A Small Molecule Scaffold Analysis: Biological Profiles of Novel, Privileged, and Promiscuous Scaffolds

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Submitted to the Graduate Faculty of

School of Pharmacy in partial fulfillment

of the requirements for the degree of

Master of Pharmaceutical Sciences

University of Pittsburgh

2013

UNIVERSITY OF PITTSBURGH

SCHOOL OF PHARMACY

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Abstract

Owing to the better understanding of physiochemical and biological challenges associated with the bioactivity of small organic molecules, novel scaffolds are becoming more extensively engineered and more highly optimized. Currently, binding specificity is becoming intensively investigated and a priority to many drug designers because it reflects the quality of scaffolds. In this thesis, we introduce a comparative analysis to benchmark the quality of four novel scaffold libraries prepared by the University of Pittsburgh Centers for Chemical Methodologies and Library Development (UPCMLD). The bioactivity profiles of these novel scaffold libraries, namely UPCMLD09A, UPCMLD02A, UPCMLD16A, and UPCMLD24A, were explored and compared with those of two privileged (benzodiazepines and dihydropyridines) and two promiscuous (rhodanines and quinolines) scaffold libraries from the literature. The approach we implemented is intended to provide an unbiased analysis and comparison of novel, privileged and promiscuous scaffold libraries. The results for three of the UPCMLD libraries, UPCMLD09A, UPCMLD16A and UPCMLD24A, indicate a comparatively high selectivity. Therefore, we suggest that the scaffolds of these libraries could be considered as privileged. In contrast, a promiscuous profile for some compounds was observed in one of the UPCMLD libraries, UPCMLD02A.

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1.0 INTRODUCTION

Many synthetic lead structures in medicinal chemistry projects are commonly designed around relatively few specific scaffolds[1], in the hope of improving the odds for developing drugs that would cure human diseases or at least enhance the quality of life in patients.

Synthetic scaffolds represent functionalized core structures from which substituents branch out. While there are many commercial building blocks available to vary these core structures, medicinal chemists are generally conservative and select those with a record of useful bioactivity. However, recent efforts to identify novel scaffolds have increased, in part due to the challenges of intellectual property protection in a patent space crowded by many generic claims,[2] and in part due to the vast expansion of drug targets that require a broader selection of potential modulators. High throughput screens (HTS) are in particular need of structurally innovative chemical collections to increase the quality of the hits.[1] Although a number of these novel scaffolds are being designed based on accidental chemical discoveries, some of them have been more rationally developed based on molecular modeling and/or assumptions about potential activities with respect to structure-activity relationships (Figure 1).[3] In any case, the ability to easily append substituents and position them in three-dimensional space also plays a vital role in improving the potency and the selectivity of the binding interaction.[4]

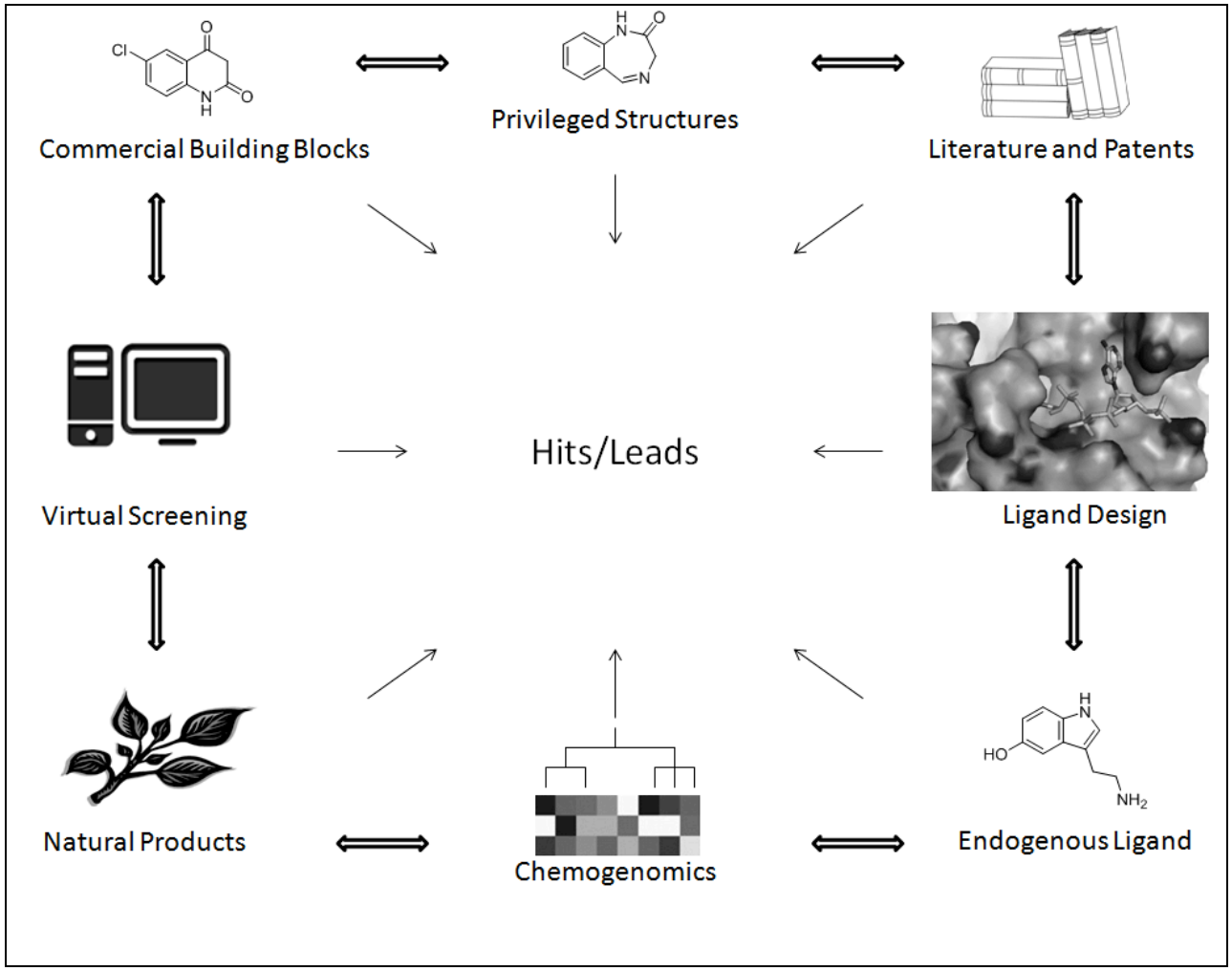


Figure 1. A representation of some of the commonly implemented approaches for the identification of hits/leads.

Regardless of the methodology used to obtain these novel scaffolds, many researchers are successful in the synthesis of unique structures that could lead to innovative, biologically active compounds. The Centers for Chemical Methodologies and Library Development (CMLD) initiative was specifically sponsored by the NIH/NIGMS to identify novel library structures.

1.1 REQUIREMENTS FOR NOVELTY

At the structural level, the newly designed novel scaffolds should meet some basic benchmarks of druglikeness, such as the Lipinski[5] and Veber rules,[6] to prove their drug development potential. Furthermore, they should not be "frequent hitters" in biological assays or demonstrate unusual reactivity or redox properties.[7] High quality core structures are readily modified by introducing a variety of substituents that can improve pharmacological properties such as potency, affinity, and specificity as well as physical properties such as solubility.[8] For example, studies have shown that halogen substituents on the aromatic moiety of the tetracaine scaffold show an enhanced potency at cyclic nucleotide-gated channels in comparison with other aromatic substitutions.[9] However, enhancing a compound's binding affinity by adding hydrophobic groups might end up decreasing its specificity.[10] Furthermore, specificity is a main concern and its lack thereof might only become apparent after extensive screening efforts or in costly late stage human trials.

An increasing amount of information is being collected on medicinal chemistry scaffolds demonstrating broad and undesirable activities in functionally unrelated assays, a hallmark of "frequent hitters". In 1988, Evans and colleagues introduced the notion of compounds with multiple activities, so called "privileged structures".[11] Although this term's definition was generalized by Evans, subsequent studies categorized it and set up the differences between privileged and "promiscuous" structures.[12,13,14] Experience-based as well as computational approaches have been dedicated to discerning the structural differences between privileged and promiscuous scaffolds.[15,16] "Privileged scaffolds" is a term used to refer to scaffolds that are able to bind to multiple targets without losing specificity, i.e. they are frequently found in hit molecules in diverse assays but their side chain composition easily allows for the introduction of

specificity.[14] Promiscuous scaffolds are frequent hitters binding to multiple targets of different families without the opportunity to gain significant selectivity or high potency through side chain variations. Often, modifying the substituents does not alter the activity substantially, or then, quite in the opposite, the activity is completely lost if substituents are varied; i.e. it is not uncommon for promiscuous scaffolds to have either unusually "flat" or "steep" SAR trends.[17]

To some extent, promiscuity is related to polypharmacology; for instance, some pharmacologists postulate that having a drug that would bind and (de)activate targets of different families to generate a more complex response pattern would be an advanced and possibly more successful approach in drug discovery, especially in cancer therapy.[18] On the other hand, medicinal chemists might be concerned that using structural features that enable lead compounds to interact with targets of different families could complicate optimization, cause pharmacokinetic and drug dosing challenges, and lead to systemic side effects due to general lack of specificity.[19]

For an extended time period, criteria to differentiate between privileged and promiscuous scaffolds have been lacking, but a recently formulated rule states that compounds which are active against at least three different target families should be considered as promiscuous.[20] In spite of this criterion, in practice the two concepts are still controversial and passionately discussed, such as the relative merits of benzodiazepines and rhodanines (Figure 2), to name a specific example for each. [21, 22]

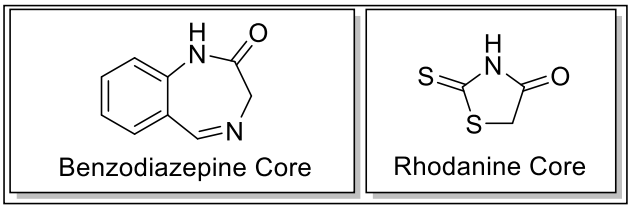


Figure 2. Benzodiazepine and rhodanine scaffolds.

The benzodiazepine nucleus was probably the first and the most important example used to describe the term "privileged structure".[11,16] Benzodiazepine derivatives are known for their wide range of pharmacological properties in clinical conditions such as anxiety disorders, ethanol withdrawal, and convulsive disorders.[23] Yet, some scientists consider several compounds containing this scaffold as non-specific binders. For example, olanzapine, a benzodiazepine antipsychotic, has been shown to bind to multiple receptors for serotonin, noradrenaline, muscarine, dopamine and histamine. Although all of the endogenous ligands of these latter receptors share the basic amine in their pharmacophores, they have major differences in their representative scaffolds which make each molecule selective to its receptor.[24,25,26] Therefore, the promiscuous profile of olanzapine would normally be unacceptable; nonetheless, the drug is approved for the treatment of schizophrenia due to its high efficacy for this disorder.[27]

Aspirin is another example of a successful promiscuous drug that is widely used. In contrast, the rhodanine scaffold gained a reputation of having insignificant value in drug discovery due to its nonselectivity.[28] Conversely, there are some rhodanine-derived drugs for the treatment of type II diabetes mellitus and diabetic complications such as epalrestat.[22] There are many contradictory observations regarding this scaffold but it is still of high interest to medicinal chemists and frequently found as a lead structure in biological studies.

Other, maybe less hotly contested examples of privileged scaffolds (such as dihydropyridine and benzenesulfonamide) and promiscuous compounds (such as quinolines and hydantoins) are being discussed in the literature without a credible justification or a standard that could be applied by others to determine their specificity and relative potential for further clinical development. Non-specificity or promiscuity of small molecules could be identified through

many approaches such as database mining,[20] lipophilicity measurement,[29] and match molecule pair (MMP) analysis[30].

In order to annotate some of the novel scaffolds prepared at the University of Pittsburgh CMLD and compare to other published scaffolds used for biological assays, we have followed a comparative analysis approach based on the interrogation of multiple screening targets.[31]

In PubChem, biological data are being collected for many novel compound classes and it is relatively simple to analyze the data and correlate them to the chemical structures.[32] Based mostly on *in vitro* bioassays, these biological data could be helpful in categorizing the behavior of compounds having particular scaffolds of interest. These activity profiles are reflected by the active hits* which are usually defined as compounds which have an activity in the range of 30 μM – 1 nM.[33] Accordingly, we selected the biological profiles of four compound libraries from the UPCMLD (UPCMLD02A, UPCMLD09A, UPCMLD16A, and UPCMLD24A) (Figure 3) and another four compound libraries from the literature for comparison. Among the latter, two were generally considered as privileged scaffolds (benzodiazepines and dihydropyridines) and the remaining two could be claimed as promiscuous (rhodanines and quinolines) (Figure 4).[28, 34]

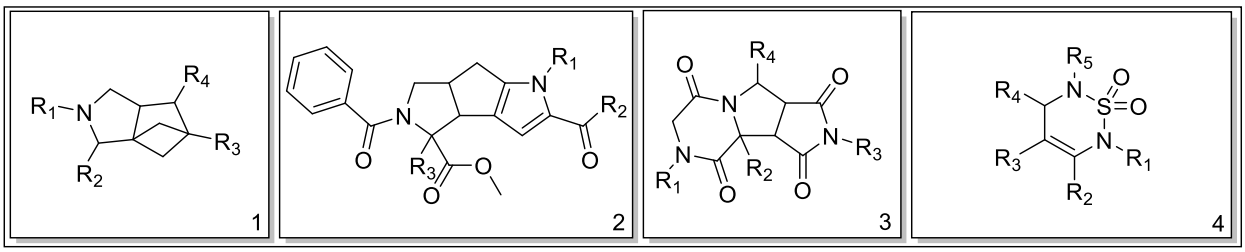


Figure 3. The scaffolds of four UPCMLD libraries. Substructures 1,2,3, and 4 are also referred to as UPCMLD09A, UPCMLD02A, UPCMLD16A, and UPCMLD24A, respectively, in the PubChem database.

*In the PubChem database, some concentration values of hits are not provided.

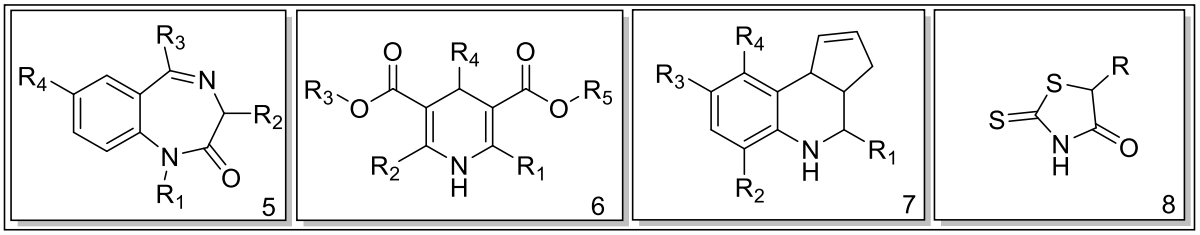


Figure 4. The scaffolds of four libraries from the literature. Substructure 5 shows the benzodiazepine nucleus, 6 is a dihydropyridine scaffold, 7 shows the quinoline nucleus, and 8 is a rhodanine. Substructures 5 and 6 are generally referred to as privileged scaffolds while compounds with substructures 7 and 8 are often considered as promiscuous.

Our general approach can be summarized as follows: the biological data of both the UPCMLD and the literature scaffold libraries were extracted from the PubChem database and analyzed. The biological data of each library contained activity profiles of compounds screened in different bioassays. Our effort was to determine if UPCMLD scaffolds would result in important screening compounds by benchmarking their libraries against the literature libraries. Literature libraries of renowned and emerging scaffolds in drug discovery (Figure 4) were used as relative references to assure a plausible analytical approach. In order to ensure an unbiased analysis, an extensive filtering process was followed.

Beginning with extracting data and excluding unshared bioassays and compounds screened in less than 100 bioassays, the eight libraries were analyzed and compared to each other. By generating graphs of the activities of individual compounds in relation to the bioassays, we managed to identify the promiscuous behavior of some scaffolds and representative compounds. This was achieved by creating specificity determinants such as the library hit rate.

2.0 METHODOLOGY

2.1 LIBRARY SELECTION

2.1.1 UPCMLD Libraries

The biological data of the UPCMLD09A library[35] was extracted from PubChem and analyzed in November 2012. The library contained 75 novel tricyclic pyrrolidine heterocycles (Appendix Table 1).

UPCMLD02A, a library of tricyclic pyrrole-2-carboxamides[36], contained 196 compounds (Appendix Table 2). Only 193 compounds were biologically tested (January, 2013).

The piperazinedione-fused tricyclic scaffold in the UPCMLD16A library[37] was contained in 62 compounds (Appendix Table 3). However, only 54 of these compounds were tested biologically (February, 2013).

In the UPCMLD24A library, the thiadiazine core was the scaffold of 79 compounds[38] (Appendix Table 4); 71 compounds were tested biologically (February, 2013).

2.1.2 Literature Libraries

The benzodiazepine library had only 60 out of 15,583 compounds that were screened in ≥100 bioassays (March, 2013) (Appendix Table 5).

The dihydropyridine scaffold library had a comparable number of compounds that were tested in ≥100 bioassays, i.e. 261 compounds (April, 2013) (Appendix Table 6).

PubChem results of the promiscuous rhodanine scaffold showed a huge number of compounds: 162,351 compounds. However, only 1,301 compounds were tested in ≥100 bioassays (May, 2013).

The tetrahydro-3H-cyclopentaquinoline library had 81 compounds tested in ≥100 bioassays in that library (June, 2013) (Appendix Table 8).

2.2 LIBRARY FILTERING

We found many duplicated bioassays at different concentrations and many similar bioassays shown as separate screens. Therefore, we excluded duplicates and similar bioassays. For example, the fluorescence-based (AID[†]:434989) and the FRET-based (AID:485270) cell-based primary HTS assay to identify antagonists of the orexin 1 receptor were considered as one bioassay.

Another issue was a significant divergence of the bioassays for different libraries; therefore we only considered common bioassays and correspondingly reanalyzed the data to facilitate the analysis process. As a result, 223 shared screening and confirmatory assays were used for all libraries (Appendix Table 9, Figure 5 and Table 1). Since not all concentration values were provided in the PubChem database, we did not include them in the analysis.

[†] AID: Pubchem bioassay accession; bioassay identification number.

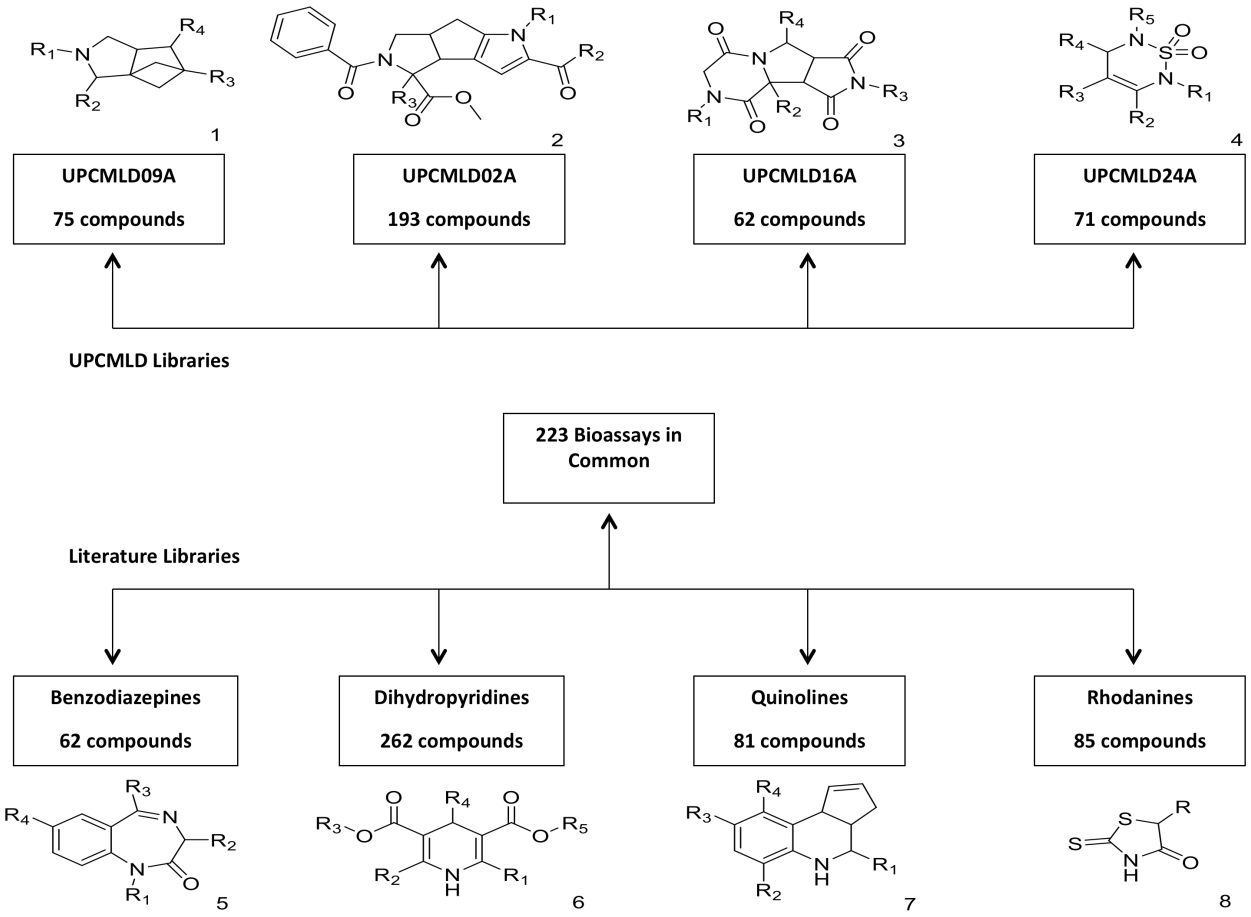


Figure 5. A summary of the unfiltered number of compounds in UPCMLD and literature libraries.

Table 1. A summary of the number of compounds in UPCMLD and literature libraries before and after filtering.

Compound Library	Number of Compounds Before Filtering	Number of Compounds After Filtering
UPCMLD09A	75	64
UPCMLD02A	193	28
UPCMLD16A	62	53
UPCMLD24A	71	71
Benzodiazepines	60	54

Dihydropyridines	261	249
Rhodanines	85	81
Quinolines	81	72

Furthermore, we excluded all library compounds that were screened in less than 100 bioassays. Due to the large number of compounds in some literature libraries, we decided not to exceed 2,000 compounds for each library to allow relevant comparison with UPCMLD libraries. Although the number of compounds in the rhodanine scaffold library did not exceed 2,000, we followed this criterion initially by filtering out substituents at the N-atom. As a result, only 85 compounds tested in ≥100 bioassays were used (Appendix Table 7).

2.3 SOFTWARE USED

Chemical and biological data were obtained from the PubChem database in spreadsheets. Literature libraries were obtained by using the substructure search in PubChem software.

Both the IBM SPSS 20 program and Microsoft Office Excel 2007 were utilized for data analysis and the generation of graphs.

2.4 SPECIFICITY DETERMINANTS

The hit rate was used to reflect the libraries' activity profiles. It was calculated using the following equation:

$$Hit\ Rate\ of\ a\ Library = \frac{number\ of\ active\ compunds}{total\ number\ of\ compounds} * 100\%$$

The number of active hits for each compound was also utilized to reflect specificity of binding.

The statistical parameters, mean and standard deviation, were used to facilitate interpretation in estimating the activity variability of libraries as well as properties. The mean indicates the average number of positive hits for compounds while the standard deviation corresponds to the variance of compounds' activity in a library.

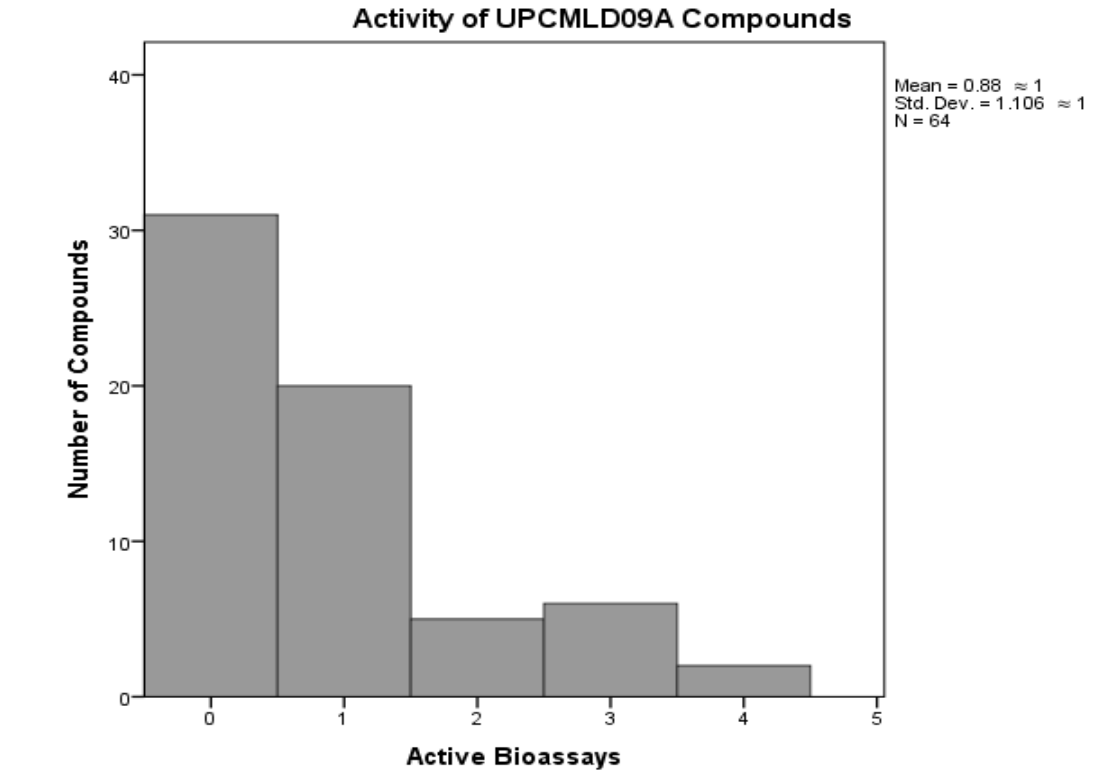
3.0 RESULTS AND DISSCUSION

In our attempt to analyze the biological behavior of compounds of some scaffold libraries, we used an approach that facilitated data analysis and interpretation.

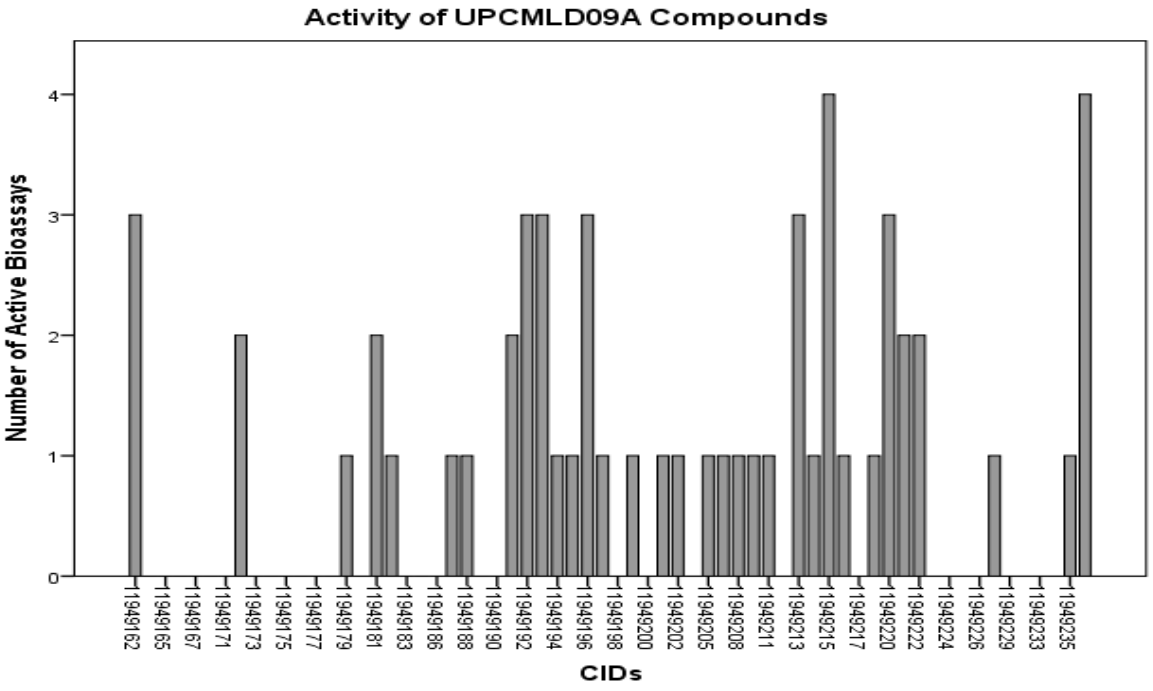
Libraries, UPCMLD09A, UPCMLD02A, UPCMLD16A, and UPCMLD24A were selected due to the considerable number of compounds and various bioassays they contained, since the other UPCMLD libraries had either few compounds or their compounds were not screened in a comparable number of bioassays; i.e. 100 bioassays or more.

After filtering the UPCMLD09A library, 64 compounds out of 75 were left. It was shown that these 64 compounds have a low number of hits individually, with 4 bioassays as the maximum number of hits (Figure 6 A and B). The UPCMLD09A library showed a relatively high hit rate, 51.6%. Since duplicate bioassays became an issue that inflated the number of total bioassays and eventually altered the hit rate and other determinants, Figure 6C was generated to ensure that these bioassays were excluded and the input data met the criterion discussed previously; i.e. only 223 shared bioassays were used.

A


Activity of UPCMLD09A Compounds
Mean = 0.88 ≈ 1
Std. Dev. = 1.106 ≈ 1
N = 64
Number of Compounds
Active Bioassays
0
10
20
30
40
0
1
2
3
4
5

B


Activity of UPCMLD09A Compounds
Number of Active Bioassays
CIDs
0
1
2
3
4
1949162
1949165
1949167
1949171
1949173
1949175
1949177
1949179
1949181
1949183
1949186
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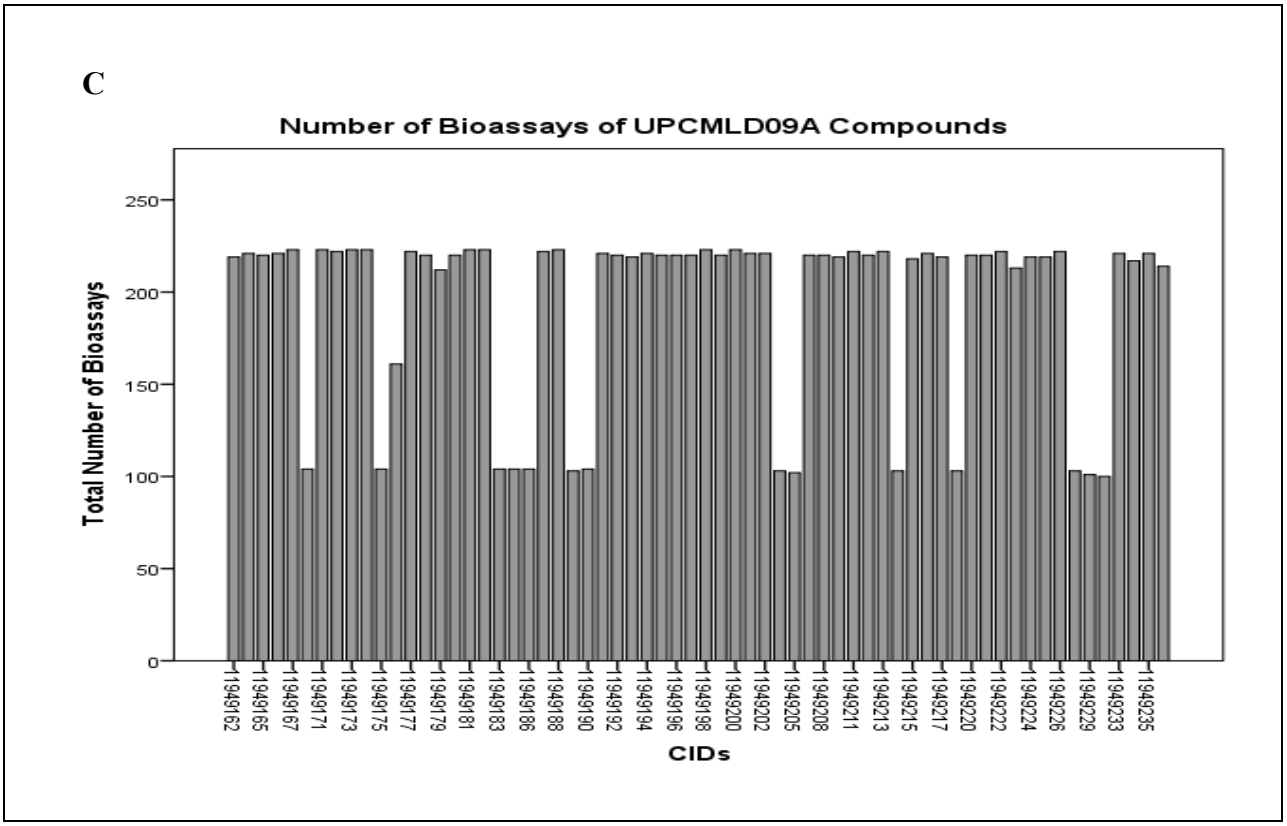


Figure 6. Graphs summarizing the bioactivity of UPCMLD09A compounds. Graph A shows the number of compounds versus the number of active bioassays indicating how many compounds are active in these bioassays (hit rate: 51.6%). Graph B shows the number of active bioassays for individual compounds in the UPCMLD09A library. CID, the PubChem compound identifier, is a unique identifier given to each chemical structure in the PubChem database. Graph C shows that compounds tested in <100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.

As stated previously, UPCMLD02A is the largest among the UPCMLD libraries and contains 196 compounds. However, an unexpected decrease in the number of its compounds after filtering was apparent. As shown in Figure 7, the number of compounds was decreased to only 28 samples. Some of these compounds were shown to interact with a considerable number of targets; CID:3247230 had 36 hits and CID:3247132 provided 12 hits (Appendix Figure 1A)**.** A modest hit rate (39.3%) and some promiscuity was observed in the UPCMLD02A library.

