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Scaffold Perception, Common Pharmacophore Model Development, And Quantitative Structure-Affinity Relationships Of Sigma Site Ligands

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SCAFFOLD PERCEPTION, COMMON PHARMACOPHORE MODEL DEVELOPMENT, AND QUANTITATIVE STRUCTURE–AFFINITY RELATIONSHIPS OF SIGMA SITE LIGANDS

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ABSTRACT

Sigma receptors are endogenous proteins with potential utility in treating psychological disorders, ischemia, the psychological and convulsive effects of drugs of abuse, and as an imaging agent for cancerous tissues, among others. Drug design efforts targeting these receptors have been hindered by a lack of structural information of the receptors themselves. Traditional ligand-based approaches have succeeded in generating many compounds with high affinity, and quite a few with selectivity for σ-1 receptors. There are few selective ligands for use as pharmacological probes for the σ-2 receptor. Much effort has gone into exploring the structure activity relationships of ligands targeting these receptors.

A critical review of the existing literature covering pharmacophore development for σ receptors was undertaken with the intent to develop computational models to assist in ligand-based drug design efforts. Inspired by the lack of pharmacophore models with general utility, and confronted by the obstacles of data heterogeneity, a database of σ ligands and their binding affinity data was collected. Cohorts of data collected under similar experimental methodologies were assembled and clustered by measures of scaffold dissimilarity. Multiple-Instance Learning techniques were used to train classification models that differentiated molecules as active or inactive, and to assist in the identification of relevant conformations of σ ligands at their macromolecular targets. Conformations of high-affinity ligands were then used to develop general pharmacophore models as part of a virtual screening approach. Structure-activity relationship models based on virtual screening alignments of known sigma ligands were developed in the search for selective σ-1 and σ-2 receptor probes.

DEDICATION

This work is dedicated to my sons Lucas and Xander. The vicissitudes of life can never the match the resolve you have given me to make this world a better place for you and your generation.

LIST OF ABBREVIATIONS OR SYMBOLS

3-HPP	3-3(-hydroxyphenyl)piperidine
3-PPP	3-(3-hydroxyphenyl)-*N*-(1-propyl)piperidine
5-HT	5-hydroxytryptamine
D_2	Dopamine 2 receptor
H_1	Histamine 1 receptor
σ-1	Sigma-1
σ-2	Sigma-2
CoMFA	Comparative Molecular Field Analysis
CoMSIA	Comparative Molecular Similarity Indices Analysis
CPU	Central Processing Unit
CSV	Comma-Separated Values
DDR	Double Data Rate
DTG	1,3-di-*o*-tolyl-guanidine
EA	External Accuracy
FPR	False Positive Rate
GB	gigabyte
GHz	gigahertz
HAL	haloperidol
IA	Internal Accuracy

kD	kilodalton
MCC	Matthews Correlation Coefficient
MD	Molecular Dynamics
MDMA	3,4-methylenedioxy methamphetamine
MHz	megahertz
MILES	Multiple Instance Learning via Embedded instance Selection
PE	Prediction Error
PGRMC1	Progesterone Receptor Membrane Component 1
PLS	Partial Least Squares
PTZ	(+)-pentazocine
QSAR	Quantitative Structure–Activity Relationship
RCSB	Research Collaboratory for Structural Bioinformatics
RMS	Root-Mean-Square
SAP	Significance Analysis of Pharmacophores
SMILES	Simplified Molecular-Input Line-Entry System
SVM	Support-Vector Machine

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1. INTRODUCTION

> Introduce such an intoxicant, and start it to ferment in humanity's blood, and it may spread from soul to soul, until, before the world is advised of its possible results, the ever-increasing potency will gain such headway as to destroy, or debase, our civilization, and even to exterminate mankind.
>
> *Etidorpha*
> John Uri Lloyd

Research into σ receptors and their ligands began in 1976 with the proposal of a "sigma opioid" class of receptors to explain aberrant behavior upon exposure to *N*-allyl-normetazocine (SKF-10047, NANM) in the chronic spinal dog model of precipitated opioid abstinence.[1] The use of racemate NANM in initial binding studies complicated matters, implicating binding to phencyclidine (PCP) sites,[2] and to multiple opioid sites.[3] In the following years, it was determined that sigma sites were distinct from opioid and PCP receptors,[4] and that the psychotomimetic effects of NANM were not a result of sigma affinity.[5]

1.1 Therapeutic potential of σ receptor ligands

Many neuroleptics and antidepressants have affinity for σ receptors and consequently their role in motor side effects of antipsychotics and as modulators of serotonergic and glutamatergic neurotransmission in depression have been well established.[6,7] In the early 1990s, σ antagonists were also demonstrated to attenuate the psychostimulant effects of cocaine[8] and methamphetamine,[9] and more recently 3,4-methylenedioxymethamphetamine (MDMA).[10] There is evidence that σ

ligands may also be of use in treating ischemia and certain cognitive disorders.[11] Sigma sites are particularly interesting targets for cancer imaging agents due to their role in apoptosis and their overexpression in a wide range of cancers, where saturation of σ-2 receptors is associated with selective cytotoxicity towards several cancer cell lines.[12]

1.2 Sigma receptor subtypes

1.2.1 Sigma-1 receptor

Sigma-1 receptors have been well characterized, displaying a rank order of affinity for haloperidol (HAL), 1,3-di-*o*-tolyl-guanidine (DTG), (+)-3-(3-hydroxyphenyl)-*N*-(1-propyl)piperidine (*R*-(+)-3-PPP), (–)-cyclazocine, (+)-NANM, PCP, etoxadrol, dexoxadrol, and MK-801.[13] These sites are distributed in both the central nervous system and peripheral tissues. The σ-1 receptor was initially cloned by Hanner et al. in 1996,[14] and was demonstrated to be a 223 amino acid 25.3 kDa peptide whose closest known homologue is the yeast C_8 sterol isomerase. To this day, the tertiary structure of σ-1 receptors or close homologs have not been elucidated by crystallography. As a consequence, structure-based drug design is not currently a viable option for the design of novel σ-1 ligands. Although a homology model has recently been developed for the σ-1 receptor,[15] ab initio and comparative modeling techniques are currently insufficient to make confident structural predictions for a protein of this size.

1.2.2 Sigma-2 receptor

In the late 1980s it became clear that the σ ligand DTG bound to a second class of receptor sites with rank order affinities to benzomorphans that contrasted themselves from classical sigma sites.[16] These sites were dubbed σ-2 sites, and for many years now, a great challenge in σ research has been to discover substances with selectivity towards this subsite. Very recently, a σ-2 receptor was putatively identified as the 21.7 kDa Progesterone Receptor Membrane Component 1 (PGRMC1).[17] PGRMC1 has a conserved cytochrome b5-like heme/steroid binding domain, and the presence of close homologs in the Research Collaboratory for Structural Bioinformatics (RCSB) Protein Data

Bank[18] suggests that homology modeling may be a feasible approach for generating models for structure-based drug design. Nevertheless, a comprehensive database of ligand structures with σ-2 binding affinities and associated scaffolds will be of significant utility for ligand-based drug design and QSAR. Until a more comprehensive correlation of PGRMC1 and σ-2 ligands is carried out, ligand-based drug design strategies may well prove more meaningful.

1.2.3 "Sigma-3"

For several years, Booth, Wyrick, Myers and others described a putative "σ-3" site with binding affinities different still from σ-1 or σ-2.[19–22] These sites were labeled by 1-phenyl-2-amino-1,2,3,4-tetrahydronaphthalenes and were later determined to be histamine H_1 receptors.[23] Subsequent literature dropped the reference to σ-3, but this points out the importance of scaffold recognition and diligent pharmacological classification of "novel" receptors.

1.3 Sigma pharmacophore and QSAR development: 1980–2011

Medicinal chemists often assess the performance of molecules in targeted biological assays in terms of a *pharmacophore*. What is meant by a "pharmacophore" can differ quite a lot from one practitioner to another. There are numerous examples of different usage of the term in the σ literature. In order to be clear about the terminology, and to explain why many of the references to pharmacophores are not included in the following review, two usages of the term are distinguished. *Pharmacophore motifs* are abstract generalizations of molecular moieties or scaffolds that attempt to explain, in a retrospective sense, *why* certain molecules possess binding affinity at a macromolecular target. *Pharmacophore models*, on the other hand, are specific, well-defined combinations of *features* that have some predictive utility in assessing the *potential* of a molecule to bind to the target.

Pharmacophore motifs were quite common in the early σ literature. To this day, ligand-based drug design efforts are couched in terms of their agreement to those motifs, and they merit review because of their longstanding influence on the interpretation of σ ligand affinity. Several very predictive pharmacophore models have also been developed over the years. Many of these models

highlight several exemplary features possessed by almost all σ ligands developed to date; others attempt to elaborate upon putative binding site features that imply complementary features of the ligands themselves. Descriptor- or fingerprint-based QSARs are not reviewed if they do not elaborate upon a pharmacophore model (for the curious, see references 24–34).

1.3.1 Non-selective σ models

1.3.1.1 Manallack topological pharmacophore model

Manallack et al.[35,36] developed the first pharmacophore models for σ ligands based on the method of Lloyd and Andrews[37] in an attempt to differentiate the binding requirements of NMDA and σ ligands. This method distinguishes three receptor features that are built around each ligand, namely two "hydrophobic" features that are aligned normal to the plane of an aromatic ring at its centroid, and a third receptor feature represented by a vector from the lone pair electrons of a ligand N to a postulated H-bond acceptor belonging to the receptor. Receptor and ligand features are presented in Figure 1.1. Conformational energies, RMS distances between receptor or ligand features, and

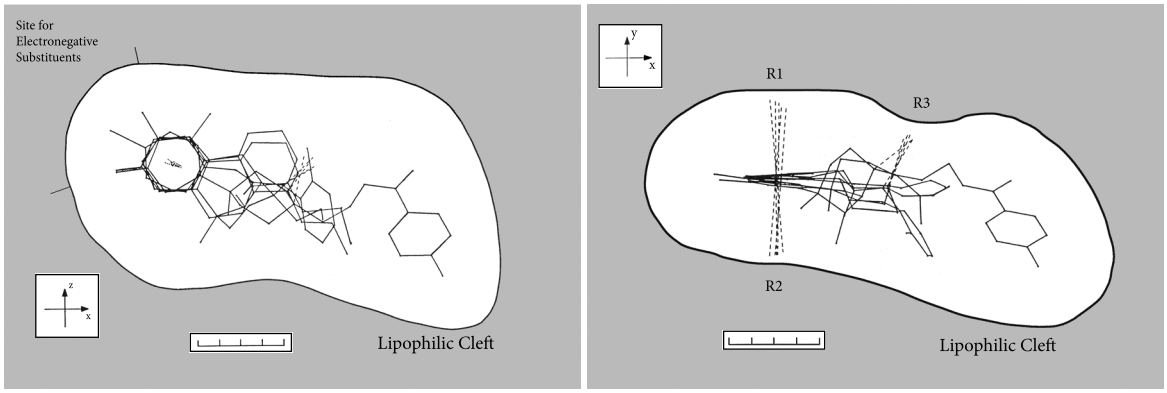


Figure 1.1: Manallack's topological pharmacophore combines receptor features R1, R2, and R3, with two ligand-based features comprising the centroid of the aromatic ring and the position of the basic nitrogen atoms. Reprinted with permission from Manallack et al.[35] Copyright (1998) American Society for Pharmacology and Experimental Therapeutics.

common volume overlaps to the template structure were used to guide the alignment process.

The model was designed around the crystal structure of *trans*-(4a*R*,10b*R*)-9-OH-*N*-*n*-propyl-octahydrobenzo[*f*]quinoline, a relatively rigid ligand that demonstrated a high eudismic ratio for σ

receptor sites.[38] High-affinity ligands towards σ sites defined by the radioligand [^{3}H](*R*)-3-PPP were selected as active analogues, although (*R*)-3-PPP was later shown to have mixed relative affinities with respect to σ-1 and σ-2 sites.[4] Crystal structures of [^{3}H](*R*)-3-PPP and *d*-NANM, and the modeled structures of DTG and HAL were used in the alignment process. Torsional analysis was required for the modeled structures and (*R*)-3-PPP, whereas the pseudochiral configuration about the N of *d*-NANM required inversion for a better fit to the template ligand.

The final model suggested a distance of 5.06 Å between the aromatic and N features. Additional electrostatic calculations were employed in their study with equivocal results depending upon the scaffold of the analogs fitted to the model. A lipophilic pocket was hypothesized to accommodate steric features of some ligands that did not detrimentally impact affinity. While the construction of a model for the "σ" receptor is useful from a conceptual standpoint, this model regrettably suffers from a paucity of ligand-based features.

1.3.1.2 Gund pharmacophore (1991)

Gund and Shukla developed a three-point pharmacophore model based upon the structures of HAL, (*R*)-3-PPP, progesterone and dextropentazocine[39] in their neutral ionization states. Conformational analysis, molecular superposition, and electrostatics were all considered in the construction of the final model. The optimal superposition of all compounds produced 4 separate pairwise pharmacophore distance measurements.

The inclusion of progesterone as an "active" compound is questionable because of its low σ affinity, and marked differences in the pharmacophore features compared to the other active ligands used in their model development. Namely, progesterone lacks both the aromatic- and N-moieties present in the other compounds. This required special alignments of the centroid of ring B to the centroid of HAL's fluorophenyl ring or alternatively to selected atoms of (*R*)-3-PPP and dextropentazocine aromatic rings. Oxygen lone pair electrons from ring D of progesterone were aligned to the N lone pairs of the other compounds. These special alignment considerations and the use of a non-selective radioligand restrict the general applicability of the resulting model.

1.3.1.3 Gund pharmacophore (1992)

Gund et al. reinvestigated their prior model[39] after the identification of PRE-084 as a selective σ ligand.[40] As part of their modification, molecules were superimposed upon a single ligand, HAL. Template features selected as references for superposition were the fluorophenyl moiety, the basic N-atom, and the lone-pair of the N-atom (Figure 1.2). As with the prior model, special alignment considerations were required, especially in the case of progesterone. The positioning of the cyclohexyl moiety of PRE-084 in their final model was hypothesized to explain its selectivity towards σ receptors.

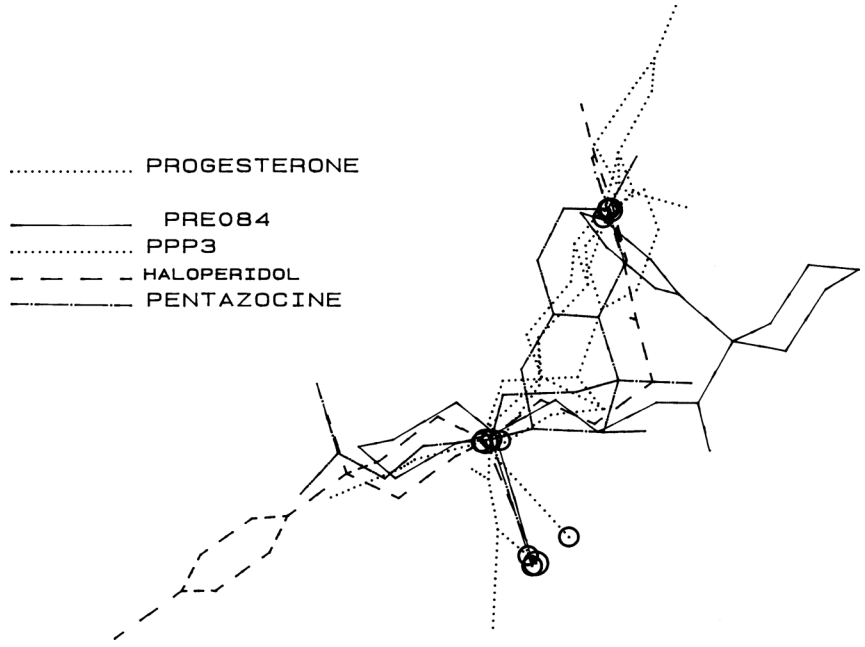


Figure 1.2: Gund's (1992) HAL-based pharmacophore model.[40] Reprinted with permission from NPP Books.[40] Copyright (1992) NPP Books.

1.3.1.4 Ablordeppy pharmacophore and CoMFA model (1992)

The model of Ablordeppey et al.[41] (Figure 1.3) was based upon *trans*-(4a*R*,10b*R*)-7-OH-*N*-*n*-propyloctahydrobenzo[*f*]quinoline, similar to the template utilized in the model of Manallack and Beart.[36] This was the first application of CoMFA[42] to σ QSAR development. Training and test set data for the study were generated from a variety of assay methodologies using the non-selective

radioligand [^{3}H]DTG without a σ-1 site masking agent. Assay variability may have been amplified in this model because of the combination of both K_i and IC_{50} data.

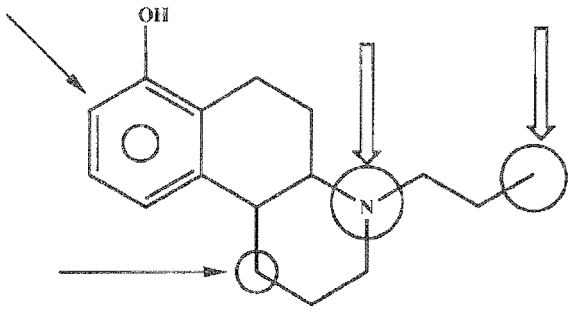


Figure 1.3: Ablordeppey's[41] template molecule *trans*-(4a*R*,10b*R*)-7-OH-*N*-*n*-propyloctahydrobenzo[*f*]quinoline, showing proposed molecular alignment sites. Reprinted with permission from Ablordeppey et al.[41] Copyright (1992) Springer SMB NL.

Basic pharmacophore features identified in their model were an aromatic ring centroid separated from a positive ionizable N by a minimum of an ethylene spacer, and an pendant propyl chain on the N-atom. Training and test set ligands were aligned to a minimum of 3 of the proposed sites, although the exact details of individual alignments were not specified. In addition, some of the ligands in the dataset possessed unresolved centers of asymmetry, and the rationale for the selection of one isomer for alignment over the other(s) was not described. A CoMFA based on the alignment of training set molecules exhibited remarkable internal consistency ($r^2 = 0.979, q^2 = 0.843$; 4 PLS components), and the external test set statistics ($Q^2 = 0.88, 0.67$; two different sets) reflected a high quality model.

1.3.1.5 Seri-Levy eudismic analysis

While not a pharmacophore model *per se,* Seri-Levy et al. employed conformational analysis and superposition of a series of 3-(3-hydroxyphenyl)piperidines (3-HPPs)[44] to investigate the stereochemical requirements of σ receptors.[43] The original data were generated from competition binding experiments using [^{3}H](*R*)-3-PPP as the radioligand. Stereoisomers of 3-HPP were aligned in two different ways for the calculation of electrostatic potential and shape chirality indices, and the superposition of the 3-hydrophenyl rings was found to be optimal. Correlation of the shape chirality

indices to eudismic indices revealed "non-Pfeiffer behavior"[45] for the homologues investigated and questioned the importance of an H-bond acceptor lying in proximity to these ligands within the σ receptor.

1.3.1.6 Beart pharmacophore model

Beart et al. examined the conformational requirements of a series of ifenprodil-related heterocyclic amino alcohols.[46] Their investigation used [^{3}H](*R*)-3-PPP as a radioligand. Receptor and ligand sites (see Figure 1.4), as well as the template ligand, were defined using the same criteria proposed by Manallack et al.[35] Low energy conformers were generated with by the application of MD or torsional analysis, and molecular models were superimposed by a three-point fit to within 0.6 Å. All of the compounds investigated fit the model well, with tight RMS fit and low energy with respect to the global minimum found through the conformer search protocols.

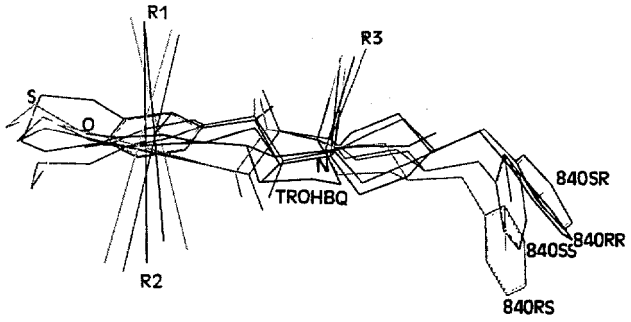


Figure 1.4: Beart's pharmacophore model[46] elaborated upon the template of Manallack,[35] focusing on the SAR of ifenprodil analogues. Reprinted with permission from Beart et al.[46] Copyright (1994) Elsevier Science Publishers

1.3.2 Sigma-1 models

1.3.2.1 Carroll pharmacophore model

Carroll et al. developed a σ-1 pharmacophore by modification of their previously proposed PCP pharmacophore motif.[47,48] While not strictly a σ-1 model, as the activity values were derived from experiments using both [^{3}H](*R*)-3-PPP and [^{3}H]dextropentazocine as radioligands, the features of

benzomorphan scaffolds aligned to their PCP model were the basis for pharmacophore development. Like the model of Manallack et al.,[35] three receptor features were assigned based upon a vector placed normal to the plane of the aromatic ring at its centroid along with a H-bond vector feature involving the lone pair on the N atom, although the exact placement of the N was deliberately left unspecified. An additional receptor feature was proposed to comprise a lipophilic pocket in the receptor capable of inducing selectivity for dextrorotatory benzomorphans depending upon the nature of the pendant N-alkyl substituents.

1.3.2.2 Elaborated Carroll pharmacophore model

Carroll et al. revisited their previous molecular modeling study[47] with a deeper investigation into the flexibility of *N*-substituted *N*-normetazocine side-chains.[49] This modification allowed the formation of additional hypotheses (see Figure 1.5) regarding the common volumes occupied by the benzomorphan side-chains and the volumes unique to the side-chains of high- and low-potency ligands.

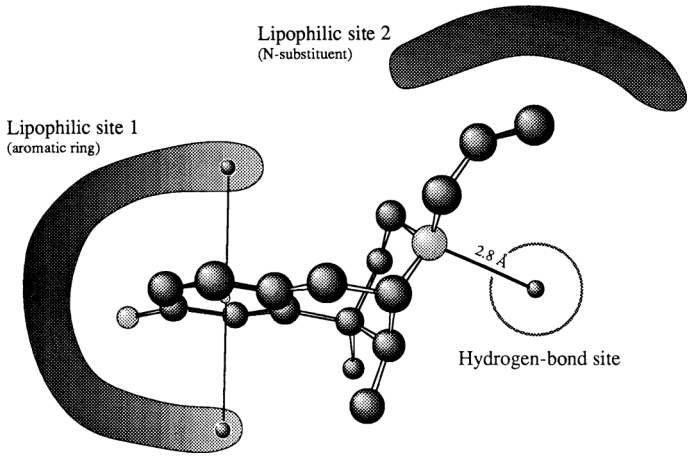


Figure 1.5: Carroll's *N*-substituted *N*-normetazocine based pharmacophore.[49] The authors investigated flexibility of side-chains at the proposed Lipophilic site 2. Reprinted with permission from NPP Books: Ann Arbor, MI, 1992.[49] Copyright (1992) NPP Books.

1.3.2.3 Gilligan pharmacophore

Gilligan et al. provided the first model explicitly investigating the nature of σ-1 binding requirements[50] utilizing *d*-NANM as a competitive binding radioligand. Based on the pharmacodynamic characteristics of 15 compounds with selectivity for σ-1 receptors over dopamine D_2 and 5-HT_{2A}, four pharmacophore features were identified as important elements for σ-1 affinity. These features comprise a basic N attached to two separate hydrophobic moieties, with an H-bonding feature between the nitrogen and its farthest hydrophobic partner (preferably an aromatic moiety).[50] The distances between such features were calculated by conformational analysis, averaged and published along with their standard deviations, all of which fell within 2 Å. While this pharmacophore is historically significant, the relative contribution of each feature is not readily apparent due to the use of a fairly congeneric series of compounds for pharmacophore elucidation and the same magnitude of receptor affinity of these compounds (8–51 nM).[50]

1.3.2.4 Hudkins pharmacophore motif

Hudkins et al.[51] described a pharmacophore based upon a set of caramiphen analogues. They proposed a "lipophilic site 1" associated closely with a N-binding site, together corresponding to ligand features of benzomorphans and 4-aryl-piperidines. A distal "lipophilic site 2" and alternative binding mode was proposed to explain the affinity of the arylcyclopentyl ester scaffold of their designed analogues and HAL. Distances were discussed in terms of methylene spacers, and no discussion of intersite angles was presented.

1.3.2.5 Glennon pharmacophore motif

Glennon et al. proposed a general three-point motif for σ-1 binding based upon a congeneric series of relatively flexible phenylalkylamines using [^{3}H]dextropentazocine as radioligand.[52] The salient features of their model include a hydrophobic site in the receptor, a proton-donating site corresponding to the almost requisite amine motif, and a secondary hydrophobic site with a propensity for accommodating bulky groups.[52] While there are three site points to this model, they were

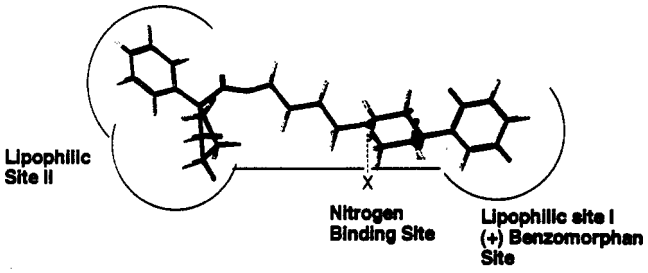


Figure 1.6: Hudkins' 3-site pharmacophore[51] recapitulates the presence of two hydrophobic sites separated by a positive-ionizable N-binding site. Reprinted with permission from Hudkins et al.[51] Copyright (1994) American Chemical Society.

presented in terms of the distances of each hydrophobic site to the N-atom. The distances between the hydrophobic groups was not stated, likely because of the wide range of distances tolerated between the primary hydrophobic site and the amine-N. This pharmacophore model was revisited in a comprehensive review of their group's σ-1 drug development strategy,[53] and also used to rationalize the SARs of 6,8-diazabicyclo[3.2.2]nonan-2-one and 6,8-diazabicylo[3.2.2]nonen-2-one derivatives.[54,55]

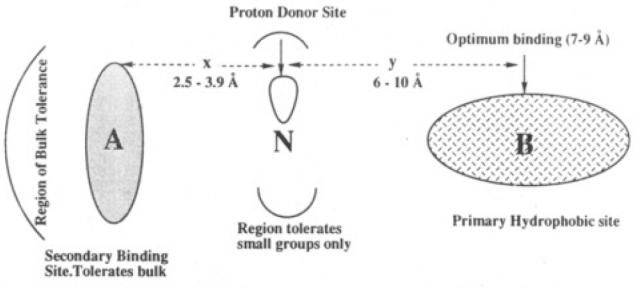


Figure 1.7: Glennon's 3-site model[52] provided general intersite distance information and proposed a receptor region tolerating hydrophobic bulk. Reprinted with permission from Glennon et al.[52] Copyright (1994) American Chemical Society.

1.3.2.6 Ablordeppey pharmacophore and CoMFA model (1998)

As part of an investigation of the configurational requirements of the *endo*- and *exo*-stereoisomers of the high-affinity ligand SC-50691, Ablordeppey et al. revisited the model of Glennon et al.[52] with a CoMFA analysis based upon dextropentazocine as a template.[56] After aligning 1-(5-phenylpentyl)-piperidine to the template, the remaining compounds in the dataset were aligned to either

the template or to the representative piperidine. The distance between the "phenyl-B" site and the amine-N of either the template or of the piperidines was held constant through a heuristic set of RMS fitting criteria while the remainder of each molecule was allowed to attain an extended conformation in the sterically accommodating "phenyl-A" region.[56]

Significantly more care was taken in the development of this model than in the their prior non-selective σ pharmacophore.[41] The training set represented alkyl- and aryl-amines, piperidines, piperazines, and a variety of compounds from different pharmacologic classes with σ-1 affinity, some with significant eudismic ratios. The test set was well sized, comprising 25% of the total number of compounds, and was also well within the domain of applicability of the training set. This was reflected in the external test statistic ($Q^2 = 0.65$) and the accurate prediction of the affinity constants of the resolved isomers of SC-50691. Their final model based on 64 total compounds demonstrated remarkable internal correlation and consistency ($r^2 = 0.989, q^2 = 0.732$; 7 PLS components).

1.3.2.7 Huang pharmacophore and CoMFA model

The work of Huang et al.[57] focused on derivatives of *N*-(1-benzylpiperidin-4-yl)-3-bromophenylacetamide (BPP). Through conformational analysis of BPP and superimposing a low-energy conformer onto pentazocine with a few manual adjustments, the authors were able to align a set of 79 BPP derivatives[57,58] for CoMFA studies. As part of their investigation, they sought to probe the importance of the carbonyl-to-N distances on σ-1 affinity. Intersite distances of BPP features in common with those present in the Glennon et al. pharmacophore[52] were also enumerated. The full matrix of intersite distances was not disclosed.

CoMFA results for 76 molecules in the dataset provided a model with superb correlation and consistency ($r^2 = 0.91, q^2 = 0.61$; 6 PLS components)[57] for the σ-1 dataset, but failed to perform suitably for the σ-2 dataset. The steric diversity around the benzyl-group corresponding to Glennon's secondary binding site was much less than that presented by the arylacetamide moieties corresponding to the primary hydrophobic site. Because of this choice, the steric tolerance of the

secondary binding site could not be corroborated. However, the steric and electrostatic nature of the primary hydrophobic receptor site were substantially more well defined by the CoMFA study.

1.3.2.8 Cao CoMFA model

Cao et al. used [3-(*cis*-3,5-Dimethyl-4-[3-phenylpropyl]-1-piperazinyl)-propyl]-*N,N*-*bis*(4-fluorophenyl)amine as template for the alignment of piperazinyl *bis*(4′-fluorophenyl)amine derivatives. Two alignments based on alternative assignment of the piperazine N-atoms as the ubiquitous amine-N feature present in σ pharmacophores were utilized, with the fluorophenyl-ring systems serving as the classic σ hydrophobic groups. The preferred alignment based upon the CoMFA results indicated that the proximal-N to the *bis*(4-fluorophenyl)amine served as a better surrogate for the requisite N-feature. Although precise intersite distances were not presented, the best CoMFA model had a respectable level of internal correlation and consistency ($r^2 = 0.929, q^2 = 0.521$; 4 PLS components).[59]

1.3.2.9 Gund pharmacophore model (2004)

The model published by Gund et al. in 2004[60] was templated upon PD144418, with superposition of spipethiane, dextropentazocine, and HAL onto the general CNS motifs described by Lloyd and Andrews[37] along with an optional O- or S- feature present in a number of the molecules. Electrostatic potential contours were used to characterize the placement of electronegative features, suggesting that the secondary binding site plays an important role in ligand affinity. The final model included a total of 3 ligand features, and the performance of σ-1 selective agents vs progesterone in fitting the pharmacophore was notable.

1.3.2.10 Jung DISCOtech pharmacophore and CoMFA model

Jung et al. employed DISCOtech on a series of spipethiane analogues, piperidine- and piperazine-analogues of caramiphen, benzoxazolones, benzothiazolones, and several notably σ-1-selective molecules from the literature to develop a pharmacophore alignment and subsequent CoMFA

model.[61] The training set comprised a total of 43 compounds and a test set of 5 compounds, and both sets represented diverse scaffolds ranging over 3 orders of magnitude in affinity for dextropentazocine defined sites. An initial 3-point pharmacophore including the aromatic ring centroid, the N-atom, and a projected H-bond from the N provided CoMFA models with poor results. They successfully overcame this obstacle by further optimization of conformers with semiemperical AM1, Hartree-Fock, DFT, or MP2 calculations, in tandem with scaling the projected H-bonding distance down to 1.4 Å. The reoptimization was followed by a very specific atom-based alignment scheme, and CoMFA analysis. AM1 charges provided better fits for electrostatic contributions, whereas the HF geometries provided more significant steric contributions to the PLS regression. The HF methodology also enhanced the external test set predictivity.

1.3.2.11 Laggner HypoGen pharmacophore model

Laggner et al. used training and test sets of diverse pharmacological classes and a wide range of activities to develop pharmacophore models for σ, emopamil binding protein, and yeast ERG2.[62] The training set of 23 compounds was deliberately chosen to reflect diverse structures and a substantial range in affinity, as encouraged by the HypoGen documentation,[63] although the σ-1 affinity data were not spread equally through the range. Pharmacophores for all three targets presented 5 common features; four hydrophobic ligand sites and a single positive ionizable N-atom. The top σ-1 model had high correlation (Pearson $r = 0.926$) and cost function analysis following response randomization indicated a high degree of confidence that the correlation was not spurious (95% confidence level). Estimated affinities were reported for a test set of 9 ligands, although the affinity of one of the σ-1 compounds was not determined. While the authors did not explicitly state the performance of the pharmacophore model on this external test set in terms of the Pearson correlation coefficient, the value is readily calculated from their data ($r = 0.403$). An agreement was found between their σ-1 pharmacophore and that developed by Glennon et al.[52] Furthermore, application of their pharmacophore model to a virtual screening protocol resulted in the discovery of 5 unique hits with $K_i \leq 100$ nM.

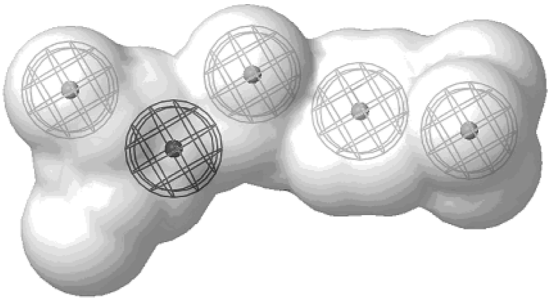


Figure 1.8: Laggner's 5-feature HypoGen pharmacophore[62] incorporated compounds from a diverse set of structural classes. Reprinted with permission from Laggner et al.[62] Copyright (2005) American Chemical Society.

This model was later applied to two series of alkenyl- and arylalkyl-amines where it was found to consistently overestimate affinity values.[64] The discrepancy in predicted vs observed binding affinity was ascribed to interlaboratory variations and the inclusion of the particularly high-affinity compound fenpropimorph in the original training set.

1.3.2.12 Zampieri HypoGen pharmacophore model

Zampieri et al. used HypoGen methodology to derive an interesting pharmacophore from a series of 31 benzooxazolones.[65] While the affinity range of training set structures and the size of the dataset fit the suggested criteria found in the HypoGen documentation,[63] the diversity of the selected structures is questionable, as the main difference in each "series" is the length of the linker from the N-feature to the benzooxazolone-N (i.e. 3–4 methylene units), and in the case of the piperidine series, the length could be interpreted as a constrained 4-methylene unit linker. Notwithstanding this caveat, the top-ranked hypothesis included five features which were all consistent with the broader σ-1 literature, such as an aliphatic hydrophobic site, two aromatic hydrophobe sites, a positive ionizable N-site, and an H-bond acceptor. Cost function analysis indicated a high confidence in a true correlation (Pearson $r = 0.896$) between predicted and experimental activities. A test set of related benzylpiperidine-4-carboxamides and σ-1 reference ligands performed remarkably well (Pearson $r = 0.882$) when aligned to the pharmacophore model. Additionally, response randomization suggested a statistical significance of 98% for the top-ranked hypothesis. This model

was later used in the refinement of the first published σ-1 homology model.[15]

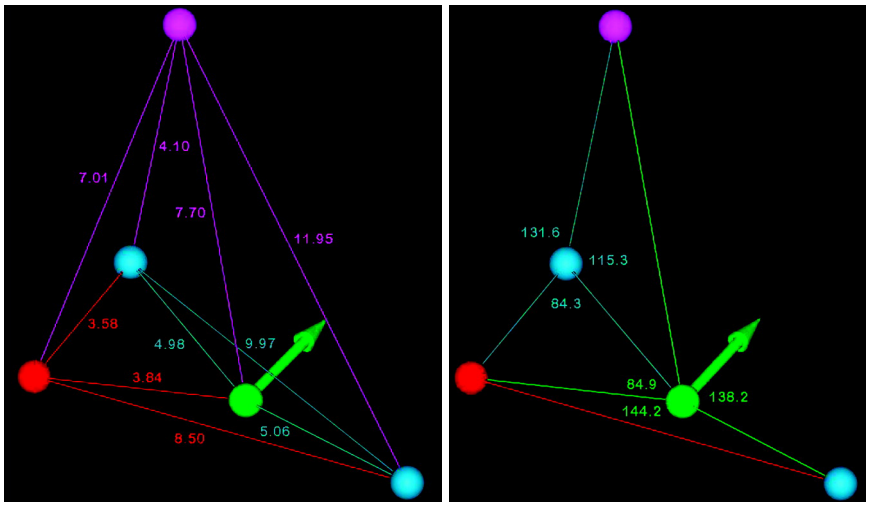


Figure 1.9: Zampieri's 5-feature benzooxazolone-based pharmacophore[65] includes an H-bond acceptor site and differentiates between aromatic and aliphatic hydrophobic features. Reprinted with permission from Zampieri et al.[65] Copyright (2009) American Chemical Society.

1.3.2.13 Oberdorf Quasar pseudoreceptor model

Oberdorf et al. used a congeneric series of spirocylic piperidines to develop a pseudoreceptor model of the σ-1 receptor.[66] Out of the 87 total structures analyzed, only 5 where achiral, whereas the remainder comprised 41 enantiomeric pairs representing the racemate compounds tested in vitro. Development of the pseudoreceptor model required the initial preparation of a pharmacophore for structure alignment. Towards this goal, structures were protonated prior to conformational analysis and alignment, making this study distinct with respect to the other σ-1 models. A unique result of this study was the perception of an H-bond acceptor feature in the pharmacophore which complemented the positive ionizable nitrogen. According to the authors, the remaining sites presented features in line with the models of Glennon[53] and Laggner et al.[62] Unfortunately, the authors did not disclose the coordinates or relative distances of the features in this pharmacophore model.

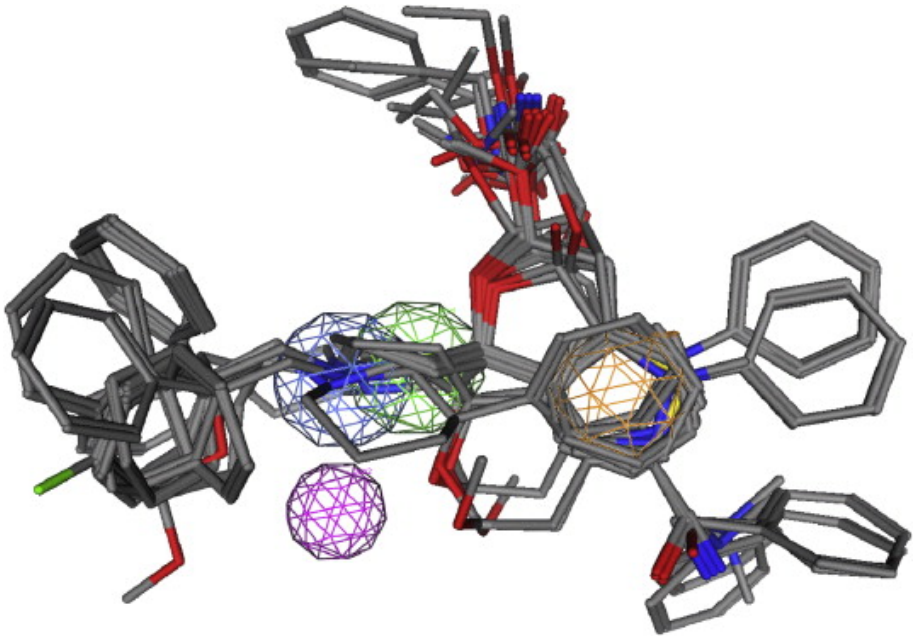


Figure 1.10: Oberdor's Quasar pseudoreceptor model.[66] Reprinted with permission from Oberdorf et al.[66] Copyright (2010) Elsevier Science.

1.3.2.14 Rossi Galahad pharmacophore model

Rossi et al. developed a 3-feature pharmacophore model from a set of congeneric arylalkenamines.[67] The most highly ranked hypothesis, according to their heuristics, possessed two hydrophobic features and a positive ionizable N. While the model was found to aid in classifying active vs inactive compounds, conventional methods of validating the model were not presented. Model parameters such as distances and coordinates between features were also not disclosed.

1.3.3 Sigma-2 models

1.3.3.1 Cratteri GRIND-based pharmacophore model

The model presented by Cratteri et al.[68] used grid-independent descriptors[69] to generate a description of the putative environment surrounding α-tropanyl derivatives in their bioactive conformations. Some of the derivatives were tested as racemate mixtures, and the decision was made to develop a model based upon the (*R*) isomers, stemming from their modestly higher eudismic ratio. A significant result of their analysis was a description of the putative dimensions of

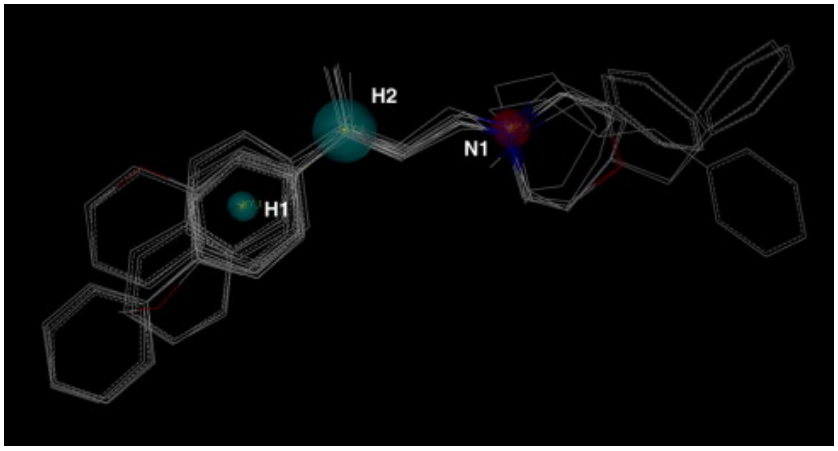


Figure 1.11: Rossi's Galahad pharmacophore[67] again proposed two hydrophobic features and a positive ionizable nitrogen, but this pharmacophore places both of the hydrophobic groups on one side of the nitrogen. Reprinted with permission from Rossi et al.[67] Copyright (2011) Pergamon.

three σ-2 receptor regions based on the selectivity of a subset of the data: distances between two hydrophobic regions, and from one of these to a H-bond donor region were disclosed. This suggests an upper limit on the total width of the binding pocket of the σ-2 receptor.

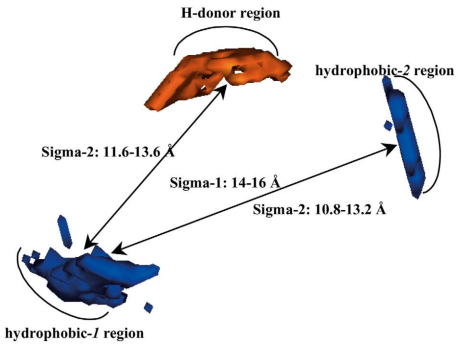


Figure 1.12: Cratteri's GRIND-based pharmacophore[68] provided a pseudoreceptor model which places some restrictions on the overall size of the binding site. Reprinted with permission from Cratteri et al.[68] Copyright (2004) Kluwer Academic Publishers.

1.3.3.2 Abate pharmacophore and CoMFA model

Abate et al. used an automated alignment of cyclohexylpiperazines and congeners to the template molecule, 1-Cyclohexyl-4-[3-(5-methoxy-1,2,3,4-tetrahydro-naphthalen-1-yl)propyl]piperazine ((*R*)-PB28), in their pursuit of a predictive CoMFA model for σ-2 ligands.[70] Initial CoMFA perfor-

mance with the automated alignment was poor, so an alternative manual alignment of the dataset to 1-Cyclohexyl-4-[3-(naphthalen-1-yl)propyl]piperazine was undertaken, with the focus not on global alignment of all features, but rather on the overlay of the piperazine ring. To simplify the alignment, and because of electrostatic considerations, the piperazine moieties were modeled in their dibasic ionization state. The manual alignment led to CoMFA models with both internal correlation and consistency, as well as external predictivity for structurally related compounds ($r^2 = 0.95, q^2 = 0.73, Q^2 = 0.55$; 4 PLS components).[70] The final model supported a SAR interpretation of the binding requirements of cyclohexylpiperazines to σ-2 receptors. Apart from suggesting an important σ-2 pharmacophore feature, no intersite distances between multiple features were proposed.

1.3.3.3 Laurini Catalyst pharmacophore model

The first ligand-based pharmacophore model specifically aimed at determining the features necessary for σ-2 affinity were recently reported by Laurini et al., based on the benzooxazolone motif.[71] This set of ligands had been previously used in the development of a σ-1 pharmacophore,[65] and share the same drawbacks with regard to the diversity represented in the training set. Affinities for σ-2 span a much narrower range than for σ-1, and are not distributed evenly through the training set.

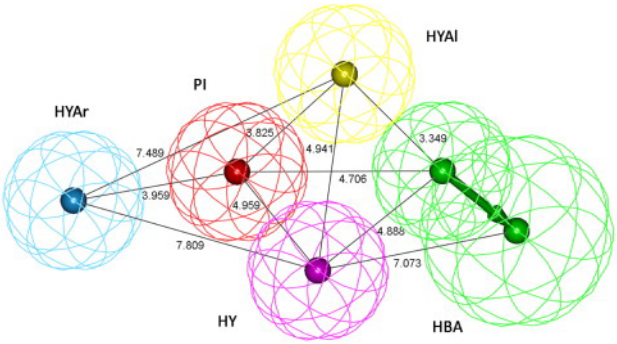


Figure 1.13: Laurini's 5-feature benzoxazolone-based σ-2 pharmacophore[71] implicated an absolute requirement of an aliphatic hydrophobic feature for σ-2 binding and revisits the H-bond acceptor feature proposed by Zampieri.[65] Reprinted with permission from Laurini et al.[71] Copyright (2010) Pergamon.

Assuming that the previous considerations do not adversely affect the regression, this is a groundbreaking pharmacophore. The model implicates an absolute requirement for an aliphatic hydrophobic moiety for high affinity, although the authors admit that σ-2 selectivity is not explained by this feature. An aromatic hydrophobic site and a general hydrophobic feature build upon this pharmacophore. The ubiquitous positive ionizable N is also present. Rounding out the 5-feature pharmacophore is an H-bond acceptor complementing the carbonyl of the benzoxazolones. Response randomization studies indicate a 95% confidence level that the hypothesis is statistically significant, and the robustness of the model is backed by leave-one-out pharmacophores showing no substantive difference from the best hypothesis.

1.3.4 "Sigma-3" model

Myers et al. used DISCO (as part of the Sybyl package) to develop a CoMFA model for a series of phenylaminotetralins which displayed affinity for a putative "σ-3" receptor.[21] Subsequently Bucholtz et al. determined that the predominant activity of these compounds was at histamine H1 receptors.[23] Accordingly, the development of their "σ-3" model and the corresponding QSARs will not be discussed, and is mentioned only for the edification of the curious reader.

1.3.5 Summary of pharmacophore models in the σ literature

As seen in Table 1.1, a great number of pharmacophore models have been proposed over the years. Many of the early pharmacophores, and several of the more recent σ-2 pharmacophores are based upon perceptions of a virtual receptor or projected points. Until the mid-nineties, these pharmacophore models were not developed with a focus on receptor subtype selectivity. Only two of the studies involved what would be regarded today as "diverse" structures; the majority were focused on elaborating the SAR of a congeneric series of molecules. Affinity prediction has also become more of a focus in the past decade. The consideration of molecular alignments has been a recurring challenge in σ pharmacophore development, requiring special consideration in many cases. When manual superposition to a template or automated alignments of congeneric series

are applied in CoMFA studies, there is a likelihood that spurious correlations will be found in the SAR because the chosen alignments do not accurately reflect the conformation of the ligands to receptor sites. Additionally, a majority of the experiments carried out with diverse scaffolds were performed with only a handful of compounds. Because of the symmetric nature of many of the 3-point pharmacophores with Hydrophobe-Nitrogen-Hydrophobe features coupled with the fact that many σ ligands possess a high degree of flexibility, the issue is raised over whether multiple binding modes may exist. Further complicating matters is the possibility of subsites on σ receptor subtypes. These factors all detract from the general utility of the majority of these models for ligand-based drug design.

1.4 Overview of σ binding assay methodology

An overwhelming number of radioligands and binding assays have been developed for imaging and competition binding studies of σ receptors.[72] Despite the preponderance of radioligands, there are few subtype selective compounds commonly used for σ-1 research, of which (+)-pentazocine is most commonly used, and only one generally-used radioligand (DTG) for σ-2 receptor assays, which is ordinarily accompanied by a modicum of PTZ to saturate residual σ-1 sites. Sigma receptors are ubiquitously expressed in all tissues with minimal specificity. While cloned σ-1 receptors have been expressed in yeast[14] and HeLa cells,[73] almost all competition binding experiments to date have been performed in brain or liver tissue homogenates from guinea pig or rat. The majority of σ-1 assays have been performed using guinea pig brain membranes, whereas rat liver membranes are generally preferred for σ-2. The diversity of assay methodologies presents a challenge for computational efforts aimed at generating QSARs and pharmacophore models, as the variability in assay performance under different conditions can lead to significant differences in perceived ligand affinity. This variability carries over as uncertainty in model development and negatively affects model performance.

Table 1.1: Overview of σ pharmacophore models

		Feature count				
Authors	Year	Receptor	Ligand	Lone pairs	QSAR	Reference
σ non-selective						
Manallack et al.	1988	3	2	0		35
Gund and Shukla	1991	0	2	1		39
Gund et al.	1992	0	2	1		40
Ablordeppey et al.	1992	0	4	0	•	41
Seri-Levy et al.	1994	0	1	0	•	43
Beart et al.	1994	3	2	0		46
σ-1 selective						
Carroll et al.	1992	3	2	0		47,49
Gilligan et al.	1992	0	4	0		50
Hudkins et al.	1994	3	0	0		51
Glennon et al.	1994	3	0	0		52
Ablordeppey et al.	1998	0	3	0	•	56
Huang et al.	2001	0	4	0	•	57
Cao et al.	2003	0	3	0	•	59
Gund et al.	2004	0	5	0		60
Jung et al.	2004	0	2	1	•	61
Laggner et al.	2005	0	5	0	•	62
Zampieri et al.	2009	0	5	0	•	65
Oberdorf et al.	2010	0	4	0	•	66
Rossi et al.	2011	0	3	0	•	67
σ-2 selective						
Cratteri et al.	2004	3	0	0	•	68
Abate et al.	2009	2	2	0	•	70
Laurini et al.	2010	0	5	0	•	71

1.5 Research Objectives

Given the lack of selective σ-2 probes and the lack of general utility of many of the modeling efforts to date, the field of σ research remains open to new discoveries. Modeling software and computational techniques have advanced significantly in recent years, and a fresh approach using curated data is overdue. That being said, σ ligand design has routinely focused on highly flexible molecules with a great degree of pharmacophore symmetry that pose challenges when there is a lack of crystallographic information to provide target structures. Virtual screening and affinity assessments, particularly efforts at identifying selective scaffolds, will require a more fundamental

understanding of the general binding requirements of σ ligands. As part of these efforts, the following objectives were established:

1. Create a database of binding competition experiments to identify experimental methodologies that are sufficiently similar for dataset collection.

2. Collect and curate data from the literature which utilize the most prevalent methodologies.

3. Use a combination of scaffold analysis, distance measures, and hierarchical clustering to generate representative training and test sets for classification of active and inactive molecules towards either σ-1 or σ-2, depending upon the underlying methodology.

4. Identify the most significant conformers of the active compounds for pharmacophore development.

5. Use these pharmacophores to clarify structural features necessary for affinity and selectivity.

2. METHODS

We have no future because our present is too volatile. We have only risk management. The spinning of the given moment's scenarios. Pattern recognition.

Pattern Recognition
William Gibson

2.1 Computational equipment

Database preparation and analysis was undertaken on a 2.8 GHz Intel Core 2 Duo Mac OS X laptop furnished with 8 GB 1067 MHz DDR3 RAM. Computational methods were performed on the same system, or on a 2.5 GHz Intel Core i5 Mac OS X desktop furnished with 4 GB 1333 MHz DDR3 RAM. CPU and memory intensive calculations were done on a Fedora Linux cluster comprising 8 Microway computers, four with 2.5 GHz 8-core Intel Xeon L5420 CPUs and 16 GB 667 MHz DDR2 RAM, and another four equipped with 2.27 GHz 16-core Intel Xeon L5520 CPUs and 32 GB 1333 MHz DDR3 RAM.

2.2 Data collection and curation

Articles with competition binding data were identified from the literature using a combination of electronic search and cross-referencing to related literature found in proceedings, books, and patents, to a limited extent. Additional sources of binding data included data generated by our lab and those generated by our colleagues. Bibliographic information as well as details concerning the

radioligand, masking ligands (if present), matrix (i.e. organism and tissue preparation), as well as PubMed ID (if available) were recorded in a PostgreSQL database (version 9.2). Records with competition binding data were analyzed to determine which experimental methodologies were most prevalent. An experimental methodology was defined as a combination radioligand, masking ligand, and matrix.

Following the identification of relevant data sources, those competition experiments with the most reliable data (e.g. K_i in lieu of IC_{50} data) were added to a project table in Maestro (version 9.3, Schrödinger, LLC, New York, NY, 2012). Molecules were sketched using the stereochemistry assigned in the original article, unless corrected for in an erratum, or unless there was evidence in the experimental section that the molecule had been incorrectly sketched in the paper. Affinity data and experimental methodology were annotated along with any assay limits, if applicable. In the case that the stereochemistry was unknown, ambiguous, or known to be tested as a racemate, the molecule was marked as racemate. Several other properties and SMILES strings were calculated using the Generate SMILES script in Maestro and QikProp (version 3.5, Schrödinger, LLC, New York, NY, 2012). Once sketched, LigPrep (version 2.5, Schrödinger, LLC, New York, NY, 2012), was used to clean up the structures and to generate relevant stereoisomers, if necessary. All molecules were double-checked for consistent stereochemistry and accurate affinity data entry. A Python script (Appendix E.1) was written to automate the processing of PubMed IDs into SMILES strings, but it was determined that the PubMed records were not reliable enough to identify molecules of interest.

2.3 Dataset composition

The initial dataset was divided into subsets representing each predominant methodology. These subsets were limited to contain molecules of unambiguous stereochemistry that were determined to have affinity within the assay limits. On occasion, a molecule would be tested more than once under a given set of experimental conditions, and thus would be replicated in the dataset. In order to deal with this situation, which was very common for reference compounds, the molecules were imported

into Canvas[74] (version 1.5, Schrödinger, LLC, New York, NY, 2012), duplicate identification was performed, and statistical analysis was carried out on the duplicates. This analysis was undertaken to determine the variability of the collated experimental data. After analysis, duplicate data points were removed, retaining the highest affinity (pK_i) measured in any experiment. This choice was made deliberately because of a classification technique (*vide infra)* used later on in the modeling process. Expurgated datasets were then exported as SMILES and CSV files.

2.3.1 Scaffold decomposition

Molecular scaffolds were decomposed by two methods implemented in Strip-It (version 1.0.1, Silicos-it, Schilde, Belgium, 2012). Initially, a canonical SMILES representation of each molecule was converted into RINGS_WITH_LINKERS_2 scaffolds preserving the ring structures, any linking chains between rings, and exolinker double bonds. Aside from these linkers, all pendant groups are eliminated in this process, which allows for a mapping of the molecule to an underlying scaffold that may be shared by other analogues. All of the unique scaffolds were then subjected to a subsequent decomposition into MURCKO_1 core scaffolds. The core scaffolds are similar to the former, with the exception that all atoms are converted to C, the bond order between connected atoms is reduced to a single bond, and exolinker double bonds are removed. This process allows for the perception of common ring and linker systems and reduces the ambiguity presented by unsaturated systems and heteroatoms. It should be noted that information about stereochemical configuration is lost in the scaffold generation process, although this is fortuitous since it allows for molecules that have identical atom connectivity to be clustered together and provides an avenue for investigating eudismic analysis.

2.3.2 Core fingerprints

A measure of the difference between scaffolds was required in order to cluster similar scaffolds. Dendritic and radial (extended-connectivity) fingerprints calculated by Canvas were evaluated for this purpose based on the moderate to high number of bits typically set “on”, and on their

performance in screening enrichment.[75] Stereochemical information was ignored in the hashing of radial fingerprints in order to be consistent with the scaffold generation process. Default atom typing (Daylight invariant and Fn functional types, respectively) were used in preparing core fingerprints. The impact of atom typing was not investigated because the core scaffolds do not distinguish atoms other than carbon, and also because bond orders were reduced by the core decomposition process.

With binary bit-strings, the minimum distance provided with this metric is 0, meaning the molecules are indistinguishable by fingerprint. The distance increases as the number of bits which are different in each fingerprint increases. Several distance measures are provided in Canvas, and it was determined that the Euclidean distance measure worked very well to distinguish clusters of molecules with similar scaffolds. Euclidean distance $D = \sqrt{A + B}$, where A is the number of bits exclusively set "on" in the bitstring of scaffold molecule **A,** and B is the number of bits exclusively set "on" in the scaffold of molecule **B.** Based on the initial results (data not shown), it was determined that radial fingerprints at the default level of 4 iterations provided a sufficient degree of distance to ensure that core scaffolds could be distinguished from one another, whereas dendritic fingerprints with the default 5-atom path length led to a small but significant proportion of cores that were not distinguished.

2.3.3 Core clustering and network visualization

Following the general procedure of Guiguemde et al.,[76] the McQuitty linkage method of hierarchical clustering was chosen in order to ensure that every core scaffold was connected to at least one other core by a node. Kelley's criterion[77] was used to select an appropriate number of clusters. This particular method is well suited for the application of common scaffold perception when paired with a suitable fingerprint and distance metric. Structures and clusters are paired based on the minimizing the average distance between members, and as clustering progresses, more distant candidates are paired incrementally in such a manner to ensure that the largest clusters of similar cores are produced. The end product of clustering is a dendrogram relating successive nodes to leaf core scaffolds and child nodes.

The visualization method of Guiguemde et al.[76] was implemented with slight modifications using custom scripts to process the scaffolds generated by Strip-It and the cluster dendrograms produced by Canvas. An edge network consisting of molecule to scaffold, and scaffold to core relationships was supplemented by core to node, and node to node edge relationships from the dendrogram. When singleton molecule to scaffold relationships were identified, they were replaced by molecule to core relationships and the original molecule to scaffold relationships were deleted from the network. No attempt was made to identify common child scaffolds. The resulting network was visualized using the yFiles circular network layout in Cytoscape[78] (version 2.8.3, Cytoscape Consortium). Binding affinity data for molecules were imported from the CSV file as node attributes. By applying node size and color mappings based upon binding affinity, clusters with a sufficiently large number of members and a suitable spread of affinity data could be selected and assigned cluster membership for pharmacophore and QSAR development in Phase. Suitable values for core-node distance for cluster discrimination were found at a Euclidean distance of ~10–12, based on the classical benzomorphan and morphinan scaffolds. Scripts for scaffold decomposition, core fingerprinting, and core clustering may be found in Appendix A.

2.3.4 Selection of classification model training and test sets

Using the range of affinity values determined from the duplicate experimental points within each individual methodology, it was possible to define a range of affinity values to classify set members as active, not determined, or inactive. The choice of selecting the highest affinity value for each molecule biases the selection of the inactive set towards truly inactive compounds while placing a handful of compounds that would have been indeterminate for classification purposes into the active set. Once suitable affinity ranges were selected, the inactive and active members of each cluster were identified, and up to three members were selected from each cluster to achieve an acceptable level of diversity among scaffold classes for training and test sets. Class membership and cluster information was exported from Cytoscape to Canvas as a CSV file, so that the original datafile could be used to generate the classification model sets.

2.4 Generation of conformers

All pharmacophore modeling approaches require a set of ligand conformations to be generated either before or during the pharmacophore elucidation step. For a useful model, the set of ligand conformers must contain conformations very near to those found in the target–ligand complex. ConfGen[79] (version 2.3, Schrödinger, LLC, New York, NY, 2012.) is a tool included in the Schrödinger Suite that is integrated in pharmacophore and docking protocols. Chen and Foloppe developed an optimized set of parameters for ConfGen that more frequently identifies conformers close to established bioactive states of two sets of ligands extracted from crystal structures.[80] These modifications have since been incorporated into the standard protocols, with the exception of two modifications to the CGO6 and CHYD parameters which control elimination of "compact" structures and hydrogen-bonding electrostatics, respectively. To this end, the CGO6 opcodes in the Macromodel file were deleted, CHYD was added and the first argument in the opcode string was set to -1. These additional "compactness-allowed" modifications were utilized because the impact on the total number of conformers generated is minimal and also because of the extension of the conformational sampling to potentially important conformations of highly-flexible ligands, which are frequently presented in the σ-literature.

2.5 Model development

2.5.1 Classification models

Multiple Instance Learning via Embedded instance Selection (MILES) is a supervised learning technique proposed by Chen et al.[81] and extended by Fu et al.[82] in the context of drug activity prediction. MILES, as applied to bags of conformers and their relationships to individual conformers, is particularly useful as a means of associating the activity of a molecule to individual conformers across a set of training molecules.

We used this technique, with a few modifications, to develop classification models for σ receptor ligands, using prototype conformational instances to generate more robust pharmacophore models.

This is particularly important for σ-1 and σ-2 ligands, as very few are rigid enough to provide simple solutions, i.e., the vast majority of active and inactive compounds are highly symmetric, flexible ligands, with little bulk or chirality to assist in interpreting how pharmacophore features might correspond to one another. Another issue with σ ligands is that no crystallographic information is presently available that might allow for structure-based perception of multiple binding modes. MILES assists in overcoming this problem by allowing for the selection of multiple significant pharmacophore configurations which can be used in traditional pharmacophore modeling applications.

2.5.2 Pharmacophore fingerprints

Pharmacophore fingerprints are a useful means of encoding the distances between potential pharmacophore features into a string of bits that represent the presence or absence of some particular combination of features. A variety of general molecular features such as hydrophobic, aromatic, positive, negative, and hydrogen bond donor or acceptor sites is typically used in tandem with binned distances to generate a hashed fingerprint. Although it is possible to calculate fingerprint data based on 3-point pharmacophores, 4-point pharmacophores, or a combination of both, only 4-point pharmacophores were used in this work. Among the reasons for selecting 4-point pharmacophores are the ability to infer the presence of chirality,[83] and by not combining them with 3-point features the impact of correlated descriptors is reduced.[84] Four-point pharmacophore fingerprints were generated using the default features defined by Phase[85] (version 3.4, Schrödinger, LLC, New York, NY, 2012), along with a custom feature matching the centroid of piperidine and piperazine moieties. In some cases, no four-point pharmacophores could be generated for a structure, and these were removed from the 1n-SVM classification modeling process. Several hundred thousand fingerprint bits are typically calculated during this process, which leads to additional computational expense when similarity measurements are calculated directly within Canvas. Given a large number of conformers and fingerprint bits, the memory and computational cost can exceed the limits of contemporary workstations.

Canvas provides several options to pre-filter fingerprints after their calculation, among them the ability to discard bits that are set by less than a certain percentage of conformers, or alternatively the most informative bits can be retained. Informative bits are decided by calculating the frequency with which each bit is turned "on" based on the total number of molecules in the collection. For classification purposes, optimally informative bits in a well constructed collection will trend towards a frequency of 50%, and thus the ranking

$$r_{\text{inf}} = |f_{\text{bit}} - 0.5|,$$

where r_{inf} is the informative bit ranking given the bit frequency f_{bit}. After the bits are ranked, informative bits are retained based on those with the least deviation from optimal. The original Significance Analysis of Pharmacophores (SAP) method described by Fu et al.[82] implemented a pre-filtering cutoff of 5% bit frequency, which can result in fingerprint lengths of several tens of thousands. Hence the option to retain informative bits was investigated to compare the utility of each approach for activity classification. One immediate benefit of the latter option is that an optimal fingerprint of arbitrary length can be determined heuristically to reduce computational overhead when applying the SAP filtering method. For comparison of fingerprint lengths and to assess the impact of SAP on the performance of MILES, a variety of fingerprint lengths were selected, including unfiltered fingerprints, those filtered by eliminating the least significant 5% of bits, and a range of informative bit string lengths from 256 to 16,384.

2.5.3 Implementation of SAP

SAP was implemented using the samr package[86] in R,[87] closely following the methods described by Li et al.[88] and Fu et al.[82] Fingerprint data were read into a data table and transposed to create an appropriately formatted matrix. The "two class unpaired" response model was selected, and activity classifications were used as outcome measurements, with 500 permutations of the activity class labels used as a control. A Δ table was computed from the data and divided into 100 intervals. Significance analysis was performed with the Δ corresponding to an estimated false positive rate (FPR) of zero at the 90$^{\text{th}}$ percentile. As shown in Figure 2.1, a sizable number of pharmacophore features can be

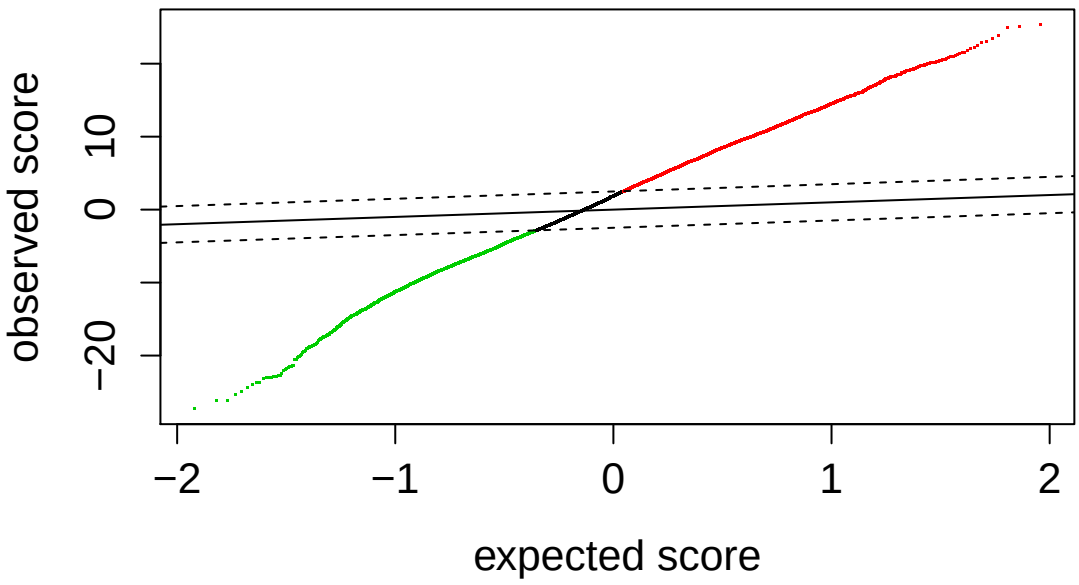


Figure 2.1: The results of SAP analysis provide two sets of bits representing pharmacophore features which are either significant (red) or insignificant (yellow) for the appropriate classification of binding activity. Insignificant bits are removed from the fingerprint and used in subsequent similarity calculations.

identified as lacking significance for accurate activity classification. In the initial experiments, care was taken to ensure that the fingerprints chosen for significance analysis were only selected from the conformers corresponding to training set molecules. Model sets were stratified between training and test in a 2:1 ratio on the complete dataset after sorting by activity. Further experiments were conducted with the inclusion of all fingerprints without regard to training or test set assignment. All pharmacophore fingerprint bits having a non-negative correlation to activity were retained for the entire set of conformers. Code detailing the SAP process is included in Appendix B.

2.5.4 Instance-based similarity mapping

In the MILES formulation, feature mapping can be described in terms of either a distance or a similarity mapping.[82] We chose to implement similarity mapping of molecules onto conformations,

such that

$$S(\mathbf{M}_i, \mathbf{C}^r) = \max_j S(\mathbf{C}_{ij}, \mathbf{C}^r),$$

where each molecule $\mathbf{M}_i$ is evaluated against every conformer $\mathbf{C}^r$ in the embedded feature space as the maximum similarity of any individual conformer $\mathbf{C}_{ij}$ in each bag to each individual conformer in every bag. By using a similarity measure, it is possible to avoid a troublesome hurdle when it comes to ranking conformers, namely that distance measures trend towards 0 if there is no perceivable difference in the pharmacophore fingerprints. When this occurs, the ranking algorithm will be unlikely to predict that the top-ranked conformations are mapped as the most active conformer, even though the weight of the support vectors may otherwise be high. This happens because the most likely conformations of an active molecule will have solutions equal to zero when mapped from their own bag. On the other hand, similarity measures trend towards higher values as the molecules share more pharmacophore fingerprint bits, even if not normalized by design or coercion, and thus the solutions have a positive correlation to the inputs in the feature mapping.

The Kulczynski similarity measure (see Table 2.1), was initially investigated as a way to ensure that the support-vector machine (SVM) correctly mapped active conformers to their parent molecules (*vide infra)*, and to average out the similarity of each conformer to the shared pharmacophore features of both partners. This measure benefits from omitting the bits from each pharmacophore fingerprint that are set "off", which is problematic in that activity prediction based on pharmacophore fingerprints is not formulated in a manner consistent with having any knowledge of what it means for a bit to be "off" when making comparisons between molecular conformers.[89] Cosine, Dice, McConnaughey, Petke, Simpson, Tanimoto, and Tversky similarity metrics were also investigated for their performance in the MILES context for similar reasons. Training and external test sets were assigned using the same stratified 2:1 approach described in 2.5.5. Conformations representing the test set were removed from the instance-based embedding. Code for instance-based similarity mapping is included in Appendix C.

Table 2.1: Measures of similarity. Canvas provides the following similarity metrics that lack an explicit count of bits that are set to 0 in both pharmacophore fingerprints.

Similarity metric	Definition[a]
Cosine	$\frac{c}{\sqrt{ab}}$
Dice	$\frac{c}{0.5(a+b)}$
Kulczynkski	$0.5\left(\frac{c}{a}+\frac{c}{b}\right)$
McConnaughey	$\frac{(c\times c)-(a-c)(b-c)}{ab}$
Petke	$\frac{c}{\max(a,b)}$
Simpson	$\frac{c}{\min(a,b)}$
Tanimoto	$\frac{c}{a+b-c}$
Tversky	$\frac{c}{\alpha(a-c)+\beta(b-c)+c}$

[a]For binary fingerprints F1 and F2, a bit is set "on" and given the value "1" if the feature represented by that bit is present in the fingerprint; otherwise, the bit is given the value "0." a is the count of bits set on in F1, b is the count of bits set on in F2, and c is the count of bits that are set on in both fingerprints. In the Tversky metric α and β are parameters used to scale the count of bits that are exclusively set on in F1 and F2, respectively.

2.5.5 Implementation of 1-norm SVM

Support vector machines are commonly used for classification purposes, and can be useful for evaluating novel compounds as "active" or "inactive" based on competition binding data. Pharmacophore fingerprints which are derived from multiple conformations of chemical entities are prone to have common spurious configurations that provide no productive information about their complexes with biological targets. In this context, 1-norm SVMs are particularly useful because they are less susceptible to over-fitting the input data, and tend to eliminate noise resulting from common but meaningless pharmacophore configurations. Linear programming (LP) techniques have previously been formulated to solve 1n-SVMs,[90–92] and have been used in the context of pharmacological classification.[81]

The parametric-cost linear program of Yao and Lee[92] uses the standard formulation:

$$\begin{aligned} \underset{\mathbf{z}\in\mathbb{R}^N}{\text{minimize}} \quad & (\mathbf{c} + \lambda\mathbf{a})'\mathbf{z} \\ \text{subject to} \quad & \mathbf{A}\mathbf{z} = \mathbf{b} \\ & \mathbf{z} \geq 0, \end{aligned}$$

along with the following definitions:

$$\begin{aligned} \mathbf{z} &\equiv (\ \beta_0^+ \ \ \beta_0^- \ \ (\boldsymbol{\beta}^+)' \ \ (\boldsymbol{\beta}^-)' \ \ (\boldsymbol{\zeta}^+)' \ \ (\boldsymbol{\zeta}^-)' \ )' \\ \mathbf{c} &\equiv (\ 0 \ \ 0 \ \ \mathbf{0}' \ \ \mathbf{0}' \ \ \mathbf{1}' \ \ \mathbf{0}' \ )' \\ \mathbf{a} &\equiv (\ 0 \ \ 0 \ \ \mathbf{1}' \ \ \mathbf{1}' \ \ \mathbf{0}' \ \ \mathbf{0}' \ )' \\ \mathbf{A} &\equiv (\ \boldsymbol{Y} \ \ -\boldsymbol{Y} \ \ \text{diag}(\boldsymbol{Y})\mathbf{X} \ \ -\text{diag}(\boldsymbol{Y})\mathbf{X} \ \ \mathbf{I}' \ \ -\mathbf{I}' \ )' \\ \mathbf{b} &\equiv 1. \end{aligned}$$

The solution, $\mathbf{z}$, minimizes the distance of support vectors from the hyperplane given the objective function. Here $\mathbf{c}$ is a vector of normalized indices of the *slack variables* used as part of calculating the objective function, $\mathbf{b}$ is a vector representing the right-hand side of the *constraint constants,* $\mathbf{a}$ is a vector used to implement the objective function, $\boldsymbol{Y}$ are the class labels, $\mathbf{X}$ is the feature matrix in the context of the MILES[81] formulation, and λ is a tunable *control parameter* of the objective function. An optimal hyperplane $\beta_0 + \boldsymbol{\beta}\mathbf{X}$ is then solved subject to the non-separable case of a 1n-SVM classifier by the introduction of the slack variable ζ that allows for some points to be misclassified. Classification of activity is based on the sign of the output, $\text{sgn}(\beta_0 + \boldsymbol{\beta}\mathbf{X})$.

Tuning of the 1n-SVM (as illustrated in Figure 2.2) was accomplished using the perry package[93] of R, with 5-fold cross-validation using random splits of the data for a total of 15 replicates. The λ parameter was initially chosen by validations over the range of 10^{-12}–10^{4} at each power of 10. Prediction error was assessed as the misclassification error rate. After narrowing down the range for λ, a second cross-validation was undertaken at 21 points ranging from the nearest lower power of 10 to the higher, spaced at arithmetic intervals between each order of magnitude. An optimal tuning parameter corresponding to the least mean cross-validation prediction error was then used to generate the 1n-SVM slack and penalty values that are necessary to calculate the accuracy of the training set and the confusion matrix of the external test set. Confusion matrices were calculated

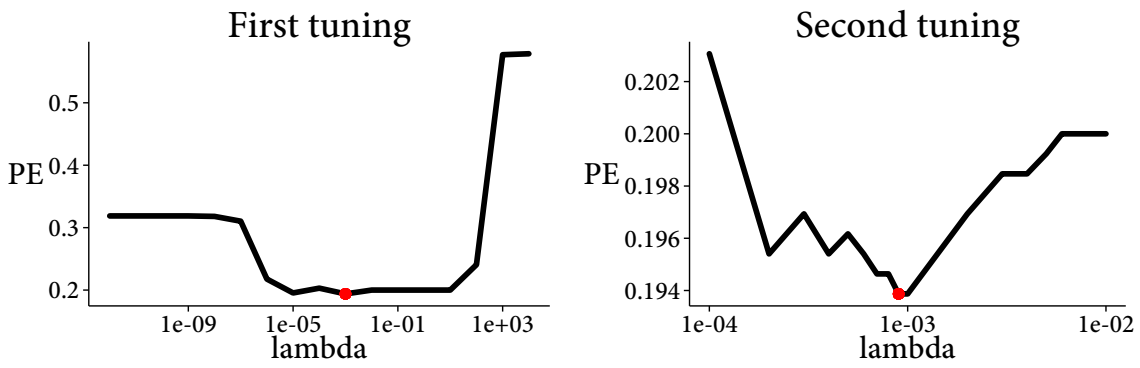


Figure 2.2: Tuning of the 1-norm SVM. The control parameter λ is selected as the minimum value (red point) at which the mean cross-validation prediction error (PE, misclassification error rate) is also minimized. The first round of tuning covers a wide order of magnitudes. A second round of tuning is performed to optimize this parameter.

using the caret package of R. The code used to implement this 1-norm SVM is included in Appendix D.

2.5.6 Selection of prototype conformers

Non-zero elements of $\boldsymbol{\beta}$ correspond to *p*rototype conformers for which molecular similarity measures contribute positively or negatively to the classification of molecular activity. Many of the conformations will have no impact on classification, and can be removed from the cohort of conformers taken on to traditional pharmacophore development. In practice, the indices of training set conformations from the original collection are congruent with the $\boldsymbol{\beta}$ so that the non-zero elements can be collected to generate a substantially smaller subset of conformers. Ranking of all conformers could be performed at this point, but the prototype conformers are sufficient for pharmacophore model development given that there are no known crystal structures for complexes of σ receptors and their ligands. After the prototype conformers are retrieved from the full set, the corresponding fingerprints for active ligands are used to generate a substantially smaller similarity matrix. This matrix is visualized as a clustered heat map to determine a practical number of active ligands that are needed to generate common pharmacophore hypotheses.

2.5.7 Pharmacophore modeling

Phase provides means for both manual and automated pharmacophore development. Individual hypotheses can be generated from each prototype conformer manually, but the development of common pharmacophore hypotheses from the entire set of prototype conformers allows for the perception of features common to subsets of entire cohort of selected conformers. Common pharmacophore hypotheses are generated and evaluated in a five-step process: generating ligand conformations, identification of pharmacophore sites, perception of common pharmacophore hypotheses, scoring of hypotheses, and building atom- or pharmacophore-based 3D QSAR models.

In structure-based pharmacophore development, the conformations of ligands are known with a high degree of certainty. Without such information, ligand-like conformations must be selected through other means, such as through the use of the ConfGen application. Highly flexible ligands, such as those found frequently in the σ literature are problematic because the number of potential common pharmacophore hypotheses rapidly becomes too great to discern any statistically significant hypotheses after the scoring step. In preliminary studies, it was not infrequent to generate tens of thousands of common 5-point hypotheses; analyzing the resulting QSAR models became an intractable task. By utilizing the prototype active and inactive conformers that were identified through MILES, the number of common pharmacophores is reduced by several orders of magnitude.

Phase provides a default set of pharmacophore sites including hydrogen bond acceptors (A), hydrogen bond donors (D), positive ionizable (P), negative ionizable (N), hydrophobic (H), and aromatic rings (R). This set was extended to include piperazine and piperidine rings (X) as group features, as was performed during the pharmacophore fingerprinting steps. After editing the feature definitions, sites were generated for all the input conformers. The prototype conformers that share a high pharmacophore fingerprint similarity will likely share many of the same features. Common pharmacophores were identified by determining an reasonable number of each type of feature, an optimal number of site points (from 3–7), and requiring matches to the number of active compounds identified from the heat map of active prototype conformers. Scoring of hypotheses was performed with the default settings in Phase, and the hypotheses that survived the initial scoring process were

taken on to pharmacophore screening and QSAR development without regard to score.

Typically atom- or pharmacophore-based QSAR models would be generated at this point. However, the common pharmacophore workflow makes it difficult to generate these models if the conformations of all other ligands in the database are not carried throughout the process. Atom-based models are best performed on cohorts of structures of limited diversity, and are not well suited to molecules with a high degree of rotational freedom. Pharmacophore-based models are more appropriate under these circumstances, but the resulting models cannot be used to infer activity when steric clashes are important to binding affinity, and there is no way to run this application outside of the common pharmacophore hypothesis workflow. On the other hand, the surviving hypotheses can be used outside of the workflow to screen through databases of ligands with known activity to retrieve cohorts of ligands which can then be utilized for QSAR development using alternative methodologies.

2.5.8 Database screening

The Phase Advanced Pharmacophore Screening application was used to retrieve pharmacophore hits from the database of all ligands. Decoy sets of 1000 drug-like ligands[94] were combined with the curated sigma database ligands and inactive ligands from the superset for calculation of enrichment. For these purposes, an affinity at 10,000 micromolar or better was considered "active". In the case of σ-2 ligands, a set with an average molecular weight of 400 was utilized, whereas the σ-1 database was more matched to the decoy set having an average molecular weight of 360. Databases were created using the same ConfGen parameters as were used in the fingerprinting and pharmacophore modeling steps. Searching of the database was performed using the existing conformers without refinement. Default matching criteria were used, with the exception that only 4 sites out of the total were required to match, and preference was given to conformers matching more sites. Four-site matches are optimal under these circumstances, as they naturally allow alignments based on chirality, but are not overly aggressive at screening out matches that contribute valuable QSAR information. Hits were scored based on default scoring fitness, but were rejected if vector features diverged at

an angle of 90˚ or more, or if the volume score was less than 0.3. These limits were determined heuristically to generate reasonable alignments without rejecting too many ligands from the database. Compound affinities were ranked according to a field-based QSAR, described below.

2.5.9 Field-based QSAR

Field-based QSAR based on the CoMFA (Force Field) and CoMSIA (Gaussian) approaches was recently incorporated into the Schrödinger software suite. Both of these approaches evaluate fields based on a rectangular grid encompassing the training set molecules. However, the Force Field method involves a Partial Least Squares (PLS) regression based on the fields evaluated at each grid point, and is very sensitive to the alignment of ligands. The Gaussian method evaluates fields based on a weighted function dependent upon the distance of atoms from the grid points, and is less sensitive to alignment artifacts. Given the diverse nature of scaffolds retrieved during the database screening steps, the Gaussian approach was used for QSAR analysis.

Each set of aligned ligands was used to develop independent QSAR models. A random split of the dataset into 50% training to test set was applied to the ligands. This ratio was chosen as it was the default for Phase, and ideally should be set high enough to generate a predictive model with a representative external test set. These sets are automatically distributed in a relatively even manner across the range of activities present in the dataset. A maximum of 3 PLS factors at a grid spacing of 1 Å were used in the regression. The grid was extended 3 Å beyond training set limits, and force fields within 2 Å of any training set atom were ignored. Steric and electrostatic fields were truncated at 30 kcal/mol. Variables with a standard deviation of less than 0.01, or with |t-value| less than 2.0 were eliminated from the regression. Cross-validation was performed with the leave-one-out technique.

3. RESULTS

> We've learned from experience that the truth will come out. Other experimenters will repeat your experiment and find out whether you were wrong or right. Nature's phenomena will agree or they'll disagree with your theory. And, although you may gain some temporary fame and excitement, you will not gain a good reputation as a scientist if you haven't tried to be very careful in this kind of work. And it's this type of integrity, this kind of care not to fool yourself, that is missing to a large extent in much of the research in cargo cult science.
>
> *Cargo Cult Science*
> Richard Feynman

3.1 Competition Binding Database

A total of 1,208 articles representing the σ literature covering the years 1981–2011 were identified as potential sources of competition binding data, which was confirmed for 564 articles. After characterizing the nature of the competition binding assay methodology, it was possible to identify the most prevalent combinations of hot ligands and masking agents as shown in Table 3.1. Furthermore, 7-OH-DPAT,7-OH-PIPAT, DTG or HAL (without a masking ligand), ifenprodil, NANM and PPP are not sufficiently target or subtype selective for the purposes of pharmacophore development. We chose to collect structural and binding data for articles containing DTG with a masking agent as σ-2 selective methodology or PTZ as a σ-1 selective ligand. In order to confidently combine

Table 3.1: Breakdown of σ research articles providing competition binding data. The following hot ligand/masking ligand combinations were only represented by a single article: 2-IPB, 4-IBP, 4-IPBS, DuP734, I-benzamide, IPAB, IPEMP, ANSTO-14, clonidine, DTG/DuP734, DTG/AC915, DTG/carbetapentane, DTG/DXM, FPS, HAL/l-sulpiride, HAL/spiroperidol/BIMU-8, IPIPAG, MS377, azido-DTG, NANM/dizoclipine, NANM/etorphine, PB28/PTZ, PPP/DXL, progesterone, PTZ/Lu28-179, SA4503, SN56, and SW120. Several of the hot ligands are now known to more effectively target other receptors.

Hot ligand	Masking ligands	No. articles
3′-iodopentazocine		2
7-OH-DPAT		2
7-OH-PIPAT	spiroperidol	2
DTG		128
DTG	DXL	55
DTG	NANM	25
DTG	PTZ	189
DXM		7
HAL		12
HAL	l-sulpiride	1
HAL	spiroperidol	24
ifenprodil		6
NANM		62
NANM	MK801	7
NE100		2
PIMBA		3
PPP		66
PTZ		356
RHM-1		6

data from different articles into sets of compounds for quantitative computational experiments, the methodologies should be as practically identical as possible. To this end, the matrix used in the σ assay is a very important consideration, so we further limited our investigations to those articles in Table 3.2 which were most widely used for competition binding experiments. Of the combinations investigated, σ-1 assays performed with PTZ on guinea pig brain tissue homogenates, and σ-2 assays run with DTG using PTZ as a masking agent on rat liver homogenates, were found to represent a sufficient number of active and inactive compounds for our computational requirements. The curated datasets included 723 unique σ-2 ligands and 1,396 curated σ-1 ligands.

Table 3.2: Breakdown of assay methodology for selective σ competition binding experiments.

Hot ligand	Masking ligand	Organism	Tissue	No. articles
DTG	DXL	rat	brain	3
DTG	DXL	rat	liver	44
DTG	NANM	guinea pig	brain	18
DTG	NANM	rat	brain	5
DTG	NANM	rat	liver	2
DTG	PTZ	guinea pig	brain	33
DTG	PTZ	guinea pig	brain plus cerebellum	1
DTG	PTZ	human	MCF-7 ADR cells	3
DTG	PTZ	rat	brain	32
DTG	PTZ	rat	brain minus cerebellum	2
DTG	PTZ	rat	liver	111
PTZ		guinea pig	brain	212
PTZ		guinea pig	brain minus cerebellum	17
PTZ		guinea pig	brain plus cerebellum	2
PTZ		guinea pig	clone in E. Coli	3
PTZ		guinea pig	clone in S. Cerevisiae	2
PTZ		guinea pig	liver	9
PTZ		human	MCF-7 cells	2
PTZ		human	brain	2
PTZ		human	jurkat cells	5
PTZ		mouse	brain	2
PTZ		rat	C6 cells	2
PTZ		rat	brain	55
PTZ		rat	brain minus cerebellum	7
PTZ		rat	liver	9

3.2 Impact of Fingerprint Length

Fingerprints of various lengths were calculated using the options available in Canvas. A σ-2 rat liver/DTG data set (Table 3.3 and Figure 3.1) was processed with the following treatments: no bit filtering, filtering out bits that are present in less than 5% of the conformers, or retaining informative bits with fingerprint lengths of 256, 512, 1,024, 2,048, 4,096, 8,192, and 16,384 bits.

Table 3.3: Statistics of the initial σ-2 classification model data set. The active and inactive compounds were selected from the curated dataset containing 723 ligands, using pK_i cutoffs of 6.0 and 8.301 for inactive and active molecules, respectively.

No. of molecules					
Training set		Test Set			
Active	Inactive	Active	Inactive	Total	Total no. of conformers
14	22	6	12	54	5,634

To determine the extent to which SAP methodology improved the calculations, each treatment was performed without SAP. SAP methodology was then used to determine a subset of significant bits, as shown in Table 3.4. Initial experiments were conducted by holding out the fingerprints from the test set, except in the case of unfiltered fingerprints. Unfiltered fingerprints could not be treated to SAP because of excessive memory resource requirements. The ratio of retained bits to informative/frequent bits following significance analysis decreases steadily from 95% down to 84% when 8,192 or more post-filtered bits are used. Retained bits also make up a very small percentage of the pre-filtered bits, ranging from 0.03% up to 2.41%. Threshold cutoffs for removal of insignificant bits tended to increase with increasing fingerprint length. Notably, repeated runs of SAP on the same fingerprints tended to generate different selections of significant bits as the fingerprint length rose above 1,024 bits (data not shown). One likely explanation for this phenomenon is that the number of random permutations of the data is fixed at 500, whereas the number of potential significant bits rises with fingerprint length. If may therefore be possible to resolve a reproducible SAP fingerprint by increasing the number of permutations if the computational cost is justifiable.

A similarity matrix using the Kulczynski metric was calculated for each treatment, and MILES

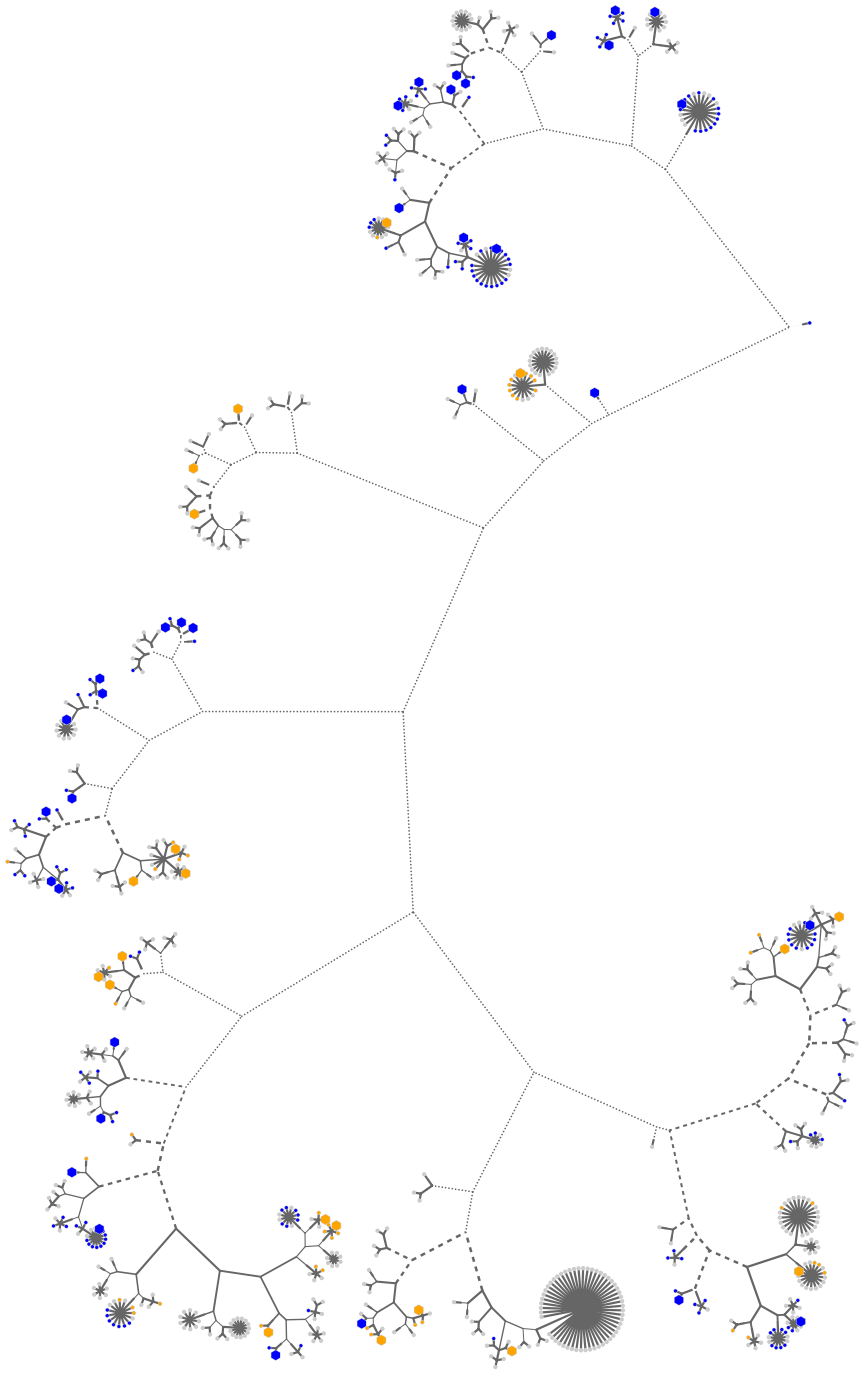


Figure 3.1: Clustered σ-2 scaffold data. Molecules classified as inactive are in blue and active molecules are colored orange; the remaining unclassified molecules are in gray. Fifty-four molecules (larger hexagons) were selected from this set for SAP and MILES performance analysis. Solid lines connect molecules and scaffolds to their cores. A clustering cutoff at a Euclidean distance of 10-12 is indicated by dashed lines. The dotted lines demonstrate the connectivity between cores and nodes in the dendrogram beyond the clustering cutoff distance.

was used to develop classification models. Confusion matrices, internal validation statistics, and cross-validation statistics were used to characterize the impact of fingerprint length on the quality of the final classification models. In order that cross-validation results remained matched across treatments, the same selection of splitting replicates were used.

Table 3.4: Significance analysis parameters after Canvas filtering and SAP: the total number of bits (b_{tot}) of the complete fingerprint was 696828.

$b_{\text{inf}} \mid b_{\text{freq}}$ [a]	b_{sap} [b]	Δ [c]
256	245	0.416
512	479	0.606
1,024	937	1.280
2,048	1,829	1.528
4,096	3,576	1.906
8,192	6,960	2.638
16,384	13,910	3.111
5% (19805)	16,794	3.108

[a]Number of informative bits, or % bits filtered by minimum frequency; [b]bits remaining after SAP; [c]selected threshold for elimination of insignificant bits

As shown in Table 3.5, regardless of whether or not SAP was performed, there was no obvious trend in λ parameter or the cross-validation prediction error. Internal accuracy of the non-SAP models was 100% (except for the 256 bit fingerprint). External accuracy and MCC were adversely affected with every treatment compared to the unfiltered fingerprint. Filtering by SAP slightly degraded internal accuracy, particularly at shorter fingerprint lengths. The external accuracy and Matthews Correlation Coefficient (MCC) measures were inconsistent, with no obvious trend towards better performance with increasing fingerprint length. At 8,192 bits with SAP filtering, the MILES classification performance was essentially identical to using raw fingerprints.

Confusion matrices and cross-validation statistics for the non- and SAP-filtered sets are presented in Tables 3.6 and 3.7, respectively. Classification of true negatives performed more poorly than that of the unfiltered fingerprint for all of the informative bit fingerprints, whereas true positive classification performed identically when the fingerprint length was set at 2,048 bits or longer. In the case of the traditional SAP method, or with a pre-filtered 8,192 bit fingerprint, the classification

Table 3.5: Tuning parameters and MILES results vary depending on the fingerprint length chosen and the application of SAP.

Pre-filtering treatment	λ^a	PE^b	IA^c	EA^d	MCC^e
no SAP treatment					
256	8e-01	0.163	0.972	0.772	0.351
512	1e-05	0.150	1.000	0.611	0.088
1,024	2e-05	0.207	1.000	0.722	0.351
2,048	7e-06	0.191	1.000	0.611	0.236
4,096	5e-05	0.196	1.000	0.722	0.403
8,192	8e-06	0.156	1.000	0.722	0.403
16,384	2e-06	0.123	1.000	0.722	0.403
5%	7e-06	0.135	1.000	0.778	0.472
raw	2e-06	0.196	1.000	0.833	0.614
processed with SAP					
256	1e02	0.144	0.944	0.667	0.316
512	1e02	0.137	0.917	0.667	0.25
1,024	9e01	0.209	0.944	0.778	0.5
2,048	1e02	0.226	0.944	0.611	0.161
4,096	1e02	0.254	0.944	0.667	0.316
8,192	9e-05	0.250	1.000	0.833	0.614
16,384	3e-02	0.252	1.000	0.778	0.472
5%	5e-05	0.265	1.000	0.833	0.614

[a]optimal tuning parameter; [b]cross-validation prediction error; [c]internal accuracy of prediction; [d]external test set accuracy; [e]Matthews Correlation Coefficient

performance was identical that of the unfiltered fingerprint. The use of SAP therefore allows the use of far fewer bits to achieve MILES classification results comparable to those found with raw fingerprints. Unfortunately there is no way to know in advance how many fingerprint bits to retain in the pre-filtering step. Some caveats with this interpretation are that only the Kulczynski metric was used in the MILES formulation for these experiments, and that the dataset was biased towards more inactive compounds. In this case, at least, the bias can be resolved by selecting fewer inactives, or by broadening the criteria for the inclusion of active compounds from the scaffold perception step.

Table 3.6: Confusion matrices of models at various fingerprint lengths without SAP filtering.

		Unfiltered		5% Cutoff		256 bits	
Reference		F	T	F	T	F	T
Prediction	F	11	2	11	3	10	3
	T	1	4	1	3	2	3

		512 bits		1,024 bits		2,048 bits	
Reference		F	T	F	T	F	T
Prediction	F	9	4	10	3	7	2
	T	3	2	2	3	5	4

		4,096 bits		8,192 bits		16,384 bits	
Reference		F	T	F	T	F	T
Prediction	F	9	2	9	2	9	2
	T	3	4	3	4	3	4

Table 3.7: Confusion matrices at various fingerprint lengths in tandem with SAP filtering.

				5% Cutoff		256 bits	
Reference				F	T	F	T
Prediction	F			11	2	8	2
	T			1	4	4	4

		512 bits		1,024 bits		2,048 bits	
Reference		F	T	F	T	F	T
Prediction	F	9	3	10	2	8	3
	T	3	3	2	4	4	3

		4,096 bits		8,192 bits		16,384 bits	
Reference		F	T	F	T	F	T
Prediction	F	8	2	11	2	11	3
	T	4	4	1	4	1	3

3.3 Comparison of Similarity Metrics

Given the mixed results using the Kulczynski metric, several other metrics were investigated in the MILES formulation. SAP-filtered fingerprints calculated previously using the 1,024 and 4,096 most informative bits were utilized in this approach. Similarity metrics were calculated using those available in Canvas that do not explicitly include the shared number of bits turned "off". Thus cosine, Dice, McConnaughey, Petke, Simpson, Tanimoto, and Tversky metrics were used to calculate similarity matrices for feature mapping. Internal validation accuracy, confusion matrices, and external test set prediction statistics were used to characterize the impact of fingerprint metric, as well as to investigate the impact of fingerprint length using these metrics.

As shown in Table 3.8, every similarity measure performed better than the original Kulcznski metric in terms of internal accuracy. Interestingly, shorter fingerprint lengths were better or equivalent to the unfiltered fingerprint at classification of the external test set with every metric except McConnaughey and Simpson. Longer fingerprints led to poorer external classification results for cosine, Petke, and Simpson metrics, but better results for the McConnaughey metric. The mean cross-validation prediction error increased with the use of longer fingerprints. Matthews Correlation Coefficients indicate performance on par with the unfiltered fingerprints using the Cosine and Petke metrics, and slightly better performance using Dice, Tanimoto, or Tversky metrics. The Dice, Tanimoto, and Tversky metrics appear to perform very well and are less sensitive to changes in fingerprint length.

3.4 Impact of training and test set size

Given the previous results, it was worthwhile to investigate the performance of SAP and MILES with a more balanced dataset. A library of 130 molecules (Table 3.11 and Figure 3.2) was assembled using all of the active ligands from every possible cluster, along with inactive molecules sampled from the remaining clusters. In many projects, it is likely that there will be many more inactive molecules than active ones. Additionally, there are some clusters which simply do not possess active

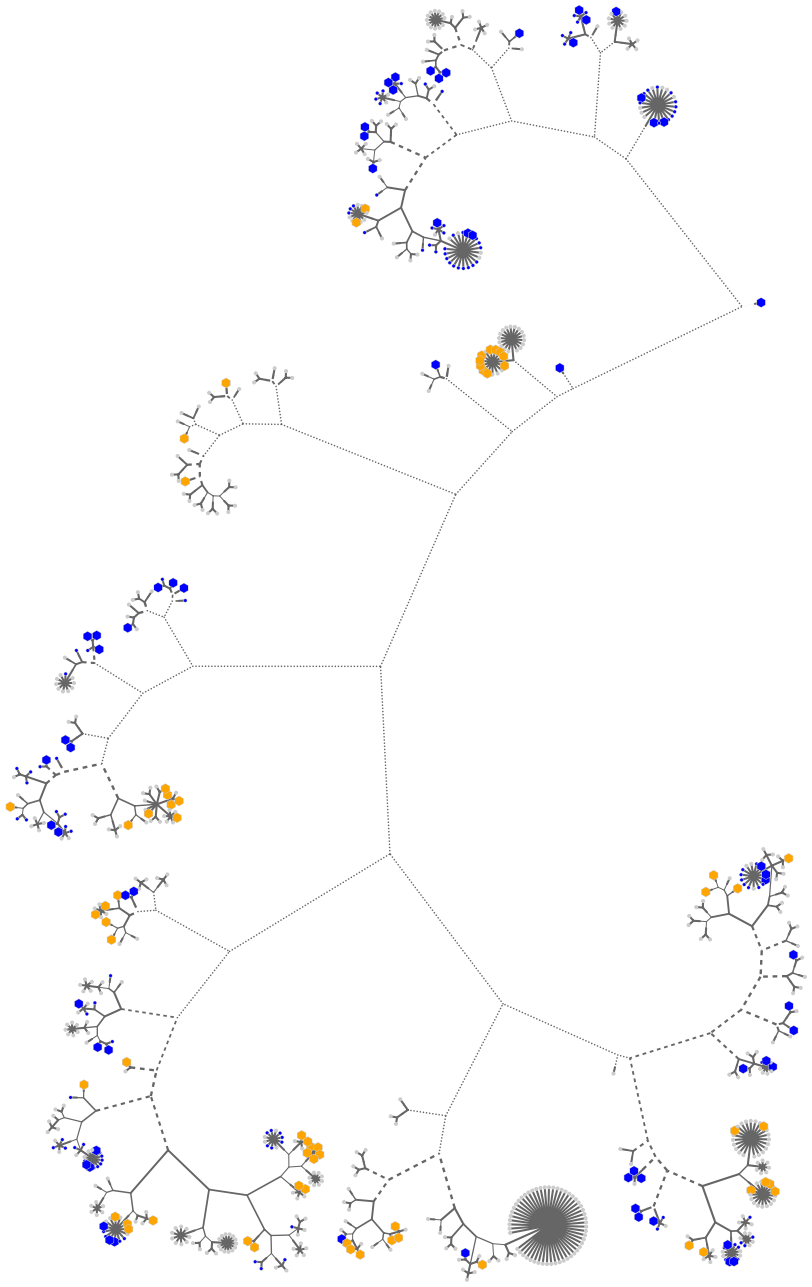


Figure 3.2: Clustered σ-2 scaffold data for the balanced dataset. Visualization details are the same as in Figure 3.1. One hundred and thirty molecules (larger hexagons) were selected from this set for SAP and MILES performance analysis. All molecules classified as active were included from all available clusters. Inactive compounds were added to roughly approximate the number of actives by selecting poor affinity ligands as evenly as possible, cluster by cluster.

Table 3.8: Stability of MILES performance utilizing alternative similarity metrics. Lower stability is associated with denominators in the similarity calculations that involve products or minimum/maximum functions.

Pre-filtering treatment	λ^a	PE^b	IA^c	EA^d	MCC^e
1,024 bit fingerprint					
Cosine	2e-07	0.185	1.000	0.833	0.614
Dice	8e-04	0.169	1.000	0.889	0.756
McConnaughey	9e-06	0.313	1.000	0.611	0.161
Petke	9e-04	0.185	1.000	0.889	0.756
Simpson	1e02	0.263	1.000	0.778	0.5
Tanimoto	1e-04	0.185	1.000	0.889	0.756
Tversky	8e-04	0.169	1.000	0.889	0.756
4,096 bit fingerprint					
Cosine	2e-03	0.209	1.000	0.778	0.5
Dice	4e-06	0.194	1.000	0.889	0.756
McConnaughey	2e-02	0.370	1.000	0.722	0.403
Petke	3e-03	0.219	1.000	0.833	0.632
Simpson	5e-03	0.287	1.000	0.556	0.
Tanimoto	4e-06	0.248	1.000	0.889	0.756
Tversky	4e-06	0.194	1.000	0.889	0.756

[a]optimal tuning parameter; [b]cross-validation prediction error; [c]internal accuracy of prediction; [d]external test set accuracy; [e]Matthews Correlation Coefficient

molecules, yet it is important that the pharmacophore information in these molecules is not lost. It is noteworthy that some molecules, particularly flexible ones, will generate many more conformers than other molecules, so while the number of compounds may be balanced, it is possible for the number of conformers to remain unbalanced.

As part of this investigation, pharmacophore fingerprints from all molecules were utilized in the significance analysis. This allows a less biased comparison to the performance of the metrics with respect to raw fingerprints, since similarity metrics calculated with Canvas will use all available bits. Experiments were run using raw fingerprints, or the 1,024 or 16,384 most informative bits. A summary of the latter fingerprints is provided in Table 3.12. The Dice, Petke, Tanimoto, and Tversky metrics were chosen because of their superior performance in the prior experiments.

Table 3.9: Confusion matrices for diverse similarity metrics using 1,024–bit fingerprints in tandem with SAP filtering. The McConnaughey metric performed notably poorer than all other metrics.

		Cosine		Dice		Kulczynski	
Reference		F	T	F	T	F	T
Prediction	F	11	2	12	2	10	2
	T	1	4	0	4	2	4

		McConnaughey		Petke		Simpson	
Reference		F	T	F	T	F	T
Prediction	F	8	3	12	2	10	2
	T	4	3	0	4	2	4

		Tanimoto		Tversky	
Reference		F	T	F	T
Prediction	F	12	2	12	2
	T	0	4	0	4

Table 3.10: Confusion matrices for diverse similarity metrics using 4,096–bit fingerprints and SAP filtering. With longer fingerprint lengths, the Kulczynski and McConnaughey metrics performed better. The Simpson metric performed notably poorer at this length.

		Cosine		Dice		Kulczynski	
Reference		F	T	F	T	F	T
Prediction	F	10	2	12	2	11	2
	T	2	4	0	4	1	4

		McConnaughey		Petke		Simpson	
Reference		F	T	F	T	F	T
Prediction	F	9	2	12	3	8	4
	T	3	4	0	3	4	2

		Tanimoto		Tversky	
Reference		F	T	F	T
Prediction	F	12	2	12	2
	T	0	4	0	4

Table 3.11: Statistics of the balanced σ-2 classification model data set.

No. of molecules					
Training set		Test Set			
Active	Inactive	Active	Inactive	Total	Total no. of conformers
43	44	21	22	130	8,576

Table 3.12: Significance analysis parameters after Canvas filtering and SAP with a more balanced dataset: the total number of bits (b_{tot}) of the complete fingerprint was 2,859,553.

b_{inf} [a]	b_{sap} [b]	Δ [c]
1,024	730	1.645
16,384	12,520	2.488

[a]Number of informative bits; [b]bits remaining after SAP; [c]selected threshold for elimination of insignificant bits

Table 3.13: Comparison of metric performance with a more balanced molecular library. Classification of the external dataset improved with larger training and test sets, but only with larger fingerprints. SAP-filtered fingerprints at 16,384 bits were comparable to the performance with raw fingerprints.

Pre-filtering treatment	λ [a]	PE [b]	IA [c]	EA [d]	MCC [e]
unfiltered fingerprint					
Dice	1e-06	0.129	1.000	0.930	0.868
Petke	9e-07	0.138	1.000	0.884	0.774
Tanimoto	8e-07	0.181	1.000	0.884	0.788
Tversky	1e-06	0.129	1.000	0.930	0.868
1,024 bit fingerprint					
Dice	3e-06	0.221	1.000	0.767	0.542
Petke	9e-07	0.138	1.000	0.884	0.774
Tanimoto	4e-05	0.211	1.000	0.791	0.612
Tversky	3e-06	0.221	1.000	0.767	0.542
16,384 bit fingerprint					
Dice	9e-04	0.194	1.000	0.884	0.788
Petke	2e-06	0.188	1.000	0.884	0.788
Tanimoto	4e-06	0.182	1.000	0.907	0.828
Tversky	8e-04	0.194	1.000	0.884	0.788

[a]optimal tuning parameter; [b]cross-validation prediction error; [c]internal accuracy of prediction; [d]external test set accuracy; [e]Matthews Correlation Coefficient

3.5 Development of σ-2 pharmacophore models and QSAR

Prototype conformers discovered in the "balanced" 16,384 bit experiment using Tanimoto similarity metrics were taken through the Develop Pharmacophore Hypothesis workflow in Phase. The heat map of active conformers indicates several clusters containing 3 distinct ligands. Matching on 6 sites with a minimum of 3 ligands allowed for up to 3 hydrogen bond acceptor moieties, and some of the most similar conformers had pairs of acceptors in close proximity, so the feature frequency of acceptors was reduced to 1. After scoring, the complete linkage clustering method was used to select representative pharmacophores with a minimum similarity of 0.9 based on survival scores. Thirty-four hypotheses were retained and used for screening the complete conformer database.

A Gaussian Field-based QSAR analysis was performed on the subsequent alignments. Two compounds 3.4 were removed from each alignment, if present, as they consistently caused problems. Compound 1 from Choi et al.[95] would occasionally pass the volume filter of the database screen, but was too large when assigned to the training set for the QSAR to run because points only associated with this compound fell far away from all other training set compounds, requiring more PLS factors than Phase was designed to accommodate. Compound 5 from Fontanilla et al. was always predicted to have a much higher affinity than observed by the original authors, at times up to 4 orders of magnitude greater.

Statistical results from these calculations are presented in Table 3.14. Standard deviations of regression were less than the average standard deviation of activity values under all circumstances, which suggests that these models are not over-fit. Higher R^2 and Q^2 statistics are preferred, as long as the RMSE is not too much greater than the SD. High leave-one-out cross-validated R^2 is no guarantee of a predictive model, although an old rule of thumb is that a model is generally only useful if R^2 CV is at least 0.5.[97] The Stability metric more precisely estimates the effect of removing molecules from the training set. In Phase, random subsets of 10% are left out and the predictions (not the observed activities) are compared to the full model; the higher this value, the less sensitive the model to changes in the training set. Very few of the resulting models show

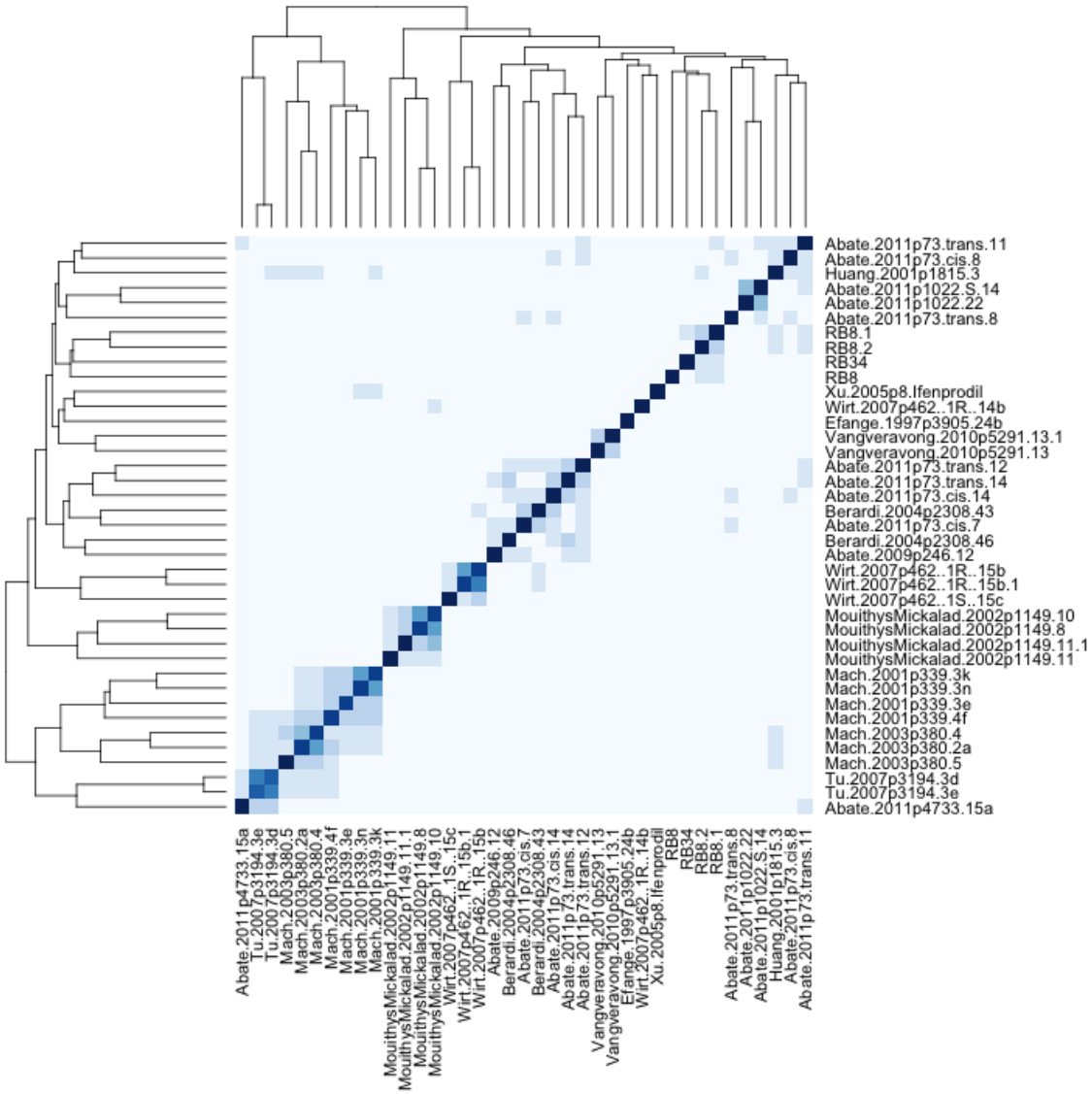
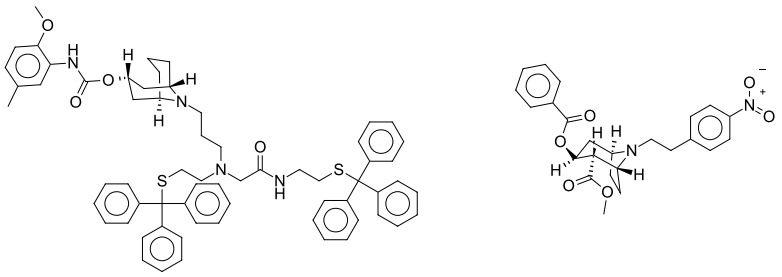


Figure 3.3: Sigma-2 prototype conformer heat map



Choi **1**
Nucl. Med. Biol. 28, 657

Fontanilla **5**
Biochemistry 47, 7205

Figure 3.4: Problem compounds for development of Gaussian QSAR from aligned datasets

appreciable sensitivity when increasing the number of PLS factors. Scrambling of activity labels should also not produce a coefficient of determination comparable to R^2, as that would indicate that the model is no better than one generated at random. Pearson-*r* is a measure of the ability of the model to predict the relative rank correctly in the external test set.

Table 3.14: Sigma-2 pharmacophore hypotheses and related statistics for regressions of 1–3 PLS factors. Each hypothesis is label with the nature of the pharmacophore features (A = H-bond acceptor, D = H-bond donor, H = hydrophobic, R = aromatic, N = negative ionizable, P = positive ionizable). The number of database screening matches within the σ-2 database is shown in parentheses. A total of 723 ligands representing the curated σ-2 data were screened.

No. Factors	SD[a]	R^{2b}	R^2 CV[c]	R^2 Scramble[d]	Stability[e]	F[f]	P[g]	RMSE[h]	Q^{2i}	Pearson-r[j]
ADHHPR.15 (470)										
1	0.8564	0.4186	0.2916	0.1568	0.971	167.1	3.82e-29	0.96	0.2381	0.5076
2	0.7584	0.5460	0.3484	0.2855	0.944	138.9	2.45e-40	0.91	0.3160	0.5809
3	0.6570	0.6608	0.3636	0.4169	0.879	149.3	9.98e-54	0.88	0.3484	0.6149
ADHHPR.17 (472)										
1	0.8098	0.4337	0.3308	0.1207	0.983	178.5	1.33e-30	0.98	0.2110	0.4782
2	0.7284	0.5439	0.3846	0.2306	0.962	138.3	2.83e-40	0.94	0.2807	0.5409
3	0.6342	0.6557	0.4180	0.3365	0.908	146.7	3.23e-53	0.92	0.3010	0.5576
ADHHPR.28 (471)										
1	0.8405	0.4074	0.2708	0.1333	0.971	160.2	2.75e-28	0.87	0.3334	0.5785
2	0.7271	0.5584	0.3541	0.2572	0.941	146.7	6.66e-42	0.84	0.3737	0.6131
3	0.6124	0.6881	0.3937	0.3486	0.872	169.9	3.68e-58	0.84	0.3819	0.6248
ADHHPR.3 (485)										
1	0.8033	0.4425	0.3035	0.1265	0.969	191.3	2.05e-32	0.91	0.2355	0.5100
2	0.7120	0.5639	0.3709	0.2309	0.949	155.1	5.68e-44	0.87	0.3012	0.5732
3	0.6227	0.6678	0.4260	0.3391	0.909	160.1	6.51e-57	0.84	0.3575	0.6055
ADHHPR.39 (483)										
1	0.7866	0.4560	0.3574	0.1346	0.983	200.3	1.94e-33	0.87	0.2942	0.5509
2	0.6899	0.5833	0.4188	0.2671	0.96	166.6	5.77e-46	0.83	0.3590	0.6158
3	0.6093	0.6764	0.4312	0.3741	0.909	165.1	8.89e-58	0.81	0.3835	0.6356
ADHHPR.43 (509)										
1	0.8055	0.4300	0.3095	0.1276	0.979	190.1	1.33e-32	0.89	0.2983	0.5477
2	0.6872	0.5868	0.3740	0.2553	0.94	178.2	6.78e-49	0.93	0.2409	0.5140
3	0.6081	0.6777	0.4157	0.3623	0.896	175.3	3.49e-61	0.92	0.2605	0.5363
ADHHPR.57 (482)										
1	0.7906	0.4654	0.3419	0.1351	0.976	208.1	2.35e-34	0.88	0.3031	0.5721
2	0.6836	0.6020	0.3891	0.2575	0.938	180.0	2.41e-48	0.81	0.4080	0.6483
3	0.6100	0.6844	0.3729	0.3630	0.863	171.3	4.48e-59	0.82	0.3893	0.6395
ADHHPR.83 (555)										
1	0.8241	0.4213	0.3240	0.1268	0.985	200.9	1.21e-34	0.88	0.3026	0.5531

2	0.7482	0.5247	0.3578	0.2477	0.964	151.8	3.83e-45	0.86	0.3253	0.5785
3	0.6656	0.6252	0.3567	0.3436	0.903	152.4	4.21e-58	0.80	0.4181	0.6492
ADHHPR.87 (490)										
1	0.7962	0.4861	0.3848	0.1306	0.983	229.8	5.45e-37	0.86	0.3519	0.5958
2	0.6884	0.6174	0.4596	0.2716	0.962	195.2	3.26e-51	0.76	0.4979	0.7060
3	0.6085	0.7023	0.4735	0.3702	0.925	189.5	4.07e-63	0.76	0.5058	0.7126
ADHPRR.30 (483)										
1	0.8250	0.3970	0.2357	0.1570	0.961	158.0	3.56e-28	0.97	0.1038	0.4020
2	0.7062	0.5601	0.3278	0.2785	0.925	152.1	2.43e-43	0.92	0.2054	0.4853
3	0.6346	0.6462	0.3239	0.3638	0.866	144.9	2.01e-53	0.88	0.2735	0.5474
ADHPRR.34 (469)										
1	0.8177	0.4255	0.3110	0.1264	0.979	172.6	7.21e-30	0.90	0.2531	0.5136
2	0.7206	0.5557	0.3631	0.2715	0.948	145.1	1.34e-41	0.85	0.3470	0.5995
3	0.6277	0.6644	0.3867	0.3716	0.887	152.4	1.71e-54	0.83	0.3677	0.6229
ADHPRR.36 (485)										
1	0.8527	0.3627	0.2797	0.1378	0.988	140.0	7.18e-26	0.96	0.1851	0.4455
2	0.7131	0.5561	0.4011	0.2385	0.965	153.5	6.22e-44	0.90	0.2767	0.5458
3	0.6237	0.6619	0.4524	0.3412	0.936	159.2	3.62e-57	0.86	0.3342	0.5881
ADHPRR.38 (494)										
1	0.8519	0.3378	0.2691	0.1345	0.991	124.4	1.27e-23	0.92	0.2700	0.5197
2	0.6968	0.5587	0.4061	0.2333	0.957	153.8	6.85e-44	0.90	0.2938	0.5583
3	0.5909	0.6840	0.4550	0.3385	0.911	174.6	3.02e-60	0.89	0.3088	0.5789
ADHPRR.40 (499)										
1	0.8094	0.4487	0.3511	0.1398	0.983	201.0	8.73e-34	0.93	0.2372	0.5107
2	0.7405	0.5404	0.3925	0.2712	0.97	144.6	2.96e-42	0.92	0.2562	0.5250
3	0.6506	0.6467	0.3703	0.3711	0.903	149.5	4.49e-55	0.89	0.2999	0.5654
ADHPRR.41 (506)										
1	0.8684	0.3677	0.2640	0.1164	0.98	146.0	8.51e-27	0.93	0.2383	0.4939
2	0.7713	0.5032	0.3323	0.2436	0.958	126.6	1.05e-38	0.90	0.2854	0.5438
3	0.6787	0.6169	0.3573	0.3404	0.911	133.6	1.33e-51	0.87	0.3373	0.5850
AHHHPR.109 (485)										
1	0.8807	0.3760	0.2821	0.1540	0.984	144.6	2.22e-26	0.93	0.2702	0.5201
2	0.7654	0.5306	0.3470	0.2704	0.951	135.1	5.63e-40	0.91	0.3036	0.5559
3	0.6580	0.6545	0.3831	0.3686	0.895	150.3	1.18e-54	0.83	0.4205	0.6485
AHHHPR.111 (482)										
1	0.8684	0.3986	0.3088	0.1335	0.986	158.4	3.31e-28	0.94	0.2609	0.5198

2	0.7702	0.5289	0.3619	0.2694	0.961	133.6	1.26e-39	0.91	0.3132	0.5752
3	0.6472	0.6687	0.4091	0.3602	0.901	159.5	1.4e-56	0.85	0.3924	0.6441
AHHHPR.113 (574)										
1	0.8764	0.3373	0.2245	0.1272	0.98	145.1	2.78e-27	0.96	0.1525	0.4349
2	0.7838	0.4717	0.3109	0.2363	0.963	126.8	4.45e-40	0.94	0.1936	0.4903
3	0.6485	0.6396	0.3853	0.3530	0.909	167.4	2.07e-62	0.88	0.3008	0.5741
AHHHPR.114 (575)										
1	0.8061	0.4241	0.2603	0.1274	0.96	210.6	3.9e-36	0.87	0.3084	0.5633
2	0.7414	0.5146	0.3224	0.2276	0.951	151.1	1.86e-45	0.85	0.3264	0.5778
3	0.6687	0.6065	0.3603	0.3276	0.923	145.9	3.25e-57	0.81	0.3891	0.6305
AHHHPR.46 (546)										
1	0.8127	0.4173	0.2958	0.1397	0.977	193.3	1.63e-33	0.89	0.2708	0.5285
2	0.6899	0.5816	0.3799	0.2482	0.945	187.0	1.27e-51	0.82	0.3821	0.6269
3	0.5596	0.7258	0.4567	0.3516	0.883	236.5	5.6e-75	0.84	0.3485	0.6236
AHHHPR.51 (538)										
1	0.8486	0.3625	0.2867	0.1268	0.99	151.2	8.07e-28	0.95	0.2298	0.4843
2	0.7565	0.4952	0.3078	0.2515	0.951	130.0	4.62e-40	0.95	0.2235	0.4880
3	0.6589	0.6185	0.3396	0.3372	0.884	142.6	5.95e-55	0.93	0.2706	0.5391
AHHHPR.53 (571)										
1	0.8344	0.3880	0.2941	0.1206	0.987	179.4	5.07e-32	0.91	0.2397	0.5051
2	0.7453	0.5135	0.3628	0.2205	0.969	148.8	7.61e-45	0.90	0.2663	0.5447
3	0.6105	0.6747	0.4098	0.3182	0.895	194.3	3.33e-68	0.87	0.3030	0.5836
AHHHPR.90 (584)										
1	0.8362	0.3927	0.3097	0.1301	0.989	186.9	3.72e-33	0.97	0.2044	0.4688
2	0.7405	0.5254	0.3587	0.2499	0.964	159.4	2.45e-47	0.92	0.2883	0.5492
3	0.6531	0.6321	0.3793	0.3546	0.912	164.4	5.15e-62	0.91	0.3010	0.5746
AHHPRR.48 (588)										
1	0.7977	0.4207	0.3186	0.1338	0.98	211.4	2.26e-36	0.96	0.1798	0.4468
2	0.7291	0.5178	0.3739	0.2216	0.967	155.7	1.17e-46	0.94	0.2261	0.4890
3	0.6018	0.6726	0.4553	0.3286	0.927	197.9	9.5e-70	0.87	0.3275	0.5808
AHHPRR.49 (584)										
1	0.8112	0.3999	0.2979	0.1074	0.983	192.6	6.64e-34	0.93	0.2246	0.4829
2	0.7324	0.5125	0.3743	0.2069	0.972	151.4	1.18e-45	0.93	0.2312	0.5031
3	0.6483	0.6193	0.4111	0.3108	0.942	155.6	6.94e-60	0.91	0.2628	0.5358
AHHPRR.50 (579)										
1	0.8690	0.3173	0.2414	0.1330	0.99	133.4	1.36e-25	1.02	0.0990	0.3498

2	0.7513	0.4915	0.3575	0.2337	0.972	138.2	9.87e-43	0.95	0.2168	0.4783
3	0.6119	0.6638	0.4187	0.3286	0.911	187.6	3.8e-67	0.93	0.2439	0.5172
AHHPRR.54 (618)										
1	0.9070	0.2783	0.2250	0.1168	0.995	118.0	1.82e-23	0.93	0.2711	0.5214
2	0.7586	0.4968	0.3613	0.2134	0.974	150.5	3.31e-46	0.85	0.3804	0.6172
3	0.6252	0.6592	0.4302	0.3069	0.924	196.0	9.66e-71	0.79	0.4642	0.6818
AHHPRR.55 (623)										
1	0.9338	0.2729	0.2197	0.1073	0.995	116.3	3.05e-23	0.97	0.1672	0.4226
2	0.7792	0.4954	0.3601	0.2035	0.972	151.7	1.28e-46	0.94	0.2209	0.5057
3	0.6848	0.6115	0.3724	0.3144	0.929	161.6	6.52e-63	0.91	0.2657	0.5515
AHHPRR.61 (414)										
1	0.8200	0.4307	0.3573	0.1587	0.991	155.1	7.08e-27	1.02	0.0551	0.3543
2	0.6735	0.6178	0.4198	0.2760	0.94	164.8	2.5e-43	0.98	0.1263	0.4496
3	0.5777	0.7202	0.4620	0.3813	0.89	174.1	7.05e-56	0.98	0.1208	0.4656
AHHPRR.62 (411)										
1	0.7923	0.4314	0.3427	0.1304	0.987	154.0	1.09e-26	0.92	0.2729	0.5237
2	0.6740	0.5906	0.4379	0.2531	0.967	145.7	6.76e-40	0.91	0.2914	0.5427
3	0.6138	0.6621	0.4400	0.3653	0.938	131.3	4.02e-47	0.89	0.3253	0.5723
AHHPRR.63 (406)										
1	0.8221	0.3896	0.2747	0.1600	0.979	127.7	3.26e-23	0.91	0.2838	0.5344
2	0.7077	0.5500	0.3558	0.2834	0.948	121.6	3.1e-35	0.88	0.3295	0.5788
3	0.5995	0.6787	0.3835	0.3854	0.888	139.4	1.43e-48	0.87	0.3442	0.6088
HHHPRR.4 (559)										
1	0.8985	0.2975	0.2088	0.1162	0.987	117.8	4.16e-23	0.98	0.1176	0.3704
2	0.7198	0.5508	0.3758	0.2340	0.954	169.8	7.24e-49	0.90	0.2626	0.5267
3	0.6119	0.6766	0.4459	0.3547	0.919	192.4	2.46e-67	0.87	0.3173	0.5746
HHHPRR.5 (562)										
1	0.9323	0.2411	0.1670	0.1360	0.99	88.3	2.15e-18	0.97	0.1366	0.3781
2	0.7843	0.4649	0.2634	0.2576	0.946	120.3	2.46e-38	0.88	0.2836	0.5347
3	0.6650	0.6166	0.2712	0.3687	0.862	148.0	3.66e-57	0.83	0.3629	0.6087
HHHPRR.6 (561)										
1	0.8535	0.3443	0.2547	0.1175	0.987	146.0	2.7e-27	0.97	0.1534	0.4115
2	0.7553	0.4883	0.3412	0.2285	0.971	132.2	4.95e-41	0.99	0.1137	0.3932
3	0.6312	0.6440	0.3795	0.3440	0.905	166.4	1.34e-61	0.96	0.1787	0.4606

[a]standard deviation of the regression; [b]coefficient of determination; [c]leave-one-out cross-validated coefficient of regression; [d]coefficient of determination using scrambled activity data; [e]stability of the model to changes in training set composition; [f]ratio of model variance to activity variance; [g]significance level of F; [h]Root-Mean-Square Error in test set predictions; [i]coefficient of determination for the external test set, [j]correlation between predicted and observed external test set activity.

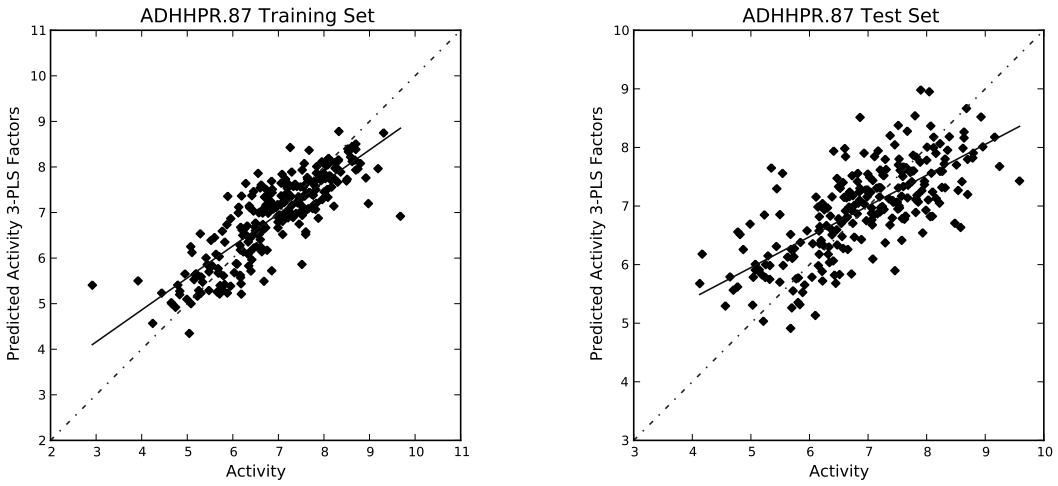


Figure 3.5: Sigma-2 training and test set regressions for the 3PLS-factor QSAR model.

Based on the battery of statistics, QSAR model ADHHPR.87 comprising either 2- or 3-PLS factors performed significantly better than the remaining models. Plots of the regression for training and tests sets are provided in Figure 3.5. This pharmacophore corresponded to a conformer of a molecule developed by Mach et al. (see Figure 3.6).[98] The Pearson-*r* of the 3-PLS factor QSAR model indicates modest relative accuracy, and the remaining statistics are acceptable. Virtual screening of the curated dataset spiked with known inactives and the set of 1,000 drug-like decoys led to a recovery of 57.6% of known active compounds. Receiver-operator characteristic and performance as percentage of the database screened are provided in Figure 3.7. After ranking based on the QSAR, enrichment factors EF_1, EF^*_1, and EF'_1 were determined to be 2.6, 42, and 65, respectively. The latter two measures indicate a robust early enrichment despite the inability to recover all known actives.

Field fractions from the 2- and 3-PLS regressions (Figure 3.15) indicate a considerable amount of steric (bulk) and hydrophobic (grease) contributions to the QSAR, followed by hydrogen bond acceptor contributions. Electronic and hydrogen bond donor contributions were minimal.