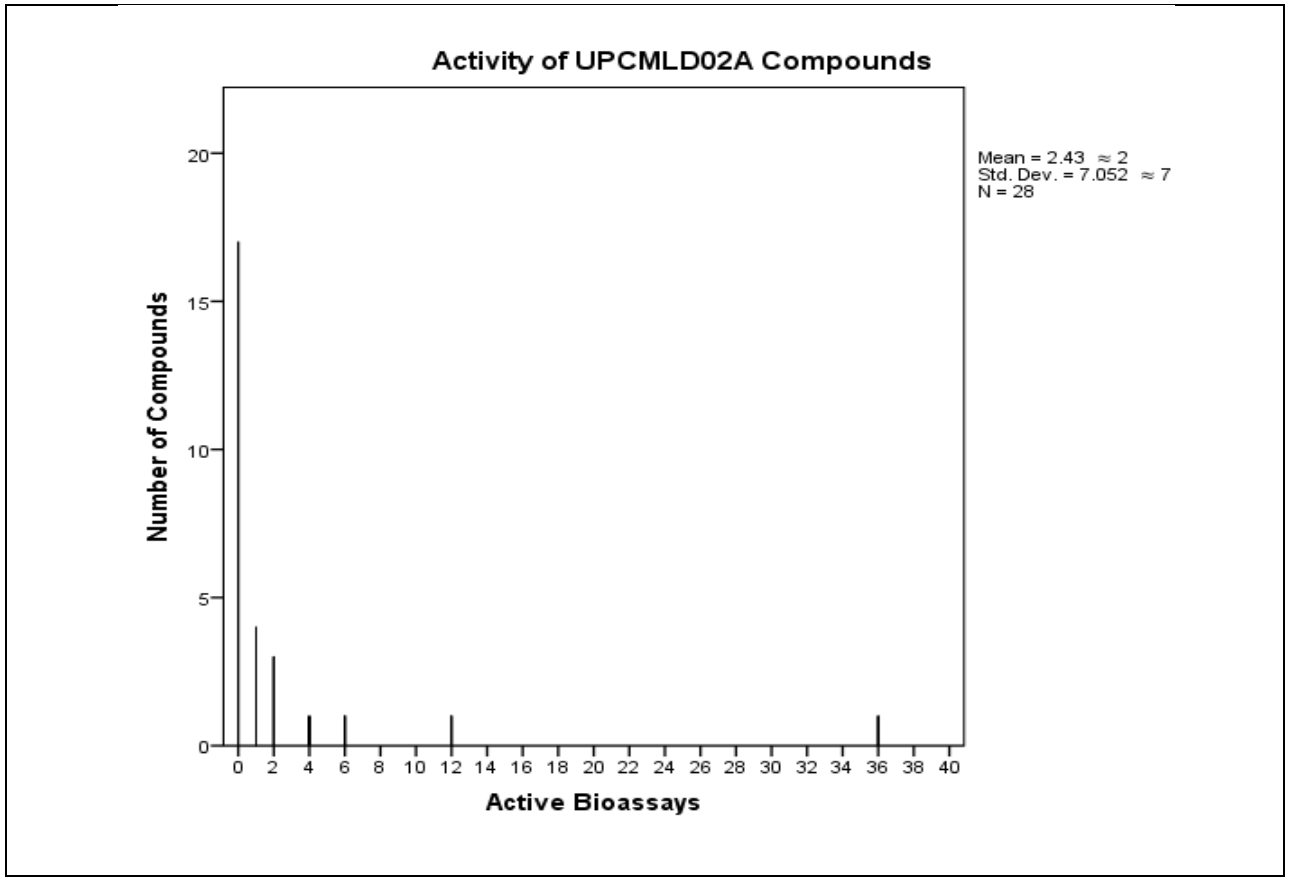


Figure 7. A graph representing the number of compounds in the UPCMLD02A library versus the number of active bioassays indicating the number of compounds that are found as active hits in different bioassays (hit rate: 39.3%).

UPCMLD16A showed somewhat better results than UPCMLD02A. 53 Compounds were included for analysis and a low number of active bioassays for individual compounds with a maximum of 3 hits was found (Figure 8). However, the majority of the compounds had no activity in any of the bioassays. Accordingly, this resulted in a relatively low hit rate; 30.2% (Appendix Figure 2A).

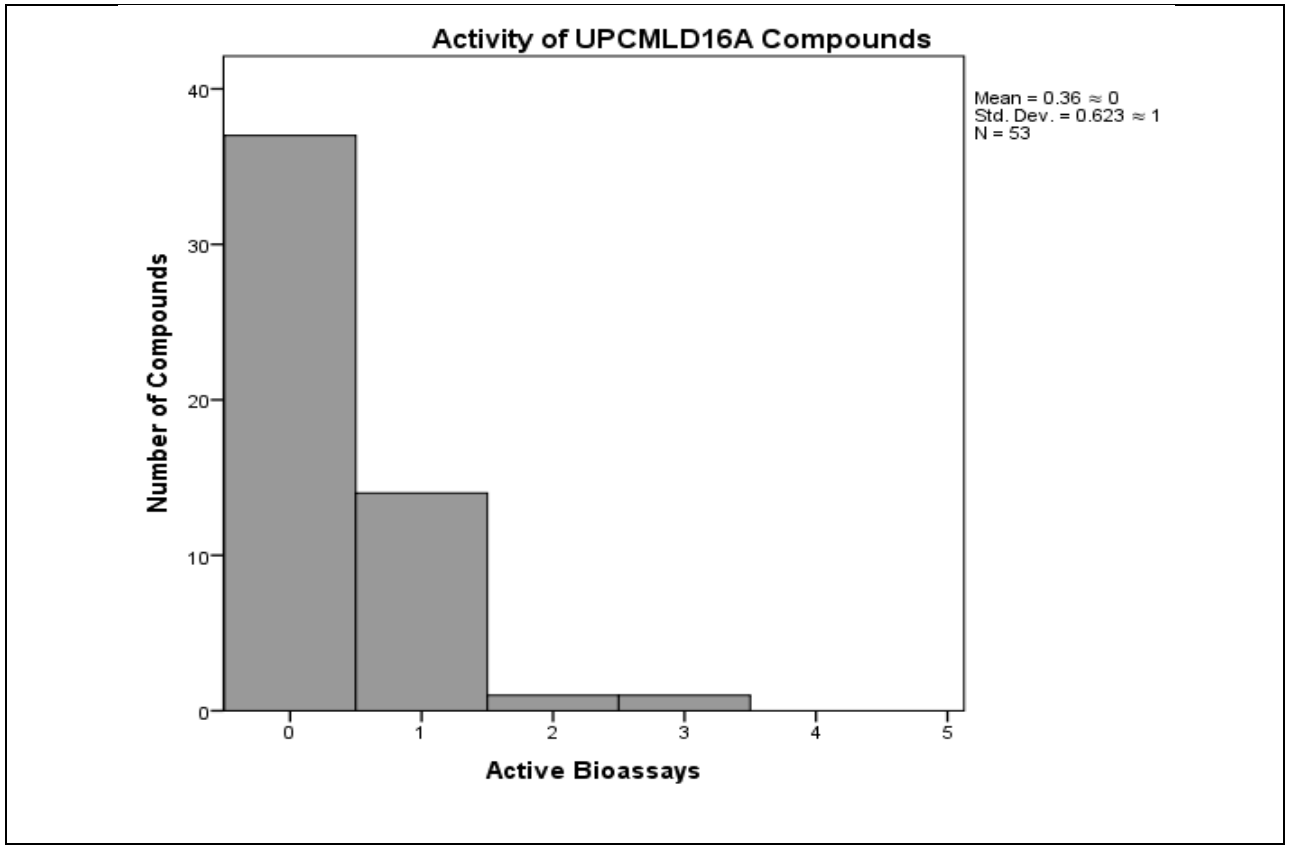


Figure 8. A graph representing the number of compounds in the UPCMLD16A library that are found as active hits in different bioassays (hit rate: 30.2%).

UPCMLD24A was the limiting library in this study since it has been less biologically explored. None of its compounds were excluded, making it the largest UPCMLD library with the greatest number of compounds after filtering (Figure 9). However, most of these compounds did not show any activity in any bioassay; this led to a comparatively low hit rate (25.4%). No more than 5 active hits for individual compounds were found (Appendix Figure 3A).

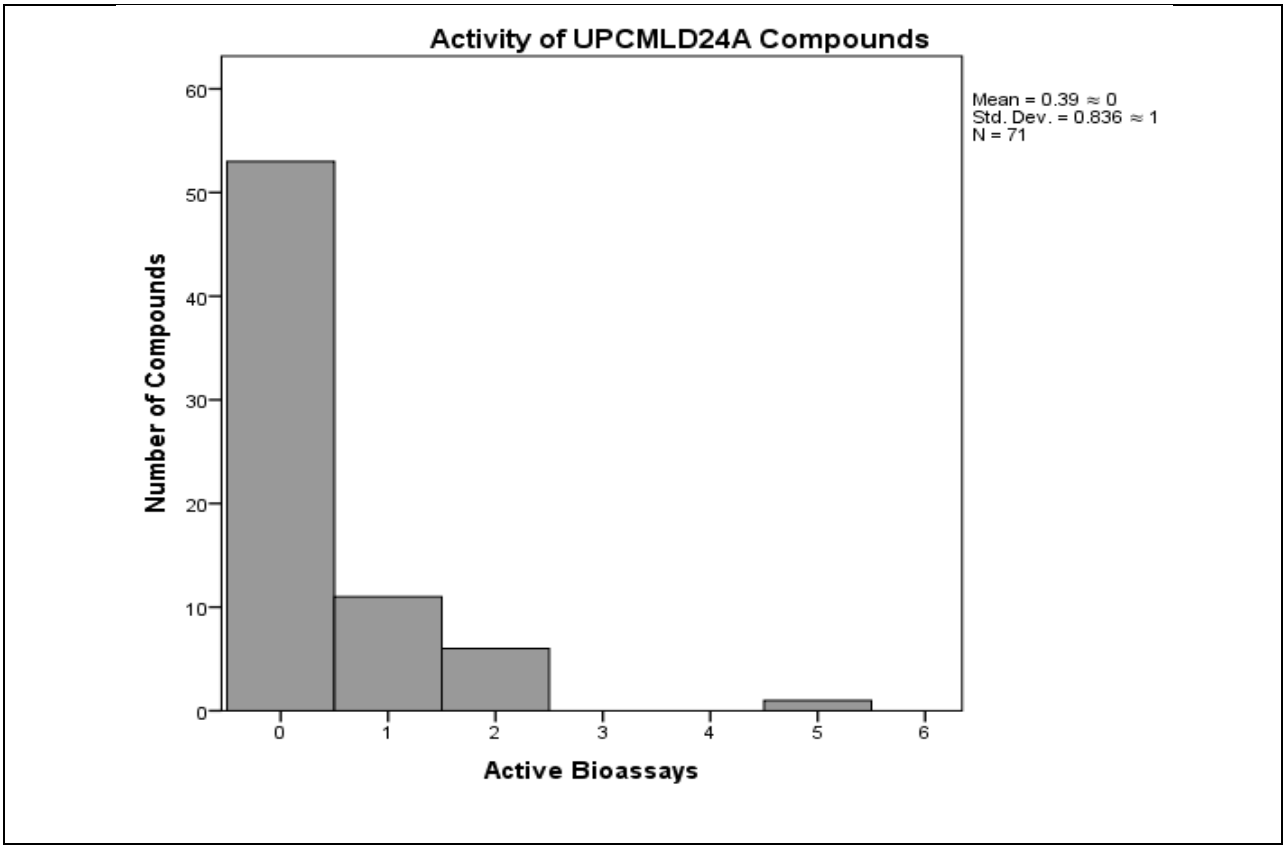


Figure 9. A graph representing the number of compounds in the UPCMLD24A library that are found as active hits in different bioassays (hit rate: 25.4%).

The results for the benzodiazepine and dihydropyridine libraries were anticipated due to their reputation as privileged scaffolds. The 54 benzodiazepines showed collectively a low number of hits (Appendix Figure 4A) and a hit rate of 35.2% (Figure 10). The dihydropyridine scaffold library contained 249 compounds after filtering and showed a positively skewed bioactivity profile with a 53.0% hit rate (Figure 11). Some dihydropyridines also showed a relatively high number of hits (Appendix Figure 5A); for example, CID: 4499 was found active in 10 bioassays.

In comparing UPCMLD libraries to these privileged literature scaffolds, it was observed that the results for the UPCMLD libraries were quite similar to the privileged compounds.

However, the UPCMLD02A library had two compounds that were exceeding the maximum number of active bioassays (10 in the dihydropyridine scaffold library) among all other libraries. Accordingly, the UPCMLD02A tricyclic pyrrole-2-carboxamides are suspected to have at least in part a promiscuous character. Another reason that led us to the latter conclusion is that only 28 compounds were tested on the shared 223 bioassays. Nonetheless, the nature of the bioassays was not explored in detail, and some compounds might be active in bioassays that are refering to multiple targets of the same family. Therefore, we analyzed the bioassays with positive results for the two UPCMLD02A compounds and found that the majority were refering to different families (Figure 12).

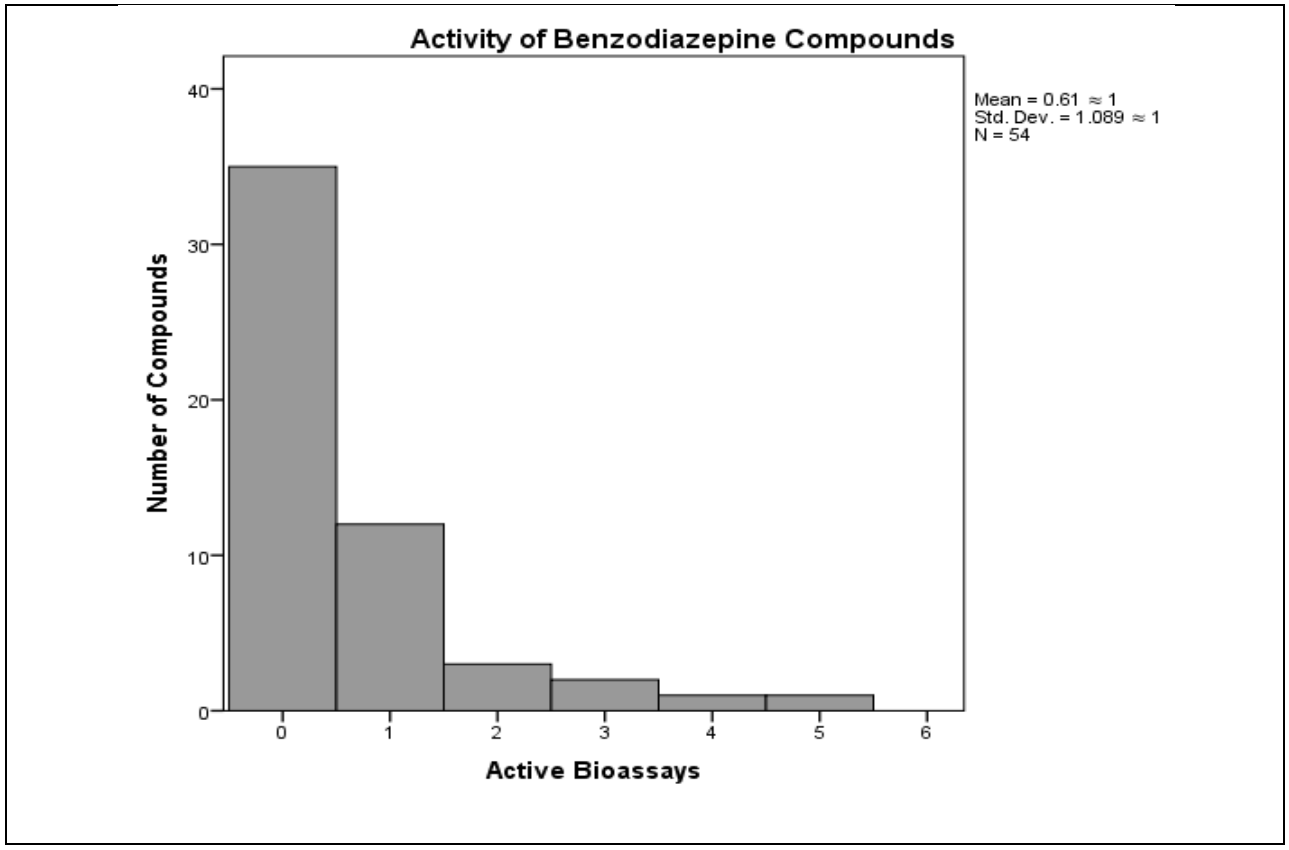


Figure 10. A graph representing the number of compounds with the benzodiazepine scaffold that are found as active hits in different bioassays (hit rate: 35.2%).

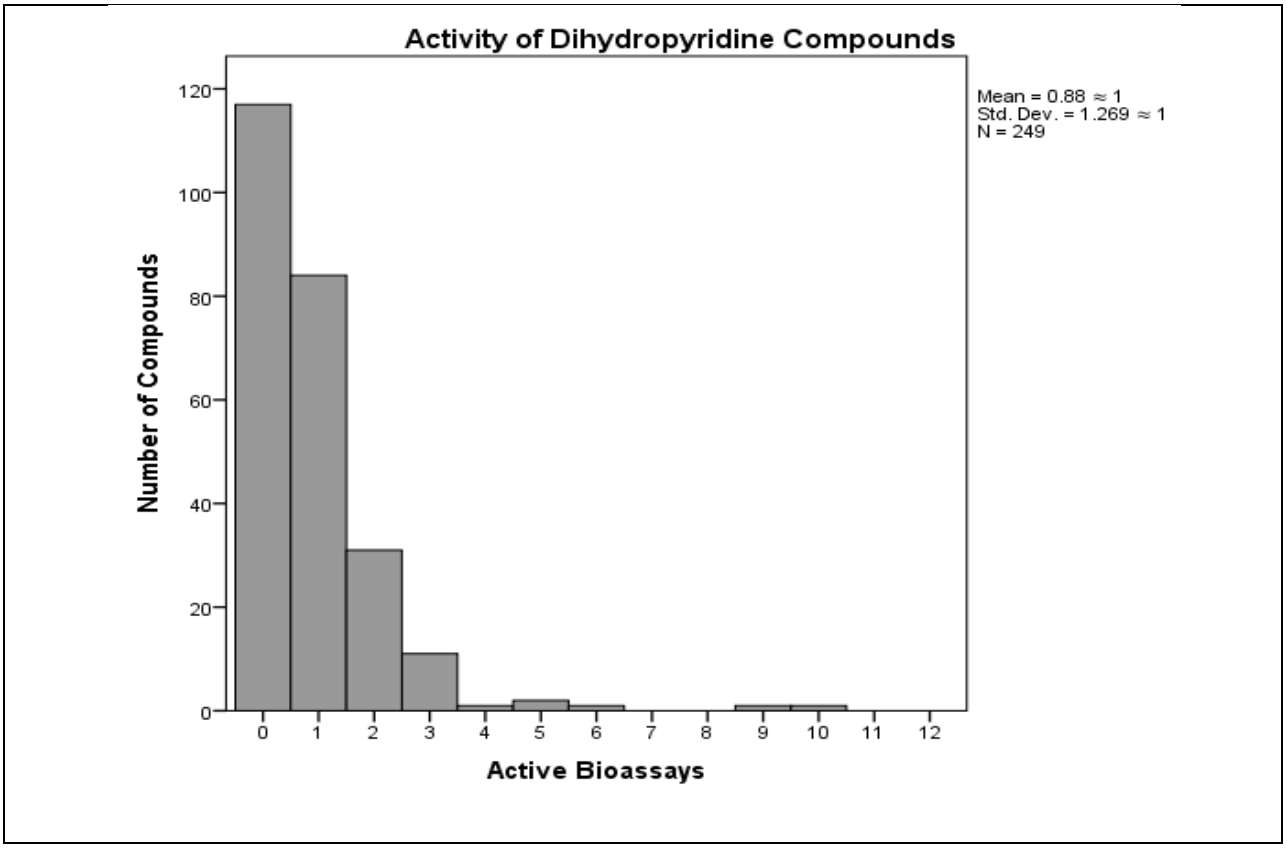


Figure 11. A graph representing the number of compounds with the dihydropyridine scaffold that are found as active hits in different bioassays (hit rate: 53.0%).

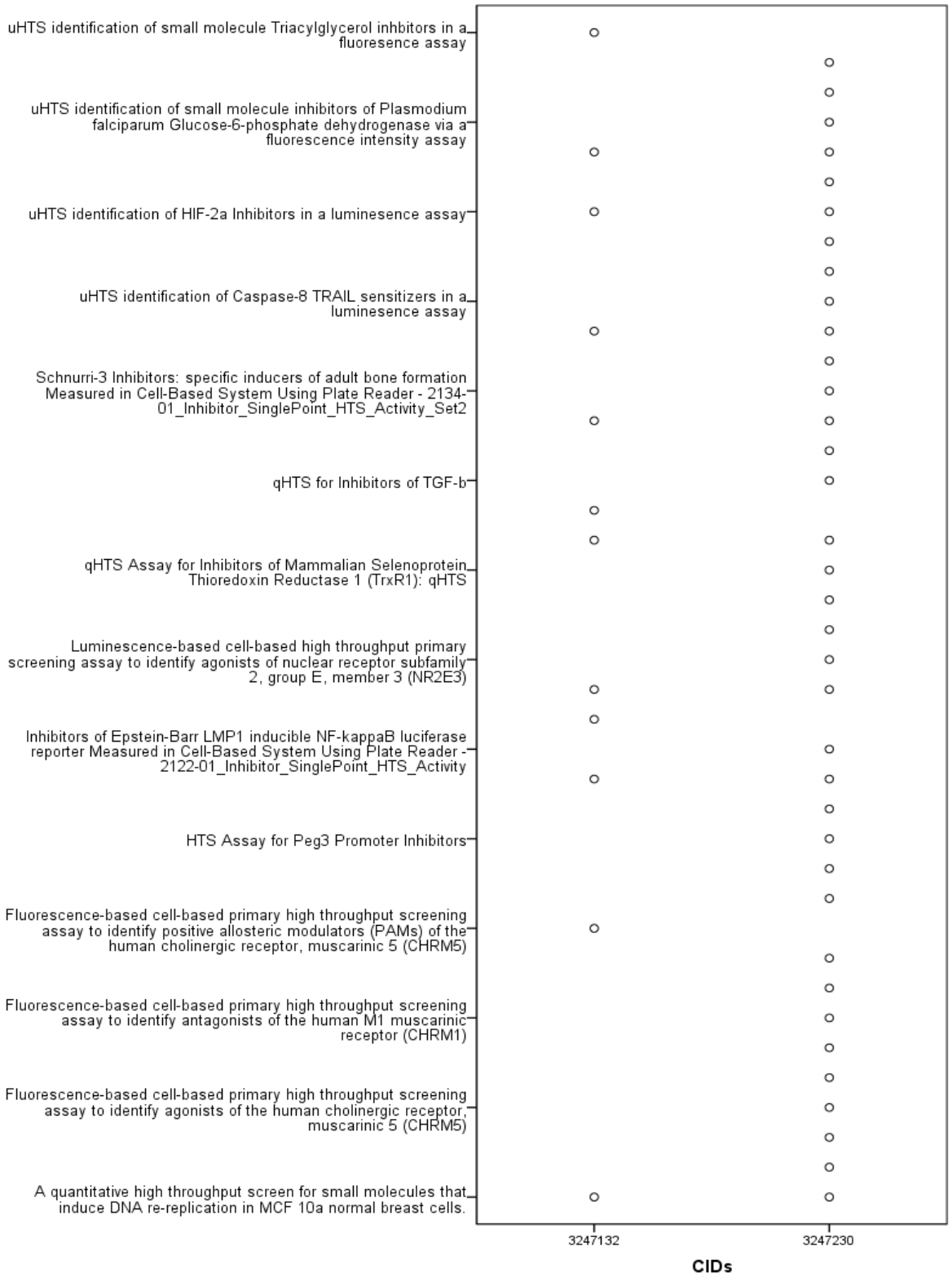


Figure 12. A representation of some of the active bioassays for two UPCMLD02A frequent hitters (not all active bioassays are shown for clarity purposes).

To avoid any bias, we compared the UPCMLD libraries to the promiscuous literature scaffold libraries. Rhodanine (Figure 13 and Appendix Figure 6) and quinoline (Figure 14 and Appendix Figure 7) scaffold libraries showed a high level of promiscuity. Although their hit rates were much higher than those of the UPCMLD libraries (86.4% for rhodanines and 80.6% for quinolines), these high numbers have little value when the cost is a loss of specificity. In addition, standard deviation values of rhodanine and quinoline scaffold libraries were considerably higher than UPCMLD09A, UPCMLD16A, and UPCMLD24A, indicating a broad variability in the bioactivity of compounds in former libraries. Owing to the high variability, the mean became an unreliable method to indicate the average number of active hits in the two promiscuous scaffold libraries.

Although the rhodanine scaffold library was initially filtered due to the large number of compounds i.e. 1,301 compounds, we did not alter the filtering process since we were expecting a promiscuous profile, and the results were as anticipated.

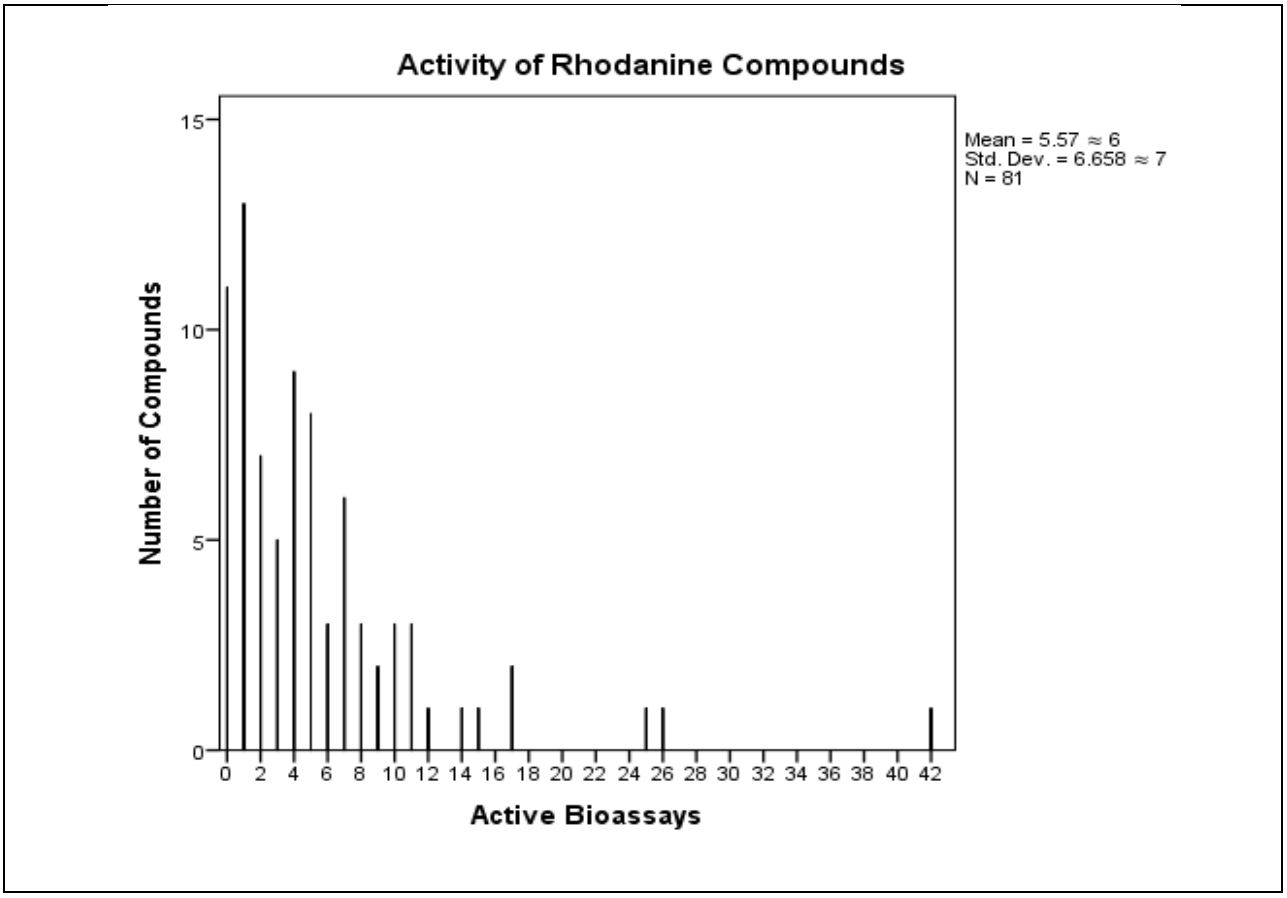


Figure 13. A graph representing the number of compounds with the rhodanine scaffold that are found as active hits in different bioassays (hit rate: 86.4%).

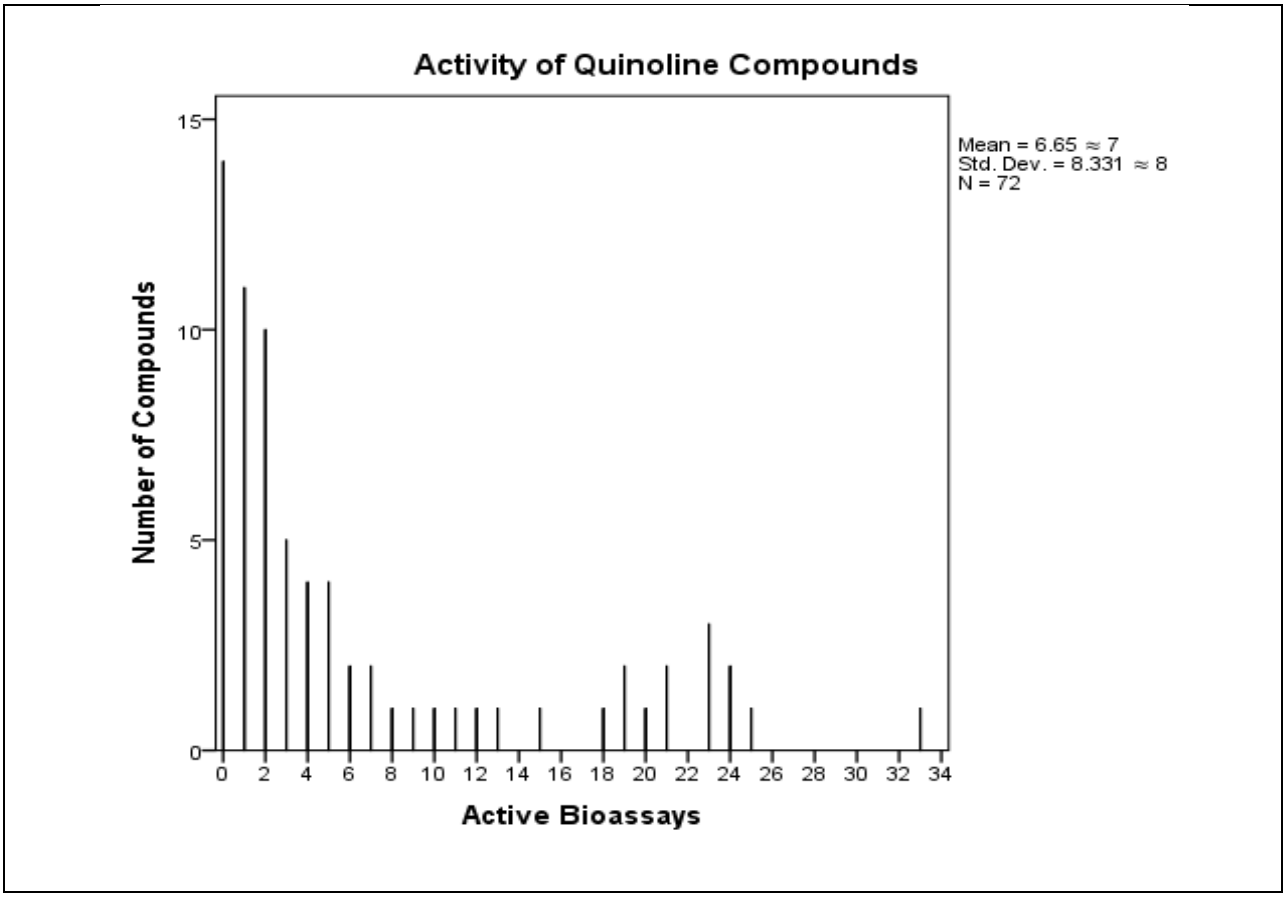


Figure 14. A graph representing the number of compounds with the quinoline scaffold that are found as active hits in different bioassays (hit rate: 80.6%).

In summary, we have implemented a comparative approach to determine the nature of the novel UPCMLD scaffold libraries as it pertains to promiscuity and/or privileged character. UPCMLD09A showed relatively high selectivity, taking into account the number of compounds involved, the library hit rate, and the low number of actives in bioassays (Table 2). Therefore, the UPCMLD09A scaffold might provide high quality screening samples. The UPCMLD02A library showed a tendency for promiscuity, although only 28 compounds were included in the comparison, due to bioassay limitations.

Table 2. A summary of the results of UPCMLD and literature scaffold libraries.

Compound Library	Library Hit Rate	Maximum Number of Hits for Individual Compounds	Mean of Hits for Individual Compounds	Standard Deviation of Hits for Individual Compounds
UPCMLD09A	51.6%	4	1	1
UPCMLD02A	39.3%	36	2	7
UPCMLD16A	30.2%	3	0	1
UPCMLD24A	25.4%	5	0	1
Benzodiazepines	35.2%	5	1	1
Dihydropyridines	53.0%	10	1	1
Rhodanines	86.4%	42	6	7
Quinolines	80.6%	33	7	8

By comparing the UPCMLD libraries with compound libraries from the literature, we learned that the novel UPCMLD scaffolds can provide high quality screening samples. However, testing the quality of novel scaffolds could be carried out considering other structural aspects, such as comparison of functionalities, rigidity, and lipophilic character.

In addition, the selection of bioassays in this research was limited since the UPCMLD libraries were less biologically explored than the literature scaffold libraries. Therefore, the selected bioassays might not be conclusive to reflect the actual nature of the libraries.

Furthermore, we disregarded concentration values of active hits bacause not all values were provided in the PubChem database. This is a potentially significant limitation due to the importance of concentration values in binding specificity.

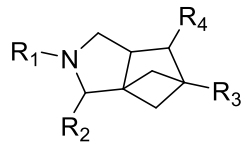
Another important aspect that might be a caveat in this study is the number of compounds representing a specific scaffold in a library. In UPCMLD02A for example, 28 compounds are too few to adequately assess the quality of the tricyclic pyrrole-2-carboxamide core structure.

Finally, based on the currently available information about privileged and promiscuous scaffolds and our knowledge regarding promiscuity, the quality of novel scaffolds could be identified by several different processes. Therefore, our approach is not a universal approach to identify quality in new scaffolds, but it certainly provides an important benchmark that reflects the biological response to structural features of organic molecules.