Visualization of the Gaussian fields superimposed on the pharmacophore and representative ligand are provided in Figures 3.8–3.12. Positive steric effects are indicated at the hydrophobic and ring aromatic sites on the east and west ends of the ligand, respectively. The impact of negative

Table 3.15: Gaussian field fractions of hypothesis ADHHPR.87

No. Factors	Steric	Electrostatic	Hydrophobic	Hbond Acceptor	Hbond Donor
1	0.407	0.054	0.314	0.177	0.047
2	0.390	0.069	0.306	0.168	0.068
3	0.328	0.081	0.309	0.190	0.091

steric contributions is negligible. An interesting combination of negative and positive electrostatic contributions demonstrates unfavorable interactions with positive partial charge surrounding the aromatic ring and continuing towards the the linker oxygen presented by the carbamate. Another unfavorable electrostatic positive partial charge field is present over the tertiary amine. Favorable positive electrostatics extend over the top of the aromatic ring and through the carbonyl of the carbamate and around the amine in a snake-like manner. Positive hydrophobic contours are present throughout the majority of the scaffold with the exception of the tertiary amine, and a small portions of the chain at the east end. Positive hydrogen bond acceptor projected point fields are expressed at the back of the aromatic ring and nestled between the amide and ester linkages of the carbamate, whereas negative contributions are made around the carbonyl and at the east end in the linker chain near the amine. Hydrogen bond donor projected point fields have an almost exclusively negative impact on the QSAR model with the exception of the back side of the 9-azabicyclo[3.3.1]nonan-3α-yl moiety.

Additional visualizations of the best alignment of one of our laboratory's active and nonselective benzo[*d*]thiazol-2(*3H*)ones[99] is provided for context of how this particular QSAR model could be used for ligand-based drug development. Due to the bent alignment, this particular conformation of RB8 is well superimposed on the positive steric and hydrophobic fields. The thiazolone moiety is also well situated within the positive electrostatic region, whereas the tertiary amine is located within the negative electrostatic region. This agrees with the relative partial charges assigned by the OPLS_2005 force field. The thiazolone carbonyl nestles a region of slightly negative hydrogen bond acceptor contours, yet the second, and particularly third carbon down the linker from the thiazolone seem particularly suited for replacement with an acceptor moiety. While RB8, aligned in this way

does not suffer from the negative hydrogen bond donor fields, one hypothetical improvement to σ-2 affinity would to be to place a donor at the pro-S hydrogen 2 carbons away from the amine on the internal linker.

3.5.1 Development of σ-1 pharmacophore models and QSAR

The σ-1 database of 1396 compounds was treated to the same workflow as described for σ-2 ligands. A subset of active and inactive compounds (Table 3.16 and Figure 3.18) was selected using up to 3 active compounds from each cluster along with sufficient inactives (3 or more) to balance the classification set. SAP was performed using 16,384 informative fingerprints bits. The Δ cutoff

Table 3.16: Statistics of the balanced σ-1 classification model data set.

No. of molecules					
Training set		Test Set			
Active	Inactive	Active	Inactive	Total	Total no. of conformers
39	44	19	22	124	10,409

was determined to be 0.761, resulting in a fingerprint length of 13,334. The Tanimoto metric was used to generate a fingerprint matrix from this file for instance-based feature mapping. An optimal λ tuning parameter of 0.006, corresponding to a prediction error of 0.224 was used to train the SVM. An internal accuracy of 1 was found, with external accuracy and an MCC of 0.732 and 0.460, respectively. In total, 52 prototype conformers were found, comprising 30 active and 22 inactive conformers.

These conformers were taken through the develop common pharmacophore process, using feature definitions including the piperidine and piperazine moieties. A maximum of 6 sites matching a minimum of three ligands, based on the heat map (Figure 3.19), produced 4 representative common pharmacophores which were used to screen the entire database of σ-1 conformers.

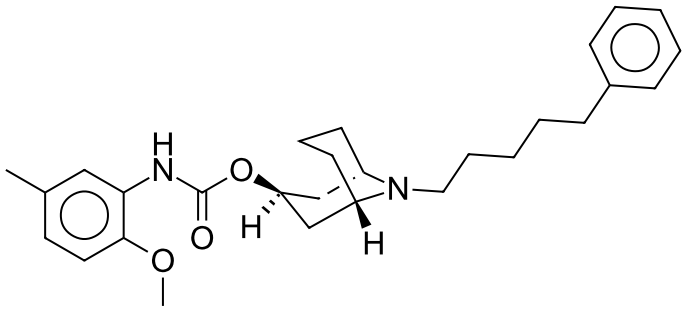


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Figure 3.6: Prototype ligand for the pharmacophore alignment ADHHPR.87

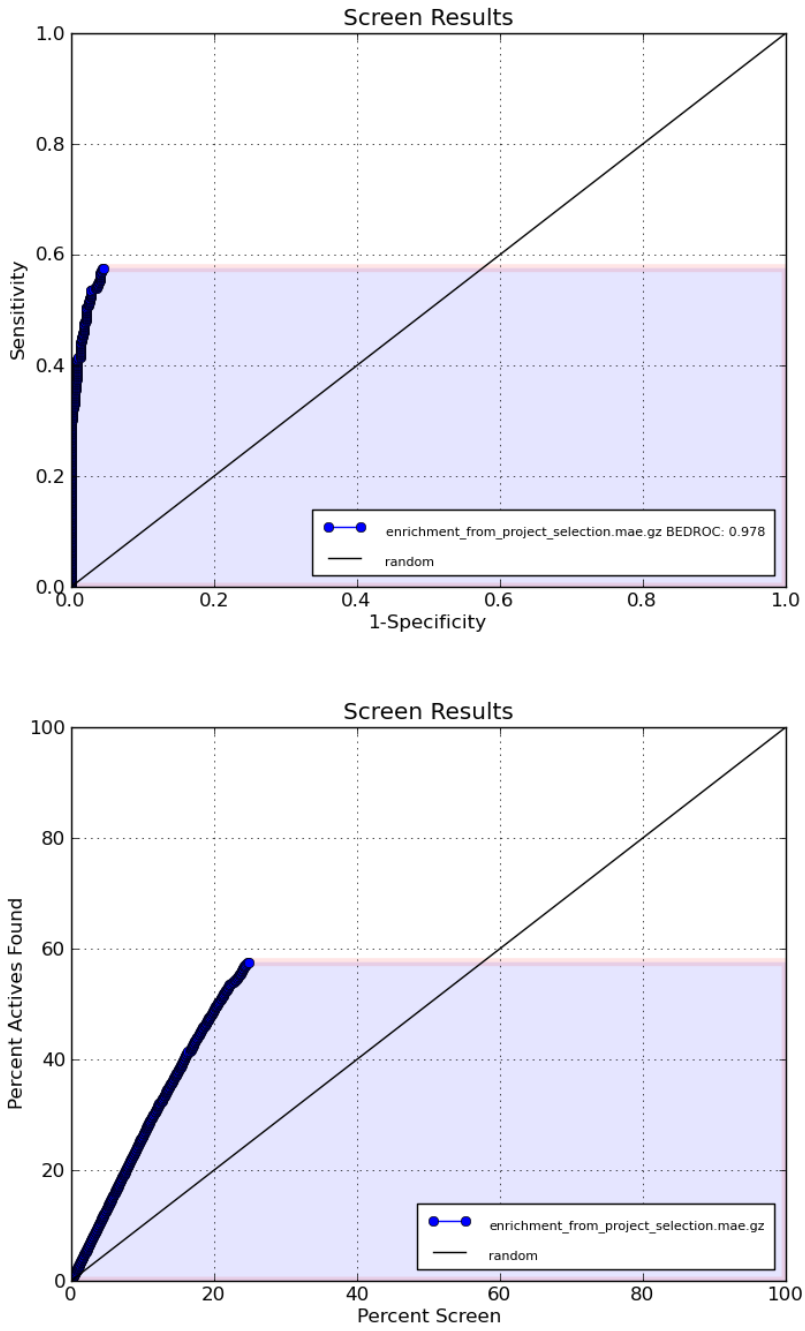

Figure 3.7: Sigma-2 virtual screening performance. Receiver-operator characteristic and screening performance as percentage of the database screened. The 45˚ line corresponds to the expected performance if the screening were no better than random.

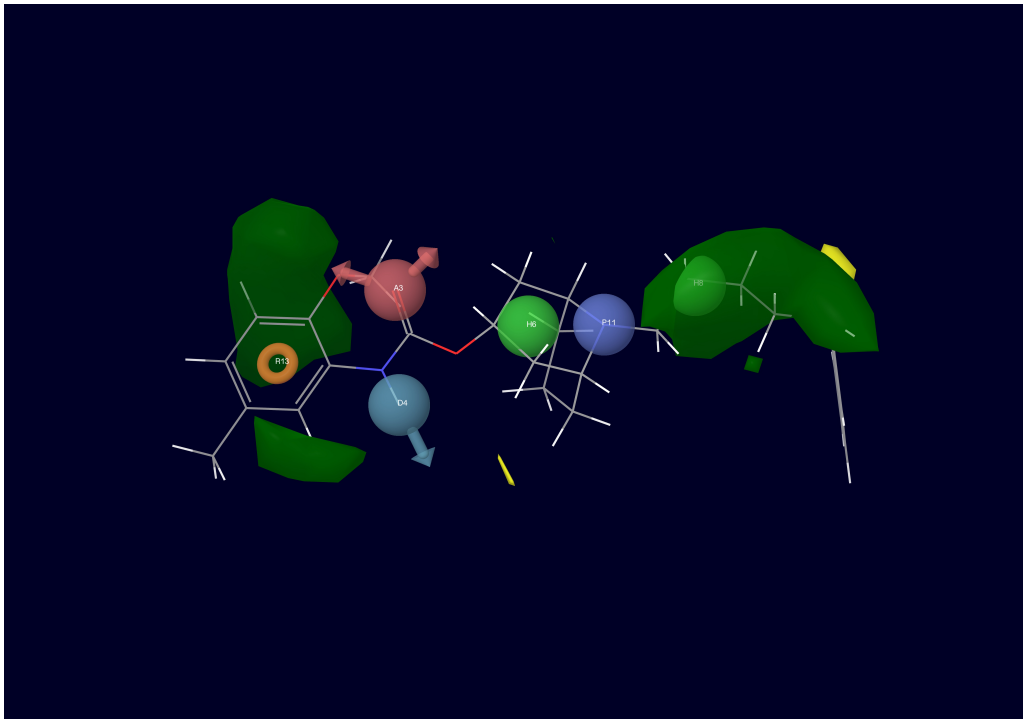

Figure 3.8: Gaussian steric fields presented by QSAR of ADHHPR.87. Positive steric field contours are shown in dark green. Negative contours are shown in yellow.

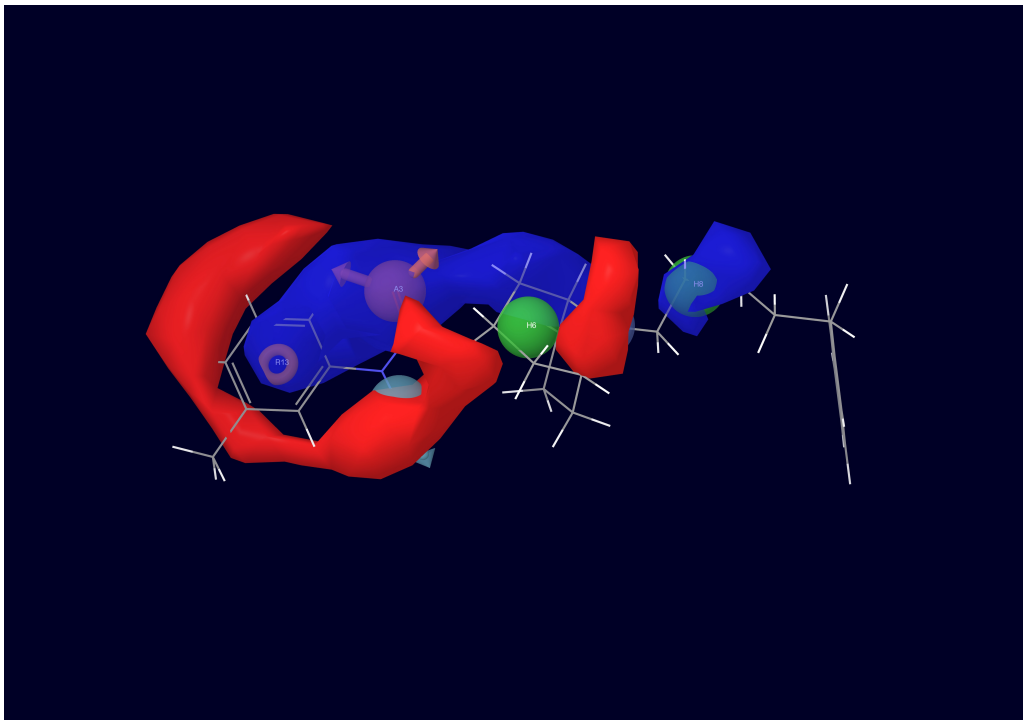

Figure 3.9: Gaussian electrostatic fields presented by QSAR of ADHHPR.87. Positive electrostatic field contours are shown in blue. Negative contours are shown in red.

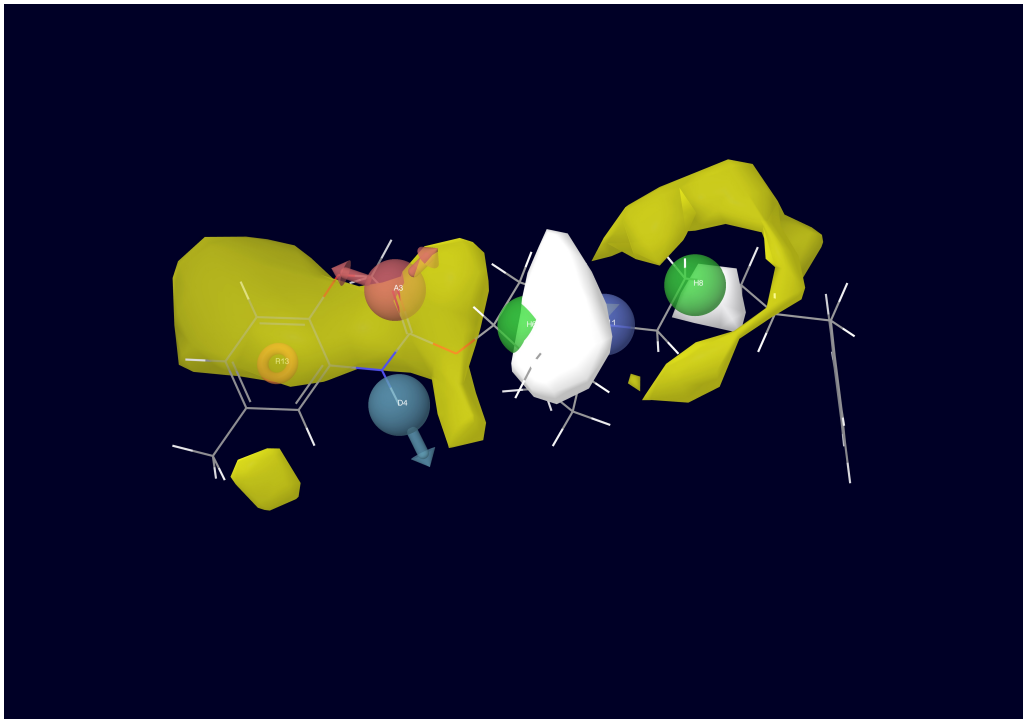

Figure 3.10: Gaussian hydrophobic fields presented by QSAR of ADHHPR.87. Positive hydrophobic field contours are shown in yellow. Negative contours are shown in white.

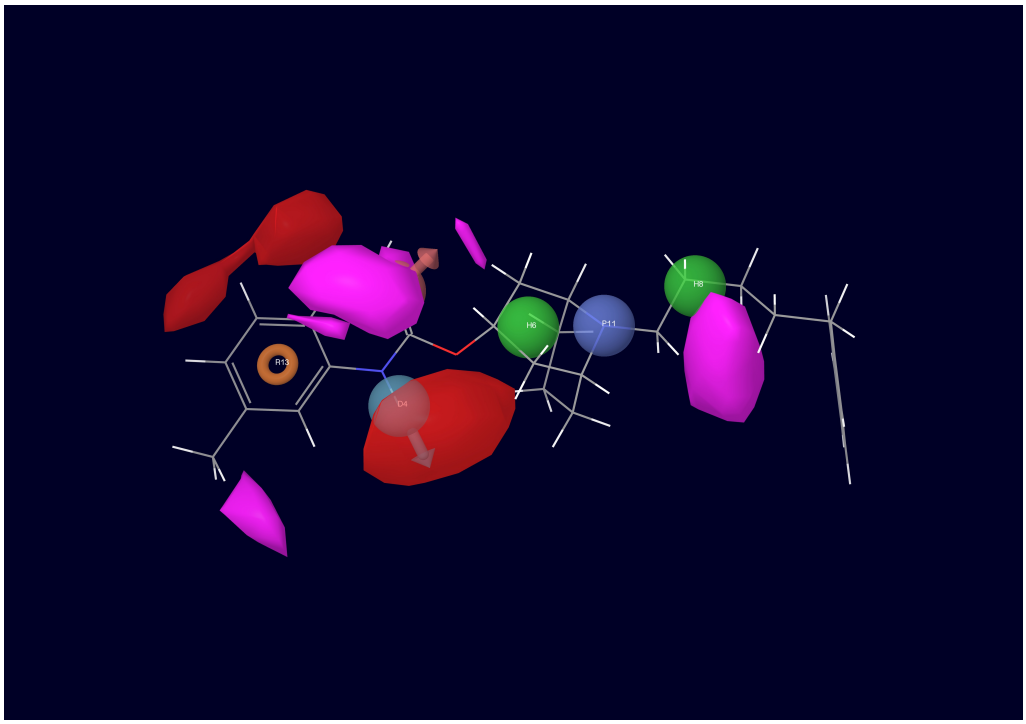

Figure 3.11: Gaussian hydrogen bond acceptor fields presented by QSAR of ADHHPR.87. Positive H-bond acceptor field contours are shown in red. Negative contours are shown in magenta.

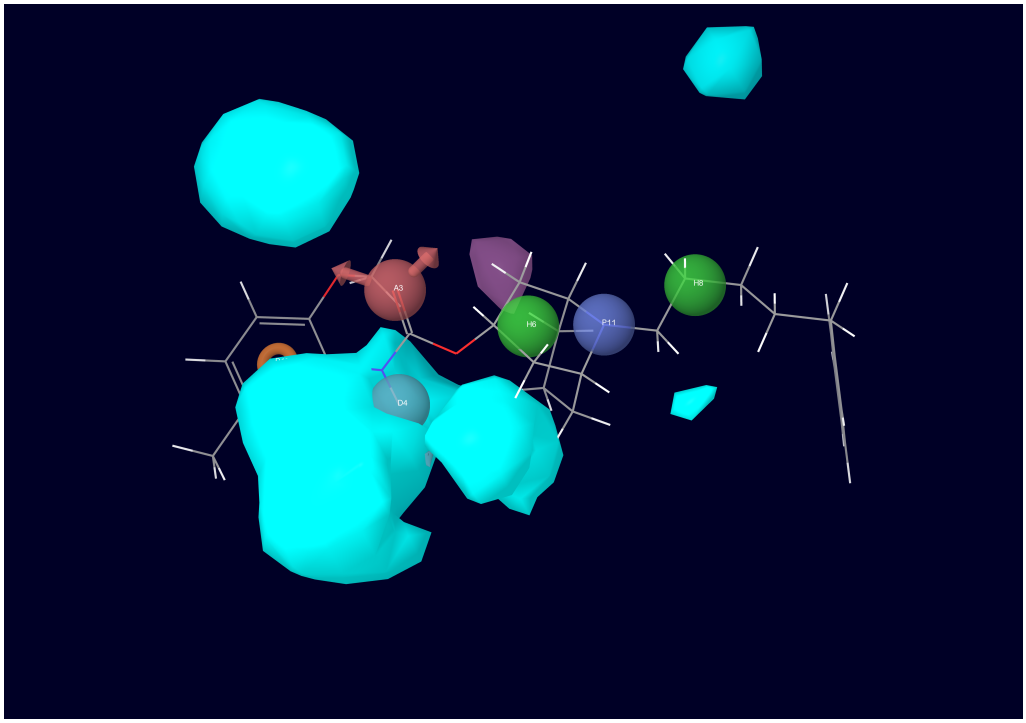

Figure 3.12: Gaussian hydrogen bond donor fields presented by QSAR of ADHHPR.87. Positive H-bond donor field contours are shown in blue-violet. Negative contours are shown in cyan.

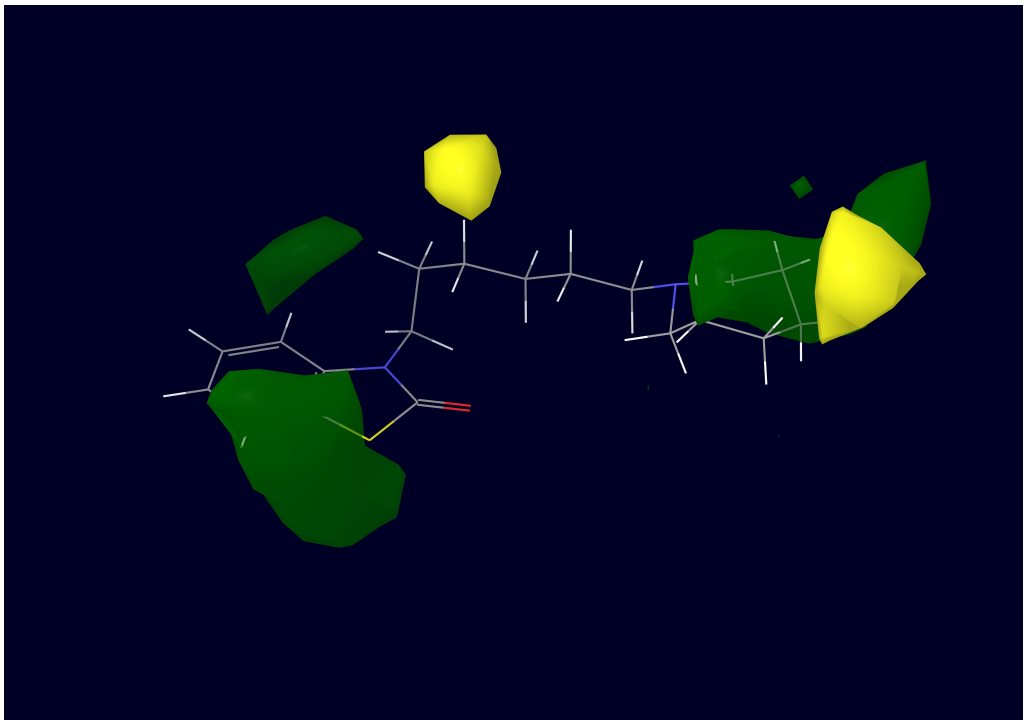

Figure 3.13: Positive steric field contours are shown in dark green. Negative contours are shown in yellow.

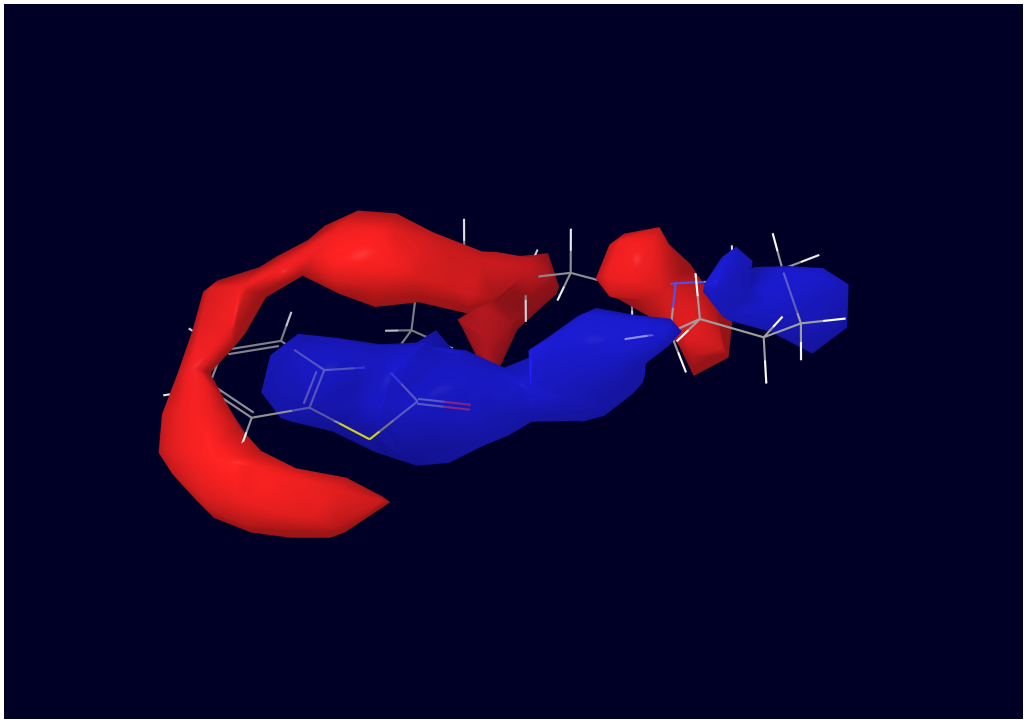

Figure 3.14: Positive electrostatic field contours are shown in blue. Negative contours are shown in red.

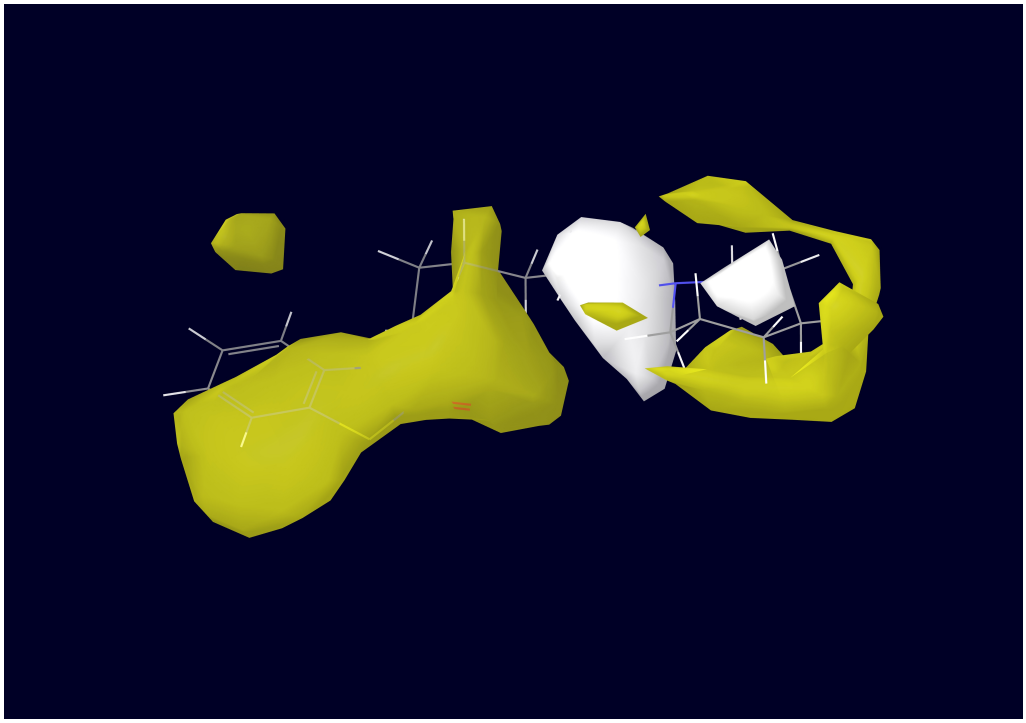

Figure 3.15: Positive hydrophobic field contours are shown in yellow. Negative contours are shown in white.

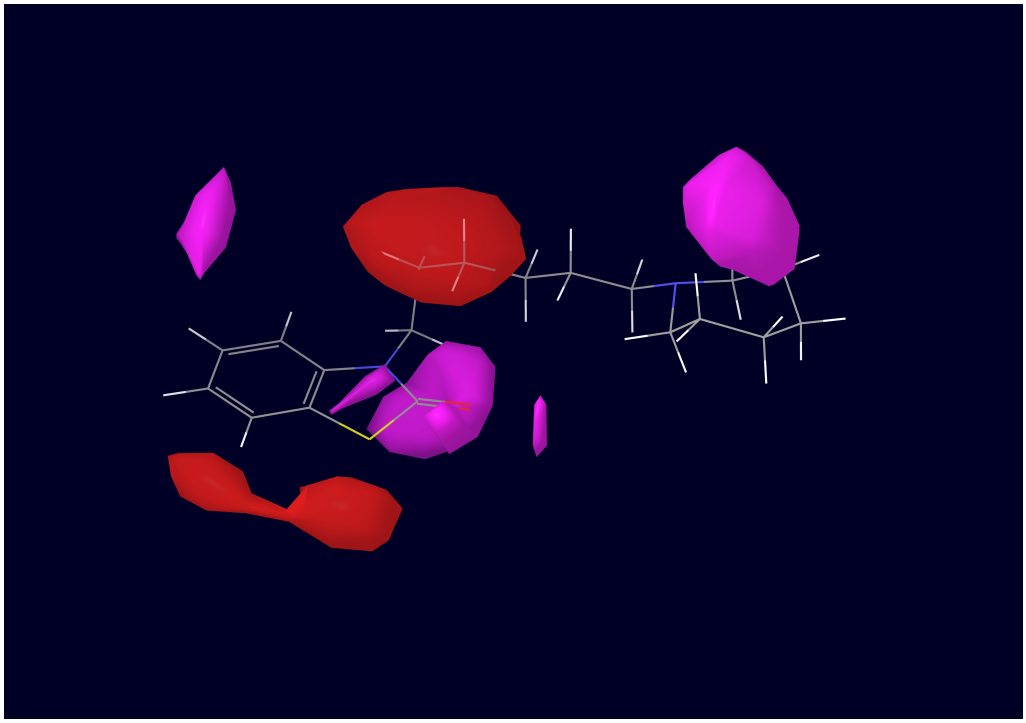

Figure 3.16: Positive H-bond acceptor field contours are shown in red. Negative contours are shown in magenta.

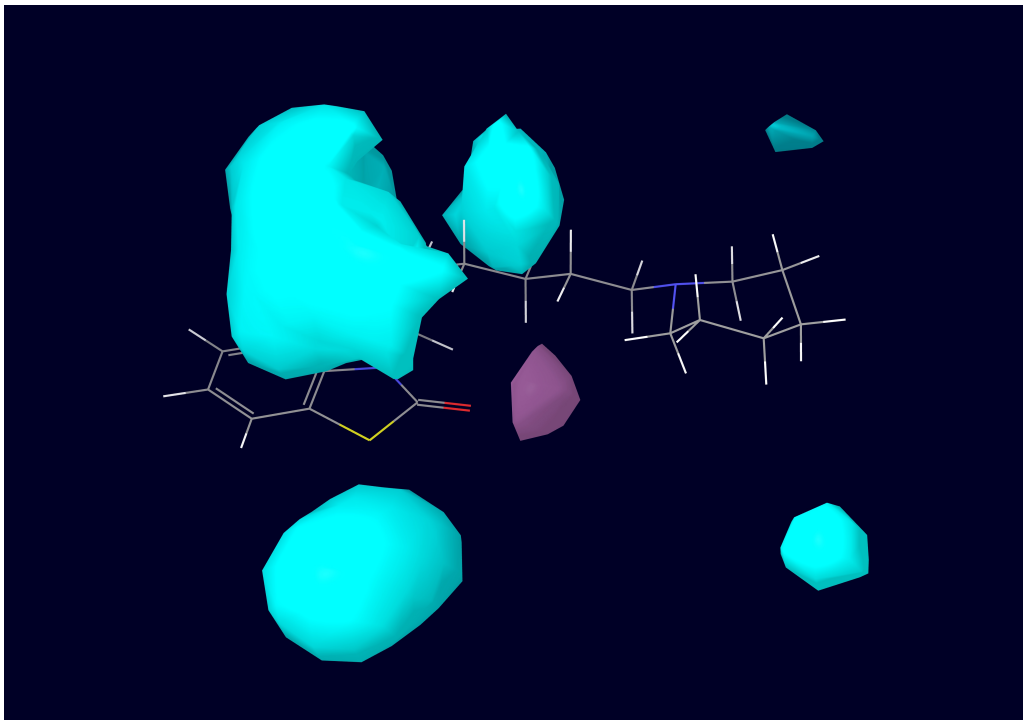

Figure 3.17: Positive H-bond donor field contours are shown in blue-violet. Negative contours are shown in cyan.

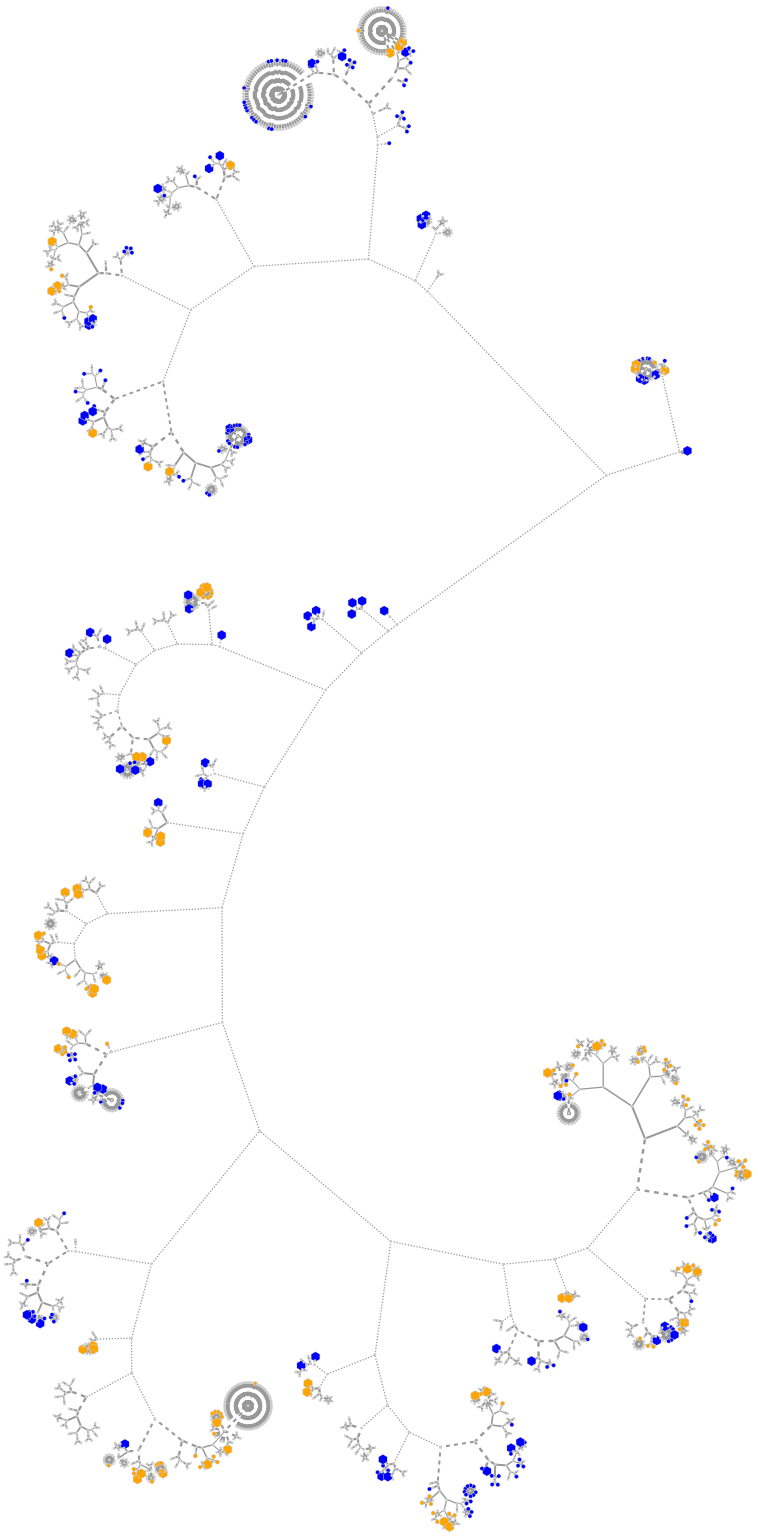

Figure 3.18: Clustered σ-2 scaffold data for the balanced dataset. Visualization details are the same as in Figure 3.1. One hundred and thirty molecules (larger hexagons) were selected from this set for SAP and MILES performance analysis.

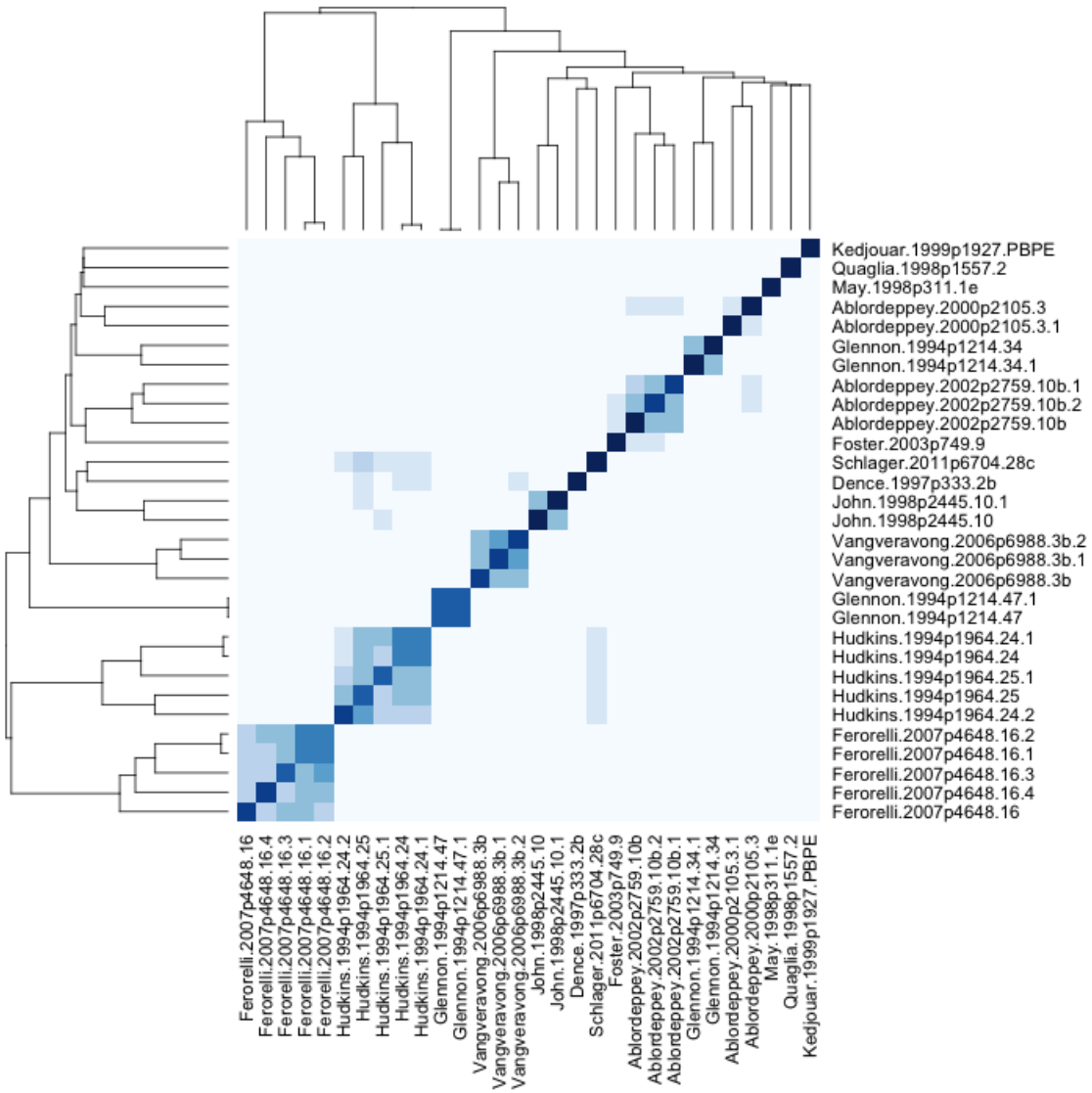

Figure 3.19: Sigma-1 prototype conformer heat map

Table 3.17: Sigma-1 pharmacophore hypotheses and related statistics for regressions of 1–3 PLS factors. Each hypothesis is label with the nature of the pharmacophore features (A = H-bond acceptor, D = H-bond donor, H = hydrophobic, R = aromatic, N = negative ionizable, P = positive ionizable). The number of database screening matches within the σ-1 database is shown in parentheses. A total of 1396 ligands representing the curated σ-1 data were screened.

No. Factors	SD[a]	R^{2b}	R^2 CV[c]	R^2 Scramble[d]	Stability[e]	F[f]	P[g]	RMSE[h]	Q^{2i}	Pearson-r[j]
AAHHPR.12 (758)										
1	1.0369	0.3573	0.2807	0.1096	0.988	209.6	4.37e-38	1.13	0.2357	0.4949
2	0.8772	0.5412	0.4082	0.2175	0.97	221.8	2.41e-64	1.08	0.3065	0.5672
3	0.7703	0.6472	0.4555	0.3127	0.942	229.3	1.84e-84	1.01	0.3876	0.6298
AAHHPR.16 (680)										
1	0.9336	0.4356	0.3491	0.1246	0.984	250.9	2.83e-42	1.10	0.2056	0.4692
2	0.8293	0.5561	0.4319	0.2421	0.974	202.9	7.38e-58	1.06	0.2622	0.5262
3	0.7484	0.6396	0.4404	0.3456	0.943	191.1	3.04e-71	1.02	0.3124	0.5715
AAHHPR.4 (795)										
1	0.9810	0.3996	0.3106	0.1081	0.986	255.5	1.87e-44	1.09	0.2405	0.5036
2	0.8617	0.5379	0.4003	0.2185	0.972	222.9	6.23e-65	1.00	0.3620	0.6080
3	0.7738	0.6283	0.4467	0.2978	0.951	215.2	1e-81	1.01	0.3439	0.6015
AAHHPR.8 (757)										
1	1.0347	0.3422	0.2501	0.1087	0.982	196.1	3.6e-36	1.12	0.2246	0.4897
2	0.9197	0.4817	0.3326	0.2367	0.964	174.7	2.21e-54	1.08	0.2777	0.5506
3	0.8125	0.5965	0.3842	0.3171	0.928	184.8	1.51e-73	1.01	0.3654	0.6178

[a]standard deviation of the regression; [b]coefficient of determination; [c]leave-one-out cross-validated coefficient of regression; [d]coefficient of determination using scrambled activity data; [e]stability of the model to changes in training set composition; [f]ratio of model variance to activity variance; [g]significance level of F; [h]Root-Mean-Square Error in test set predictions; [i]coefficient of determination for the external test set, [j]correlation between predicted and observed external test set activity.

Gaussian field-based QSARs were developed for alignments to all hypotheses, and statistics for the chosen 3 PLS-factor model are given in Table 3.17. Plots of the regression for training and tests sets are provided in Figure 3.20.

Hypothesis AAHHPR.12 performed slightly better than the remaining hypotheses, all of which shared the same number of features. The Gaussian field fractions (Table 3.18), much like those of the the σ-2 QSAR, indicate a high level of steric, hydrophobic character, although the hydrogen bond field fraction is noticeably more predominant. Virtual screening of the curated dataset spiked

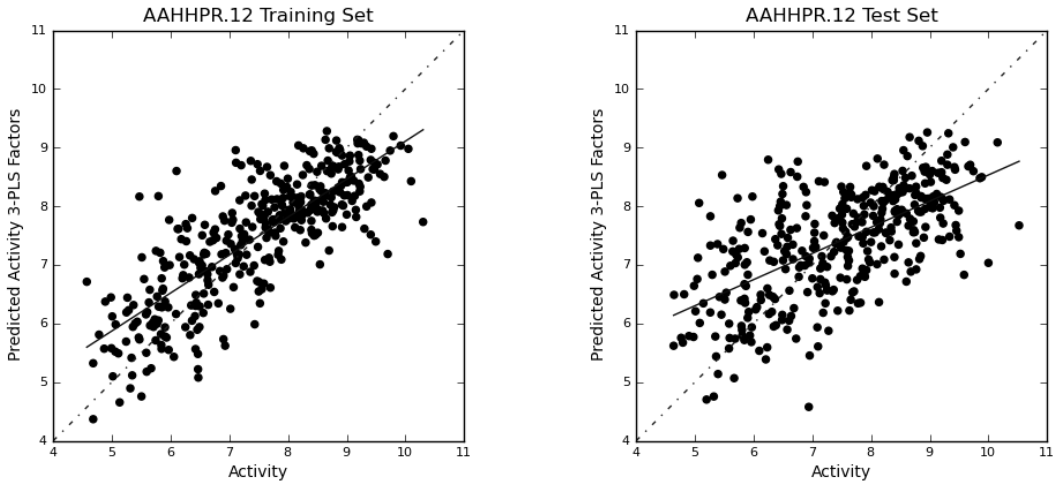

Figure 3.20: Sigma-1 training and test set regressions for the 3PLS-factor QSAR model.

with known inactives and the set of 1,000 drug-like decoys led to a recovery of 54.4% of known active compounds. After ranking based on the QSAR, enrichment factors EF_1, EF^*_1, and EF'_1 were determined to be 1.8, 12, and 23, respectively. The latter two measures indicate a robust early enrichment despite the inability to recover all known actives. Receiver-operator characteristic and performance as percentage of the database screened are provided in Figure 3.21.

Table 3.18: Gaussian field fractions of hypothesis AAHHPR.12

No. Factors	Steric	Electrostatic	Hydrophobic	Hbond Acceptor	Hbond Donor
1	0.399	0.042	0.229	0.252	0.079
2	0.401	0.045	0.276	0.208	0.069
3	0.377	0.054	0.265	0.215	0.090

Visualization of the Gaussian fields superimposed on the pharmacophore and representative ligand are provided in Figures 3.23–3.27. Interestingly, although the feature types of the underlying pharmacophore are very similar to the σ-2 pharmacophore, there are some important differences in the Gaussian fields. Sterically, the only favorable interaction is located very near to the positive ionizable feature. The remaining steric interactions form a pocket around the reference ligand of Hudkins et al.[51] (see Figure 3.22). Again, negative electrostatics are favored around the positive ionizable feature. Hydrophobic features extend through much of the scaffold except for the location

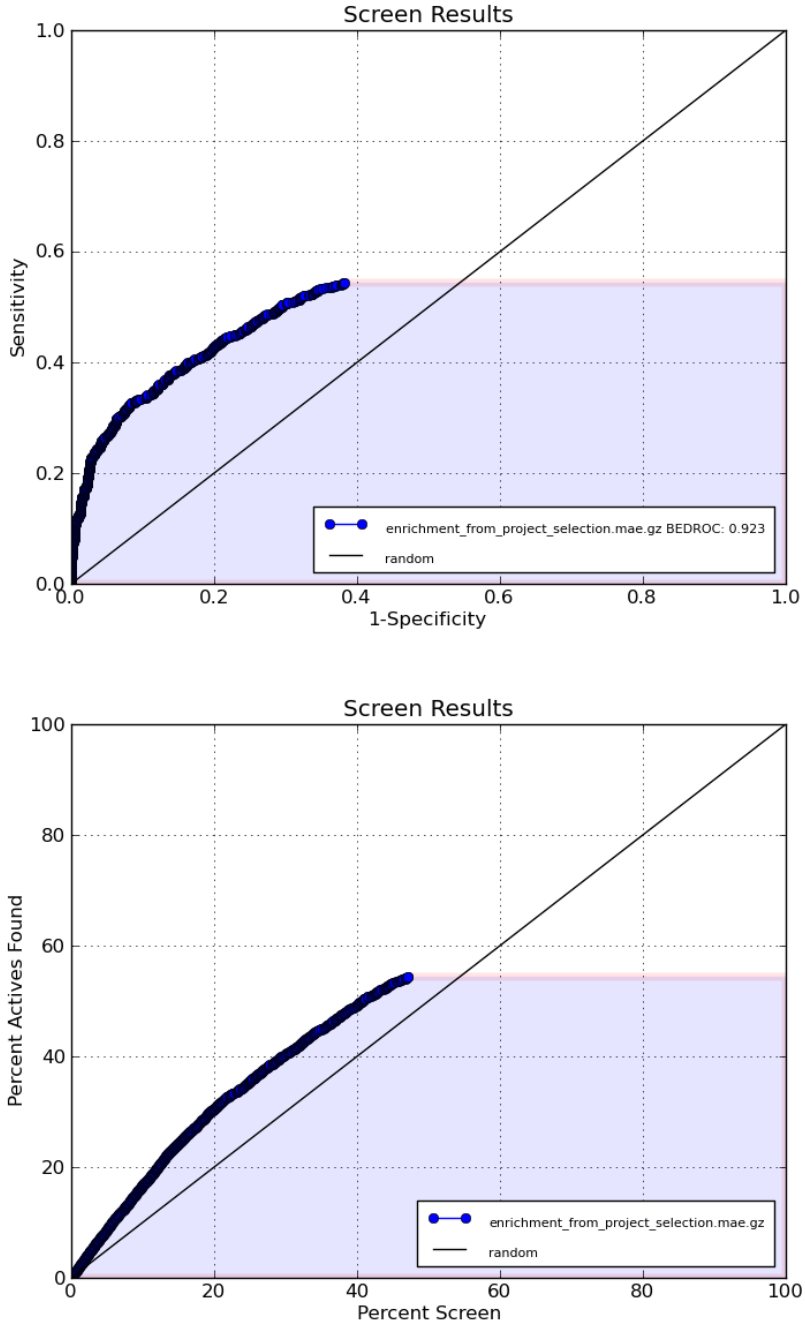

Figure 3.21: Sigma-1 virtual screening performance. Receiver-operator characteristic and screening performance as percentage of the database screened.

of the positive ionizable feature and the ring aromatic at the west end. Acceptor fields are favored near the ester oxygens, in the same areas which are disfavored sterically. Donor contours show a strong unfavorable interaction on the west end in the vicinity of the ring aromatic pharmacophore site.

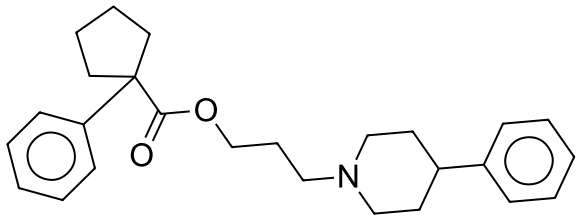

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Figure 3.22: Prototype ligand for the pharmacophore alignment AAHHPR.12

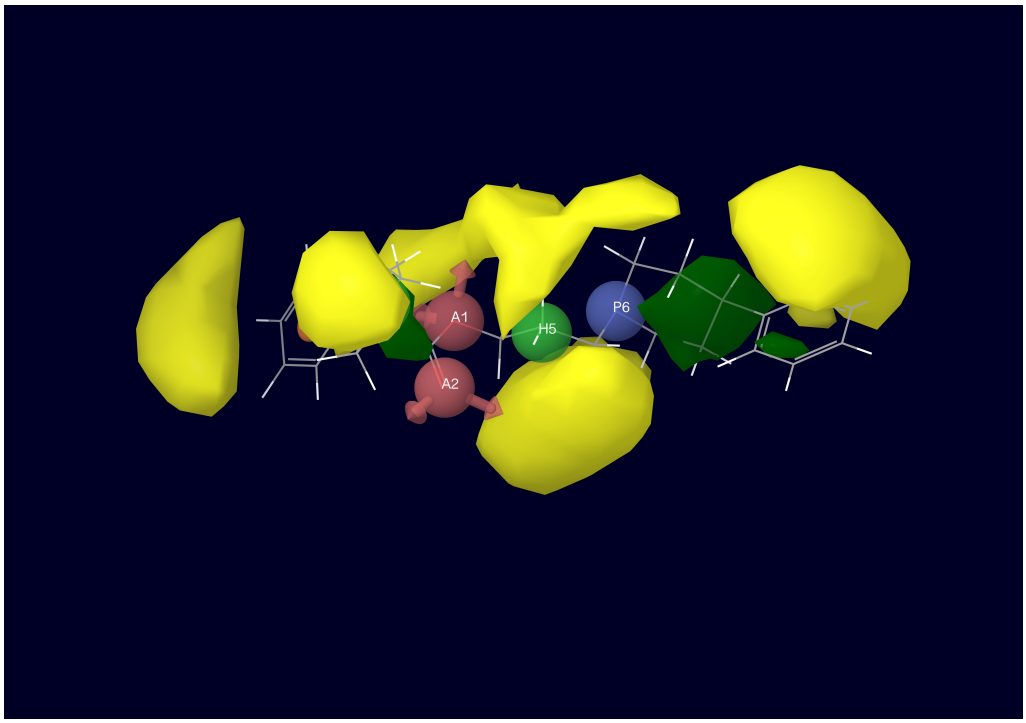

Figure 3.23: Gaussian steric fields presented by QSAR of AAHHPR.12. Positive steric field contours are shown in dark green. Negative contours are shown in yellow.

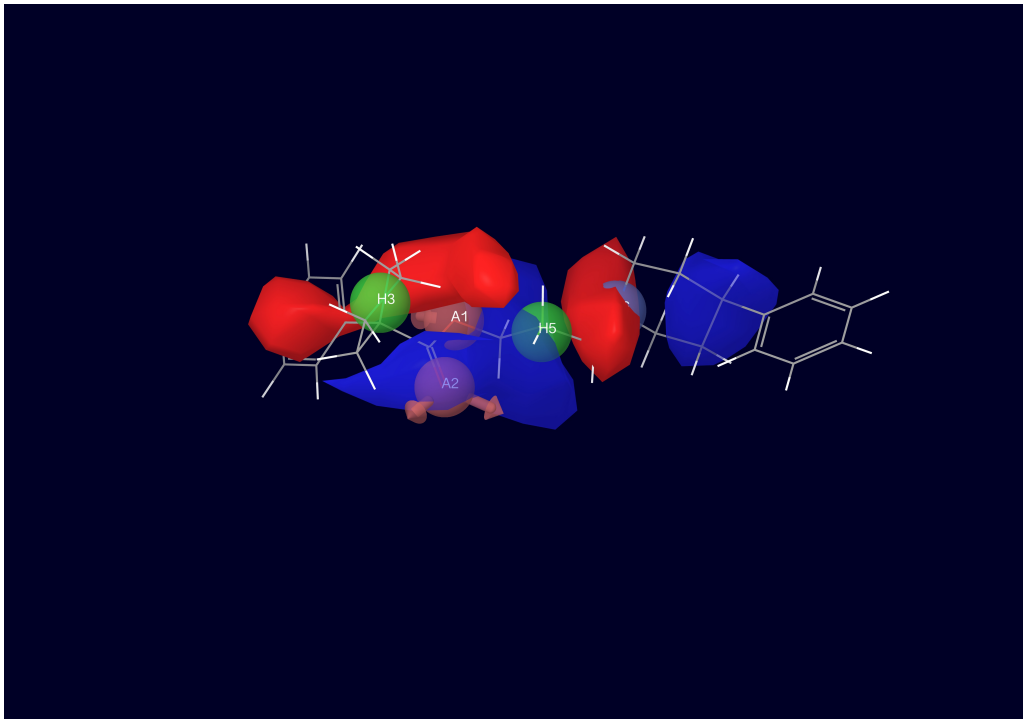

Figure 3.24: Gaussian electrostatic fields presented by QSAR of AAHHPR.12. Positive electrostatic field contours are shown in blue. Negative contours are shown in red.

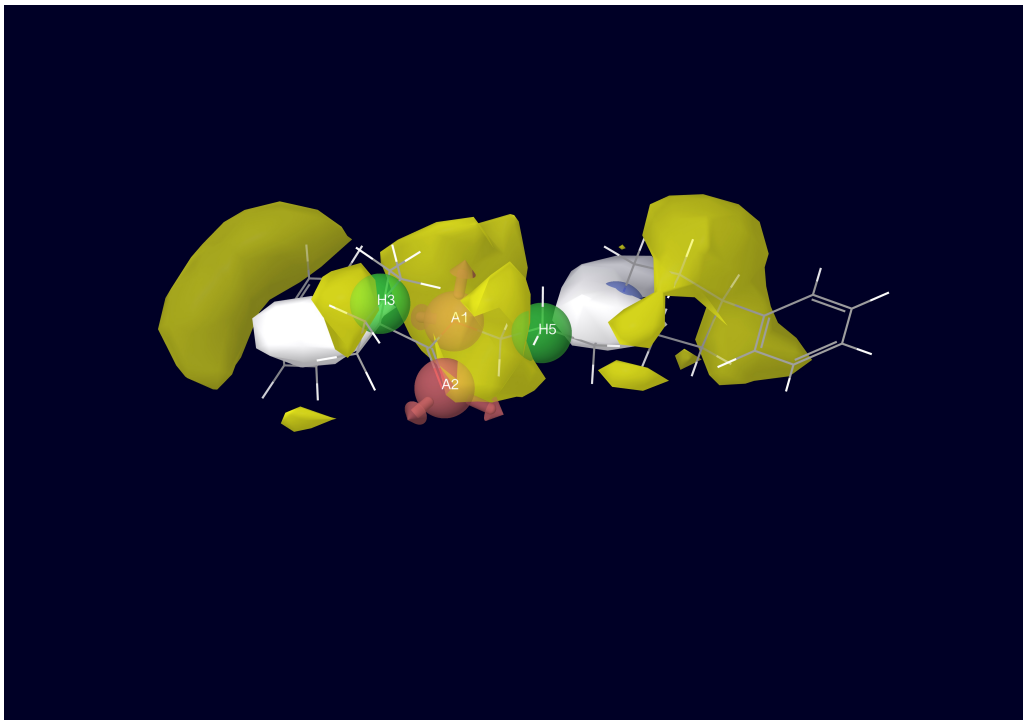

Figure 3.25: Gaussian hydrophobic fields presented by QSAR of AAHHPR.12. Positive hydrophobic field contours are shown in yellow. Negative contours are shown in white.

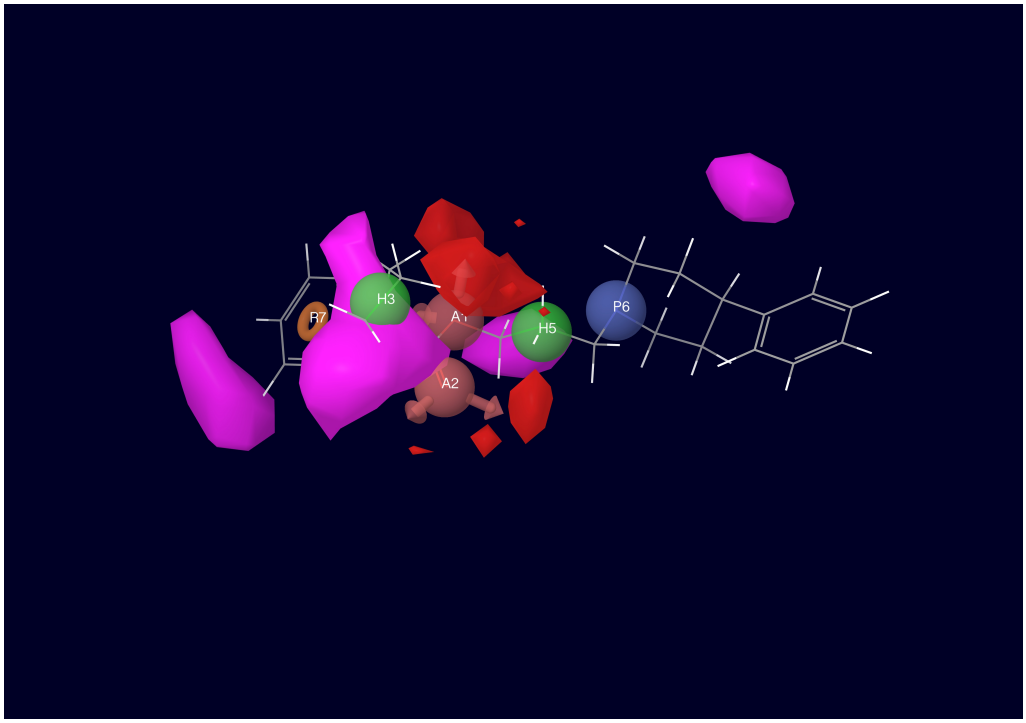

Figure 3.26: Gaussian hydrogen bond acceptor fields presented by QSAR of AAHHPR.12. Positive H-bond acceptor field contours are shown in red. Negative contours are shown in magenta.

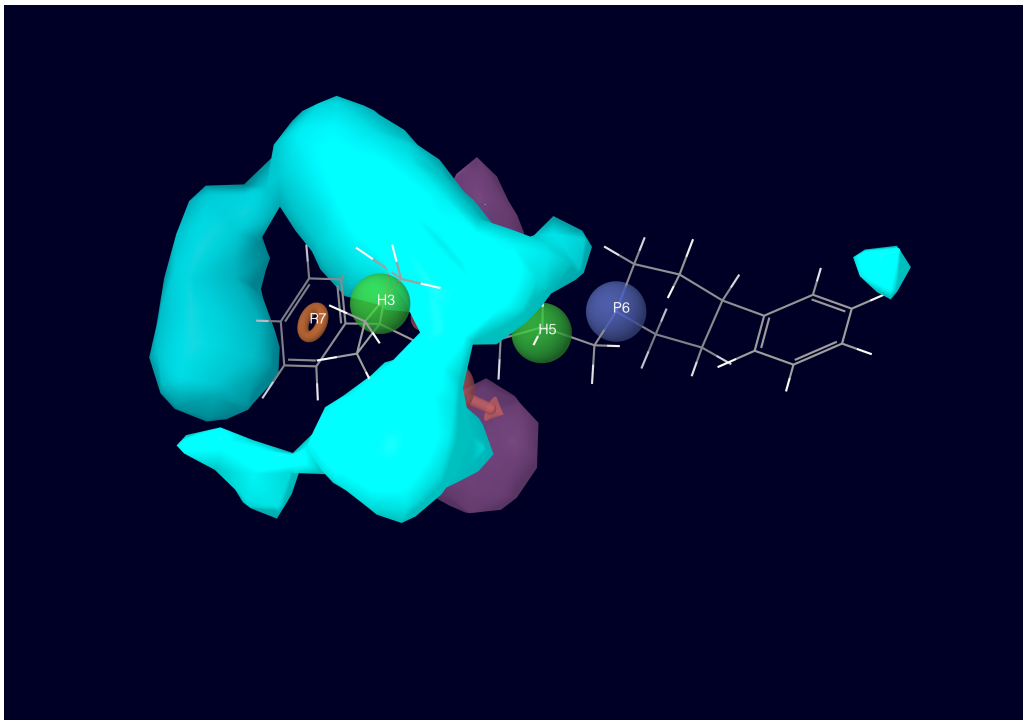

Figure 3.27: Gaussian hydrogen bond donor fields presented by QSAR of AAHHPR.12. Positive H-bond donor field contours are shown in blue-violet. Negative contours are shown in cyan.

4. CONCLUSIONS AND FUTURE WORK

The large print giveth, and the small print taketh away

Step Right Up
Tom Waits

4.1 Conclusions

Computational techniques for ligand-based drug design based on pharmacophore modeling, virtual screening, and QSARs have met with many challenges over the years when applied to σ receptor targets. One of the major hurdles, having a database of the extensive number of ligands presented in the literature since σ research began, will undoubtably help to overcome the cause of many inconsistencies in computational analyses, namely, data heterogeneity. Curated set of σ data, based on K_i values, and using comparable analytical methods is now available.

Clustering of the datasets by scaffold allowed for a sensible way of generating diverse training and test sets of active and inactive compounds in an efficient manner. This technique, pioneered by Guiguemde et al.[76] has the advantage of hierarchically assembling a dendrogram of structures by related scaffold, and provides an intuitive way of visualizing properties associated with structural changes at the core of a database of ligands.

The modeling approach described here has met with a modicum of success, particularly for σ-2 classification techniques. Pharmacophore fingerprints performed very well when used for the classification of active and inactive compounds through the Multiple-instance learning via embedded subset selection protocol. Significance Analysis of Pharmacophores has the potential to

allow for a greatly reduced fingerprint bit length, although care must be taken to pick an appropriate metric, whether it be a distance or similarity measure. In particular, implementing MILES with measures which use products of bits from each instance or that use a maximum or minimum similarity are problematic if SAP has been utilized to reduce the fingerprint length. While the pharmacophore features which lead to better SAP classification accuracy can readily be calculated at some computational expense, the original implementation was designed for microarray data. The number of wells in a microarray is much smaller than the number of instances in a SAP analysis, and the SAM method which SAP is based upon uses the Γ function for permutation analysis. As the number of instances grows, this function causes an overflow and triggers an error, calling some question into the validity of the statistical analysis.

Aggressive reduction in fingerprint length tends to reduce classification accuracy, particularly with larger numbers of instances. A cursory analysis of the results of this research suggests that no fewer "informative bits" are used than the total number of conformers. The elimination of bits with a frequency of less than 5%, as implemented by Fu et al. [82] produced slightly more bits than the levels we investigated. This may partially explain the comparable classification performance with the 54-molecule dataset used at higher fingerprint lengths.

An issue with purely ligand-based design projects is how to identify active conformers of ligands for pharmacophore development, shape-screening, virtual screening, and other methods that depend on good knowledge of the 3D coordinates of active molecules at the biomolecular target. In preliminary experiments using a complete set of conformers, the number of pharmacophores surviving the common pharmacophore perception step was overwhelming, and model assessment at this point was unjustifiable. The MILES method, as implemented here, provided a set of prototype conformers that was useful in reducing the overhead of pharmacophore generation with very flexible molecules. Consequentially, number of common pharmacophores generated incorporating the MILES approach was orders of magnitude smaller than when using a complete set of conformers. Virtual screening of with the surviving pharmacophore hypotheses allowed for the retrieval of much of the original datasets, indicating a general utility for screening σ-like molecules. Quantitative

structure-activity relationships built upon the aligned hits provided provided virtual screening rankings that retrieved over 50% of the known actives for both σ-1 and σ-2 targets. While this level of performance is not ideal, it does suggest that multiple binding modes or binding sites are present on both receptors. It may be possible to eliminate the retrieved actives from the pharmacophore modeling process and build new models which capture the pharmacophore features of these alternate binding sites. These pharmacophore models and their related QSARs will be useful tools for further virtual screening projects targeted at discovering more diverse scaffolds from which to build upon.

4.2 Future Work

Identification of alternative pharmacophore models based on the set of ligands not retrieved with the current pharmacophore models is needed for a comprehensive description of the σ binding motifs. As it stands, the virtual screening performance is suitable for screening a large database of commercially available compounds. Careful consideration of the hits retrieved in such a screen will be useful for identifying more diverse scaffolds for the exploration of σ site probes. Small modifications of the procedures used in this work will also be useful for developing selectivity- rather than affinity-based models. It will also be interesting to expand this work to identify binding requirements of agonists versus antagonists, although the existing literature is sometimes vague or contradictory when it comes to determining the pharmacological outcomes that are used for such a classification.

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LIST OF APPENDICES

APPENDIX A. HIERARCHICAL CLUSTERING SCRIPTS

APPENDIX A. HIERARCHICAL CLUSTERING SCRIPTS

The following directory listings, Makefile, and python files implement hierarchical clustering. Prerequisites for this process are Canvas, Strip-It, Python, and Make. A SMILES input file named `SMILES.smi` which contains only unique structures is required. An output file `cytoscape.net` that contains the requisite network table data for visualization with Cytoscape is generated by the Makefile.

A.1 hcviz directory listing

```
xibalba:hcviz dewatson$ ls -lR
total 8
-rw-r--r--  1 dewatson  staff  1567 Jun 22 15:25 Makefile
drwxr-xr-x  6 dewatson  staff   204 Sep 12 19:47 bin
drwxr-xr-x  4 dewatson  staff   136 Jun 22 14:15 lib

./bin:
total 32
-rwxr-xr-x  1 dewatson  staff  1378 Jun 22 13:04 network_cores.py
-rwxr-xr-x  1 dewatson  staff  1341 Jun 22 13:52 network_linkage.py
-rwxr-xr-x  1 dewatson  staff  1826 Jun 22 14:43 network_scaffolds.py
-rwxr-xr-x  1 dewatson  staff  1414 Jun 22 13:04 singletons.py

./lib:
total 16
-rw-r--r--  1 dewatson  staff   9 Jun 22 13:02 MURCKO1.def
-rw-r--r--  1 dewatson  staff  21 Jun 22 13:03 RWL2.def
```

A.2 Makefile

```
##
# Makefile
#
# Driver to control the processing of molecular SMILES into
#     a complete edge network
#
# author     David Watson
# email      dewatson@icloud.com
# copyright  Copyright (c) 2013, David Watson
##

all: stripit canvas network

stripit:
        @echo Running Strip-It and creating scaffold files
```

```
        strip-it --input SMILES.smi --output RWL2.strip \
                 --scaffolds ./lib/RWL2.def
        grep -v -e "-$$" RWL2.strip > RWL2.scaf
        awk '{ print $$3 " " $$3 }' RWL2.scaf | grep -v "RINGS" | \
            sort -u > MURCKO1.smi
        strip-it --input MURCKO1.smi --output MURCKO1.scaf \
                 --scaffolds ./lib/MURCKO1.def
        awk '{ print $$3 " " $$3 }' MURCKO1.scaf | grep -v "MURCKO" | \
            sort -u > RADIAL.smi

network:
        ./bin/network_scaffolds.py -i RWL2.scaf -o radial.net
        strip-it --input singletons.smi --output singletons.scaf \
            --scaffolds ./lib/MURCKO1.def
        ./bin/network_cores.py -i MURCKO1.scaf -o radial.net
        ./bin/network_linkage.py -i radial.tree -o radial.net
        ./bin/singletons.py -i singletons.scaf -o radial.net
        sed 's/\[/\\[/g' singletons.sed | sed 's/\]/\\]/g' > singletons.grep
        grep -v -f singletons.grep radial.net > cytoscape.net

canvas:
        $$SCHRODINGER/utilities/canvasFPGen -ismi RADIAL.smi -o radial.fp \
            -fptype radial -nostereo
        $$SCHRODINGER/utilities/canvasFPMatrix -ifp radial.fp \
            -ocsv radial.csv -metric euclidean
        $$SCHRODINGER/utilities/canvasHC -im radial.csv -linkage mcquitty \
            -ot radial.tree -kelley

mostly-clean: stripit-clean network-clean canvas-clean

stripit-clean:
        -rm -f RWL2.strip RWL2.scaf MURCKO1.smi MURCKO1.scaf RADIAL.smi

network-clean:
        -rm -f radial.net singletons.smi singletons.sed singletons.scaf \
               singletons.grep

canvas-clean:
        -rm -f radial.fp radial.csv radial.tree

all-clean: mostly-clean
        -rm -f cytoscape.net
```

A.3 network_cores.py

```
#!/usr/bin/env python
"""
```

```
    network_cores.py

    Creates network core node entries based on a Strip-it scaffold file

    author      David Watson
    email       dewatson@icloud.com
    copyright   Copyright (c) 2013, David Watson
"""
import sys
import argparse

parser = argparse.ArgumentParser(description =
    'Create a hierarchy of RWL2_Murcko1 interactions from a murko_1 strip-it' \
    ' file.')
parser.add_argument('-i', metavar = 'infile', type = argparse.FileType('r'),
                    help = 'Strip-It murcko1 file', required = True,
                    dest = 'murcko')
parser.add_argument('-o', metavar = 'outfile', type = argparse.FileType('a'),
                    help = 'Cytoscape network table', required = True,
                    dest = 'cytoscape')
try:
    args = parser.parse_args()
except IOError, msg:
    parser.error(str(msg))

cytoscape = '%s %s %s %s\n'

try:
    stripped = next(args.murcko)
except StopIteration:
    sys.exit('Strip-it file appears empty')

if not stripped.startswith('NAME'):
    sys.exit('Strip-it file appears to be invalid')

murcko = {}

while True:
    try:
        murckoline = next(args.murcko).rstrip().split("\t")
    except StopIteration:
        break

    while not murckoline[2] in murcko:
        murcko[murckoline[2]] = [murckoline[0]]
        break
    else:
```

```
        murcko[murckoline[2]].append(murckoline[0])

for smiles in murcko.keys():
     for molecule in range(0, len(murcko[smiles]), 1):
         args.cytoscape.write(cytoscape % (murcko[smiles][molecule], 'S_C',
                              smiles, '10.0'))
```

A.4 network_linkage.py

```
#!/usr/bin/env python
"""
    network_linkage.py

    Converts a Canvas dendrogram to a Cytoscape edge network

    author      David Watson
    email       dewatson@icloud.com
    copyright   Copyright (c) 2013, David Watson
"""
import sys
import argparse

parser = argparse.ArgumentParser(description =
    'Create dendrogram leaf-node and node-node linkages from a Canvas tree ' \
    'file.')
parser.add_argument('-i', metavar = 'infile', type = argparse.FileType('r'),
                    help = 'Canvas tree file', required = True, dest = 'tree')
parser.add_argument('-o', metavar = 'outfile', type = argparse.FileType('a'),
                    help = 'Cytoscape network table', required = True,
                    dest = 'cytoscape')
try:
    args=parser.parse_args()
except IOError, msg:
    parser.error(str(msg))

cytoscape = '%s %s%s %s %s\n'

try:
    stripped = next(args.tree)
except StopIteration:
    sys.exit('Tree file appears empty')

if not stripped.startswith('0'):
    sys.exit('Tree file appears to be invalid')

args.tree.seek(0)
```

```
while True:
    try:
        nodeline = next(args.tree).rstrip().split()
    except StopIteration:
        break

    node = 'N' + nodeline[0]
    weight = nodeline[1].rstrip()

    for linked in range(2):
        childline = next(args.tree).rstrip().split()
        if childline[0].startswith('C'):
            prefix = 'N'
        else:
            prefix = ''
        args.cytoscape.write(cytoscape % (prefix + childline[1], childline[0],
                             '_N', node, weight))
```

A.5 network_scaffolds.py

```
#!/usr/bin/env python
"""
    network_scaffolds.py

    Create Cytoscape network node entries based on scaffolds

    author      David Watson
    email       dewatson@icloud.com
    copyright   Copyright (c) 2013, David Watson
"""
import sys
import argparse

parser = argparse.ArgumentParser(
    description = 'Creates an edge network of molecule-scaffold from ' \
                  ' Strip-It RINGS_WITH_LINKERS_2 output.')
parser.add_argument('-i', metavar = 'infile', type = argparse.FileType('r'),
                    help = 'Strip-It rwl2 file', required = True, dest = 'rwl')
parser.add_argument('-o', metavar = 'outfile', type = argparse.FileType('w'),
                    help = 'Cytoscape network table', required = True,
                    dest = 'cytoscape')
try:
    args = parser.parse_args()
except IOError, msg:
    parser.error(str(msg))

cytoscape = '%s %s %s %s\n'
```

```
singletons = open('singletons.smi', 'w')
patterns = open('singletons.sed', 'w')

try:
    stripped = next(args.rwl)
except StopIteration:
    sys.exit("Strip-it file appears empty")

if not stripped.startswith('NAME'):
    sys.exit("Strip-it file appears to be invalid")

rings_with_linkers = {}
args.cytoscape.write(cytoscape % ("source", "interaction", "target", "weight"))

while True:
    try:
        rwlline = next(args.rwl).rstrip().split("\t")
    except StopIteration:
        break

    while not rwlline[2] in rings_with_linkers:
        rings_with_linkers[rwlline[2]] = [rwlline[0]]
        break
    else:
        rings_with_linkers[rwlline[2]].append(rwlline[0])

for smiles in rings_with_linkers.keys():
    for molecule in range(0, len(rings_with_linkers[smiles]), 1):
        if len(rings_with_linkers[smiles]) == 1:
            singletons.write("%s %s\n" % (smiles,
                            rings_with_linkers[smiles][0]))
            patterns.write("^%s \n" % (smiles))
        else:
            args.cytoscape.write(cytoscape % (rings_with_linkers[smiles][molecule],
                                "M_S", smiles, "10.0"))
```

A.6 singletons.py

```
#!/usr/bin/env python
"""
    singletons.py

    Replace molecule-scaffold and scaffold-core mappings when there
    is only a single molecule representing a core

    author     David Watson
```

```
    email       dewatson@icloud.com
    copyright   Copyright (c) 2013, David Watson
"""
import sys
import argparse

parser = argparse.ArgumentParser(
    description = 'Create an edge network of molecule-core interactions ' \
                  'from a Strip-It MURCKO_1 file containing singletons.')
parser.add_argument('-i', metavar = 'infile', type = argparse.FileType('r'),
                    help = 'Strip-It MURCKO_1 file', required = True,
                    dest = 'murcko')
parser.add_argument('-o', metavar = 'outfile', type = argparse.FileType('a'),
                    help = 'Cytoscape network table', required = True,
                    dest='cytoscape')
try:
    args = parser.parse_args()
except IOError, msg:
    parser.error(str(msg))

cytoscape = '%s %s %s %s\n'

try:
    stripped = next(args.murcko)
except StopIteration:
    sys.exit("Strip-it file appears empty")

if not stripped.startswith('NAME'):
    sys.exit("Strip-it file appears to be invalid")

murcko = {}

while True:
    try:
        murckoline = next(args.murcko).rstrip().split("\t")
    except StopIteration:
        break

    while not murckoline[2] in murcko:
        murcko[murckoline[2]] = [murckoline[0]]
        break
    else:
        murcko[murckoline[2]].append(murckoline[0])

for smiles in murcko.keys():
    for molecule in range(0,len(murcko[smiles]),1):
        args.cytoscape.write(cytoscape % (murcko[smiles][molecule], "M_C",
```

```
                                smiles, "10.0"))
```

A.7 MURCKO1.def

Configuration file for Strip-it

```
MURCKO_1
```

A.8 RWL2.def

Configuration file for Strip-it

```
RINGS_WITH_LINKERS_2
```

APPENDIX B. SAP IMPLEMENTATION

APPENDIX B. SAP IMPLEMENTATION

B.1 Makefile

Given a set of conformations produced by ConfGen, the following Makefile will attempt to generate fingerprints for all conformers, and if unsuccessful, will deal with removing failed fingerprint properties.

```
# #
# Makefile
#
# Prepare Canvas fingerprints for SAP analysis
#
# author     David Watson
# email      dewatson@icloud.com
# copyright  Copyright (c) 2013, David Watson
#
##

fingerprints:
        $$SCHRODINGER/utilities/canvasPharmFP \
            -fp sigmaPforeFeatures.def -imae superset.maegz \
            -odata conformers.fp -4pt -mostSig 16384  1>&2 2> pharmFPerrors.txt
        $$SCHRODINGER/utilities/canvasFPBinary2CSV \
            -i conformers.fp -o conformers.csv -off 0 -notot
        -grep index pharmFPerrors.txt >duds.txt
        -awk '{ print $$9 }' duds.txt >duds.conformers
        $$SCHRODINGER/utilities/proplister -c -noheader -p s_m_title \
            -p i_user_model_set -p i_user_activity_class superset.maegz -o props.csv
        python bin/strip_3pt_pfores.py
```

B.2 bin/strip_3pt_pfores.py

This script takes care of removing the entries of failed fingerprint generation from the properties file.

```
"""
    strip_3pt_pfores.py

    Removes property information from the property file if Canvas is unable
    to generate a fingerprint for some reason

    author     David Watson
    email      dewatson@icloud.com
    copyright  Copyright (c) 2013, David Watson
"""
```

```
import subprocess

# The following function was contributed by Olafur Waage to the website
# http://stackoverflow.com/questions/845058/how-to-get-line-count-cheaply-in-python
# This uses a subprocess to execute the Unix command "wc -l" to determine
# the file length
def file_len(fname):
    p = subprocess.Popen(['wc', '-l', fname], stdout=subprocess.PIPE,
                                              stderr=subprocess.PIPE)
    result, err = p.communicate()
    if p.returncode != 0:
        raise IOError(err)
    return int(result.strip().split()[0])

myFile = "props.csv"

totallength = file_len(myFile)
totalRange = range(1, totallength + 1)

duds = [int(line.rstrip()) for line in open("duds.conformers", "r")]

for myDud in duds:
    totalRange.remove(myDud)

propsFile = open("propsSubset.csv", "w")
props = [line for line in open('props.csv', 'r')]
for conformer in totalRange:
    propsFile.write(props[conformer - 1])
propsFile.close()
```

B.3 significanceAnalysis.R

This script is a driver for converting the Canvas fingerprints into a subset of significant fingerprints.

```
# #
# significanceAnalysis.R
#
# Implements SAP as described by Fu, et al. in BMC Bioinformatics 13, S3
#
# author     David Watson
# email      dewatson@icloud.com
# copyright Copyright (c) 2013, David Watson
#
##

# begin with a set of fingerprints and properties extracted from the superset
# load the SAP driver code
```

```
source(”bin/sap.R”)

# read in the raw fingerprints
FPs <- read.csv(”conformers.csv”,header=TRUE)

# read in the activity assignments: 1 := active, 2 := inactive
ACs <- read.csv(”props.csv”)
colnames(ACs) <- c(”s_m_title”, ”i_user_model_set”, ”i_user_activity_class”)

# determine the indices of the training set
attach(ACs)
modelSets <- 1:length(i_user_model_set) * (i_user_model_set != 2)
detach(ACs)

# generate a table containing the bags
uniqueActivities <- unique(ACs)

# classify bags as active and inactive
acActivity <- assignActivities(uniqueActivities)

# divide up the bags
intTrainClass <- acActivity[uniqueActivities$i_user_model_set == 1]
extTestClass <- acActivity[uniqueActivities$i_user_model_set == 2]

# generate significant fingerprints (”sigFPs.csv”)
determineSAP(FPsubset, ACsubset)
```

B.4 sap.R

```
# #
# sap.R
#
# Implements SAP as described by Fu, et al. in BMC Bioinformatics 13, S3
#
# author     David Watson
# email      dewatson@icloud.com
# copyright Copyright (c) 2013, David Watson
#
##

library(”matrixStats”)
library(”samr”)
determineSAP <- function(rawFPs, ACs) {
  # transpose the fingerprint
  tFPs <- as.matrix(t(subset(rawFPs,select=-name)))
  attach(ACs)
  SAPFdata <- list(x = tFPs, y = i_user_activity_class,
```

```
    geneid = as.character(1:nrow(tFPs)),
    genenames = colnames(subset(rawFPs,select = -name)),
    logged2 = FALSE)
  detach(ACs)
  SAP <- samr(SAPFdata,
    resp.type = "Two class unpaired",
    nperms = 500)
  save(SAP, file = "SAP.RData")
  DELTAs <-samr.compute.delta.table(SAP, nvals = 100)
  save(DELTAs, file = "DELTAs.RData")
  DELTArow <- sum(DELTAs[1:nrow(DELTAs), 3] != 0) + 1
  DELTA <- DELTAs[DELTArow, 1]
  write.csv(DELTA, file = "DELTA.csv",
    quote = FALSE, row.names = FALSE)
  par(pch = ".")
  # Be sure a proper graphics terminal is open or comment the next line
  samr.plot(SAP, DELTA)
  SAPresults <- samr.compute.siggenes.table(SAP, DELTA, SAPFdata, DELTAs)
  keepbits <- !colnames(FPs) %in% SAPresults$genes.lo[,2]
  sigFPs <- subset(FPs, select=colnames(FPs[keepbits == TRUE]))
  write.csv(sigFPs, file = "sigFPs.csv", quote = FALSE,row.names = FALSE)
  cat("Significant fingerprint bits were saved to sigFPs.csv")
}

assignActivities <- function (acTable) {
  attach(acTable)
  activeBits <- 1*s_m_title %in% s_m_title[i_user_activity_class == 1]
  inactiveBits <- -1*!s_m_title %in% s_m_title[i_user_activity_class == 1]
  detach(acTable)
  activityAssignment <- activeBits + inactiveBits
  activityAssignment
}
```

APPENDIX C. FEATURE MAPPING IMPLEMENTATION

APPENDIX C. FEATURE MAPPING IMPLEMENTATION

C.1 Makefile

Canvas is used to convert the significant fingerprints in CSV form into a native format, and then a fingerprint matrix is generated. Suitable metrics are cosine, dice, kulczynski, mcconnaughey, petke, simpson, tanimoto, and tversky. When working from unfiltered fingerprints, only the matrix step needs to be run.

```
# #
# Makefile
#
# Convert fingerprints into binary form and calculate similarity matrix
#
# author     David Watson
# email      dewatson@icloud.com
# copyright Copyright (c) 2013, David Watson
#
##

features:
        $$SCHRODINGER/utilities/canvasCSV2FPBinary -icsv sigFPs.csv -o sigFPs.fp
        $$SCHRODINGER/utilities/canvasFPMatrix \
            -ifp sigFPs.fp -ocsv FPmatrix.csv -metric tanimoto
```

C.2 features.R

```
# #
# features.R
#
# Map bags to instances and return a feature matrix
#
# author     David Watson
# email      dewatson@icloud.com
# copyright Copyright (c) 2013, David Watson
#
##

featureMap <- function(FPmatrix, activityClasses) {
  trainSet <-
      unique(subset(activityClasses, i_user_model_set == 1, select=s_m_title))
  featureVector <-
      vector(mode = "numeric", length = (length(unique(canvas)) *
      nrow(activityClasses)))
  count <- 0
  moleculeCount <- 0
```

```
  for ( i in unique(canvas))  {
    moleculeCount <- moleculeCount + 1
    message("Evaluating molecule ", moleculeCount)
    for ( j in 1:nrow(activityClasses)) {
      count <- count + 1
      featureVector[count] <-
          max(subset(FPmatrix, canvas == as.character(i), select=j+1) )
    }
  }
  interimMatrix <-
      matrix(featureVector, nrow = length(unique(canvas)),
      ncol = length(canvas),
      dimnames = list(unique(canvas),canvas), byrow = TRUE)
  keepFeatures <-  colnames(interimMatrix) %in% trainSet$s_m_title
  subset(interimMatrix, select=keepFeatures)
}

conformerMap <- function(FPmatrix, activityClasses) {
  trainSet <- unique(subset(activityClasses,
      i_user_model_set == 1, select = s_m_title))
  conformerCount <- 0
  count <- 0
  featureVector <- vector(mode = "numeric", length = (nrow(activityClasses)^2))
  for ( i in 1:nrow(FPmatrix)) {
    conformerCount <- conformerCount + 1
    message("Evaluating conformer ", conformerCount)
    for ( j in 1:nrow(activityClasses)) {
      count <- count + 1
      featureVector[count] <- FPmatrix[i, j + 1]
    }
  }
  interimMatrix <-
      matrix(featureVector, nrow = nrow(activityClasses), ncol = nrow(activityClasses),
      dimnames = list(FPmatrix$canvas, FPmatrix$canvas), byrow = TRUE)
  keepFeatures <-  colnames(interimMatrix) %in% trainSet$s_m_title
  subset(interimMatrix, select = keepFeatures)
}
```

C.3 mapping.R

This is the driver for the instance-based feature mapping

```
# #
# mapping.R
#
# Interactive workflow for feature mapping
#
# author     David Watson
```

```
# email      dewatson@icloud.com
# copyright Copyright (c) 2013, David Watson
#
##

# read in the fingerprint similarity matrix and should be run directly after the SAP
# code otherwise read in the properties as in the SAP driver
FPmatrix <- read.csv(”FPmatrix.csv”, header = TRUE)
attach(FPmatrix)

# perform the instance-based feature mapping
FPfeatures <- featureMap(FPmatrix, ACs)
detach(FPmatrix)
```

APPENDIX D. 1-NORM SVM IMPLEMENTATION

APPENDIX D. 1-NORM SVM IMPLEMENTATION

D.1 bin/1norm.R

rconsole

```
# #
# 1norm.R
#
# Implementation of Yao and Lee's parametric 1-norm SVM as an LP
#      Another Look at Linear Programming for Feature Selection
#      via Methods of Regularization, Technical Report No. 800r,
#      Department of Statistics, Ohio State University, 2010.
#
#      See section 4.2, equation 17
#
# author     David Watson
# email      dewatson@icloud.com
# copyright Copyright (c) 2013, David Watson
#
##

library("Rglpk")
library("perry")
library("caret")

oneNormSVM <- function (trialMatrix, activityAssignment, lambda) {
  trialRows <- nrow(trialMatrix)
  trialCols <- ncol(trialMatrix)
  cost <- c(rep(0, 2), rep(0, trialCols*2),
    rep(1/trialRows, trialRows), rep(0, trialRows))
  a <- c(rep(0, 2), rep(1, trialCols*2), rep(0, trialRows), rep(0, trialRows))
  A <- cbind(activityAssignment, -activityAssignment,
    activityAssignment*trialMatrix, -activityAssignment*trialMatrix,
    diag(rep(1, trialRows)), -diag(rep(1, trialRows)))
  b <- c(rep(1, trialRows))
  oFx <- cost + (lambda*a/trialCols)
  dir <- c(rep("==", trialRows))
  ulbounds <- list(lower = list(ind = c(1L, 2L), val=c(-Inf, -Inf)))
  onensvm <- Rglpk_solve_LP(oFx, A, dir, b, bounds = ulbounds)
  solution <- list()
  solution$hyperplane <- onensvm$solution[3:(trialCols+2)] -
    onensvm$solution[(3 + trialCols):(2 * trialCols + 2)]
  solution$margin <- onensvm$solution[1] - onensvm$solution[2]
  solution$error <-
    onensvm$solution[(2 * trialCols + 3):(2 * trialCols + trialRows + 2)] -
```

```
    onensvm$solution[(3 + 2 * trialCols + trialRows):
    (2 * trialCols + 2 * trialRows + 2)]
  class(solution) <- ”1nsvm”
  solution
}

# Prediction method for class 1nsvm
predict.1nsvm <- function (object, testSet) {
  hyperplane <- object$hyperplane
  margin <- object$margin
  as.vector(sign(margin + testSet %*% hyperplane))
}

# Internal accuracy calculation for a tuned 1-norm SVM
internalAccuracy <- function (internalTest, internalAssignment) {
  validSet <- vector(mode=”numeric”)
  for (itSol in rownames(internalTest)) {
    tempSol <- sign(mySlack + internalTest[as.character(itSol),] %*% myPenalty)
    validSet <- append(validSet, tempSol)
  }

  cat(validSet)
  # The following will calculate the percent of correctly assigned activities
  classificationAccuracy <- sum((validSet * internalAssignment) == 1) /
    nrow(internalTest)
}

# cost function for SVM tuning
svmCost <- function(true,predicted) {
  (length(predicted)-sum(diag(table(true,predicted))))/length(predicted)
}

# Matthews Correlation Coefficient for balanced measure of classification
# performance
MCC <- function (TP, TN, FP, FN) {
  ((TP*TN)-(FP*FN))/sqrt((TP+FP)*(TP+FN)*(TN+FP)*(TN+FN))
}
```

D.2 1nSVM.R

This is the driver for the 1-norm SVM. It should be run immediately after the SAP and instance-based feature selection protocols.

```
source(bin/1norm.R)
# #
# 1norm.R
#
# Interactive workflow for tuning 1-norm SVM
```

```
#
# author     David Watson
# email      dewatson@icloud.com
# copyright Copyright (c) 2013, David Watson
#
##

# divide the feature space between training and test sets
InternalMatrix <- subset(FPfeatures, subset = uniqueActivities$i_user_model_set == 1)
ExtTesting <- subset(FPfeatures, subset = uniqueActivities$i_user_model_set == 2)

# generate random splits of for 5-fold cross-validation
mySplits <- cvFolds(n = nrow(InternalMatrix), K = 5, R = 15, type = ”random”)

# perform initial tuning of the SVM
tuning <- list(lambda = c(10^(-12:4)))
# the tuning process may be split among multiple cores on SMP systems
firstTuning <- perryTuning(oneNormSVM, x = InternalMatrix,
  y = intTrainClass, tuning = tuning, cost = svmCost, splits = mySplits,
  names = c(”trialMatrix”, ”activityAssignment”), ncores = 2)

# examine the tuning parameter
tuning

# perform the second round of tuning
# note that this is an interactive process and the next line must be edited
tuning <- list(lambda = unique(c(seq(from = 1e-7, to = 1e-6, by = (1e-6 - 1e-7)/9),
  seq(from = 1e-6, to = 1e-5, by = (1e-5 - 1e-6)/9))))

secondTuning <- perryTuning(oneNormSVM, x = InternalMatrix,
  y = intTrainClass, tuning = tuning, cost = svmCost, splits = mySplits,
  names = c(”trialMatrix”, ”activityAssignment”), ncores = 2)

# inspect the tuning parameter
secondTuning

# note that the following is interactive and the lambda parameter must be edited
tunedSVM <- oneNormSVM(InternalMatrix, intTrainClass, 7e-07)

mySlack <- tunedSVM$margin
myPenalty <- tunedSVM$hyperplane

tunedAccuracy <- internalAccuracy(InternalMatrix, intTrainClass)
tunedAccuracy

# perform external accuracy calculation
extPrediction <- predict(tunedSVM, ExtTesting)
```

```
confusionMatrix(extPrediction, extTestClass, positive = ”1”)

# calculate Matthews Correlation Coefficient
# note that this is interactive, replace with values from the confusion matrix
MCC(8,2,4,5)

# retrieve the model set compound indices
subsetRange <- seq(from = 1, to = nrow(Acs))
subsetSelect <- subsetRange[modelSets != 0]

# retrieve the prototype conformers
 conformerRange <- subsetSelect[myPenalty != 0]

 # write to a file for retrieval
 write.csv(conformerRange, file=”prototypes.csv”, quote = FALSE,row.names = FALSE)
```

APPENDIX E. ADDITIONAL SCRIPTS

APPENDIX E. ADDITIONAL SCRIPTS

E.1 pubmed_cids.py

The following script was developed to retrieve a SMILES file containing known PubChem compounds that have been curated by PubMed IDs. This script takes advantage of the PubChem Power User Gateway.

```
"""
    pubmed_cids.py

    Retrieves a SMILES file containing known PubChem compounds
    referenced back to a PubMed ID.

    author     David Watson
    email      dewatson@icloud.com
    copyright Copyright (c) 2013, David Watson
"""
#!/usr/bin/env python
import sys
import argparse
import urllib
import nltk
import xml.dom.minidom
import time

parser = argparse.ArgumentParser(
               description='Resolves compound lists in SMILES format based
               upon associated PubMed IDs through PubChem.')
parser.add_argument('-i', metavar='infile', type=argparse.FileType('r'),
               help='PubMed UID file', required=True, dest='pmid')
args=parser.parse_args()

PUBMED = "http://www.ncbi.nlm.nih.gov/pubmed?"
PUG = "http://pubchem.ncbi.nlm.nih.gov/pug/pug.cgi"

PUG_WAITING_HEAD = """\
<PCT-Data>
  <PCT-Data_input>
    <PCT-InputData>
      <PCT-InputData_request>
        <PCT-Request>
"""

PUG_WAITING_TAIL = """\
          <PCT-Request_type value="status"/>
```

```
        </PCT-Request>
      </PCT-InputData_request>
    </PCT-InputData>
  </PCT-Data_input>
</PCT-Data>
"""

PUG_DL_HEAD = """\
<PCT-Data>
  <PCT-Data_input>
    <PCT-InputData>
      <PCT-InputData_download>
        <PCT-Download>
          <PCT-Download_uids>
            <PCT-QueryUids>
              <PCT-QueryUids_ids>
                <PCT-ID-List>
                  <PCT-ID-List_db>pccompound</PCT-ID-List_db>
                  <PCT-ID-List_uids>
"""

PUG_DL_TAIL = """\
                  </PCT-ID-List_uids>
                </PCT-ID-List>
              </PCT-QueryUids_ids>
            </PCT-QueryUids>
          </PCT-Download_uids>
          <PCT-Download_format value="smiles"/>
          <PCT-Download_compression value="none"/>
          <PCT-Download_use-3d value="false"/>
        </PCT-Download>
      </PCT-InputData_download>
    </PCT-InputData>
  </PCT-Data_input>
</PCT-Data>
"""

def processUidFile():
 try:
  for pmid in args.pmid.readlines():
   print "Processing " + pmid
   cids = getCIDsFromUID(pmid.strip())
   if len(cids) > 0:
    processCids(pmid, cids)
 except StopIteration:
  sys.exit("PubMed UID file appears to be empty")
```

```
def getCIDsFromUID(UID):
 params = urllib.urlencode({'Db': 'pccompound',
                'DbFrom': 'pubmed', 'Cmd': 'Link',
                'LinkName': 'pubmed_pccompound_mesh', 'format': 'text',
                'report': 'uilist', 'IdsFromResult': UID})
 pubcrawl = urllib.urlopen(PUBMED, params).read()
 raw = nltk.clean_html(pubcrawl)
 tokens = nltk.word_tokenize(raw)
 return(tokens)

def processCids(smilesName, cidlist):
 querystring = ""
 for cid in cidlist:
  querystring += "                    <PCT-ID-List_uids_E>"
              + cid + "</PCT-ID-List_uids_E>\n"
 pubquery = PUG_DL_HEAD + querystring + PUG_DL_TAIL
 pub = urllib.urlopen(PUG, pubquery).read()
 pubdom = xml.dom.minidom.parseString(pub)
 handleResponse(smilesName, pubdom)

def getText(nodelist):
    rc = ""
    for node in nodelist:
        if node.nodeType == node.TEXT_NODE:
            rc = rc + node.data
    return rc

def handleResponse(smilesName, dom):
 waitingXml = dom.getElementsByTagName("PCT-Waiting_reqid")
 if waitingXml.length > 0:
  for wait in waitingXml:
   waiturl = getText(wait.childNodes)
   handleWait(smilesName, waiturl)
 else:
  downloadXml = dom.getElementsByTagName("PCT-Download-URL_url")
  print "Received download URL for " + smilesName
  processDownload(smilesName, downloadXml)

def handleWait(smilesName, waitReq):
 print "Waiting on response for job " + smilesName
 waitquery = "          <PCT-Request_reqid>"
           + waitReq + "</PCT-Request_reqid>\n"
 PCT_QUERY = PUG_WAITING_HEAD + waitquery + PUG_WAITING_TAIL
 time.sleep(3)
 newquery = urllib.urlopen(PUG, PCT_QUERY).read()
 newdom = xml.dom.minidom.parseString(newquery)
 handleResponse(smilesName, newdom)
```

```
def processDownload(smilesName, downloadXml):
 dlurl = ""
 for node in downloadXml:
  dlurl = getText(node.childNodes)
 smilesFile = smilesName.rstrip() + ".smi"
 urllib.urlretrieve(dlurl, smilesFile)

processUidFile()
```

E.2 tanimoto_cluster.py

The following script clusters compounds based on a user-specified Tanimoto similarity cutoff. A Canvas distance matrix file is required, which should have been generated using Tanimoto similarity measures. The output is a Cytoscape network file that may be useful for visualizing the clusters in the network.

```
#!/usr/bin/env python
"""
    tanimoto_cluster.py

    Cluster compounds based on a specified Tanimoto similarity cutoff

    author      David Watson
    email       dewatson@icloud.com
    copyright Copyright (c) 2013, David Watson
"""
import sys
import argparse

parser = argparse.ArgumentParser(
               description='Convert a Canvas distance matrix
               to Cytoscape network.')
parser.add_argument('-i', metavar='infile', type=argparse.FileType('r'),
               help='Canvas distance matrix', required=True, dest='canvas')
parser.add_argument('-o', metavar='outfile', type=argparse.FileType('w'),
               help='Cytoscape network', required=True, dest='cytoscape')
parser.add_argument('-s', metavar='similarity', type=float,
               help='Tanimoto similarity cutoff (default: 0.70)',
               dest='similarity', default=0.70)
args=parser.parse_args()

cytoscape = '%s %s %s\n'

try:
 compounds = next(args.canvas).rstrip().split(',')
except StopIteration:
 sys.exit("Canvas input file does not contain header information")
```

```
if len(compounds) <= 1 or compounds[0] != 'canvas':
 sys.exit("The Canvas input file does not appear to be valid")

line_index=0
compound_index=1

while True:
 line_index+=1
 compound_index=line_index+1
 if (line_index == len(compounds)):
  break

 try:
  distances = next(args.canvas).rstrip().split(',')
 except StopIteration:
  sys.exit("The input file appears corrupt")

 while compound_index < len(compounds):
  if (args.similarity <= float(distances[compound_index])):
   args.cytoscape.write(cytoscape % (compounds[line_index],
               compounds[compound_index], distances[compound_index]))
  compound_index+=1
```

APPENDIX F. BINDING AFFINITY DATA SETS

APPENDIX F. BINDING AFFINITY DATA SETS

Table F.1: Sigma 1: PTZ guinea pig brain dataset

SMILES	Name	pK_i	Ref.
c1cc(I)ccc1C[C@@H](C)NCCCc2ccccc2	2	7.745	56
c1ccccc1CCCCNCc2ccccc2	4	8.013	56
c1ccccc1CCCNCCc2ccccc2	7	7.959	56
c1ccccc1C[C@@H](C)[N+](C)(C)CCCc2ccccc2	14	6.873	56
CN(C)CCCCCc1ccccc1	16	9.237	56
c1ccccc1C[C@H](C)N(Cc2ccccc2)CCCc3ccccc3	17	6.893	56
c1ccccc1C[C@H](C)NCCCCc2ccccc2	22	7.721	56
c1ccccc1C[C@H](C)NCCCc2ccccc2	23	7.292	56
c1ccccc1CCCNCCCc2ccccc2	24	7.959	56
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-pentazocine	8.796	56
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-pentazocine	6.943	56
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.387	56
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	9.328	56
c1cc(O)ccc1[C@@H](O)[C@@H](C)N(CC2)CCC2Cc3ccccc3	Ifenprodil	8.237	56
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	Dextromethorphan	6.282	56
CC(C)(C)[C@@](C1)(O)CCN([C@H]1c2c34)C[C@@H]4c5c(cccc5)CCc3ccc2	R-Butaclamol	7.161	56
CC(C)(C)[C@](C1)(O)CCN([C@@H]1c2c34)C[C@H]4c5c(cccc5)CCc3ccc2	S-Butaclamol	6.234	56
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-NANM	6.830	56
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-NANM	5.439	56
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	R-3PPP	7.319	56
CCCN(C1)CCC[C@H]1c2cc(O)ccc2	S-3PPP	6.506	56
OCCN(CC1)CCN1CCCN2c(cccc3)c3Sc(c24)ccc(Cl)c4	Perphenazine	7.602	56
CCN(CC)CCCN1c(cccc2)c2Sc(c13)cccc3	Chlorpromazine	6.474	56
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2cccc3)c(c4c23)cccc4	Rimcazole	5.937	56
c1ccccc1CCCN(CC2)CCC2(O)c3cc(Cl)ccc3	42	7.824	56
CCCN1CCN(CC1)c2ccccc2	43	7.086	56
c1ccccc1CCCCCN(CC2)CCC2Cc3ccccc3	44	9.237	56
c1ccccc1C[C@@H](C)[N+](C)(C)CCCc(c2)ccc(c23)cccc3	46	8.569	56
C1CCCCN1CCCc2ccccc2	47	7.310	56
CCCCCNCCc1ccccc1	49	7.930	56
c1ccccc1CCCCCN(C)CCc2ccccc2	51	9.690	56
CNCCCCc1ccccc1	52	7.380	56
c1ccc(Cl)cc1C(=O)CCCCN(CC2)CCC2c3ccccc3	53	8.110	56
c1ccc(Cl)cc1C(=O)CCCCN2CCCCC2	54	9.660	56
c1ccccc1C(=O)CCCCN(CC2)CCC2c3ccccc3	55	10.050	56
c1cc(Cl)ccc1CCCCCN(CC2)CCC2c3ccccc3	56	9.820	56
c1cc(Cl)ccc1C(=O)CCCCN(CC2)CCC2c3ccccc3	57	9.920	56
c1cc(Cl)ccc1C(=O)CCCCN2CCCCC2	58	9.740	56
c1ccccc1CCCN(CC2)CCC2c3ccccc3	59	9.520	56
c1ccccc1CCCCN(CC2)CCC2c3ccccc3	60	9.660	56
c1ccccc1CCCN2CCN(CC2)c3ccccc3	62	7.990	56
c1ccccc1CCCCN2CCN(CC2)Cc3ccccc3	3	9.699	100
c1ccccc1C(=O)N2CCN(CC2)CCCCc3ccccc3	4	6.903	100
c1ccccc1CCCCN(CC2)CCC2Cc3ccccc3	5	9.097	100
c1ccccc1CCCCCN2CCN(CC2)Cc3ccccc3	6	9.398	100
C1CN(C)CCN1CCCCCc2ccccc2	8	8.854	100
CC1CCN(CC1)CCCCCc2ccccc2	9	10.155	100
C1CN(C)CCC1CCCCCc2ccccc2	10	8.886	100
C1CCCCN1CCCCCc2ccc(N)cc2	13	7.420	100
C1CCCCN1C\C=C\C=C\c(c2)ccc(c23)OCO3	14	9.066	100
C1CCCCN1CCCCCc(c2)ccc(c23)OCO3	15	9.495	100
c1ccccc1CCCCC[N@@+]2(C)CC[C@@H](CC2)Cc3ccccc3	16	8.569	100
[C@H]12CC[C@H](CC1)CN(C2)CCCCCc3ccccc3	2	9.000	101
CCN(CC)CCCCCc1ccccc1	4	8.222	101
CCCN(C)CCCCCc1ccccc1	5	9.602	101
CN(C)CCCCCc1ccccc1	6b	7.854	101
c1ccccc1CCCCCNCc2ccccc2	8a	9.770	101
c1ccccc1CCCCCN(C)CCCc2ccccc2	10b	9.444	101

c1ccccc1CCCCCN(CC2)CCC2c3ccccc3	14	9.796	101
c1ccccc1CCCN(CC2)CCC2Cc3ccccc3	21	9.398	101
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	1	6.458	102
CC(C)(C)OC(=O)COc(c1)ccc(C=C[C@H]2CCCC3)c1[C@@]23CCN(C)C(=O)OC(C)(C)C	5	7.854	102
CC(C)(C)OC(=O)CN(C)CC[C@]12c3c(ccc(c3)OC)C=C[C@H]1CCCC2	6a	7.432	102
CN(C)CC[C@]12c3c(ccc(c3)OC)C=C[C@H]1CCCC2	6b	6.611	102
C=CCN(C)CC[C@]12c3c(ccc(c3)OC)C=C[C@H]1CCCC2	6c	7.310	102
COCCN(C)CC[C@]12c3c(ccc(c3)OC)C=C[C@H]1CCCC2	6d	7.310	102
C1CCC[C@@H]2C=Cc(ccc(c3)OC)c3[C@]12CCN(C)CCOCc4ccccc4	6e	6.618	102
CNCC[C@]12c3c(ccc(c3)OC)C=C[C@H]1CCCC2	6g	6.341	102
OCCN(C)CC[C@]12c3c(ccc(c3)OC)C=C[C@H]1CCCC2	6i	6.793	102
CC(C)(C)OC(=O)CN(C)CC[C@]12c3c(ccc(c3)OC)CC[C@H]1CCCC2	6j	6.428	102
CC(C)(C)OC(=O)COc(c1)ccc(C=C[C@@H]2CCCC3)c1[C@]23CCN(C)C(=O)OC(C)(C)C	6k	6.939	102
c1ccccc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	9	5.839	103
c1ccc(F)cc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	10	6.064	103
c1cc(F)ccc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	11	6.187	103
c1ccc(OC)cc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	12	5.710	103
COc(cc1)ccc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	13	5.907	103
c1ccc(F)cc1CCN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	14	6.631	103
c1cc(F)ccc1CCN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	15	6.609	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4ccccc4	23	7.538	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4cc(F)ccc4	24	7.658	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4ccc(F)cc4	25	7.921	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4cc(OC)ccc4	26	6.622	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4ccc(cc4)OC	27	7.907	103
c1ccc(F)cc1CCN([C@@H](C2)C3)[C@H](C4)C[C@@H]3C[C@@H]24	28	8.081	103
c1cc(F)ccc1CCN([C@@H](C2)C3)[C@H](C4)C[C@@H]3C[C@@H]24	29	7.893	103
CC(=O)Nc1ccc(cc1)N(CC2)CCN2CCCCNS(=O)(=O)CC3CCCCC3	20m	7.000	104
CCCCN(C1)CCN([C@H]12)C(=O)CC2	14b	6.462	105
C1CN(C)[C@@H](C2)CC(=O)C[C@]12c3cc(O)ccc3	(+)-(1S,5S)-4	6.118	106
C1CN(C)[C@H](C2)CC(=O)C[C@@]12c3cc(O)ccc3	(-)-(1R,5R)-4	4.498	106
c1ccccc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-(1R,5R)-5	8.027	106
c1ccccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-(1R,5R)-5	5.886	106
c1cc(Cl)c(Cl)cc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-(1R,5R)-6	7.495	106
c1cc(Cl)c(Cl)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-(1R,5R)-6	5.495	106
c1ccccc1/C=C([C@H](C2)[N+](C)(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-(1R,5R)-7	5.268	106
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	SKF10047	7.658	107
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	Dextromethorphan	6.438	107
c1ccccc1C2(CCCC2)C(=O)OCCOCCN(CC)CC	Carbetapentane	7.125	107
c1ccccc1C2(CCCCC2)C(=O)OCCN3CCOCC3	PRE-084	8.046	107
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)C	BD1047	8.812	107
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.987	108
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-pentazocine	8.592	108
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)C	BD1047	8.276	108
CCCN(CCC)CCc1cc(c(cc1)OC)OCCc2ccccc2	NE100	7.897	108
c1cc(Cl)c(Cl)cc1CCN2CCN(C)CC2	BD1063	7.786	108
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.192	108
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-3-PPP	7.125	108
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	SKF-10,047	6.824	108
c1ccccc1C2(CCCCC2)C(=O)OCCN3CCOCC3	PRE-084	6.821	108
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	dextromethorphan	6.643	108
CC(=O)[C@H]1CC[C@H]([C@@]12C)[C@H]3[C@H](CC2)[C@]4(C)C(CC3)=CC(=O)CC4	progesterone	5.841	108
N#Cc1ccc(cc1)OCC2CCN(CC2)CCCF	2	8.367	109
CC(C)(C)[C@@](C1)(O)CCN([C@H]1c2c34)C[C@@H]4c5c(cccc5)CCc3ccc2	(-)-Butaclamol	7.377	110
CC(C)(C)[C@](C1)(O)CCN([C@@H]1c2c34)C[C@H]4c5c(cccc5)CCc3ccc2	(+)-Butaclamol	6.321	110
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	Dextromethorphan	6.642	110
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)O	Dextrorphan	6.387	110
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	6.971	110
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	9.252	110
c1cc(F)ccc1C(=O)CCCN2CCN(CC2)c(c3)ncc(c34)cccc4	HR-375	7.495	110
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-3-PPP	7.097	110
CCCN(C1)CCC[C@H]1c2cc(O)ccc2	(-)-3-PPP	6.133	110
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2cccc3)c(c4c23)cccc4	Rimcazole	6.078	110
CN(C)CCC=C1c(cccc2)c2CCc(c13)cccc3	Amitryptiline	5.792	110
CCN(CC)CCCN1c(cccc2)c2Sc(c13)cccc3	Chlorpromazine	6.379	110
CN(C)CCCN(c(c12)cccc1)c3c(CC2)cccc3	Imipramine	6.491	110
OCCN(CC1)CCN1CCCN2c(cccc3)c3Sc(c24)ccc(Cl)c4	Perphenazine	7.481	110
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN4CCN(C)CC4	Trifluoperazine	6.662	110

FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN(C)C	Trifluopromazine	6.110	110
C1CC1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	(+)-alpha-Cyclazocine	7.721	110
C1CC1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-alpha-Cyclazocine	5.994	110
C1CC1CN(CC2)[C@H]([C@@H]3C)Cc(c4[C@@]23C)ccc(c4)O	(+)-beta-Cyclazocine	5.131	110
C1CC1CN(CC2)[C@@H]([C@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-beta-Cyclazocine	4.544	110
CC[C@]12c3c(ccc(c3)O)C(=O)[C@@H]([C@H]1C)N(CC2)CC4CC4	(+)ethylketocyclazocine	6.686	110
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-alpha-Pentazocine	8.678	110
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-alpha-Pentazocine	6.951	110
CC(C)=CCN(CC1)[C@H]([C@@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-beta-Pentazocine	6.108	110
CC(C)=CCN(CC1)[C@@H]([C@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-beta-Pentazocine	5.157	110
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-SKF-10,047	6.740	110
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-SKF-10,047	5.325	110
CCCCCC(=O)CC[C@@]1(C)[C@@H](N(C)CC2)Cc(c3[C@]12C)ccc(c3)O	(+)-Tonazocine	5.582	110
CCCCCC(=O)CC[C@]1(C)[C@H](N(C)CC2)Cc(c3[C@@]12C)ccc(c3)O	(-)-Tonazocine	4.571	110
CC(C)CCC(=O)CC[C@@]1(C)[C@@H](N(C)CC2)Cc(c3[C@]12C)ccc(c3)O	(+)-Zenazocine	5.484	110
c1cc(F)ccc1C(c2ccc(F)cc2)OCCN(CC3)CCN3CCCc4ccccc4	GBR-12909	7.658	110
C1CN(C)CCC1(C(=O)OCC)c2ccccc2	Meperidine	5.763	110
O1[C@H]2[C@@H](O)C=C[C@H]3[C@H](N(C)CC4)Cc5ccc(O)c1c5[C@@]234	Morphine	5.004	110
c1ccccc1C2(CCCCC2)N3CCCCC3	Phencyclidine	5.857	110
c1cc(Cl)c(Cl)cc1CC(=O)N(C)[C@@H]2[C@H](CCCC2)N3CCCC3	U-50,488H	5.730	110
CCN(CC)CCOC(=O)C1(CCCC1)c2ccc(N)cc2	Aminocaramiphen	7.167	111
CCN(CC)CCOC(=O)C1(CCCC1)c2ccc(I)cc2	Iodocaramiphen	8.750	111
CCN(CC)CCOC(=O)C1(CCCC1)c2ccc(cc2)N3CCCC3	4	6.939	111
CCN(CC)CC#CCOC(=O)C1(CCCC1)c2ccccc2	7	7.108	111
c1ccccc1C2(CCCC2)C(=O)OCCCN(CC)CC	8	8.437	111
C1CN(C)CCC1OC(=O)C2(CCCC2)c3ccccc3	9	6.100	111
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(C2)Cc(c23)cc(OC)c(c3)OC	3	5.841	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)CCc(c23)cc(OC)c(c3)OC	4	5.295	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)c(c23)cc(OC)c(c3)OC	5	5.345	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CCC2)Cc(c23)cc(OC)c(c3)OC	6	5.684	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CCCC2)c(c23)cc(OC)c(c3)OC	7	5.591	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CCC2)c(c23)cc(OC)c(c3)OC	8	5.347	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(C)CCc2cc(OC)c(cc2)OC	9	6.234	112
c1ccccc1C[C@@H](C)NCCc2ccccc2	(-)4	7.360	52
c1ccccc1C[C@H](C)NCCc2ccccc2	(+)4	7.866	52
c1ccccc1C[C@@H](C)N(C)CCc2ccccc2	(-)5	7.785	52
c1ccccc1C[C@H](C)N(C)CCc2ccccc2	(+)5	8.237	52
c1ccccc1C[C@@H](C)NCCCc2ccccc2	(-)3	7.967	52
c1ccccc1C[C@H](C)NCCCc2ccccc2	(+)3	7.409	52
c1ccccc1C[C@H](C)N(C)CCCc2ccccc2	(+)6	8.886	52
c1ccccc1C[C@H](C)N(Cc2ccccc2)CCCc3ccccc3	(+)7	6.886	52
c1ccccc1C[C@@H](C)[N+](C)(C)CCCc2ccccc2	(-)8	6.870	52
c1cc(I)ccc1C[C@@H](C)NCCCc2ccccc2	(-)11	7.752	52
c1ccccc1C[C@@H](C)NCCCCc2ccccc2	(-)16	8.131	52
c1ccccc1C[C@H](C)NCCCCc2ccccc2	(+)16	7.712	52
c1ccccc1C[C@@H](C)NCCCCCc2ccccc2	(-)18	9.301	52
c1ccccc1C[C@H](C)NCCCCCc2ccccc2	(+)18	9.046	52
c1cccc(c12)ccc(c2)CCCN(C)CCCc(c3)ccc(c34)cccc4	21	7.523	52
c1ccccc1C[C@@H](C)NCCCc2cccc(c23)cccc3	(-)22	8.066	52
c1ccccc1C[C@@H](C)NCCCc(c2)ccc(c23)cccc3	(-)23	8.244	52
c1ccccc1CCCNCCc2ccccc2	24	7.947	52
c1ccccc1CCCNCCCc2ccccc2	25	7.943	52
c1ccccc1CCCCNCc2ccccc2	26	8.018	52
c1ccccc1CCCCNCCc2ccccc2	27	8.585	52
c1ccccc1CCCCCNCc2ccccc2	28	9.495	52
c1ccccc1CCCCCN(C)Cc2ccccc2	29	9.721	52
c1ccccc1CCCCCNCCc2ccccc2	30	9.770	52
c1ccccc1CCCCCN(C)CCc2ccccc2	31	9.602	52
c1ccccc1CCCCCNCCCc2ccccc2	32	9.553	52
c1ccccc1CCCCCN(C)CCCc2ccccc2	33	9.420	52
c1ccccc1CCCCCNCCCCc2ccccc2	34	9.319	52
c1ccccc1CCCCCCCNCc2ccccc2	35	8.638	52
c1ccccc1CCCCCCCNCCc2ccccc2	36	8.824	52
CCCCCNCCc1ccccc1	37	7.317	52
CCCN(C)CCCCCc1ccccc1	38	9.538	52
CN(C)CCCCCc1ccccc1	39	7.932	52
CNCCCCCc1ccccc1	40	6.379	52
C1CCCN1CCCCCc2ccccc2	41	9.119	52

C1CCCCN1CCCCCc2ccccc2	42	9.319	52
c1ccccc1CCNCCN2CCCC2	45	7.081	52
C1CCCCC1CCCCCNCc2ccccc2	46	9.092	52
CN(C)CCCCCC1CCCCC1	47	9.585	52
CNCCCCCC1CCCCC1	48	8.167	52
NCCCCCC1CCCCC1	49	6.721	52
c1cccc(c12)sc(c2)C3(N)CCCCC3	4	5.499	113
c1cccc(c12)sc(c2)C3(CCCCC3)N4CCCC4	7	6.775	113
c1cccc(c12)sc(c2)C3(CCCCC3)N4CCCCCC4	8	6.171	113
c1cccc(c12)sc(c2)C3(CCCC3)N4CCCC4	9	6.903	113
c1cccc(c12)sc(c2)C3(CCCC3)N4CCCCC4	10	5.959	113
c1cccc(c12)sc(c2)C3(CCCC3)N4CCCCCC4	11	5.539	113
c1cccc(c12)sc(c2)C3(N4CCCC4)CCCCCC3	12	6.143	113
c1cccc(c12)sc(c2)C3(CCCCCC3)N4CCCCC4	13	5.652	113
c1cccc(c12)sc(c2)C3(CCCCCC3)N4CCCCCC4	14	5.567	113
c1cccc(c12)sc(c2)C3(N)CCCC3	17	5.762	113
c1cccc(c12)sc(c2)C3(N)CCCCCC3	20	5.038	113
c1ccccc1C2(CCCC2)C(=O)OCCOCCN(CC)CC	Carbetapentane	7.495	114
c1ccccc1C(C)(c2ccccc2)C(=O)CCN(CC3)CCC3c4ccccc4	7	8.102	115
c1ccccc1C(C)(c2ccccc2)C(=O)CCCN(CC3)CCC3c4ccccc4	8	8.585	115
c1ccccc1C(C)(c2ccccc2)C(=O)CCCCN(CC3)CCC3c4ccccc4	9	9.018	115
C1CCCCC1C2(CCCCC2)C(=O)CCN(CC3)CCC3c4ccccc4	10	7.921	115
C1CCCCC1C2(CCCCC2)C(=O)CCCN(CC3)CCC3c4ccccc4	11	8.174	115
C1CCCCC1C2(CCCCC2)C(=O)CCCCN(CC3)CCC3c4ccccc4	12	8.387	115
CCN(CC)CCC(=O)C(C)(c1ccccc1)c2ccccc2	Aprophen	7.585	115
CCN(CC)CCC(=O)C1(CCCCC1)C2CCCCC2	Dicyclomine	7.921	115
c1ccccc1C2(CCCC2)C(=O)OCCN(CC3)CCC3c4ccccc4	14	8.403	51
c1cc([N+]([O-])=O)ccc1C2(CCCC2)C(=O)OCCN(CC3)CCC3c4ccccc4	15	10.301	51
c1cc(I)ccc1C2(CCCC2)C(=O)OCCN(CC3)CCC3c4ccccc4	16	8.842	51
N#Cc1ccc(cc1)C2(CCCC2)C(=O)OCCN(CC3)CCC3c4ccccc4	17	8.886	51
c1cc(Cl)ccc1C2(CCCC2)C(=O)OCCN(CC3)CCC3c4ccccc4	18	8.873	51
COc(cc1)ccc1C2(CCCC2)C(=O)OCCN(CC3)CCC3c4ccccc4	19	8.991	51
c1ccccc1C2(CCCC2)C(=O)OCCN3CCN(CC3)c4ccccc4	20	7.202	51
c1cc([N+]([O-])=O)ccc1C2(CCCC2)C(=O)OCCN3CCN(CC3)c4ccccc4	21	8.556	51
c1cc(I)ccc1C2(CCCC2)C(=O)OCCN3CCN(CC3)c4ccccc4	22	7.642	51
c1cc(Cl)ccc1C2(CCCC2)C(=O)OCCN3CCN(CC3)c4ccccc4	23	7.114	51
c1ccccc1C2(CCCC2)C(=O)OCCCN(CC3)CCC3c4ccccc4	24	9.301	51
c1cc([N+]([O-])=O)ccc1C2(CCCC2)C(=O)OCCCN(CC3)CCC3c4ccccc4	25	9.569	51
c1cc(Cl)ccc1C2(CCCC2)C(=O)OCCCN(CC3)CCC3c4ccccc4	26	8.821	51
c1cc(I)ccc1C2(CCCC2)C(=O)OCCCN(CC3)CCC3c4ccccc4	27	9.056	51
COc(cc1)ccc1C2(CCCC2)C(=O)OCCCN(CC3)CCC3c4ccccc4	28	9.187	51
c1ccccc1C2(CCCC2)C(=O)OCCCCN(CC3)CCC3c4ccccc4	32	9.292	51
c1ccccc1C2(CCCC2)C(=O)OCCCCCN(CC3)CCC3c4ccccc4	33	9.215	51
c1ccccc1C2(CCCC2)C(=O)OCCCCCCN(CC3)CCC3c4ccccc4	33	8.917	51
CCN(CC)CCOC(=O)C1(CCCC1)c2ccccc2	caramiphen	7.585	51
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCN(CC4)CCC4c5ccccc5	9	7.770	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCCN(CC4)CCC4c5ccccc5	10	7.658	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCCCN(CC4)CCC4c5ccccc5	11	8.000	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCCCCN(CC4)CCC4c5ccccc5	12	9.155	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCCCCCN(CC4)CCC4c5ccccc5	13	9.229	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCN4CCN(CC4)c5ccccc5	14	6.178	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCCCN4CCN(CC4)c5ccccc5	15	6.484	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCCCCN4CCN(CC4)c5ccccc5	16	7.721	116
c1ccccc1C2(c3ccccc3)C(=O)N(C(=O)N2)CCCCCCN4CCN(CC4)c5ccccc5	17	7.886	116
O=C(O)/C(C)=C/C=C/C(C)=C/C=C/C=C(C)/C=C/C=C(C)/C(=O)O	Crocetin	5.796	117
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-Pentazocine	8.721	117
c1cc(O)ccc1[C@@H](O)[C@@H](C)N(CC2)CCC2Cc3ccccc3	Ifenprodil	7.972	118
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	9.046	118
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.450	118
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OC	SA4503	8.334	118
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OCCF	FE-SA4503	8.095	118
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-Pentazocine	8.790	118
c1cc(F)ccc1C(c2ccc(F)cc2)O[C@@H](C3)C[C@H](CC[C@H]34)N4CCc5c[nH]c(c56)cccc6	GA 1-69	6.367	119
CC(C)[C@@H](N)CN1[C@@H](CC[C@@H]12)C[C@H](C2)OC(c3ccc(F)cc3)c4ccc(F)cc4	GA 2-50	7.917	119
c1cc(F)ccc1C(c2ccc(F)cc2)O[C@@H](C3)C[C@H](CC[C@H]34)N4CCN	GA 2-99	6.889	119
c1cc(F)ccc1C(c2ccc(F)cc2)O[C@@H](C3)C[C@H](CC[C@H]34)N4CC5CC5	JWH 013	8.161	119
c1cccc(c1[C@]23C)[C@H](N3)Cc4c2cccc4	(+)-3	4.228	120
S=C=Nc(cc1)cc2c1C[C@@H](N3)c(c4[C@]23C)cccc4	(+)-8a	5.317	120

c1ncc(I)cc1C(=O)NCCN(CC)CC	1	5.509	121
c1nc(I)ccc1C(=O)NCCN(CC)CC	2	6.328	121
c1ncc(I)cc1C(=O)NCCCCN(CC)CC	3	6.201	121
c1ncc(I)cc1C(=O)N2CCN(CC2)Cc3ccccc3	4	6.538	121
c1cccc(c12)ncc(c2)C(=O)N3CCN(CC3)Cc4ccc(I)cc4	5	6.481	121
c1ccccc1[C@@]2(CO)[C@@H](C2)CN(C)C34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(+)-18	8.900	122
c1ccccc1[C@]2(CO)[C@H](C2)CN(C)C34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(-)-18	8.857	122
c1ccccc1[C@@]2(C(=O)OC)[C@@H](C2)CN(C)C34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(+)-4	7.410	123
c1ccccc1[C@]2(C(=O)OC)[C@H](C2)CN(C)C34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(-)-4	8.678	123
c1ccccc1[C@@]2(CO)[C@@H](C2)CNC34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(+)-5	7.936	123
c1ccccc1[C@]2(CO)[C@H](C2)CNC34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(-)-5	8.187	123
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3	9.174	25
c1cc(F)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	5	9.013	25
c1cccc(F)c1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	6	8.839	25
N#Cc1ccc(cc1)CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	7	8.815	25
c1cc(C)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	8	8.682	25
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	9	8.660	25
c1cc(Cl)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	10	8.625	25
COc(cc1)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	11	8.539	25
c1cc(Br)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	12	8.507	25
c1cccc(C)c1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	13	7.892	25
c1cc(I)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	14	7.782	25
c1cc(N)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	15	7.776	25
FC(F)(F)c1ccc(cc1)CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	16	7.688	25
c1ccc(I)cc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	17	7.565	25
CC(=O)Nc(cc1)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	18	7.328	25
CN(C)c(cc1)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	19	6.993	25
c1cc(I)c([N+]([O-])=O)cc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	20	6.413	25
c1cccc(I)c1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	21	6.032	25
CC(C)(C)c1ccc(cc1)CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	22	5.972	25
c1c(O)ccc(c1[C@]23C)C[C@@H]([C@H]2C)NCC3	1l	5.563	124
c1c(O)ccc(c1[C@]23C)C[C@@H]([C@H]2C)N(C)CC3	1m	5.876	124
CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1n	5.963	124
CCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1o	7.367	124
CCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1p	8.222	124
CCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1q	8.420	124
CCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1r	8.638	124
CCCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1s	8.721	124
CCCCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1t	8.553	124
CCCCCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1u	7.921	124
CCCCCCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	1v	7.161	124
c1c(O)ccc(c1[C@@]23C)C[C@H]([C@@H]2C)NCC3	1a	5.171	124
c1c(O)ccc(c1[C@@]23C)C[C@H]([C@@H]2C)N(C)CC3	1b	4.742	124
CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1c	4.780	124
CCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1d	6.131	124
CCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1e	6.983	124
CCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1f	7.347	124
CCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1g	7.398	124
CCCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1h	7.310	124
CCCCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1i	7.456	124
CCCCCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1j	7.495	124
CCCCCCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	1k	7.420	124
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.921	125
c1ccccc1CCCN2CCN(CC2)Cc3ccccc3	3a	9.180	34
c1ccccc1CCCN2CCN(CC2)Cc3c(Br)cccc3	3b	9.222	34
c1ccccc1CCCN2CCN(CC2)Cc3c([N+]([O-])=O)cccc3	3c	8.553	34
c1ccccc1CCCN2CCN(CC2)Cc3cc(I)ccc3	3d	9.409	34
c1ccccc1CCCN2CCN(CC2)Cc3cc(F)ccc3	3e	8.866	34
c1ccccc1CCCN2CCN(CC2)Cc3cc(OC)ccc3	3f	9.060	34
c1ccccc1CCCN2CCN(CC2)Cc3cc([N+]([O-])=O)ccc3	3g	9.032	34
c1ccccc1CCCN2CCN(CC2)Cc3ccc(cc3)OC	3h	9.119	34
c1ccccc1CCCN2CCN(CC2)Cc3ccc([N+]([O-])=O)cc3	3i	9.432	34
c1ccccc1CCCN2CCN(CC2)Cc3ccc(C)cc3	3j	8.932	34
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	9.081	34
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OC	SA4503	8.363	34
c1cc(Cl)ccc1[C@]2(C(=O)OC)[C@H](C2)CN(CC3)[C@@H]([C@@H]4C)Cc(c5[C@]34C)ccc(c5)O	CCB	5.979	126
O=C1CCCc(c12)cc(cc2)CC(=O)N3CCCC[C@H]3CN(C)C	BRL 53001	5.916	126
c1ccccc1[C@]2(C(=O)OC)[C@H](C2)CN(CC3)[C@H]([C@H]4C)Cc(c5[C@@]34C)ccc(c5)O	(1R,2S)-6a	7.176	127