APPENDIX A

SUPPLEMENTARY DATA

Appendix Table 1. A list of the compounds in the UPCMLD09A library



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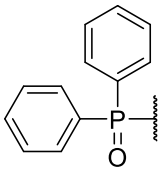
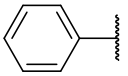
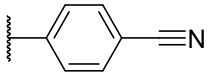
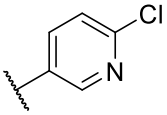
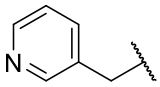
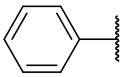
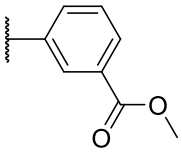
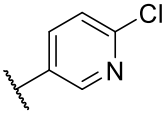
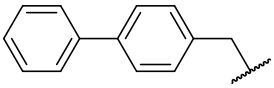
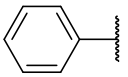
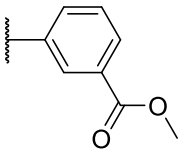
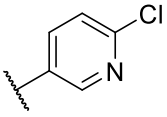
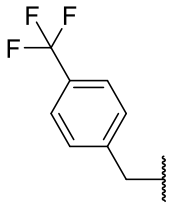
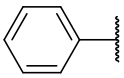
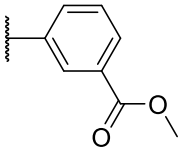
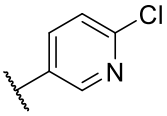
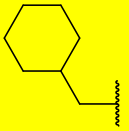
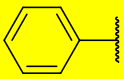
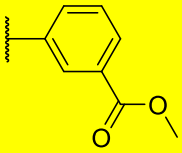
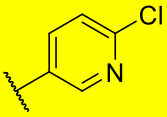
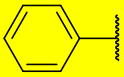
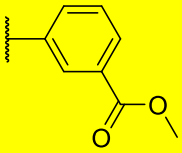
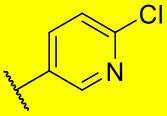
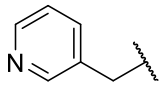
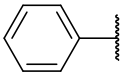
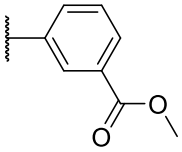
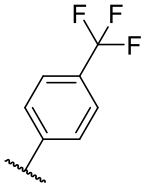
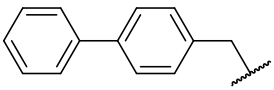
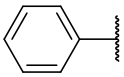
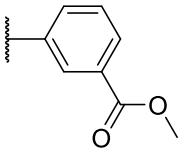
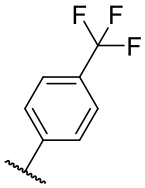
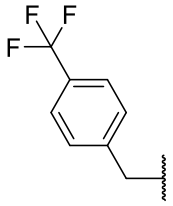
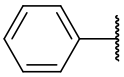
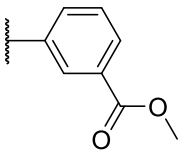
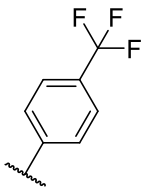
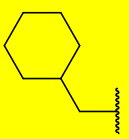
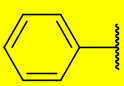
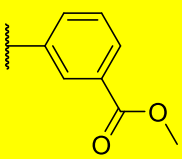
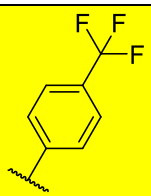
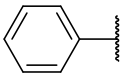
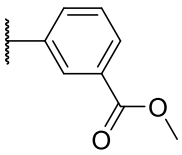
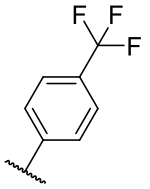
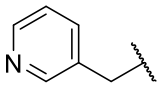
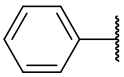
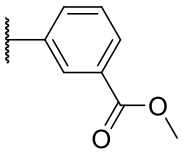
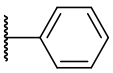
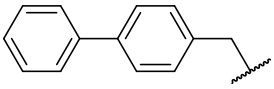
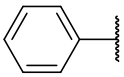
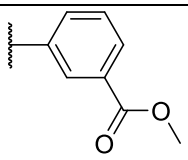
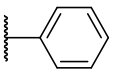
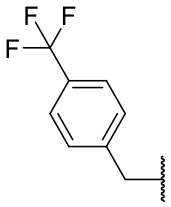
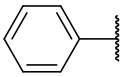
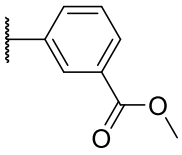
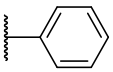
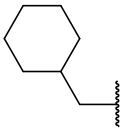
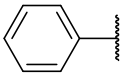
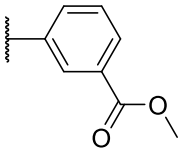
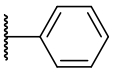
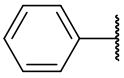
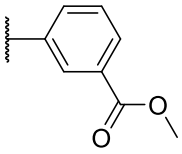
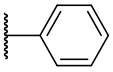
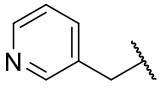
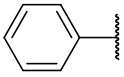
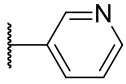
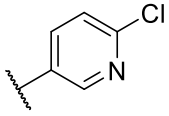
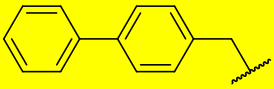
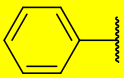
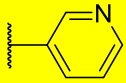
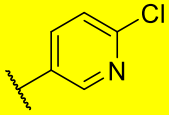
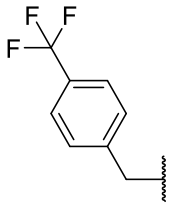
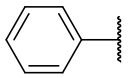
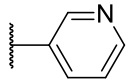
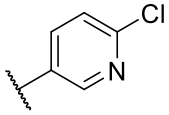
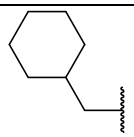
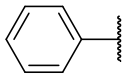
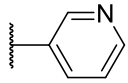
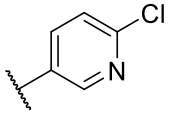
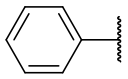
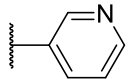
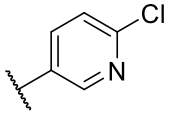
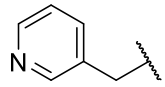
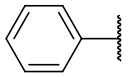
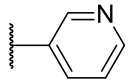
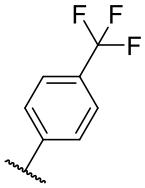
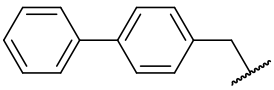
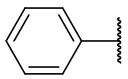
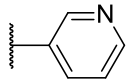
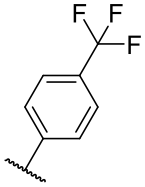
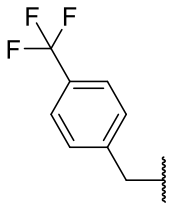
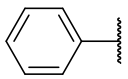
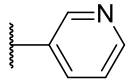
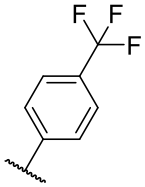
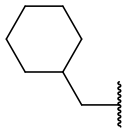
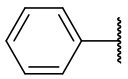
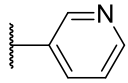
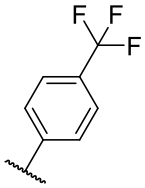
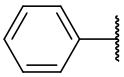
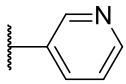
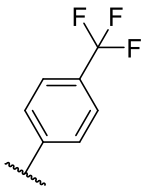
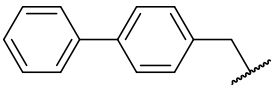
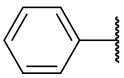
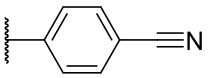
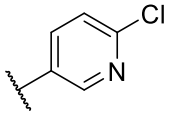
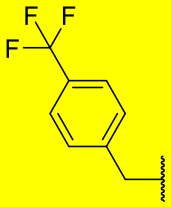
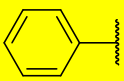
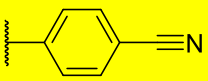
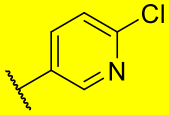
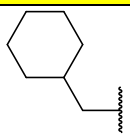
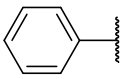
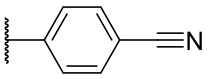
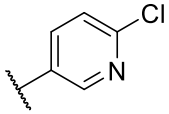
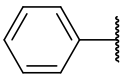
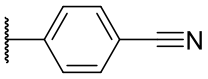
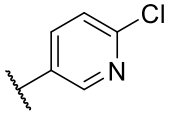
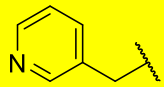
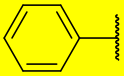
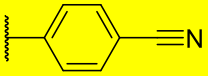
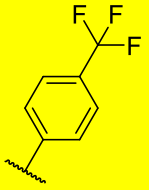
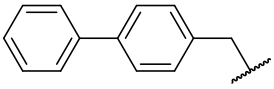
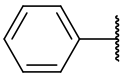
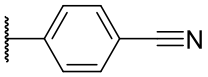
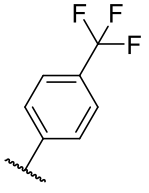
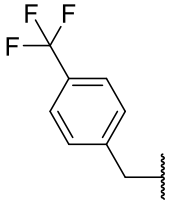
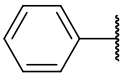
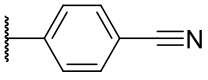
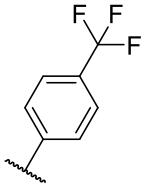
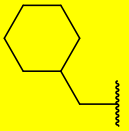
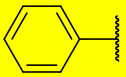
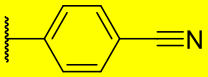
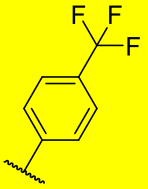
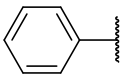
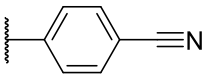
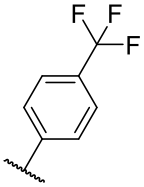
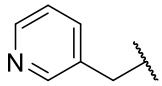
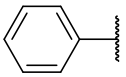
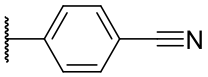
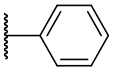
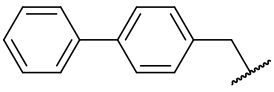
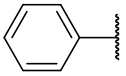
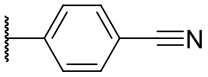
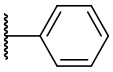
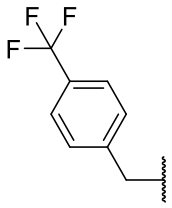
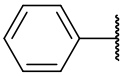
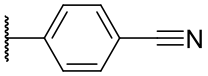
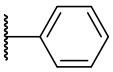
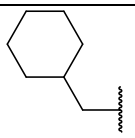
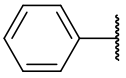
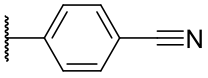
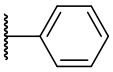
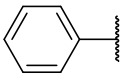
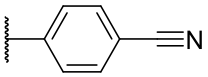
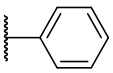
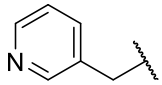
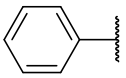
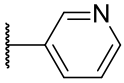
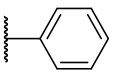
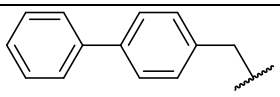
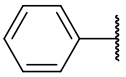
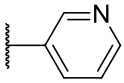
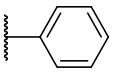
11949236				
11949235				
11949234				

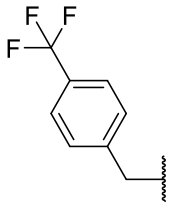
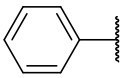
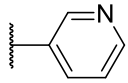
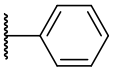
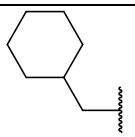
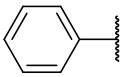
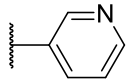
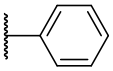
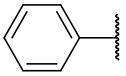
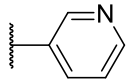
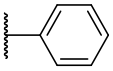
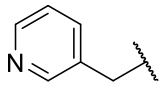
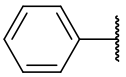
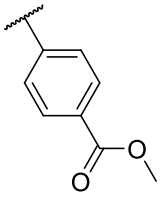
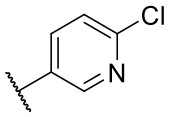
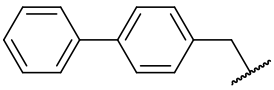
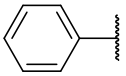
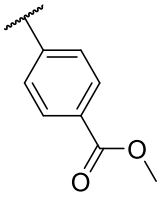
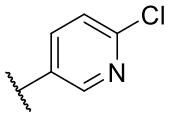
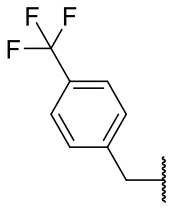
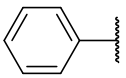
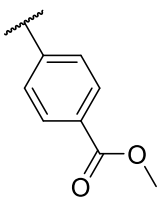
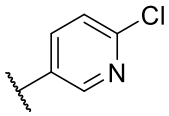
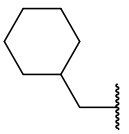
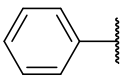
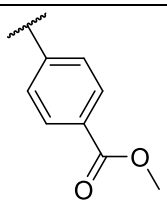
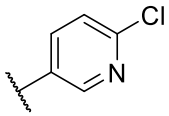
11949233				
11949232				
11949231				
11949230				
11949229				
11949228				
11949227				

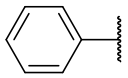
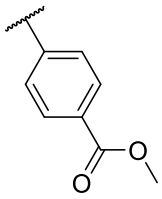
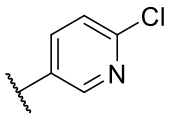
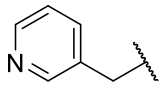
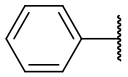
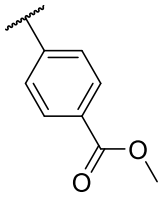
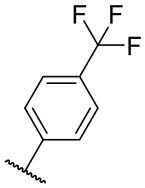
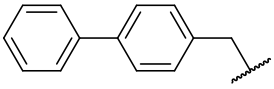
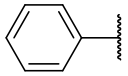
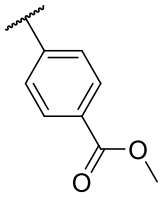
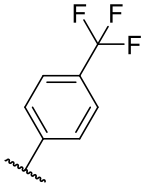
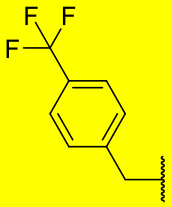
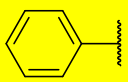
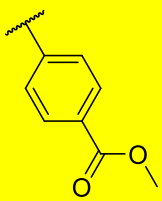
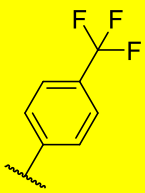
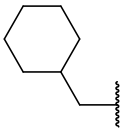
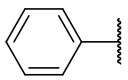
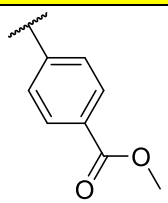
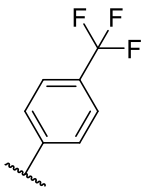
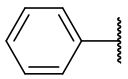
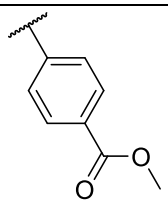
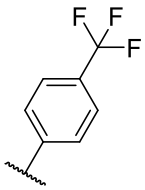
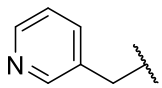
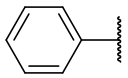
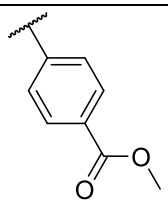
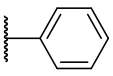
11949226				
11949225				
11949224				
11949223				
11949222				
11949221				
11949220				
11949219				

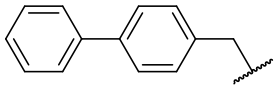
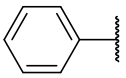
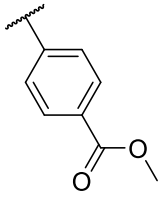
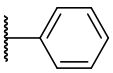
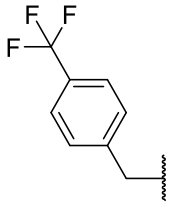
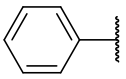
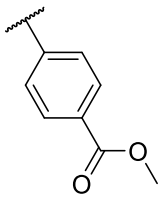
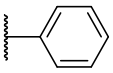
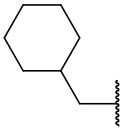
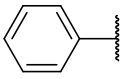
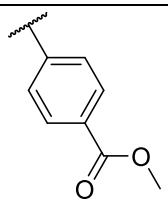
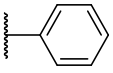
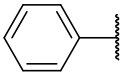
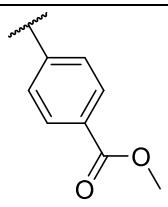
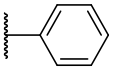
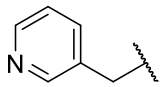
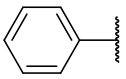
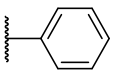
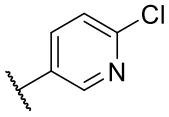
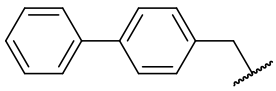
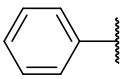
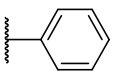
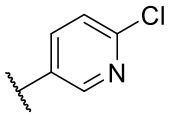
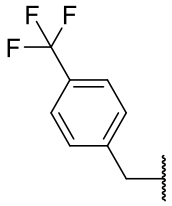
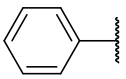
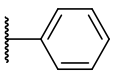
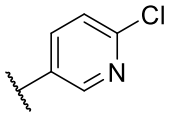
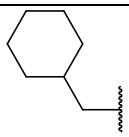
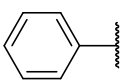
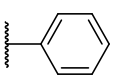
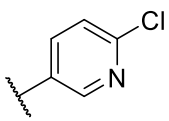
11949218				
11949217				
11949216				
11949215				
11949214				
11949213				
11949212				

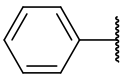
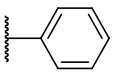
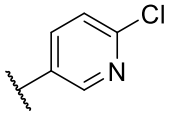
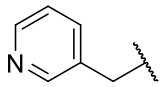
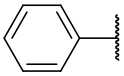
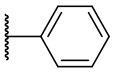
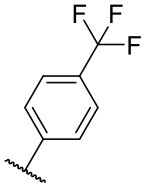
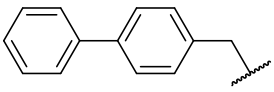
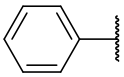
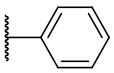
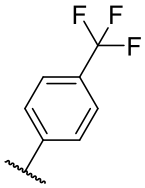
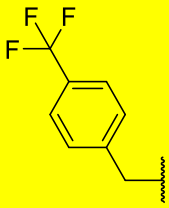
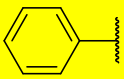
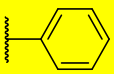
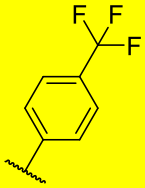
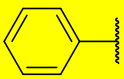
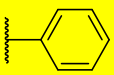
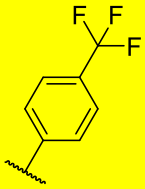
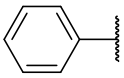
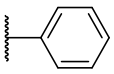
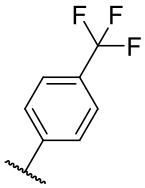
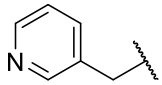
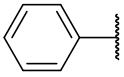
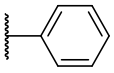
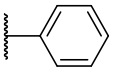
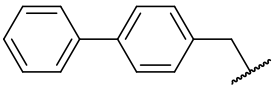
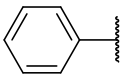
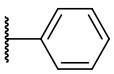
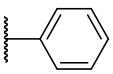
11949211				
11949210				
11949209				
11949208				
11949207				
11949206				
11949205				
11949204				

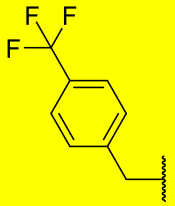
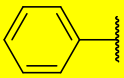
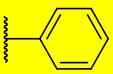
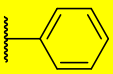
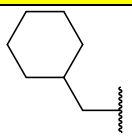
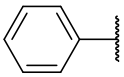
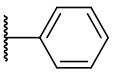
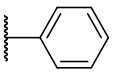
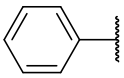
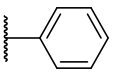
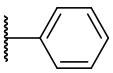
11949203				
11949202				
11949201				
11949200				
11949199				
11949198				
11949197				
11949196				
11949195				

11949194				
11949193				
11949192				
11949191				
11949190				
11949189				
11949188				

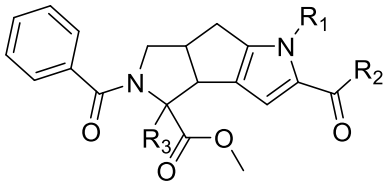
11949187				
11949186				
11949185				
11949184				
11949183				
11949182				
11949181				

11949180				
11949179				
11949178				
11949177				
11949176				
11949175				
11949174				
11949173				

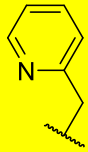
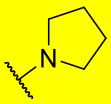
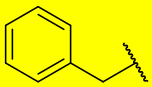
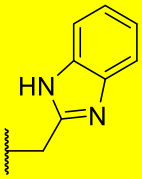
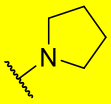
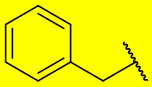
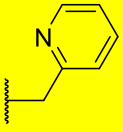
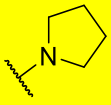
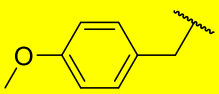
11949172				
11949171				
11949170				
11949169				
11949168				
11949167				
11949166				
11949165				

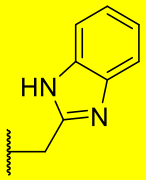
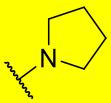
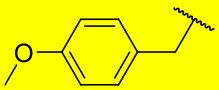
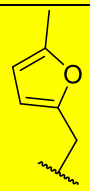
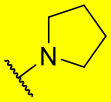
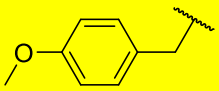
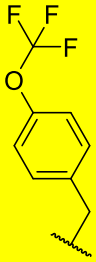
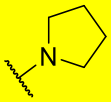
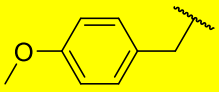
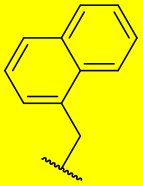
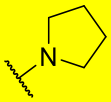
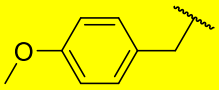
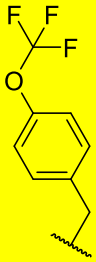
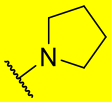
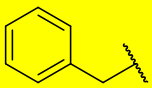
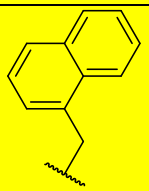
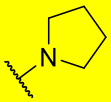
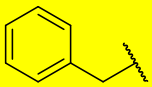
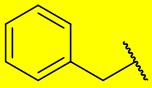
11949164				
11949163				
11949162				

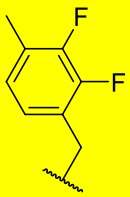
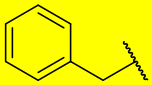
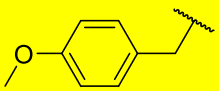
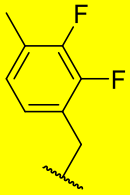
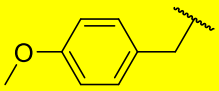
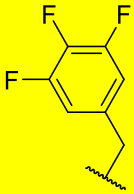
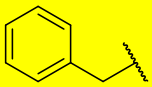
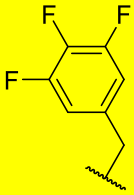
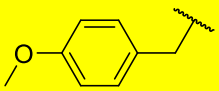
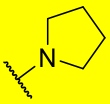
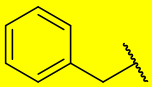
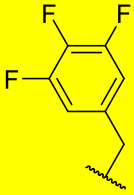
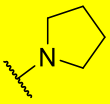
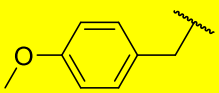
Appendix Table 2a. A list of compounds for the primary scaffold in the UPCMLD02A library

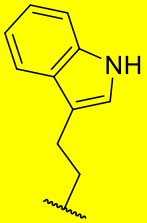
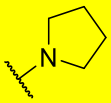
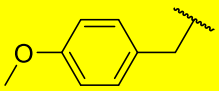
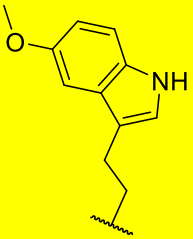
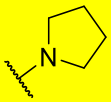
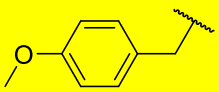
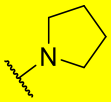
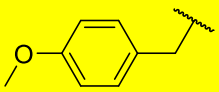
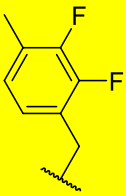
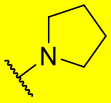
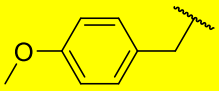
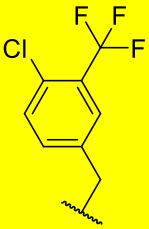
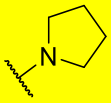
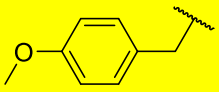
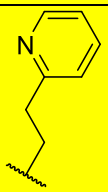
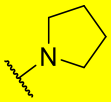
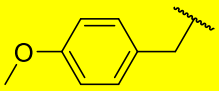


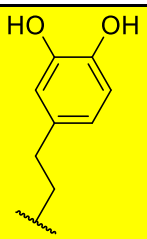
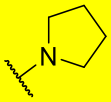
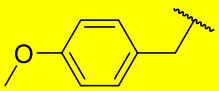
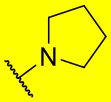
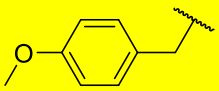
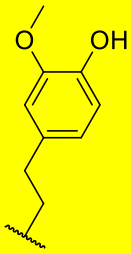
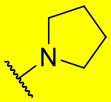
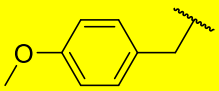
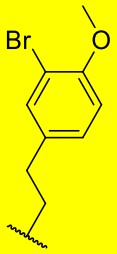
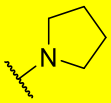
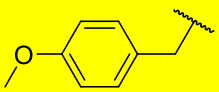
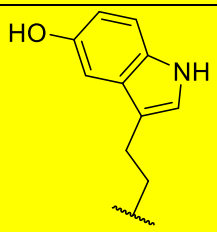
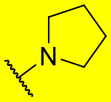
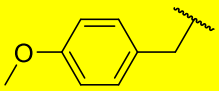
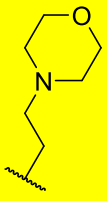
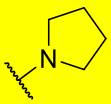
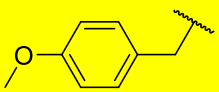
2

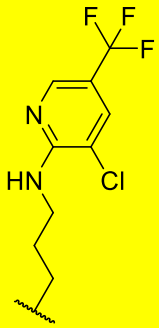
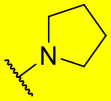
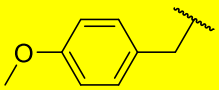
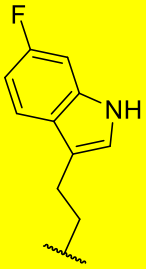
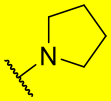
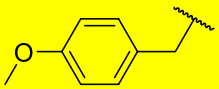
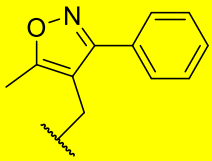
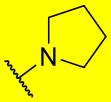
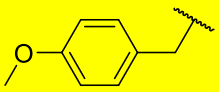
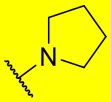
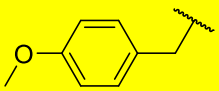
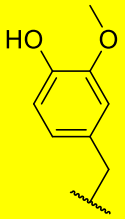
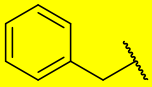
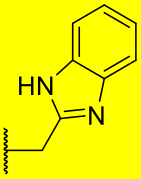
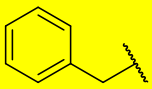
CID	R_1	R_2	R_3
3247074			
3247075			
3247076			

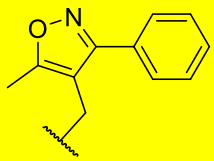
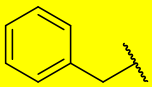
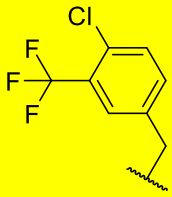
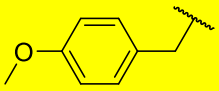
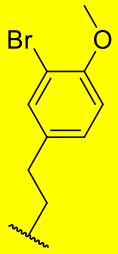
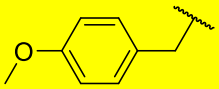
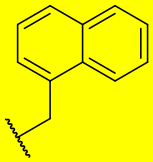
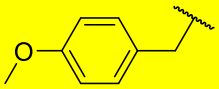
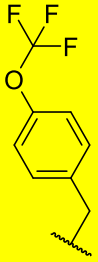
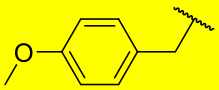
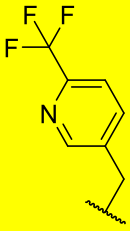
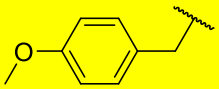
3247077			
3247078			
3247079			
3247080			
3247081			
3247082			
3247083			

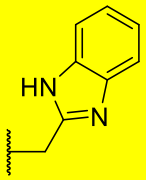
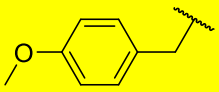
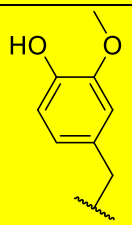
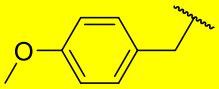
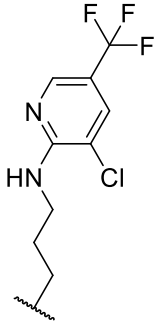
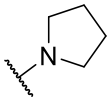
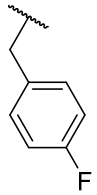
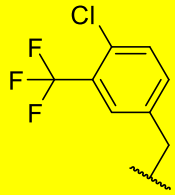
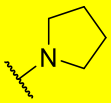
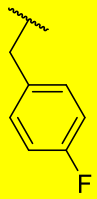
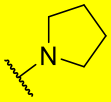
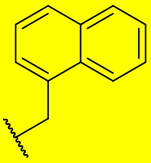
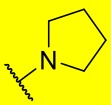
3247084			
3247085			
3247086			
3247087			
3247088			
3247089			
3247090			

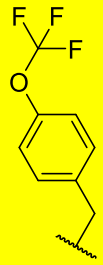
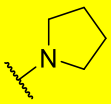
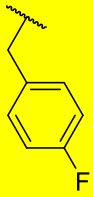
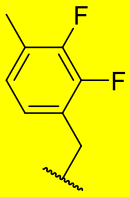
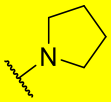
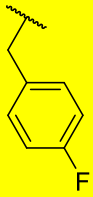
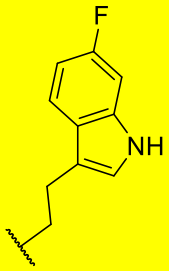
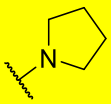
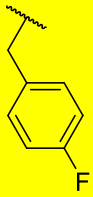
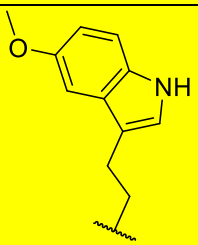
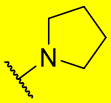
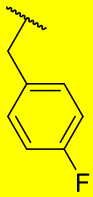
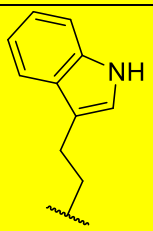
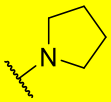
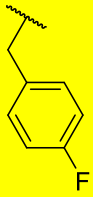
3247091			
3247092			
3247093			
3247094			
3247095			
3247096			

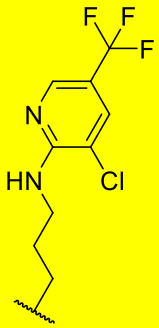
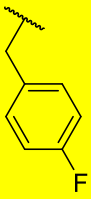
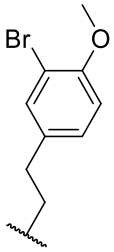
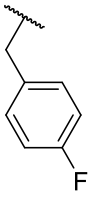
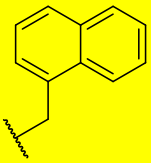
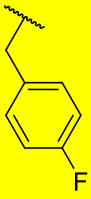
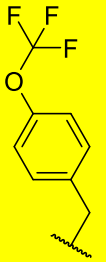
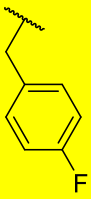
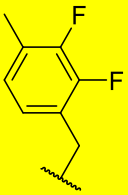
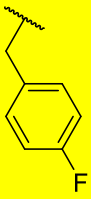
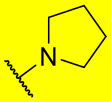
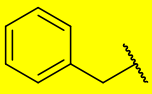
3247097			
3247098			
3247099			
3247100			
3247101			
3247102			

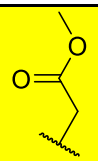
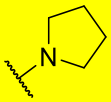
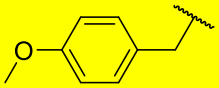
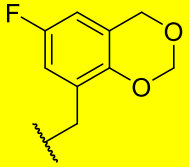
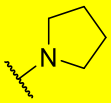
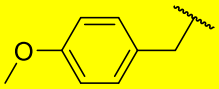
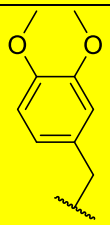
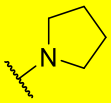
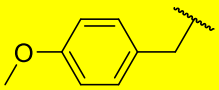
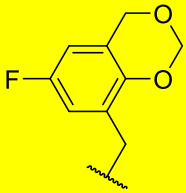
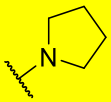
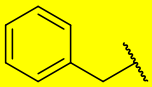
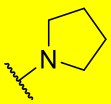
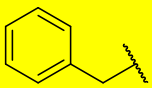
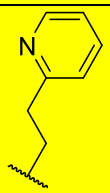
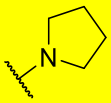
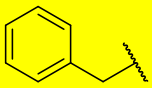
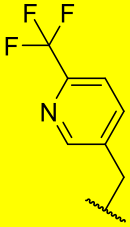
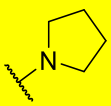
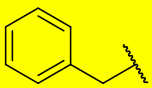
3247103			
3247104			
3247105			
3247106			
3247107			
3247108			

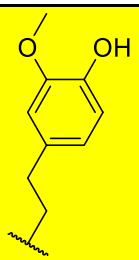
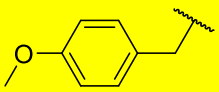
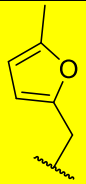
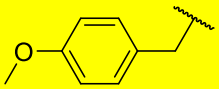
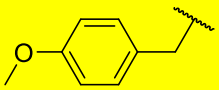
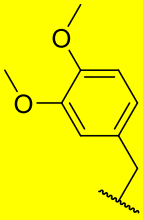
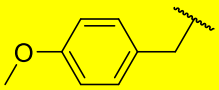
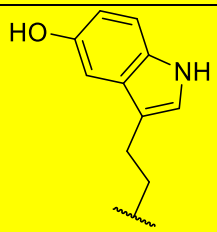
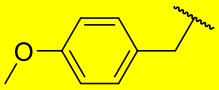
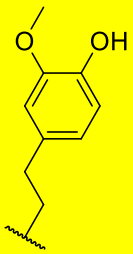
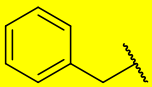
3247109			
3247110			
3247111			
3247112			
3247113			
3247114			

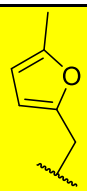
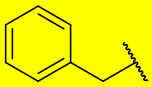
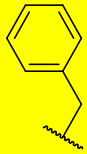
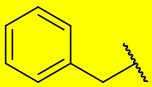
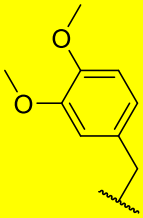
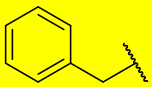
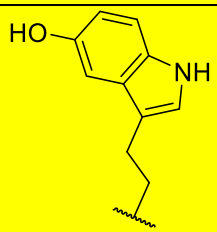
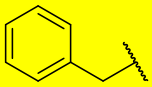
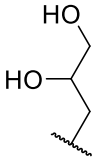
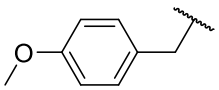
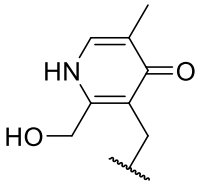
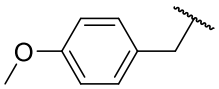
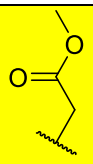
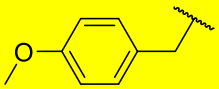
3247115			
3247116			
3247117			
3247118			
3247119			
3247120			

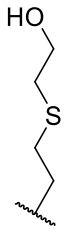
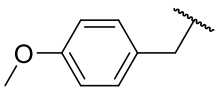
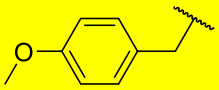
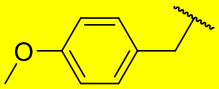
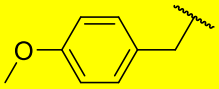
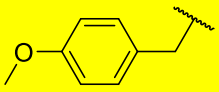
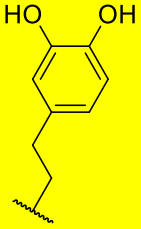
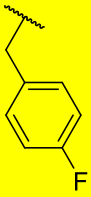
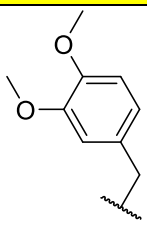
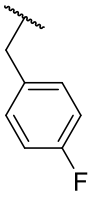
3247121			
3247122			
3247123			
3247124			
3247125			

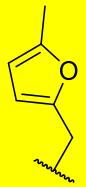
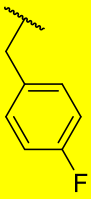
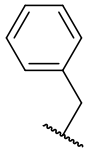
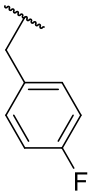
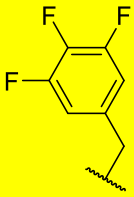
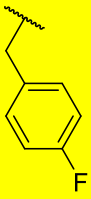
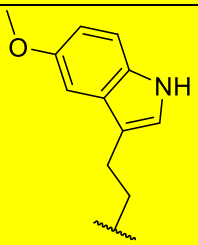
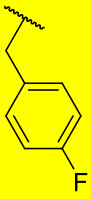
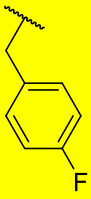
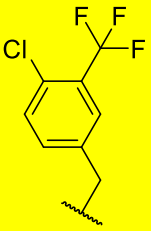
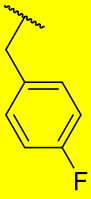
3247126			
3247127			
3247128			
3247129			
3247130			
3247131			