c1ccccc1[C@@]2(C(=O)OC)[C@@H](C2)CN(CC3)[C@H]([C@H]4C)Cc(c5[C@@]34C)ccc(c5)O	(1S,2R)-6a	5.860	127
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)–SKF10047	6.772	127
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	6.801	127
c1cccc([N+]([O-])=O)c1C(=O)NC2CCN(CC2)Cc3ccccc3	1	7.876	128
c1cc([N+]([O-])=O)ccc1C(=O)NC2CCN(CC2)Cc3ccccc3	2	8.408	128
c1cccc(F)c1C(=O)NC2CCN(CC2)Cc3ccccc3	3	8.470	128
c1cc(F)ccc1C(=O)NC2CCN(CC2)Cc3ccccc3	4	8.588	128
c1cc(Cl)c(Cl)cc1CC(=O)N2CCN(CCCC)C[C@@H]2[C@H](C)N3CCCC3	(R,S)-22	7.396	129
c1cc(Cl)c(Cl)cc1CC(=O)N2CCN(CCCC)C[C@H]2[C@@H](C)N3CCCC3	(S,R)-22	7.092	129
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.658	129
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)–pentazocine	8.446	129
c1cc(F)ccc1C(=O)C[C@@H]2CCCN([C@@H]23)CCCC3	8alpha-b	6.582	130
c1cc(F)ccc1C(=O)C[C@H]2CCCN([C@@H]23)CCCC3	8beta-b	6.119	130
c1ccccc1/C=C/[C@@H]2CCCN([C@@H]23)CCCC3	9alpha-a	6.893	130
c1ccccc1/C=C/[C@H]2CCCN([C@@H]23)CCCC3	9beta-a	7.387	130
c1ccccc1CC[C@@H]2CCCN([C@@H]23)CCCC3	10alpha-a	7.420	130
c1cc(F)ccc1CC[C@@H]2CCCN([C@@H]23)CCCC3	10alpha-b	8.180	130
COc(cc1)ccc1CC[C@@H]2CCCN([C@@H]23)CCCC3	10alpha-c	7.553	130
c1ccccc1CC[C@H]2CCCN([C@@H]23)CCCC3	10beta-a	8.187	130
c1cc(F)ccc1CC[C@H]2CCCN([C@@H]23)CCCC3	10beta-b	8.432	130
COc(cc1)ccc1CC[C@H]2CCCN([C@@H]23)CCCC3	10beta-c	7.854	130
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.439	130
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.097	130
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.697	130
c1ccccc1C[C@@H]2CCCN([C@@H]23)CCCC3	1	7.453	131
c1ccccc1CCC[C@@H]2CCCN([C@@H]23)CCCC3	4	8.377	131
c1ccccc1SC[C@@H]2CCCN([C@@H]23)CCCC3	5	7.051	131
Fc1ccc(cc1)SC[C@@H]2CCCN([C@@H]23)CCCC3	6	7.879	131
c1ccccc1CSC[C@@H]2CCCN([C@@H]23)CCCC3	7	8.495	131
c1cc(Cl)ccc1CSC[C@@H]2CCCN([C@@H]23)CCCC3	8	9.000	131
c1ccccc1CCSC[C@@H]2CCCN([C@@H]23)CCCC3	9	9.201	131
c1cc(F)ccc1CCSC[C@@H]2CCCN([C@@H]23)CCCC3	10	9.201	131
c1ccccc1SC[C@H]2CCCN([C@@H]23)CCCC3	14	8.000	131
Fc1ccc(cc1)SC[C@H]2CCCN([C@@H]23)CCCC3	15	8.357	131
c1ccccc1CSC[C@H]2CCCN([C@@H]23)CCCC3	16	9.284	131
c1cc(Cl)ccc1CSC[C@H]2CCCN([C@@H]23)CCCC3	17	9.638	131
c1ccccc1CCSC[C@H]2CCCN([C@@H]23)CCCC3	18	9.420	131
c1ccccc1CC(=O)C[C@@H]2CCCN([C@@H]23)CCCC3	19	7.991	131
c1cc(F)ccc1C(=O)CSC[C@@H]2CCCN([C@@H]23)CCCC3	20	8.046	131
c1cc(Cl)ccc1OCC(=O)OC[C@@H]2CCCN([C@@H]23)CCCC3	22	7.433	131
c1cc(Cl)ccc1SCC(=O)OC[C@@H]2CCCN([C@@H]23)CCCC3	23	7.616	131
c1cc(F)ccc1C(c2ccc(F)cc2)C[C@@H]3CCCN([C@@H]34)CCCC4	24	7.310	131
c1cc(F)ccc1C(c2ccc(F)cc2)SC[C@@H]3CCCN([C@@H]34)CCCC4	25	8.194	131
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.357	131
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.839	131
COCCN1CCN(CC1)C[C@H](C2=O)CCN2c3ccc(Cl)cc3	MS-377	7.137	132
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.481	132
C1CCCn(c12)c(=O)c(c(n2)C)CCN(CC3)CCC3c4noc(c45)cc(F)cc5	Risperidone	4.886	132
CC(C)NC[C@H](O)COc1cccc(c12)ccc(C)c2	(+-)-Propranolol	6.149	133
CC(C)NC[C@@H](O)COc1cccc(c12)ccc(C)c2	(+-)-Propranolol	6.149	133
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.553	133
OCCN(CC1)CCC1COc2ccc(I)cc2	3	8.638	134
N#Cc1ccc(cc1)CN(CC2)CCC2COC/C=C/I	1	9.420	135
N#Cc1ccc(cc1)OCC2CCN(CC2)C/C=C/I	2	9.174	136
c1cc(I)ccc1C(=O)OC2CCN(CC2)CCCF	4	8.914	136
N#Cc1ccc(cc1)OCC2CCN(CCF)CC2	1	7.614	137
N#Cc1ccc(cc1)OCC2CCN(CC2)Cc3ccc(F)cc3	3	9.119	137
N#Cc1ccc(cc1)OCC2CCN(CC2)Cc3c(Br)cccc3	5	8.695	137
N#Cc1ccc(cc1)OCC2CCN(CC2)Cc3c(I)cccc3	6	8.034	137
c1cc(F)ccc1CN(CC2)CCC2COc(cc3)ccc3[N+]([O-])=O	7	8.921	137
FCCN(CC1)CCC1COc2ccc(I)cc2	8	9.076	137
C1CC1CN(CC2)CCC2COc3ccc(I)cc3	10	9.301	137
N#Cc1cc(ccc1)CN(CC2)CCC2COc3ccc(I)cc3	11	8.538	137
c1cccc(c1C#N)CN(CC2)CCC2COc3ccc(I)cc3	12	7.979	137
FCCCN(CC1)CCC1COc2ccc(Br)cc2	13	9.420	137
C1CC1CN(CC2)CCC2COc3ccc(Br)cc3	14	9.222	137
C1CC1CN(CC2)CCC2COc3cc(Br)ccc3	15	9.056	137
FCCCN(CC1)CCC1COc2c(F)c(F)c(F)c(F)c2F	16	8.770	137

c1cc(F)ccc1CN(CC2)CCC2COc3c(F)c(F)c(F)c(F)c3F	17	8.444	137
c1ccc(F)cc1CN(CC2)CCC2COc3c(F)c(F)c(F)c(F)c3F	18	8.481	137
FCCC[C@H](O1)c(cccc2)c2C13CCN(CC3)Cc4ccccc4	S-2	9.229	138
FCCC[C@@H](O1)c(cccc2)c2C13CCN(CC3)Cc4ccccc4	R-2	8.745	138
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 CCCCCCNc4ccc([N+]([O-])=O)c(c45)non5	K05-138	5.959	139
c1cc(Cl)c(Cl)cc1CCN(C)[C@@H]2[C@@H](CCCC2)N3CCCC3	(-)-2	8.109	140
c1cc(Cl)c(Cl)cc1CCN(C)[C@H]2[C@H](CCCC2)N3CCCC3	(+)-2	7.729	140
c1cc(Cl)c(Cl)cc1CCN(C)[C@@H]2[C@H](CCCC2)N3CCCC3	(+)-4	6.370	140
c1cc(Cl)c(Cl)cc1CCN(C)[C@H]2[C@@H](CCCC2)N3CCCC3	(-)-4	6.342	140
c1cc(Cl)c(Cl)cc1CCN(C)CCN2CCCC2	1	8.678	140
c1cc(Cl)c(Cl)cc1CCN2CCC[C@H]2CN3CCCC3	(-)-8	8.757	140
c1cc(Cl)c(Cl)cc1CCN2CCC[C@@H]2CN3CCCC3	(+)-8	8.363	140
C1CCCN1CCN(CC2)Cc(c23)cc(Cl)c(Cl)c3	12	8.873	140
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-pentazocine	8.509	140
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	1,3-di-o-tolylguanidine	7.558	140
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.432	140
c1ccccc1C2(CCCCC2)N3CCCCC3	1	5.963	141
C1CCCCN1[C@](C2)(C[C@@H]([C@@H]23)C3)c4ccccc4	6	5.429	141
C1CCCCN1[C@@](C2)(C[C@@H]([C@@H]23)C3)c4ccccc4	7	4.788	141
C1CCCCN1[C@]2(CC[C@@H]([C@@H]23)C3)c4ccccc4	(+)-8	5.138	141
C1CCCCN1[C@@]2(CC[C@H]([C@H]23)C3)c4ccccc4	(-)-8	5.947	141
c1cc(Cl)c(Cl)cc1CCN2CCNCC2	3	6.924	142
c1cc(Cl)c(Cl)cc1CCN2CCN(C)CC2	4	8.039	142
c1cc(Cl)c(Cl)cc1CCN2CCN(CC)CC2	5	8.796	142
CCCN1CCN(CC1)CCc2cc(Cl)c(Cl)cc2	6	8.921	142
CCCCN1CCN(CC1)CCc2cc(Cl)c(Cl)cc2	7	9.260	142
CCCCCN1CCN(CC1)CCc2cc(Cl)c(Cl)cc2	8	8.770	142
c1cc(Cl)c(Cl)cc1CCN2CCN(CC2)CCc3cc(Cl)c(Cl)cc3	9	8.770	142
c1cc(Cl)c(Cl)cc1CCN2CCCNCC2	10	6.812	142
c1cc(Cl)c(Cl)cc1CCN2CCCN(C)CC2	11	6.759	142
c1cc(Cl)c(Cl)cc1CCN(C2)CCN([C@H]23)CCC3	(-)-12	8.268	142
c1cc(Cl)c(Cl)cc1CCN(C2)CCN([C@@H]23)CCC3	(+)-12	8.854	142
c1cc(Cl)c(Cl)cc1CCN2CCN(CC3)CCC23	16	6.184	142
c1cc(Cl)c(Cl)cc1CCNCC2(CCCCC2)N3CCCCC3	17	7.788	142
c1cc(Cl)c(Cl)cc1CCN(C)CC2(CCCCC2)N3CCCCC3	18	7.108	142
c1ccccc1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-7	10.377	143
c1ccccc1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-7	10.347	143
COc(cc1)ccc1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-8	9.092	143
COc(cc1)ccc1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-8	9.638	143
c1ccc(OC)cc1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-9	9.301	143
c1ccc(OC)cc1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-9	10.000	143
c1cccc(OC)c1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-10	9.523	143
c1cccc(OC)c1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-10	8.389	143
COc1cccc(OC)c1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-11	9.585	143
COc1cccc(OC)c1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-11	9.495	143
Fc1cccc(F)c1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-12	9.201	143
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.548	143
COc1cccc(c12)[C@@H](CCC2)NC(=O)CN3CCN(CC3)C4CCCCC4	R-9	7.690	144
COc1cccc(c12)[C@H](CCC2)NC(=O)CN3CCN(CC3)C4CCCCC4	S-9	7.024	144
COc1cccc(c12)[C@@H](CCC2)NCCN3CCN(CC3)C4CCCCC4	R-11	7.866	144
COc1cccc(c12)[C@H](CCC2)NCCN3CCN(CC3)C4CCCCC4	S-11	7.633	144
C1CCCCC1N(CC2)CCN2CCO[C@H](CCC3)c(c34)cccc4OC	R-14	8.664	144
C1CCCCC1N(CC2)CCN2CCO[C@@H](CCC3)c(c34)cccc4OC	S-14	8.489	144
c1ccc(OC)c(c12)cccc2NC(=O)CN3CCN(CC3)C4CCCCC4	20	7.371	144
c1ccc(OC)c(c12)cccc2NCCN3CCN(CC3)C4CCCCC4	21	8.264	144
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.523	144
Cc(c1)ccc(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	2	5.668	145
Cc(c1)ccc(OC)c1C(=O)NCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	11a	6.272	145
Cc(c1)ccc(OC)c1C(=O)NCCCN2CCN(CC2)C3CCCCC3	11b	7.342	145
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	12a	5.357	145
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCN2CCN(CC2)C3CCCCC3	12b	7.588	145
COc(c1)c(OC)cc(Br)c1C(=O)NCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	13a	5.590	145
COc(c1)c(OC)cc(Br)c1C(=O)NCCCN2CCN(CC2)C3CCCCC3	13b	6.572	145
c1cccc(c12)CCN(C2=O)CCCN(CC3)Cc(c34)cc(OC)c(c4)OC	15a	6.149	145
c1cccc(c12)CCN(C2=O)CCCN3CCN(CC3)C4CCCCC4	15b	7.607	145
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.510	145
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.582	146

CCCN(C1)CCC=C1c(on2)cc2-c(cc3)ccc3C	PD 144418	10.097	147
c1ccccc1CC/C(=N\O)C2=CCCN(C2)CCC	PD 128298	9.137	147
c1cc(F)ccc1C(=O)CC2CCN(CC2)CC3CC3	DuP 734	9.041	147
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.921	147
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-Pentazocine	8.237	147
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-3-PPP	7.625	147
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.582	147
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-SKF10047	7.445	147
OC1CCN(CC1)CCCCCCOc2cccc(c23)oc(cc3=O)-c4ccccc4	NPC 16377	7.294	147
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	Dextromethorphan	7.254	147
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-Pentazocine	7.092	147
CC(C)(C)[C@@](C1)(O)CCN([C@H]1c2c34)C[C@@H]4c5c(cccc5)CCc3ccc2	(-)-Butaclamol	7.019	147
CCCN(C1)CCC[C@H]1c2cc(O)ccc2	(-)-3-PPP	6.532	147
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-SKF10047	6.098	147
CC(C)(C)[C@](C1)(O)CCN([C@@H]1c2c34)C[C@H]4c5c(cccc5)CCc3ccc2	(+)-Butaclamol	6.097	147
c1ccccc1C2(CCCCC2)N3CCCCC3	PCP	5.841	147
c1cc(F)ccc1C(=O)CCCN(CC2)CCC23C(=O)NCN3c4ccccc4	Spiperone	5.644	147
Fc1ccc(cc1)SC[C@H]2CCCN([C@@H]23)CCCC3	ANS-4	8.222	148
Fc1ccc(cc1)SC[C@@H]2CCCN([C@@H]23)CCCC3	ANS-5	7.721	148
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.444	148
CCCCN(C[C@@H]1O)CCN1Cc2ccccc2	3b	6.529	149
c1ccccc1CN2CCN(C[C@@H]2O)Cc3ccccc3	3c	7.417	149
c1ccccc1CN2CCN(C[C@@H]2O)Cc3ccc(cc3)OC	3d	7.907	149
c1ccccc1CCN(C[C@@H]2O)CCN2Cc3ccccc3	3e	7.434	149
c1ccccc1CN2CCN(C[C@@H]2O)C3CCCCC3	3f	7.236	149
CCC(=O)CN(C[C@@H]1O)CCN1Cc2ccccc2	3n	5.802	149
c1cc(Cl)c(Cl)cc1CC(=O)NC[C@H]2CN(CC(=O)OCC)CCN2Cc3ccccc3	17a	5.873	150
c1cc(Cl)c(Cl)cc1CC(=O)N(C)C[C@H]2CN(CC(=O)OCC)CCN2Cc3ccccc3	17b	6.742	150
c1cc(Cl)c(Cl)cc1CC(=O)N(C2)CN([C@@H]23)CCN(C3)CC(=O)OCC	19	6.042	150
c1ccccc1CN2CCCN(C[C@@H]2CO)Cc3ccccc3	4a	8.131	151
COC(OC)CN(C[C@@H]1CO)CCCN1Cc2ccccc2	4b	6.495	151
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.963	152
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.719	152
CC1(C)CCCN(C1)CCC[C@H](CCC2)c(c23)cccc3OC	S-39	7.936	152
CC1(C)CCCN(C1)CCC[C@@H](CCC2)c(c23)cccc3OC	R-39	7.479	152
CCCN(CCC)CCc1cc(c(cc1)OC)OCCc2ccccc2	NE100	8.987	152
c1cc(Cl)c(Cl)cc1CCN(C)CCN2CCCC2	BD1008	8.764	152
CC1(C)CCCN(C1)CCCC2=CCc(c23)cccc3	23	7.636	152
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.569	153
c1cc(Cl)c(Cl)cc1CC(=O)OCCN2CCCC2	AC915	8.600	153
CC1CCN(CC1)CCOc2ccc(Cl)cc2	12	9.066	153
CC1CCN(CC1)C[C@@H](C)Oc2ccc(Cl)cc2	R-13	7.900	153
CC1CCN(CC1)C[C@H](C)Oc2ccc(Cl)cc2	S-13	8.742	153
c1cc(Cl)ccc1O[C@H](C)CCN(CC2)CCC2C	R-14	8.738	153
c1cc(Cl)ccc1O[C@@H](C)CCN(CC2)CCC2C	S-14	8.854	153
CC1CCN(CC1)CCCOc2ccc(Cl)cc2	15	8.750	153
CC1CCN(CC1)C[C@@H](C)COc2ccc(Cl)cc2	R-16	8.963	153
CC1CCN(CC1)C[C@H](C)COc2ccc(Cl)cc2	S-16	8.770	153
CC1CCN(CC1)[C@H](C)COc2ccc(Cl)cc2	R-17	8.928	153
CC1CCN(CC1)[C@@H](C)COc2ccc(Cl)cc2	S-17	9.469	153
CC1CCN(CC1)[C@H](C)CCOc2ccc(Cl)cc2	R-18	8.656	153
CC1CCN(CC1)[C@@H](C)CCOc2ccc(Cl)cc2	S-18	8.570	153
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.516	154
c1ccccc1CCN2CCCCC2	AC927	6.510	154
COc1cccc(c12)[C@@H](CCC2)CCCN3CCN(CC3)C4CCCCC4	S-33	8.611	154
COc1cccc(c12)[C@H](CCC2)CCCN3CCN(CC3)C4CCCCC4	R-33	8.256	154
c1cccc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	43	8.666	154
c1ccc(OC)c(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	44	8.804	154
c1cccc(c12)cccc2CCCCN3CCN(CC3)C4CCCCC4	45	9.658	154
c1cccc(c12)cccc2CCCCCN3CCN(CC3)C4CCCCC4	46	8.620	154
C1CCCCN1CCCc2cccc(c23)cc(cc3)OC	21	8.108	155
CC1(C)CCCN(C1)CCCc2cccc(c23)cc(cc3)OC	26	9.456	155
CC1(C)CCCCN1CCCc2cccc(c23)cc(cc3)OC	25	5.975	155
CC1CCN(CC1)CCCc2cccc(c23)cc(cc3)OC	24	8.824	155
CC1(C)CCN(CC1)CCCc2cccc(c23)cc(cc3)OC	27	8.833	155
C1CCCCN1CCCCc2cccc(c23)cc(cc3)OC	28	8.943	155
CC1(C)CCCN(C1)CCCCc2cccc(c23)cc(cc3)OC	33	9.444	155
CC1(C)CCCCN1CCCCc2cccc(c23)cc(cc3)OC	32	7.654	155

CC1CCN(CC1)CCCCc2cccc(c23)cc(cc3)OC	31	10.523	155
CC1(C)CCN(CC1)CCCCc2cccc(c23)cc(cc3)OC	34	8.648	155
C[C@@H]1CCCN(C1)CCCc2cccc(c23)cc(cc3)OC	23R	8.870	155
C[C@H]1CCCN(C1)CCCc2cccc(c23)cc(cc3)OC	23S	8.479	155
C[C@@H]1CCCCN1CCCc2cccc(c23)cc(cc3)OC	22R	8.738	155
C[C@H]1CCCCN1CCCc2cccc(c23)cc(cc3)OC	22S	8.152	155
C[C@@H]1CCCN(C1)CCCCc2cccc(c23)cc(cc3)OC	30R	9.620	155
C[C@H]1CCCN(C1)CCCCc2cccc(c23)cc(cc3)OC	30S	9.180	155
C[C@@H]1CCCCN1CCCCc2cccc(c23)cc(cc3)OC	29R	8.845	155
C[C@H]1CCCCN1CCCCc2cccc(c23)cc(cc3)OC	29S	9.301	155
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.553	155
n1ccccc1OCCN[C@@H](CC2)CC[C@@H]2c3ccccc3	cis-14	8.113	156
c1ccc(OC)cc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4cccc(c45)cccc5	cis-17	6.620	156
c1cccc(OC)c1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-19	6.433	156
c1ccc(OC)cc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-20	6.750	156
COc(cc1)ccc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-21	6.712	156
c1ccccc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-29	6.096	156
Cc1ccc(cc1)[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-30	6.000	156
c1cc(Cl)ccc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-31	5.963	156
Fc1cccc(F)c1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-32	5.287	156
c1ccc(C)c(c1C)[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-34	8.199	156
c1cccc(OC)c1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-19	8.544	156
c1ccc(OC)cc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-20	7.606	156
COc(cc1)ccc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-21	6.536	156
c1ccccc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-29	6.983	156
Cc1ccc(cc1)[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-30	7.513	156
c1cc(Cl)ccc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-31	6.721	156
Fc1cccc(F)c1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-32	6.721	156
COc1cccc(OC)c1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-33	6.668	156
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.618	156
c1cccc(c12)CCC[C@@H]2CCCN3CCN(CC3)C4CCCCC4	R-3	9.201	157
c1cccc(c12)CCC[C@H]2CCCN3CCN(CC3)C4CCCCC4	S-3	9.886	157
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.480	158
CCN1CCN(CC1)C2CCCCC2	55	7.205	158
C1CCCCC1N2CCN(CC2)C3CCCCC3	57	8.688	158
C1CCCCC1C(=O)N2CCN(CC2)C3CCCCC3	58	8.445	158
C1CCCCC1CCCN2CCN(CC2)C3CCCCC3	59	9.602	158
c1cc(I)ccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-8	5.767	159
c1ccc(I)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-9	5.790	159
c1ccccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(OC)ccc4	(+)-10	6.839	159
COc(cc1)ccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-4	5.719	159
c1ccc(OC)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-6	5.222	159
c1ccc(Cl)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-7	5.509	159
c1cc(Cl)ccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-5	6.120	159
COc(cc1)ccc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-4	8.108	159
c1cc(Cl)ccc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-5	7.735	159
c1ccc(OC)cc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-6	8.237	159
c1ccc(Cl)cc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-7	7.519	159
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN4CCN(CC4)CCO	Fluphenazine	7.587	160
CC(C)(C)[C@](C1)(O)CCN([C@@H]1c2c34)C[C@H]4c5c(cccc5)CCc3ccc2	(+)-Butaclamol	5.630	160
CC(C)(C)[C@@](C1)(O)CCN([C@H]1c2c34)C[C@@H]4c5c(cccc5)CCc3ccc2	(-)-Butaclamol	7.077	160
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-PPP	7.530	160
CCCN(C1)CCC[C@H]1c2cc(O)ccc2	(-)-PPP	6.733	160
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-Pentazocine	7.080	160
C1CCC[C@@H]2[C@@H](N(CC3)CC=C)Cc(c4[C@]123)ccc(c4)O	Dextrallorphan	7.870	160
C1CC1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	(+)-Cyclazocine	7.764	160
C1CC1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-Cyclazocine	5.577	160
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-SKF10047	7.224	160
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-SKF10047	5.285	160
c1ccccc1C2(CCCCC2)N3CCCCC3	PCP	5.753	160
c1ccccc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	CB-64L	7.979	161
c1cc(Cl)c(Cl)cc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	CB-182	7.564	161
c1ccccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	CB-64D	5.514	161
c1cc(Cl)c(Cl)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	CB-184	5.129	161
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	Ibogaine	5.068	162
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4ccc(c5)O	O-des-methyl-Ibogaine	4.824	162
C1CNC(C)=C(C1=c23)N=c2cc(cc3)OC	Harmaline	5.264	162
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4cc(cc5)OC	Tabernanthine	5.542	162

CC(C)(C)Oc(c1)ccc2[nH]c(c3c12)[C@H]4[C@H]5N(CC3)C[C@@H](C4)C[C@@H]5CC	10-t-butoxy-ibogamine	5.313	163
C[C@@H]1CN(C[C@H](C)N1)CCCN(c2ccc(F)cc2)c3ccc(F)cc3	10	6.907	59
c1ccccc1CCCN2[C@@H](C)CN(C[C@H]2C)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	11	7.955	59
c1cc(F)ccc1N(c2ccc(F)cc2)CCCN(C[C@H]3C)C[C@@H](C)N3CCc4cc(Cl)c(Cl)cc4	12	7.488	59
c1ccccc1N(c2ccccc2)CCCN(C[C@H]3C)C[C@H](C)N3CCc4cc(Cl)c(Cl)cc4	13	7.529	59
C1CNCCN1CCCN(c2ccc(F)cc2)c3ccc(F)cc3	15	5.857	59
c1ccccc1CCCN2CCN(CC2)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	16	7.179	59
c1cc(F)ccc1N(c2ccc(F)cc2)CCCN3CCN(CC3)Cc4ccccc4	17	7.883	59
c1ccccc1C[C@H](O)CN2CCN(CC2)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	6a	7.551	164
c1ccccc1C[C@@H](O)CN2CCN(CC2)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	6b	7.476	164
c1ccccc1C[C@H](OC(=O)C)CN2CCN(CC2)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	7a	7.125	164
c1ccccc1C[C@H](OC(=O)CC)CN2CCN(CC2)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	7b	7.087	164
c1ccccc1C[C@H](OC(=O)CCC)CN2CCN(CC2)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	7c	6.535	164
c1ccccc1C[C@H](OC(=O)C=C)CN2CCN(CC2)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	7d	7.342	164
c1ccccc1CC(=O)O[C@@H](Cc2ccccc2)CN3CCN(CC3)CCCN(c4ccc(F)cc4)c5ccc(F)cc5	7e	7.058	164
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.252	164
CCCN(CCC)CCc1cc(c(cc1)OC)OCCc2ccccc2	NE100	8.623	164
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	l-pentazocine	7.079	164
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2cccc3)c(c4c23)cccc4	rimcazole	6.049	164
c1cc(F)ccc1C(c2ccc(F)cc2)OCCN(CC3)CCN3CCCc4ccccc4	GBR12909	7.294	164
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-1d	7.081	165
c1ccccc1CN2CC[C@@H]3[C@@H](C)[C@H]2Cc(c34)cccc4	(-)-2a	9.018	165
c1ccccc1CN2CC[C@H]3[C@H](C)[C@@H]2Cc(c34)cccc4	(+)-2a	8.241	165
c1cccc(c12)C[C@@H]3[C@H](CC)[C@H]2CCN3Cc4ccccc4	(-)-2b	8.474	165
c1cccc(c12)C[C@H]3[C@@H](CC)[C@@H]2CCN3Cc4ccccc4	(+)-2b	7.573	165
c1cccc(c12)C[C@@H]3[C@H](C(C)C)[C@H]2CCN3Cc4ccccc4	(-)-2c	7.499	165
c1cccc(c12)C[C@H]3[C@@H](C(C)C)[C@@H]2CCN3Cc4ccccc4	(+)-2c	6.777	165
c1cccc(c12)[C@H]([C@H](C)C=C2)CCNCc3ccccc3	(+)-10a	7.708	165
c1cccc(c12)[C@@H]([C@@H](C)C=C2)CCNCc3ccccc3	(-)-10a	7.762	165
c1cccc(c12)[C@H]([C@H](CC)C=C2)CCNCc3ccccc3	(+)-10b	7.780	165
c1cccc(c12)[C@@H]([C@@H](CC)C=C2)CCNCc3ccccc3	(-)-10b	7.830	165
c1cccc(c12)[C@H]([C@H](C(C)C)C=C2)CCNCc3ccccc3	(+)-10c	7.921	165
c1cccc(c12)[C@@H]([C@@H](C(C)C)C=C2)CCNCc3ccccc3	(-)-10c	7.932	165
c1cc(I)ccc1CN(CC2)CCC23c4c(CO3)cccc4	Spiro-I	8.561	166
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.609	95
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.419	95
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	9.022	95
c1ccccc1C(c2ccccc2)(c3ccccc3)SCCNC(=O)CN(CCSC(c4ccccc4)(c5ccccc5) c6ccccc6)CCCN7C(CCC8)CC(CC78)OC(=O)Nc(c(cc9)OC)cc9C	1	5.320	95
I\C=C\CN(CCC)[C@H](C1)CCc(c12)ccc(c2)O	S-trans-7-OH-PIPAT	8.412	95
s1cccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12a	5.844	167
CN(C)c(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12b	5.900	167
c1nc(Cl)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12d	5.898	167
c1cccc(c12)[nH]c(c2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12e	5.745	167
c1cccc(c12)ncc(n2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12f	5.131	167
c1cccc(c12)oc(c2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12g	5.966	167
c1cccc(c12)sc(c2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12h	5.841	167
FCCc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12i	5.451	167
Cc(s1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12j	5.961	167
s1c(Br)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12k	6.466	167
c1cc(Cl)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13a	5.642	167
c1cc(F)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13b	6.034	167
COc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13d	5.063	167
c1cccc(c12)oc(c2)C(=O)NCCCCN3CCN(CC3)c(c4Cl)cccc4Cl	13f	5.246	167
FCCc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13g	5.057	167
Cc(s1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13h	5.847	167
s1c(Br)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13i	6.213	167
CCCCNCCCc1ccccc1	1a	7.137	168
CCCCCCCNCCCc1ccccc1	2a	7.824	168
CCCCCCCCCCCCCNCCCc1ccccc1	3a	5.276	168
CCCCCCCCCCCCCCCCCCCCNCCCc1ccccc1	4a	4.463	168
CCCCNCCCc1ccc([N+]([O-])=O)cc1	1b	8.523	168
CCCCCCCNCCCc1ccc([N+]([O-])=O)cc1	2b	8.000	168
CCCCCCCCCCCCCNCCCc1ccc([N+]([O-])=O)cc1	3b	5.292	168
CCCCCCCCCCCCCCCCCCCCNCCCc1ccc([N+]([O-])=O)cc1	4b	4.570	168
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.903	169
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.053	169
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.939	169

CCCN(CCC)CCc1cc(c(cc1)OC)OCCc2ccccc2	NE100	8.959	169
c1cc(Cl)c(Cl)cc1CC(=O)OCCN2CCCC2	AC915	8.662	169
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	dextromethorphan	7.036	169
CN(C)C/C=C(\C)c(c1)ccc(c12)cccc2	2	7.703	64
CN(C)C/C=C(\C)c1cccc(c12)cccc2	3	6.991	64
CN(C)C/C=C(\C)c(c1)ccc(c12)cc(O)cc2	4	6.640	64
CN(C)C/C=C(\C)c(c1)ccc(c12)cc(cc2)OC	5	7.670	64
CN(C)C/C=C(\C)c1ccc(cc1)-c2ccccc2	6	8.854	64
c1cccc(c12)ccc(c2)C(\C)=C\CN(C)Cc3ccccc3	12	8.103	64
c1ccccc1-c(cc2)ccc2C(\C)=C\CN(C)Cc3ccccc3	13	8.199	64
C1CCCCN1C/C=C/2CCCc(c23)n(nc3)-c4ccccc4	17a	8.215	170
C1COCCN1C/C=C/2CCCc(c23)n(nc3)-c4ccccc4	17b	7.644	170
C1CCCCCN1C/C=C/2CCCc(c23)n(nc3)-c4ccccc4	17c	8.824	170
CC1CCN(CC1)C/C=C/2CCCc(c23)n(nc3)-c4ccccc4	17d	8.357	170
CCN(CC)C/C=C/1CCCc(c12)n(nc2)-c3ccccc3	17e	7.936	170
C1CCCCC1N(CC2)CCN2C/C=C/3CCCc(c34)n(nc4)-c5ccccc5	17f	7.955	170
C[C@@H]1CN(C[C@@H](O1)C)C/C=C/2CCCc(c23)n(nc3)-c4ccccc4	17g	7.710	170
c1ccccc1C2CCN(CC2)C/C=C/3CCCc(c34)n(nc4)-c5ccccc5	17h	8.602	170
c1ccccc1N(CC2)CCN2C/C=C/3CCCc(c34)n(nc4)-c5ccccc5	17i	7.380	170
c1cccc(CO2)c1C23CCN(CC3)C/C=C/4CCCc(c45)n(nc5)-c6ccccc6	17k	8.310	170
c1cccc(c12)CN(CC2)C/C=C/3CCCc(c34)n(nc4)-c5ccccc5	17m	7.395	170
c1ccccc1CN(C)C/C=C/2CCCc(c23)n(nc3)-c4ccccc4	17n	7.870	170
c1cccc(c12)CN(C2)C/C=C/3CCCc(c34)n(nc4)-c5ccccc5	17p	7.338	170
C1CCCCN1C/C=C/2CCCc(c23)n(nc3)-c(c4)ccc(Cl)c4Cl	17q	8.215	170
C1COCCN1C/C=C/2CCCc(c23)n(nc3)-c(c4)ccc(Cl)c4Cl	17r	7.226	170
C[C@@H]1CN(C[C@@H](O1)C)C/C=C/2CCCc(c23)n(nc3)-c(c4)ccc(Cl)c4Cl	17s	7.251	170
c1c(O)ccc(c1[C@]23C)C[C@@H]([C@H]2C)N(C)CC3	(+)-1a	5.678	26
CC(=O)Nc(c1)ccc(c1[C@]23C)C[C@@H]([C@H]2C)N(CC3)Cc4ccccc4	(+)-3a	8.246	26
c1cccc(c1[C@]23C)C[C@@H]([C@H]2C)N(C)CC3	(+)-2a	6.317	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(F)c4	(+)-3e	8.419	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)N(C)C	(+)-3c	8.757	26
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cccc3	(+)-2c	7.084	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(Br)c4	(+)-3g	7.733	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)N	(+)-3b	8.833	26
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cccc3	(+)-2b	8.804	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(Cl)c4	(+)-3f	8.145	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)NS(=O)(=O)C	(+)-3d	7.983	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cccc4	(+)-2d	7.735	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(I)c4	(+)-3h	6.884	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(F)c4	(-)-3e	7.708	26
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)cccc3	(-)-2b	7.578	26
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(F)c3	(-)-4a	7.516	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-1f	7.438	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(Cl)c4	(-)-3f	7.397	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-2d	7.232	26
CC(C)CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(F)c3	(-)-4b	8.330	26
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(F)c3	(+)-4a	8.830	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)CC(=C4[C@@]23C)CCC(=O)C4	(+)-10	7.947	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(Br)c(c4Br)O	(+)-2a	7.151	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4Br)O	(+)-3a	8.757	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(Br)c(c4)O	(+)-4a	7.164	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(I)c(c4)O	(+)-5a	6.636	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(Cl)c(c4Cl)O	(+)-6a	7.146	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4Cl)O	(+)-7a	8.764	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cc(Br)c(c3Br)O	(+)-2b	6.921	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3Br)O	(+)-3b	8.604	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cc(Br)c(c3)O	(+)-4b	6.943	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cc(I)c(c3)O	(+)-5b	6.025	171
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)cc(Br)c(c3)O	(-)-4b	7.427	171
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)cc(I)c(c3)O	(-)-5b	7.453	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3Cl)O	(+)-7b	8.582	171
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3CCF	11a	5.698	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3CC=C	11b	5.901	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccncc4	11c	5.806	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4cccnc4	11d	5.630	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(F)nc4	11e	5.600	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(cc4)SC	11f	5.694	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(cc4)OC	11g	6.490	172

Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(cc4)OC	11h	6.350	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(CCF)cc4	11i	5.579	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(cc4)N(C)C	11j	5.728	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(cc4)N(C)C	WC-26	5.843	172
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc(cc4)ccc4CCF	WC-59	5.767	172
CCN(CC)CCOC(=O)C(CCC)(c1ccccc1)c2ccccc2	l-Lobeline	7.276	173
c1ccccc1C(=O)C[C@H]2CCC[C@H](N2C)C[C@H](O)c3ccccc3	Proadifen	7.523	173
C1CCCN([C@@H]1[C@@H]23)C[C@H](C2)[C@@H]4N(C3)CCCC4	(-)Sparteine	5.087	173
C=C[C@H]([C@H]12)CN(CC2)[C@H](C1)[C@@H](O)c3ccnc(c34)cccc4	Quinidine	4.780	173
c1cc(I)ccc1C(=O)NC2CCN(CC2)Cc3ccc(F)cc3	2a	9.051	174
c1cc(I)ccc1C(=O)NC2CCN(CC2)Cc3c(F)cccc3	2b	9.420	174
c1cc(Br)ccc1C(=O)NC2CCN(CC2)Cc3ccc(F)cc3	2c	9.076	174
c1cc(Br)ccc1C(=O)NC2CCN(CC2)Cc3c(F)cccc3	2d	9.222	174
c1cc(Br)ccc1C(=O)NC2CCN(CC2)Cc3ccccc3	1b	9.009	174
c1cc(F)ccc1C(=O)CN2[C@@H](CC[C@@H]23)C[C@@H](C3)c4ccccc4	11	6.552	175
c1cc(F)ccc1C(=O)CCCN2[C@@H](CC[C@@H]23)C[C@@H](C3)c4ccccc4	12	7.467	175
c1cc(F)ccc1C(=O)CCCN(CC2)CCC23c4c(N(C)C3)cccc4	24a	6.957	175
c1cc(F)ccc1C(=O)CCCN(CC2)CCC23c4c(CC3)cccc4	24b	8.745	175
c1c(Br)c(N)c(I)c(OC)c1C(=O)NCCN(CC)CC	2	6.556	176
COc(cc1)c(I)cc1C(=O)NCCN(CC)CC	IMBA	6.604	176
CC(=O)Nc(c(I)c1)cc(OC)c1C(=O)NCCN(CC)CC	6	5.285	176
c1c(I)c(N)cc(OC)c1C(=O)NCCN(CC)CC	7	6.315	176
CC(=O)Nc(cc1)c(I)cc1C(=O)NCCN(CC)CC	9	5.333	176
CCN(CC)CCNC(=O)c1c(I)ccc(c1)OC	12	6.342	176
c1c(I)ccc(OC)c1C(=O)NCCN(CC)CC	15	7.036	176
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.530	176
CC1(C)CCCN(C1)CCCc2cccc(c23)c(OC)ccc3	11	7.348	177
CC1(C)CCCN(C1)CCCc2cccc(c23)ccc(c3)OC	13	6.939	177
COc(cc1)cc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	15	8.500	177
C1CCCCC1N(CC2)CCN2CCCc3cccc(c34)ccc(c4)OC	16	9.046	177
CC1(C)CCCN(C1)CCCc2cccc(c23)cc(O)cc3	17	6.469	177
CC1(C)CCCN(C1)CCCc2cccc(c23)ccc(c3)O	18	6.135	177
c1cc(O)cc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	19	8.169	177
c1c(O)ccc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	20	8.261	177
c1cccc2n(c(c3c12)cccc3)CCCN(C4)CCCC4(C)C	26	5.695	177
c1cccc2n(c(c3c12)cccc3)CCCCN(C4)CCCC4(C)C	27	6.757	177
c1cccc2n(c(c3c12)cccc3)CCCCCN(C4)CCCC4(C)C	28	6.860	177
c1cccc2n(c(c3c12)cccc3)CCCN4CCN(CC4)C5CCCCC5	29	5.462	177
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.489	177
CC1(C)CCCN(C1)CCCc2cccc(c23)occ3	16	7.197	178
CC1(C)CCCN(C1)CCCc2cccc(c23)scc3	17	7.284	178
CC1(C)CCCN(C1)Cc(c2)oc(c23)cccc3	22	5.433	178
c1cccc(c12)n(cc2)CCCN(C3)CCCC3(C)C	28	7.293	178
c1cccc(c12)n(nn2)CCCN(C3)CCCC3(C)C	29	6.470	178
c1cccc(c12)n(cc2C)CCCN(C3)CCCC3(C)C	30	7.381	178
C1CCCCC1CCCCN(C2)CCCC2(C)C	31	8.991	178
CC1(C)CCCN(C1)CCNc(n2)sc(c23)cccc3	37	6.247	178
s1ccnc1NCCN(C2)CCCC2(C)C	38	6.338	178
CC1(C)CCCN(C1)CCCCN(C2)CCCC2(C)C	41	7.851	178
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.500	178
c1ccccc1CN2CCN(CC2)Cc3ccccc3	3	8.236	179
c1ccc(OC)cc1CN2CCN(CC2)Cc3ccccc3	4	9.409	179
COc(cc1)ccc1CN2CCN(CC2)Cc3ccccc3	5	9.328	179
c1cccc(Cl)c1CN2CCN(CC2)Cc3ccccc3	6	8.276	179
c1ccc(Cl)cc1CN2CCN(CC2)Cc3ccccc3	7	9.337	179
c1cc(Cl)ccc1CN2CCN(CC2)Cc3ccccc3	8	8.854	179
c1cc(Cl)c(Cl)cc1CN2CCN(CC2)Cc3ccccc3	9	9.237	179
c1cc(Cl)cc(Cl)c1CN2CCN(CC2)Cc3ccccc3	10	8.119	179
COc(cc1)ccc1CN2C[C@@H](CC[C@@H]3O)N(C[C@H]23)Cc4ccccc4	15	8.125	180
COc(cc1)ccc1CN2C[C@H](CC[C@H]3O)N(C[C@@H]23)Cc4ccccc4	ent-15	8.187	180
COc(cc1)ccc1CN2C[C@@H](CC[C@H]3O)N(C[C@H]23)Cc4ccccc4	20	6.928	180
COc(cc1)ccc1CN2C[C@H](CC[C@@H]3O)N(C[C@@H]23)Cc4ccccc4	ent-20	6.903	180
COc(cc1)ccc1CN2C[C@@H](CC[C@@H]3OC)N(C[C@H]23)Cc4ccccc4	17	6.588	180
COc(cc1)ccc1CN2C[C@H](CC[C@H]3OC)N(C[C@@H]23)Cc4ccccc4	ent-17	7.585	180
COc(cc1)ccc1CN2C[C@@H](CC[C@H]3OC)N(C[C@H]23)Cc4ccccc4	22	6.900	180
COc(cc1)ccc1CN2C[C@H](CC[C@@H]3OC)N(C[C@@H]23)Cc4ccccc4	ent-22	7.602	180
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@H](CC[C@@H]3N4CCCC4)N(C[C@@H]23)C c5ccccc5	19	6.364	181

c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@H](CC[C@H]3N4CCCC4)N(C[C@@H]23)C c5ccccc5	20	6.703	181
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@@H](CC[C@@H]3N4CCCC4)N(C[C@H]23)C c5ccccc5	ent-20	5.432	181
c1ccccc1\C=C\CCN2CCN(C)CC2	3a	7.538	182
CC1CCN(CC1)CCC=C2c(cccc3)c3Sc(c24)cccc4	5	9.097	182
c1ccccc1C(c2ccccc2)=CCCN(CC3)CCC3C	6	8.721	182
c1ccccc1C(c2ccccc2)CCCN(CC3)CCC3C	7	8.959	182
c1ccccc1C(c2ccccc2)=CCCCN(CC3)CCC3C	8	9.886	182
c1ccccc1C(c2ccccc2)CCCCN(CC3)CCC3C	9	10.046	182
CCN(CC)CCOC(=O)C(CCC)(c1ccccc1)c2ccccc2	11	7.770	182
c1ccccc1C(O)(c2ccccc2)CCCCN(CC)CC	13	7.921	182
c1ccccc1C(c2ccccc2)CCCCN(CC)CC	14	8.854	182
c1ccccc1C(c2ccccc2)=CCCCN(C)CCc3ccccc3	15a	9.051	182
c1ccccc1C(c2ccccc2)=CCCCNCCc3ccccc3	15b	8.886	182
c1ccccc1C(c2ccccc2)CCCCN(C)CCc3ccccc3	16a	9.319	182
c1ccccc1C(c2ccccc2)CCCCNCCc3ccccc3	16b	9.180	182
c1ccccc1CCCCN2CCN(C)CC2	4	7.699	182
c1ccccc1/C=C\CCN2CCN(C)CC2	3b	7.538	182
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	Ditolylguanidine	7.721	14
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	Dextrometorphan	7.357	14
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-SKF,10047	7.387	14
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	9.699	14
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-SKF,10047	5.706	14
c1cc(O)ccc1[C@@H](O)[C@@H](C)N(CC2)CCC2Cc3ccccc3	Ifenprodil	8.699	14
OCCN(CC1)CCN1CCCN(c(c23)cccc2)c4c(C=C3)cccc4	Opipramol	9.699	14
c1ccccc1[C@](C#N)(C(C)C)CCCN(C)CCc2ccccc2	(+)-Emopamil	8.959	14
c1ccccc1[C@@](C#N)(C(C)C)CCCN(C)CCc2ccccc2	(-)-Emopamil	8.222	14
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN4CCN(C)CC4	Trifluoperazine	7.678	14
O[C@H]1CC[C@H]([C@@]12C)[C@H]3[C@H](CC2)[C@]4(C)C(CC3)=CC(=O)CC4	Testosterone	5.854	14
CC(=O)[C@H]1CC[C@H]([C@@]12C)[C@H]3[C@H](CC2)[C@]4(C)C(CC3)=CC(=O)CC4	Progesterone	6.471	14
OCC(=O)[C@H]1CC[C@H]([C@@]12C)[C@H]3[C@H]([C@H](C2)O) [C@]4(C)C(CC3)=CC(=O)CC4	Corticosterone	4.553	14
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-3-PPP	8.155	14
c1ccc(I)cc1CCN(C)CCN2CCCC2	2	8.602	183
c1cc(I)ccc1CCN(C)CCN2CCCC2	3	8.602	183
C1CCCN1CCN(C)Cc2c(I)cccc2	4	7.575	183
C1CCCN1CCN(C)Cc2cc(I)ccc2	5	8.444	183
C1CCCN1CCN(C)Cc2ccc(I)cc2	6	8.699	183
c1ccc(Br)cc1CCN(C)CCN2CCCC2	9	8.367	183
c1cc(Br)ccc1CCN(C)CCN2CCCC2	10	8.538	183
C1CCCN1CCN(C)Cc2cc(Br)ccc2	11	8.051	183
c1ccc(F)cc1CCN(C)CCN2CCCC2	12	8.268	183
c1cc(F)ccc1CCN(C)CCN2CCCC2	13	8.222	183
c1ccc(Cl)cc1CCN(C)CCN2CCCC2	14	8.658	183
c1cc(Cl)ccc1CCN(C)CCN2CCCC2	15	8.620	183
C=CCN(C[C@H]12)[C@@H](CC=C1)CN2Cc3ccc(cc3)OC	2	8.036	55
C=CCN(C[C@@H]12)[C@H](CC=C1)CN2Cc3ccc(cc3)OC	ent-2	6.544	55
COc(cc1)ccc1CN2C[C@H](CC=C3)N(C[C@@H]23)Cc4ccccc4	3	9.041	55
COc(cc1)ccc1CN2C[C@@H](CC=C3)N(C[C@H]23)Cc4ccccc4	ent-3	8.357	55
C=CCN1C[C@H](CCC2)N(C[C@@H]12)Cc3ccc(cc3)OC	23a	7.959	184
C=CCN1C[C@@H](CCC2)N(C[C@H]12)Cc3ccc(cc3)OC	ent-23a	7.569	184
COC1(OC)CC[C@H](N(C[C@H]12)CC=C)CN2Cc3ccc(cc3)OC	11	5.903	184
COC1(OC)CC[C@@H](N(C[C@@H]12)CC=C)CN2Cc3ccc(cc3)OC	ent-11	6.231	184
C=CCN(C[C@H]12)[C@@H](CCC1=O)CN2Cc3ccc(cc3)OC	12	5.796	184
C=CCN(C[C@@H]12)[C@H](CCC1=O)CN2Cc3ccc(cc3)OC	ent-12	6.261	184
C=CCN(C[C@H]12)[C@@H](CC[C@H]1O)CN2Cc3ccc(cc3)OC	15a	5.650	184
C=CCN(C[C@@H]12)[C@H](CC[C@@H]1O)CN2Cc3ccc(cc3)OC	ent-15a	6.465	184
C=CCN(C[C@H]12)[C@@H](CC[C@H]1O)CN2Cc3c(OC)cc(cc3)OC	15b	5.039	184
C=CCN(C[C@@H]12)[C@H](CC[C@@H]1O)CN2Cc3c(OC)cc(cc3)OC	ent-15b	5.015	184
CO[C@@H]1CC[C@H](N(C[C@H]12)CC=C)CN2Cc3ccc(cc3)OC	16a	5.395	184
CO[C@H]1CC[C@@H](N(C[C@@H]12)CC=C)CN2Cc3ccc(cc3)OC	ent-16a	4.793	184
C=CCN(C[C@H]12)[C@@H](CC[C@@H]1O)CN2Cc3ccc(cc3)OC	20a	4.636	184
C=CCN(C[C@@H]12)[C@H](CC[C@H]1O)CN2Cc3ccc(cc3)OC	ent-20a	4.764	184
CO[C@H]1CC[C@H](N(C[C@H]12)CC=C)CN2Cc3ccc(cc3)OC	21a	5.456	184
CO[C@@H]1CC[C@@H](N(C[C@@H]12)CC=C)CN2Cc3ccc(cc3)OC	ent-21a	5.082	184
CO[C@H]1CC[C@H](N(C[C@H]12)CC=C)CN2Cc3c(OC)cc(cc3)OC	21b	5.241	184
CO[C@@H]1CC[C@@H](N(C[C@@H]12)CC=C)CN2Cc3c(OC)cc(cc3)OC	ent-21b	4.975	184

C=CCN1C[C@H](CCC2)N(C[C@@H]12)Cc3c(OC)cc(cc3)OC	23b	6.573	184
C=CCN1C[C@@H](CCC2)N(C[C@H]12)Cc3c(OC)cc(cc3)OC	ent-23b	6.251	184
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.377	184
CCCN(C[C@H]12)[C@@H](CCC1=O)CN2Cc3ccc(cc3)OC	7	6.488	54
CCCN(C[C@@H]12)[C@H](CCC1=O)CN2Cc3ccc(cc3)OC	ent-7	7.174	54
CC(C)=CCN(C[C@H]12)[C@@H](CCC1=O)CN2Cc3ccc(cc3)OC	12	7.699	54
CC(C)=CCN(C[C@@H]12)[C@H](CCC1=O)CN2Cc3ccc(cc3)OC	ent-12	7.770	54
COc(cc1)ccc1CN2C[C@H](CCC3=O)N(C[C@@H]23)Cc4ccccc4	14	7.276	54
COc(cc1)ccc1CN2C[C@@H](CCC3=O)N(C[C@H]23)Cc4ccccc4	ent-14	6.876	54
COc(cc1)ccc1CN2C[C@H](CCC3=O)N(C[C@@H]23)c4ccccc4	16	5.204	54
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@H](N(C[C@H]23)CC=C)CCC\3=C\c4ccccc4	15	6.499	185
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3OC c4ccccc4	12	6.609	185
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@@H](N(C[C@@H]23)CC=C)CCC\3=C\ c4ccccc4	ent-15	5.348	185
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3OC c4ccccc4	ent-12	5.783	185
CCN(CC)C(=O)c1ccc(cc1)[C@H](c2ccccc2)N3C[C@H](CCC4)N(C[C@@H]34)CC=C	ent-25	6.607	185
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3OCc4ccccc4	8a	6.437	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3OCc4ccccc4	11a	6.812	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3Oc4ccccc4	13a	5.674	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3OC c4ccccc4	11b	6.415	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3Oc4ccccc4	13b	5.393	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3Oc4ccccc4	15a	5.263	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3Oc4ccccc4	15b	5.801	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CCC\3=C\c4ccccc4	17a	5.921	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CCC\3=C\c4ccccc4	17b	6.333	186
COc(cc1)ccc1CN2C[C@H](C3)N(CC=C)C[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	21a	4.979	186
COc(cc1)cc(OC)c1CN2C[C@H](C3)N(CC=C)C[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	21b	5.197	186
COc(cc1)ccc1CN([C@@H]2CN3CC=C)C[C@@H]3Cc(c4C)c2nc(c45)cccc5	23a	5.788	186
COc(cc1)cc(OC)c1CN([C@@H]2CN3CC=C)C[C@@H]3Cc(c4C)c2nc(c45)cccc5	23b	5.263	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@@H]3OCc4ccccc4	ent-8a	5.983	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3OCc4ccccc4	ent-11a	7.041	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3OCc4ccccc4	ent-11b	5.896	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3Oc4ccccc4	ent-15a	5.790	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3Oc4ccccc4	ent-15b	5.547	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CCC\3=C\c4ccccc4	ent-17a	6.983	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CCC\3=C\c4ccccc4	ent-17b	6.500	186
COc(cc1)cc(OC)c1CN([C@H]2CN3CC=C)C[C@H]3Cc(c4C)c2nc(c45)cccc5	ent-23b	5.788	186
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	1	8.409	58
c1cccc(Cl)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	2	8.511	58
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	3	8.854	58
c1cc(Cl)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	4	8.190	58
c1cc(Cl)c(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	5	8.282	58
c1cc(Cl)cc(Cl)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	6	8.015	58
Clc1cccc(Cl)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	7	8.138	58
c1cccc(Br)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	8	8.539	58
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	9	9.060	58
c1cc(Br)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	10	8.401	58
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	11	8.449	58
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	12	8.611	58
c1cc(F)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	13	8.465	58
c1cc(F)cc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	14	8.412	58
c1c(F)ccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	15	8.376	58
Fc1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	16	8.237	58
c1cc(F)c(F)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	17	8.499	58
c1c(F)cc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	18	8.117	58
c1cccc(c1C(F)(F)F)CC(=O)NC2CCN(CC2)Cc3ccccc3	19	8.060	58
FC(F)(F)c1cc(ccc1)CC(=O)NC2CCN(CC2)Cc3ccccc3	20	8.407	58
FC(F)(F)c1ccc(cc1)CC(=O)NC2CCN(CC2)Cc3ccccc3	21	8.007	58
c1cccc([N+]([O-])=O)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	22	7.570	58
c1ccc([N+]([O-])=O)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	23	8.341	58
c1cc([N+]([O-])=O)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	24	7.745	58
c1cc([N+]([O-])=O)cc([N+]([O-])=O)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	25	7.848	58
c1cccc(O)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	26	7.726	58
c1ccc(O)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	27	6.959	58
c1cc(O)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	28	6.543	58

c1cc(O)c(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	30	7.623	58
c1cccc(OC)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	31	7.511	58
c1ccc(OC)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	32	7.979	58
COc(cc1)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	33	7.178	58
COc(c1)ccc(OC)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	34	7.363	58
COc(cc1)c(OC)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	35	6.453	58
COc(c1)cc(OC)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	36	6.917	58
COc(c1)c(OC)c(OC)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	37	7.097	58
O1COc(c12)ccc(c2)CC(=O)NC3CCN(CC3)Cc4ccccc4	38	8.135	58
COc(cc1)cc(OC)c1NC(=O)NC2CCN(CC2)Cc3ccccc3	39	7.521	58
CSc(cc1)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	41	7.567	58
CSc(cc1)ccc1NC(=O)NC2CCN(CC2)Cc3ccccc3	42	7.194	58
c1cc(N)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	43	6.328	58
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.597	58
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)Cc4ccccc4	1	8.252	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)C4CCCC4	2	8.921	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)C4CCCCC4	3	8.959	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)C4CCCCCC4	4	8.959	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	5	8.721	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)[C@@H]([C@@H]45)[C@H]6C[C@@H](C5)C[C@@H](C4)C6	6	6.917	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)Cc4ccccc4	7	8.495	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)C4CCCC4	8	8.444	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)C4CCCCC4	9	8.237	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)C4CCCCCC4	10	8.319	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	11	6.398	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)[C@@H]([C@@H]45) [C@H]6C[C@@H](C5)C[C@@H](C4)C6	12	7.553	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)Cc4ccccc4	13	8.229	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)C4CCCC4	14	9.155	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)C4CCCCC4	15	8.921	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)C4CCCCCC4	16	8.770	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	17	8.208	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)[C@@H]([C@@H]45) [C@H]6C[C@@H](C5)C[C@@H](C4)C6	18	8.208	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3Cc4ccccc4	19	7.252	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCC4	20	8.398	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCCC4	21	8.602	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCCCC4	22	7.244	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCCCCC4	23	7.896	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	24	7.777	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3[C@@H]([C@@H]45) [C@H]6C[C@@H](C5)C[C@@H](C4)C6	25	7.631	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3Cc4ccccc4	26	6.638	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCC4	27	7.319	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCCC4	28	7.509	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCCCC4	29	7.684	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCCCCC4	30	7.229	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3[C@@H]([C@@H]45) [C@H]6C[C@@H](C5)C[C@@H](C4)C6	31	6.426	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]([C@H]34)[C@@H](CCC3)CN(C4) C5CCCCC5	32	7.161	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]([C@H]34)[C@@H](CCC3)CN(C4) C5CCCCCC5	33	7.018	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]([C@H]34)[C@@H](CCC3)CN(C4) Cc5ccccc5	37	7.131	187
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.824	187
c1ccccc1CN(C)Cc2cnc([nH]2)-c3c(OC)c(OC)ccc3	5a	7.777	188
c1ccc(OC)c(OC)c1-c([nH]2)ncc2CNC3CCN(CC3)Cc4ccccc4	5c	7.474	188
c1c(Br)cc(OC)c(OC)c1-c([nH]2)ncc2CNC3CCN(CC3)Cc4ccccc4	5d	7.072	188
c1ccc(OC)c(OC)c1-c([nH]2)ncc2CN[C@@H](C[C@H]34)C[C@@H](CCC3) N4Cc5ccccc5	5e	6.232	188
c1cc(Cl)ccc1C2(O)CCN(CC2)Cc3cnc([nH]3)-c4c(OC)c(OC)cc(Br)c4	5n	6.627	188
c1ccccc1C2CCN(CC2)Cc3cnc([nH]3)-c4c(OC)c(OC)cc(Br)c4	5l	6.266	188
c1ccccc1CN(CC2)CCC2c(on3)nc3-c4c(OC)c(OC)ccc4	7d	8.180	188
c1sccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	2	8.143	57
s1cccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	1	8.406	57
n1c[nH]cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	3	6.605	57
n1ccccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	4	6.628	57

c1cccc(c12)[nH]cc2CC(=O)NC3CCN(CC3)Cc4ccccc4	10	7.963	57
c1ncccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	5	6.570	57
c1cnccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	6	6.525	57
c1cccc(c12)cccc2CC(=O)NC3CCN(CC3)Cc4ccccc4	7	8.333	57
c1cccc(c12)cccc2NC(=O)NC3CCN(CC3)Cc4ccccc4	8	7.645	57
c1cccc(c12)ccc(c2)CC(=O)NC3CCN(CC3)Cc4ccccc4	9	7.209	57
c1cc(I)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	16	7.859	57
c1c(Br)ccc(c12)[nH]cc2CC(=O)NC3CCN(CC3)Cc4ccccc4	11	7.284	57
COc(c1)ccc(c12)[nH]cc2CC(=O)NC3CCN(CC3)Cc4ccccc4	12	6.902	57
n1cccnc1SCC(=O)NC2CCN(CC2)Cc3ccccc3	15	6.824	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3c(F)cccc3	17	7.993	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3cc(F)ccc3	18	8.085	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	19	8.181	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3c(I)cccc3	20	6.460	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	21	8.171	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	22	8.044	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(cc3C(F)(F)F)ccc3	24	6.850	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(cc3)ccc3C(F)(F)F	25	7.060	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccc([N+]([O-])=O)cc3	26	7.720	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3cc(Cl)c(Cl)cc3	27	8.140	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3cc(F)c(F)cc3	28	8.201	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(c3)ccc(c34)OCO4	29	8.401	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(c3)ccc(c34)cccc4	30	7.622	57
c1ccccc1CC(=O)NC2CCN(CC2)CCc3ccccc3	31	7.505	57
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	32	8.502	57
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	33	7.812	57
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	34	8.377	57
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	35	8.259	57
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	36	8.368	57
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	37	8.648	57
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	38	8.939	57
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	39	8.636	57
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	40	8.493	57
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	41	8.917	57
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	42	8.457	57
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	43	8.750	57
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.252	189
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.050	189
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.201	189
c1ccccc1C[C@H]2CN[C@H](C)Cc(c23)cccc3	14a	5.983	189
c1cccc(c12)C[C@@H](CCCC)NC[C@@H]2Cc3ccccc3	14c	6.539	189
c1ccccc1C[C@H]2CN[C@H](c3ccccc3)Cc(c24)cccc4	14d	5.978	189
c1ccccc1C[C@@H]2CN[C@@H](C)Cc(c23)cccc3	ent-14a	5.976	189
c1cccc(c12)C[C@H](CC)NC[C@H]2Cc3ccccc3	ent-14b	6.682	189
c1cccc(c12)C[C@H](CCCC)NC[C@H]2Cc3ccccc3	ent-14c	7.585	189
C[C@H](C1)NCCc(c12)cccc2	12a	5.435	190
C[C@@H](C1)NCCc(c12)cccc2	ent-12a	6.524	190
CCCC[C@H](C1)NCCc(c12)cccc2	12c	7.796	190
CCCC[C@@H](C1)NCCc(c12)cccc2	ent-12c	6.056	190
c1cccc(c12)CCN[C@@H](C2)c3ccccc3	12d	7.301	190
c1ccccc1CCCN2[C@@H](C)CN(C[C@H]2C)CCCN(c3ccccc3)c4ccccc4	25	7.012	191
c1cc(F)ccc1C(c2ccc(F)cc2)OCCN(CC3)CCN3CCCc4ccccc4	3	6.511	191
c1ccccc1CCCN2[C@@H](C)CN(C[C@H]2C)CCCn(c3cccc4)c(c5c34)cccc5	11	6.983	191
C[C@@H]1CN(C[C@H](C)N1)CCCN(c2ccccc2)c3ccccc3	24	6.860	191
CN1[C@@H](C)CN(C[C@H]1C)CCCn(c2cccc3)c(c4c23)cccc4	10	6.258	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2ccc(c3)[N+]([O-])=O)c(c4c23)cccc4	7	6.225	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2cccc3)c(c4c23)cccc4	1	6.042	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2ccc(Br)c3)c(c4c23)ccc(Br)c4	5	5.355	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2ccc(c3)N)c(c4c23)cccc4	8	5.243	191
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.658	192
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.721	192
COc(cc1)ccc1N(C2=O)C[C@@H](O2)CN(CC3)CCC3(O)c(c4)ccc(c45)OCO5	panamesine	6.955	192
COc(cc1)ccc1N(C2=O)C[C@@H](O2)CN(CC3)CC[Si]3(O)c(c4)ccc(c45)OCO5	sila-panamesine	7.432	192
c1cc(I)ccc1C(=O)NCCN(CC)CC	IDAB	7.959	193
c1cc(I)ccc1C(=O)NCCN2CCCCC2	IPAB	8.590	193
c1cc(I)ccc1C(=O)NC2CCN(CC2)Cc3ccccc3	4-IBP	8.770	194
c1ccc(I)cc1C(=O)NC2CCN(CC2)Cc3ccccc3	3-IBP	8.520	194
c1cccc(I)c1C(=O)NC2CCN(CC2)Cc3ccccc3	2-IBP	8.785	194

c1cc(Br)ccc1CCN(C)CCN2CCCCC2	BrPEMP	8.524	195
c1cc(I)ccc1CCN(C)CCN2CCCCC2	IPEMP	9.086	195
CCN(CC)CCNS(=O)(=O)c1ccc(Br)cc1	1	7.996	196
CCN(CC)CCNS(=O)(=O)c1ccc(I)cc1	2	8.304	196
C1CCCN1CCNS(=O)(=O)c2ccc(Br)cc2	3	8.177	196
C1CCCN1CCNS(=O)(=O)c2ccc(I)cc2	4	8.372	196
C1CCCCN1CCNS(=O)(=O)c2ccc(Br)cc2	5	8.812	196
C1CCCCN1CCNS(=O)(=O)c2ccc(I)cc2	6	9.337	196
C1CCCCCN1CCNS(=O)(=O)c2ccc(Br)cc2	7	9.201	196
C1CCCCCN1CCNS(=O)(=O)c2ccc(I)cc2	8	8.879	196
C1CCCCCN1CCN(C)S(=O)(=O)c2ccc(Br)cc2	9	9.745	196
C1CCCCCN1CCN(C)S(=O)(=O)c2ccc(I)cc2	10	9.854	196
C1CCCCN1CCNS(=O)(=O)c(cc2)cc(I)c2OC	11	7.379	196
C1CCCCCN1CCN(C)S(=O)(=O)c(cc2)cc(I)c2OC	12	8.507	196
COc(cc1)c(I)cc1C(=O)NCCN2CCCCC2	PIMBA	7.927	197
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-pentazocine	8.174	198
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.129	198
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-3-PPP	7.101	198
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.721	198
c1ccccc1C(\CC)=C(c2ccccc2)/c3ccc(cc3)OCCN(C)C	Tamoxifen	6.572	198
C1CCCN1CCOc(cc2)ccc2Cc3ccccc3	PBPE	9.620	198
c1ccccc1C(C)(C)c2ccc(cc2)OCCN3CCCC3	PCPE	8.983	198
c1ccccc1Cc2ccc(cc2)OCCN3CCOCC3	MBPE	8.759	198
c1ccccc1C(C)(C)c2ccc(cc2)OCCN3CCOCC3	MCPE	7.832	198
CCCSc(nsn1)c1C2=CCCNC2	P-TZTP	7.730	199
FCCCSc(nsn1)c1C2=CCCNC2	FP-TZTP	7.207	199
FCCSc(nsn1)c1C2=CCCNC2	FE-TZTP	7.664	199
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.752	200
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	ibogaine	5.031	200
c1ccccc1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-Vesamicol	7.588	201
c1cc(F)ccc1CN(C2)CC[C@@H](O)[C@@H]2N(CC3)CCC3c4ccccc4	(+)-FBT	7.666	201
c1cc(F)ccc1CN(C2)CC[C@H](O)[C@H]2N(CC3)CCC3c4ccccc4	(-)-FBT	7.654	201
c1ccccc1C(c2ccccc2)O[C@@H](C3)C[C@@H](N4C)CC[C@H]34	Benztropine	6.503	202
Clc1c(Cl)ccc(c1)NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6a	6.885	203
Clc1c(Cl)ccc(c1)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3a	7.275	203
COc(c(Cl)c1)cc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3b	7.500	203
c1cc(Cl)cc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3c	7.590	203
c1ccc(Br)cc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3d	7.907	203
c1cc(Br)ccc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3	8.201	203
Cc1c(C)cccc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3f	8.215	203
c1cc(C)cc(c1C)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3g	8.036	203
CCc1ccc(cc1)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3h	7.602	203
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3i	7.842	203
[O-][N+](=O)c(c1)ccc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3 Cc4ccccc4	3j	7.421	203
c1cc([N+]([O-])=O)cc(c1C)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3 Cc4ccccc4	3n	7.780	203
CCCCc1ccc(cc1)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3l	8.208	203
c1ccc(SC)cc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3m	8.167	203
c1cccc(Br)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3o	8.398	203
COc(cc1)ccc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3p	7.487	203
Clc1c(Cl)ccc(c1)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4a	7.511	203
COc(c(Cl)c1)cc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4cc-ccc4	4b	6.630	203
c1ccc(Br)cc1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4d	8.180	203
c1cc(Br)ccc1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4e	7.889	203
Cc1c(C)cccc1NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4f	7.939	203
c1cc(C)cc(c1C)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4g	8.222	203
CCc1ccc(cc1)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4h	7.764	203
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4i	7.034	203
[O-][N+](=O)c(c1)ccc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3C c4ccccc4	4j	7.169	203
c1cc([N+]([O-])=O)cc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 Cc4ccccc4	4k	7.676	203
CCCCc1ccc(cc1)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4l	7.393	203
c1ccc(SC)cc1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4m	7.876	203
[O-][N+](=O)c1cccc(c1C)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 Cc4ccccc4	4n	8.523	203

COc(c1)ccc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4o	6.483	203
CC(C)c(cc1)cc(c1CC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4p	7.606	203
c1ccc(Br)cc1NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6c	7.048	203
Brc1cccc(c1OC)NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6f	6.889	203
c1cc(Br)ccc1NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6d	6.421	203
c1cc([N+]([O-])=O)cc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3C c4ccccc4	3k	8.102	203
CCN(CC)Cc1ccc([nH]1)-c2c(OC)c(OC)cc(Br)c2	6g	6.561	204
c1ccccc1CN(Cc2ccccc2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6h	6.866	204
C1CCCCN1Cc2ccc([nH]2)-c3c(OC)c(OC)cc(Br)c3	6i	6.780	204
c1ccccc1C2CCN(CC2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6j	6.777	204
c1ccccc1CC2CCN(CC2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6k	6.951	204
c1cccc(c12)CN(C2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6q	6.409	204
c1cccc(c12)CN(C2)Cc3ccc([nH]3)-c(c4OC)cc(Br)c(c45)cccc5	11d	6.510	204
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	1b	6.695	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccccc4	2a	7.223	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCc4ccccc4	3	7.137	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCc4ccccc4	4	7.184	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCC c4ccccc4	5	7.762	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCC c4ccccc4	6	6.670	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCC c4ccccc4	7	6.638	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(F)cc4	2b	6.582	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(I)cc4	2c	6.757	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc([N+]([O-])=O)cc4	2e	6.668	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(N)cc4	2f	5.648	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4cc(F)ccc4	1d	6.492	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(I)cc4	1e	6.343	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4cc(I)ccc4	1g	5.868	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(C)cc4	1h	6.564	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc([N+]([O-])=O)cc4	1i	6.268	98
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCN(CC3)Cc(c34)cccc4	11a	7.821	205
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCN(CC3)Cc(c34)cc(OC)c(c4)OC	11b	6.723	205
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	12	5.936	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCN(CC2)Cc(c23)cccc3	13a	6.558	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	13b	5.533	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	14	4.889	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)CCC2c(c3Cl)cccc3Cl	15	6.092	205
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCCCN(CC3)CCC3c(c4Cl)cccc4Cl	16	6.124	205
c1c(Br)ccc(OC)c1C(=O)NCCN(CC2)Cc(c23)cccc3	17	7.662	205
c1c(Br)ccc(OC)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	18	5.261	205
Cc(c1)ccc(OC)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	19	4.982	205
Cc(c1)ccc(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	20	5.512	205
c1cc(F)ccc1CN(CC2)CCC23c4c(C(=O)O3)cccc4	2c	8.114	206
c1cc(F)ccc1CN(CC2)CCC23c4c(CO3)cccc4	2d	9.745	206
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.244	207
c1ccccc1CN(CC2)CCC23c4c(CC(=O)O3)cccc4	18	7.533	208
c1ccccc1CN(CC2)CCC23c4c(C=CO3)cccc4	19	8.728	208
c1ccccc1CN(CC2)CCC23c4c(CCO3)cccc4	20	9.161	208
c1ccccc1CN(CC2)CCC23c4c(C(=O)O3)cccc4	25	7.672	208
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	6.785	208
c1ccccc1[C@]23[C@H](C2)CN(C3)C4CCCCC4	(+)-(1R,2S)-14	9.041	209
c1ccccc1[C@@]23[C@@H](C2)CN(C3)C4CCCCC4	(-)-(1S,2R)-14	7.836	209
C1CCCCC1CN(C2)C[C@@H](C3)[C@]23c4ccccc4	(+)-(1R,2S)-15	8.638	209
C1CCCCC1CN(C2)C[C@H](C3)[C@@]23c4ccccc4	(-)-(1S,2R)-15	8.032	209
c1ccccc1CCN(C2)C[C@@H](C3)[C@]23c4ccccc4	(+)-(1R,2S)-18	7.260	209
c1ccccc1CCN(C2)C[C@H](C3)[C@@]23c4ccccc4	(-)-(1S,2R)-18	6.785	209
c1ccccc1CCCN(C2)C[C@@H](C3)[C@]23c4ccccc4	(+)-(1R,2S)-19	7.796	209
c1ccccc1CCCN(C2)C[C@H](C3)[C@@]23c4ccccc4	(-)-(1S,2R)-19	7.319	209
c1ccccc1[C@]2(C(=O)OC)[C@H](C2)CN(CC3)CCC3(O)c4ccc(Cl)cc4	(+)-1	8.403	210
c1ccccc1[C@]2(C(=O)OC)[C@H](C2)CN(CC3)CCC3(O)c4ccccc4	(+)-8	8.299	210
c1ccccc1[C@@]2(C(=O)OC)[C@@H](C2)CN(CC3)CCC3(O)c4ccccc4	(-)-8	8.154	210
c1ccccc1[C@]2(C(=O)OC)[C@H](C2)CN3[C@@H](CC[C@@H]34)C[C@](C4)(O)c5ccc(Cl)cc5	(+)-9	7.357	210
c1ccccc1[C@@]2(C(=O)OC)[C@@H](C2)CN3[C@@H](CC[C@@H]34)C[C@](C4)(O)c5ccc(Cl)cc5	(-)-9	6.284	210
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.159	210
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)C	BD1047	9.032	211

[C@@]123c4c5c(OC)ccc4C[C@H](NCC3)[C@H]2CCC(=O)[C@H]1O5	(+)-nordihydrocodeinone	4.777	212
c1cc(Cl)c(Cl)cc1CCN[C@H]2[C@H](CCCC2)N3CCCC3	LR132	8.699	213
c1cc(Cl)c(Cl)cc1CCNCCN2CCCC2	BD1060	8.523	214
C1CCCN1CCN(CC=C)CCc2cc(Cl)c(Cl)cc2	BD1052	8.699	214
c1cc(Cl)c(Cl)cc1CCN(CC)CCN2CCCC2	BD1067	8.699	214
c1cccc(OC)c1CCN(CC)CCN2CCCCC2	UMB98	7.602	215
c1ccc(OC)cc1CCN(CC)CCN2CCCCC2	UMB99	7.796	215
COc(cc1)ccc1CCN(CC)CCN2CCCCC2	UMB100	7.620	215
c1cccc(OC)c1CCN(C)CCN2CCCCC2	UMB101	7.495	215
c1ccc(OC)cc1CCN(C)CCN2CCCCC2	UMB102	7.602	215
COc(cc1)ccc1CCN(C)CCN2CCCCC2	UMB103	7.678	215
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccccc3	1a	9.310	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc(cc3)OC	1b	8.975	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc(O)cc3	1c	8.347	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc(F)cc3	1d	9.143	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc([N+]([O-])=O)cc3	1e	9.268	216
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2a	7.061	216
COc(cc1)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2b	7.003	216
c1cc(O)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2c	7.207	216
c1cc(F)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2d	7.500	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2e	7.011	216
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3a	9.237	216
COc(cc1)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3b	8.658	216
c1cc(O)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3c	7.807	216
c1cc(F)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3d	9.237	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3e	9.081	216
c1ccccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4a	7.585	216
COc(cc1)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4b	7.693	216
c1cc(O)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4c	7.678	216
c1cc(F)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4d	8.143	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4e	7.444	216
c1ccccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5a	8.921	216
COc(cc1)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5b	8.602	216
c1cc(O)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5c	7.896	216
c1cc(F)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5d	8.854	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5e	9.092	216
N#CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	2	4.886	217
N#CCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	3	5.009	217
N#CCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	4	5.770	217
N#CCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	5	6.310	217
N#CCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	6	6.194	217
N#CCCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	7	7.097	217
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	8	4.959	217
C=CCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	9	5.796	217
C=CCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	10	7.301	217
C=CCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	11	7.658	217
CC#CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	12	5.009	217
C#CCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	13	5.229	217
C#CCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	14	6.699	217
N#CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	16	4.959	217
N#CCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	17	6.602	217
N#CCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	18	7.699	217
N#CCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	19	7.444	217
N#CCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	20	7.481	217
N#CCCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	21	7.796	217
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	22	6.523	217
C=CCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	23	7.824	217
C=CCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	24	8.678	217
C=CCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	25	8.959	217
CC#CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	26	6.796	217
C#CCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	27	6.959	217
C#CCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	28	7.745	217
c1cc(Cl)c(Cl)cc1CCN(C)CCN2CCCCCC2	LR172	9.398	218
c1cc(F)ccc1-n(c(c23)cccc2)c(=O)n3CCCCN(CC4)Cc(c45)cc(OC)c(c5)OC	CM353	5.903	219
c1cccc(c12)n(C)c(=O)n2CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	CM398	5.821	219
c1cccc(c12)n(C)c(=O)n2CCCCN(CC3)CCC34c5c(CO4)cccc5	CM699	7.857	219
CCCCCn1c(=O)n(c(c12)cccc2)CCCCN3CCN(CC3)c4ccc(F)cc4	CM775	6.564	219
c1cccc(c12)n(CCC)c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM777	6.447	219

c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c5ccccc5	3a	8.347	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c5ccc(cc5)OC	3b	8.824	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c(cc5)ccc5C	3c	8.444	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c5ccc([N+]([O-])=O)cc5	3d	8.770	220
N#Cc1ccc(cc1)-c(sc2)c(CCO3)c2C34CCN(CC4)Cc5ccccc5	3e	8.469	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c5cccc(c56)cccc6	3f	8.398	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)csc4	5	9.456	220
c1ccccc1CN(CC2)CCC23c4c(C=CO3)csc4	14	8.721	220
c1ccccc1C(\CC)=C(c2ccccc2)/c3ccc(cc3)OCCN(C)C	Tamoxifen	7.585	221
c1cccc(c12)oc(CCCC)c2C(=O)c3cc(I)c(c(I)c3)OCCN(CC)CC	Amiodarone	8.678	221
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c(cc3C(F)(F)F)ccc3	Trifluperidol	8.886	221
c1cccc(Cl)c1CNC[C@H]2CC[C@@H](CC2)CNCc3c(Cl)cccc3	AY-9944	9.337	221
c1ccccc1/C(Cl)=C(c2ccccc2)\c3ccc(cc3)OCCN(CC)CC	Enclomiphene	7.921	221
c1ccccc1\C(Cl)=C(c2ccccc2)\c3ccc(cc3)OCCN(CC)CC	Zuclomiphene	8.260	221
CCCCN(CC1)CCC12c3c(CCC2)cccc3	L-609,404	9.222	221
Cn1c(=O)sc(c12)cc(cc2)CCN(CC3)CCC3c4ccccc4	6	7.699	222
Cn1c(=O)sc(c12)cc(cc2)CCCCN3CCN(CC3)Cc4ccccc4	11	7.429	222
Cn1c(=O)sc(c12)cc(cc2)CCCCN3CCN(CC3)Cc4cc(Cl)c(Cl)cc4	15	6.857	222
NC12C[C@@H]3C[C@H](C1)C[C@H](C2)C3	amantadine	4.853	223
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.469	223
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.770	223
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.886	223
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	dextromethorphan	6.569	223
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)O	dextrorphan	6.408	223
C1CN(C)CCC12N=Nc3c(N2)cccc3	1	5.467	224
c1ccccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	2	8.553	224
c1cc(F)ccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	3	8.553	224
c1cc(Cl)ccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	4	8.903	224
c1cc(C)ccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	5	8.602	224
COc(cc1)ccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	6	8.398	224
c1ccccc1CCN(CC2)CCC23N=Nc4c(N3)cccc4	7	8.398	224
c1ccccc1CCCCN(CC2)CCC23N=Nc4c(N3)cccc4	8	8.420	224
c1ccccc1CCCCCN(CC2)CCC23N=Nc4c(N3)cccc4	9	9.027	224
c1ccccc1C(=O)CCCN(CC2)CCC23N=Nc4c(N3)cccc4	10	7.854	224
c1cc(F)ccc1C(=O)CCCN(CC2)CCC23N=Nc4c(N3)cccc4	11	7.921	224
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.222	224
c1ccccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	2	9.222	224
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.215	225
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.409	225
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.928	226
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.030	226
c1cccc(O)c1C(=O)CCCCCN2CCN(CC2)c3noc(c34)cccc4	40	7.215	227
c1cccc(OC)c1C(=O)CCCCCN2CCN(CC2)c3noc(c34)cccc4	43	5.367	227
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.161	228
[C@@H]12CC[C@H](N2C)C[C@H](C1)OC(=O)[C@@H](C)Oc3ccc(F)cc3	R(+)1	6.446	228
[C@@H]12CC[C@H](N2C)C[C@H](C1)OC(=O)[C@H](C)Sc3ccc(Cl)cc3	S(-)16	6.427	228
Cc1ccc(cc1)[C@]2(C(=O)OC)[C@H](C2)CN(CC3)CCC3(O)c4ccccc4	(+)-7	8.721	229
Cc1ccc(cc1)[C@@]2(C(=O)OC)[C@@H](C2)CN(CC3)CCC3(O)c4ccccc4	(-)-7	7.886	229
c1ccccc1CN(CC2)CCC23C(=O)c4c(CC3)cccc4	1	8.854	230
c1ccccc1CN(CC2)CCC23CCc4c(S3)cccc4	2	9.301	230
c1ccccc1CN(CC2)CCC23CCc4c(S3(=O)=O)cccc4	4	7.699	230
c1ccccc1CN(CC2)CCC23CCc4c(O3)cccc4	5	9.208	230
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	8.495	230
CN1CCN(CC1)C2=Nc(cc(Cl)cc3)c3Nc(c24)cccc4	clozapine	5.071	230
c1cc(F)ccc1C(=O)NCCN(CC)CC	F-FBZA	5.051	231
C1CCCCN1CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	1a	8.018	232
C1COCCN1CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	2a	7.873	232
C1CCCCCN1CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3a	7.697	232
C1CCCN1CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	4a	8.131	232
CCN(CC)CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	5a	7.818	232
CN(C)CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	6a	7.703	232
C1CCCCC1NCCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	7c	7.381	232
c1ccccc1NCCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	8c	8.229	232
c1ccccc1N(C)CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	9c	8.252	232
c1ccccc1N(CC)CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	10c	7.375	232
c1ccccc1CNCCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	11c	7.529	232
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.796	232
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-pentazocine	8.215	232

c1ccccc1[C@@]2(C(=O)OC)[C@@H](C2)CNC34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(-)-cis-18	8.398	233
c1ccccc1[C@]2(C(=O)OC)[C@H](C2)CNC34C[C@@H]5C[C@H](C3)C[C@H](C4)C5	(+)-cis-18	6.631	233
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.229	233
C1CCCCN1CCN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-1a	5.342	234
C1CCCN1CCN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-1b	5.143	234
C1CCCCN1CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cccc4	(+)-3a	7.699	234
C1CCCCN1CCN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-3a	7.495	234
C1CCCN1CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cccc4	(+)-3b	7.469	234
C1CCCN1CCN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-3b	6.599	234
c1ccccc1NCCN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)7a	5.648	234
c1ccccc1NCCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cccc4	(+)-8a	7.678	234
c1ccccc1NCCN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-8a	7.237	234
c1ccccc1N(C)CCN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cccc4	(+)-8b	7.041	234
c1ccccc1N(C)CCN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-8b	6.854	234
c1ccccc1[C@]2(C(=O)OC)[C@H](C2)CN(CC3)CCC3(O)c4ccc(Cl)cc4	(+)-7(MR 200)	8.821	235
c1ccccc1[C@@]2(C(=O)OC)[C@@H](C2)CN(CC3)CCC3(O)c4ccc(Cl)cc4	(-)-7(MR 201)	8.252	235
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.658	235
CN(C)C/C=C(\C)c1ccc(cc1)OC	11	6.094	67
c1ccccc1C(\C)=C\CN(C)Cc2ccccc2	13	7.036	67
COc(cc1)ccc1C(\C)=C\CN(C)Cc2ccccc2	14	8.280	67
c1ccc(OC)cc1C(\C)=C\CN(C)Cc2ccccc2	15	8.000	67
C1CCCCN1C/C=C(\C)c(c2)ccc(c23)cccc3	16	9.013	67
C1CCCCN1C/C=C(\C)c2ccc(cc2)-c3ccccc3	17	9.066	67
c1ccccc1C(\C)=C\CN2CCCCC2	18	6.338	67
COc(cc1)ccc1C(\C)=C\CN2CCCCC2	19	7.854	67
c1ccc(OC)cc1C(\C)=C\CN2CCCCC2	20	7.041	67
c1cccc(c12)ccc(c2)C(\C)=C\CN(CC3)CCC3Cc4ccccc4	21	7.638	67
c1ccccc1-c(cc2)ccc2C(\C)=C\CN(CC3)CCC3Cc4ccccc4	22	8.154	67
c1ccccc1C(\C)=C\CN(CC2)CCC2Cc3ccccc3	23	8.971	67
COc(cc1)ccc1C(\C)=C\CN(CC2)CCC2Cc3ccccc3	24	8.383	67
c1ccc(OC)cc1C(\C)=C\CN(CC2)CCC2Cc3ccccc3	25	8.114	67
C1COCCN1C/C=C(\C)c(c2)ccc(c23)cccc3	26	8.018	67
C1COCCN1C/C=C(\C)c2ccc(cc2)-c3ccccc3	27	7.936	67
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	6.751	236
c1ccccc1CN(CC2)CCC23c4c(C=CO3)n(nc4)-c5ccccc5	26	8.830	237
c1ccccc1CN(CC2)CCC23c4c(C=CO3)n(C)nc4	27	7.921	237
c1ccccc1Cn(nc2)c(CCO3)c2C34CCN(CC4)Cc5ccccc5	28a	8.767	237
c1ccccc1CCCN(CC2)CCC23c4c(CCO3)n(nc4)Cc5ccccc5	28c	9.092	237
c1ccccc1Cn(nc2)c(CCO3)c2C34CCN(CC4)CC5CCCCC5	28d	9.367	237
CC(C)CCN(CC1)CCC12c3c(CCO2)n(nc3)Cc4ccccc4	28e	9.009	237
CC(C)=CCN(CC1)CCC12c3c(CCO2)n(nc3)Cc4ccccc4	28f	9.013	237
c1ccccc1CN(CC2)CCC23c4c(CCO3)n(C)nc4	29a	8.036	237
c1ccccc1CCCN(CC2)CCC23c4c(CCO3)n(C)nc4	29c	7.770	237
CC(C)CCN(CC1)CCC12c3c(CCO2)n(C)nc3	29d	7.523	237
CC(C)=CCN(CC1)CCC12c3c(CCO2)n(C)nc3	29e	7.854	237
CC(=O)[C@H]1CC[C@H]([C@@]12C)[C@H]3[C@H](CC2)[C@]4(C)C(CC3)=CC(=O)CC4	progesterone	6.180	237
c1cc(F)ccc1C(=O)CCCN(CC2)CC[Si]2(O)c3ccc(Cl)cc3	sila-haloperidol	8.469	238
Cc(c1)ccc(OCCF)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3a	4.643	239
c1c(Br)cc(OC)c(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3b	4.815	239
Cc(c1)ccc(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3c	6.481	239
c1c(Br)ccc(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3d	5.968	239
c1c(I)ccc(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3e	5.886	239
c1c(I)cc(OC)c(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3f	5.668	239
c1cc(F)ccc1C(=O)C2CCN(CC2)[C@@H](C3)[C@@H](O)Cc(c34)cccc4	(-)-9e	6.181	240
c1cc(F)ccc1C(=O)C2CCN(CC2)[C@H](C3)[C@H](O)Cc(c34)cccc4	(+)-9e	6.731	240
FCCOc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OCCF)cccc3	20c	5.361	241
FCCOCCOCCOc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	18c	5.312	241
FCCOc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	18a	5.321	241
CN(C)c(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OCCF)cccc3	20a	5.708	241
c1sccc1-c(cc2)ccc2C(=O)NCCCCN3CCN(CC3)c4c(OCCF)cccc4	20e	4.680	241
FCCc(cc1)ccc1C(=O)NC/C=C/CN2CCN(CC2)c3c(OCCF)cccc3	21b	5.143	241
c1sccc1-c(cc2)ccc2C(=O)NC/C=C/CN3CCN(CC3)c4c(OCCF)cccc4	21e	5.109	241
CCCc(cc1)cc(c12)sc(=O)n2CCN3CCCCC3	1	9.222	242
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCCN3CCCCC3	2	8.638	242
CCC(=O)c(cc1)cc(c12)oc(=O)n2CCCN3CCCCC3	3	8.071	242
CCCCC(=O)c(cc1)cc(c12)oc(=O)n2CCN3CCCCC3	4	7.638	242
CCCCC(=O)c(cc1)cc(c12)oc(=O)n2CCCN3CCCCC3	5	7.398	242
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCN3CCCCC3	6	7.328	242

CCCCC(=O)c(cc1)cc(c12)sc(=O)n2CCN3CCCCC3	7	7.310	242
c1ccccc1C(=O)c(cc2)cc(c23)sc(=O)n3CCN4CCCC4	8	7.268	242
CCC(=O)c(cc1)cc(c12)sc(=O)n2C(=O)CC	9	7.201	242
CCC(=O)c(cc1)cc(c12)oc(=O)n2CCN3CCCCC3	10	7.143	242
C1COCCN1CCn2c(=O)oc(c23)cc(cc3)Cc4ccccc4	11	7.143	242
c1ccccc1C(=O)c(cc2)cc(c23)sc(=O)n3CCN4CCCCC4	12	7.081	242
c1ccccc1C(=O)c(cc2)cc(c23)sc(=O)n3CCN(C)C	13	6.979	242
CCCCCc(cc1)cc(c12)oc(=O)n2CCN3CCOCC3	14	6.752	242
c1ccccc1C(=O)c(cc2)cc(c23)oc(=O)n3CCN4CCCC4	15	6.733	242
c1ccccc1C(=O)c(cc2)cc(c23)oc(=O)n3CCN4CCCCC4	16	6.627	242
CCCCC(=O)c(cc1)cc(c12)oc(=O)n2CCN3CCCC3	17	6.491	242
c1ccccc1C(=O)c(cc2)cc(c23)oc(=O)n3CCN(C)C	18	6.438	242
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCN3CCCC3	19	6.243	242
CCC(=O)c(cc1)cc(c12)oc(=O)n2CCN3CCCC3	20	6.210	242
CCCCC(=O)c(cc1)cc(c12)sc(=O)n2CCN(C)C	21	6.202	242
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	8.456	243
c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Cl)cc4	2	7.714	244
c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	7	7.917	244
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Cl)cc4	6	6.616	244
c1cc(Br)ccc1C2(O)CCN(CC2)Cc3c[nH]c(c34)cccc4OC	8	5.592	244
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	9	6.967	244
COc1cccc(c12)[nH]cc2CN(CC3)CCC34C(=O)N(C)CN4c5ccccc5	14	5.502	244
c1cccc(c12)[nH]cc2CN(CC3)CCC3c4ccccc4	17	6.480	244
c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(cc4)SC	20	7.402	244
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(cc4)SC	21	6.627	244
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCN	1a	5.604	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCN	1b	5.848	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 CCCCCCCCCCN	1c	6.872	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCNC c4cc(Br)ccc4	2a	7.179	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 CCCCNCc4cc(F)ccc4	2b	9.523	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 CCCCNCc4cc(I)ccc4	2c	7.195	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCNC c4ccc(Br)cc4	2d	8.770	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCNC c4ccc(F)cc4	2e	7.655	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 CCCCNCc4ccc(I)cc4	2f	9.469	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCNC c4cc(Br)ccc4	3a	6.949	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCNC c4cc(F)ccc4	3b	9.337	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCNCc 4cc(I)ccc4	3c	9.252	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCNC c4ccc(Br)cc4	3d	7.365	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCNC c4ccc(F)cc4	3e	9.000	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCCNC c4ccc(I)cc4	3f	9.187	245
c1cc(Cl)ccc1C(=O)NCCCCCCN2[C@H](CCC3)C[C@@H](C[C@@H]23)OC(=O)Nc(c(cc4)OC)cc4C	4a	5.855	245
c1cc(Br)ccc1C(=O)NCCCCCCN2[C@H](CCC3)C[C@@H](C[C@@H]23)OC(=O)Nc(c(cc4)OC)cc4C	4b	5.690	245
c1cc(F)ccc1C(=O)NCCCCCCN2[C@H](CCC3)C[C@@H](C[C@@H]23)OC(=O)Nc(c(cc4)OC)cc4C	4c	5.906	245
c1cc(I)ccc1C(=O)NCCCCCCN2[C@H](CCC3)C[C@@H](C[C@@H]23)OC(=O)Nc(c(cc4)OC)cc4C	4d	5.850	245
N1C(=O)N[C@@H]([C@@H]12)CS[C@@H]2CCCCC(=O)NCCCCCCN3 [C@H](CCC4)C[C@@H](C[C@@H]34)OC(=O)Nc(c(cc5)OC)cc5C	5	5.468	245
N1C(=O)N[C@@H]([C@@H]12)CS[C@@H]2CCCCC(=O)NCCCCCCCC CCN3[C@H](CCC4)C[C@@H](C[C@@H]34)OC(=O)Nc(c(cc5)OC)cc5C	6	4.990	245
N1C(=O)N[C@@H]([C@@H]12)CS[C@@H]2CCCC(=O)N CCCCCC(=O)NCCCCCCN3[C@H](CCC4)C[C@@H](C[C@@H]34)OC(=O)Nc(c(cc5)OC)cc5C	7	4.984	245
N1C(=O)N[C@@H]([C@@H]12)CS[C@@H]2CCCC(=O)NCCCCCC(=O)N CCCCCCCCCCN3[C@H](CCC4)C[C@@H](C[C@@H]34)OC(=O)Nc(c(cc5)OC)cc5C	8	5.418	245
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3 CCCCCCNS(=O)(=O)c(ccc4)c(c45)cccc5N(C)C	9	4.898	245
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.839	245

c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(I)cc4	5	8.699	246
c1cc(I)ccc1C2(O)CCN(CC2)Cc3c[nH]c(c34)cccc4OC	6	6.055	246
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(I)cc4	7	6.706	246
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccccc4	8	5.816	246
FCCOc1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	9	5.492	246
FCCOc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	10	6.644	246
COc1cccc(c12)[nH]cc2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	11	5.384	246
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	12	5.753	246
c1ccnc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	13	7.821	246
c1ccnc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(I)cc4	14	8.921	246
c1ccnc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(cc4)SC	15	8.093	246
c1cccc(c12)oc(c2)CN(CC3)CCC3(O)c4ccc(Br)cc4	18	8.611	246
c1cccc(c12)oc(c2)CN(CC3)CCC3(O)c4ccc(I)cc4	19	8.851	246
c1cccc(c12)sc(c2)CN(CC3)CCC3(O)c4ccc(Br)cc4	20	8.672	246
c1cccc(c12)occ2CN(CC3)CCC3(O)c4ccc(Br)cc4	21	9.229	246
c1cccc(c12)occ2CN(CC3)CCC3(O)c4ccc(I)cc4	22	9.292	246
c1cccc(c12)occ2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	23	5.750	246
c1cccc(c12)scc2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	24	5.726	246
c1cccc(c12)occ2CN(CC3)CCC34C(=O)N(C)CN4c5ccccc5	25	6.150	246
c1ccccc1N2CN(CCF)C(=O)C23CCN(CC3)Cc4coc(c45)cccc5	26	7.553	246
c1cccc(c12)scc2CN(CC3)CCC34C(=O)N(C)CN4c5ccccc5	27	6.480	246
c1ccccc1N2CN(Cc3cn(nn3)CCF)C(=O)C24CCN(CC4)Cc5coc(c56)cccc6	29	6.096	246
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC3(O)c4ccc(Cl)cc4	2	6.380	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	3	6.364	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC3n4c(=O)[nH]c(c45)cc(Cl)cc5	4	6.801	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC34C(=O)NCN4c5ccccc5	5	5.510	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OC)cccc4	6	5.930	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OCCF)cccc4	7	4.867	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4ccc(cc4)OC	8	6.770	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OC)cc(cc4)OC	9	6.208	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c(cc4)c(OC)cc4C	10	6.424	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OC)cccc4	11	5.580	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OCCF)cccc4	12	4.680	247
C1CC(=O)Nc(c12)cc(cc2)OCCCN3CCN(CC3)c4c(OC)cccc4	13	6.120	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCN3CCN(CC3)c4c(OC)cccc4	14	5.585	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCCN3CCN(CC3)c4c(OC)cccc4	15	5.870	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCCCN3CCN(CC3)c4c(OC)cccc4	16	5.792	247
c1ccccc1CCN(C[C@@H]2CCCO)CCN2Cc3ccccc3	15	7.180	248
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@H]2N(C)C	19a	7.623	249
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@@H]2N(C)C	19b	6.620	249
c1cc(Cl)c(Cl)cc1CC(=O)N[C@@H]2CC[C@@H](CN3C)N(C[C@H]23)Cc4ccccc4	22a	6.883	249
c1cc(Cl)c(Cl)cc1CC(=O)N[C@H]2CC[C@@H](CN3C)N(C[C@H]23)Cc4ccccc4	22b	6.735	249
O[C@@H]1CC[C@@H](CN2C)N(C[C@H]12)Cc3ccccc3	8a(2R)	5.620	250
O[C@H]1CC[C@@H](CN2C)N(C[C@H]12)Cc3ccccc3	8a(2S)	5.304	250
c1ccccc1CCN2C[C@H](CC[C@H]3O)N(C[C@@H]23)Cc4ccccc4	8c(2R)	7.530	250
c1ccccc1CCN2C[C@H](CC[C@@H]3O)N(C[C@@H]23)Cc4ccccc4	8c(2S)	7.478	250
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@H]2OC	12a(2R)	5.870	250
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@H]2OCc4ccccc4	13a(2R)	7.790	250
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CCC2(OC)OC	15a	5.456	250
c1cc(Cl)c(Cl)cc1CC(=O)NCC[C@@H]2C[C@@H](C[C@@H](O2)OC)NCc3ccccc3	22beta	7.081	251
c1cc(Cl)c(Cl)cc1CC(=O)NCC[C@@H]2C[C@@H](NC)C[C@@H](O2)OC	25beta	5.848	251
c1ccccc1CC(=O)NCC[C@@H]2C[C@H](C[C@H](O2)OC)NCc3ccccc3	29alpha	6.602	251
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@@H]3Cc4ccccc4	(1R)-14a	8.420	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@@H]3CCc4ccccc4	(1R)-14b	8.569	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@H]3Cc4c(C)cccc4	(1S)-14c	8.301	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@@H]3Cc4ccc(cc4)OC	(1R)-14d	7.886	252
c1ccccc1[C@H](CO)N(C[C@@H]2C)CCc(c23)cccc3	(1R)-14e	9.161	252
c1ccccc1[C@H](CO)N(C[C@H]2C)CCc(c23)cccc3	(1S)-14e	8.678	252
c1ccccc1C[C@H]2CNCCc(c23)cccc3	(1R)-15a	8.469	252
c1ccccc1C[C@@H]2CNCCc(c23)cccc3	(1S)-15a	7.585	252
c1ccccc1CC[C@H]2CNCCc(c23)cccc3	(1R)-15b	8.276	252
c1cccc(C)c1C[C@H]2CNCCc(c23)cccc3	(1R)-15c	7.854	252
c1cccc(C)c1C[C@@H]2CNCCc(c23)cccc3	(1S)-15c	8.244	252
COc(cc1)ccc1C[C@H]2CNCCc(c23)cccc3	(1R)-15d	8.638	252
COc(cc1)ccc1C[C@@H]2CNCCc(c23)cccc3	(1S)-15d	8.081	252
C[C@H]1CNCCc(c12)cccc2	(1R)-15e	8.000	252
C[C@@H]1CNCCc(c12)cccc2	(1S)-15e	8.046	252
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	1	6.055	253

c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(C2)CCc(c3)c2cc(c34)OCO4	2	7.085	253
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc4c(c3)OCCO4	3	6.471	253
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc4c(c3)OCCCO4	4	5.845	253
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCNCCc2cc(OC)c(cc2)OC	5	6.056	253
c1cccc(c12)[nH]cc2CN3CCN(CC3)c4ccc(F)cc4	1a	5.439	254
c1cccc(c12)[nH]cc2CN3CCN(CC3)c4c(F)ccc(F)c4	1b	6.666	254
c1cccc(c12)[nH]cc2CN3CCN(CC3)c(c4)ccc(Cl)c4Cl	1c	6.900	254
c1cc(F)ccc1N(CC2)CCN2Cc3cn(c(c34)cccc4)CN5CCN(CC5)c6ccc(F)cc6	2a	5.570	254
c1cccc(c12)n(cc2C)CN3CCN(CC3)c4ccc(F)cc4	3a	6.000	254
c1ccccc1CCN2CCN(CC2)Cn(cc3C)c(c34)cccc4	3b	7.848	254
c1cccc(c12)n(cc2)CCCN3CCN(CC3)c4ccc(F)cc4	4a	6.341	254
c1cccc(c12)n(cc2)CCCN3CCN(CC3)c4c(F)cccc4	4b	6.578	254
c1cccc(c12)n(cc2)CCCN3CCN(CC3)c4ccccc4	4c	5.826	254
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.036	255
CCCc(cc1)cc(c12)sc(=O)n2CCN3CCCCCC3	9	9.252	255
CCCCc(cc1)cc(c12)sc(=O)n2CCN3CCCCC3	10	8.432	255
C1CCCCN1CCCn2c(=O)sc(c23)cc(cc3)CCC	11	8.921	255
C1CCCCN1CCCCn2c(=O)sc(c23)cc(cc3)CCC	12	8.538	255
CCCc(cc1)cc(c12)sc(=O)n2CCN(C3)C[C@](C)([C@]34C)CCC4	13	8.854	255
CCCc(cc1)cc(c12)OCC(=O)N2CCN3CCCCC3	16	7.553	255
c1cccc(OC)c1CC(=O)N(C)CCN2CCCC2	4	5.263	256
c1ccc(OC)cc1CC(=O)N(C)CCN2CCCC2	5	5.509	256
COc(cc1)ccc1CC(=O)N(C)CCN2CCCC2	6	5.654	256
c1cccc([N+]([O-])=O)c1CC(=O)N(C)CCN2CCCC2	7	6.133	256
c1ccc([N+]([O-])=O)cc1CC(=O)N(C)CCN2CCCC2	8	5.733	256
c1cc([N+]([O-])=O)ccc1CC(=O)N(C)CCN2CCCC2	9	6.061	256
c1cccc(OC)c1CCN(C)CCN2CCCC2	10	7.804	256
c1ccc(OC)cc1CCN(C)CCN2CCCC2	11	7.623	256
COc(cc1)ccc1CCN(C)CCN2CCCC2	12	7.519	256
c1cccc([N+]([O-])=O)c1CCN(C)CCN2CCCC2	13	8.114	256
c1ccc([N+]([O-])=O)cc1CCN(C)CCN2CCCC2	14	8.194	256
c1cc([N+]([O-])=O)ccc1CCN(C)CCN2CCCC2	15	8.367	256
c1cccc(N)c1CCN(C)CCN2CCCC2	16	6.536	256
c1ccc(N)cc1CCN(C)CCN2CCCC2	17	6.237	256
c1cc(N)ccc1CCN(C)CCN2CCCC2	18	6.559	256
c1cc(Cl)c(Cl)cc1CC(=O)N2CCN(CC2)CCCc3ccccc3	1	7.553	257
c1cccc([N+]([O-])=O)c1CC(=O)N2CCN(CC2)CCCc3ccccc3	2	8.102	257
c1ccc([N+]([O-])=O)cc1CC(=O)N2CCN(CC2)CCCc3ccccc3	3	8.119	257
c1cc([N+]([O-])=O)ccc1CC(=O)N2CCN(CC2)CCCc3ccccc3	4	7.854	257
c1cccc(OC)c1CC(=O)N2CCN(CC2)CCCc3ccccc3	5	7.252	257
c1ccc(OC)cc1CC(=O)N2CCN(CC2)CCCc3ccccc3	6	7.585	257
COc(cc1)ccc1CC(=O)N2CCN(CC2)CCCc3ccccc3	7	7.886	257
c1ccccc1CCCN2CCN(CC2)CCc3cc(Cl)c(Cl)cc3	8	8.658	257
c1ccccc1CCCN2CCN(CC2)CCc3c([N+]([O-])=O)cccc3	9	8.921	257
c1ccccc1CCCN2CCN(CC2)CCc3cc([N+]([O-])=O)ccc3	10	9.143	257
c1ccccc1CCCN2CCN(CC2)CCc3ccc([N+]([O-])=O)cc3	11	8.585	257
c1ccccc1CCCN2CCN(CC2)CCc3c(N)cccc3	12	8.319	257
c1ccccc1CCCN2CCN(CC2)CCc3cc(N)ccc3	13	8.699	257
c1ccccc1CCCN2CCN(CC2)CCc3ccc(N)cc3	14	8.387	257
c1ccccc1CCCN2CCN(CC2)CCc3c(OC)cccc3	15	8.409	257
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)ccc3	16	8.854	257
c1ccccc1CCCN2CCN(CC2)CCc3ccc(cc3)OC	17	8.886	257
c1cccc(OC)c1CC(=O)N2CCN(CC2)C(=O)Cc3c(OC)cccc3	18	5.834	257
c1cccc(OC)c1CCN2CCN(CC2)CCc3c(OC)cccc3	21	6.839	257
c1ccc(OC)cc1CCN2CCN(CC2)CCc3cc(OC)ccc3	22	8.276	257
COc(cc1)ccc1CCN2CCN(CC2)CCc3ccc(cc3)OC	23	8.086	257
CC(C)(C)OC(=O)NCCC(=O)N1CCN(CC1)CCCc2ccccc2	25	7.066	257
CC(C)(C)OC(=O)NCCCC(=O)N1CCN(CC1)CCCc2ccccc2	26	9.495	257
NCC(=O)N1CCN(CC1)CCCc2ccccc2	27	8.387	257
NCCC(=O)N1CCN(CC1)CCCc2ccccc2	28	6.830	257
NCCCC(=O)N1CCN(CC1)CCCc2ccccc2	29	6.695	257
c1ccccc1CCCN2CCN(CC2)CCN	30	8.585	257
c1ccccc1CCCN2CCN(CC2)CCCN	31	6.742	257
NCCCCN1CCN(CC1)CCCc2ccccc2	32	6.752	257
c1cc(Cl)c(Cl)cc1CCN2CCCC2	4	7.542	258
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)CCN2CCCC2	5	7.860	258
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)CCN(C)CCN2CCCC2	6	6.959	258
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)CCN(C)CCN(C)CCN2CCCC2	7	6.644	258

C1CCCN1CCCN(C)CCN(C)Cc2cc(Cl)c(Cl)cc2	8	7.524	258
c1cc(Cl)c(Cl)cc1CN(C)CCCN(C)CCN2CCCC2	9	8.097	258
C1CCCN1CCN(C)CCN(C)Cc2cc(Cl)c(Cl)cc2	10	8.827	258
c1cc(Cl)c(Cl)cc1CCN(C)CCCN(C)CCCN2CCCC2	11	7.111	258
C1CCCN1CCCCN(C)CCCN(C)CCc2cc(Cl)c(Cl)cc2	12	6.893	258
c1cc(Cl)c(Cl)cc1CCN(C)CCCCN(C)CCCCN2CCCC2	13	5.950	258
c1cc(Cl)c(Cl)cc1CCN(CCN)CCN2CCCC2	14	7.390	258
NCCNCCc1cc(Cl)c(Cl)cc1	15	6.409	258
c1cc(Cl)c(Cl)cc1CCNCCNCCN	16	6.614	258
c1cc(Cl)c(Cl)cc1CCNCCNCCN2CCCC2	17	7.268	258

Table F.2: Sigma 2: DTG/DXL rat liver dataset

SMILES	Name	pK_i	Ref.
c1cc(I)ccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-8	7.279	159
c1ccc(I)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-9	7.620	159
c1ccccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(OC)ccc4	(+)-10	7.284	159
COc(cc1)ccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-4	7.666	159
c1ccc(OC)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-6	7.418	159
c1ccc(Cl)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-7	7.650	159
c1cc(Cl)ccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	(+)-5	8.194	159
COc(cc1)ccc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-4	7.090	159
c1cc(Cl)ccc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-5	7.577	159
c1ccc(OC)cc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-6	7.334	159
c1ccc(Cl)cc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	(-)-7	6.910	159
C1CN(C)[C@H](C2)CC(=O)C[C@@]12c3cc(O)ccc3	(-)-1	4.602	159
c1ccccc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	CB-64L	6.812	161
c1cc(Cl)c(Cl)cc1/C=C([C@H](C2)N(C)CC3)/C(=O)C[C@@]23c4cc(O)ccc4	CB-182	7.450	161
c1ccccc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	CB-64D	7.783	161
c1cc(Cl)c(Cl)cc1/C=C([C@@H](C2)N(C)CC3)/C(=O)C[C@]23c4cc(O)ccc4	CB-184	7.873	161
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	Ibogaine	6.697	162
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4ccc(c5)O	O-des-methyl-Ibogaine	5.282	162
C1CNC(C)=C(C1=c23)N=c2cc(cc3)OC	Harmaline	4.703	162
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4cc(cc5)OC	Tabernanthine	6.712	162
CC(C)(C)Oc(c1)ccc2[nH]c(c3c12)[C@H]4[C@H]5N(CC3)C[C@@H](C4)C[C@@H]5CC	10-t-butoxy-ibogamine	6.607	163
c1ccccc1C(=O)O[C@H]([C@@H]2C(=O)OC)C[C@@H](N3C)CC[C@H]23	cocaine	5.054	59
CCCN(C1)CCC[C@H]1c2cc(O)ccc2	S(-)-3-PPP	6.631	59
c1ccccc1C2(CCCC2)C(=O)OCCOCCN(CC)CC	carbetapentane	7.710	59
CCN(CC)CCOC(=O)C1(CCCC1)c2ccccc2	caramiphen	7.810	59
c1ccccc1CCCN2[C@@H](C)CN(C[C@H]2C)CCCN(c3ccc(F)cc3)c4ccc(F)cc4	11	7.730	59
c1cc(F)ccc1N(c2ccc(F)cc2)CCCN(C[C@H]3C)C[C@@H](C)N3CCc4cc(Cl)c(Cl)cc4	12	5.932	59
c1ccccc1N(c2ccccc2)CCCN(C[C@H]3C)C[C@H](C)N3CCc4cc(Cl)c(Cl)cc4	13	6.666	59
C1CNCCN1CCCN(c2ccc(F)cc2)c3ccc(F)cc3	15	6.415	59
c1cc(F)ccc1N(c2ccc(F)cc2)CCCN3CCN(CC3)Cc4ccccc4	17	7.107	59
c1ccccc1C2(CCCCC2)C(=O)OCCN3CCOCC3	PRE084	7.333	59
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-1d	6.827	165
c1ccccc1CN2CC[C@@H]3[C@@H](C)[C@H]2Cc(c34)cccc4	(-)-2a	6.883	165
c1ccccc1CN2CC[C@H]3[C@H](C)[C@@H]2Cc(c34)cccc4	(+)-2a	6.231	165
c1ccccc(c12)C[C@@H]3[C@H](CC)[C@H]2CCN3Cc4ccccc4	(-)-2b	6.939	165
c1ccccc(c12)C[C@H]3[C@@H](CC)[C@@H]2CCN3Cc4ccccc4	(+)-2b	6.321	165
c1ccccc(c12)C[C@@H]3[C@H](C(C)C)[C@H]2CCN3Cc4ccccc4	(-)-2c	6.876	165
c1ccccc(c12)C[C@H]3[C@@H](C(C)C)[C@@H]2CCN3Cc4ccccc4	(+)-2c	6.025	165
c1ccccc(c12)[C@H]([C@H](C)C=C2)CCNCc3ccccc3	(+)-10a	6.217	165
c1ccccc(c12)[C@@H]([C@@H](C)C=C2)CCNCc3ccccc3	(-)-10a	6.431	165
c1ccccc(c12)[C@H]([C@H](CC)C=C2)CCNCc3ccccc3	(+)-10b	6.120	165
c1ccccc(c12)[C@@H]([C@@H](CC)C=C2)CCNCc3ccccc3	(-)-10b	6.071	165
c1ccccc(c12)[C@H]([C@H](C(C)C)C=C2)CCNCc3ccccc3	(+)-10c	6.069	165
c1ccccc(c12)[C@@H]([C@@H](C(C)C)C=C2)CCNCc3ccccc3	(-)-10c	6.105	165
CC(=O)Nc(c1)ccc(c1[C@]23C)C[C@@H]([C@H]2C)N(CC3)Cc4ccccc4	(+)-3a	5.851	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(F)c4	(+)-3e	6.578	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)N(C)C	(+)-3c	6.588	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(Br)c4	(+)-3g	6.300	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)N	(+)-3b	6.080	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(Cl)c4	(+)-3f	6.368	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	(+)-1f	5.767	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)NS(=O)(=O)C	(+)-3d	5.721	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cccc4	(+)-2d	6.312	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(I)c4	(+)-3h	5.691	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(F)c4	(-)-3e	7.367	26
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)cccc3	(-)-2b	6.530	26
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(F)c3	(-)-4a	7.286	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-1f	6.717	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(Cl)c4	(-)-3f	6.419	26
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)cccc4	(-)-2d	6.638	26
CC(C)CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(F)c3	(-)-4b	7.249	26
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(F)c3	(+)-4a	6.812	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)CC(=C4[C@@]23C)CCC(=O)C4	(+)-10	6.161	26
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(Br)c(c4Br)O	(+)-2a	5.697	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4Br)O	(+)-3a	6.461	171

c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(Br)c(c4)O	(+)-4a	5.914	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(I)c(c4)O	(+)-5a	6.224	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)cc(Cl)c(c4Cl)O	(+)-6a	5.664	171
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4Cl)O	(+)-7a	6.117	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cc(Br)c(c3Br)O	(+)-2b	6.676	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3Br)O	(+)-3b	6.548	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cc(Br)c(c3)O	(+)-4b	6.438	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)cc(I)c(c3)O	(+)-5b	6.652	171
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)cc(Br)c(c3)O	(-)-4b	7.138	171
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)cc(I)c(c3)O	(-)-5b	7.027	171
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3Cl)O	(+)-7b	5.305	171
c1cc(I)ccc1C(=O)NC2CCN(CC2)Cc3ccc(F)cc3	2a	8.424	174
c1cc(I)ccc1C(=O)NC2CCN(CC2)Cc3c(F)cccc3	2b	7.693	174
c1cc(Br)ccc1C(=O)NC2CCN(CC2)Cc3ccc(F)cc3	2c	8.396	174
c1cc(Br)ccc1C(=O)NC2CCN(CC2)Cc3c(F)cccc3	2d	7.642	174
c1c(Br)c(N)c(I)c(OC)c1C(=O)NCCN(CC)CC	2	5.629	176
COc(cc1)c(I)cc1C(=O)NCCN(CC)CC	IMBA	5.186	176
CC(=O)Nc(c(I)c1)cc(OC)c1C(=O)NCCN(CC)CC	6	3.939	176
c1c(I)c(N)cc(OC)c1C(=O)NCCN(CC)CC	7	4.670	176
CC(=O)Nc(cc1)c(I)cc1C(=O)NCCN(CC)CC	9	3.830	176
CCN(CC)CCNC(=O)c1c(I)ccc(c1)OC	12	6.460	176
c1c(I)ccc(OC)c1C(=O)NCCN(CC)CC	15	5.991	176
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.333	176
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.453	259
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.616	259
c1ccccc1CN2CCN(CC2)Cc3ccccc3	3	5.895	179
c1ccc(OC)cc1CN2CCN(CC2)Cc3ccccc3	4	6.967	179
COc(cc1)ccc1CN2CCN(CC2)Cc3ccccc3	5	6.793	179
c1cccc(Cl)c1CN2CCN(CC2)Cc3ccccc3	6	6.278	179
c1ccc(Cl)cc1CN2CCN(CC2)Cc3ccccc3	7	7.249	179
c1cc(Cl)ccc1CN2CCN(CC2)Cc3ccccc3	8	6.728	179
c1cc(Cl)c(Cl)cc1CN2CCN(CC2)Cc3ccccc3	9	8.123	179
c1cc(Cl)cc(Cl)c1CN2CCN(CC2)Cc3ccccc3	10	6.910	179
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	5.812	183
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.893	183
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.921	183
c1cc(Cl)c(Cl)cc1CCN(C)CCN2CCCC2	1	8.092	183
c1ccc(I)cc1CCN(C)CCN2CCCC2	2	8.041	183
c1cc(I)ccc1CCN(C)CCN2CCCC2	3	7.366	183
C1CCCN1CCN(C)Cc2c(I)cccc2	4	7.317	183
C1CCCN1CCN(C)Cc2cc(I)ccc2	5	7.472	183
C1CCCN1CCN(C)Cc2ccc(I)cc2	6	7.611	183
c1ccc(Br)cc1CCN(C)CCN2CCCC2	9	7.223	183
c1cc(Br)ccc1CCN(C)CCN2CCCC2	10	7.488	183
C1CCCN1CCN(C)Cc2cc(Br)ccc2	11	6.658	183
c1ccc(F)cc1CCN(C)CCN2CCCC2	12	6.985	183
c1cc(F)ccc1CCN(C)CCN2CCCC2	13	6.907	183
c1ccc(Cl)cc1CCN(C)CCN2CCCC2	14	7.548	183
c1cc(Cl)ccc1CCN(C)CCN2CCCC2	15	7.297	183
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-3-PPP	6.860	260
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-l-pentazocine	7.438	260
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN4CCN(CC4)CCO	Fluphenazine	7.577	260
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-SKF10047	5.575	260
C1CC1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	(+)-Cyclazocine	4.982	260
C1CC1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	(-)-Cyclazocine	5.920	260
c1ccccc1CCCN2[C@@H](C)CN(C[C@H]2C)CCCN(c3ccccc3)c4ccccc4	25	6.738	191
c1cc(F)ccc1C(c2ccc(F)cc2)OCCN(CC3)CCN3CCCc4ccccc4	3	6.936	191
c1ccccc1CCCN2[C@@H](C)CN(C[C@H]2C)CCCn(c3cccc4)c(c5c34)cccc5	11	6.839	191
C[C@@H]1CN(C[C@H](C)N1)CCCN(c2ccccc2)c3ccccc3	24	6.455	191
CN1[C@@H](C)CN(C[C@H]1C)CCCn(c2cccc3)c(c4c23)cccc4	10	6.638	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2ccc(c3)[N+]([O-])=O)c(c4c23)cccc4	7	6.714	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2cccc3)c(c4c23)cccc4	1	6.520	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2ccc(Br)c3)c(c4c23)ccc(Br)c4	5	6.171	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2ccc(c3)N)c(c4c23)cccc4	8	5.780	191
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2c(Br)cc(Br)c3)c(c4c23)ccc(Br)c4	6	5.701	191
c1cc(I)ccc1C(=O)NCCN(CC)CC	IDAB	5.690	193
c1cc(I)ccc1C(=O)NCCN2CCCCC2	IPAB	6.688	193
c1cc(Br)ccc1CCN(C)CCN2CCCCC2	BrPEMP	8.072	195

c1cc(I)ccc1CCN(C)CCN2CCCCC2	IPEMP	7.818	195
CCN(CC)CCNS(=O)(=O)c1ccc(Br)cc1	1	5.549	196
CCN(CC)CCNS(=O)(=O)c1ccc(I)cc1	2	5.621	196
C1CCCN1CCNS(=O)(=O)c2ccc(Br)cc2	3	5.828	196
C1CCCN1CCNS(=O)(=O)c2ccc(I)cc2	4	5.999	196
C1CCCCN1CCNS(=O)(=O)c2ccc(Br)cc2	5	6.338	196
C1CCCCN1CCNS(=O)(=O)c2ccc(I)cc2	6	6.686	196
C1CCCCCN1CCNS(=O)(=O)c2ccc(Br)cc2	7	6.703	196
C1CCCCCN1CCNS(=O)(=O)c2ccc(I)cc2	8	6.724	196
C1CCCCCN1CCN(C)S(=O)(=O)c2ccc(Br)cc2	9	7.353	196
C1CCCCCN1CCN(C)S(=O)(=O)c2ccc(I)cc2	10	7.629	196
C1CCCCN1CCNS(=O)(=O)c(cc2)cc(I)c2OC	11	6.348	196
C1CCCCCN1CCN(C)S(=O)(=O)c(cc2)cc(I)c2OC	12	6.472	196
COc(cc1)c(I)cc1C(=O)NCCN2CCCCC2	PIMBA	6.686	197
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-pentazocine	5.866	198
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.213	198
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)-3-PPP	6.921	198
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	7.098	198
c1ccccc1C(\CC)=C(c2ccccc2)/c3ccc(cc3)OCCN(C)C	Tamoxifen	6.870	198
C1CCCN1CCOc(cc2)ccc2Cc3ccccc3	PBPE	6.917	198
c1ccccc1C(C)(C)c2ccc(cc2)OCCN3CCCC3	PCPE	6.921	198
c1ccccc1Cc2ccc(cc2)OCCN3CCOCC3	MBPE	5.732	198
c1ccccc1C(C)(C)c2ccc(cc2)OCCN3CCOCC3	MCPE	5.871	198
CCCSc(nsn1)c1C2=CCCNC2	P-TZTP	6.398	199
c1cc(F)ccc1-n(c(c23)cccc3)cc2CCCCN4CCN(CC4)c5ccc(I)cc5	Indole-I	6.790	261
O1COc(c12)ccc(c2)CN3CCN(CC3)Cc4ccc(I)cc4	BP-I	7.214	262
O1COc(c12)ccc(c2)CN3CCN(CC3)Cc4ccc(F)cc4	BP-F	7.282	262
O1COc(c12)ccc(c2)CN3CCN(CC3)Cc4ccc(C)cc4	BP-CH3	7.303	262
O1COc(c12)ccc(c2)CN3CCN(CC3)Cc4ccc([N+]([O-])=O)cc4	BP-NO2	7.393	262
O1COc(c12)ccc(c2)CN3CCN(CC3)Cc4ccc(Br)cc4	BP-Br	7.393	262
c1ccccc1CCN2CCCCC2	9	6.951	263
C1CCCCN1CCCc2ccccc2	10	7.602	263
c1ccccc1CCN(CC2)CCC2C	13	7.478	263
CC1CCN(CC1)CCCc2ccccc2	14	7.917	263
c1ccccc1CCN(CC2)Cc(c23)cccc3	15	7.242	263
c1ccccc1CCCN(CC2)Cc(c23)cccc3	16	7.848	263
c1ccccc1CCN2CCN(CC2)c3ccccn3	17	6.924	263
c1ccccc1CCCN2CCN(CC2)c3ccccn3	18	8.309	263
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)C	BD1047	7.328	211
c1cc(Cl)c(Cl)cc1CCN2CCN(C)CC2	BD1063	6.348	211
c1cc(Cl)c(Cl)cc1CCN(C2)CCN([C@H]23)CCC3	BD1018	7.310	213
c1cc(Cl)c(Cl)cc1CCN(C2)CCN([C@@H]23)CCC3	BD1031	7.097	213
c1cc(Cl)c(Cl)cc1CCN[C@H]2[C@H](CCCC2)N3CCCC3	LR132	6.154	213
c1cc(Cl)c(Cl)cc1CCNCCN2CCCC2	BD1060	8.523	214
C1CCCN1CCN(CC=C)CCc2cc(Cl)c(Cl)cc2	BD1052	8.699	214
c1cc(Cl)c(Cl)cc1CCN(CC)CCN2CCCC2	BD1067	8.699	214
c1cccc(OC)c1CCN(CC)CCN2CCCCC2	UMB98	6.148	215
c1ccc(OC)cc1CCN(CC)CCN2CCCCC2	UMB99	5.994	215
COc(cc1)ccc1CCN(CC)CCN2CCCCC2	UMB100	6.020	215
c1cccc(OC)c1CCN(C)CCN2CCCCC2	UMB101	6.412	215
c1ccc(OC)cc1CCN(C)CCN2CCCCC2	UMB102	6.421	215
COc(cc1)ccc1CCN(C)CCN2CCCCC2	UMB103	6.376	215
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccccc3	1a	6.590	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc(cc3)OC	1b	6.569	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc(O)cc3	1c	6.293	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc(F)cc3	1d	6.827	216
c1ccc(O)cc1C2(C(=O)CC)CCN(CC2)Cc3ccc([N+]([O-])=O)cc3	1e	6.421	216
c1ccccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2a	6.661	216
COc(cc1)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2b	5.992	216
c1cc(O)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2c	5.655	216
c1cc(F)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2d	6.152	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@@H]([C@@H]3C)Cc(c4[C@]23C)ccc(c4)O	2e	5.966	216
c1ccccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3a	5.771	216
COc(cc1)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3b	6.348	216
c1cc(O)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3c	5.798	216
c1cc(F)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3d	5.878	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	3e	6.101	216
c1ccccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4a	6.018	216

COc(cc1)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4b	6.004	216
c1cc(O)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4c	5.567	216
c1cc(F)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4d	6.310	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@@H]([C@@H]3CCCC4)Cc(c5[C@]234)ccc(c5)O	4e	5.928	216
c1ccccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5a	5.742	216
COc(cc1)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5b	5.821	216
c1cc(O)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5c	5.835	216
c1cc(F)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5d	5.876	216
c1cc([N+]([O-])=O)ccc1CN(CC2)[C@H]([C@H]3CCCC4)Cc(c5[C@@]234)ccc(c5)O	5e	5.661	216
N#CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	2	4.721	217
N#CCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	3	4.292	217
N#CCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	4	5.076	217
N#CCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	5	5.553	217
N#CCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	6	6.420	217
N#CCCCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	7	6.824	217
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	8	5.495	217
C=CCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	9	6.208	217
C=CCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	10	6.745	217
C=CCCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	11	7.097	217
CC#CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	12	5.357	217
C#CCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	13	5.658	217
C#CCCCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	14	6.357	217
N#CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	16	4.032	217
N#CCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	18	4.469	217
N#CCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	19	4.886	217
N#CCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	20	5.244	217
N#CCCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	21	5.721	217
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	22	4.569	217
C=CCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	23	5.119	217
C=CCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	24	5.602	217
C=CCCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	25	6.119	217
CC#CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	26	4.921	217
C#CCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	27	4.824	217
C#CCCCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	28	5.456	217
c1cc(Cl)c(Cl)cc1CCN(C)CCN2CCCCCC2	LR172	8.699	218
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-Pentazocine	5.713	264
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.538	264
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-pentazocine	7.886	264
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	7.420	264
C=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-SKF10047	5.364	264
c1cccc(OC)c1CC(=O)N(C)CCN2CCCC2	4	5.499	256
c1ccc(OC)cc1CC(=O)N(C)CCN2CCCC2	5	5.955	256
COc(cc1)ccc1CC(=O)N(C)CCN2CCCC2	6	5.914	256
c1cccc([N+]([O-])=O)c1CC(=O)N(C)CCN2CCCC2	7	5.827	256
c1ccc([N+]([O-])=O)cc1CC(=O)N(C)CCN2CCCC2	8	6.268	256
c1cc([N+]([O-])=O)ccc1CC(=O)N(C)CCN2CCCC2	9	6.225	256
c1cccc(OC)c1CCN(C)CCN2CCCC2	10	6.842	256
c1ccc(OC)cc1CCN(C)CCN2CCCC2	11	6.680	256
COc(cc1)ccc1CCN(C)CCN2CCCC2	12	6.592	256
c1cccc([N+]([O-])=O)c1CCN(C)CCN2CCCC2	13	6.507	256
c1ccc([N+]([O-])=O)cc1CCN(C)CCN2CCCC2	14	7.021	256
c1cc([N+]([O-])=O)ccc1CCN(C)CCN2CCCC2	15	7.203	256
c1cccc(N)c1CCN(C)CCN2CCCC2	16	6.194	256
c1ccc(N)cc1CCN(C)CCN2CCCC2	17	5.650	256
c1cc(N)ccc1CCN(C)CCN2CCCC2	18	6.011	256
c1cc(Cl)c(Cl)cc1CC(=O)N2CCN(CC2)CCCc3ccccc3	1	7.108	257
c1cccc([N+]([O-])=O)c1CC(=O)N2CCN(CC2)CCCc3ccccc3	2	7.119	257
c1ccc([N+]([O-])=O)cc1CC(=O)N2CCN(CC2)CCCc3ccccc3	3	7.187	257
c1cc([N+]([O-])=O)ccc1CC(=O)N2CCN(CC2)CCCc3ccccc3	4	6.777	257
c1cccc(OC)c1CC(=O)N2CCN(CC2)CCCc3ccccc3	5	6.532	257
c1ccc(OC)cc1CC(=O)N2CCN(CC2)CCCc3ccccc3	6	6.686	257
COc(cc1)ccc1CC(=O)N2CCN(CC2)CCCc3ccccc3	7	6.333	257
c1ccccc1CCCN2CCN(CC2)CCc3cc(Cl)c(Cl)cc3	8	7.411	257
c1ccccc1CCCN2CCN(CC2)CCc3c([N+]([O-])=O)cccc3	9	8.310	257
c1ccccc1CCCN2CCN(CC2)CCc3cc([N+]([O-])=O)ccc3	10	8.027	257
c1ccccc1CCCN2CCN(CC2)CCc3ccc([N+]([O-])=O)cc3	11	7.602	257
c1ccccc1CCCN2CCN(CC2)CCc3c(N)cccc3	12	7.745	257
c1ccccc1CCCN2CCN(CC2)CCc3cc(N)ccc3	13	7.432	257

c1ccccc1CCCN2CCN(CC2)CCc3ccc(N)cc3	14	7.854	257
c1ccccc1CCCN2CCN(CC2)CCc3c(OC)cccc3	15	8.125	257
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)ccc3	16	7.991	257
c1ccccc1CCCN2CCN(CC2)CCc3ccc(cc3)OC	17	7.544	257
c1ccc(OC)cc1CC(=O)N2CCN(CC2)C(=O)Cc3cc(OC)ccc3	19	7.928	257
COc(cc1)ccc1CC(=O)N2CCN(CC2)C(=O)Cc3ccc(cc3)OC	20	6.128	257
c1cccc(OC)c1CCN2CCN(CC2)CCc3c(OC)cccc3	21	7.770	257
c1ccc(OC)cc1CCN2CCN(CC2)CCc3cc(OC)ccc3	22	7.538	257
COc(cc1)ccc1CCN2CCN(CC2)CCc3ccc(cc3)OC	23	7.004	257
CC(C)(C)OC(=O)NCC(=O)N1CCN(CC1)CCCc2ccccc2	24	6.757	257
CC(C)(C)OC(=O)NCCC(=O)N1CCN(CC1)CCCc2ccccc2	25	5.341	257
CC(C)(C)OC(=O)NCCCC(=O)N1CCN(CC1)CCCc2ccccc2	26	6.900	257
NCC(=O)N1CCN(CC1)CCCc2ccccc2	27	6.519	257
NCCC(=O)N1CCN(CC1)CCCc2ccccc2	28	5.749	257
NCCCC(=O)N1CCN(CC1)CCCc2ccccc2	29	5.416	257
c1ccccc1CCCN2CCN(CC2)CCN	30	6.726	257
c1ccccc1CCCN2CCN(CC2)CCCN	31	5.699	257
NCCCCN1CCN(CC1)CCCc2ccccc2	32	6.000	257
c1cc(Cl)c(Cl)cc1CCN2CCCC2	4	7.111	258
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)CCN2CCCC2	5	7.842	258
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)CCN(C)CCN2CCCC2	6	7.271	258
c1cc(Cl)c(Cl)cc1CCN(C)CCN(C)CCN(C)CCN(C)CCN2CCCC2	7	6.790	258
C1CCCN1CCCN(C)CCN(C)Cc2cc(Cl)c(Cl)cc2	8	7.738	258
c1cc(Cl)c(Cl)cc1CN(C)CCCN(C)CCN2CCCC2	9	7.279	258
C1CCCN1CCN(C)CCN(C)Cc2cc(Cl)c(Cl)cc2	10	7.917	258
c1cc(Cl)c(Cl)cc1CCN(C)CCCN(C)CCCN2CCCC2	11	7.827	258
C1CCCN1CCCCN(C)CCCN(C)CCc2cc(Cl)c(Cl)cc2	12	6.818	258
c1cc(Cl)c(Cl)cc1CCN(C)CCCCN(C)CCCCN2CCCC2	13	6.939	258
c1cc(Cl)c(Cl)cc1CCN(CCN)CCN2CCCC2	14	6.870	258
NCCNCCc1cc(Cl)c(Cl)cc1	15	5.626	258
c1cc(Cl)c(Cl)cc1CCNCCNCCN	16	6.270	258
c1cc(Cl)c(Cl)cc1CCNCCNCCN2CCCC2	17	6.955	258