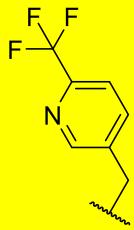
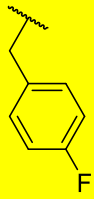
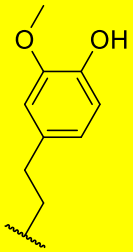
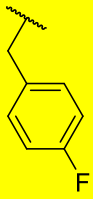
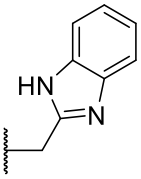
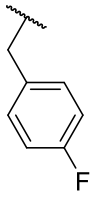
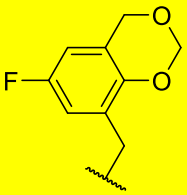
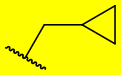
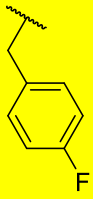
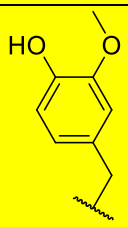
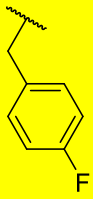
3247134			
3247136			
3247138			
3247139			
3247140			
3247141			
3247142			

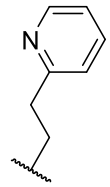
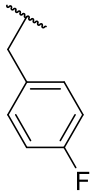
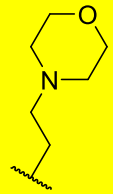
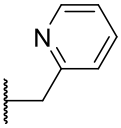
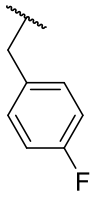
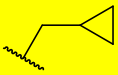
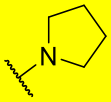
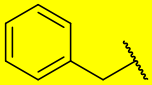
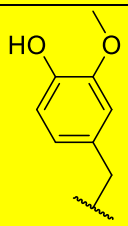
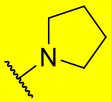
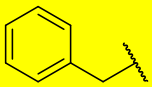
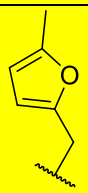
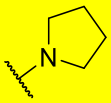
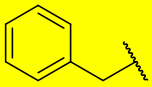
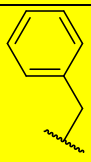
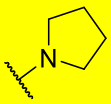
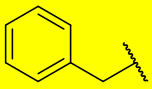
3247144			
3247145			
3247146			
3247147			
3247148			
3247149			

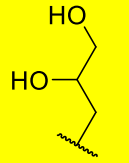
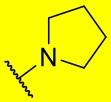
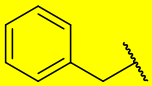
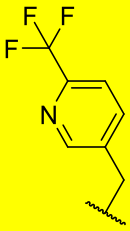
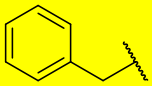
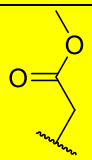
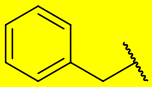
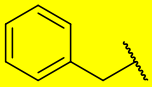
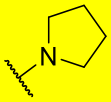
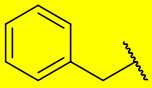
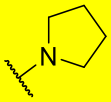
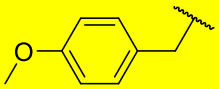
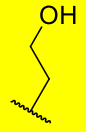
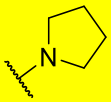
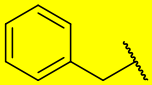
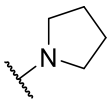
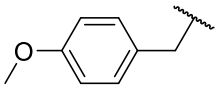
3247150			
3247151			
3247152			
3247153			
3247159			
3247160			
3247161			

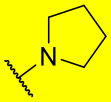
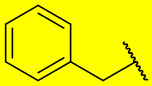
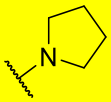
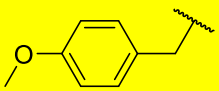
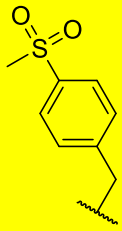
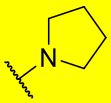
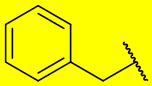
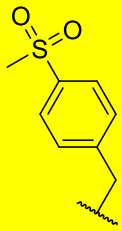
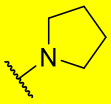
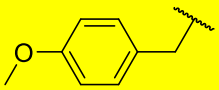
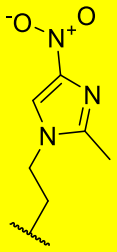
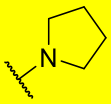
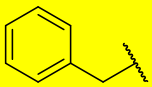
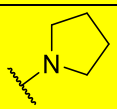
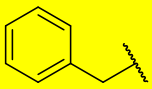
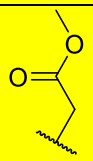
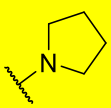
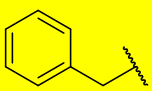
3247162			
3247163			
3247164			
3247165			
3247166			
3247168			
3247169			

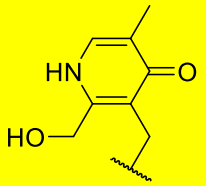
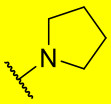
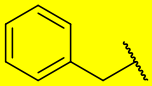
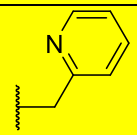
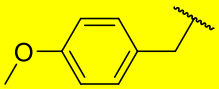
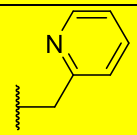
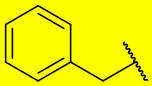
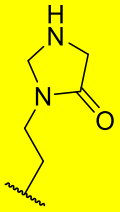
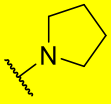
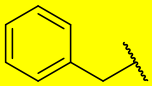
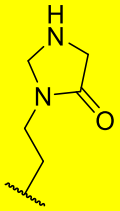
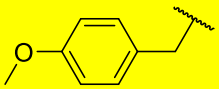
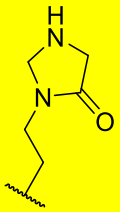
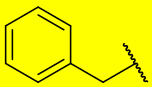
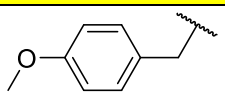
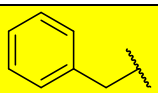
3247170			
3247171			
3247172			
3247173			
3247174			
3247175			

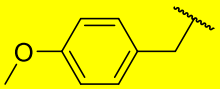
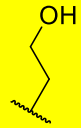
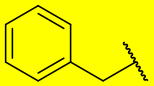
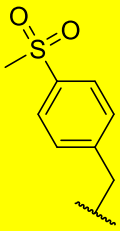
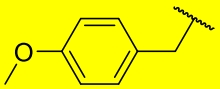
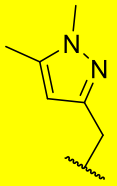
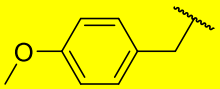
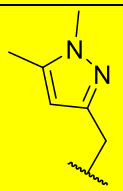
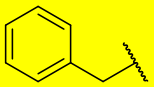
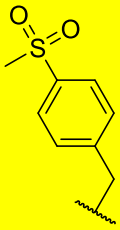
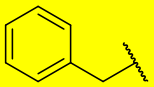
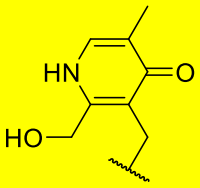
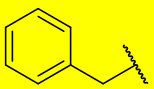
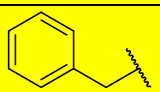
3247176			
3247177			
3247178			
3247179			
3247180			
3247181			

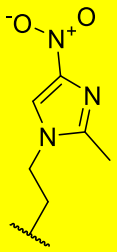
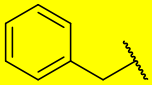
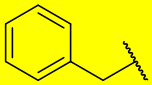
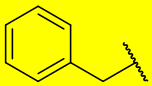
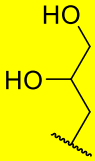
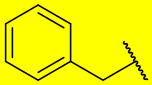
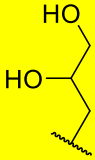
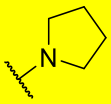
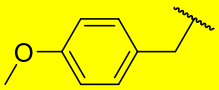
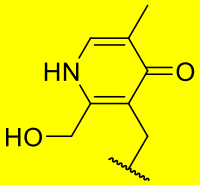
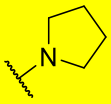
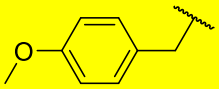
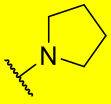
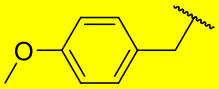
3247182			
3247183			
3247184			
3247185			
3247186			
3247187			
3247188			

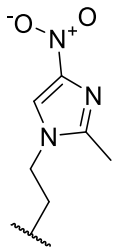
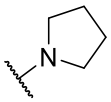
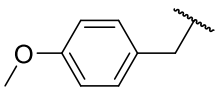
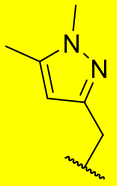
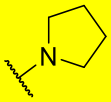
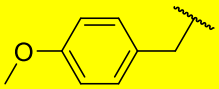
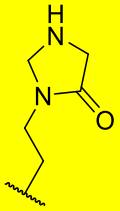
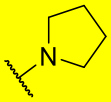
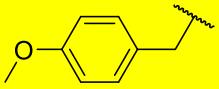
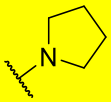
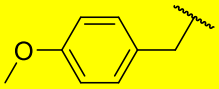
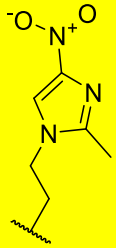
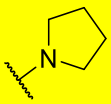
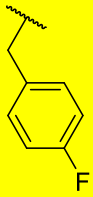
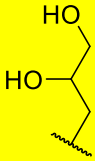
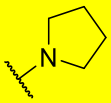
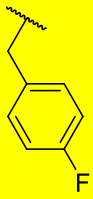
3247189			
3247190			
3247191			
3247192			
3247193	H		
3247194	H		
3247195			
3247196			

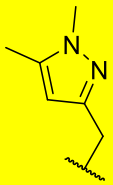
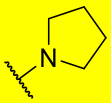
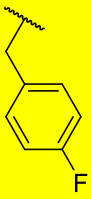
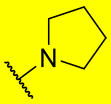
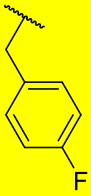
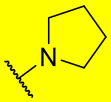
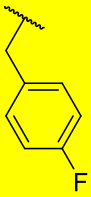
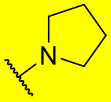
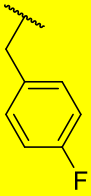
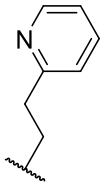
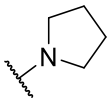
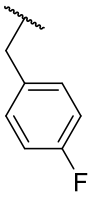
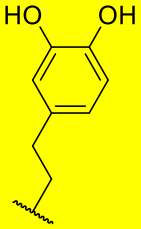
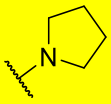
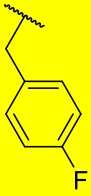
3247197			
3247198			
3247199			
3247200			
3247201			
3247202			
3247203			

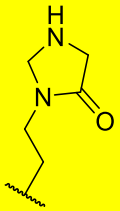
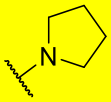
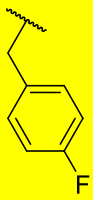
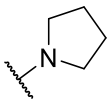
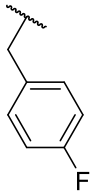
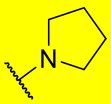
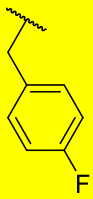
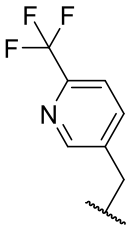
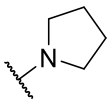
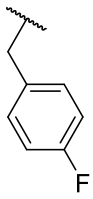
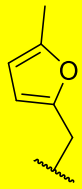
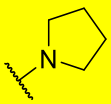
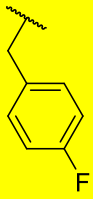
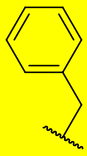
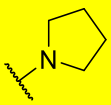
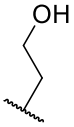
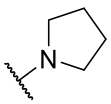
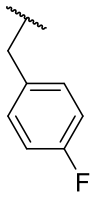
3247204			
3247205			
3247206			
3247207			
3247208			
3247209			
3247210	H		
3247211	H		

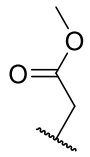
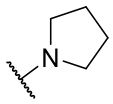
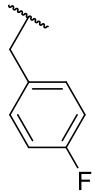
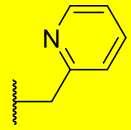
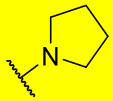
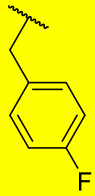
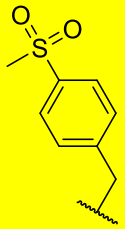
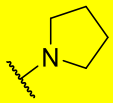
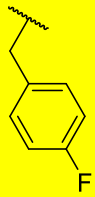
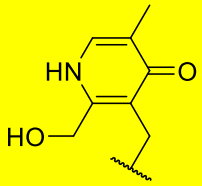
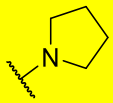
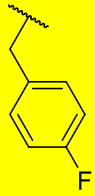
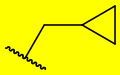
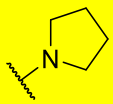
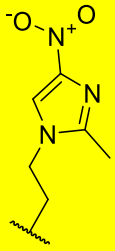
3247212			
3247213			
3247214			
3247215			
3247216			
3247217			
3247218			
3247219			

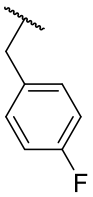
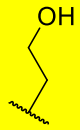
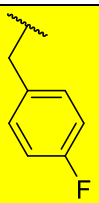
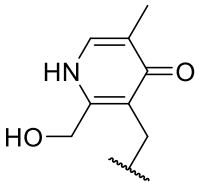
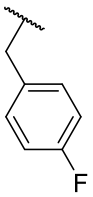
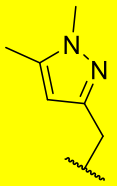
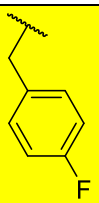
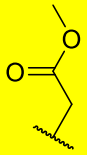
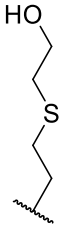
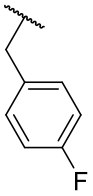
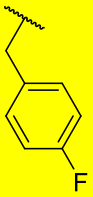
3247220			
3247221			
3247222			
3247223			
3247224			
3247225			
3247226			

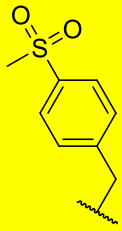
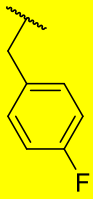
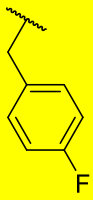
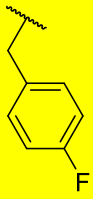
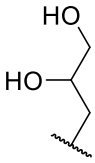
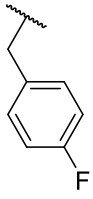
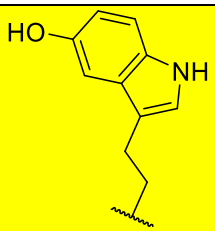
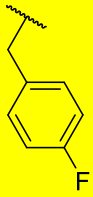
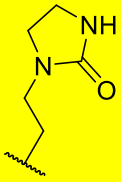
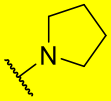
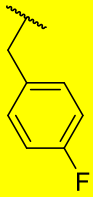
3247227			
3247228			
3247231			
3247232			
3247233			
3247234			

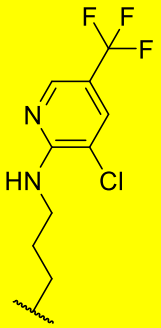
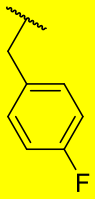
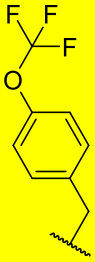
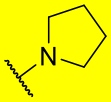
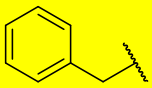
3247235			
3247236			
3247237			
3247238			
3247239			
3247240			

3247241			
3247242			
3247243			
3247244			
3247245			
3247246			
3247247			

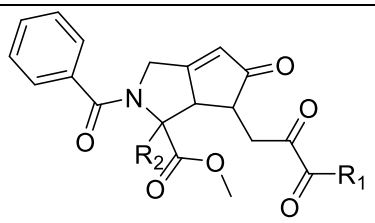
3247248			
3247249			
3247250			
3247251			
3247252			
3247253			

3247254	H		
3247255			
3247256			
3247257			
3247258			
3247259			
3247260			

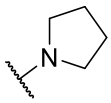
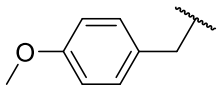
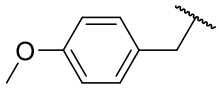
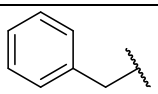
3247261			
3247262			
3247263			
11949594			
50919303			
15965408			

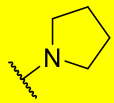
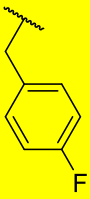
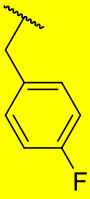
15965404			
11972257			

Appendix Table 2b. A list of compounds for a secondary scaffold in the UPCMLD02A library

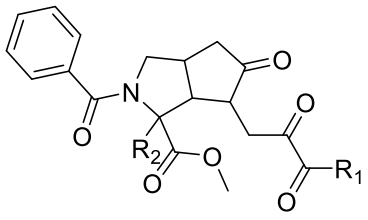


9

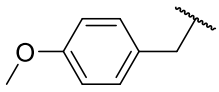
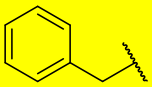
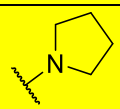
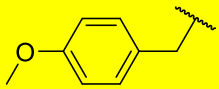
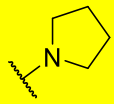
CID	R_1	R_2
3247132		
3247133		
3247143		

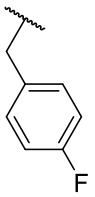
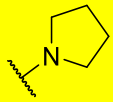
3247156		
3247158		

Appendix Table 2b. A list of compounds for a secondary scaffold in the UPCMLD02A library

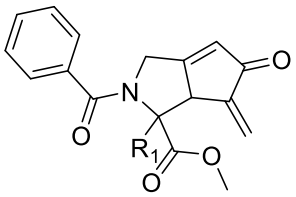


10

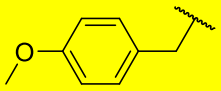
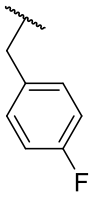
CID	R_1	R_2
3247135		
3247154		
3247155		
3247157[±]		

3247167		
50919302±		

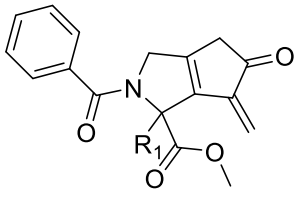
Appendix Table 2d. A list of compounds for a secondary scaffold in the UPCMLD02A library



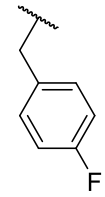
11

CID	R_1
3247229	
3247230	

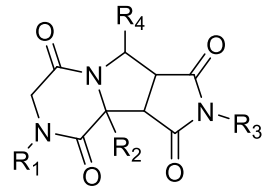
Appendix Table 2e. A list of a secondary scaffold in the UPCMLD02A library



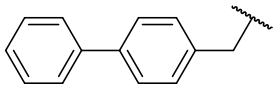
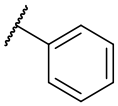
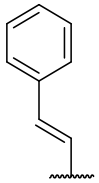
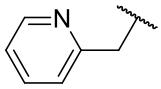
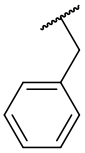
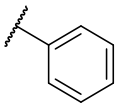
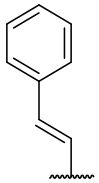
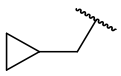
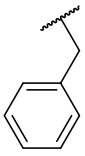
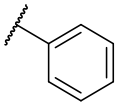
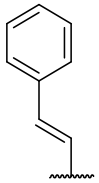
12

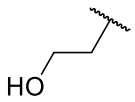
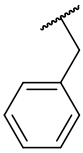
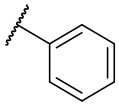
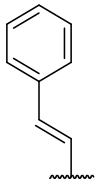
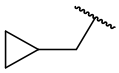
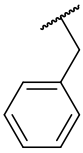
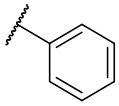
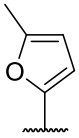
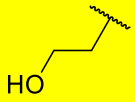
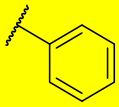
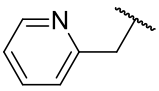
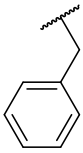
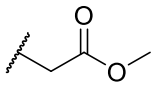
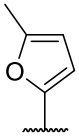
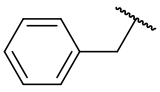
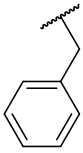
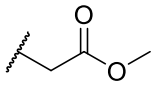
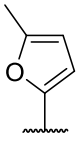
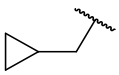
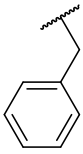
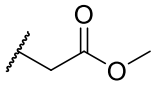
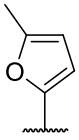
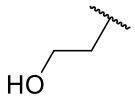
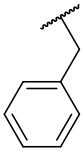
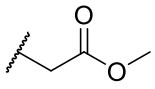
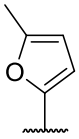
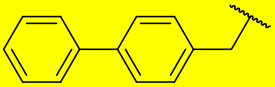
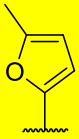
CID	R_1
50919301	

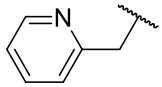
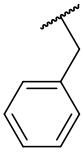
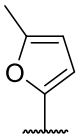
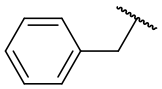
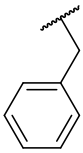
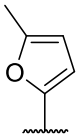
Appendix Table 3. A list of the compounds in the UPCMLD16A library



3

CID	R_1	R_2	R_3	R_4
23731318				
23731357				
23731356				

23731355				
23731354				
23731353				
23731352				
23731351				
23731350				
23731349				
23731348				

23731347				
23731346				
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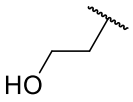
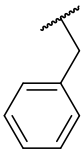
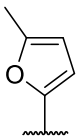
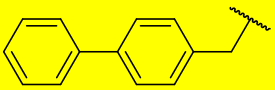
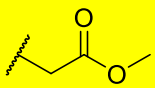
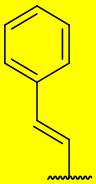
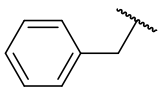
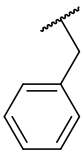
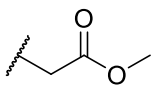
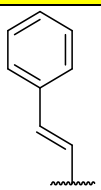
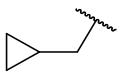
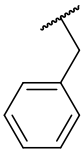
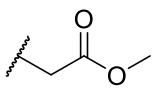
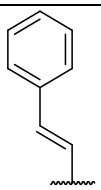
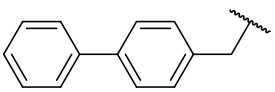
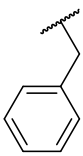
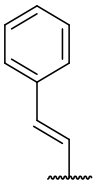
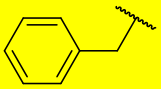
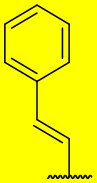
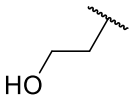
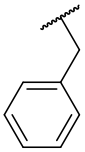
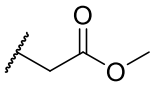
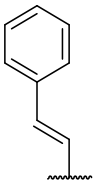
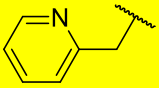
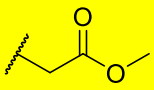
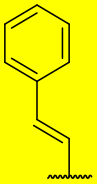
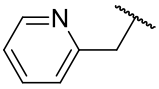
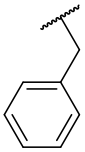
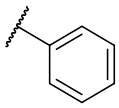
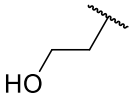
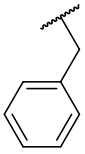
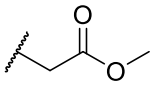
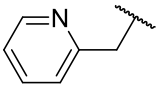
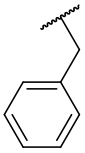
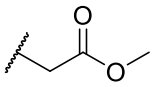
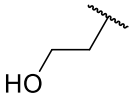
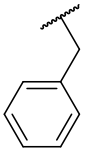
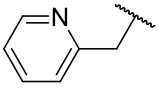
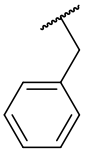
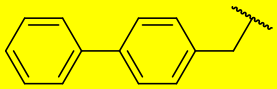
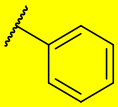
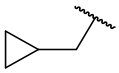
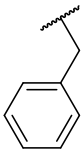
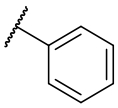
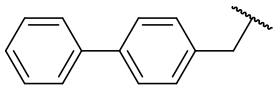
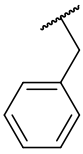
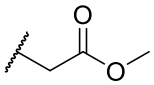
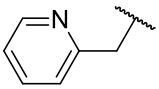
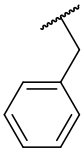
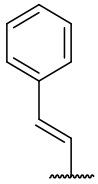
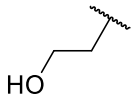
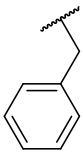
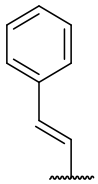
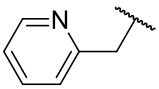
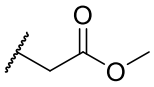
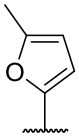
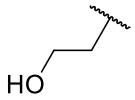
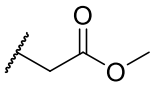
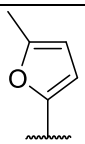
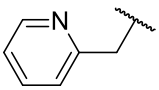
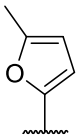
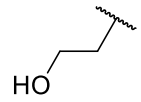
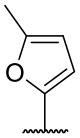
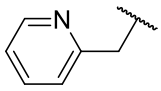
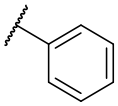
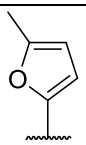
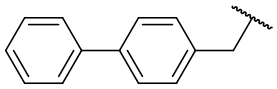
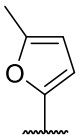
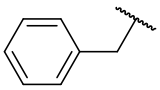
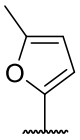
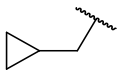
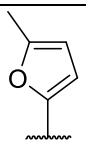
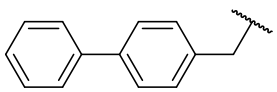
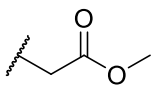
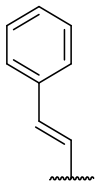
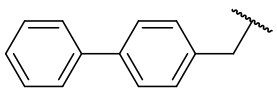
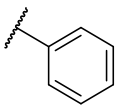
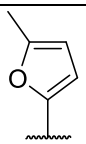
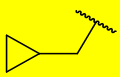
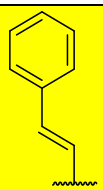
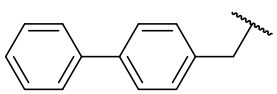
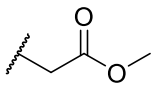
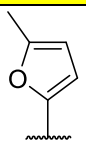
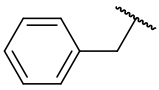
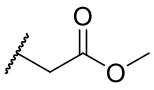
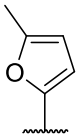
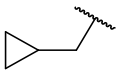
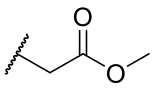
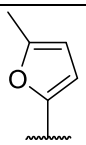
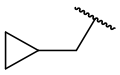
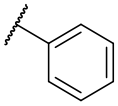
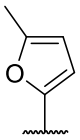
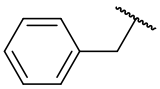
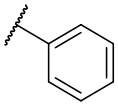
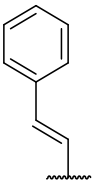
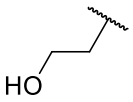
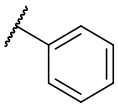
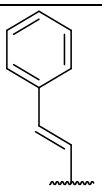
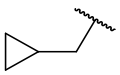
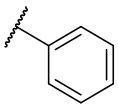
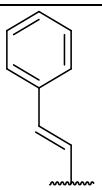
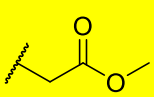
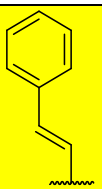
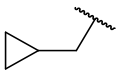
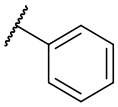
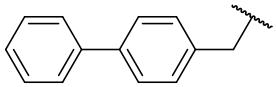
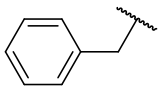
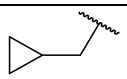
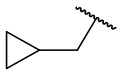
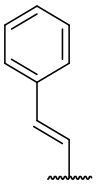
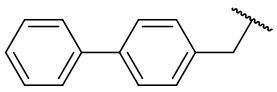
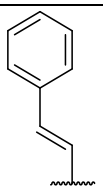
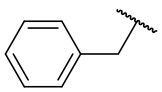
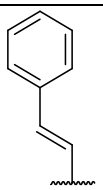
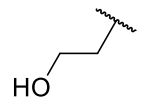
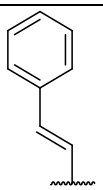
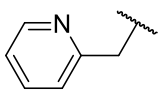
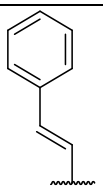
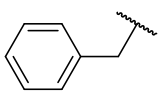
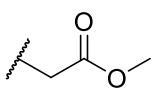
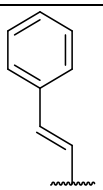
23731344				
23731343				
23731342				
23731341				
23731340				

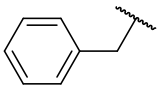
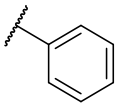
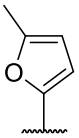
23731339				
23731338				
23731337				
23731336				
23731335				
23731334				
23731333				
23731332				

23731331				
23731330				
23731329				
23731328				
23731327				
23731326				
23731325				
23731324				

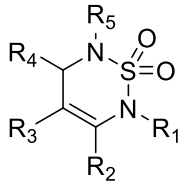
23731323				
23731322				
23731321				
23731320				
23731319				
23731317				
23731316				
23731315				
23731314				

23731313				
23731312				
23731311				
23731310				
23731309				
23731308				
23731307				
23731306				
23731305				

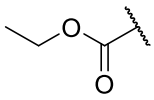
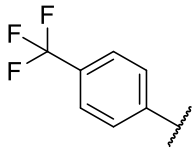
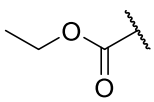
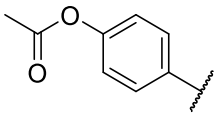
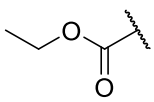
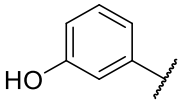
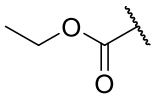
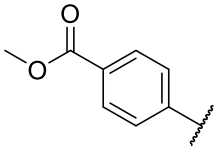
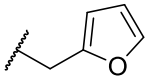
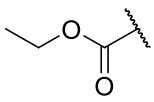
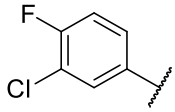
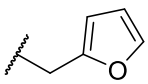
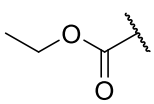
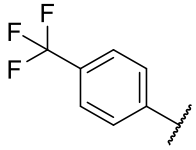
23731304				
23731303				
23731302				
23731301				
23731300				
23731299				
23731298				
23731297				

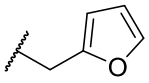
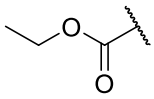
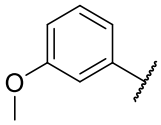
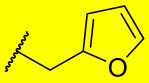
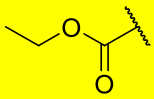
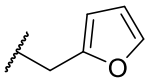
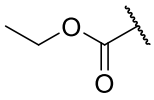
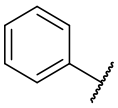
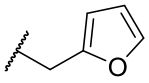
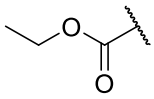
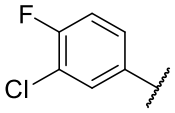
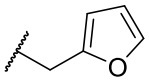
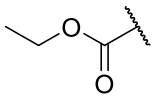
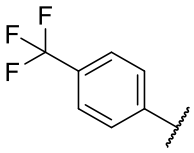
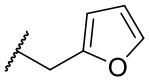
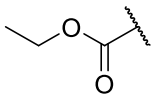
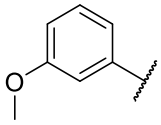
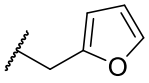
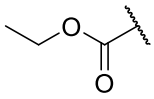
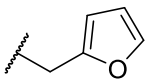
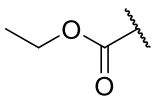
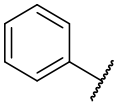
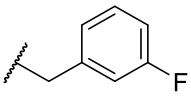
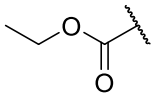
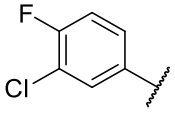
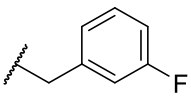
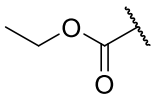
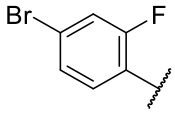
23731296				

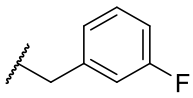
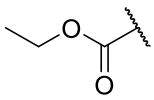
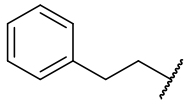
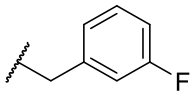
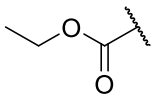
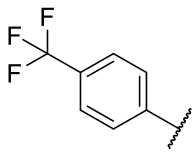
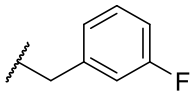
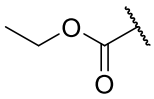
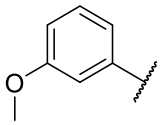
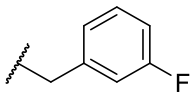
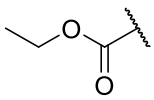
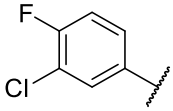
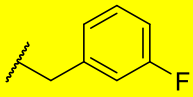
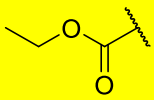
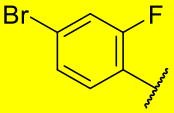
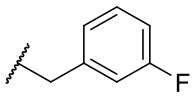
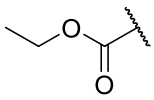
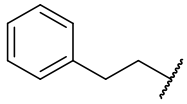
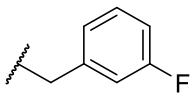
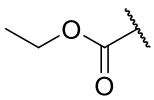
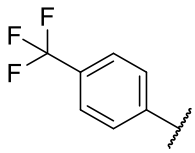
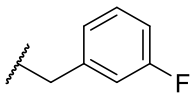
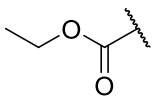
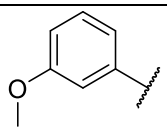
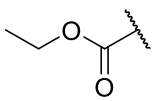
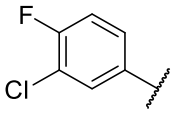
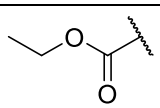
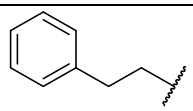
Appendix Table 4a. A list of compounds for the primary scaffold in the UPCMLD24A library

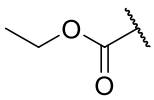
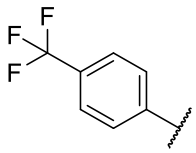
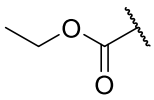
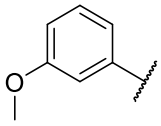
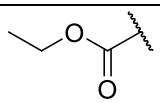
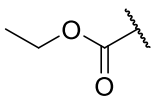
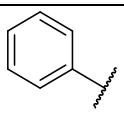
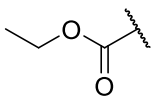
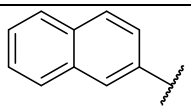
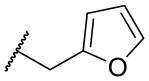
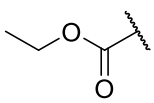
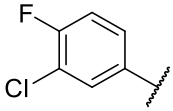
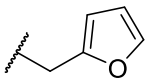
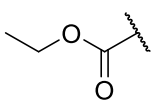
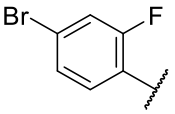
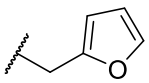
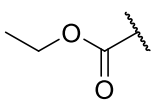
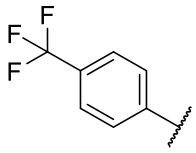
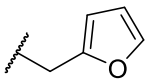
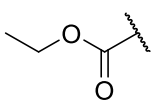
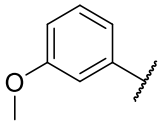
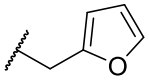
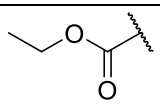