Table F.3: Sigma 2: DTG/PTZ rat brain dataset

SMILES	Name	pK_i	Ref.
FC(F)(F)Oc(cc1)ccc1CCN(C)CCN2CCCC2	9	7.444	265
FC(F)(F)Oc(cc1)ccc1CCN(CC)CCN2CCCC2	10	7.495	265
FC(F)(F)Oc(cc1)ccc1CCN(C)CCN2CCCCC2	11	7.602	265
FC(F)(F)Oc(cc1)ccc1CCN(CC)CCN2CCCCC2	12	7.585	265
c1cccc(OC(F)(F)F)c1CCN(C)CCN2CCCC2	18	7.367	265
c1cccc(OC(F)(F)F)c1CCN(CC)CCN2CCCC2	19	7.086	265
c1cccc(OC(F)(F)F)c1CCN(C)CCN2CCCCC2	20	7.237	265
c1cccc(OC(F)(F)F)c1CCN(CC)CCN2CCCCC2	21	7.260	265
c1ccc(OC(F)(F)F)cc1CCN(C)CCN2CCCC2	27	7.398	265
c1ccc(OC(F)(F)F)cc1CCN(CC)CCN2CCCC2	28	7.367	265
c1ccc(OC(F)(F)F)cc1CCN(C)CCN2CCCCC2	29	7.509	265
c1ccc(OC(F)(F)F)cc1CCN(CC)CCN2CCCCC2	30	7.824	265
c1cc(F)ccc1CC[C@H]2CCCN([C@@H]23)CCCC3	10beta-b	5.887	130
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.055	130
c1cc(Cl)ccc1CSC[C@@H]2CCCN([C@@H]23)CCCC3	8	6.730	131
c1ccccc1CCSC[C@@H]2CCCN([C@@H]23)CCCC3	9	6.808	131
c1cc(F)ccc1CCSC[C@@H]2CCCN([C@@H]23)CCCC3	10	6.833	131
c1cc(Cl)ccc1CSC[C@H]2CCCN([C@@H]23)CCCC3	17	6.632	131
c1ccccc1CCSC[C@H]2CCCN([C@@H]23)CCCC3	18	6.859	131
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.104	131
COCCN1CCN(CC1)C[C@H](C2=O)CCN2c3ccc(Cl)cc3	MS-377	5.161	132
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	6.569	132
C1CCCn(c12)c(=O)c(c(n2)C)CCN(CC3)CCC3c4noc(c45)cc(F)cc5	Risperidone	5.276	132
c1ccccc1CN(C)CCCN(C2=O)CN([C@H]23)Cc4c(C3)cccc4	1	6.254	266
c1ccccc1CN(C)CCCN(C2=O)CN([C@@H]23)Cc4c(C3)cccc4	2	6.085	266
C[C@@]12C(C)(C)[C@@H](CC1)CN(C2)C3CCCCC3	3	8.959	267
C1CCCCC1CN(C2)C[C@H](CC3)C(C)(C)[C@@]23C	4	8.503	267
C1CCCCC1CN(C2)C[C@@H](CC3)C(C)(C)[C@]23C	5	8.451	267
C1CCCCC1CCN(C2)C[C@H](CC3)C(C)(C)[C@@]23C	6	9.553	267
C1CCCCC1CCN(C2)C[C@@H](CC3)C(C)(C)[C@]23C	7	9.638	267
C1CCCCC1CCCN(C2)C[C@H](CC3)C(C)(C)[C@@]23C	8	9.252	267
C1CCCCC1CCCCN(C2)C[C@H](CC3)C(C)(C)[C@@]23C	9	8.168	267
C1CCCC1CCN(C2)C[C@H](CC3)C(C)(C)[C@@]23C	10	9.155	267
C1CCCCCC1CCN(C2)C[C@H](CC3)C(C)(C)[C@@]23C	11	9.602	267
C[C@@]12C(C)(C)[C@@H](CC1)CN(C2)CCC3CCCCCCC3	12	9.481	267
C1[C@@H](C2)C[C@H](C3)C[C@@H]2[C@H]([C@@H]13)CCN(C4)C[C@H](CC5)C(C)(C)[C@@]45C	13	9.114	267
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.775	267
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.157	267
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-SKF10047	4.848	267
c1ccccc1CC[C@H]2CCCN([C@@H]23)CCCC3	ANS-1	6.127	148
c1ccccc1CC[C@@H]2CCCN([C@@H]23)CCCC3	ANS-2	6.523	148
c1cc(F)ccc1CC[C@@H]2CCCN([C@@H]23)CCCC3	ANS-3	6.658	148
Fc1ccc(cc1)SC[C@H]2CCCN([C@@H]23)CCCC3	ANS-4	6.365	148
Fc1ccc(cc1)SC[C@@H]2CCCN([C@@H]23)CCCC3	ANS-5	6.461	148
c1ccccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	FN/C-1	6.194	148
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.041	148
c1cc(Cl)c(Cl)cc1CCN2CCN(C)CC2	BD1063	6.357	10
COc(cc1)ccc1CCN(CC)CCN2CCCC2	UMB115	5.521	268
c1ccc(OC)cc1CCN(CC)CCN2CCCC2	UMB116	6.712	268
c1cccc(OC)c1CCN(CC)CCN2CCCC2	UMB117	6.883	268
C1CN(C)C[C@@H]2CCC[C@@H]3Oc(c4[C@]123)c(OC)ccc4	(-)-3a	5.126	269
C1CC1CN(CC2)C[C@@H]3CCC[C@@H]4Oc(c5[C@]234)c(OC)ccc5	(-)-3b	5.485	269
c1ccccc1CCN(CC2)C[C@@H]3CCC[C@@H]4Oc(c5[C@]234)c(OC)ccc5	(-)-3c	5.485	269
C1CC1CN(CC2)C[C@H]3CCC[C@H]4Oc(c5[C@@]234)c(OC)ccc5	(+)-3b	5.360	269
c1ccccc1CCN(CC2)C[C@H]3CCC[C@H]4Oc(c5[C@@]234)c(OC)ccc5	(+)-3c	5.593	269
c1ccccc1CCN(CC2)C[C@@H]3CCC[C@@H]4Oc(c5[C@]234)c(O)ccc5	(-)-1c	5.269	269
C1CC1CN(CC2)C[C@H]3CCC[C@H]4Oc(c5[C@@]234)c(O)ccc5	(+)-1b	5.987	269
c1ccccc1CCN(CC2)C[C@H]3CCC[C@H]4Oc(c5[C@@]234)c(O)ccc5	(+)-1c	6.580	269
CC(C)=CCN(CC1)[C@@H]([C@@H]2C)Cc(c3[C@]12C)ccc(c3)O	(-)-pentazocine	7.252	269
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-pentazocine	5.866	269
COc1ccc(Br)c(OC)c1C(=O)NC[C@@H]2CCCN2CC	Remoxipride	6.496	6
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)C\2=C\CCN4CCN(CC4)CCO	Cis-(z)-flupenthixol	6.572	6
C[C@@H]1CN(C[C@H](C)N1)CCCn(c2cccc3)c(c4c23)cccc4	Rimcazole	5.935	6
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c(cc3C(F)(F)F)ccc3	Trifluperidol	6.917	6
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN4CCN(CC4)CCO	Fluphenazine	6.682	6

FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN4CCN(C)CC4	Trifluoperazine	6.241	6
CN(C)CCCN1c(cccc2)c2Sc(c13)ccc(Cl)c3	Chlorpromazine	5.788	6
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN(C)C	Trifluopromazine	5.727	6
C1CCCn(c12)c(=O)c(c(n2)C)CCN(CC3)CCC3c4noc(c45)cc(F)cc5	Risperidone	5.766	6
c1cc(F)ccc1C(c2ccc(F)cc2)CCCN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	Pimozide	5.485	6
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	7.268	6
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.367	6
c1ccccc1C(=O)O[C@H]([C@@H]2C(=O)OC)C[C@@H](N3C)CC[C@H]23	cocaine	4.888	270
C1CCCN1C[C@@H](C)N(C)CCc2cc(Cl)c(Cl)cc2	LR176	7.357	270
S=C=NCCN1[C@@H](C)CN(C[C@H]1C)CCCn(c2cccc3)c(c4c23)cccc4	SH1/57	5.522	270
C[C@@H]1CN(C[C@H](C)N1)CCCN(c2ccccc2)c3ccccc3	SH2/21	6.057	270
c1ccccc1CCCN2[C@@H](C)CN(C[C@H]2C)CCCN(c3ccccc3)c4ccccc4	SH3/24	6.793	270
c1ccccc1CCN2CCN(CC2)c3ccccn3	UMB24	6.770	271
c1cccc(c12)n(cc2)CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	CM360	9.678	272
c1cc(F)ccc1-c2cn(c(c23)cccc3)CCCCN(CC4)Cc(c45)cc(OC)c(c5)OC	CM361	8.360	272
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN(CC3)CC=C3c4ccc(F)cc4	CM401	9.180	272
c1cccc(c12)oc(=O)n2CCCCN(CC3)CC=C3c4ccc(F)cc4	CM406	9.244	272
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(cc4)OC	CM407	7.460	272
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4c(F)cccc4	CM408	8.399	272
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(cc4)OC	CM433	7.551	272
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4cc(OC)ccc4	CM442	7.722	272
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c(c4Cl)cccc4Cl	CM449	7.622	272
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c(c4Cl)cccc4Cl	CM450	7.689	272
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c(c4Cl)cccc4Cl	CM452	6.388	272
c1cccc(c12)oc(=S)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM454	8.879	272
c1cc([N+]([O-])=O)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM458	8.876	272
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4c(Br)cc(F)cc4	CM461	8.996	272
COc(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM464	8.708	272
COc(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM465	8.152	272
c1cc(F)ccc1N(CC2)CCN2CCCCn3c(=O)oc(c34)cc(cc4)OCc5ccccc5	CM483	8.366	272
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4cc(F)ccc4	CM490	8.428	272
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4cc(F)ccc4	CM491	8.000	272
CC(=O)c1cccc(c12)n(c(=O)o2)CCCCN3CCN(CC3)c4ccc(F)cc4	CM498	8.189	272
c1c(Br)ccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM539	8.519	272
c1cc(F)ccc1N(CC2)CCN2CCCCn3c(=O)oc(c34)ccc(c4)-c5ccc(F)cc5	CM540	7.896	272
CC(=O)c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM564	8.268	272
CS(=O)(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM567	6.952	272
c1cc(F)ccc1N(CC2)CCN2CCCCn3c(=O)oc(c34)cc(cc4)S(=O)(=O)N5CCCC5	CM569	8.080	272
S=C=Nc(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM572	8.172	272
c1cccc(c12)n(C)c(=O)n2CCCCN3CCN(CC3)c(c4[N+]([O-])=O)ccc(F)c4	CM585	8.435	272
c1cccc(c12)sc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	MES71	8.523	272
CCC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4c(F)cc(F)cc4	MES74	8.327	272
c1cccc(c12)n(C)c(=O)n2CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	CM398	9.367	273
c1cccc(c12)n(C)c(=O)n2CCCCN(CC3)CCC34c5c(CO4)cccc5	CM699	10.854	273
CCCCCn1c(=O)n(c(c12)cccc2)CCCCN3CCN(CC3)c4ccc(F)cc4	CM775	8.370	273
c1cccc(c12)n(CCC)c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM777	9.178	274
c1ccccc1-n(c(c23)cccc2)c(=O)n3CCCCN4CCN(CC4)c5ccc(F)cc5	CM778	8.175	274
CCCCCCCCCCn1c(=O)n(c(c12)cccc2)CCCCN3CCN(CC3)c4ccc(F)cc4	CM781	8.342	274
c1cc(F)ccc1-n2c(=O)n(c(c23)ccc(c3)C(=O)C)CCCCN4CCN(CC4)c5ccc(F)cc5	CM782	7.164	274
CC(=O)c(c1)ccc(c12)n(c(=O)n2CCC)CCCCN3CCN(CC3)c4ccc(F)cc4	NF12	6.431	274
CCCCCn1c(=O)n(c(c12)ccc(c2)C(=O)C)CCCCN3CCN(CC3)c4ccc(F)cc4	NF8	8.668	274
c1cc(F)cc(c12)sc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	AZ-68	9.660	275
c1cc(F)cc(c12)sc(=S)n2CCCCN3CCN(CC3)C4CCCCC4	AZ-78	9.300	275
c1cc(F)cc(c12)sc(n2)SCCCCN3CCN(CC3)C4CCCCC4	AZ-81	7.860	275
c1cc(F)cc(c12)SCC(=O)N2CCCCN3CCN(CC3)C4CCCCC4	AZ-87	8.191	275
c1cc(Br)cc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM138	8.350	275
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM142	8.152	275
CCc(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM146	8.592	275
O=C1CCN(CC1)CCCCn2c(=O)oc(c23)cccc3	CM152	7.105	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)Cc4ccccc4	CM159	7.333	275
C1CN(C)CCN1CCCCn2c(=O)oc(c23)cccc3	CM160	5.623	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)CC4CC4	CM162	7.330	275
c1cccc(c12)oc(=O)n2CCCCN(CC3)CC=C3c4ccc(Cl)cc4	CM165	7.840	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)CCc4ccccc4	CM166	7.033	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c(cc4)ccc4[N+]([O-])=O	CM167	6.646	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccccn4	CM168	6.892	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(Cl)cc4	CM169	6.617	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM170	9.155	275

c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)CC4CCCCC4	CM171	7.856	275
c1cccc(c12)oc(=O)n2CCCCN(CC3)CCC3c4ccccc4	CM172	7.764	275
CCc(c1)ccc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM174	7.235	275
c1cccc(c12)oc(=O)n2CCN(CC3)CC=C3c4ccc(Cl)cc4	CM175	6.210	275
c1ccccc1CCN2CCN(CC2)CCn3c(=O)oc(c34)cccc4	CM176	7.663	275
c1cccc(c12)oc(=O)n2CCN3CCN(CC3)c4ccc(Cl)cc4	CM179	5.646	275
c1cccc(c12)oc(=O)n2CCN3CCN(CC3)CC4CCCCC4	CM181	8.054	275
c1cccc(c12)oc(=O)n2CCN(CC3)CCC3c4ccccc4	CM182	6.109	275
CC(=O)c(c1)ccc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM184	7.983	275
c1cc([N+]([O-])=O)cc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM188	8.609	275
CC(=O)Nc(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM191	7.111	275
c1cccc(c12)oc(=O)n2CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	CM295	8.818	275
FCCCc(cc1)cc(c12)sc(=O)n2CCN3CCCCCC3	CM304	6.439	275
c1cccc(c12)sc(=S)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM307	8.180	275
c1cccc(c12)sc(=S)n2CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	CM308	9.252	275
c1cc(F)ccc1-n(c(c23)cccc2)c(=O)n3CCCCN4CCN(CC4)c5ccc(F)cc5	CM322	8.777	275
c1cc(F)ccc1-n(c(c23)cccc2)c(=O)n3CCCCN4CCN(CC4)C5CCCCC5	CM325	8.674	275
C1CCCCC1N(CC2)CCN2CCCCn3c(=O)oc(c34)cc(cc4)-c5ccc(F)cc5	CM343	7.419	275
CC(=O)c(c1)ccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM356	8.917	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4c(F)cccc4	CM362	8.554	275
c1c(Br)ccc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM365	10.260	275
C1CCCCC1N(CC2)CCN2CCCCn3c(=O)oc(c34)ccc(c4)-c5ccc(F)cc5	CM366	11.215	275
c1cccc(c12)n(C)c(=O)n2CCCCN3CCN(CC3)C4CCCCC4	CM396	8.590	275
c1cccc(c12)n(C)c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM397	9.337	275
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c(c4[N+]([O-])=O)ccc(F)c4	CM592	8.201	275
c1cccc(c12)n(C)c(=O)n2CCCCN3CCN(CC3)c(c4N)ccc(F)c4	CM599	8.445	275
[O-][N+](=O)c(c1)ccc(c12)n(C)c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM608	8.326	275
c1c(N)ccc(c12)n(C)c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM609	7.575	275
S=C=Nc(c1)ccc(c12)n(C)c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM617	7.521	275
c1c(F)ccc(c1N=C=S)N(CC2)CCN2CCCCn3c(=O)n(C)c(c34)cccc4	CM621	7.900	275
CC(=O)c1cc(O)c(cc1)NCCCCN2CCN(CC2)c3ccc(F)cc3	CM623	7.356	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4c(F)cc(F)cc4	CM624	8.708	275
CC(=O)c(cc1)cc(c12)oc(=S)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM625	8.726	275
CC(=O)c(cc1)cc(c12)OCC(=O)N2CCCCN3CCN(CC3)c4ccc(F)cc4	CM627	8.198	275
CC(=O)c(cc1)cc(c12)oc(=O)n2CCCCN3CCCN(CC3)c4ccc(F)cc4	CM673	7.296	275
c1cccc(c12)[nH]c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM728	7.529	275
CCCCCCCc(cc1)cc(c12)sc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	SN-55	7.503	275
CCCCCCC(=O)c(cc1)cc(c12)sc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	SN-57	7.533	275
C1CCCCN1CCCCn2c(=O)oc(c23)cccc3	SN-60	6.672	275
c1cccc(c12)oc(=O)n2CCCCCCN3CCN(CC3)Cc4ccccc4	SN-61	6.970	275
CCC(=O)c(c1)ccc(c12)oc(=O)n2CCN3CCCCCC3	SN-71	5.630	275
CCCc(c1)ccc(c12)oc(=O)n2CCN3CCCCCC3	SN-72	5.742	275
c1ccccc1C(=O)c(cc2)cc(c23)sc(=O)n3CCN4CCCCCC4	SN-78	6.066	275
C1CCCCCN1CCn2c(=O)sc(c23)cc(cc3)Cc4ccccc4	SN-81	6.649	275
c1cc(N)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	SN-228	6.751	275
CC(=O)Nc(cc1)cc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	SN-248	7.318	275
FC(F)(F)c1ccc(cc1)N(CC2)CCN2CCCCn3c(=O)oc(c34)cccc4	SN-250	7.005	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c4ccccc4	SN-251	7.942	275
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)c(cc4)ccc4C	SN-252	6.971	275
C1CN(C)CCC1(C#N)c2ccccc2	2	5.669	276
c1ccccc1C2(C#N)CCN(CC2)CC=C	3	6.179	276
c1ccccc1C2(C#N)CCN(CC2)CCC	4	6.845	276
c1ccccc1C2(C#N)CCN(CC2)CC(=C)C	5	6.317	276
c1ccccc1C2(C#N)CCN(CC2)CC(C)C	6	7.201	276
c1ccccc1C2(C#N)CCN(CC2)Cc3ccccc3	7	6.182	276
c1ccccc1C2(C#N)CCN(CC2)CCc3ccccc3	8	6.928	276
c1ccccc1C2(C#N)CCN(CC2)CCCc3ccccc3	9	7.337	276
c1ccccc1C2(C#N)CCN(CC2)CCCCc3ccccc3	10	5.883	276
c1ccccc1CCN2CCCCC2	AC927	6.860	276
c1cccc(c12)oc(=O)n2CCN3CCN(CC3)C4CCCCC4	5a	8.265	277
c1cccc(c12)sc(=O)n2CCN3CCN(CC3)C4CCCCC4	5b	8.648	277
c1cccc(c12)oc(=O)n2CCCN3CCN(CC3)C4CCCCC4	5c	8.058	277
c1cccc(c12)sc(=O)n2CCCN3CCN(CC3)C4CCCCC4	5d	8.516	277
c1cccc(c12)oc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	5e	8.738	277
c1cccc(c12)sc(=O)n2CCCCN3CCN(CC3)C4CCCCC4	5f	9.409	277
c1cccc(c12)oc(=O)n2CCCCCN3CCN(CC3)C4CCCCC4	5g	8.230	277
c1cccc(c12)sc(=O)n2CCCCCN3CCN(CC3)C4CCCCC4	5h	8.613	277
c1cccc(c12)oc(=O)n2CCCCCCN3CCN(CC3)C4CCCCC4	5i	8.514	277

c1cccc(c12)sc(=O)n2CCCCCCN3CCN(CC3)C4CCCCC4	5j	8.827	277
c1cccc(c12)oc(n2)SCCCCN3CCN(CC3)C4CCCCC4	8	8.424	277
c1cccc(c12)oc(=S)n2CCCCN3CCN(CC3)C4CCCCC4	13a	9.114	277
c1cccc(c12)sc(=S)n2CCCCN3CCN(CC3)C4CCCCC4	13b	9.260	277
CCCc(cc1)cc(c12)sc(=O)n2CCN3CCCCCC3	1	6.080	277
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.094	277
c1cccc(c12)n(cc2)CCCCN3CCN(CC3)C4CCCCC4	4a	8.721	278
c1cccc(c12)n(cc2)CCCCN3CCN(CC3)c4ccc(F)cc4	4b	7.875	278
c1cccc(c12)n(cc2)CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	4c	8.437	278
CC(=O)c(c1)ccc(c12)n(cc2)CCCCN3CCN(CC3)C4CCCCC4	4d	8.636	278
CC(=O)c(c1)ccc(c12)n(cc2)CCCCN3CCN(CC3)c4ccc(F)cc4	4e	8.481	278
CC(=O)c(c1)ccc(c12)n(cc2)CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	4f	8.848	278
c1ccccc1-c2cn(c(c23)cccc3)CCCCN4CCN(CC4)C5CCCCC5	9a	7.910	278
c1ccccc1-c2cn(c(c23)cccc3)CCCCN4CCN(CC4)c5ccc(F)cc5	9b	8.002	278
c1ccccc1-c2cn(c(c23)cccc3)CCCCN(CC4)Cc(c45)cc(OC)c(c5)OC	9c	7.335	278
c1cc(F)ccc1-c2cn(c(c23)cccc3)CCCCN4CCN(CC4)C5CCCCC5	9d	7.647	278
c1cc(F)ccc1-c2cn(c(c23)cccc3)CCCCN4CCN(CC4)c5ccc(F)cc5	9e	7.079	278
c1cc(F)ccc1-c2cn(c(c23)cccc3)CCCCN(CC4)Cc(c45)cc(OC)c(c5)OC	9f	8.128	278
c1occc1-c2cn(c(c23)cccc3)CCCCN4CCN(CC4)C5CCCCC5	9g	7.997	278
c1occc1-c2cn(c(c23)cccc3)CCCCN4CCN(CC4)c5ccc(F)cc5	9h	6.804	278
c1occc1-c2cn(c(c23)cccc3)CCCCN(CC4)Cc(c45)cc(OC)c(c5)OC	9i	7.920	278
c1cc(C(F)(F)F)ccc1C(=N\OCCN)\CCCCOC	Fluvoxamine	5.074	279
c1cccc(c12)[C@@H](NC)CC[C@H]2c(c3)ccc(Cl)c3Cl	Sertraline	5.276	279
FC(F)(F)c1ccc(cc1)O[C@@H](CCNC)c2ccccc2	S(+)-Fluoxetine	5.261	279
CN(C)CCCN(c(c12)cccc1)c3c(CC2)cccc3	Imipramine	5.676	279
O1COc(c12)ccc(c2)OC[C@H]3[C@@H](CCNC3)c4ccc(F)cc4	Paroxetine	4.641	279
CNCCCN(c(c12)cccc1)c3c(CC2)cccc3	Desipramine	4.942	279
FC(F)(F)c1ccc(cc1)O[C@H](CCNC)c2ccccc2	R(-)-Fluoxetine	4.618	279
CN[C@@H](C)Cc1ccccc1	METH	7.331	280
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.229	224
c1cc(Cl)ccc1CN(CC2)CCC23N=Nc4c(N3)cccc4	4	6.461	224
c1ccccc1CCCCN(CC2)CCC23N=Nc4c(N3)cccc4	8	7.367	224
c1ccccc1CCCCCN(CC2)CCC23N=Nc4c(N3)cccc4	9	7.284	224
c1ccccc1C(=O)CCCN(CC2)CCC23N=Nc4c(N3)cccc4	10	6.558	224
c1ccccc1CN(CC2)CCC23CCc4c(S3)cccc4	1(Spipithane)	6.400	281
c1ccccc1CN(CC2)CCC23CCc4c(O3)cccc4	2	7.660	281
c1ccccc1CN(CC2)CCC23Cc4c(CC3)cccc4	3	7.850	281
c1ccccc1CN(CC2)CCC23OCc4c(S3)cccc4	4	6.650	281
c1ccccc1CN(CC2)CCC23Oc4c(CO3)cccc4	5	6.640	281
c1ccccc1CN(CC2)CCC23CC(=O)c4c(O3)cccc4	6	6.520	281
c1ccccc1CN(CC2)CCC2[C@@H](CC3)Sc(c34)cccc4	7	7.240	281
c1ccccc1CN(CC2)CCC2[C@H](CC3)Sc(c34)cccc4	7	7.240	281
c1ccccc1CN(CC2)CCC2[C@@H](CC3=O)Oc(c34)cccc4	8	6.760	281
c1ccccc1CN(CC2)CCC2[C@H](CC3=O)Oc(c34)cccc4	8	6.760	281
c1ccccc1CN(CC2)CCC2[C@@H](CC3=O)Sc(c34)cccc4	9	5.810	281
c1ccccc1CN(CC2)CCC2[C@H](CC3=O)Sc(c34)cccc4	9	5.810	281
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	6.950	281
c1ccccc1CCN2CCN(CC2)c3ccncc3	1	7.157	282
c1ccccc1CCCN2CCN(CC2)c3ccncc3	2	7.076	282
c1ccccc1CCN2CCN(CC2)c3cccnc3	3	6.357	282
c1ccccc1CCCN2CCN(CC2)c3cccnc3	4	6.959	282
C1CCCCN1CCCc2ccccc2	UMB23	7.495	283
c1cc(Cl)c(Cl)cc1CCN(CC)CCN2CCCCC2	UMB82	7.538	283

Table F.4: Sigma 2: DTG/PTZ rat liver dataset

SMILES	Name	pK_i	Ref.
c1ccccc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	9	5.991	103
c1ccc(F)cc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	10	6.152	103
c1cc(F)ccc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	11	6.083	103
c1ccc(OC)cc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	12	6.452	103
COc(cc1)ccc1CN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	13	6.371	103
c1ccc(F)cc1CCN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	14	6.602	103
c1cc(F)ccc1CCN2[C@H](C3)C[C@@H](C4)C[C@H]3C[C@]24O	15	6.697	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4ccccc4	23	7.022	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4cc(F)ccc4	24	6.879	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4ccc(F)cc4	25	7.046	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4cc(OC)ccc4	26	7.194	103
[C@H]12C[C@H]3C[C@@H](C2)N([C@@H](C1)C3)Cc4ccc(cc4)OC	27	7.268	103
c1ccc(F)cc1CCN([C@@H](C2)C3)[C@H](C4)C[C@@H]3C[C@@H]24	28	7.398	103
c1cc(F)ccc1CCN([C@@H](C2)C3)[C@H](C4)C[C@@H]3C[C@@H]24	29	7.469	103
COc1cccc(c12)[C@@H](CCC2)N3CCN(CC3)C4CCCCC4	R-4	7.708	70
COc1cccc(c12)[C@H](CCC2)N3CCN(CC3)C4CCCCC4	S-4	7.747	70
COc1cccc(c12)[C@@H](CCC2)CN(CC3)CCC3N4CCCCC4	R-10	7.592	70
COc1cccc(c12)[C@H](CCC2)CN(CC3)CCC3N4CCCCC4	S-10	7.730	70
COc1cccc(c12)[C@H](CCC2)CCN3CCN(CC3)C4CCCCC4	R-11	8.036	70
COc1cccc(c12)[C@@H](CCC2)CCN3CCN(CC3)C4CCCCC4	S-11	7.801	70
CCN1CCN(CC1)C2CCCCC2	13	6.457	70
C1CCCCC1CCCN2CCN(CC2)C3CCCCC3	12	8.328	70
C1CCCCC1N2CCN(CC2)C3CCCCC3	24	7.939	70
C1CCCCC1C(=O)N2CCN(CC2)C3CCCCC3	26	6.697	70
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.590	143
c1ccccc1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-7	8.437	143
c1ccccc1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-7	8.321	143
COc(cc1)ccc1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-8	8.799	143
COc(cc1)ccc1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-8	8.917	143
c1ccc(OC)cc1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-9	8.688	143
c1cccc(OC)c1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-10	8.162	143
COc1cccc(OC)c1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-11	8.101	143
COc1cccc(OC)c1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-11	9.678	143
Fc1cccc(F)c1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-12	7.851	143
Fc1cccc(F)c1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-12	8.714	143
c1cccc(Cl)c1[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-13	7.676	143
c1cccc(Cl)c1[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-13	8.305	143
c1cccc(c1C)[C@H]2CC[C@H](CC2)N3CCN(CC3)C4CCCCC4	cis-14	8.780	143
c1cccc(c1C)[C@H]2CC[C@@H](CC2)N3CCN(CC3)C4CCCCC4	trans-14	8.783	143
COc1cccc(c12)[C@@H](CCC2)NC(=O)CN3CCN(CC3)C4CCCCC4	R-9	7.996	144
COc1cccc(c12)[C@H](CCC2)NC(=O)CN3CCN(CC3)C4CCCCC4	S-9	8.228	144
COc1cccc(c12)[C@@H](CCC2)NCCN3CCN(CC3)C4CCCCC4	R-11	7.842	144
COc1cccc(c12)[C@H](CCC2)NCCN3CCN(CC3)C4CCCCC4	S-11	8.070	144
C1CCCCC1N(CC2)CCN2CCO[C@H](CCC3)c(c34)cccc4OC	R-14	7.955	144
C1CCCCC1N(CC2)CCN2CCO[C@@H](CCC3)c(c34)cccc4OC	S-14	8.327	144
c1ccc(OC)c(c12)cccc2NC(=O)CN3CCN(CC3)C4CCCCC4	20	7.635	144
c1ccc(OC)c(c12)cccc2NCCN3CCN(CC3)C4CCCCC4	21	7.733	144
C1CCCCC1N(CC2)CCN2CCOc3cccc(c34)c(OC)ccc4	22	8.620	144
Cc(c1)ccc(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	2	8.061	145
Cc(c1)ccc(OC)c1C(=O)NCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	11a	8.580	145
Cc(c1)ccc(OC)c1C(=O)NCCCN2CCN(CC2)C3CCCCC3	11b	7.583	145
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	12a	7.889	145
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCN2CCN(CC2)C3CCCCC3	12b	7.674	145
COc(c1)c(OC)cc(Br)c1C(=O)NCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	13a	7.293	145
COc(c1)c(OC)cc(Br)c1C(=O)NCCCN2CCN(CC2)C3CCCCC3	13b	6.331	145
c1cccc(c12)CCN(C2=O)CCCN(CC3)Cc(c34)cc(OC)c(c4)OC	15a	8.315	145
c1cccc(c12)CCN(C2=O)CCCN3CCN(CC3)C4CCCCC4	15b	7.575	145
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.580	145
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.609	146
CCCCN(C[C@@H]1O)CCN1Cc2ccccc2	3b	6.290	149
c1ccccc1CN2CCN(C[C@@H]2O)Cc3ccccc3	3c	6.752	149
c1ccccc1CN2CCN(C[C@@H]2O)Cc3ccc(cc3)OC	3d	7.153	149
c1ccccc1CCN(C[C@@H]2O)CCN2Cc3ccccc3	3e	6.879	149
c1ccccc1CN2CCN(C[C@@H]2O)C3CCCCC3	3f	6.967	149
c1ccccc1CN2CCCN(C[C@@H]2CO)Cc3ccccc3	4a	6.427	151

COC(OC)CN(C[C@@H]1CO)CCCN1Cc2ccccc2	4b	5.045	151
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.595	152
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OC	SA4503	7.111	152
CC1(C)CCCN(C1)CCC[C@H](CCC2)c(c23)cccc3OC	S-39	6.660	152
CC1(C)CCCN(C1)CCC[C@@H](CCC2)c(c23)cccc3OC	R-39	6.759	152
CCCN(CCC)CCc1cc(c(cc1)OC)OCCc2ccccc2	NE100	6.674	152
c1cc(Cl)c(Cl)cc1CCN(C)CCN2CCCC2	BD1008	7.082	152
CC1(C)CCCN(C1)CCCC2=CCc(c23)cccc3	23	6.456	152
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.506	153
CC1CCN(CC1)CCOc2ccc(Cl)cc2	12	6.622	153
CC1CCN(CC1)C[C@@H](C)Oc2ccc(Cl)cc2	R-13	6.479	153
CC1CCN(CC1)C[C@H](C)Oc2ccc(Cl)cc2	S-13	6.498	153
c1cc(Cl)ccc1O[C@H](C)CCN(CC2)CCC2C	R-14	7.181	153
c1cc(Cl)ccc1O[C@@H](C)CCN(CC2)CCC2C	S-14	7.857	153
CC1CCN(CC1)CCCOc2ccc(Cl)cc2	15	7.413	153
CC1CCN(CC1)C[C@@H](C)COc2ccc(Cl)cc2	R-16	7.389	153
CC1CCN(CC1)C[C@H](C)COc2ccc(Cl)cc2	S-16	7.208	153
CC1CCN(CC1)[C@H](C)COc2ccc(Cl)cc2	R-17	7.281	153
CC1CCN(CC1)[C@@H](C)COc2ccc(Cl)cc2	S-17	6.730	153
CC1CCN(CC1)[C@H](C)CCOc2ccc(Cl)cc2	R-18	7.821	153
CC1CCN(CC1)[C@@H](C)CCOc2ccc(Cl)cc2	S-18	7.500	153
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.550	154
c1ccccc1CCN2CCCCC2	AC927	6.712	154
COc1cccc(c12)[C@@H](CCC2)CCCN3CCN(CC3)C4CCCCC4	S-33	8.063	154
COc1cccc(c12)[C@H](CCC2)CCCN3CCN(CC3)C4CCCCC4	R-33	8.680	154
c1cccc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	43	9.161	154
c1ccc(OC)c(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	44	8.034	154
c1cccc(c12)cccc2CCCCN3CCN(CC3)C4CCCCC4	45	7.516	154
c1cccc(c12)cccc2CCCCCN3CCN(CC3)C4CCCCC4	46	9.244	154
C1CCCCN1CCCc2cccc(c23)cc(cc3)OC	21	6.757	155
CC1(C)CCCN(C1)CCCc2cccc(c23)cc(cc3)OC	26	6.623	155
CC1(C)CCCCN1CCCc2cccc(c23)cc(cc3)OC	25	7.027	155
CC1CCN(CC1)CCCc2cccc(c23)cc(cc3)OC	24	7.410	155
CC1(C)CCN(CC1)CCCc2cccc(c23)cc(cc3)OC	27	7.580	155
C1CCCCN1CCCCc2cccc(c23)cc(cc3)OC	28	6.821	155
CC1(C)CCCN(C1)CCCCc2cccc(c23)cc(cc3)OC	33	7.171	155
CC1(C)CCCCN1CCCCc2cccc(c23)cc(cc3)OC	32	7.544	155
CC1CCN(CC1)CCCCc2cccc(c23)cc(cc3)OC	31	7.747	155
CC1(C)CCN(CC1)CCCCc2cccc(c23)cc(cc3)OC	34	7.747	155
C[C@@H]1CCCN(C1)CCCc2cccc(c23)cc(cc3)OC	23R	7.220	155
C[C@H]1CCCN(C1)CCCc2cccc(c23)cc(cc3)OC	23S	7.227	155
C[C@@H]1CCCCN1CCCc2cccc(c23)cc(cc3)OC	22R	7.064	155
C[C@H]1CCCCN1CCCc2cccc(c23)cc(cc3)OC	22S	6.983	155
C[C@@H]1CCCN(C1)CCCCc2cccc(c23)cc(cc3)OC	30R	7.194	155
C[C@H]1CCCN(C1)CCCCc2cccc(c23)cc(cc3)OC	30S	7.485	155
C[C@@H]1CCCCN1CCCCc2cccc(c23)cc(cc3)OC	29R	7.308	155
C[C@H]1CCCCN1CCCCc2cccc(c23)cc(cc3)OC	29S	7.269	155
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.491	155
c1cccc(OC)c1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-19	6.616	156
c1ccc(OC)cc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-20	7.442	156
COc(cc1)ccc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-21	7.195	156
c1ccccc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-29	7.208	156
Cc1ccc(cc1)[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-30	7.149	156
c1cc(Cl)ccc1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-31	6.824	156
Fc1cccc(F)c1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-32	6.357	156
COc1cccc(OC)c1[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-33	6.163	156
c1ccc(C)c(c1C)[C@H]2CC[C@H](CC2)N(CC3)CCN3c4ccccn4	cis-34	7.220	156
c1cccc(OC)c1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-19	7.523	156
c1ccc(OC)cc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-20	7.660	156
COc(cc1)ccc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-21	6.654	156
c1ccccc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-29	7.570	156
Cc1ccc(cc1)[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-30	7.529	156
c1cc(Cl)ccc1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-31	7.536	156
Fc1cccc(F)c1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-32	6.860	156
COc1cccc(OC)c1[C@H]2CC[C@@H](CC2)N(CC3)CCN3c4ccccn4	trans-33	7.602	156
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.507	156
c1cccc(c12)CCC[C@@H]2CCCN3CCN(CC3)C4CCCCC4	R-3	9.310	157
c1cccc(c12)CCC[C@H]2CCCN3CCN(CC3)C4CCCCC4	S-3	8.928	157

c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.495	158
c1cc(I)ccc1CN(CC2)CCC23c4c(CO3)cccc4	Spiro-I	6.469	166
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	5.716	95
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.740	95
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.420	95
c1ccccc1C(c2ccccc2)(c3ccccc3)SCCNC(=O)CN(CCSC(c4ccccc4)(c5ccccc5) c6ccccc6)CCCN7[C@H](CCC8)C[C@@H](C[C@@H]78)OC(=O)Nc(c(cc9)OC)cc9C	1	5.871	95
I\C=C\CN(CCC)[C@H](C1)CCc(c12)ccc(c2)O	S-trans-7-OH-PIPAT	6.449	95
s1cccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12a	5.337	167
CN(C)c(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12b	5.805	167
CSc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12c	5.698	167
c1nc(Cl)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12d	5.754	167
c1cccc(c12)[nH]c(c2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12e	5.711	167
c1cccc(c12)ncc(n2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12f	6.350	167
c1cccc(c12)oc(c2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12g	6.169	167
c1cccc(c12)sc(c2)C(=O)NCCCCN3CCN(CC3)c4c(OC)cccc4	12h	5.846	167
FCCc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12i	5.657	167
Cc(s1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12j	6.034	167
s1c(Br)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	12k	6.417	167
c1cc(Cl)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13a	5.253	167
c1cc(F)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13b	5.795	167
CN(C)c(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13c	5.170	167
COc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13d	5.151	167
CSc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13e	5.075	167
c1cccc(c12)oc(c2)C(=O)NCCCCN3CCN(CC3)c(c4Cl)cccc4Cl	13f	5.435	167
FCCc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13g	5.142	167
Cc(s1)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13h	5.438	167
s1c(Br)ccc1C(=O)NCCCCN2CCN(CC2)c(c3Cl)cccc3Cl	13i	5.521	167
CCCCNCCCc1ccccc1	1a	7.824	168
CCCCCCCNCCCc1ccccc1	2a	7.481	168
CCCCCCCCCCCCNCCCc1ccccc1	3a	5.678	168
CCCCCCCCCCCCCCCCCCCNCCCc1ccccc1	4a	4.699	168
CCCCNCCCc1ccc([N+]([O-])=O)cc1	1b	7.658	168
CCCCCCCNCCCc1ccc([N+]([O-])=O)cc1	2b	7.959	168
CCCCCCCCCCCCNCCCc1ccc([N+]([O-])=O)cc1	3b	5.620	168
CCCCCCCCCCCCCCCCCCNCCCc1ccc([N+]([O-])=O)cc1	4b	5.046	168
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.453	169
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.375	169
CCCN(CCC)CCc1cc(c(cc1)OC)OCCc2ccccc2	NE100	6.770	169
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	dextromethorphan	5.466	169
c1cc(F)ccc1C(=O)CN2[C@@H](CC[C@@H]23)C[C@@H](C3)c4ccccc4	11	7.135	175
c1cc(F)ccc1C(=O)CCCN2[C@@H](CC[C@@H]23)C[C@@H](C3)c4ccccc4	12	7.814	175
c1cc(F)ccc1C(=O)CCCN(CC2)CCC23c4c(N(C)C3)cccc4	24a	7.216	175
c1cc(F)ccc1C(=O)CCCN(CC2)CCC23c4c(CC3)cccc4	24b	8.481	175
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.511	177
CC1(C)CCCN(C1)CCCc2cccc(c23)c(OC)ccc3	11	6.192	177
CC1(C)CCCN(C1)CCCc2cccc(c23)ccc(c3)OC	13	6.173	177
COc(cc1)cc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	15	8.045	177
C1CCCCC1N(CC2)CCN2CCCc3cccc(c34)ccc(c4)OC	16	8.082	177
CC1(C)CCCN(C1)CCCc2cccc(c23)cc(O)cc3	17	6.222	177
CC1(C)CCCN(C1)CCCc2cccc(c23)ccc(c3)O	18	6.385	177
c1cc(O)cc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	19	7.578	177
c1c(O)ccc(c12)cccc2CCCN3CCN(CC3)C4CCCCC4	20	7.928	177
c1cccc2n(c(c3c12)cccc3)CCCN(C4)CCCC4(C)C	26	5.349	177
c1cccc2n(c(c3c12)cccc3)CCCCN(C4)CCCC4(C)C	27	6.284	177
c1cccc2n(c(c3c12)cccc3)CCCCCN(C4)CCCC4(C)C	28	6.932	177
c1cccc2n(c(c3c12)cccc3)CCCN4CCN(CC4)C5CCCCC5	29	7.900	177
CC1(C)CCCN(C1)CCCc2cccc(c23)occ3	16	7.374	178
CC1(C)CCCN(C1)CCCc2cccc(c23)scc3	17	7.197	178
CC1(C)CCCN(C1)Cc(c2)oc(c23)cccc3	22	5.742	178
c1cccc(c12)n(cc2)CCCN(C3)CCCC3(C)C	28	6.712	178
c1cccc(c12)n(nn2)CCCN(C3)CCCC3(C)C	29	5.701	178
c1cccc(c12)n(cc2C)CCCN(C3)CCCC3(C)C	30	6.959	178
C1CCCCC1CCCCN(C2)CCCC2(C)C	31	7.708	178
CC1(C)CCCN(C1)CCNc(n2)sc(c23)cccc3	37	6.130	178
s1ccnc1NCCN(C2)CCCC2(C)C	38	5.478	178
CC1(C)CCCN(C1)CCCCN(C2)CCCC2(C)C	41	6.383	178
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.465	178

C1CCCCCN1CCCn2c(=O)sc(c23)cccc3	RB2	6.752	284
C1CCCCCN1CCCCn2c(=O)sc(c23)cccc3	RB4	6.996	284
C1CCCCCN1CCCCCn2c(=O)sc(c23)cccc3	RB6	8.602	284
C1CCCCCN1CCCCCCn2c(=O)sc(c23)cccc3	RB8	8.620	284
C1CCCCCN1CCCn2c(=O)sc(c23)cc(cc3)CCC	RB10	7.764	284
C1CCCCCN1CCCCn2c(=O)sc(c23)cc(cc3)CCC	RB14	8.367	284
C1CCCCCN1CCCCCn2c(=O)sc(c23)cc(cc3)CCC	RB16	8.796	284
C1CCCCCN1CCCCCCn2c(=O)sc(c23)cc(cc3)CCC	RB18	8.638	284
CCCCc(cc1)cc(c12)sc(=O)n2CCCN3CCCCCC3	RB20	7.815	284
C1CCCCCN1CCCCCCn2c(=O)sc(c23)cc(cc3)CCCC	RB24	8.387	284
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCCN3CCCCCC3	RB26	6.516	284
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCCCN3CCCCCC3	RB28	7.519	284
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCCCCN3CCCCCC3	RB30	8.081	284
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCCCCCN3CCCCCC3	RB32	8.959	284
C1CCCCCN1CCCCn2c(=O)sc(c23)cc(cc3)CCCC	RB34	8.357	284
CCCC(=O)c(cc1)cc(c12)sc(=O)n2CCCN3CCCCCC3	RB36	6.983	284
CCCC(=O)c(cc1)cc(c12)sc(=O)n2CCCCN3CCCCCC3	RB38	7.666	284
CCCC(=O)c(cc1)cc(c12)sc(=O)n2CCCCCN3CCCCCC3	RB40	8.244	284
C1CCCN1CCn2c(=O)sc(c23)cccc3	RB65	5.083	284
C1CCCCCN1CCn2c(=O)sc(c23)cccc3	RB67	6.145	284
CCCC(=O)c(cc1)cc(c12)sc(=O)n2CCCCCCN3CCCCCC3	RB70	8.638	284
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCN3CCCCCC3	RB74	5.661	284
CCC(=O)c(cc1)cc(c12)sc(=O)n2CCN3CCCC3	RB75	5.320	284
CCCc(cc1)cc(c12)sc(=O)n2CCN3CCCCCC3	SN-56	6.569	284
c1ccccc1C(=O)O[C@H]([C@@H]2C(=O)OC)C[C@H](CC[C@H]23)N3CCc4ccc([N+]([O-])=O)cc4	5	2.272	96
c1ccccc1C(=O)O[C@H]([C@@H]2C(=O)OC)C[C@H](CC[C@H]23)N3CCc4ccc(N)cc4	6	4.777	96
c1cc(F)ccc1CCC(=O)N(CCC)CCc2ccc([N+]([O-])=O)cc2	11	4.905	96
c1cc(F)ccc1CCCN(CCC)CCc2ccc(N)cc2	13	6.921	96
c1cc(F)ccc1CCCN(CCC)CCc2cc(I)c(N)cc2	14	4.377	96
c1cc(F)ccc1CCCN(CCC)CCc2cc(I)c(cc2)N=[N+]=[N-]	15	5.889	96
NCCc1c[nH]c(c12)cccc2	tryptamine	5.309	285
CN(C)CCc1c[nH]c(c12)cccc2	N,N'-dimethyltryptamine	4.663	285
CNCCc1c[nH]c(c12)cccc2	N-methyltryptamine	4.892	285
NCCc1ccccc1	PEA	5.136	285
CNCCc1ccccc1	N-methylPEA	4.659	285
CN(C)CCc1ccccc1	N,N'-dimethylPEA	4.674	285
NCCc1ccc(O)cc1	tyramine	3.217	285
CNCCc1ccc(O)cc1	N-methyltyramine	5.180	285
CN(C)CCc1ccc(O)cc1	N,N'-dimethyltyramine	4.192	285
COc(cc1)ccc1CN2C[C@@H](CC[C@@H]3O)N(C[C@H]23)Cc4ccccc4	15	5.770	180
COc(cc1)ccc1CN2C[C@H](CC[C@H]3O)N(C[C@@H]23)Cc4ccccc4	ent-15	6.094	180
COc(cc1)ccc1CN2C[C@@H](CC[C@H]3O)N(C[C@H]23)Cc4ccccc4	20	6.356	180
COc(cc1)ccc1CN2C[C@H](CC[C@@H]3O)N(C[C@@H]23)Cc4ccccc4	ent-20	6.152	180
COc(cc1)ccc1CN2C[C@@H](CC[C@@H]3OC)N(C[C@H]23)Cc4ccccc4	17	5.614	180
COc(cc1)ccc1CN2C[C@H](CC[C@H]3OC)N(C[C@@H]23)Cc4ccccc4	ent-17	6.242	180
COc(cc1)ccc1CN2C[C@@H](CC[C@H]3OC)N(C[C@H]23)Cc4ccccc4	22	5.842	180
COc(cc1)ccc1CN2C[C@H](CC[C@@H]3OC)N(C[C@@H]23)Cc4ccccc4	ent-22	6.488	180
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@H](CC[C@@H]3N4CCCC4)N(C[C@@H]23)Cc5cc-ccc5	19	6.056	181
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@H](CC[C@H]3N4CCCC4)N(C[C@@H]23)Cc5cc-ccc5	20	5.770	181
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@@H](N(C[C@@H]23)C(=O)OC)CC[C@H]3N4CCCC4	24	6.205	181
C1CCCN1[C@@H]2CC[C@H](N(C[C@H]23)C(=O)CC)CN3C(=O)Cc4cc(Cl)c(Cl)cc4	26	5.959	181
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@@H](CC[C@H]3N4CCCC4)N(C[C@H]23)Cc5cc-ccc5	ent-19	5.495	181
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@@H](CC[C@@H]3N4CCCC4)N(C[C@H]23)Cc5cc-ccc5	ent-20	5.292	181
c1cc(Cl)c(Cl)cc1CC(=O)N2C[C@H](N(C[C@H]23)C(=O)OC)CC[C@@H]3N4CCCC4	ent-24	5.824	181
C1CCCN1[C@H]2CC[C@@H](N(C[C@@H]23)C(=O)CC)CN3C(=O)Cc4cc(Cl)c(Cl)cc4	ent-26	5.678	181
CCCN(CCC)CCc1ccc([N+]([O-])=O)cc1	2	4.271	286
CCCCN(CCCC)CCCc1ccc([N+]([O-])=O)cc1	3	6.394	286
CCCCN(CCCC)C(=O)CCc1ccc(F)cc1	4	3.898	286
c1cc([N+]([O-])=O)ccc1CN(CCC)C(=O)CCc2ccc(F)cc2	6	3.627	286
CCCCN(CCCC)CCCc1ccc(F)cc1	9	6.164	286
CCCCCCCCN(CCCCCCCC)CCCc1ccc(F)cc1	10	5.782	286
CCCNCCCc1ccc(F)cc1	13	6.638	286
c1cc(F)ccc1CCCN(CCC)Cc2ccc(N)cc2	14	5.668	286
c1cc(F)ccc1CCCN(CCC)Cc2cc(I)c(N)cc2	16	3.875	286

c1cc([N+]([O-])=O)ccc1CCCN(CCC)CCc2ccc(N)cc2	20	7.078	286
c1cccc(c12)C(=O)N(C2=O)CCCCN(C3)CCc(c34)ccc(c4)[N+]([O-])=O	3b	7.058	287
c1ccc([N+]([O-])=O)cc1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	5a	2.917	287
c1cc([N+]([O-])=O)ccc1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	5d	4.833	287
c1ccc(OC)c(O)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	5i	4.169	287
COc(cc1)c(OC)c(OC)c1C(=O)NCCCCN(C2)CCc(c23)ccc(c3)[N+]([O-])=O	5e	4.986	287
c1ccc(OC)c(OC)c1C(=O)NCCCCN(C2)CCc(c23)ccc(c3)[N+]([O-])=O	5f	5.104	287
c1cc(I)c(OC)c(O)c1C(=O)NCCCCN(C2)CCc(c23)ccc(c3)[N+]([O-])=O	5g	4.127	287
c1ccc(OC)c(O)c1C(=O)NCCCCN(C2)CCc(c23)ccc(c3)[N+]([O-])=O	5h	4.951	287
C=CCN(C[C@H]12)[C@@H](CC=C1)CN2Cc3ccc(cc3)OC	2	5.625	55
C=CCN(C[C@@H]12)[C@H](CC=C1)CN2Cc3ccc(cc3)OC	ent-2	5.613	55
COc(cc1)ccc1CN2C[C@H](CC=C3)N(C[C@@H]23)Cc4ccccc4	3	7.409	55
COc(cc1)ccc1CN2C[C@@H](CC=C3)N(C[C@H]23)Cc4ccccc4	ent-3	6.372	55
C=CCN1C[C@H](CCC2)N(C[C@@H]12)Cc3ccc(cc3)OC	23	6.693	184
C=CCN1C[C@@H](CCC2)N(C[C@H]12)Cc3ccc(cc3)OC	ent-23	6.475	184
C=CCN(C[C@H]12)[C@@H](CCC1=O)CN2Cc3ccc(cc3)OC	12	5.041	184
C=CCN(C[C@@H]12)[C@H](CCC1=O)CN2Cc3ccc(cc3)OC	ent-12	5.721	184
C=CCN(C[C@H]12)[C@@H](CC[C@H]1O)CN2Cc3ccc(cc3)OC	15a	5.321	184
C=CCN(C[C@@H]12)[C@H](CC[C@@H]1O)CN2Cc3ccc(cc3)OC	ent-15a	5.917	184
C=CCN(C[C@H]12)[C@@H](CC[C@H]1O)CN2Cc3c(OC)cc(cc3)OC	15b	5.836	184
C=CCN(C[C@@H]12)[C@H](CC[C@@H]1O)CN2Cc3c(OC)cc(cc3)OC	ent-15b	5.287	184
CO[C@@H]1CC[C@H](N(C[C@H]12)CC=C)CN2Cc3ccc(cc3)OC	16a	5.772	184
CO[C@H]1CC[C@@H](N(C[C@@H]12)CC=C)CN2Cc3ccc(cc3)OC	ent-16a	5.810	184
CO[C@@H]1CC[C@H](N(C[C@H]12)CC=C)CN2Cc3c(OC)cc(cc3)OC	16b	5.678	184
CO[C@H]1CC[C@@H](N(C[C@@H]12)CC=C)CN2Cc3c(OC)cc(cc3)OC	ent-16b	4.870	184
CO[C@H]1CC[C@H](N(C[C@H]12)CC=C)CN2Cc3ccc(cc3)OC	21a	5.678	184
CO[C@@H]1CC[C@@H](N(C[C@@H]12)CC=C)CN2Cc3ccc(cc3)OC	ent-21a	4.650	184
CO[C@H]1CC[C@H](N(C[C@H]12)CC=C)CN2Cc3c(OC)cc(cc3)OC	21b	5.116	184
C=CCN1C[C@H](CCC2)N(C[C@@H]12)Cc3c(OC)cc(cc3)OC	23b	5.631	184
C=CCN1C[C@@H](CCC2)N(C[C@H]12)Cc3c(OC)cc(cc3)OC	ent-23b	5.733	184
CCCN(C[C@@H]12)[C@H](CCC1=O)CN2Cc3ccc(cc3)OC	ent-7	5.745	54
CC(C)=CCN(C[C@H]12)[C@@H](CCC1=O)CN2Cc3ccc(cc3)OC	12	6.075	54
CC(C)=CCN(C[C@@H]12)[C@H](CCC1=O)CN2Cc3ccc(cc3)OC	ent-12	5.886	54
COc(cc1)ccc1CN2C[C@H](CCC3=O)N(C[C@@H]23)Cc4ccccc4	14	6.152	54
COc(cc1)ccc1CN2C[C@@H](CCC3=O)N(C[C@H]23)Cc4ccccc4	ent-14	5.444	54
COc(cc1)ccc1CN2C[C@H](CCC3=O)N(C[C@@H]23)c4ccccc4	16	5.423	54
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@H](N(C[C@H]23)CC=C)CC[C@@H]3 OCc4ccccc4	9	4.815	185
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3 OCc4ccccc4	12	4.660	185
CCN(CC)C(=O)c1ccc(cc1)[C@H](c2ccccc2)N3C[C@@H](CCC4)N(C[C@H]34)CC=C	24	6.910	185
CCN(CC)C(=O)c1ccc(cc1)[C@@H](c2ccccc2)N3C[C@@H](CCC4)N(C[C@H]34)CC=C	25	7.081	185
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3 OCc4ccccc4	ent-9	5.821	185
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@@H](N(C[C@@H]23)CC=C)CCC\3=C\ c4ccccc4	ent-15	5.561	185
CCN(CC)C(=O)c1ccc(cc1)CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3 OCc4ccccc4	ent-12	5.810	185
CCN(CC)C(=O)c1ccc(cc1)[C@@H](c2ccccc2)N3C[C@H](CCC4)N(C[C@@H]34)CC=C	ent-24	6.163	185
CCN(CC)C(=O)c1ccc(cc1)[C@H](c2ccccc2)N3C[C@H](CCC4)N(C[C@@H]34)CC=C	ent-25	6.545	185
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3OCc4ccccc4	8a	6.096	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3OCc4ccccc4	8b	6.398	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3OCc4ccccc4	11a	6.238	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3Oc4ccccc4	13a	6.320	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3OCc4cc- ccc4	11b	6.231	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@H]3Oc4ccccc4	13b	6.329	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3Oc4ccccc4	15a	5.076	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CC[C@@H]3Oc4ccccc4	15b	5.680	186
COc(cc1)ccc1CN2C[C@@H](N(C[C@@H]23)CC=C)CCC\3=C\c4ccccc4	17a	6.240	186
COc(cc1)cc(OC)c1CN2C[C@@H](N(C[C@@H]23)CC=C)CCC\3=C\c4ccccc4	17b	6.799	186
c1cccc2[nH]c(c3c12)[C@H]4CN(CC=C)[C@@H](C3)CN4Cc5ccc(cc5)OC	20a	4.627	186
c1cccc2[nH]c(c3c12)[C@H]4CN(CC=C)[C@@H](C3)CN4Cc5c(OC)cc(cc5)OC	20b	5.475	186
COc(cc1)cc(OC)c1CN2C[C@H](C3)N(CC=C)C[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	21b	5.030	186
COc(cc1)ccc1CN([C@@H]2CN3CC=C)C[C@@H]3Cc(c4C)c2nc(c45)cccc5	23a	5.251	186
COc(cc1)cc(OC)c1CN([C@@H]2CN3CC=C)C[C@@H]3Cc(c4C)c2nc(c45)cccc5	23b	5.076	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@@H]3OCc4ccccc4	ent-8a	5.323	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@@H]3OCc4ccccc4	ent-8b	5.551	186

COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3OCc4ccccc4	ent-11a	5.190	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@@H]3Oc4ccccc4	ent-13a	6.064	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3OCc4ccccc4	ent-11b	4.644	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@@H]3Oc4ccccc4	ent-13b	5.231	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3Oc4ccccc4	ent-15a	6.162	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CC[C@H]3Oc4ccccc4	ent-15b	6.042	186
COc(cc1)ccc1CN2C[C@H](N(C[C@H]23)CC=C)CCC\3=C\c4ccccc4	ent-17a	6.247	186
COc(cc1)cc(OC)c1CN2C[C@H](N(C[C@H]23)CC=C)CCC\3=C\c4ccccc4	ent-17b	6.168	186
c1cccc2[nH]c(c3c12)[C@@H]4CN(CC=C)[C@H](C3)CN4Cc5c(OC)cc(cc5)OC	ent-20b	5.493	186
COc(cc1)cc(OC)c1CN2C[C@@H](C3)N(CC=C)C[C@H]2c(c3c45)[nH]c4ccc(c5)OC	ent-21b	4.991	186
COc(cc1)ccc1CN([C@H]2CN3CC=C)C[C@H]3Cc(c4C)c2nc(c45)cccc5	ent-23a	4.243	186
COc(cc1)cc(OC)c1CN([C@H]2CN3CC=C)C[C@H]3Cc(c4C)c2nc(c45)cccc5	ent-23b	5.251	186
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	1	6.620	58
c1cccc(Cl)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	2	6.759	58
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	3	7.433	58
c1cc(Cl)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	4	7.093	58
c1cc(Cl)c(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	5	7.836	58
c1cc(Cl)cc(Cl)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	6	7.611	58
Clc1cccc(Cl)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	7	7.150	58
c1cccc(Br)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	8	7.062	58
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	9	7.818	58
c1cc(Br)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	10	7.622	58
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	11	6.176	58
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	12	6.815	58
c1cc(F)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	13	7.160	58
c1cc(F)cc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	14	6.886	58
c1c(F)ccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	15	6.888	58
Fc1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	16	6.684	58
c1cc(F)c(F)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	17	7.272	58
c1c(F)cc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	18	7.428	58
c1cccc(c1C(F)(F)F)CC(=O)NC2CCN(CC2)Cc3ccccc3	19	7.208	58
FC(F)(F)c1cc(ccc1)CC(=O)NC2CCN(CC2)Cc3ccccc3	20	7.423	58
FC(F)(F)c1ccc(cc1)CC(=O)NC2CCN(CC2)Cc3ccccc3	21	7.272	58
c1cccc([N+]([O-])=O)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	22	6.307	58
c1ccc([N+]([O-])=O)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	23	7.101	58
c1cc([N+]([O-])=O)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	24	6.977	58
c1cc([N+]([O-])=O)cc([N+]([O-])=O)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	25	6.614	58
c1cccc(O)c1CC(=O)NC2CCN(CC2)Cc3ccccc3	26	6.465	58
c1cc(O)c(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	30	6.121	58
c1ccc(OC)cc1CC(=O)NC2CCN(CC2)Cc3ccccc3	32	6.487	58
COc(cc1)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	33	6.316	58
O1COc(c12)ccc(c2)CC(=O)NC3CCN(CC3)Cc4ccccc4	38	6.538	58
COc(cc1)cc(OC)c1NC(=O)NC2CCN(CC2)Cc3ccccc3	39	6.644	58
CSc(cc1)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	41	7.079	58
CSc(cc1)ccc1NC(=O)NC2CCN(CC2)Cc3ccccc3	42	7.094	58
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)Cc4ccccc4	1	7.456	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)C4CCCC4	2	8.167	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)C4CCCCC4	3	8.678	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)C4CCCCCC4	4	8.585	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	5	8.620	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC3CCN(CC3)[C@@H]([C@@H]45)[C@H]6C[C@@H](C5)C[C@@H](C4)C6	6	7.260	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)Cc4ccccc4	7	7.377	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)C4CCCC4	8	7.569	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)C4CCCCC4	9	7.602	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)C4CCCCCC4	10	7.770	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	11	6.863	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@H]3CCN(C3)[C@@H]([C@@H]45)[C@H]6C[C@@H](C5)C[C@@H](C4)C6	12	7.155	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)Cc4ccccc4	13	7.682	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)C4CCCC4	14	7.815	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)C4CCCCC4	15	8.009	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)C4CCCCCC4	16	8.000	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	17	6.554	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]3CCN(C3)[C@@H]([C@@H]45)[C@H]6C[C@@H](C5)C[C@@H](C4)C6	18	7.670	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3Cc4ccccc4	19	6.654	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCC4	20	6.818	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCCC4	21	7.292	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCCCC4	22	6.833	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3C4CCCCCC4	23	7.357	187

c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3[C@@H]([C@@H]45)[C@@H](CCC5)CCC4	24	6.573	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@@H]3CCCN3[C@@H]([C@@H]45)[C@H]6C[C@@H](C5)C[C@@H](C4)C6	25	6.851	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3Cc4ccccc4	26	6.684	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCC4	27	7.022	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCCC4	28	7.456	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCCCC4	29	7.602	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3C4CCCCCC4	30	7.244	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)NC[C@H]3CCCN3[C@@H]([C@@H]45)[C@H]6C[C@@H](C5)C[C@@H](C4)C6	31	6.499	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]([C@H]34)[C@@H](CCC3)CN(C4) C5CCCCC5	32	8.319	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]([C@H]34)[C@@H](CCC3)CN(C4) C5CCCCCC5	33	8.102	187
c1cccc(c12)c(Br)cc(c2OC)C(=O)N[C@@H]([C@H]34)[C@@H](CCC3)CN(C4)C c5ccccc5	37	6.602	187
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.770	187
c1ccc(OC)c(OC)c1-c([nH]2)ncc2CNC3CCN(CC3)Cc4ccccc4	5c	6.854	188
c1ccccc1CC2CCN(CC2)Cc3cnc([nH]3)-c4c(OC)c(OC)cc(Br)c4	5m	6.947	188
c1ccccc1C2CCN(CC2)Cc3cnc([nH]3)-c4c(OC)c(OC)cc(Br)c4	5l	6.385	188
c1ccccc1CN(CC2)CCC2c(on3)nc3-c4c(OC)c(OC)ccc4	7d	6.600	188
c1c(I)cc(OC)c(OC)c1C(=O)N[C@@H]([C@H]23)[C@@H](CCC2)CN(C3)C c4ccccc4	IABN	6.377	188
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.545	57
c1sccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	2	6.473	57
s1cccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	1	6.406	57
c1cccc(c12)cccc2CC(=O)NC3CCN(CC3)Cc4ccccc4	7	7.404	57
c1cccc(c12)cccc2NC(=O)NC3CCN(CC3)Cc4ccccc4	8	7.602	57
c1cccc(c12)ccc(c2)CC(=O)NC3CCN(CC3)Cc4ccccc4	9	6.952	57
c1cc(I)ccc1CC(=O)NC2CCN(CC2)Cc3ccccc3	16	7.212	57
c1c(Br)ccc(c12)[nH]cc2CC(=O)NC3CCN(CC3)Cc4ccccc4	11	6.169	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3c(F)cccc3	17	6.166	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	19	7.081	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3c(I)cccc3	20	6.200	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	21	6.719	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	22	6.159	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(cc3C(F)(F)F)ccc3	24	6.290	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(cc3)ccc3C(F)(F)F	25	6.522	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3ccc([N+]([O-])=O)cc3	26	6.496	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3cc(Cl)c(Cl)cc3	27	6.373	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc3cc(F)c(F)cc3	28	6.635	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(c3)ccc(c34)OCO4	29	6.766	57
c1ccccc1CC(=O)NC2CCN(CC2)Cc(c3)ccc(c34)cccc4	30	6.722	57
c1ccccc1CC(=O)NC2CCN(CC2)CCc3ccccc3	31	6.971	57
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	32	6.855	57
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	33	6.742	57
c1cccc(F)c1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	34	6.634	57
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	35	7.508	57
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	36	7.299	57
c1ccc(F)cc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	37	6.776	57
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	38	8.028	57
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	39	7.518	57
c1ccc(Cl)cc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	40	6.591	57
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3ccc(F)cc3	41	8.218	57
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3cc(I)ccc3	42	7.227	57
c1ccc(Br)cc1CC(=O)NC2CCN(CC2)Cc3ccc(I)cc3	43	7.044	57
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.240	189
c1ccccc1C[C@H]2CN[C@H](C)Cc(c23)cccc3	14a	5.512	189
c1cccc(c12)C[C@@H](CC)NC[C@@H]2Cc3ccccc3	14b	5.988	189
c1cccc(c12)C[C@@H](CCCC)NC[C@@H]2Cc3ccccc3	14c	6.110	189
c1ccccc1C[C@H]2CN[C@H](c3ccccc3)Cc(c24)cccc4	14d	5.633	189
c1ccccc1C[C@@H]2CN[C@@H](C)Cc(c23)cccc3	ent-14a	5.986	189
c1cccc(c12)C[C@H](CC)NC[C@H]2Cc3ccccc3	ent-14b	6.688	189
c1cccc(c12)C[C@H](CCCC)NC[C@H]2Cc3ccccc3	ent-14c	7.387	189
c1ccccc1C[C@@H]2CN[C@@H](c3ccccc3)Cc(c24)cccc4	ent-14d	6.553	189
C[C@H](C1)NCCc(c12)cccc2	12a	5.515	190
CC[C@H](C1)NCCc(c12)cccc2	12b	5.983	190
CCCC[C@H](C1)NCCc(c12)cccc2	12c	5.519	190
CCCC[C@@H](C1)NCCc(c12)cccc2	ent-12c	5.686	190
c1cccc(c12)CCN[C@@H](C2)c3ccccc3	12d	6.210	190