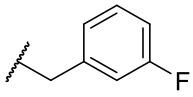
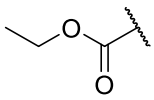
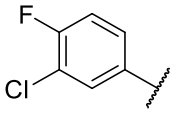
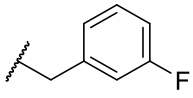
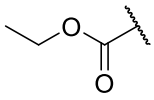
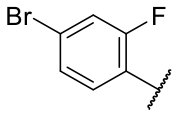
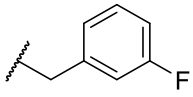
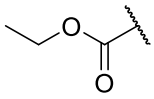
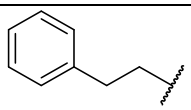
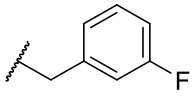
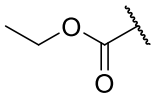
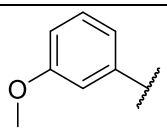
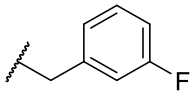
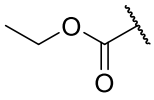
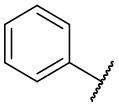
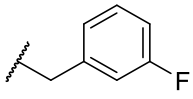
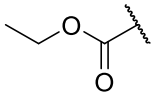
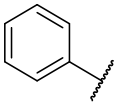
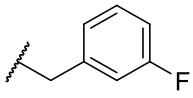
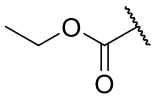
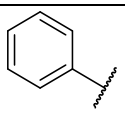
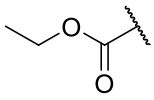
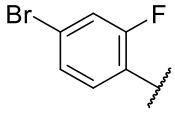
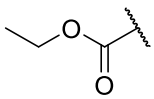
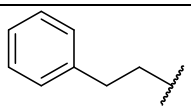
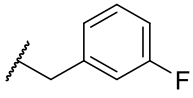
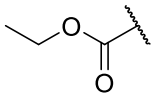
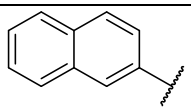
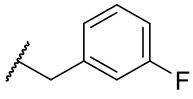
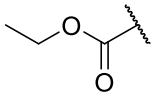
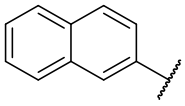
4

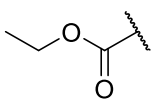
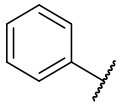
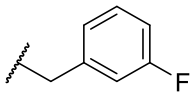
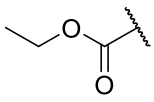
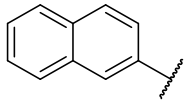
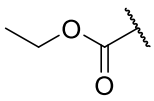
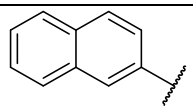
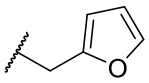
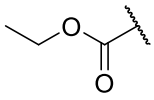
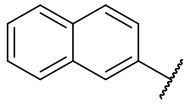
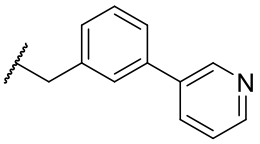
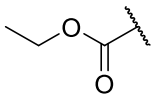
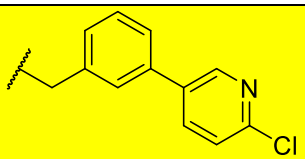
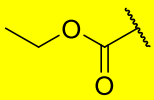
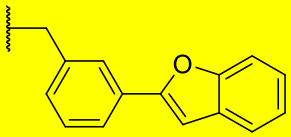
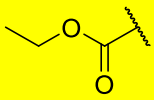
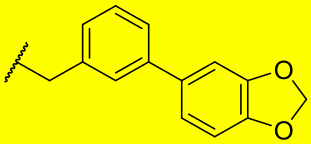
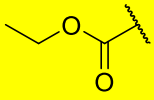
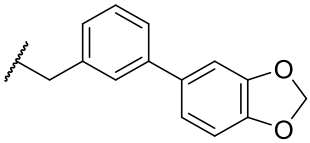
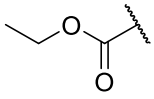
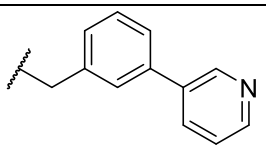
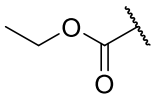
CID	R_1	R_2	R_3	R_4	R_5
42628032	H	H			H
42628031	H	H			H
42628030	H	H			H
42628029	H	H			H
42628028		H			
42628027		H			

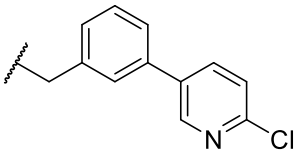
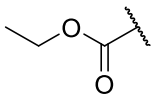
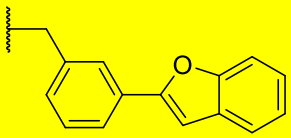
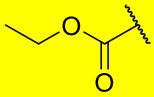
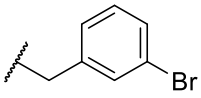
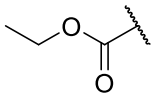
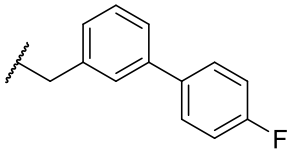
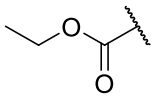
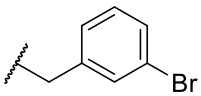
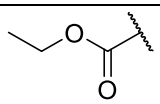
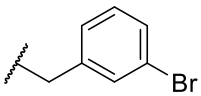
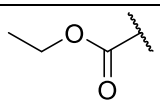
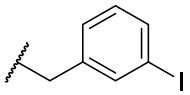
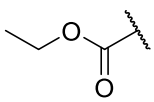
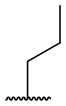
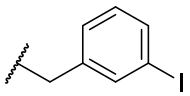
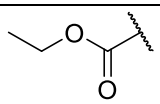
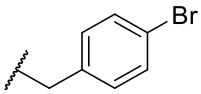
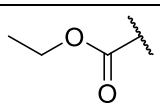
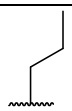
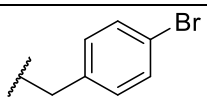
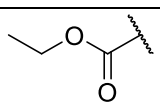
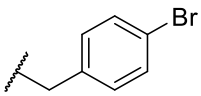
42628026		H			
42628025		H			
42628024		H			
42628023		H			
42628022		H			
42628021		H			
42628020		H			
42628019		H			
42628018		H			
42628017		H			

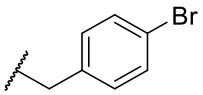
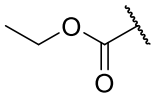
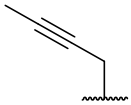
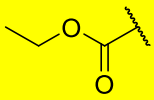
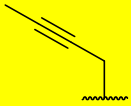
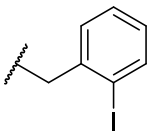
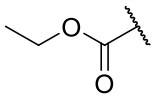
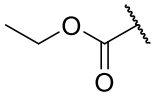
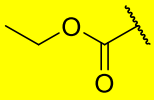
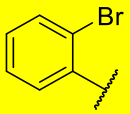
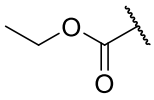
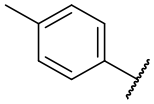
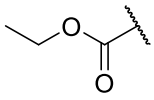
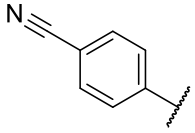
42628016		H			
42628015		H			
42628014		H			
42628013		H			
42628012		H			
42628011		H			
42628010		H			
42628009		H			
42628008		H			H
42628007		H			H

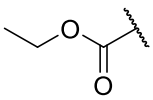
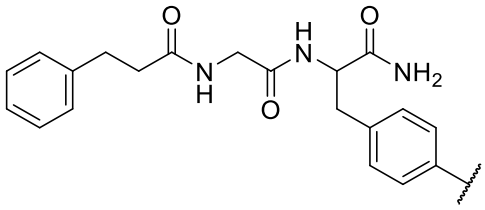
42628006		H			H
42628005		H			H
42628004		H			H
42628003		H			H
42628002		H			H
42628001		H			H
42628000		H			H
42627999		H			H
42627998		H			H
42627997		H			H

42627996		H			H
42627995		H			H
42627994		H			H
42627993		H			H
42627992		H			
42627991		H			
42627990		H			H
42627989	H	H			H
42627988	H	H			H
42627987		H			
42627986		H			H

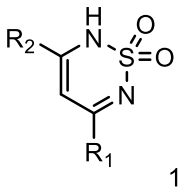
42627985	H	H			H
42627984		H			
42627983	H	H			H
42627982		H			
42627981		H			
42627980		H			
42627979		H			H
42627978		H			H
42627977		H			
42627976		H			

42627975		H			
42627974		H			
42627973		H			
42627972		H			
42627971		H			
42627970		H			H
42627969		H			
42627968		H			
42627967		H			
42627966		H			
42627965		H			H

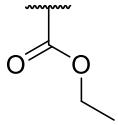
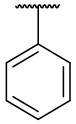
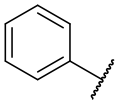
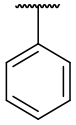
42627964				H	
42627963	H			H	
42627962				H	
42627961	H			H	
42627960	H	H			H
42627959	H	H			H
42627958	H	H			H

CID	R_1	R_2	R_3	R_4	R_5
42628033	H	H			H

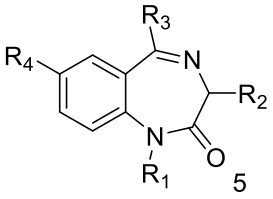
Appendix Table 4b. A list of compounds for a secondary scaffold in the UPCMLD24A library



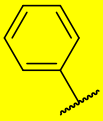
13

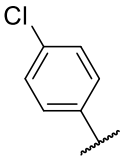
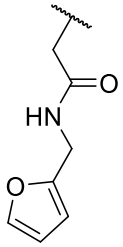
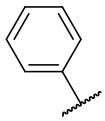
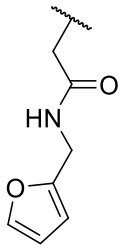
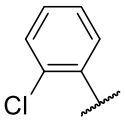
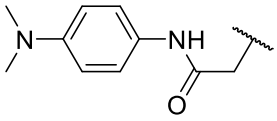
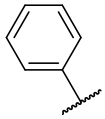
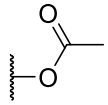
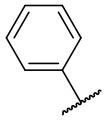
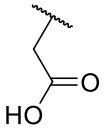
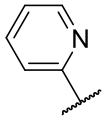
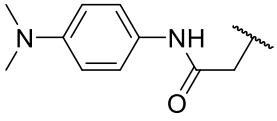
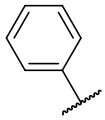
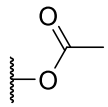
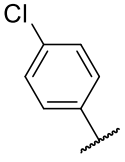
CID	R_1	R_2
18526094		
12196531		
12196529		

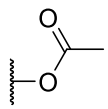
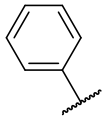
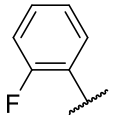
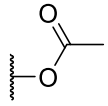
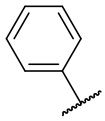
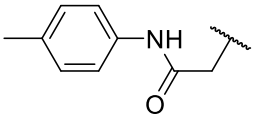
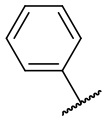
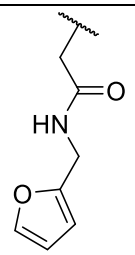
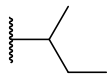
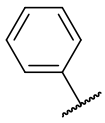
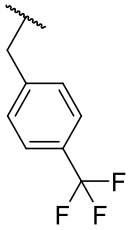
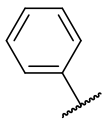
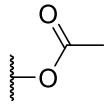
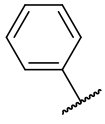
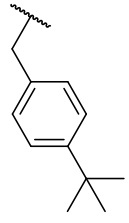
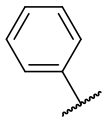
Appendix Table 5a. A list of compounds for the primary scaffold in the benzodiazepines library that was screened in ≥100 bioassays

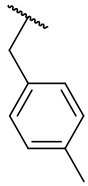
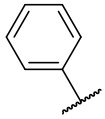
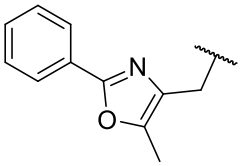
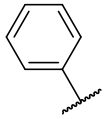
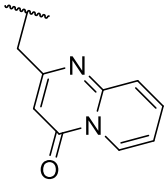
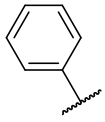
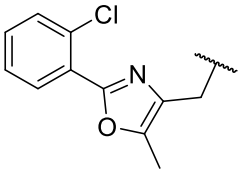
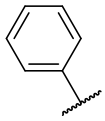
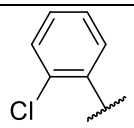
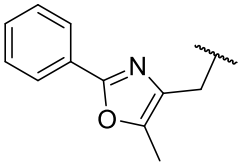
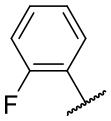
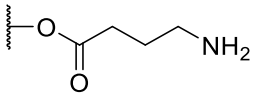
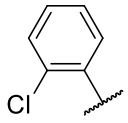
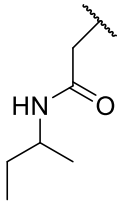
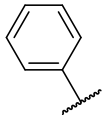


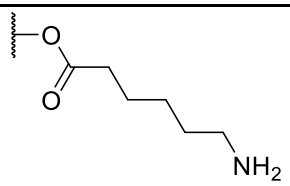
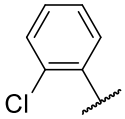
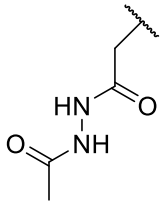
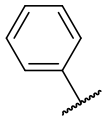
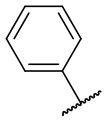
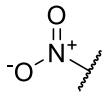
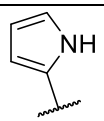
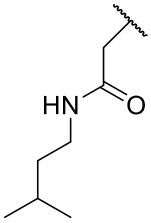
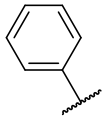
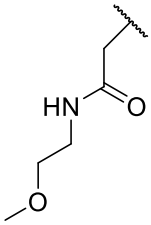
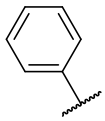
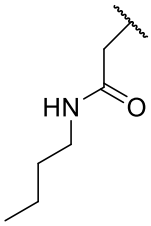
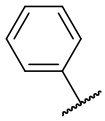
5

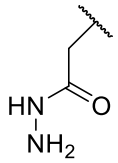
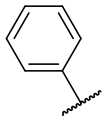
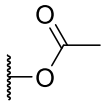
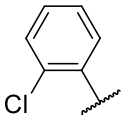
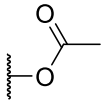
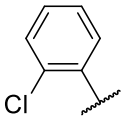
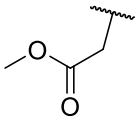
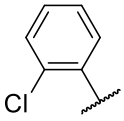
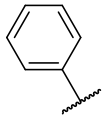
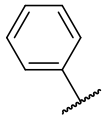
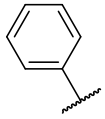
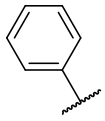
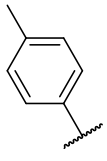
CID	R_1	R_2	R_3	R_4
3016		H		Cl

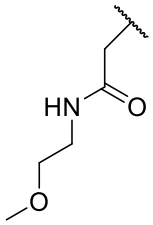
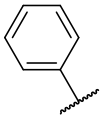
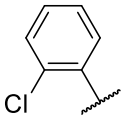
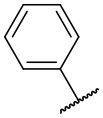
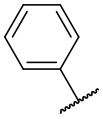
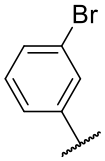
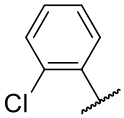
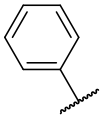
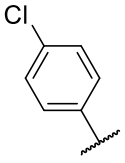
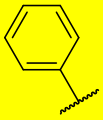
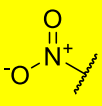
1688		H		Cl
3239992		H		H
3242322		H		Cl
3241670		H		H
661451	H			H
292106		H		Cl
4067095		H		Cl
3769982	H			Br

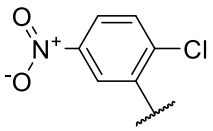
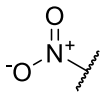
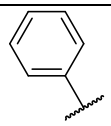
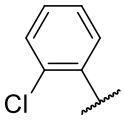
627336	H			Br
4540	H	H		Cl
3763028	H			
4227629		H		Cl
9550458				Cl
3812960		H		H
629081				Br
3780845		H		H

3782732		H		H
4053467		H		H
3645286		H		Br
15945564		H		H
125820	H	OH		Br
15945507				Cl
2912834	H			Br
15992383		H		H

16188013	H			Br
627086		H		Br
4506	H	H		
64983	H	H		Cl
4227633		H		H
4231220		H		H
4231219		H		H

121919		H		Br
631729				Br
630731	H			Br
1985588		H		Br
76175	H	H		H
76167	H	H		Br
625577	H			Br
613848	H	H		
781348	H	H		Br

3525607				Cl
632515		H		Br
614001	H	OH		H
627325	H	OH		Br
633837	H	H		Br
629437	H			Br
617083		OH		H
3676999	H	OH		Br
4496		H		

2835734	H	H		
1108855		H		
40113	H	H		Br
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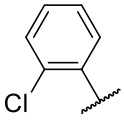
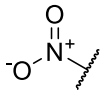
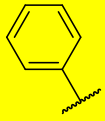
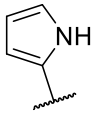
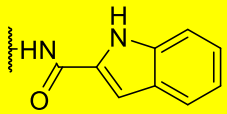
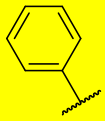
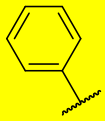
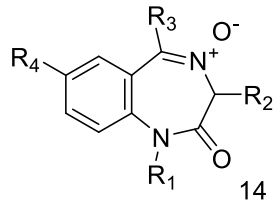
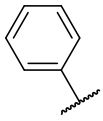
2802	H	H		
4616	H	OH		Cl
457993		H		Cl
443375				H
5391		OH		Cl

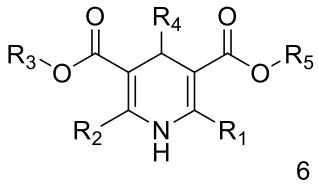
Appendix Table 5b. A list of a secondary scaffold in the benzodiazepines library that was screened in ≥100 bioassays



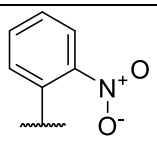
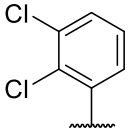
14

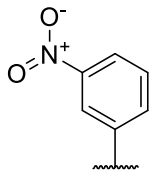
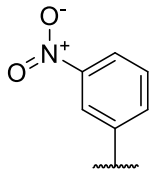
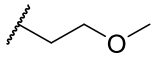
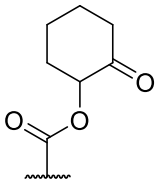
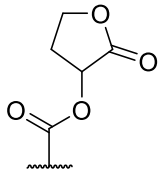
CID	R_1	R_2	R_3	R_4
72793		H		Cl

Appendix Table 6a. A list of compounds for the primary scaffold in the dihydropyridines library that was screened in ≥100 bioassays



6

CID	R_1	R_2	R_3	R_4	R_5
4485					
3333					

4507±					
4497					
2998930					
2998073					
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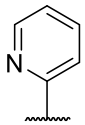
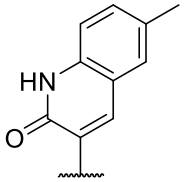
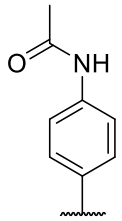
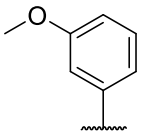
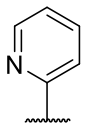
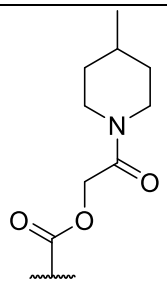
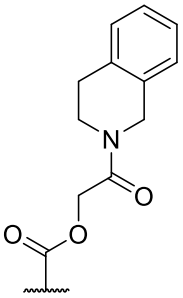
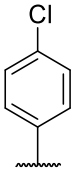
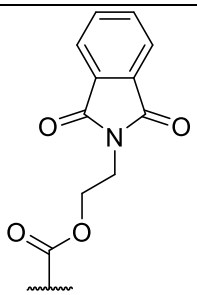
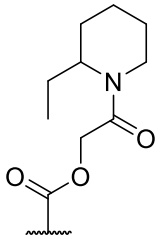
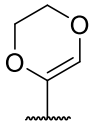
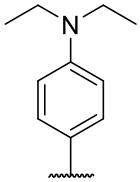
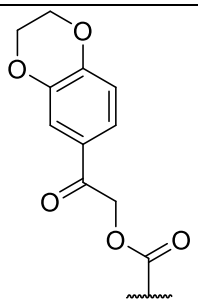
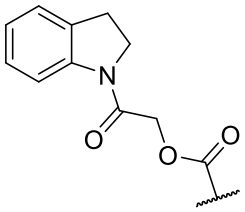
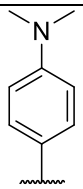
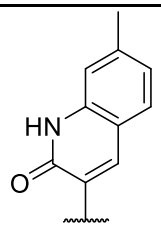
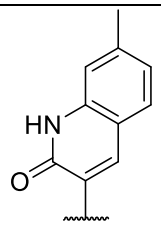
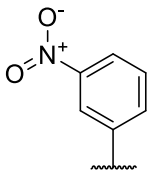
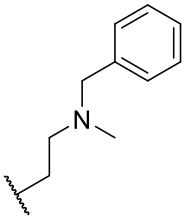
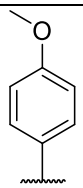
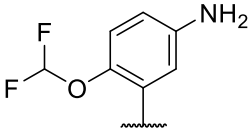
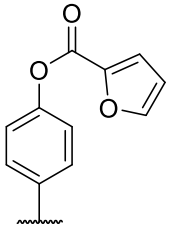
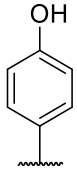
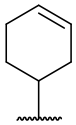
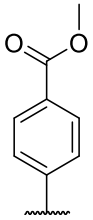
99955					
645054					
356261					

674174	H	H			
614258					
2997634					
3000076					
715615	H	H			
2998190					

2998245					
654190					
653396					
2998525					
2998988					
646414					

652775					
646662					
41114±					
97201					
1179153					
2873602					
619963					

2874327					
607320	H	H			
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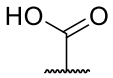
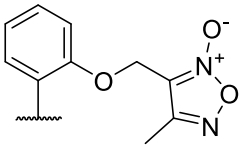
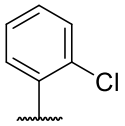
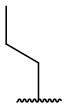
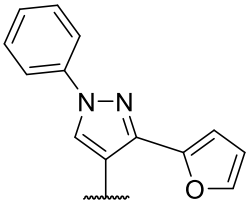
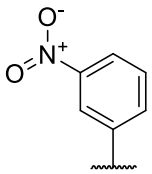
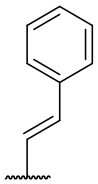
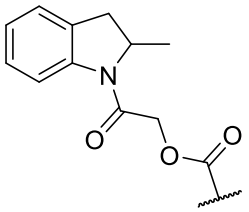
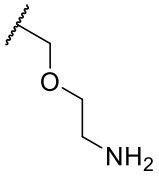
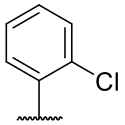
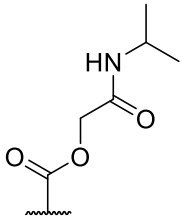
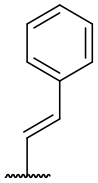
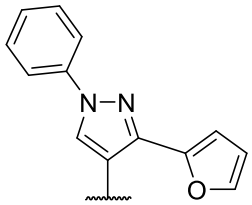
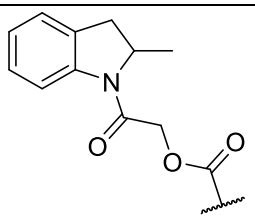
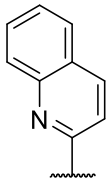
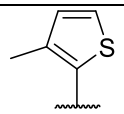
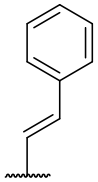
168683					
2999719					
299857	H	H			
101991					
980133					
89082					

980118					
4372140					
2162±					
3552238					
741918					
2891841					
5036384					

1481403					
741915					
5349621					
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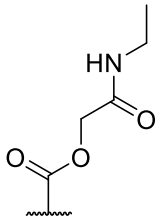
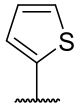
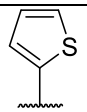
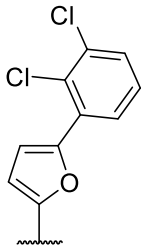
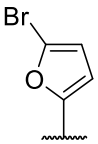
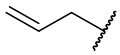
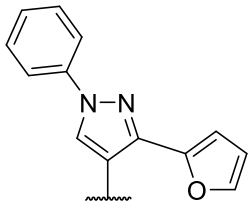
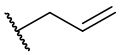
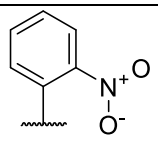
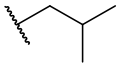
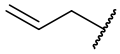
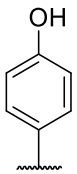
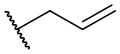
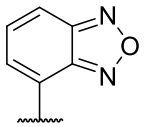
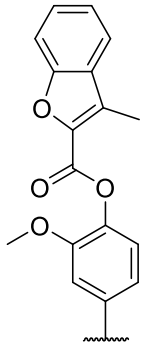
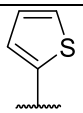
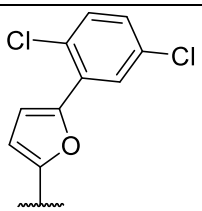
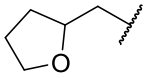
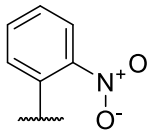
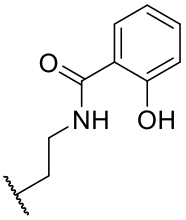
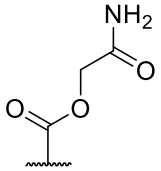
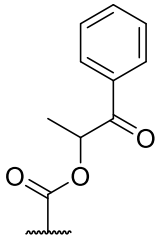
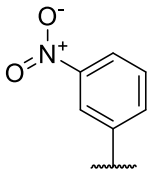
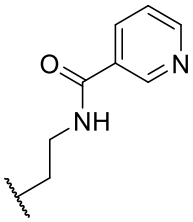
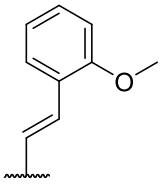
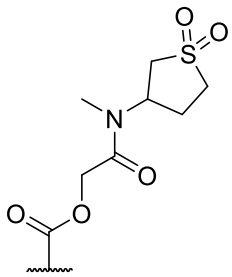
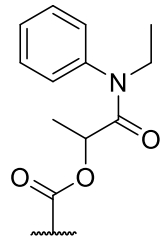
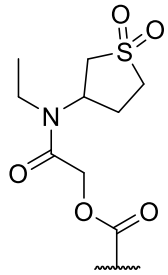
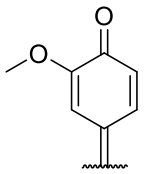
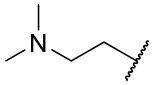
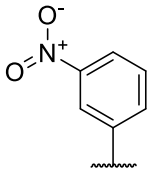
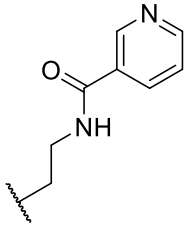
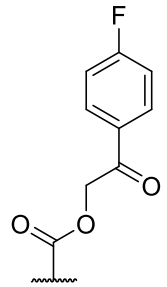
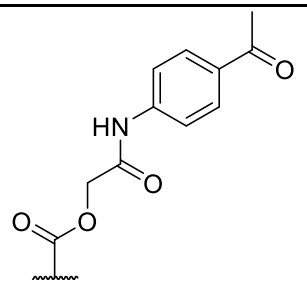
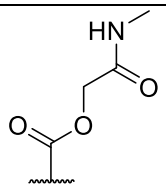
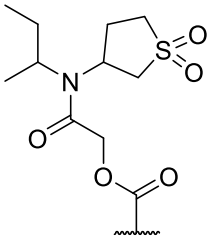
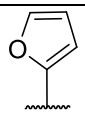
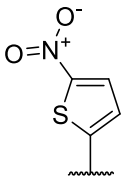
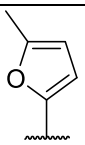
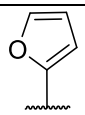
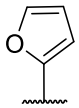
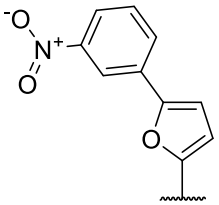
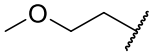
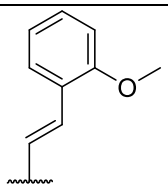
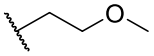
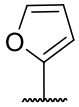
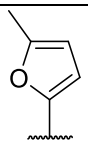
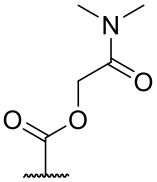
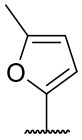
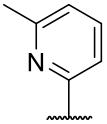
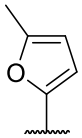
4542777					
2891805					
1116476					
979574					
979103					

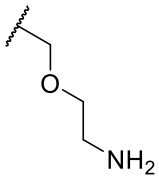
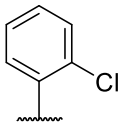
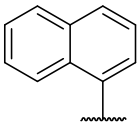
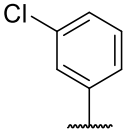
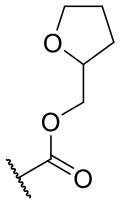
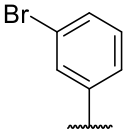
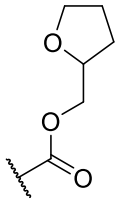
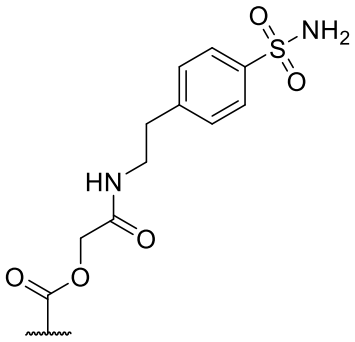
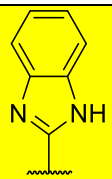
3713405					
4499					
3139744					
3784					
1521795					
211447					
1523976					

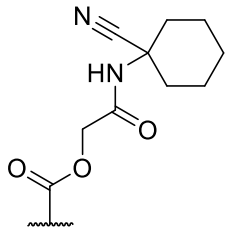
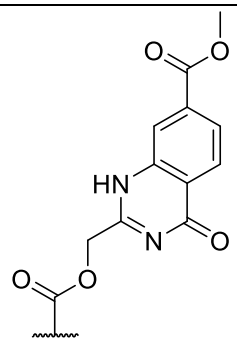
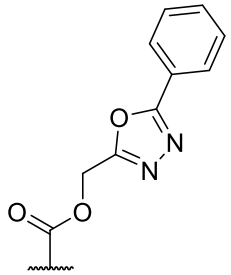
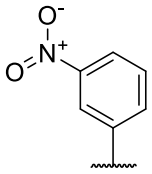
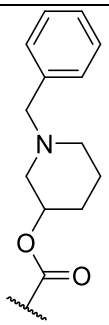
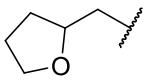
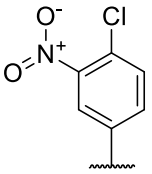
4225909					
4640338					
4876664					
3655532					
1330517					
3527455					

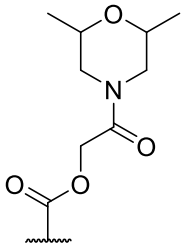
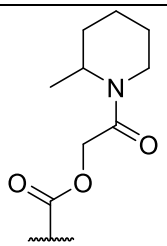
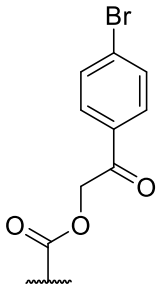
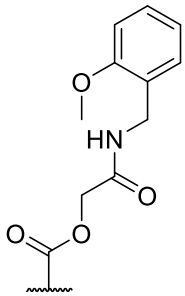
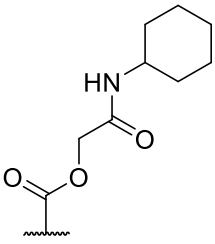
4882233					
3278447					
5457261					
15944995					
4291090					

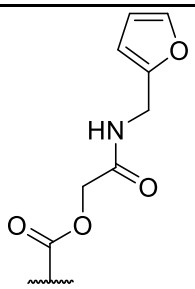
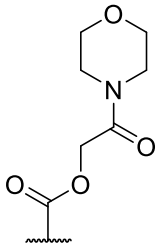
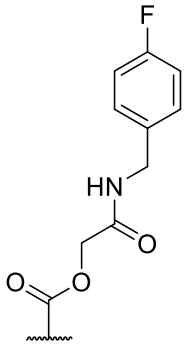
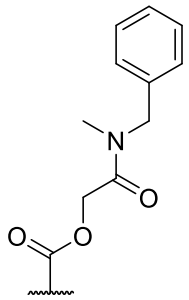
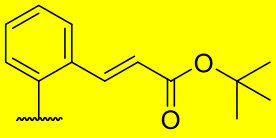
4037186					
5040203					
4833026					
211446					
330513					
2891790					
2891717					
2832255					

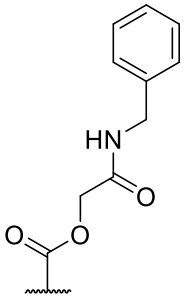
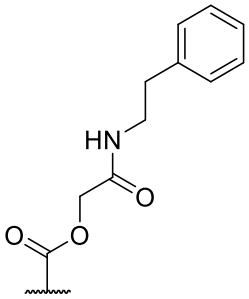
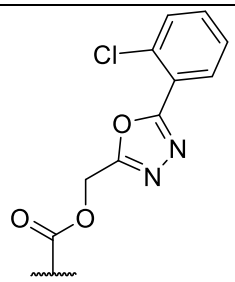
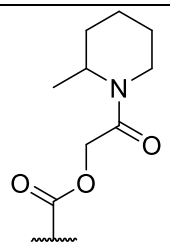
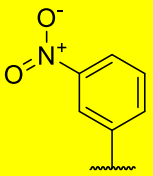
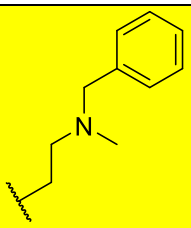
1042586					
5788116					
206197					
680018					
4874926					
979325					
2729685					
698276					

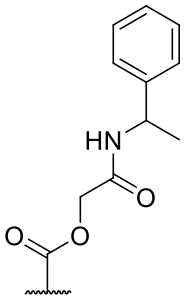
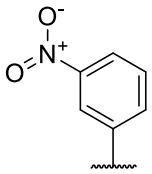
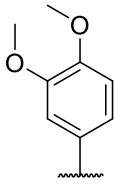
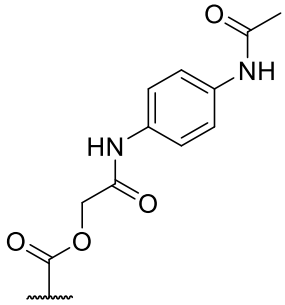
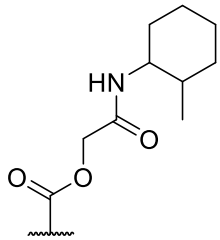
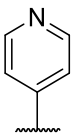
60496±					
607376	H	H			
3290996					
4597530					
24980278					
1355281					

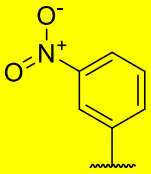
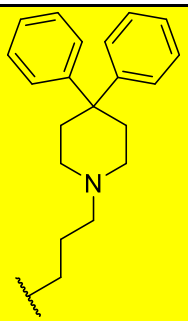
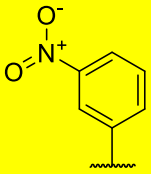
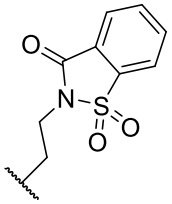
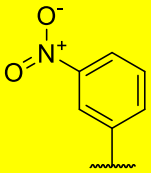
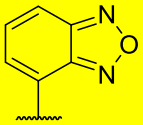
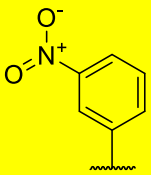
16235098					
16269372					
16303100					
656667					
5178648					

4377834					
4877032					
16251224					
3952096					
5206524					

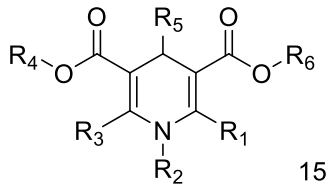
3952099					
3952101					
4010124					
4350308					
5311217					

4003931					
4527347					
16331146					
4878417					
4474[±]					

3924081					
282663					
323302					
3578429					
3954720					
322224					

60602					
157704[±]					
124236					
5282138					
158617					
157132					

Appendix Table 6b. A list of compounds for a secondary scaffold in the dihydropyridines library that was screened in ≥100 bioassays



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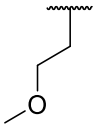
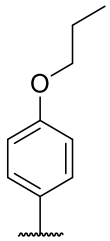
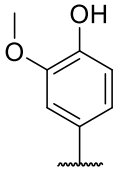
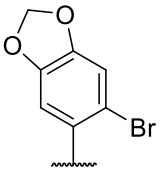
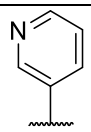
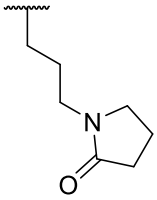
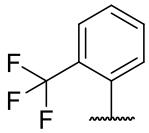
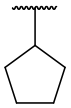
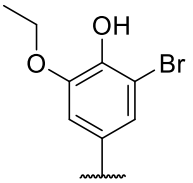
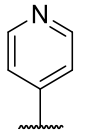
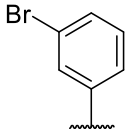
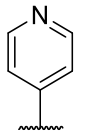
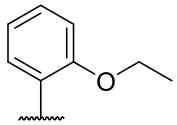
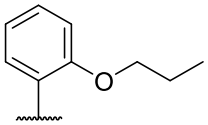
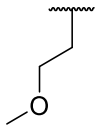
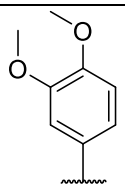
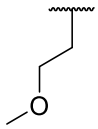
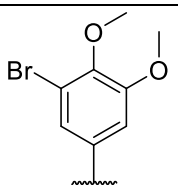
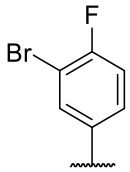
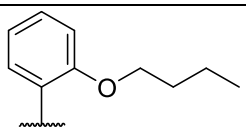
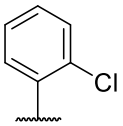
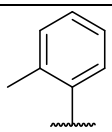
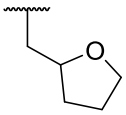
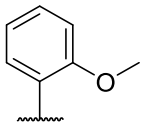
2172352	H		H			
647803	H		H			
2171942	H		H			
758229						
1515332	H		H			

1313404	H		H			
742390						
2265768						
40672						
649789	H		H			
2221501	H		H			
2055736	H		H			
2172338	H		H			

1368638						
2172337	H		H			
610962	H		H			
743917						
2906112	H		H			
616915	H		H			
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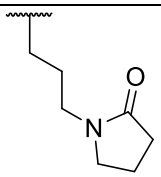
653593	H		H			
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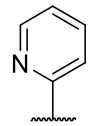
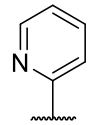
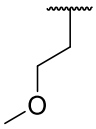
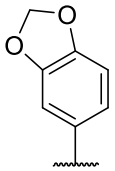
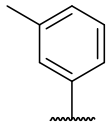
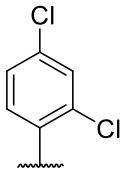
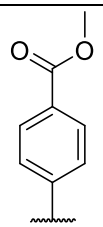
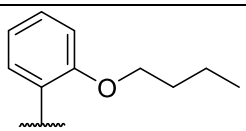
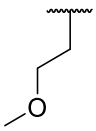
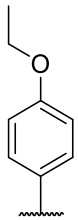
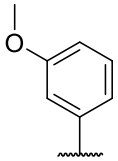
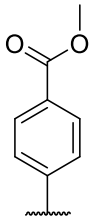
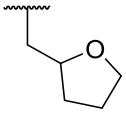
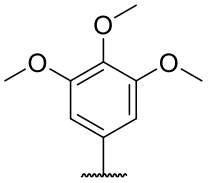
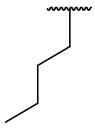
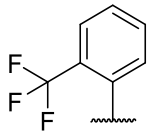
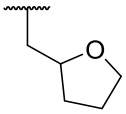
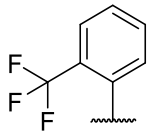
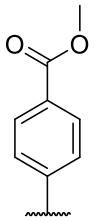
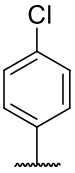
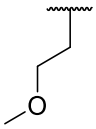
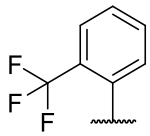
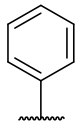
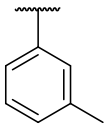
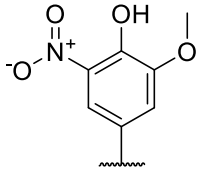
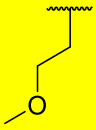
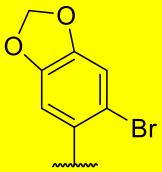
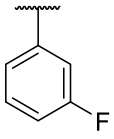
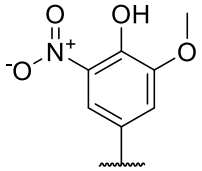
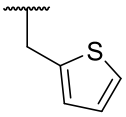
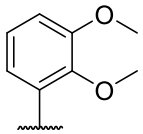
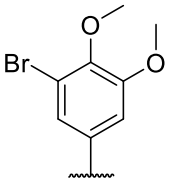
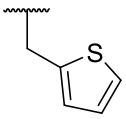
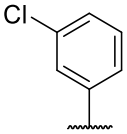
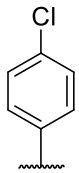
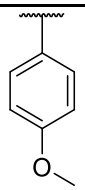
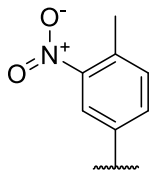
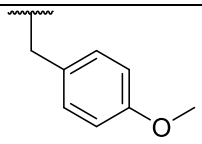
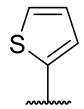
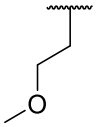
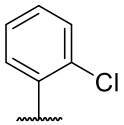
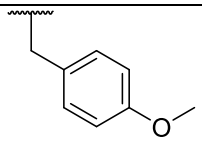
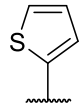
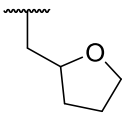
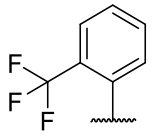
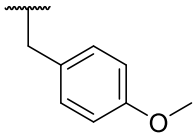
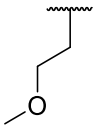
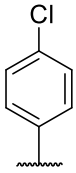
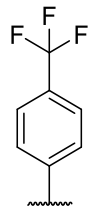
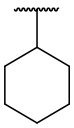
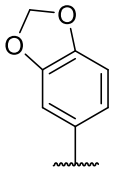
674186						
714587						
2052813	H		H			
614266	H		H			
1336353	H		H			
1087398						
617111						
2291187	H		H			

775764	H		H			
616871	H		H			
644677	H		H			
2195084	H		H			
2936404	H		H			
1043709						
625873						
2168053	H		H			

623049						
1294819	H		H			
2052819	H		H			
2233519	H		H			
1043689	H		H			
3684684	H		H			
2936351	H		H			
325406						

1297295	H		H			
1073334	H		H			
2169339	H		H			
2172353	H		H			
2976701	H		H			
1073346	H		H			
2052604	H		H			
1073796	H		H			

1094573	H		H			
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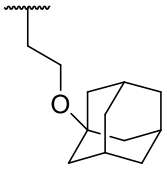
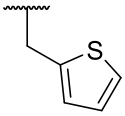
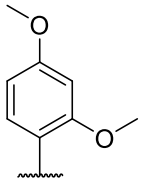
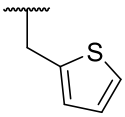
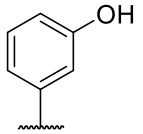
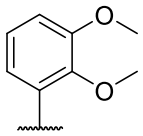
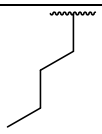
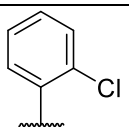
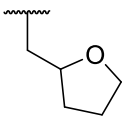
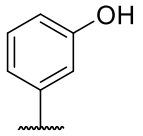
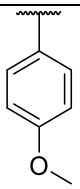
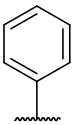
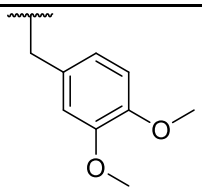
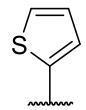
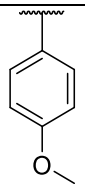
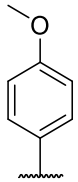
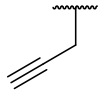
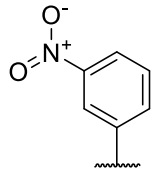
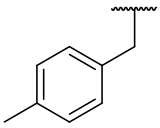
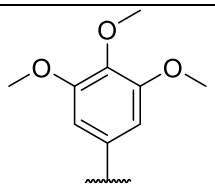
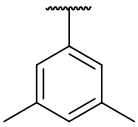
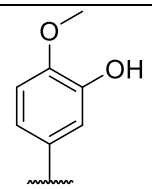
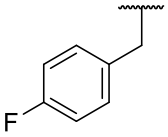
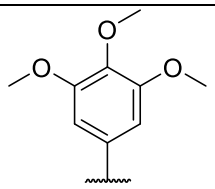
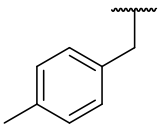
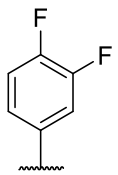
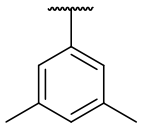
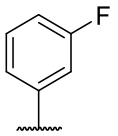
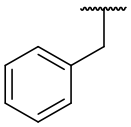
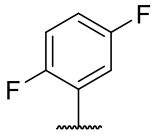
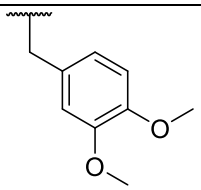
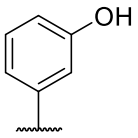
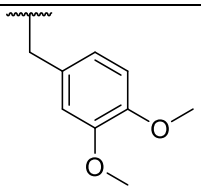
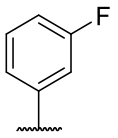
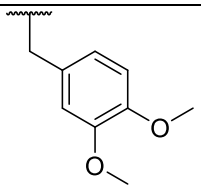
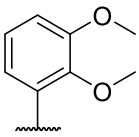
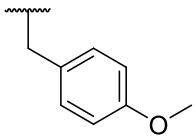
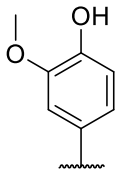
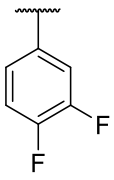
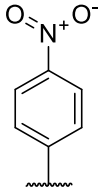
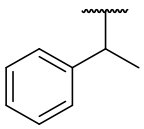
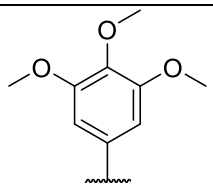
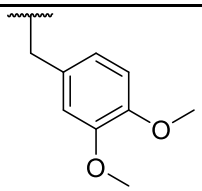
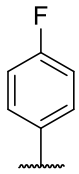
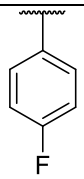
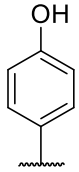
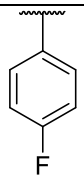
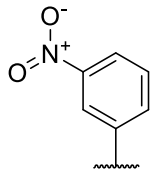
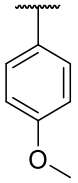
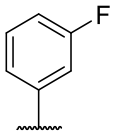
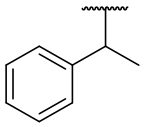
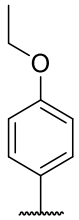
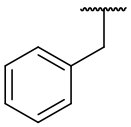
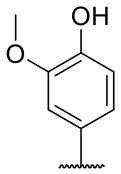
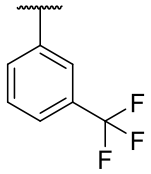
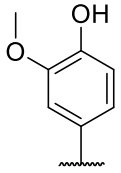
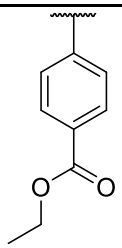
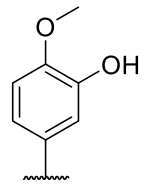
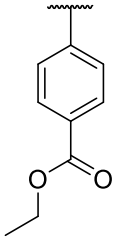
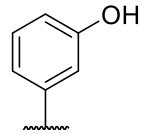
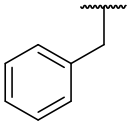
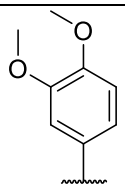
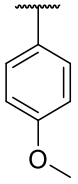
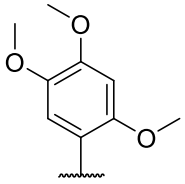
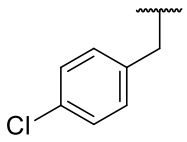
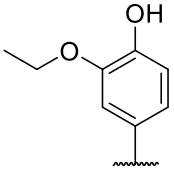
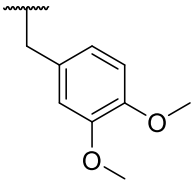
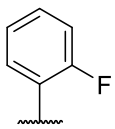
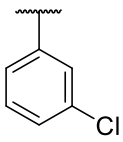
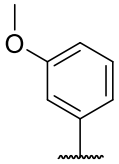
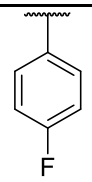
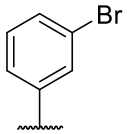
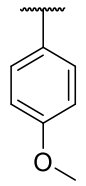
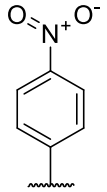
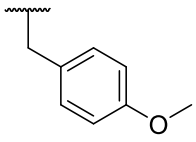
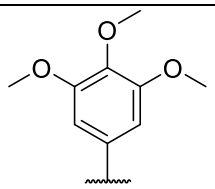
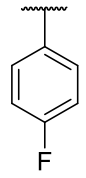
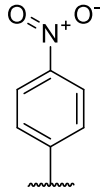
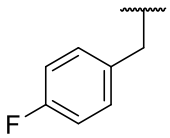
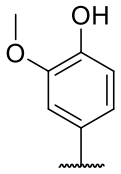
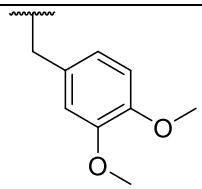
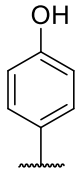
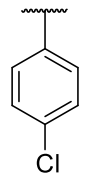
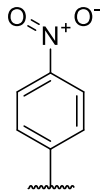
5131501	H		H			
1158246	H		H			
2233288	H		H			
1336608	H		H			
2194667	H		H			
2917066	H		H			
1547954						

1272579	H		H			
1357611						
11538542						
1073338	H		H			
1294867	H		H			
1073328	H		H			
3692778	H		H			

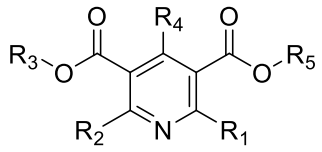
1298163	H		H			
1336676	H		H			
1050959	H		H			
1094423	H		H			
1201780	H		H			
3158412	H		H			
1313969	H		H			
2897978	H		H			

1094429	H		H			
1261225	H		H			
1322301	H		H			
1094572	H		H			
2898344	H		H			
1094619	H		H			
1262626	H		H			

1202534	H		H			
1262617	H		H			
1073349	H		H			
1295422	H		H			
1531944	H		H			
1094686	H		H			
1295694	H		H			

1295301	H		H			
1298115	H		H			
1349549	H		H			
1296864	H		H			
1094770	H		H			
1094685	H		H			
1296921	H		H			

Appendix Table 6c. A list of compounds for a secondary scaffold in the dihydropyridines library that was screened in ≥100 bioassays



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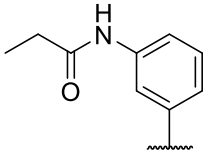
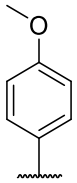
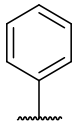
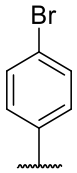
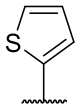
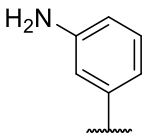
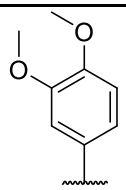
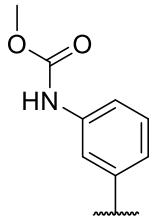
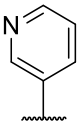
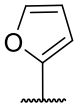
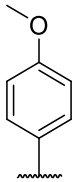
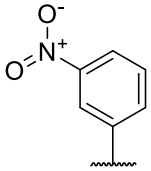
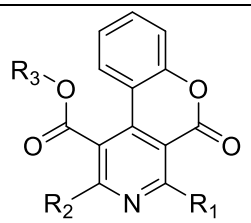
CID	R_1	R_2	R_3	R_4	R_5
1519307					
226671					
629929					
1547825					
714649					
2229373					

632200					
1511235					
323487					
684250					
2739835					
2739782					
282662					

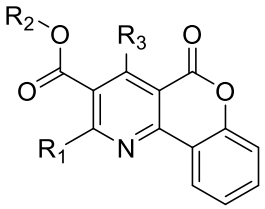
Appendix Table 6d. A list of compounds for a secondary scaffold in the dihydropyridines library that was screened in ≥100 bioassays



17

CID	R_1	R_2	R_3
721596			
1508705			

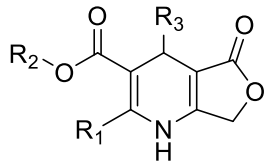
Appendix Table 6d. A list of a secondary scaffold in the dihydropyridines library that was screened in ≥100 bioassays



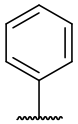
18

CID	R_1	R_2	R_3
766691			

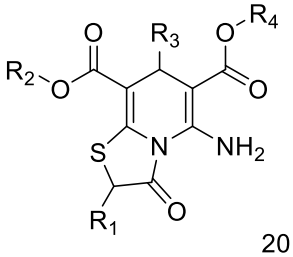
Appendix Table 6e. A list of a secondary scaffold in the dihydropyridines library that was screened in ≥100 bioassays



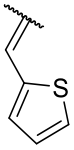
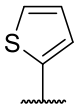
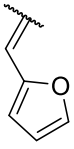
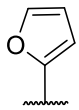
19

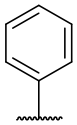
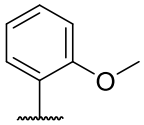
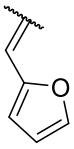
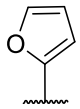
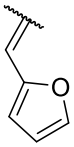
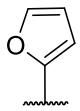
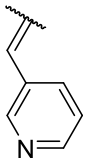
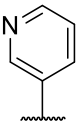
CID	R_1	R_2	R_3
4621225			

Appendix Table 6f. A list of compounds for a secondary scaffold in the dihydropyridines library that was screened in ≥100 bioassays



20

CID	R_1	R_2	R_3	R_4
5863694				
16410242				

2968682				
2966579				
660793	H		H	
5940036				
5917962				
5789170				
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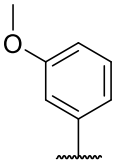
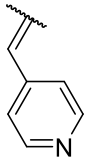
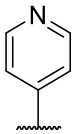
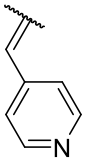
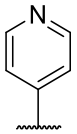
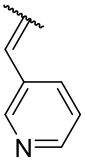
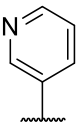
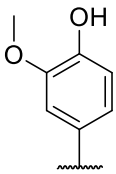
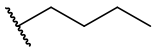
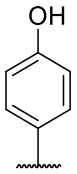
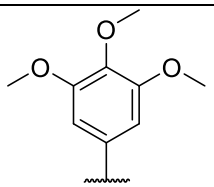
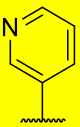
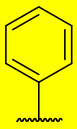
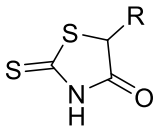
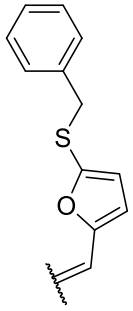
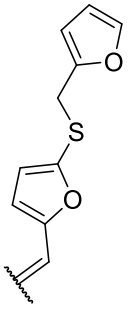
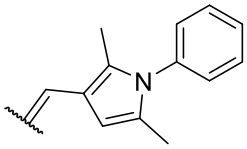
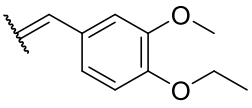
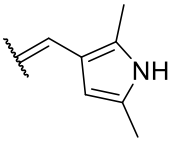
4587577				
5761865				

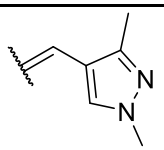
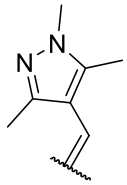
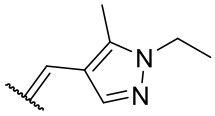
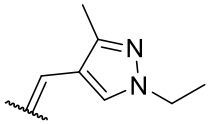
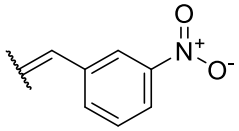
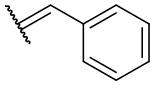
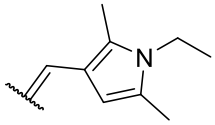
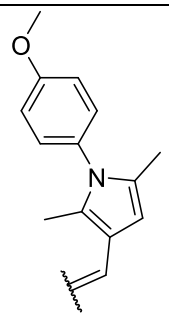
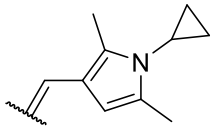
5929786				
5929103				
5189086				
3487882				
2969954				
5939372				
5702971				
5783507				

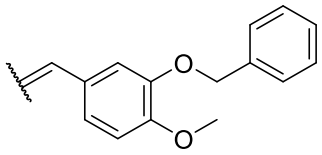
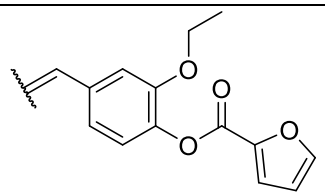
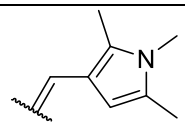
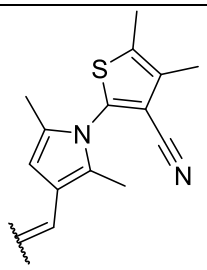
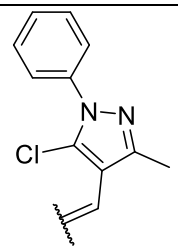
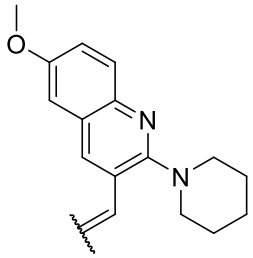
Appendix Table 7. A list of the compounds in the rhodanine scaffold library that was screened in ≥100 bioassays

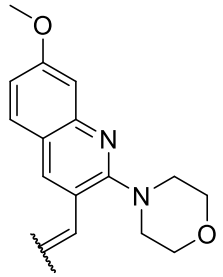
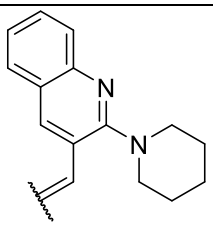
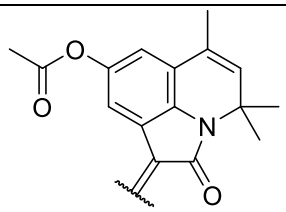
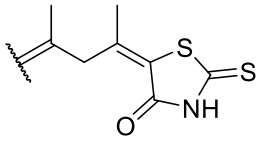
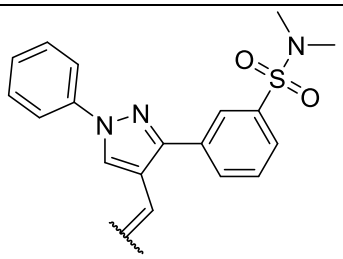
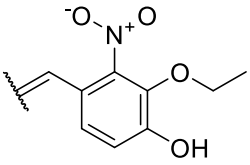


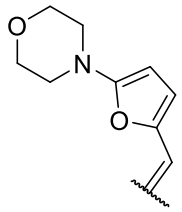
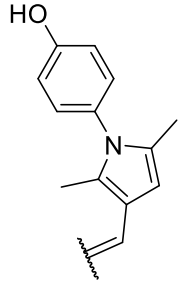
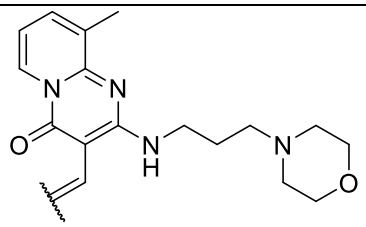
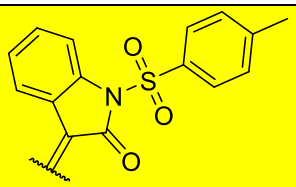
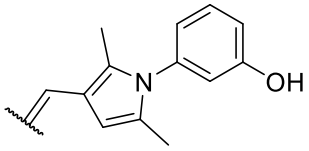
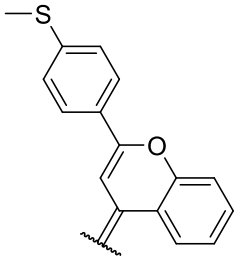
8

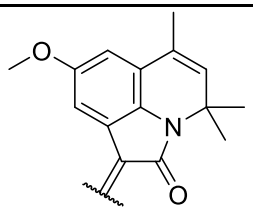
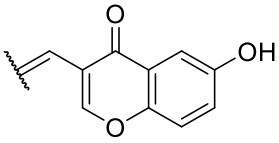
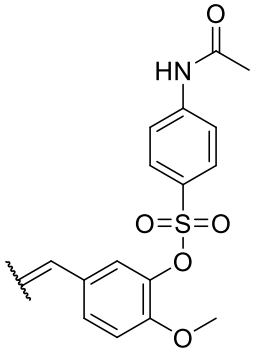
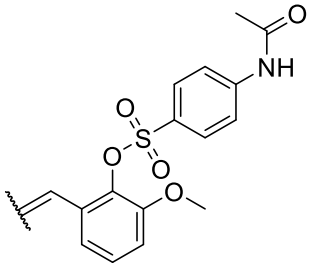
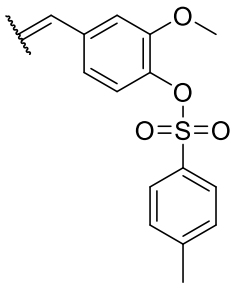
CID	R
12004907	
12005023	
1201546	H
1201959	
1205767	
1206896	

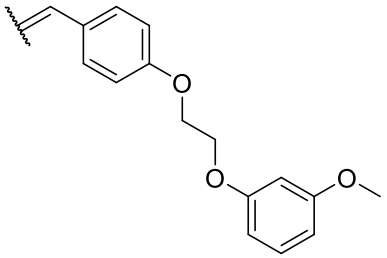
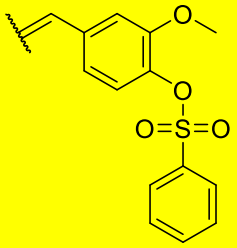
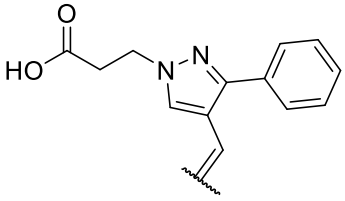
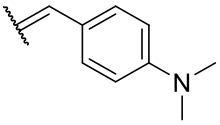
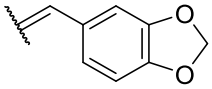
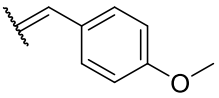
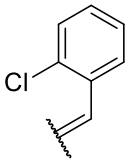
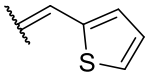
1235243	
1236046	
1236050	
1237580	
1241127	
1273210	
1309706	
1329072	
1331044	

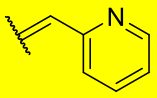
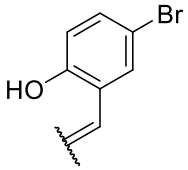
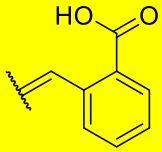
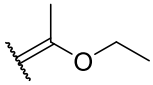
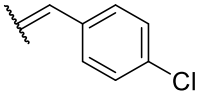
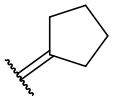
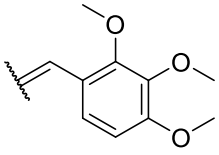
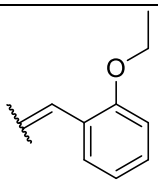
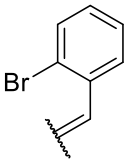
1350270	
1367790	
1370241	
1370249	
1381466	
1385343	

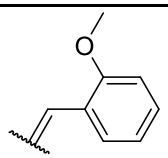
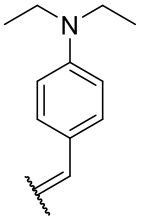
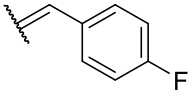
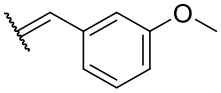
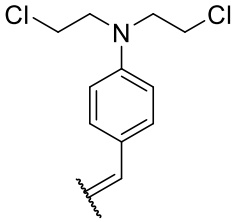
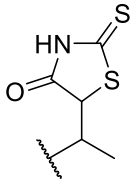
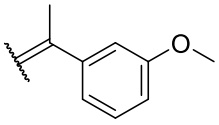
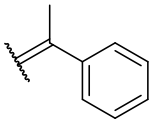
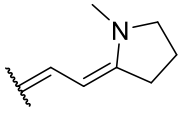
1388377	
1420281	
1613528	
16195300	
1624667	
1742917	

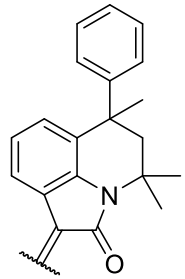
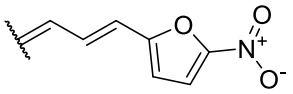
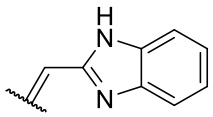
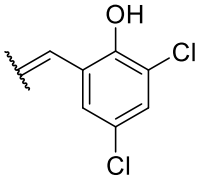
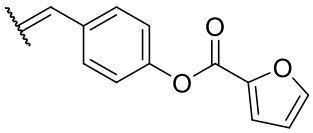
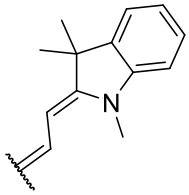
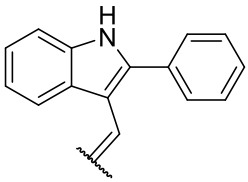
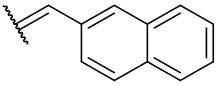
1849004	
1855553	
1863779	
1922475	
1960206	
1962679	

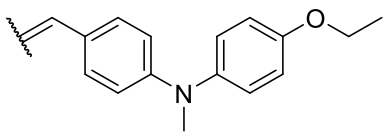
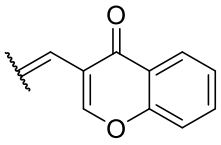
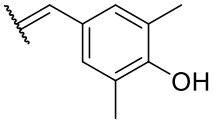
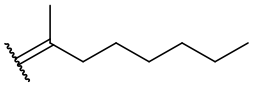
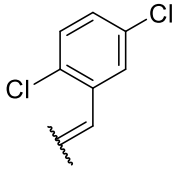
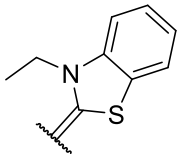
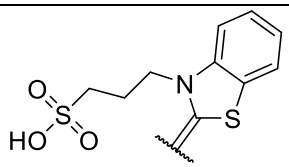
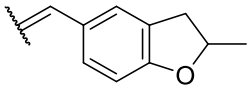
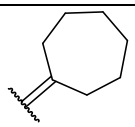
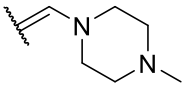
2000865	
2030134	
2163119	
2175545	
2268032	

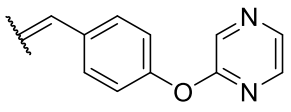
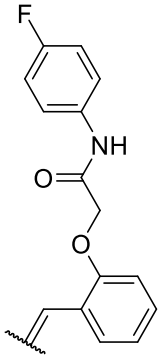
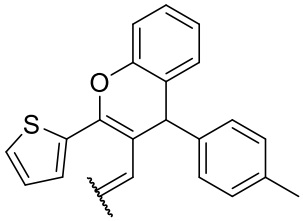
2272421	
2272534	
2387166	
2723826	
2785114	
2787034	
2787053	
2796945	

2796946	
2796949	
2826383	
2826563	
2830585	
2844976	
2848355	
2859659	
2864576	

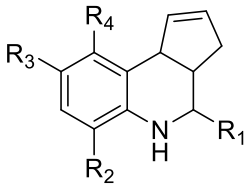
3004477	
3034543	
3034572	
3095430	
4302151	
5042127	
5151023	
5178496	
5292926	

5293996	
5335985	
5585899	
5712384	
5751473	
5756549	
5756550	
5757257	

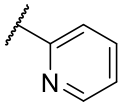
5767616	
5913361	
5953071	
6007691	
6243032	
6300280	
6398921	
6532825	
659551	
664780	

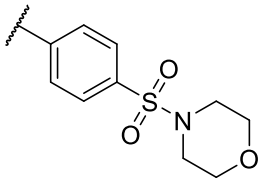
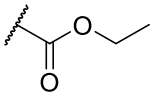
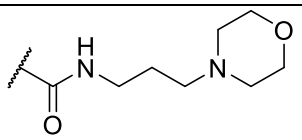
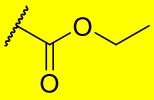
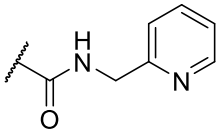
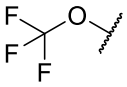
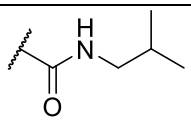
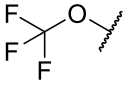
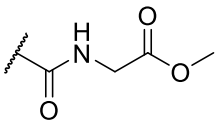
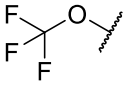
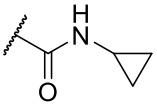
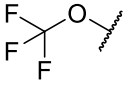
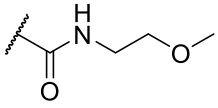
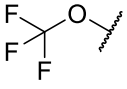
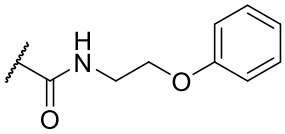
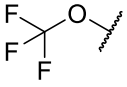
7101311	
7185334	
9551861	

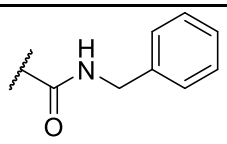
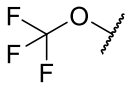
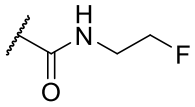
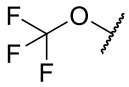
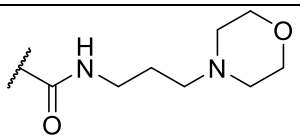
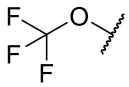
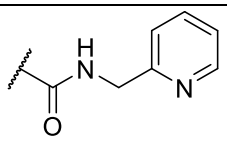
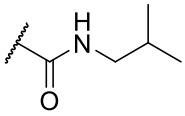
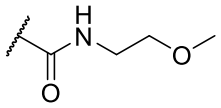
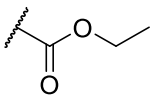
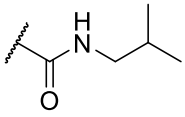
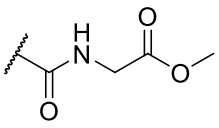
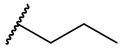
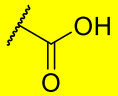
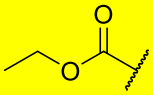
Appendix Table 8a. A list of compounds for the primary scaffold in the quinolines library that was screened in ≥100 bioassays

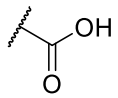
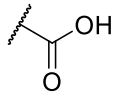
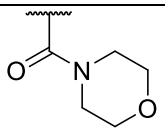
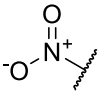


7

CID	R_1	R_2	R_3	R_4
1203912		H		H

15945793		Cl		H
16738614		H		H
16738622		H		H
16738628		F		H
16738630		H		H
16738632		H		H
16738633		H		H
16738634		H		H
16738635		H		H
16738636		H		H

16738638		H		H
16738640		H		H
16738641		H		H
16738647		H		H
16738649		H		H
16738651		H		H
16738654		H		H
16738663		H	H	H
16738667		H	H	H
2839743		H		H
2859888		H		H

2865731		Cl	Cl	H
2872045			H	H
2873402	H			H
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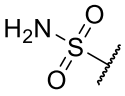
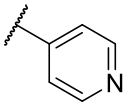
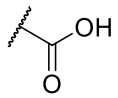
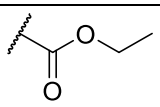
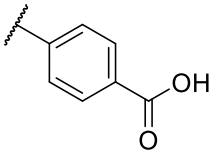
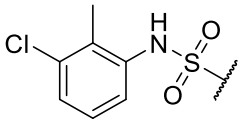
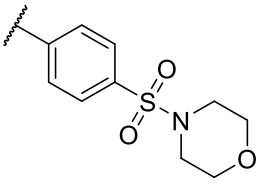
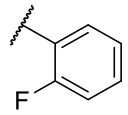
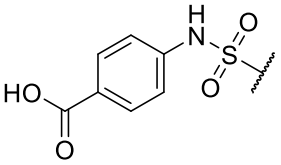
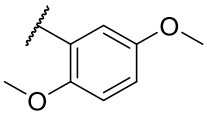
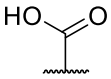
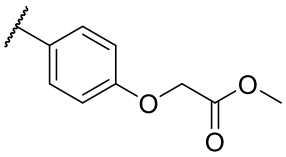
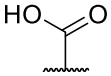
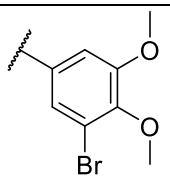
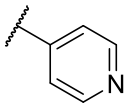
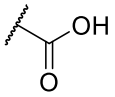
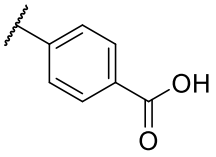
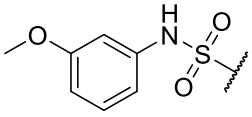
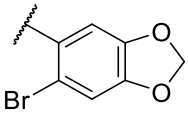
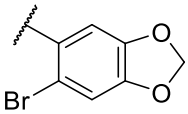
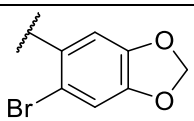
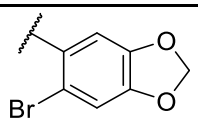
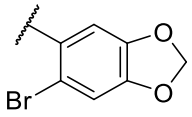
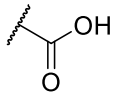
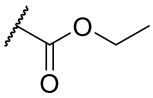
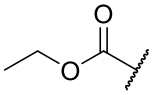
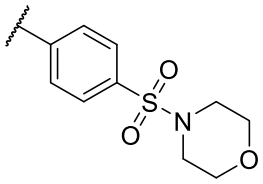
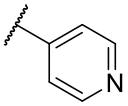
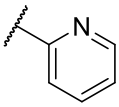
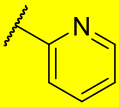
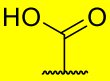
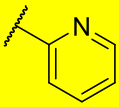
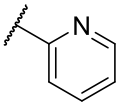
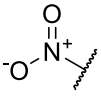
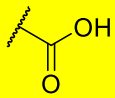
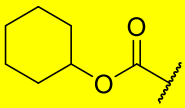
2874832		H		H
2947620		H		H
2975102		Cl	Cl	Cl
2975117		H	Br	H
2975144		H		H
2975162				H

2978460		H		H
2980797		Cl	H	
2982494		Cl	H	
2984654		F	H	H
3136296		H		H
3136298		H		H
3136304		H		H
3136748		H		H
3136783		H	F	H
3136844		H	H	H

3136846		H		H
3136849		H		H
3136927		H	Br	H
3136931		H		H
3145169		H		H
3154276		H		H
3154395		Cl	H	
3154407		Cl	H	
3154424				
3154430				H
3243550		H		H

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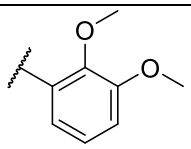
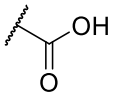
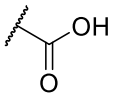
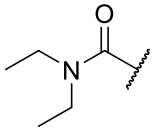
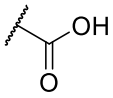
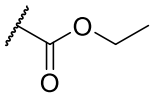
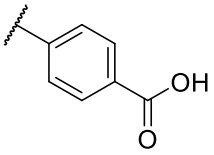
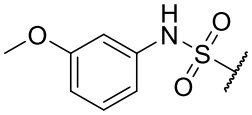
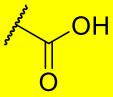
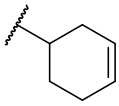
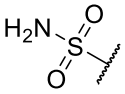
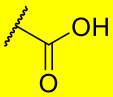
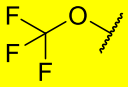
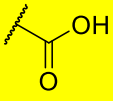
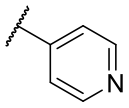
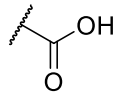
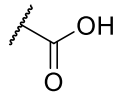
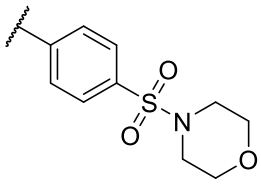
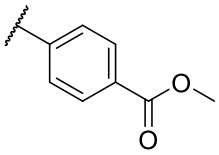
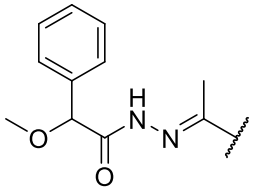
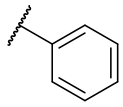
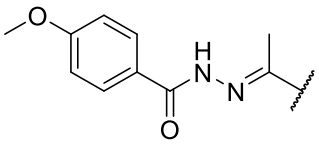
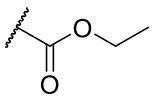
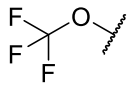
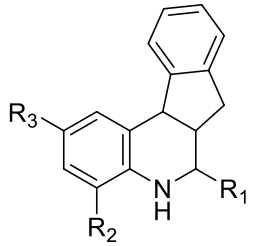
3437213		F	Br	H
3453217		OH	Cl	
3797563		H		H
3845516			H	Cl
3850620		H		H
5322407		H		H
617227			H	H
619328		H		H
620366		H		H
646096		H		H

647392		H	H	H
652912			H	H
654089		OH	H	H
7349533				H
9594283		H		H
9594287		H		H
9973697		H		H

Appendix Table 8b. A list of compounds for a secondary scaffold in the quinolines library that was screened in ≥100 bioassays



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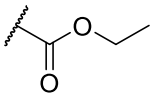
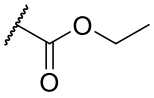
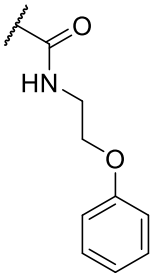
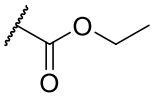
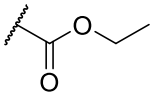
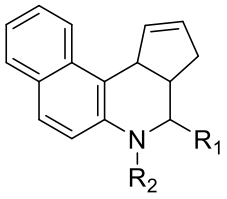
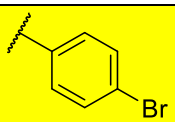
CID	R_1	R_2	R_3
16738615		F	
16738637		H	
16738642		H	
16738659			
495051		H	H

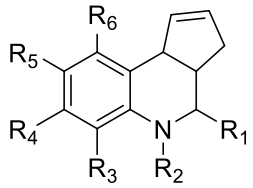
Appendix Table 8c. A list of a secondary scaffold in the quinolines library that was screened in ≥100 bioassays



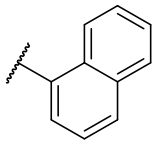
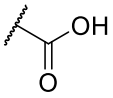
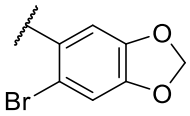
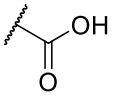
22

CID	R_1	R_2
2882083		

Appendix Table 8d. A list of compounds for a secondary scaffold in the quinolines library that was screened in ≥100 bioassays



23

CID	R_1	R_2	R_3	R_4	R_5	R_6
2882119			H	H	Cl	H
3125599		H	H		H	
3136845		H	H		H	
646406		H			H	H

NB:

- Yollow colored boxes refer to compounds that were excluded after filtering.
- CIDs followed by ± are compounds with different enantiomeric forms.

Appendix Table 9. A list of the shared bioassays; 223 bioassays.

AID	Bioassay
2690	A yeast HTS for caloric restriction mimetics that inhibit age-related superoxide
2805	uHTS Luminescent assay for identification of activators of mouse intestinal alkaline phosphatase
2806	uHTS Luminescent assay for identification of inhibitors of mouse intestinal alkaline phosphatase
434973	uHTS Luminescent assay for identification of inhibitors of Sentrin-specific protease 7 (SENP7)
434989	Fluorescence-based cell-based primary high throughput screening assay to identify antagonists of the orexin 1 receptor (OX1R; HCRTR1)
435022	uHTS luminescence assay for the identification of chemical inhibitors of B-cell specific antigen receptor-induced NF-kB activation
435030	Absorbance-based primary bacterial cell-based high throughput screening assay to identify inhibitors of AddAB recombination protein complex
449763	uHTS identification of small molecule activators of the apoptotic arm of the Unfolded Protein response via a luminescent-based reporter assay
463079	Fluorescence-based counterscreen for orexin 1 receptor (OX1R) antagonists: cell-based assay to identify antagonists of the parental CHO cell line
463082	Fluorescence polarization-based primary biochemical high throughput screening assay to identify inhibitors of the plasma platelet activating factor acetylhydrolase (pPAFAH)
463104	uHTS identification of small molecule activators of the adaptive arm of the Unfolded Protein response via a luminescent-based reporter assay
463141	Absorbance-based primary biochemical high throughput screening assay to identify activators of procaspase-3

463190	uHTS identification of small molecule inhibitors of tim10-1 yeast via a luminescent assay
463195	uHTS identification of small molecule inhibitors of tim10 yeast via a luminescent assay
463212	uHTS identification of small molecule inhibitors of tim23-1 yeast via a luminescent assay
463254	qHTS Assay for Inhibitors of Ubiquitin-specific Protease USP2a Using CHOP2 as the Reporter
485272	Fluorescence polarization-based primary biochemical high throughput screening assay to identify inhibitors of Protein Arginine Deiminase 4 (PAD4) (1536 HTS)
485275	Phenotypic HTS multiplex for antifungal efflux pump inhibitors
485290	qHTS Assay for Inhibitors of Tyrosyl-DNA Phosphodiesterase (TDP1)
485341	qHTS Inhibitors of AmpC Beta-Lactamase (assay without detergent)
485346	uHTS for identification of Inhibitors of Mdm2/MdmX interaction in luminescent format.
485349	qHTS Assay for Identifying a Potential Treatment of Ataxia-Telangiectasia
485353	qHTS of Yeast-based Assay for SARS-CoV PLP
485367	qHTS Assay to Find Inhibitors of T. brucei phosphofructokinase
488837	qHTS Assay for Inhibitors of the Phosphatase Activity of Eya2
488839	Development of CDK5 inhibitors Measured in Biochemical System Using Plate Reader - 2083-01_Inhibitor_SinglePoint_HTS_Activity
488847	RNA aptamer-based HTS for inhibitors of GRK2
488862	Inhibitors of Prion Protein 5' UTR mRNA Measured in Cell-Based System Using Plate Reader - 2078-01_Inhibitor_SinglePoint_HTS_Activity
488895	High Throughput Screen for Tat Transport Inhibitors Measured in Microorganism System Using Plate Reader - 2093-

	01_Inhibitor_SinglePoint_HTS_Activity
488896	HTS using DiI-HDL to assay lipid transfer in ldlA[SR-BI] cells Measured in Cell-Based System Using Plate Reader - 2085-01_Inhibitor_SinglePoint_HTS_Activity
488899	MITF Measured in Cell-Based System Using Plate Reader - 2084-01_Inhibitor_SinglePoint_HTS_Activity
488965	Fluorescent Biochemical Primary HTS to Identify Inhibitors of P. aeruginosa PvdQ acylase Measured in Biochemical System Using Plate Reader and Imaging Combination - 2091-01_Inhibitor_SinglePoint_HTS_Activity
488966	Primary and Confirmatory Screening for Inhibitors of Bacterial Capsule Biogenesis
489030	uHTS Fluorescent assay for identification of inhibitors of Apaf-1
489031	uHTS Fluorescent assay for identification of activators of Apaf-1
492947	qHTS assay of beta-arrestin-biased ligands of beta2-adrenergic receptor
492953	Fluorescence polarization-based primary biochemical high throughput screening assay to identify inhibitors of human platelet-activating factor acetylhydrolase 1b, catalytic subunit 2 (PAFAH1B2)
492956	Fluorescence polarization-based primary biochemical high throughput screening assay to identify inhibitors of human platelet activating factor acetylhydrolase 2 (PAFAH2)
492972	Fluorescence polarization-based primary biochemical high throughput screening assay to identify inhibitors of human platelet-activating factor acetylhydrolase 1B, catalytic subunit 3 (PAFAH1B3)
493005	qHTS Assay for Iinhibitors of HIV-1 Budding by Blocking the Interaction of PTAP/TSG101
493008	Fluorescence-based biochemical primary high throughput screening assay to identify activators of the calcium sensitivity of cardiac Regulated Thin Filaments (RTF)
493011	uHTS identification of APOBEC3A DNA Deaminase Inhibitors via a fluorescence-based single-stranded DNA deaminase assay

493012	uHTS identification of APOBEC3G DNA Deaminase Inhibitors via a fluorescence-based single-stranded DNA deaminase assay
493014	qHTS Assay to Find Inhibitors of Chronic Active B-Cell Receptor Signaling
493036	Image-Based HTS for Selective Agonists for NTR1
493087	Fluorescence polarization-based cell-based primary high throughput screening assay to identify activators of insulin-degrading enzyme (IDE)
493091	uHTS Colorimetric assay for identification of inhibitors of Scp-1
493098	uHTS identification of small molecule antagonists of the CCR6 receptor via a luminescent beta-arrestin assay
493131	Activator for delta FosB/delta FosB homodimer Measured in Biochemical System Using Plate Reader - 2072-01_Activator_SinglePoint_HTS_Activity
493160	uHTS Fluorescent assay for identification of inhibitors of hexokinase domain containing I (HKDC1)
493187	uHTS Fluorescent assay for identification of activators of hexokinase domain containing I (HKDC1)
493244	Fluorescence-based biochemical primary high throughput screening assay to identify inhibitors of the calcium sensitivity of cardiac Regulated Thin Filaments (RTF)
504326	Luminescence-based cell-based primary high throughput screening assay to identify agonists of heterodimerization of the mu 1 (OPRM1) and delta 1 (OPRD1) opioid receptors
504327	qHTS Assay for Inhibitors of GCN5L2
504329	Discovery of Small Molecule Probes for H1N1 Influenza NS1A
504339	qHTS Assay for Inhibitors of JMJD2A-Tudor Domain
504357	Luminescence-based cell-based primary high throughput screening assay to identify inverse agonists of heterodimerization of the mu 1 (OPRM1) and delta 1 (OPRD1) opioid receptors

504411	Fluorescence-based primary biochemical high throughput screening assay to identify inhibitors of human diacylglycerol lipase, beta (DAGLB)
504423	C-LANA FP assay Measured in Biochemical System Using Plate Reader - 2117-01_Inhibitor_SinglePoint_HTS_Activity
504441	Dyrk1 A HTS Measured in Biochemical System Using Plate Reader - 2124-01_Inhibitor_SinglePoint_HTS_Activity
504444	Nrf2 qHTS screen for inhibitors
504454	HTS for Beta-2AR agonists via FAP method
504462	uHTS fluorescent assay for identification of inhibitors of ATG4B
504466	qHTS screen for small molecules that induce genotoxicity in human embryonic kidney (HEK293T) cells expressing luciferase-tagged ELG1
504467	qHTS screen for small molecules that inhibit ELG1-dependent DNA repair in human embryonic kidney (HEK293T) cells expressing luciferase-tagged ELG1
504490	Assay for Inhibitors of the beta-Arrestin-Adaptor Protein 2 Interaction That Mediate GPCR Degradation and Recycling
504523	Fluorescence polarization to screen for inhibitors that disrupt the protein-protein interaction between Keap1 and Nrf2 Measured in Biochemical System Using Plate Reader - 2119-01_Inhibitor_SinglePoint_HTS_Activity
504558	Inhibitors of Epstein-Barr LMP1 inducible NF-kappaB luciferase reporter Measured in Cell-Based System Using Plate Reader - 2122-01_Inhibitor_SinglePoint_HTS_Activity
504577	HTS of Small Molecules that Regulate V-ATPase Proton Transport in Yeast using pHLuorin
504582	In vivo-based yeast HTS to detect compounds rescuing yeast growth/survival of Plasmodium Falciparum HSP40-mediated toxicity Measured in Whole Organism System Using Plate Reader - 2120-01_Inhibitor_SinglePoint_HTS_Activity
504621	Anti-Malarial Hsp90 Inhibitors Measured in Microorganism System

	Using Plate Reader - 2121-01_Inhibitor_SinglePoint_HTS_Activity_Set2
504634	Counterscreen for inverse agonists of OPRM1-OPRD1 heterodimerization: luminescence-based cell-based full-deck high throughput screening assay to identify inverse agonists of 5-hydroxytryptamine (serotonin) 5A receptor (HTR5A)
504690	uHTS identification of small molecule inhibitors of Plasmodium falciparum Glucose-6-phosphate dehydrogenase via a fluorescence intensity assay
504692	Counterscreen for agonists of OPRM1-OPRD1 heterodimerization: luminescence-based cell-based full-deck high throughput screening assay to identify agonists of 5-hydroxytryptamine (serotonin) 5A receptor (HTR5A)
504700	Fluorescence polarization-based biochemical primary high throughput screening assay to identify activators of the Protein Kinase A-R2B (PKA-R2B) complex
504706	qHTS assay for re-activators of p53 using a Luc reporter
504707	Fluorescence polarization-based biochemical primary high throughput screening assay to identify activators of the Protein Kinase A-R1A (PKA-R1A) complex
504720	uHTS identification of MazEF TA System activators via a fluorescence-based single-stranded RNase assay
504734	Fluorescence-based cell-based primary high throughput screening assay to identify inhibitors of TLR9-MyD88 binding.
504766	Luminescence-based primary cell-based high throughput screening assay to identify inhibitors of the orphan nuclear receptor subfamily 0, group B, member 1 (DAX1; NR0B1)
504775	HTS using DiI-HDL to assay lipid transfer in ldlA[SR-BI] cells Measured in Cell-Based System Using Plate Reader - 2085-01_Activator_SinglePoint_HTS_Activity
504803	Fluorescence polarization-based primary biochemical high throughput screening assay to identify inhibitors of the HTRA serine peptidase 1

	(HTRA1)
504810	Antagonists of the Thyroid Stimulating Hormone Receptor: HTS campaign
504812	Inverse Agonists of the Thyroid Stimulating Hormone Receptor: HTS campaign
504842	Inhibitors of TCP-1 ring complex (TRiC) of Methanococcus maripaludis (MmCpn): qHTS
504845	Inhibitors of Regulator of G Protein Signaling (RGS) 4: qHTS
504847	Inhibitors of the vitamin D receptor (VDR): qHTS
504884	Inhibitors of Y. pestis Topo-I using cleavage product accumulation Measured in Biochemical System Using Plate Reader - 2123-01_Inhibitor_SinglePoint_HTS_Activity
504891	qHTS Assay to Find Inhibitors of Pin1
504894	Activators of T cell receptors: qHTS campaign
540253	qHTS Assay for Inhibitors of RanGTP induced Rango (Ran-regulated importin-beta cargo) - Importin beta complex dissociation
540263	qHTS Assay for Inhibitors of Rango (Ran-regulated importin-beta cargo) - Importin beta complex formation
540267	Small Molecules that selectively kill Giardia lamblia: qHTS
540295	TRFRET-based cell-based primary high throughput screening assay to identify biased ligands of the melanocortin 4 receptor (MC4R): antagonists of MC4R
540303	qHTS for Inhibitors of Cell Surface uPA Generation
540308	Luminescence-based cell-based primary high throughput screening assay to identify biased ligands of the melanocortin 4 receptor (MC4R): agonists of MC4R
540317	HTS for Inhibitors of HP1-beta Chromodomain Interactions with Methylated Histone Tails

540336	Rtt109/Vps75 Measured in Biochemical System Using Plate Reader - 2106-01_Inhibitor_SinglePoint_HTS_Activity
540364	Luminescence-based cell-based primary high throughput screening assay to identify activators of the GAA850 frataxin (FXN) promoter
588334	MITF Measured in Cell-Based System Using Plate Reader - 2084-01_Activator_SinglePoint_HTS_Activity
588335	Counterscreen for inhibitors of the fructose-bisphosphate aldolase (FBA) of M. tuberculosis: Absorbance-based biochemical high throughput Glycerophosphate Dehydrogenase-Triosephosphate Isomerase (GDH-TPI) full deck assay to identify assay artifacts
588352	Luminescence-based cell-based primary high throughput screening assay to identify inhibitors of the Steroid Receptor Coactivator 3 (SRC3; NCOA3)
588354	Luminescence-based cell-based primary high throughput screening assay to identify inhibitors of the Steroid Receptor Coactivator 1 (SRC1; NCOA1)
588358	HTS to Find Inhibitors of Pathogenic Pemphigus Antibodies
588391	Turbidometric Biochemical Primary HTS to identify inhibitors of Protein Disulfide Isomerase Measured in Biochemical System Using Plate Reader - 2137-01_Inhibitor_SinglePoint_HTS_Activity
588405	HTS Assay for Peg3 Promoter Inhibitors
588413	uHTS identification of Gli-Sufu Antagonists in a luminescence reporter assay
588436	Cholera Quorum: HTS for inducers of light production in the absence ofautoinducers using BH1578 (luxS deficient, cqsA deficient) Measured in Microorganism System Using Plate Reader - 2132-01_Agonist_SinglePoint_HTS_Activity
588453	qHTS Assay for Inhibitors of Mammalian Selenoprotein Thioredoxin Reductase 1 (TrxR1): qHTS
588456	qHTS Assay for Substrates of Mammalian Selenoprotein Thioredoxin Reductase 1 (TrxR1): qHTS

588458	uHTS identification of DNMT1 inhibitors in a Fluorescent Molecular Beacon assay
588473	uHTS identification of agonists of the CRF-binding protein and CRF-R2 receptor complex
588475	uHTS identification of antagonists of the CRF-binding protein and CRF-R2 receptor complex
588478	A screen for small molecule inhibitors of the human deubiquitinating enzyme, UCH37
588489	uHTS identification of microRNA-mediated mRNA deadenylation inhibitors by fluoresence polarization assay
588492	uHTS identification of small molecule modulators of myocardial damage
588493	uHTS identification of inhibitors of Rpn11 in a Fluorescent Polarization assay
588497	High-throughput multiplex microsphere screening for inhibitors of toxin protease, specifically Botulinum neurotoxin light chain F protease, MLPCN compound set
588499	High-throughput multiplex microsphere screening for inhibitors of toxin protease, specifically Botulinum neurotoxin light chain A protease, MLPCN compound set
588501	High-throughput multiplex microsphere screening for inhibitors of toxin protease, specifically Lethal Factor Protease, MLPCN compound set
588549	Fluorescence polarization to screen for inhibitor that competite the binding of FadD28 to bisubstrate Measured in Biochemical System Using Plate Reader - 2147-01_Inhibitor_SinglePoint_HTS_Activity
588579	qHTS for Inhibitors of Polymerase Kappa
588590	qHTS for Inhibitors of Polymerase Iota
588591	qHTS for Inhibitors of Polymerase Eta
588621	uHTS identification of small molecule inhibitors of Striatal-Enriched

	Phosphatase via a fluorescence intensity assay
588664	TRFRET-based biochemical primary high throughput screening assay to identify inhibitors of the interaction of the Ras and Rab interactor 1 protein (Rin1) and the c-abl oncogene 1, non-receptor tyrosine kinase (Abl)
588674	Schnurri-3 Inhibitors: specific inducers of adult bone formation Measured in Cell-Based System Using Plate Reader - 2134-01_Inhibitor_SinglePoint_HTS_Activity_Set2
588689	Primary and Confirmatory Screening for Flavivirus Genomic Capping Enzyme Inhibition
588692	Luciferase Reporter Cell Based HTS to identify inhibitors of N-linked Glycosylation Measured in Cell-Based System Using Plate Reader - 2146-01_Inhibitor_SinglePoint_HTS_Activity_Set2
588727	A Cell-Based Confirmatory Screen for Compounds that Inhibit VEEV, TC-83
588795	qHTS Assay for the Inhibitors of Human Flap endonuclease 1 (FEN1).
588814	Fluorescence-based cell-based primary high throughput screening assay to identify agonists of the human cholinergic receptor, muscarinic 1 (CHRM1)
588819	Fluorescence-based cell-based primary high throughput screening assay to identify positive allosteric modulators (PAMs) of the human M1 muscarinic receptor (CHRM1).
588852	Fluorescence-based cell-based primary high throughput screening assay to identify antagonists of the human M1 muscarinic receptor (CHRM1)
588855	qHTS for Inhibitors of TGF-b
602123	Fluorescence polarization-based primary biochemical high throughput screening assay to identify inhibitors of Escherichia coli DNA-binding ATP-dependent protease La (eLon)
602141	uHTS determination of small molecule cytotoxicity in a fluorescence assay to identify cystic fibrosis induced NFkb Inhibitors
602162	Flow Cytometric HTS Screen for inhibitors of the ABC transporter

	ABCB6 for MLPCN Compound Set
602163	Absorbance-based biochemical primary high throughput screening assay to identify activators of Methionine sulfoxide reductase A (MsrA)
602179	qHTS for Inhibitors of mutant isocitrate dehydrogenase 1 (IDH1): qHTS
602229	Luminescence-based cell-based high throughput primary screening assay to identify agonists of nuclear receptor subfamily 2, group E, member 3 (NR2E3)
602233	qHTS Assay to Find Inhibitors of Phosphoglycerate Kinase
602244	uHTS identification of CXCR6 Inhibitors in a B-arrestin luminescence assay
602247	Full deck counterscreen for positive allosteric modulators (PAMs) of the human M1 muscarinic receptor (CHRM1): Fluorescence-based cell-based high throughput screening assay to identify nonselective activators and assay artifacts using the parental CHOK1 cell line
602248	Full deck counterscreen for agonists of the human M1 muscarinic receptor (CHRM1): Fluorescence-based cell-based high throughput screening assay to identify nonselective activators and assay artifacts using the parental CHOK1 cell line
602250	Full deck counterscreen for antagonists of the human M1 muscarinic receptor (CHRM1): Fluorescence-based cell-based high throughput screening assay to identify nonselective inhibitors and assay artifacts using the parental CHOK1 cell line
602252	Fluorescence Polarization with CAL-PDZ Measured in Biochemical System Using Plate Reader - 2109-02_Inhibitor_SinglePoint_HTS_Activity
602261	uHTS identification of small molecule inhibitors of the thioesterase domain of fatty acid synthase via a fluorescence intensity assay
602274	uHTS luminescent assay for identification of compounds that enhance the survival of human induced pluripotent stem cells when cultured as single cells

602281	Luminescence-based biochemical primary high throughput screening assay to identify inhibitors of the interaction of the lipase co-activator protein, abhydrolase domain containing 5 (ABHD5) with perilipin-5 (MLDP; PLIN5)
602310	qHTS for Inhibitors of Vif-A3G Interactions: qHTS
602313	qHTS for Inhibitors of Vif-A3F Interactions: qHTS
602329	Identification of inhibitors of RAD54 Measured in Biochemical System Using Plate Reader - 2159-01_Inhibitor_SinglePoint_HTS_Activity
602332	qHTS for Inducers of the Endoplasmic Reticulum Stress Response (ERSR) in Human Glioma: qHTS
602340	HTS for suppressors of simvastatin-induced mytoxicity in differentiated C2C12 cells Measured in Cell-Based System Using Plate Reader - 2112-01_Suppressor_SinglePoint_HTS_Activity
602342	Small molecule inhibitors of miR122 Measured in Cell-Based System Using Plate Reader - 2144-01_Inhibitor_SinglePoint_HTS_Activity
602346	Identification of VIF Inhibitors Measured in Cell-Based System Using Imaging - 2108-01_Inhibitor_SinglePoint_HTS_Activity
602363	Whole cell Yeast HTS to identify compounds modulating the fidelity of the start codon recognition in eukaryotes. Measured in Whole Organism System Using Plate Reader - 2155-01_Other_SinglePoint_HTS_Activity
602393	Screen for inhibitors of the SWI/SNF chromatin remodeling complex (esBAF) in mouse embryonic stem cells with Luciferase reporter assay Measured in Cell-Based System Using Plate Reader - 2141-01_Inhibitor_SinglePoint_HTS_Activity
602396	Luminescence-based cell-based primary high throughput screening assay to identify inverse agonists of the liver receptor homolog-1 (LRH-1; NR5A2)
602399	uHTS identification of inhibitors of NadD in a Colorimetric assay
602405	PgID: DNTB colorimetric HTS to detect inhibitor of PgID Measured in Biochemical System Using Plate Reader - 2164-

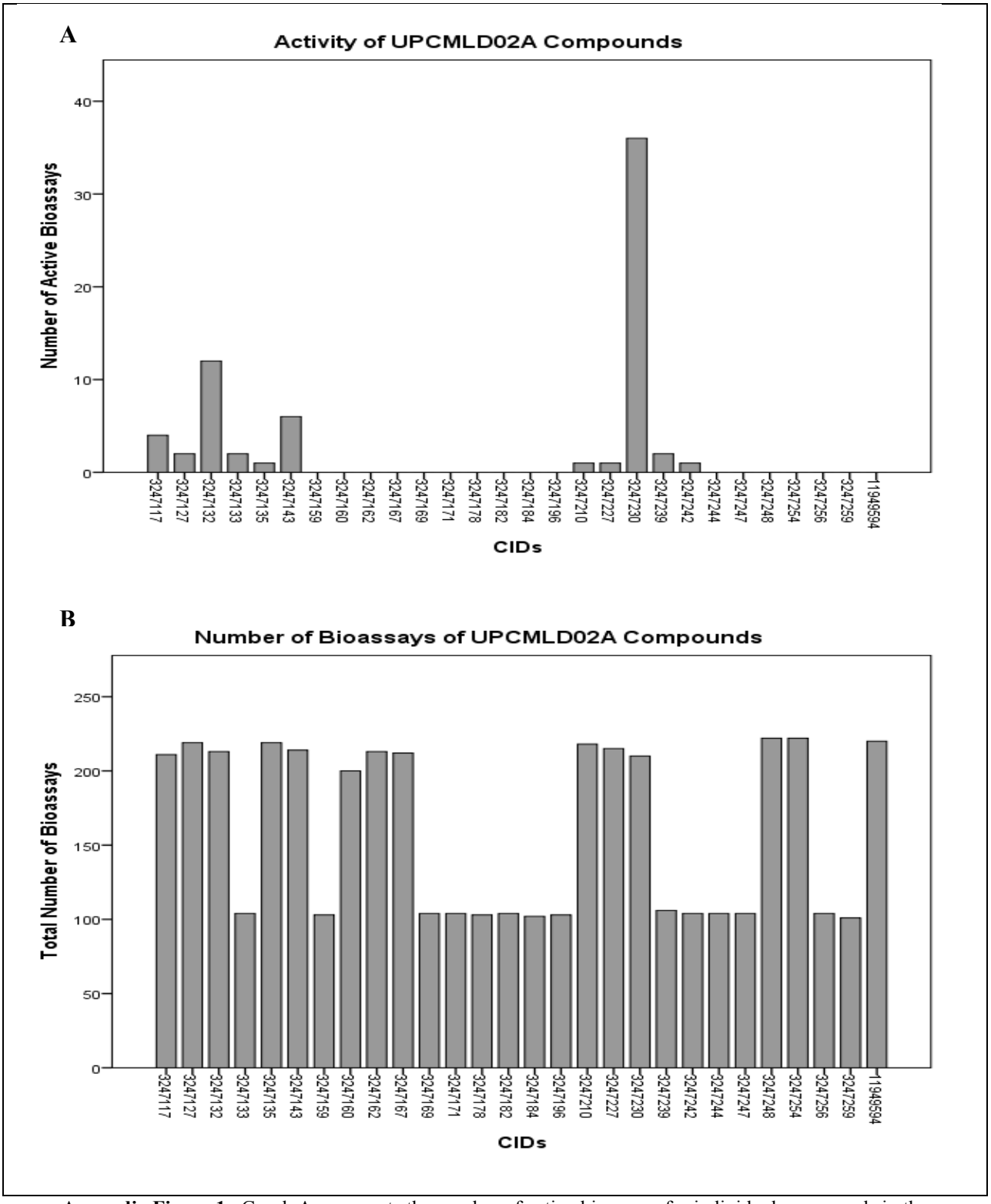
	01_Inhibitor_SinglePoint_HTS_Activity
602410	Primary cell-based screen for identification of compounds that inhibit the two-pore domain potassium channel KCNK3
602429	uHTS identification of SUMO1-mediated protein-protein interactions
602438	uHTS identification of modulators of interaction between CendR and NRP-1 using Fluorescence Polarization assay
602440	uHTS Fluorescent Assay Using Nedd8 Protein Substrate for Identification of Inhibitors of Sentrin-Specific Protease 8 (SENP8)
602449	uHTS identification of small molecule inhibitors of the mitochondrial permeability transition pore via an absorbance assay
602481	Mycobacterium tuberculosis BioA enzyme inhibitor Measured in Biochemical System Using Plate Reader - 2163-01_Inhibitor_SinglePoint_HTS_Activity
623870	ARNT-TAC3: AlphaScreen HTS to detect disruption of ARNT/TAC3 interactions Measured in Biochemical System Using Plate Reader - 2158-01_Inhibitor_SinglePoint_HTS_Activity
623877	Primary cell-based high-throughput screening for identification of compounds that activate/potentiate calcium-activated chloride channels (TMEM16A)
623901	Small molecule inhibitors of miR122 Measured in Cell-Based System Using Plate Reader - 2144-01_Activator_SinglePoint_HTS_Activity
624037	Fluorescence-based cell-based primary high throughput screening assay to identify agonists of the human cholinergic receptor, muscarinic 5 (CHRM5)
624038	Fluorescence-based cell-based primary high throughput screening assay to identify positive allosteric modulators (PAMs) of the human cholinergic receptor, muscarinic 5 (CHRM5)
624040	Fluorescence-based cell-based primary high throughput screening assay to identify antagonists of the human cholinergic receptor, muscarinic 5 (CHRM5)
624125	Fluorescence-based cell-based primary high throughput screening assay to identify antagonists of the human cholinergic receptor, muscarinic 4

	(CHRM4)
624126	Fluorescence-based cell-based primary high throughput screening assay to identify positive allosteric modulators (PAMs) of the human cholinergic receptor, muscarinic 4 (CHRM4)
624127	Fluorescence-based cell-based primary high throughput screening assay to identify agonists of the human cholinergic receptor, muscarinic 4 (CHRM4)
624168	uHTS identification of small molecule activators of alpha dystroglycan glycosylation
624169	Luminescence-based cell-based primary high throughput screening assay to identify agonists of the mouse 5-hydroxytryptamine (serotonin) receptor 2A (HTR2A)
624170	qHTS for Inhibitors of Glutaminase (GLS)
624171	qHTS of Nrf2 Activators
624172	qHTS of GLP-1 Receptor Agonists
624173	qHTS of Trypanosoma Brucei Inhibitors
624178	qHTS for Inhibitors of Human Acid Sphingomyelinase Assay: Native Substrate
624202	qHTS Assay to Identify Small Molecule Activators of BRCA1 Expression
624204	uHTS identification of small molecule inhibitors of the catalytic domain of the SUMO protease, SENP1 in a FRET assay
624246	qHTS for Small Molecule Inhibitors of the ERG Ets/DNA interaction
624256	HTS to identify compounds that promote myeloid differentiation with MLPCN compound set
624263	A Quantitative High throughput Screen to Identify Chemical Modulators of PINK1 Expression
624267	Fluorescence-based cell-based primary high throughput screening assay to identify inhibitors of the interaction of nucleotide-binding oligomerization domain containing 2 (NOD2) and the receptor-

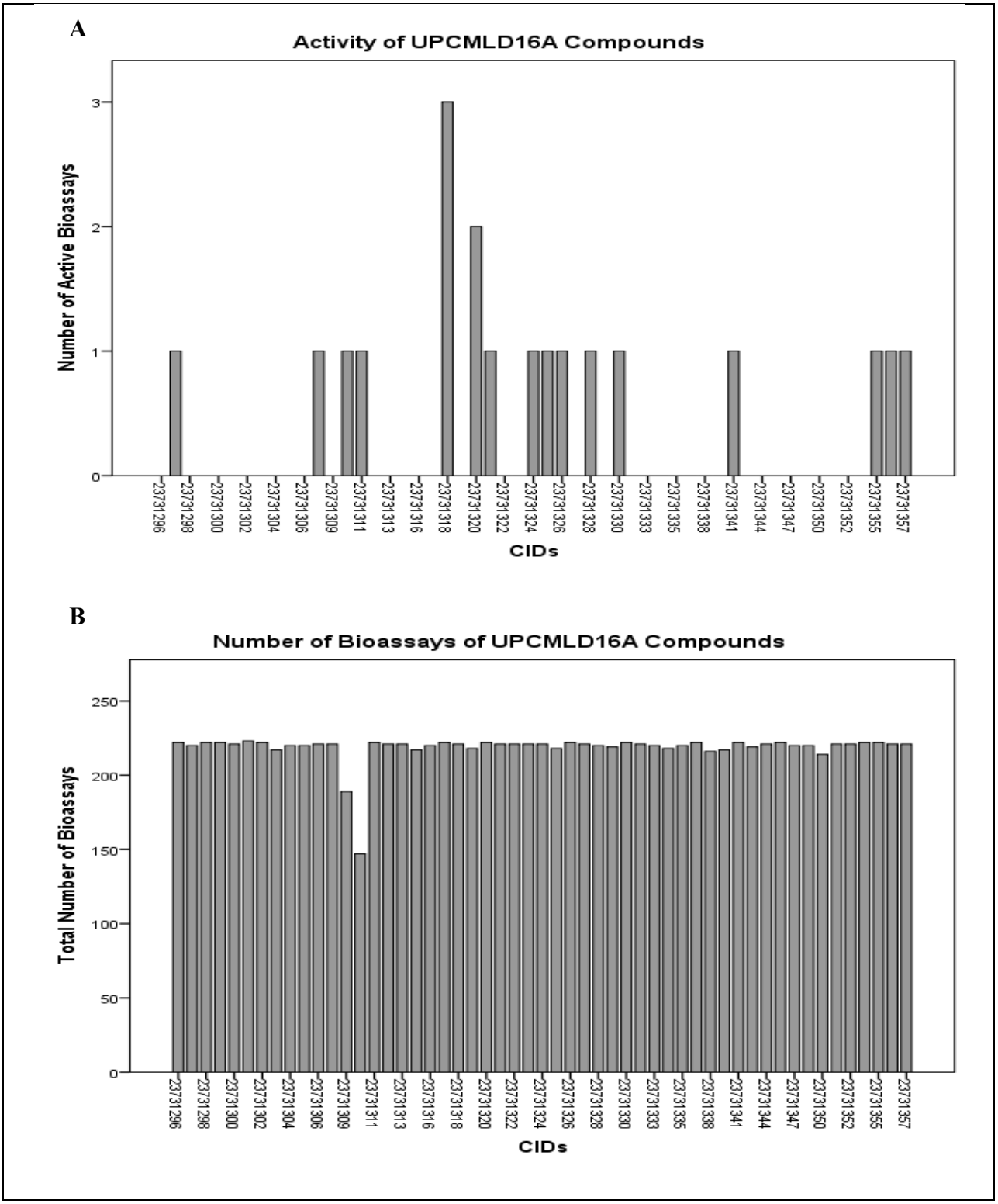
	interacting serine-threonine kinase 2 (RIPK2)
624268	Luminescence-based biochemical primary high throughput screening assay to identify inhibitors of Trypanosoma brucei methionyl tRNA synthetase (MetRS)
624288	qHTS for Antagonists of gsp, the Etiologic Mutation Responsible for Fibrous Dysplasia/McCune-Albright Syndrome: qHTS
624291	qHTS for Activators of Integrin-Mediated Alleviation for Muscular Dystrophy
624296	A quantitative high throughput screen for small molecules that induce DNA re-replication in MCF 10a normal breast cells.
624304	uHTS identification of SKN-1 Inhibitors in a fluoresence assay
624330	Discovery of small molecule inhibitors of the oncogenic and cytokinetic protein MgcRacGAP - Primary and Confirmatory Screens
624352	uHTS identification of HIF-2a Inhibitors in a luminesence assay
624354	uHTS identification of Caspase-8 TRAIL sensitizers in a luminesence assay
624377	Fluorescence polarization-based biochemical primary high throughput screening assay to identify inhibitors of ArfGAP with SH3 domain, ankyrin repeat and PH domain 1 (ASAP1)
624414	qHTS for Agonists of the Human Mucolipin Transient Receptor Potential 1 (TRPML1)
624415	qHTS for Inhibitors of the Human Mucolipin Transient Receptor Potential 1 (TRPML1)
624416	TRFRET-based biochemical primary high throughput screening assay to identify small molecules that bind to the HIV-1-gp120 binding antibody, PG9
624417	qHTS of GLP-1 Receptor Inverse Agonists (Inhibition Mode)
624463	Beta-Arrestin HTS for Positive Allosteric Modulators of the Human D2 Dopamine Receptor: Antagonists

624464	Beta-Arrestin HTS for Positive Allosteric Modulators of the Human D2 Dopamine Receptor: Potentiators
624465	Beta-Arrestin HTS for Positive Allosteric Modulators of the Human D2 Dopamine Receptor: Agonists
624466	Fluorescence-based cell-based primary high throughput screening assay to identify antagonists of the human trace amine associated receptor 1 (TAAR1)
624467	Fluorescence-based cell-based primary high throughput screening assay to identify agonists of the human trace amine associated receptor 1 (TAAR1)
624483	Counterscreen of compound fluorescence effects on High-throughput multiplex microsphere screening for inhibitors of toxin protease
651550	HTS Assay for Inhibitors of Akt Phophorylation: Primary Screen
651560	uHTS identification of small molecule inhibitors of Low Molecular Weight Protein Tyrosine Phosphatase, LMPTP, via a fluorescence intensity assay
651572	Fluorescence polarization-based biochemical primary high throughput screening assay to identify inhibitors of ADP-ribosylation factor GTPase activating protein 1 (ARFGAP1)
651582	uHTS identification of small molecule Triacylglycerol inhbitors in a fluoresence assay
651602	Absorbance-based primary bacterial cell-based high throughput screening assay to identify inhibitors of RecBCD (with phage)
651610	HIV entry: Env-mediated Cell Fusion Measured in Cell-Based System Using Plate Reader - 7013-01_Inhibitor_SinglePoint_HTS_Activity
651635	qHTS for Inhibitors of ATXN expression
651636	uHTS identification of small molecule antagonists of the EBI2 receptor via a luminescent beta-arrestin assay
651640	DENV2 CPE-Based HTS Measured in Cell-Based and Microorganism Combination System Using Plate Reader - 2149-01_Other_SinglePoint_HTS_Activity

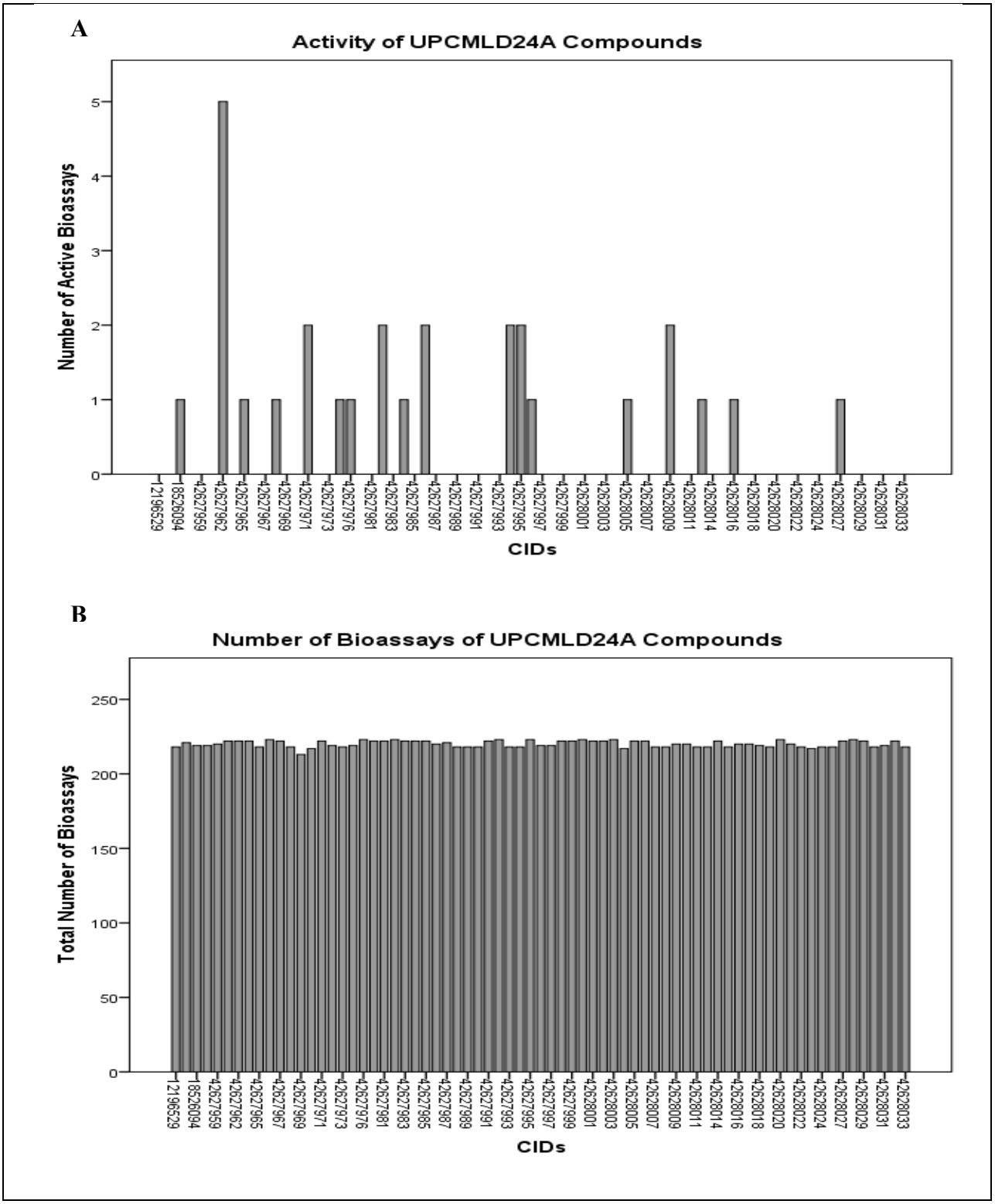
651644	qHTS Assay for Inhibitors of the HIV-1 protein Vpr
651647	uHTS identification of inhibitors of MT1-MMP activation in a fluoresence assay
651654	HTS for the detection of C. neoformans cell lysis via adenylate kinase (AK) release Measured in Microorganism System Using Plate Reader - 2162-01_Inhibitor_SinglePoint_HTS_Activity
651658	Small Molecule Inhibitors of FGF22-Mediated Excitatory Synaptogenesis & Epilepsy Measured in Biochemical System Using RT-PCR - 7012-01_Inhibitor_SinglePoint_HTS_Activity
651687	MLPCN PGC1a Modulators Measured in Cell-Based System Using Plate Reader - 2139-01_Inhibitor_SinglePoint_HTS_Activity



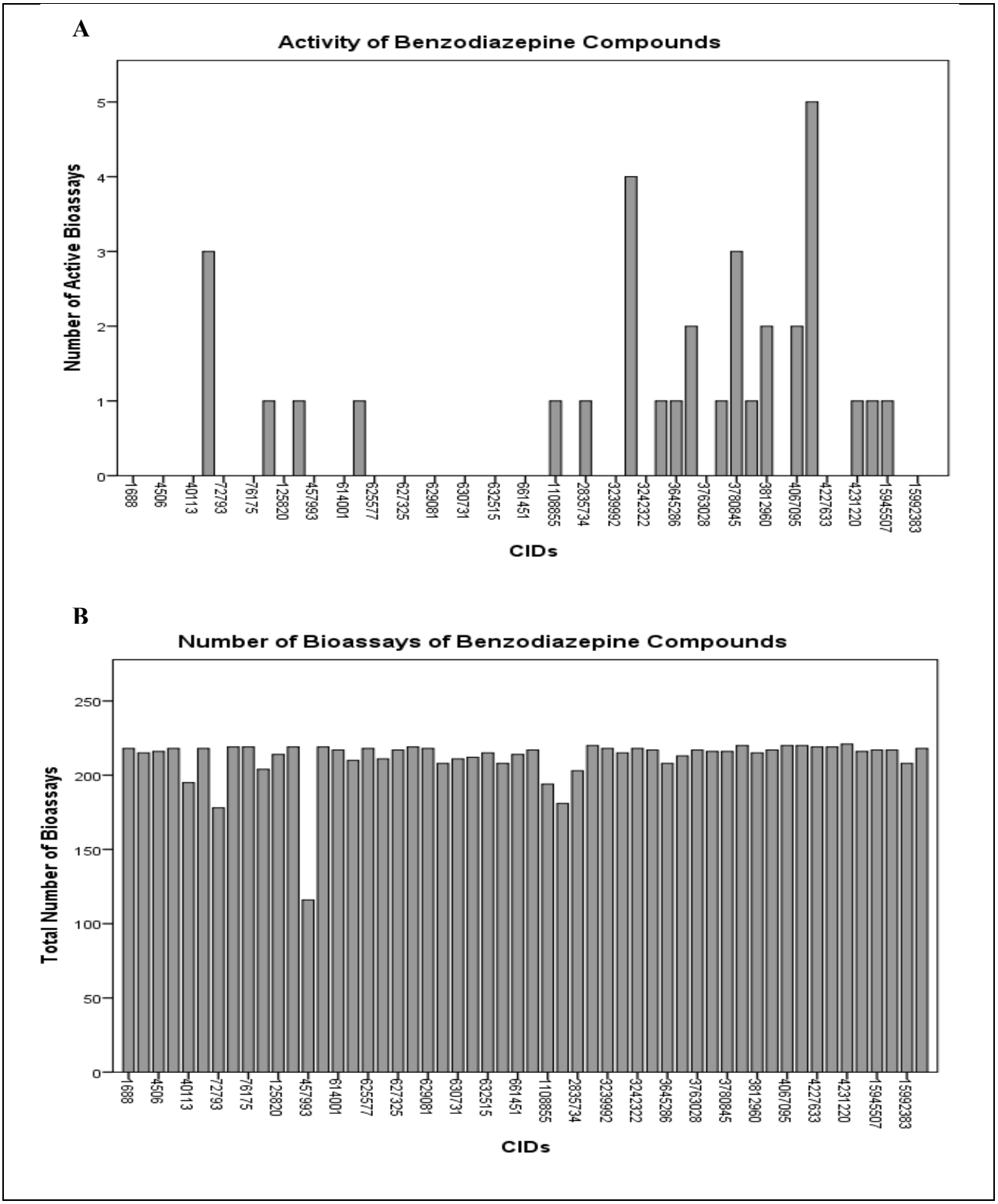
Appendix Figure 1. Graph A represents the number of active bioassays for individual compounds in the UPCMLD02A library. Graph B demonstrates that compounds tested in less than 100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.



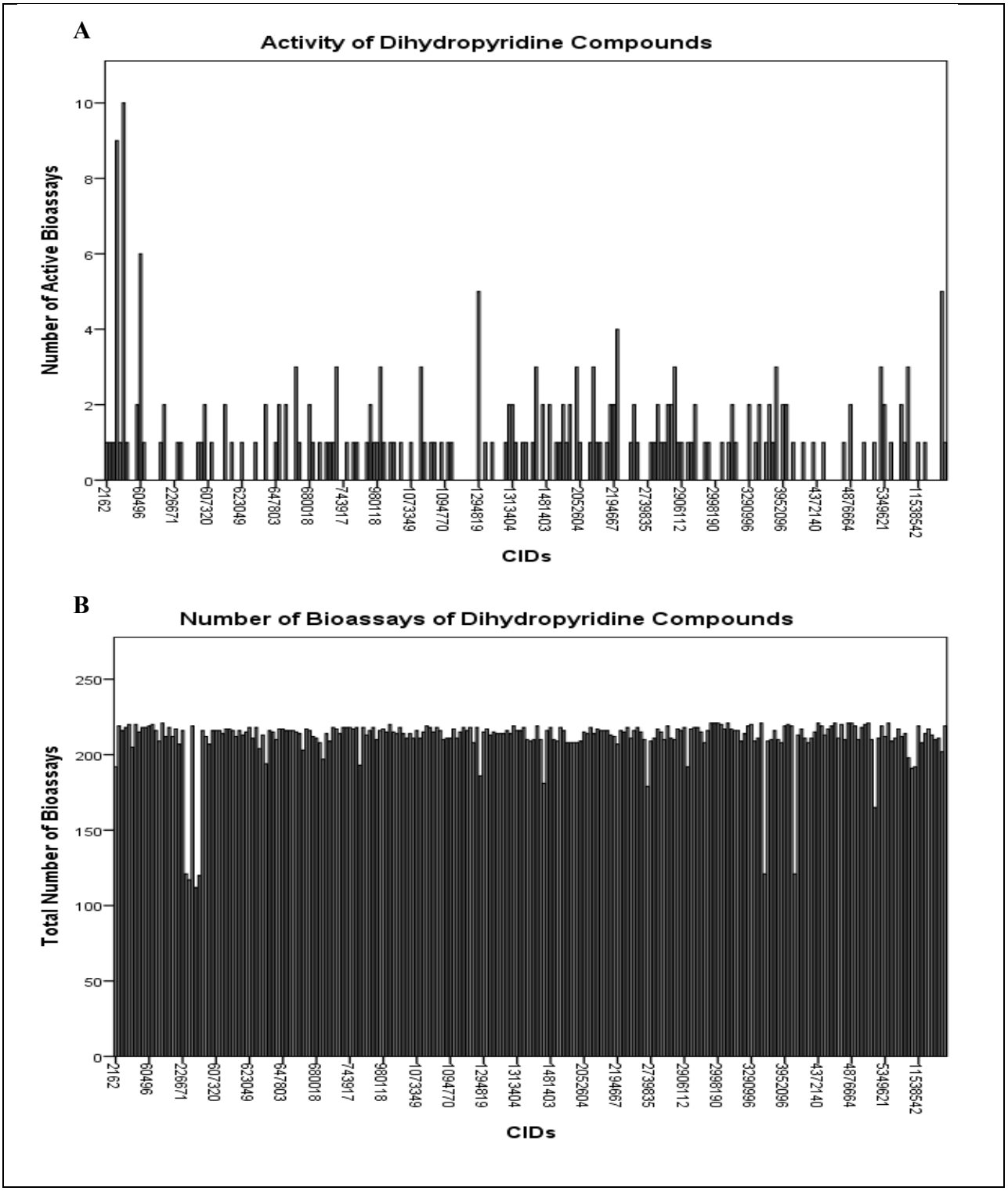
Appendix Figure 2. Graph A represents the number of active bioassays for individual compounds in the UPCMLD16A library. Graph B demonstrates that compounds tested in less than 100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.



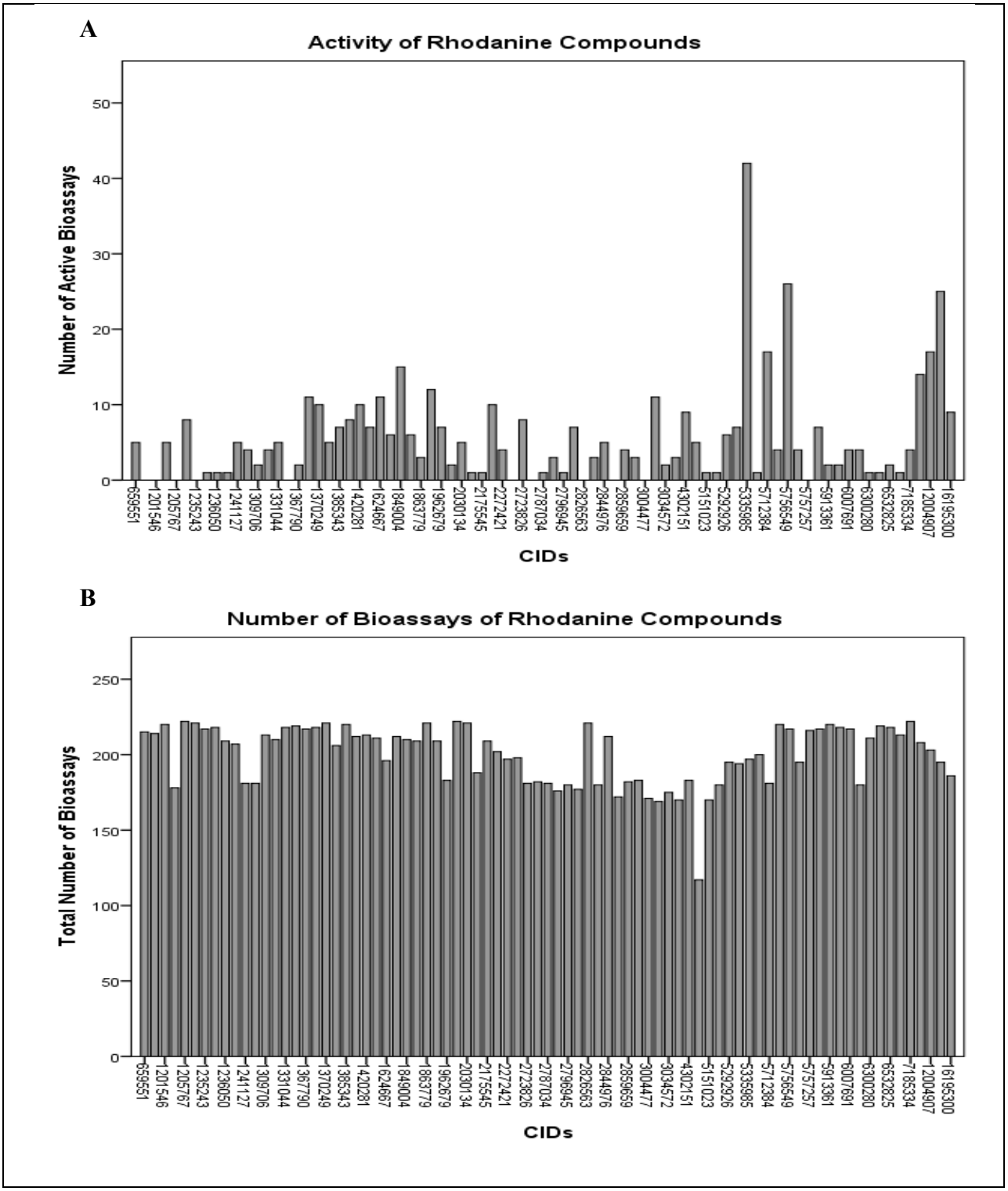
Appendix Figure 3. Graph A represents the number of active bioassays for individual compounds in the UPCMLD24A library. Graph B demonstrates that compounds tested in less than 100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.



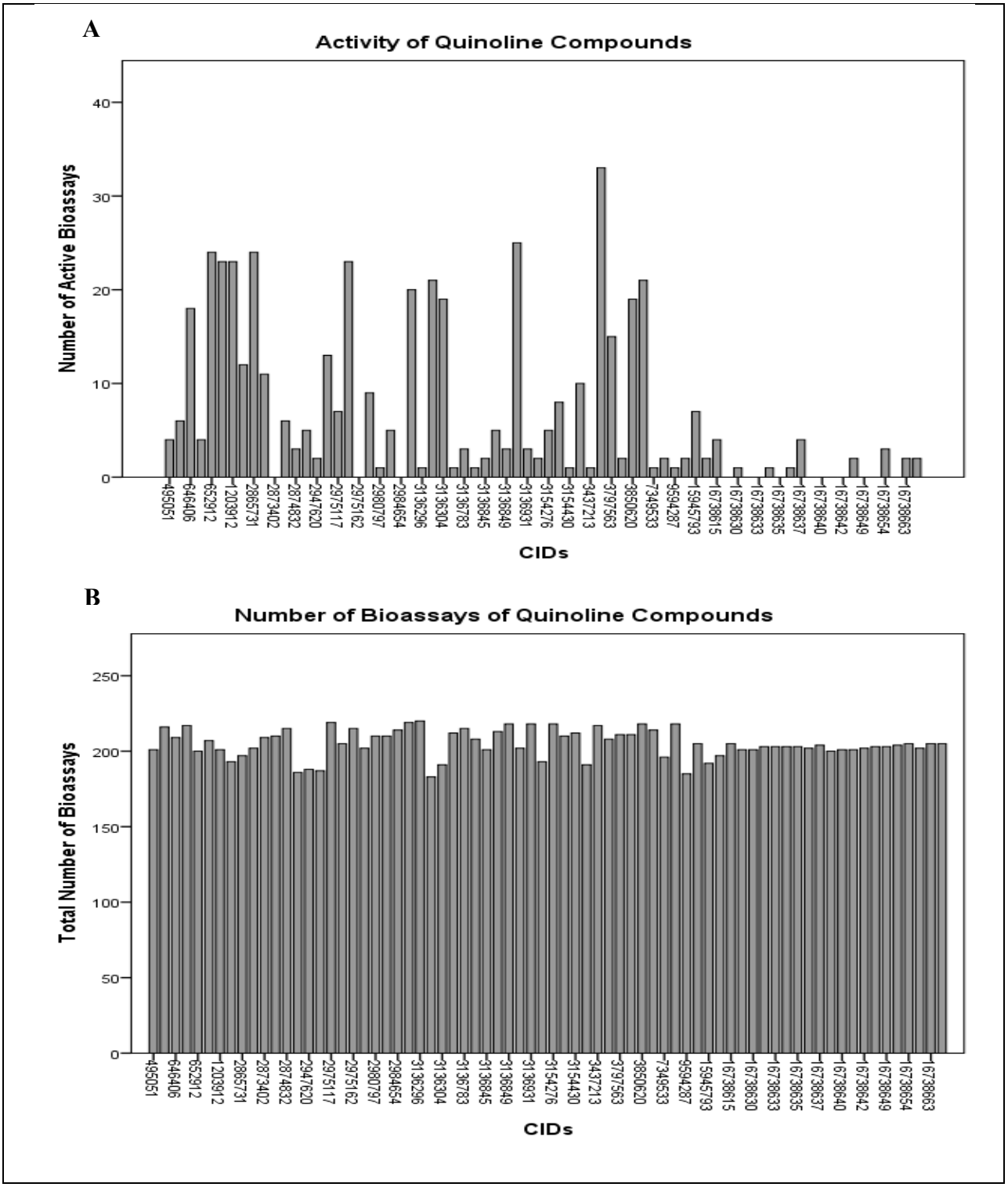
Appendix Figure 4. Graph A represents the number of active bioassays for individual compounds in the benzodiazebine scaffold library. Graph B demonstrates that compounds tested in less than 100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.



Appendix Figure 5. Graph A represents the number of active bioassays for individual compounds in the dihydropyridine scaffold library. Graph B demonstrates that compounds tested in less than 100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.



Appendix Figure 6. Graph A represents the number of active bioassays for individual compounds in the rhodanine scaffold library. Graph B demonstrates that compounds tested in less than 100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.



Appendix Figure 7. Graph A represents the number of active bioassays for individual compounds in the quinoline scaffold library. Graph B demonstrates that compounds tested in less than 100 bioassays were filtered out and that only the shared 223 bioassays were included in the analysis.

BIBLIOGRAPHY

[1] Leeson, P. D.; Davis, A. M.; Steele J. Drug-Like Properties: Guiding Principles for Design – or Chemical Prejudice? *Drug Discov. Today: Technol.* **2004**, *1*, 189-195.

[2] Langdon, S. R.; Brown, N.; Blagg, J. Scaffold Diversity of Exemplified Medicinal Chemistry Space. *J. Chem. Inf. Model.* **2011**, *51*, 2174-2185.

[3] Bleicher, K. H.; Böhm, H. J.; Müller K.; Alanine, A. I. A Guide to Drug Discovery: Hit and Lead Generation: Beyond High-Throughput Screening. *Nat. Rev. Drug Discov.* **2003**, *2*, 369-378.

[4] Patrick, G. L. *An Introduction to Medicinal Chemistry*. New York: Oxford University Press, 2009, 225-227.

[5] Lipinski, C. A. Lead- and Drug-Like Compounds: the Rule-of-Five Revolution. *Drug Discov. Today: Technol.* **2004**, *1*, 337-341.

[6] Veber, D. F.; Johnson, S. R.; Cheng, H. Y.; Smith, B. R.; Ward, K. W.; Kopple K. D. Molecular Properties that Influence the Oral Bioavailability of Drug Candidates. *J. Med. Chem.* **2002**, *45*, 2615-2623.

[7] Rishton, G. M. Nonleadlikeness and Leadlikeness in Biochemical Screening. *Drug Discov. Today* **2003**, *8*, 86-96.

[8] Jhoti, H.; Leach, A. R. *Structure Based Drug Discovery.* Netherlands: Springer, 2007, 129-153.

[9] Kirk, S. R.; Andrade, A. L.; Melich, K.; Jackson, E. P.; Cuellar, E.; Karpen, J. W. Halogen Substituents on the Aromatic Moiety of the Tetracaine Scaffold Improve

Potency of Cyclic Nucleotide-Gated Channel Block. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 6417-6419.

[10] Patrick, G. L. *An Introduction to Medicinal Chemistry*. New York: Oxford University Press, 2009, 379-382.

[11] Evans, B.E.; Rittle, K.E.; Bock, M.G.; DiPardo, R. M.; Freidinger, R. M.; Whitter, W. L.; Lundell, G. F.; Veber, D. F.; Anderson, P. S.; Chang, R. S. L.; Lotti, V. J.; Cerino, D. J.; Chen, T. B.; Kling, P. J.; Kunkel, K. A.; Springer, J. P.; Hirshfieldt, J. Methods for Drug Discovery: Development of Potent, Selective, Orally Effective Cholecystokinin Antagonists. *J. Med. Chem.* **1988**, *31*, 2235-2346.

[12] Patchett, A. A.; Nargund, R. P. Privileged Structures — An Update. *Annu. Rep. Med. Chem.* **2000**, *35*, 289-298.

[13] DeSimone, R. W.; Currie, K. S.; Mitchell, S.A.; Darrow, J.W.; Pippin, D.A. Privileged Structures: Applications in Drug Discovery. *Comb. Chem. High Throughput Screen.* **2004**, *7*, 473-493.

[14] Welsch, M. E.; Snyder, S. A.; Stockwell B. R. Privileged Scaffolds for Library Design and Drug Discovery. *Curr. Opin. Chem. Biol.* **2010**, *14*, 347-361.

[15] Lounkine, E.; Keiser, M. J.; Whitebread S.; Mikhailov, D.; Hamon, J.; Jenkins, J. L.; Lavan, P.; Weber, E.; Doak, A. K.; Cote, S.; Shoichet, B. K.; Urban, L. Large Scale Prediction and Testing of Drug Activity on Side-Effect Targets. *Nature* **2012**, *486*, 361-367.

[16] Rognan, D. Chemogenomic Approaches to Rational Drug Design. *Br. J. Pharmacol*. **2007**, *152*, 38–52.

[17] McGovern, S. L. *Virtual Screening in Drug Discovery*. Florida: CRC Press, 2005, 107-116.

[18] Boran, A. D.; Iyengar, R. Systems Approaches to Polypharmacology and Drug Discovery. *Curr. Opin. Drug Discov. Devel.* **2010**, *13*, 297-309.

[19] Peters, J. U. Polypharmacology - Foe or Friend? *J. Med. Chem.* **2013**, *56*, 8955-8971.

[20] Hu, Y.; Bajorath, J. Polypharmacology Directed Compound Data Mining: Identification of Promiscuous Chemotypes with Different Activity Profiles and Comparison to Approved Drugs. *J. Chem. Inf. Model.* **2010**, *50*, 2112-2118.

[21] Klekota, J.; Roth, F. P. Chemical Substructures that Enrich for Biological Activity. *Bioinformatics* **2008**, *24*, 2518-2525.

[22] Tomasić, T.; Masic, L.P. Rhodanine as a Privileged Scaffold in Drug Discovery. *Curr. Med. Chem.* **2009**, *16*, 1596-629.

[23] Lacy, C. F. *Drug Information Handbook.* Ohio: Lexicomp, 2011, 498-500.

[24] Cannon, J. G. Structure-Activity Relationships of Dopamine Agonists. *Ann. Rev. Pharmacol. Toxicol.* **1963**, *23*, 103-130.

[25] Patrick, G. L. *An Introduction to Medicinal Chemistry*. New York: Oxford University Press, 2009, 336-337.

[26] Patrick, G. L. *An Introduction to Medicinal Chemistry*. New York: Oxford University Press, 2009, 44.

[27] Patrick, G. L. *An Introduction to Medicinal Chemistry*. New York: Oxford University Press, 2009, 192.

[28] Mendgen, T.; Steuer, C.; Klein, C. Privileged Scaffolds or Promiscuous Binders: A Comperative Study on Rhodanines and Related Heterocycles in Medicinal Chemistry. *J. Med. Chem.* **2012**, *55*, 743-753.

[29] Leeson, P. D.; Springthorpe, B. The Influence of Drug-Like Concepts on Decision-Making in Medicinal Chemistry. *Nat. Rev. Drug Discov.* **2007**, *6*, 881-890.

[30] Dimova, D.; Hu, Y.; Bajorath, J. Matched Molecular Pair Analysis of Small Molecule Microarray Data Identifies Promiscuity Cliffs and Reveals Molecular Origins of Extreme Compound Promiscuity. *J. Med. Chem.* **2012**, *55*, 10220-10228.

[31] Wipf, P.; Fang, Z.; Ferrié, L.; Ueda, M.; Walczak, M. A. A.; Yan, Y.; Yang, M. Cycloadditions in Heterocycle and Alkaloid Synthesis. *Pure Appl. Chem.* **2013**, *85*, 1079-1087.

[32] Xie, X. Exploiting PubChem for Virtual Screening. *Expert Opin. Drug Discov.* **2010**, *5*, 1205-1220.

[33] Patrick, G. L. *An Introduction to Medicinal Chemistry*. New York: Oxford University Press, 2009, 194.

[34] Böcker, A.; Bonneau, P. R.; Edwards, P. J. HTS Promiscuity Analyses for Accelerating Decision Making. *J. Biomol. Screen.* **2011**, *16*, 765-774.

[35] Wipf, P.; Walczak, M. A. A. Pericyclic Cascade Reactions of (Bicyclo[1.1.0]butylmethyl)amines. *Angew. Chem. Int. Ed.*. **2006**, *45*, 4172–4175.

[36] Werner, S.; Iyer, P.S.; Fodor, M.D.; Coleman, C. M.; Twining, L. A.; Mitasev, B.; Brummond, K. M. Solution-Phase Synthesis of a Tricyclic Pyrrole-2-Carboxamide

Discovery Library Applying a Stetter-Paal-Knorr Reaction Sequence. *J. Comb. Chem.* **2006**, *8*, 368-380.

[37] Werner, S.; Nielsen, S.D.; Wipf, P.; Turner, D. M.; Chambers, P. G.; Geib, S. J.; Curran, D. P.; Zhang, W. Fluorous Parallel Synthesis of a Piperazinedione-Fused Tricyclic Compound Library. *J. Comb. Chem.* **2009**, *11,* 452-459.

[38] Rosenker, C. J.; Johnstone, L.; Zhang, L.; Quade, B.; Wipf, P. Synthesis and Selective Functionalization of a Heterocyclic Thiadiazine Library. (In Preparation)