c1cccc(c12)CCN[C@H](C2)c3ccccc3	ent-12d	6.370	190
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.695	192
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.107	192
c1cc(I)ccc1C(=O)NC2CCN(CC2)Cc3ccccc3	4-IBP	7.599	194
c1ccc(I)cc1C(=O)NC2CCN(CC2)Cc3ccccc3	3-IBP	7.073	194
c1cccc(I)c1C(=O)NC2CCN(CC2)Cc3ccccc3	2-IBP	7.529	194
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OCF	FM-SA4503	6.602	288
CN(C)[C@H]([C@H]1O2)CC[C@H]2Cc(c13)cccc3	12	5.538	289
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.662	200
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	ibogaine	7.044	200
c1ccccc1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-Vesamicol	7.462	201
c1cc(F)ccc1CN(C2)CC[C@@H](O)[C@@H]2N(CC3)CCC3c4ccccc4	(+)-FBT	7.445	201
c1cc(F)ccc1CN(C2)CC[C@H](O)[C@H]2N(CC3)CCC3c4ccccc4	(-)-FBT	6.960	201
c1ccccc1C(c2ccccc2)O[C@@H](C3)C[C@@H](N4C)CC[C@H]34	Benztropine	7.458	202
Clc1c(Cl)ccc(c1)NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6a	6.676	203
Clc1c(Cl)ccc(c1)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3a	7.548	203
COc(c(Cl)c1)cc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3b	8.137	203
c1cc(Cl)cc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3c	7.996	203
c1ccc(Br)cc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3d	7.821	203
c1cc(Br)ccc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3e	8.538	203
Cc1c(C)cccc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3f	7.821	203
c1cc(C)cc(c1C)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3g	7.836	203
CCc1ccc(cc1)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3h	7.917	203
Cc1cc(c(cc1)OC)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3i	8.495	203
[O-][N+](=O)c(c1)ccc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3C c4ccccc4	3j	8.268	203
c1cc([N+]([O-])=O)cc(c1C)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3C c4ccccc4	3n	8.509	203
CCCCc1ccc(cc1)NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3l	7.963	203
c1ccc(SC)cc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3m	7.652	203
c1cccc(Br)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3o	7.529	203
COc(cc1)ccc1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3Cc4ccccc4	3p	7.415	203
Clc1c(Cl)ccc(c1)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4a	7.060	203
COc(c(Cl)c1)cc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3C c4ccccc4	4b	7.640	203
c1cc(O)cc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4c	7.197	203
c1ccc(Br)cc1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4d	7.963	203
c1cc(Br)ccc1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4e	7.963	203
Cc1c(C)cccc1NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4f	8.310	203
c1cc(C)cc(c1C)NC(=O)O[C@@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4g	8.119	203
CCc1ccc(cc1)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4h	7.836	203
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4i	8.509	203
[O-][N+](=O)c(c1)ccc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3C c4ccccc4	4j	7.777	203
c1cc([N+]([O-])=O)cc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3C [c4ccccc4	4k	8.260	203
CCCCc1ccc(cc1)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4l	7.578	203
c1ccc(SC)cc1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4m	8.076	203
[O-][N+](=O)c1cccc(c1C)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3C c4ccccc4	4n	7.721	203
COc(c1)ccc(OC)c1NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3C c4ccccc4	4o	7.572	203
CC(C)c(cc1)cc(c1CC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	4p	8.229	203
COc(c1)ccc(OC)c1NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6e	6.219	203
c1ccc(Br)cc1NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6c	6.993	203
Brc1cccc(c1OC)NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6f	6.820	203
c1cc(Br)ccc1NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6d	6.395	203
COc(c(Cl)c1)cc(OC)c1NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3C c4ccccc4	6h	6.362	203
c1c(Cl)ccc(OC)c1NC(=O)N[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	6i	6.191	203
c1cc([N+]([O-])=O)cc(OC)c1NC(=O)O[C@@H](C2)C[C@H](CC[C@H]23)N3C c4ccccc4	3k	8.699	203
COc(c1)c(OC)cc(c12)CN(CC2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6b	6.337	204
CCN(CC)Cc1ccc([nH]1)-c2c(OC)c(OC)cc(Br)c2	6g	6.152	204
c1ccccc1CN(Cc2ccccc2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6h	6.544	204
C1CCCCN1Cc2ccc([nH]2)-c3c(OC)c(OC)cc(Br)c3	6i	6.291	204
c1ccccc1C2CCN(CC2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6j	6.660	204
c1ccccc1CC2CCN(CC2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6k	6.453	204

c1cccc(c12)CN(C2)Cc3ccc([nH]3)-c4c(OC)c(OC)cc(Br)c4	6q	6.513	204
COc(c1)c(OC)cc(c12)CN(CC2)Cc3ccc([nH]3)-c(c4OC)cc(Br)c(c45)cccc5	11a	7.585	204
c1cccc(c12)CN(C2)Cc3ccc([nH]3)-c(c4OC)cc(Br)c(c45)cccc5	11d	7.060	204
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	1b	7.523	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccccc4	2a	8.921	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCc4ccccc4	3	8.699	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCc4ccccc4	4	8.538	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCC c4ccccc4	5	8.745	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCCC c4ccccc4	6	8.119	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCCCC-CCc4ccccc4	7	8.119	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(F)cc4	2b	8.229	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(I)cc4	2c	6.851	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(C)cc4	2d	7.081	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc([N+]([O-])=O)cc4	2e	7.939	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(N)cc4	2f	8.301	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4c(F)cccc4	1c	6.686	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4cc(F)ccc4	1d	6.498	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(I)cc4	1e	7.514	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4cc(I)ccc4	1g	7.293	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc(C)cc4	1h	7.810	98
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccc([N+]([O-])=O)cc4	1i	7.599	98
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCN(CC3)Cc(c34)cccc4	11a	7.321	205
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCN(CC3)Cc(c34)cc(OC)c(c4)OC	11b	7.674	205
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	12	7.754	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCN(CC2)Cc(c23)cccc3	13a	6.145	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	13b	7.785	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	14	8.086	205
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)CCC2c(c3Cl)cccc3Cl	15	7.125	205
c1cccc(c12)c(Br)cc(c2OC)C(=O)NCCCCN(CC3)CCC3c(c4Cl)cccc4Cl	16	7.578	205
c1c(Br)ccc(OC)c1C(=O)NCCN(CC2)Cc(c23)cccc3	17	7.049	205
c1c(Br)ccc(OC)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	18	7.907	205
Cc(c1)ccc(OC)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	19	7.876	205
Cc(c1)ccc(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	20	7.987	205
c1cc(F)ccc1CN(CC2)CCC23c4c(C(=O)O3)cccc4	2c	5.717	206
c1cc(F)ccc1CN(CC2)CCC23c4c(CO3)cccc4	2d	6.883	206
c1ccccc1CN(CC2)CCC23c4c(CC(=O)O3)cccc4	18	5.937	208
c1ccccc1CN(CC2)CCC23c4c(C=CO3)cccc4	19	6.520	208
c1ccccc1CN(CC2)CCC23c4c(CCO3)cccc4	20	7.001	208
c1ccccc1CN(CC2)CCC23c4c(C(=O)O3)cccc4	25	5.836	208
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.194	208
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.466	208
c1ccccc1CN(C)CCCc2cn(c(c23)cccc3)-c4ccc(F)cc4	1a	6.352	290
c1ccc(Cl)cc1CN(C)CCCc2cn(c(c23)cccc3)-c4ccc(F)cc4	1c	6.908	290
c1cc(C)cc(C)c1CN(C)CCCc2cn(c(c23)cccc3)-c4ccc(F)cc4	1l	7.329	290
c1ccccc1CN(C)CCCCc2cn(c(c23)cccc3)-c4ccc(F)cc4	2a	7.239	290
c1ccc(Cl)cc1CN(C)CCCCc2cn(c(c23)cccc3)-c4ccc(F)cc4	2c	7.592	290
c1cc(F)ccc1-n(c(c23)cccc3)cc2CCCCN(C)Cc4c(C)cc(C)cc4	2l	8.229	290
c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c5ccc(cc5)OC	3b	6.033	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c(cc5)ccc5C	3c	5.796	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)c(sc4)-c5cccc(c56)cccc6	3f	7.292	220
c1ccccc1CN(CC2)CCC23c4c(CCO3)csc4	5	6.638	220
c1ccccc1CN(CC2)CCC23c4c(C=CO3)csc4	14	7.073	220
Cn1c(=O)sc(c12)cc(cc2)CCN(CC3)CCC3Cc4ccccc4	8	8.301	222
Cn1c(=O)sc(c12)cc(cc2)CCN3CCN(CC3)Cc4ccccc4	10	8.523	222
Cn1c(=O)sc(c12)cc(cc2)CCN3CCN(CC3)Cc4c(Cl)cc(Cl)cc4	12	8.097	222
Cn1c(=O)sc(c12)cc(cc2)CCN3CCN(CC3)Cc4cc(Cl)c(Cl)cc4	14	8.301	222
C[C@@H]1CN(C[C@H](C)N1)CCc(cc2)cc(c23)sc(=O)n3C	16	5.699	222
Cn1c(=O)sc(c12)cc(cc2)CCCCN(CC3)CCC3c4ccccc4	7	8.523	222
Cn1c(=O)sc(c12)cc(cc2)CCCCN(CC3)CCC3Cc4ccccc4	9	8.301	222
Cn1c(=O)sc(c12)cc(cc2)CCCCN3CCN(CC3)Cc4c(Cl)cc(Cl)cc4	13	8.046	222
C[C@@H]1CN(C[C@H](C)N1)CCCCc(cc2)cc(c23)sc(=O)n3C	17	7.000	222
Cn1c(=O)sc(c12)cc(cc2)CCN(CC3)CCC3c4ccccc4	6	8.699	222
Cn1c(=O)sc(c12)cc(cc2)CCCCN3CCN(CC3)Cc4ccccc4	11	8.699	222
Cn1c(=O)sc(c12)cc(cc2)CCCCN3CCN(CC3)Cc4cc(Cl)c(Cl)cc4	15	8.699	222
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.377	225

c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.446	226
c1cccc(O)c1C(=O)CCCCCN2CCN(CC2)c3noc(c34)cccc4	40	6.740	227
c1cccc(OC)c1C(=O)CCCCCN2CCN(CC2)c3noc(c34)cccc4	43	6.833	227
c1cc(F)ccc1C(=O)NCCN(CC)CC	F-FBZA	3.921	231
CN(C)C/C=C(\C)c(c1)ccc(c12)cc(cc2)OC	2a	6.151	291
COc(cc1)cc(c12)ccc(c2)C(\C)=C\CN(C)Cc3ccccc3	2b	6.246	291
C1CCCCN1C/C=C(\C)c(c2)ccc(c23)cc(cc3)OC	2c	6.866	291
c1ccccc1-c(cc2)ccc2C(\C)=C\CN(C)Cc3ccccc3	2d	6.510	291
c1ccccc1CN(CC2)CCC23c4c(C=CO3)n(nc4)-c5ccccc5	26	6.254	237
c1ccccc1CN(CC2)CCC23c4c(C=CO3)n(C)nc4	27	6.368	237
c1ccccc1Cn(nc2)c(CCO3)c2C34CCN(CC4)Cc5ccccc5	28a	6.112	237
c1ccccc1CCCN(CC2)CCC23c4c(CCO3)n(nc4)Cc5ccccc5	28c	6.991	237
c1ccccc1Cn(nc2)c(CCO3)c2C34CCN(CC4)CC5CCCCC5	28d	7.367	237
CC(C)CCN(CC1)CCC12c3c(CCO2)n(nc3)Cc4ccccc4	28e	7.081	237
CC(C)=CCN(CC1)CCC12c3c(CCO2)n(nc3)Cc4ccccc4	28f	6.570	237
c1ccccc1CN(CC2)CCC23c4c(CCO3)n(C)nc4	29a	6.719	237
c1cccc(I)c1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-oIV	6.256	292
c1cccc(I)c1C2CCN(CC2)[C@@H]3[C@@H](O)CCCC3	(+)-oIV	6.703	292
c1ccc(I)cc1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-mIV	7.368	292
c1ccc(I)cc1C2CCN(CC2)[C@@H]3[C@@H](O)CCCC3	(+)-mIV	7.398	292
c1cc(I)ccc1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-pIV	7.638	292
c1ccccc1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-Vesamicol	6.376	292
c1ccccc1C2CCN(CC2)[C@@H]3[C@@H](O)CCCC3	(+)-Vesamicol	6.445	292
c1cc(I)ccc1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-pIV	7.551	293
c1cc(I)ccc1C2CCN(CC2)[C@@H]3[C@@H](O)CCCC3	(+)-pIV	7.690	293
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	5.572	293
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.648	293
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	6.959	293
c1ccccc1C2CCN(CC2)[C@@H]3[C@@H](O)CCCC3	(+)-Vesamicol	6.481	294
c1ccccc1C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-Vesamicol	6.461	294
c1cccc(c1C)C2CCN(CC2)[C@@H]3[C@@H](O)CCCC3	(+)-OMV	6.662	294
c1cccc(c1C)C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-OMV	6.575	294
Cc1ccc(cc1)C2CCN(CC2)[C@@H]3[C@@H](O)CCCC3	(+)-PMV	7.390	294
Cc1ccc(cc1)C2CCN(CC2)[C@H]3[C@H](O)CCCC3	(-)-PMV	7.373	294
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	5.607	294
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.684	294
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	6.777	294
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OC	SA4503	6.616	294
c1cc(F)ccc1C(=O)CCCN(CC2)CC[Si]2(O)c3ccc(Cl)cc3	sila-haloperidol	6.510	238
c1cc(O)ccc1[C@H](O)[C@H](C)N(CC2)CCC2Cc3ccccc3	1	7.007	295
Cc(c1)ccc(OCCF)c1C(=O)NCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3a	6.991	239
c1c(Br)cc(OC)c(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3b	6.413	239
Cc(c1)ccc(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3c	8.158	239
c1c(Br)ccc(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3d	9.187	239
c1c(I)ccc(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3e	8.975	239
c1c(I)cc(OC)c(OCCF)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	3f	9.585	239
c1cc(F)ccc1C(=O)C2CCN(CC2)[C@@H](C3)[C@@H](O)Cc(c34)cccc4	(-)-9e	6.496	240
c1cc(F)ccc1C(=O)C2CCN(CC2)[C@H](C3)[C@H](O)Cc(c34)cccc4	(+)-9e	6.556	240
FCCOc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OCCF)cccc3	20c	6.100	241
FCCOCCOCCOc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	18c	5.951	241
FCCOc(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OC)cccc3	18a	6.180	241
CN(C)c(cc1)ccc1C(=O)NCCCCN2CCN(CC2)c3c(OCCF)cccc3	20a	6.187	241
c1sccc1-c(cc2)ccc2C(=O)NCCCCN3CCN(CC3)c4c(OCCF)cccc4	20e	5.225	241
FCCc(cc1)ccc1C(=O)NC/C=C/CN2CCN(CC2)c3c(OCCF)cccc3	21b	5.695	241
c1sccc1-c(cc2)ccc2C(=O)NC/C=C/CN3CCN(CC3)c4c(OCCF)cccc4	21e	5.879	241
c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Cl)cc4	2	5.742	244
c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	7	5.671	244
c1cc(Cl)ccc1C2(O)CCN(CC2)Cc3c[nH]c(c34)cccc4OC	5	5.904	244
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Cl)cc4	6	5.721	244
c1cc(Br)ccc1C2(O)CCN(CC2)Cc3c[nH]c(c34)cccc4OC	8	6.025	244
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	9	5.568	244
c1cccc(c12)[nH]cc2CN(CC3)CCC3c4ccccc4	17	5.862	244
c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(cc4)SC	20	6.054	244
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.616	246
c1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(I)cc4	5	5.658	246
c1cc(I)ccc1C2(O)CCN(CC2)Cc3c[nH]c(c34)cccc4OC	6	6.013	246
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(I)cc4	7	5.487	246
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccccc4	8	5.559	246

FCCOc1cccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	9	5.022	246
FCCOc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	10	4.982	246
COc1cccc(c12)[nH]cc2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	11	4.792	246
COc(c1)ccc(c12)[nH]cc2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	12	4.565	246
c1ccnc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(Br)cc4	13	8.721	246
c1ccnc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(I)cc4	14	8.257	246
c1ccnc(c12)[nH]cc2CN(CC3)CCC3(O)c4ccc(cc4)SC	15	8.111	246
c1cccc(c12)oc(c2)CN(CC3)CCC3(O)c4ccc(Br)cc4	18	5.854	246
c1cccc(c12)oc(c2)CN(CC3)CCC3(O)c4ccc(I)cc4	19	5.626	246
c1cccc(c12)sc(c2)CN(CC3)CCC3(O)c4ccc(Br)cc4	20	5.707	246
c1cccc(c12)occ2CN(CC3)CCC3(O)c4ccc(Br)cc4	21	6.424	246
c1cccc(c12)occ2CN(CC3)CCC3(O)c4ccc(I)cc4	22	6.406	246
c1cccc(c12)occ2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	23	4.743	246
c1cccc(c12)scc2CN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	24	4.836	246
c1cccc(c12)occ2CN(CC3)CCC34C(=O)N(C)CN4c5ccccc5	25	4.604	246
c1ccccc1N2CN(CCF)C(=O)C23CCN(CC3)Cc4coc(c45)cccc5	26	4.993	246
c1cccc(c12)scc2CN(CC3)CCC34C(=O)N(C)CN4c5ccccc5	27	4.694	246
c1ccccc1N2CN(Cc3cn(nn3)CCF)C(=O)C24CCN(CC4)Cc5coc(c56)cccc6	29	4.657	246
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC3(O)c4ccc(Cl)cc4	2	5.083	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC3n4c(=O)[nH]c(c45)cccc5	3	4.439	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC3n4c(=O)[nH]c(c45)cc(Cl)cc5	4	4.772	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN(CC3)CCC34C(=O)NCN4c5ccccc5	5	4.700	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OC)cccc4	6	6.223	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OCCF)cccc4	7	5.302	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4ccc(cc4)OC	8	6.177	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OC)cc(cc4)OC	9	5.476	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCN3CCN(CC3)c(cc4)c(OC)cc4C	10	5.194	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OC)cccc4	11	5.883	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCCN3CCN(CC3)c4c(OCCF)cccc4	12	5.305	247
C1CC(=O)Nc(c12)cc(cc2)OCCCN3CCN(CC3)c4c(OC)cccc4	13	5.720	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCN3CCN(CC3)c4c(OC)cccc4	14	5.547	247
C1CC(=O)Nc(c12)cc(cc2)OCCCCCN3CCN(CC3)c4c(OC)cccc4	15	6.636	247
c1cc(=O)[nH]c(c12)cc(cc2)OCCCCCN3CCN(CC3)c4c(OC)cccc4	16	6.216	247
c1ccccc1CCN(C[C@@H]2CCCO)CCN2Cc3ccccc3	15	5.924	248
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@H]2N(C)C	19a	6.452	249
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@@H]2N(C)C	19b	5.854	249
c1cc(Cl)c(Cl)cc1CC(=O)N[C@@H]2CC[C@@H](CN3C)N(C[C@H]23)Cc4ccccc4	22a	5.955	249
c1cc(Cl)c(Cl)cc1CC(=O)N[C@H]2CC[C@@H](CN3C)N(C[C@H]23)Cc4ccccc4	22b	6.580	249
O[C@@H]1CC[C@@H](CN2C)N(C[C@H]12)Cc3ccccc3	8a(2R)	5.379	250
O[C@H]1CC[C@@H](CN2C)N(C[C@H]12)Cc3ccccc3	8a(2S)	5.539	250
c1ccccc1CCN2C[C@H](CC[C@H]3O)N(C[C@@H]23)Cc4ccccc4	8c(2R)	6.231	250
c1ccccc1CCN2C[C@H](CC[C@@H]3O)N(C[C@@H]23)Cc4ccccc4	8c(2S)	6.465	250
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@H]2OC	12a(2R)	6.485	250
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CC[C@H]2OCc4ccccc4	13a(2R)	7.517	250
c1ccccc1CN(C[C@H]23)[C@H](CN3C)CCC2(OC)OC	15a	5.738	250
c1cc(Cl)c(Cl)cc1CC(=O)NCC[C@@H]2C[C@@H](C[C@@H](O2)OC)NCc3ccccc3	22beta	5.599	251
c1ccccc1CC(=O)NCC[C@@H]2C[C@H](C[C@H](O2)OC)NCc3ccccc3	29alpha	5.213	251
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@@H]3Cc4ccccc4	(1R)-14a	8.013	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@H]3Cc4ccccc4	(1S)-14a	7.886	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@@H]3CCc4ccccc4	(1R)-14b	8.444	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@H]3CCc4ccccc4	(1S)-14b	7.456	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@H]3Cc4c(C)cccc4	(1S)-14c	7.538	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@@H]3Cc4ccc(cc4)OC	(1R)-14d	7.824	252
c1ccccc1[C@H](CO)N(CCc(c23)cccc2)C[C@H]3Cc4ccc(cc4)OC	(1S)-14d	8.602	252
c1ccccc1[C@H](CO)N(C[C@@H]2C)CCc(c23)cccc3	(1R)-14e	8.229	252
c1ccccc1C[C@H]2CNCCc(c23)cccc3	(1R)-15a	8.394	252
c1ccccc1C[C@@H]2CNCCc(c23)cccc3	(1S)-15a	8.237	252
c1ccccc1CC[C@H]2CNCCc(c23)cccc3	(1R)-15b	8.959	252
c1ccccc1CC[C@@H]2CNCCc(c23)cccc3	(1S)-15b	8.377	252
c1ccccc(C)c1C[C@H]2CNCCc(c23)cccc3	(1R)-15c	8.284	252
c1ccccc(C)c1C[C@@H]2CNCCc(c23)cccc3	(1S)-15c	8.553	252
COc(cc1)ccc1C[C@H]2CNCCc(c23)cccc3	(1R)-15d	8.102	252
COc(cc1)ccc1C[C@@H]2CNCCc(c23)cccc3	(1S)-15d	8.155	252
C[C@H]1CNCCc(c12)cccc2	(1R)-15e	8.000	252
C[C@@H]1CNCCc(c12)cccc2	(1S)-15e	7.699	252
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3Cc4ccccc4	1a	8.314	296
Cc1cc(c(cc1)OC)NC(=O)O[C@H](C[C@H]23)C[C@@H](CCC2)N3CCc4ccc(N)cc4	2f	8.785	296
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.557	296

c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	7.326	296
c1cc(O)ccc1[C@@H](O)[C@@H](C)N(CC2)CCC2Cc3ccccc3	Ifenprodil	8.569	296
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-Pentazocine	5.842	296
[C@@H]12CC[C@H](N2C)C[C@H](C1)OC(=O)c3c[nH]c(c34)cccc4	3-Tropanylindole-3-carboxylate	5.413	296
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	Dextromethorphan	5.543	296
c1cccc(c12)n(C)cc2C(=O)OCC3CCN(CC3)CCNS(=O)(=O)C	GR113808	6.863	296
CN(C)CCCc(c(O)cc1)cc1C(=O)Nc(cc2)ccc2-c3ccncc3	GR55562	5.247	296
c1cc(F)ccc1C(=O)C2CCN(CC2)CCn(c3=O)c(=O)[nH]c(c34)cccc4	Ketanserin	5.627	296
c1c(Cl)cc(Cl)cc1C(=O)O[C@@H](C2)C[C@@H](N3C)CC[C@H]23	MDL72222	7.932	296
CC(C)NC[C@H](O)COc1cccc(c12)[nH]cc2	Pindolol	5.706	296
C1CCCCC1C(=O)N(c2ccccn2)CCN3CCN(CC3)c4c(OC)cccc4	Way100635	5.442	296
Cc(c1)ccc(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	RHM-1	8.220	296
c1cccc(c12)[nH]cc2CN3CCN(CC3)c4ccc(F)cc4	1a	6.180	254
c1cccc(c12)[nH]cc2CN3CCN(CC3)c4c(F)ccc(F)c4	1b	6.379	254
c1cccc(c12)[nH]cc2CN3CCN(CC3)c(c4)ccc(Cl)c4Cl	1c	6.886	254
c1cc(F)ccc1N(CC2)CCN2Cc3cn(c(c34)cccc4)CN5CCN(CC5)c6ccc(F)cc6	2a	6.000	254
c1ccccc1CCN2CCN(CC2)Cn(cc3C)c(c34)cccc4	3b	7.253	254
c1cccc(c12)n(cc2)CCCN3CCN(CC3)c4ccc(F)cc4	4a	7.699	254
c1cccc(c12)n(cc2)CCCN3CCN(CC3)c4c(F)cccc4	4b	8.004	254
c1cccc(c12)n(cc2)CCCN3CCN(CC3)c4ccccc4	4c	7.125	254
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	d-pentazocine	6.485	297
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	6.886	297
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	6.629	297
c1ccccc1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1a	6.609	297
c1cccc(Cl)c1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1b	6.524	297
c1cc(Cl)ccc1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1c	6.370	297
c1cc(Cl)cc(Cl)c1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1d	6.418	297
c1cccc(F)c1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1e	6.672	297
c1cc(C)ccc1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1h	6.936	297
c1cccc(C)c1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1g	6.471	297
c1cc(F)ccc1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1f	6.770	297
c1cc(C)cc(C)c1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1i	6.728	297
Cc1cc(C)cc(C)c1CN(CC2)CCC2Cn3c(=O)oc(c34)cccc4	1j	5.540	297
c1cccc(c12)cccc2CN(CC3)CCC3Cn4c(=O)oc(c45)cccc5	1l	5.889	297
c1ccccc1CN(C)CCCn2c(=O)oc(c23)cccc3	2a	5.950	65
c1cccc(Cl)c1CN(C)CCCn2c(=O)oc(c23)cccc3	2b	6.341	65
c1ccc(Cl)cc1CN(C)CCCn2c(=O)oc(c23)cccc3	2c	5.951	65
c1cc(Cl)ccc1CN(C)CCCn2c(=O)oc(c23)cccc3	2d	6.341	65
c1cccc(OC)c1CN(C)CCCn2c(=O)oc(c23)cccc3	2e	6.717	65
c1ccc(OC)cc1CN(C)CCCn2c(=O)oc(c23)cccc3	2f	5.672	65
c1cccc(c12)oc(=O)n2CCCN(C)Cc3ccc(cc3)OC	2g	5.585	65
c1cccc(C)c1CN(C)CCCn2c(=O)oc(c23)cccc3	2h	5.871	65
c1ccc(C)cc1CN(C)CCCn2c(=O)oc(c23)cccc3	2i	5.566	65
c1cc(C)ccc1CN(C)CCCn2c(=O)oc(c23)cccc3	2j	6.004	65
c1cc(C)cc(C)c1CN(C)CCCn2c(=O)oc(c23)cccc3	2k	5.685	65
c1ccccc1CN(C)CCCCn2c(=O)oc(c23)cccc3	3a	6.921	65
c1cccc(Cl)c1CN(C)CCCCn2c(=O)oc(c23)cccc3	3b	7.427	65
c1cc(Cl)ccc1CN(C)CCCCn2c(=O)oc(c23)cccc3	3d	7.441	65
c1ccc(OC)cc1CN(C)CCCCn2c(=O)oc(c23)cccc3	3f	6.728	65
COc(cc1)ccc1CN(C)CCCCn2c(=O)oc(c23)cccc3	3g	7.682	65
c1ccc(C)cc1CN(C)CCCCn2c(=O)oc(c23)cccc3	3i	7.498	65
c1cc(C)ccc1CN(C)CCCCn2c(=O)oc(c23)cccc3	3j	7.640	65
c1cc(C)cc(C)c1CN(C)CCCCn2c(=O)oc(c23)cccc3	3k	8.159	65

Table F.5: Sigma 2: DTG/PTZ guinea pig brain dataset

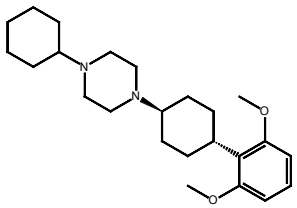
SMILES	Name	pK_i	Ref.
c1ccccc1CCCCN(CC2)CCC2Cc3ccccc3	5	8.509	100
c1ccccc1CCCCCN(CC2)CCC2Cc3ccccc3	7	8.553	100
C1CN(C)CCN1CCCCCc2ccccc2	8	7.102	100
CC1CCN(CC1)CCCCCc2ccccc2	9	8.155	100
C1CN(C)CCC1CCCCCc2ccccc2	10	7.013	100
C1CCCCN1CCCCCc2ccccc2	11	7.301	100
C1CCCCC1CCCCCc2ccc(N)cc2	12	4.264	100
C1CCCCN1CCCCCc2ccc(N)cc2	13	6.081	100
C1CCCCN1C\C=C\C=C\c(c2)ccc(c23)OCO3	14	6.256	100
C1CCCCN1CCCCCc(c2)ccc(c23)OCO3	15	7.201	100
C1CCCN1CCCCCc2ccccc2	3	7.155	101
CCN(CC)CCCCCc1ccccc1	4	7.051	101
CNCCCCCc1ccccc1	6a	5.101	101
CN(C)CCCCCc1ccccc1	6b	6.015	101
c1ccccc1CCCCCN(C)CCc2ccccc2	7	8.301	101
c1ccccc1CCCCCNCc2ccccc2	8a	7.469	101
c1ccccc1CCCCCN(C)Cc2ccccc2	8b	7.886	101
c1ccccc1CCCCCNCCc2ccccc2	9	7.824	101
c1ccccc1CCCCCNCCCc2ccccc2	10a	8.009	101
c1ccccc1CCCCCN(C)CCCc2ccccc2	10b	8.201	101
c1ccccc1CCCCCNCCCCc2ccccc2	11	7.167	101
c1ccccc1CCCN(CC2)CCC2Cc3ccccc3	21	8.481	101
N#Cc1ccc(cc1)OCC2CCN(CC2)CCCF	2	6.842	109
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(C2)Cc(c23)cc(OC)c(c3)OC	3	9.086	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)CCc(c23)cc(OC)c(c3)OC	4	6.134	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)c(c23)cc(OC)c(c3)OC	5	5.014	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CCC2)Cc(c23)cc(OC)c(c3)OC	6	6.502	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CCCC2)c(c23)cc(OC)c(c3)OC	7	5.048	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CCC2)c(c23)cc(OC)c(c3)OC	8	5.235	112
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(C)CCc2cc(OC)c(cc2)OC	9	5.672	112
c1ccccc1C[C@@H](C)NCCCc2ccccc2	5(R)	7.215	298
c1ccccc1C[C@H](C)NCCCc2ccccc2	5(S)	7.420	298
c1ccccc1C[C@@H](C)NCCCCc2ccccc2	6(R)	7.319	298
c1ccccc1C[C@H](C)NCCCCc2ccccc2	6(S)	7.444	298
c1ccccc1C[C@@H](C)NCCCCCc2ccccc2	7(R)	8.000	298
c1ccccc1C[C@H](C)NCCCCCc2ccccc2	7(S)	7.721	298
c1ccccc1CCCCCCCNCc2ccccc2	22	7.409	298
c1ccccc1CCCNCCc2ccccc2	23	7.046	298
c1ccccc1CCCCNCCc2ccccc2	24	6.921	298
c1ccccc1CCCCCCCNCCc2ccccc2	27	7.481	298
c1ccccc1CCCNCCCc2ccccc2	28	7.194	298
CCCCCNCCCc1ccccc1	32	6.620	298
CCCN(C)CCCCCc1ccccc1	33	7.398	298
CN(C)CCCCCC1CCCCC1	38	6.710	298
CNCCCCCC1CCCCC1	39	6.456	298
FC(F)(F)c1cc(ccc1)CCN(C)CCCCCc2ccccc2	41	7.854	298
FC(F)(F)c1cc(ccc1)CCCCCN(C)CCc2ccccc2	42	8.444	298
c1ccc(C(F)(F)F)cc1C(=O)CCCCN(C)CCc2ccccc2	43	8.886	298
c1ccccc1C(=O)CCCCN(CC)CC	46	6.125	298
c1ccccc1C(=O)CCCCN(CC2)CCC2c3ccccc3	57	8.509	298
c1ccc(Cl)cc1C(=O)CCCCN2CCCCC2	58	7.481	298
c1ccc(Cl)cc1C(=O)CCCCN(CC2)CCC2c3ccccc3	59	8.796	298
c1cc(Cl)ccc1C(=O)CCCCN2CCCCC2	60	7.602	298
c1cc(Cl)ccc1C(=O)CCCCN(CC2)CCC2c3ccccc3	61	9.000	298
c1cc(Cl)ccc1CCCCCN(CC2)CCC2c3ccccc3	62	8.678	298
c1ccccc1C(=O)C2CCN(CC2)CCCCc3ccccc3	65	7.959	298
c1ccccc1C(c2ccccc2)C3CCN(CC3)CCCCc4ccccc4	67	6.629	298
c1ccccc1CCCCCN2CCN(CC2)Cc3ccccc3	68	7.959	298
c1ccccc1CCCCN2CCN(CC2)Cc3ccccc3	69	8.086	298
c1ccccc1C(=O)N2CCN(CC2)CCCCc3ccccc3	72	6.015	298
c1cccc(c12)C(=O)N(C2=O)CCCN(CC3)CCC3Cc4ccccc4	80	7.886	298
c1cccc(c12)C(=O)N(C2=O)CCCN3CCN(CC3)Cc4ccccc4	81	6.538	298
c1cccc(c12)C(=O)N(C2=O)CCCN(CC3)CCC3c4ccccc4	82	7.921	298
c1cccc(c12)C(=O)N(C2=O)CCCN3CCN(CC3)c4ccccc4	83	6.827	298
c1cccc(c12)C(=O)N(C2=O)CCCCN3CCN(CC3)c4ccccc4	84	7.699	298

c1cc(O)ccc1CCN(CC2)CCC2Cc3ccccc3	85	9.155	298
CCCN1CCN(CC1)c2ccccc2	86	6.268	298
NCCCN1CCN(CC1)c2ccccc2	87	4.870	298
c1ccccc1C(=O)NCCCN2CCN(CC2)c3ccccc3	88	6.310	298
c1cc(Cl)ccc1C(=O)NCCCN2CCN(CC2)c3ccccc3	89	7.051	298
COc(cc1)ccc1C(=O)NCCCN2CCN(CC2)c3ccccc3	90	6.190	298
c1ccccc1CNCCCN2CCN(CC2)c3ccccc3	91	7.000	298
c1ccccc1CN(C(=O)C)CCCN2CCN(CC2)c3ccccc3	92	6.730	298
O=C1CCCC(=O)N1CCCN2CCN(CC2)c3ccccc3	93	6.015	298
O=C1CCC(=O)N1CCCN2CCN(CC2)c3ccccc3	94	5.658	298
c1cc([N+]([O-])=O)ccc1C2(CCCC2)C(=O)OCCN(CC3)CCC3c4ccccc4	RLH-033	6.979	114
CCN(CC)CCOC(=O)C1(CCCC1)c2ccccc2	Caramiphen	5.790	114
c1ccccc1C2(CCCC2)C(=O)OCCOCCN(CC)CC	Carbetapentane	6.037	114
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.174	114
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	7.854	114
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)Pentazocine	5.870	114
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	(+)3-PPP	5.945	114
c1cc(O)ccc1[C@@H](O)[C@@H](C)N(CC2)CCC2Cc3ccccc3	Ifenprodil	8.967	118
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.101	118
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.399	118
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OC	SA4503	7.200	118
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OCCF	FE-SA4503	6.946	118
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-Pentazocine	6.138	118
c1cc(F)ccc1C(c2ccc(F)cc2)O[C@@H](C3)C[C@H](CC[C@H]34)N4CCc5c[nH]c(c56)cccc6	GA1-69	7.182	119
CC(C)[C@@H](N)CN1[C@@H](CC[C@@H]12)C[C@H](C2)OC(c3ccc(F)cc3)c4ccc(F)cc4	GA2-50	7.742	119
c1cc(F)ccc1C(c2ccc(F)cc2)O[C@@H](C3)C[C@H](CC[C@H]34)N4CCN	GA2-99	6.807	119
c1cc(F)ccc1C(c2ccc(F)cc2)O[C@@H](C3)C[C@H](CC[C@H]34)N4CC5CC5	JHW013	7.587	119
c1ccccc1CCCN2CCN(CC2)Cc3ccccc3	3a	7.464	34
c1ccccc1CCCN2CCN(CC2)Cc3c(Br)cccc3	3b	8.385	34
c1ccccc1CCCN2CCN(CC2)Cc3c([N+]([O-])=O)cccc3	3c	8.421	34
c1ccccc1CCCN2CCN(CC2)Cc3cc(I)ccc3	3d	8.987	34
c1ccccc1CCCN2CCN(CC2)Cc3cc(F)ccc3	3e	7.859	34
c1ccccc1CCCN2CCN(CC2)Cc3cc(OC)ccc3	3f	7.848	34
c1ccccc1CCCN2CCN(CC2)Cc3cc([N+]([O-])=O)ccc3	3g	8.799	34
c1ccccc1CCCN2CCN(CC2)Cc3ccc(cc3)OC	3h	7.484	34
c1ccccc1CCCN2CCN(CC2)Cc3ccc([N+]([O-])=O)cc3	3i	8.483	34
c1ccccc1CCCN2CCN(CC2)Cc3ccc(C)cc3	3j	7.757	34
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	8.019	34
c1ccccc1CCCN2CCN(CC2)CCc3cc(OC)c(cc3)OC	SA4503	7.048	34
c1cc([N+]([O-])=O)ccc1C(=O)NC2CCN(CC2)Cc3ccccc3	2	7.319	128
c1cccc(F)c1C(=O)NC2CCN(CC2)Cc3ccccc3	3	6.391	128
c1cc(F)ccc1C(=O)NC2CCN(CC2)Cc3ccccc3	4	6.833	128
OCCN(CC1)CCC1COc2ccc(I)cc2	3	6.857	134
N#Cc1ccc(cc1)CN(CC2)CCC2COC/C=C/I	1	7.672	135
N#Cc1ccc(cc1)OCC2CCN(CC2)C/C=C/I	2	7.411	136
c1cc(I)ccc1C(=O)OC2CCN(CC2)CCCF	4	7.138	136
N#Cc1ccc(cc1)OCC2CCN(CCF)CC2	1	6.442	137
N#Cc1ccc(cc1)OCC2CCN(CC2)Cc3ccc(F)cc3	3	8.284	137
N#Cc1ccc(cc1)OCC2CCN(CC2)Cc3c(Br)cccc3	5	7.507	137
N#Cc1ccc(cc1)OCC2CCN(CC2)Cc3c(I)cccc3	6	7.029	137
c1cc(F)ccc1CN(CC2)CCC2COc(cc3)ccc3[N+]([O-])=O	7	8.409	137
FCCN(CC1)CCC1COc2ccc(I)cc2	8	6.991	137
C1CC1CN(CC2)CCC2COc3ccc(I)cc3	10	7.932	137
N#Cc1cc(ccc1)CN(CC2)CCC2COc3ccc(I)cc3	11	7.158	137
c1cccc(c1C#N)CN(CC2)CCC2COc3ccc(I)cc3	12	6.848	137
FCCCN(CC1)CCC1COc2ccc(Br)cc2	13	7.883	137
C1CC1CN(CC2)CCC2COc3ccc(Br)cc3	14	7.866	137
C1CC1CN(CC2)CCC2COc3cc(Br)ccc3	15	8.004	137
FCCCN(CC1)CCC1COc2c(F)c(F)c(F)c(F)c2F	16	8.276	137
c1cc(F)ccc1CN(CC2)CCC2COc3c(F)c(F)c(F)c(F)c3F	17	8.367	137
c1ccc(F)cc1CN(CC2)CCC2COc3c(F)c(F)c(F)c(F)c3F	18	7.620	137
CC1CCN(CC1)CCC=C2c(cccc3)c3Sc(c24)ccccc4	5	7.585	182
c1ccccc1C(c2ccccc2)=CCCN(CC3)CCC3C	6	7.553	182
c1ccccc1C(c2ccccc2)CCCN(CC3)CCC3C	7	7.553	182
c1ccccc1C(c2ccccc2)=CCCCN(CC3)CCC3C	8	7.602	182
c1ccccc1C(c2ccccc2)CCCCN(CC3)CCC3C	9	7.770	182
CCN(CC)CCOC(=O)C(CCC)(c1ccccc1)c2ccccc2	11	5.959	182
c1ccccc1C(O)(c2ccccc2)CCCCN(CC)CC	13	6.097	182

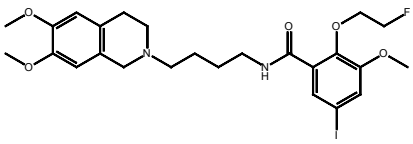
c1ccccc1C(c2ccccc2)CCCCN(CC)CC	14	7.292	182
c1ccccc1C(c2ccccc2)=CCCCN(C)CCc3ccccc3	15a	7.387	182
c1ccccc1C(c2ccccc2)=CCCCNCCc3ccccc3	15b	6.848	182
c1ccccc1C(c2ccccc2)CCCCN(C)CCc3ccccc3	16a	7.495	182
c1ccccc1C(c2ccccc2)CCCCNCCc3ccccc3	16b	7.000	182
c1ccccc1CCCCN2CCN(C)CC2	4	6.046	182
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.848	200
CC[C@H]1C[C@H](C2)CN(CC3)[C@@H]1[C@@H]2c(c3c45)[nH]c4ccc(c5)OC	ibogaine	6.602	200
c1cc(F)ccc1-c2cn(c(c23)cccc3)CCCCN(CC4)Cc(c45)cc(OC)c(c5)OC	CM353	8.349	219
c1cccc(c12)n(C)c(=O)n2CCCCN(CC3)Cc(c34)cc(OC)c(c4)OC	CM398	8.347	219
c1cccc(c12)n(C)c(=O)n2CCCCN(CC3)CCC34c5c(CO4)cccc5	CM699	8.638	219
CCCCCn1c(=O)n(c(c12)cccc2)CCCCN3CCN(CC3)c4ccc(F)cc4	CM775	8.644	219
c1cccc(c12)n(CCC)c(=O)n2CCCCN3CCN(CC3)c4ccc(F)cc4	CM777	7.719	219
NC12C[C@@H]3C[C@H](C1)C[C@H](C2)C3	amantadine	4.582	223
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	dtg	7.041	223
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	haloperidol	7.879	223
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	dextromethorphan	4.081	223
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)O	dextrorphan	4.993	223
c1cc(F)ccc1C(=O)CCCN(CC2)CCC2(O)c3ccc(Cl)cc3	Haloperidol	7.442	299
CC(C)=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-Pentazocine	6.341	299
CCCN(C1)CCC[C@@H]1c2cc(O)ccc2	R-(+)-PPP	6.355	299
c1ccccc1C2(CCCC2)C(=O)OCCOCCN(CC)CC	Carbetapentane	5.817	299
c1cc(Cl)c(Cl)cc1CCN(C)[C@H]2[C@H](CCCC2)N3CCCC3	BD738	6.726	299
c1cc(Cl)c(Cl)cc1CCN(C)[C@@H]2[C@@H](CCCC2)N3CCCC3	BD737	6.299	299
FC(F)(F)c(c1)ccc(c12)Sc3c(cccc3)N2CCCN4CCN(CC4)CCO	Fluphenazine	6.357	299
C1CCC[C@@H]2[C@@H](N(CC3)CC=C)Cc(c4[C@]123)ccc(c4)O	Dextrallorphan	5.730	299
OCCN(CC1)CCN1CCCN2c(cccc3)c3Sc(c24)ccc(Cl)c4	Perphenazine	6.368	299
c1cccc(c1C)NC(=N)Nc(c2C)cccc2	DTG	7.425	299
CCCN(C1)CCC[C@H]1c2cc(O)ccc2	S-(-)-PPP	5.811	299
C1CCC[C@@H]2[C@@H](N(CC3)CC=C)Cc(c4[C@]123)ccc(c4)OC	KCR-11-240.1	5.854	299
C=CCN(CC1)[C@H]([C@H]2C)Cc(c3[C@@]12C)ccc(c3)O	(+)-SKF10047	5.370	299
c1cc(Cl)c(Cl)cc1CC(=O)N(C)[C@@H]2[C@@H](CCCC2)N3CCCC3	BD446	5.859	299
CC(C)(C)[C@@](C1)(O)CCN([C@H]1c2c34)C[C@@H]4c5c(cccc5)CCc3ccc2	(-)-Butaclamol	5.438	299
CCN(CC)CCOC(=O)C1(CCCC1)c2ccccc2	Caramiphen	5.543	299
C1CC1CN(CC2)[C@H]([C@H]3C)Cc(c4[C@@]23C)ccc(c4)O	(+)-Cyclazocine	5.907	299
C1CCCC12CC(=O)N(C(=O)C2)CCCCN3CCN(CC3)c4ncccn4	Buspirone	6.128	299
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)OC	Dextromethorphan	4.272	299
c1cc(Cl)c(Cl)cc1CC(=O)N(C)[C@H]2[C@H](CCCC2)N3CCCC3	BD445	5.383	299
O1[C@@H]2C(=O)CC[C@@H]3[C@@H](N(CC4)CC5CC5)Cc6ccc(c1c6[C@]234)OC	KCR-12-83.1	4.739	299
O1[C@@H]2C(=O)CC[C@@H]3[C@@H](N(CC4)CC5CC5)Cc6ccc(O)c1c6[C@]234	KCR-12-84.1	4.534	299
C1CCC[C@@H]2[C@@H](N(C)CC3)Cc(c4[C@]123)ccc(c4)O	Dextrorphan	4.944	299
C1CCC[C@H]2[C@H](N(CC3)CC=C)Cc(c4[C@@]123)ccc(c4)O	Levallorphan	4.864	299
COc(c1)ccc(c1[C@@]234)C[C@H](NCC4)[C@H]2CCCC3	KCR-11-239.1	4.728	299
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc(OC)c(c3)OC	1	8.569	253
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(C2)CCc(c3)c2cc(c34)OCO4	2	7.684	253
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc4c(c3)OCCO4	3	7.664	253
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCN(CC2)Cc(c23)cc4c(c3)OCCCO4	4	7.487	253
c1c(Br)cc(OC)c(OC)c1C(=O)NCCCCNCCc2cc(OC)c(cc2)OC	5	5.336	253

APPENDIX G. SIGMA-2 TRAINING/TEST SETS

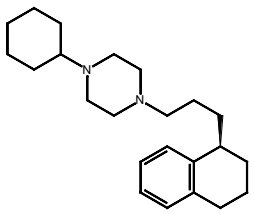
APPENDIX G. SIGMA-2 TRAINING/TEST SETS



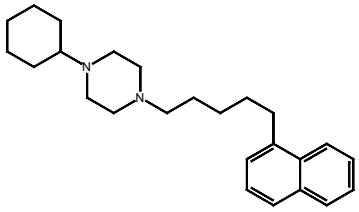
title: Abate:2011p73:trans-11
pKi: 9.678
model set: 1



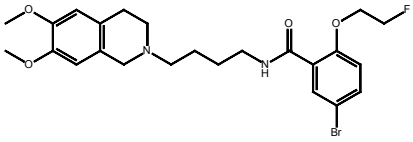
title: Tu:2007p3194:3f
pKi: 9.585
model set: 2



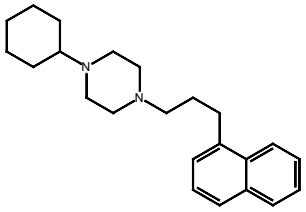
title: Berardi:2009p205:R-3
pKi: 9.31
model set: 2



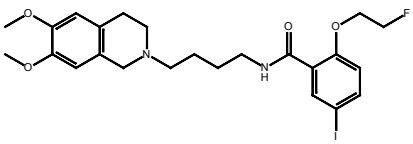
title: Berardi:2004p2308:46
pKi: 9.244
model set: 1



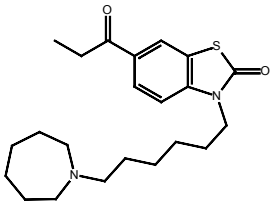
title: Tu:2007p3194:3d
pKi: 9.187
model set: 1



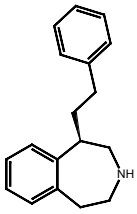
title: Berardi:2004p2308:43
pKi: 9.161
model set: 1



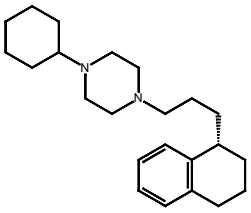
title: Tu:2007p3194:3e
pKi: 8.975
model set: 1



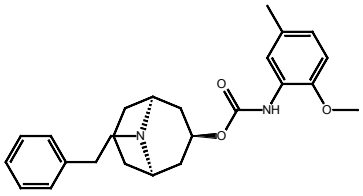
title: RB32
pKi: 8.959
model set: 1



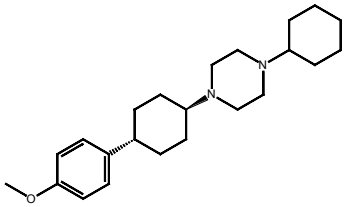
title: Wirt:2007p462:(1R)-15b
pKi: 8.959
model set: 1



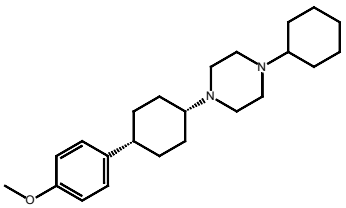
title: Berardi:2009p205:S-3
pKi: 8.928
model set: 1



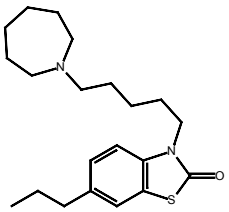
title: Mach:2003p380:2a
pKi: 8.921
model set: 1



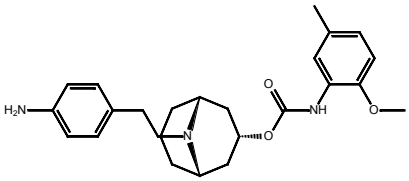
title: Abate:2011p73:trans-8
pKi: 8.917
model set: 1



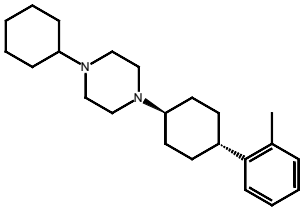
title: Abate:2011p73:cis-8
pKi: 8.799
model set: 1



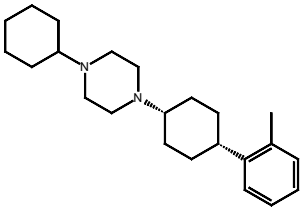
title: RB16
pKi: 8.796
model set: 1



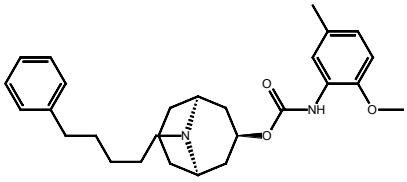
title: Xu:2005p8:2f
pKi: 8.785
model set: 2



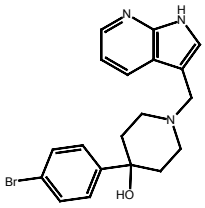
title: Abate:2011p73:trans-14
pKi: 8.783
model set: 1



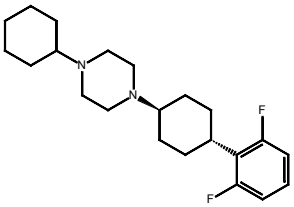
title: Abate:2011p73:cis-14
pKi: 8.78
model set: 1



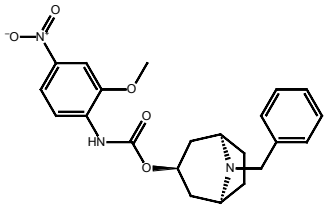
title: Mach:2003p380:5
pKi: 8.745
model set: 1



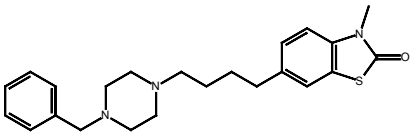
title: Vangveravong:2010p5291:13
pKi: 8.721
model set: 1



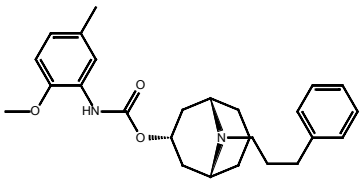
title: Abate:2011p73:trans-12
pKi: 8.714
model set: 1



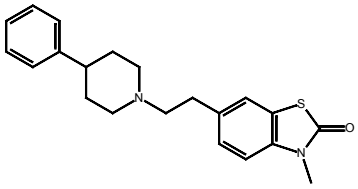
title: Mach:2001p339:3k
pKi: 8.699
model set: 1



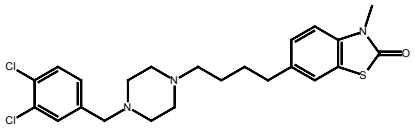
title: MouithysMickalad:2002p1149:1k
pKi: 8.699
model set: 1



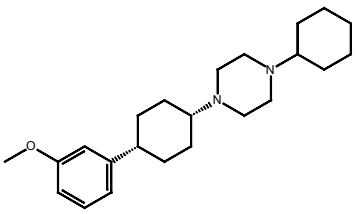
title: Mach:2003p380:3
pKi: 8.699
model set: 2



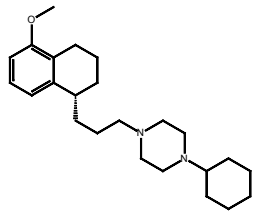
title: MouithysMickalad:2002p1149:6
pKi: 8.699
model set: 2



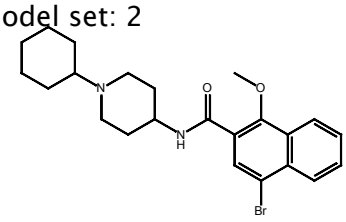
title: MouithysMickalad:2002p1149:15
pKi: 8.699
model set: 2



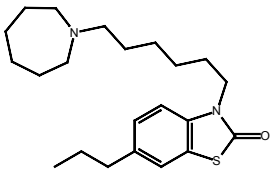
title: Abate:2011p73:cis-9
pKi: 8.688
model set: 2



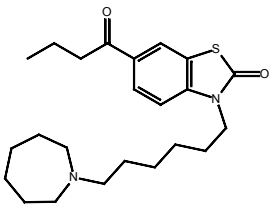
title: Berardi:2004p2308:R-33
pKi: 8.68
model set: 2



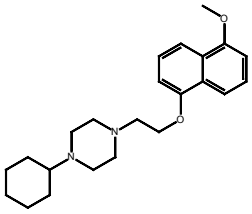
title: Huang:2001p1815:3
pKi: 8.678
model set: 1



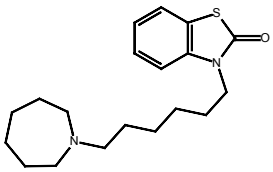
title: RB18
pKi: 8.638
model set: 1



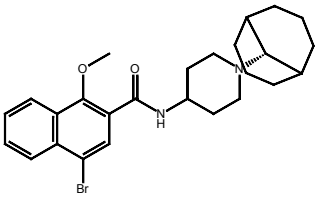
title: RB70
pKi: 8.638
model set: 2



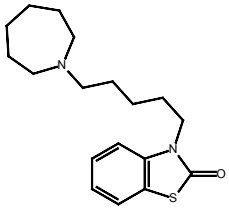
title: Abate:2011p1022:22
pKi: 8.62
model set: 1



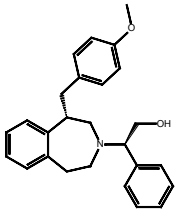
title: RB8
pKi: 8.62
model set: 1



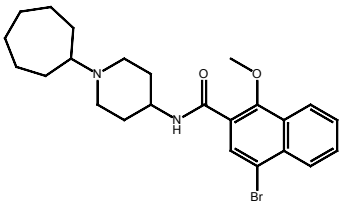
title: Huang:2001p1815:5
pKi: 8.62
model set: 1



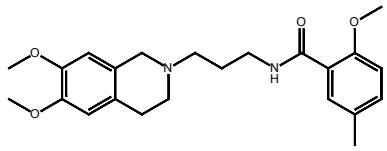
title: RB6
pKi: 8.602
model set: 1



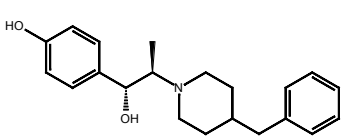
title: Wirt:2007p462:(1S)-14d
pKi: 8.602
model set: 2



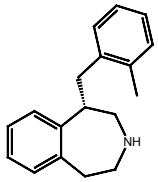
title: Huang:2001p1815:4
pKi: 8.585
model set: 1



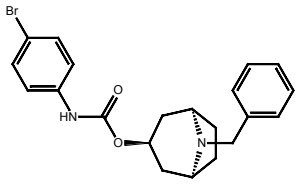
title: Abate:2011p4733:11a
pKi: 8.58
model set: 2



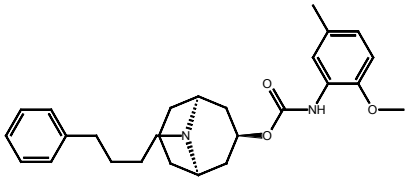
title: Xu:2005p8:Ifenprodil
pKi: 8.569
model set: 1



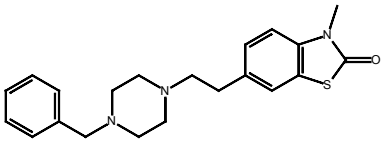
title: Wirt:2007p462:(1S)-15c
pKi: 8.553
model set: 1



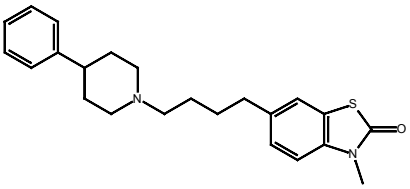
title: Mach:2001p339:3e
pKi: 8.538
model set: 1



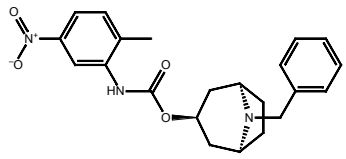
title: Mach:2003p380:4
pKi: 8.538
model set: 1



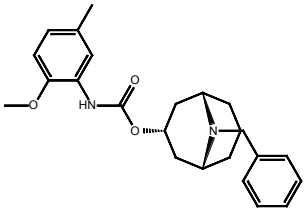
title: MouithysMickalad:2002p1149:1
pKi: 8.523
model set: 1



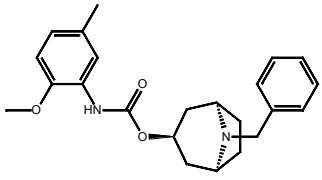
title: MouithysMickalad:2002p1149:7
pKi: 8.523
model set: 2



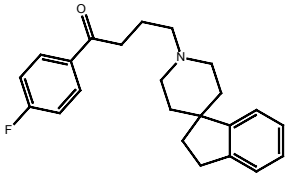
title: Mach:2001p339:3n
pKi: 8.509
model set: 1



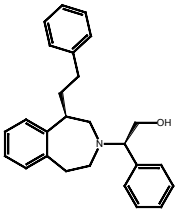
title: Mach:2001p339:4i
pKi: 8.509
model set: 2



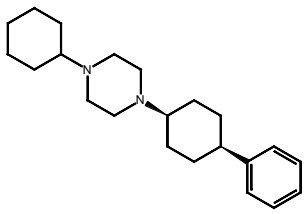
title: Mach:2001p339:3i
pKi: 8.495
model set: 2



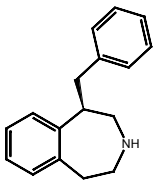
title: Efange:1997p3905:24b
pKi: 8.481
model set: 1



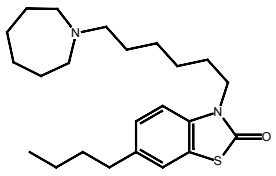
title: Wirt:2007p462:(1R)-14b
pKi: 8.444
model set: 1



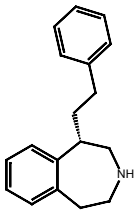
title: Abate:2011p73:cis-7
pKi: 8.437
model set: 1



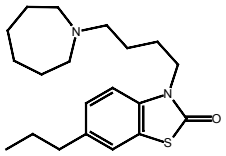
title: Wirt:2007p462:(1R)-15a
pKi: 8.394
model set: 2



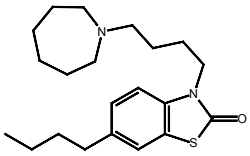
title: RB24
pKi: 8.387
model set: 2



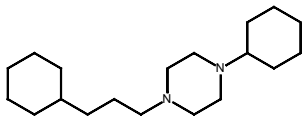
title: Wirt:2007p462:(1S)-15b
pKi: 8.377
model set: 1



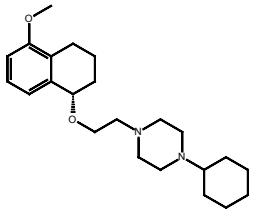
title: RB14
pKi: 8.367
model set: 2



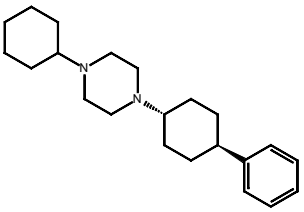
title: RB34
pKi: 8.357
model set: 1



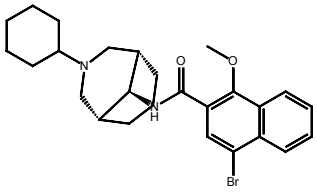
title: Abate:2009p246:12
pKi: 8.328
model set: 1



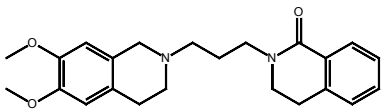
title: Abate:2011p1022:S-14
pKi: 8.327
model set: 1



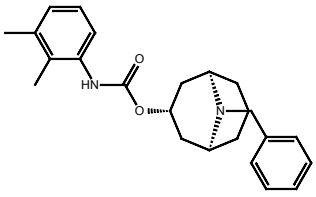
title: Abate:2011p73:trans-7
pKi: 8.321
model set: 2



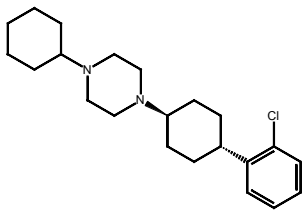
title: Huang:2001p1815:32
pKi: 8.319
model set: 2



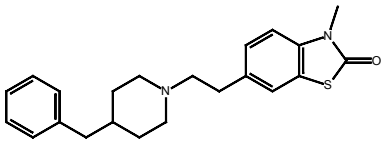
title: Abate:2011p4733:15a
pKi: 8.315
model set: 1



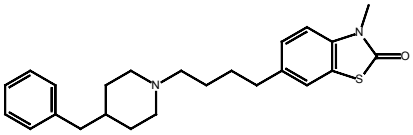
title: Mach:2001p339:4f
pKi: 8.31
model set: 1



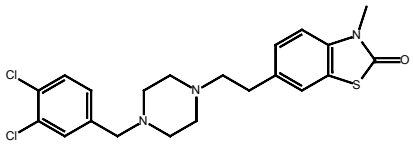
title: Abate:2011p73:trans-13
pKi: 8.305
model set: 2



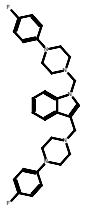
title: MouithysMickalad:2002p1149:8
pKi: 8.301
model set: 1



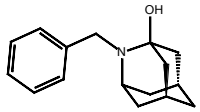
title: MouithysMickalad:2002p1149:9
pKi: 8.301
model set: 1



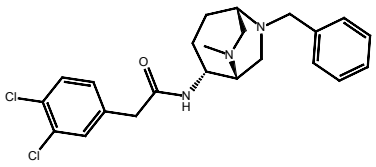
title: MouithysMickalad:2002p1149:14
pKi: 8.301
model set: 2



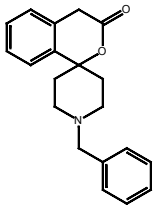
title: Yarim:2011p869:2a
pKi: 6.0
model set: 2



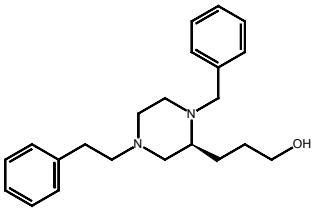
title: Banister:2011p5289:9
pKi: 5.991
model set: 1



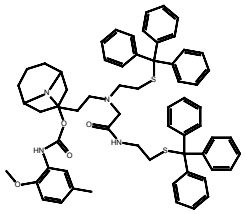
title: Weigl:2002p2245:22a
pKi: 5.955
model set: 1



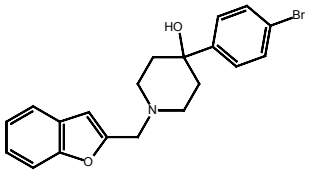
title: Maier:2002p438:18
pKi: 5.937
model set: 1



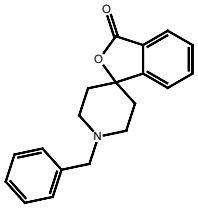
title: Weigl:2002p1173:15
pKi: 5.924
model set: 1



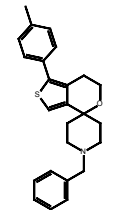
title: Choi:2001p657:1
pKi: 5.871
model set: 1



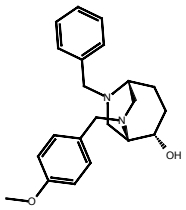
title: Vangveravong:2010p5291:18
pKi: 5.854
model set: 1



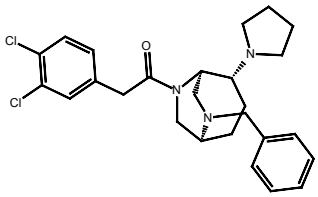
title: Maier:2002p438:25
pKi: 5.836
model set: 2



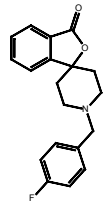
title: Meyer:2010p8016:3c
pKi: 5.796
model set: 1



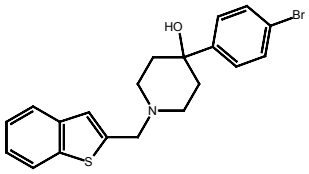
title: Geiger:2007p6144:15
pKi: 5.77
model set: 1



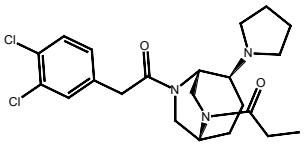
title: Geiger:2010p4212:20
pKi: 5.77
model set: 1



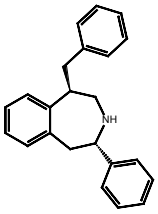
title: Maestrup:2009p3630:2c
pKi: 5.717
model set: 1



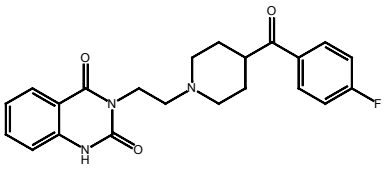
title: Vangveravong:2010p5291:20
pKi: 5.707
model set: 2



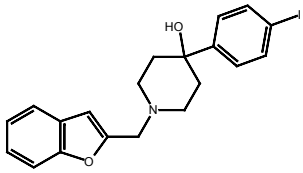
title: Geiger:2010p4212:ent-26
pKi: 5.678
model set: 2



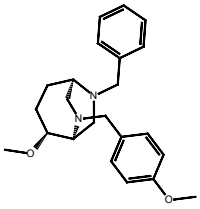
title: Husain:2009p1383:14d
pKi: 5.633
model set: 2



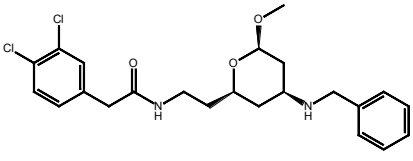
title: Xu:2005p8:Ketanserin
pKi: 5.627
model set: 1



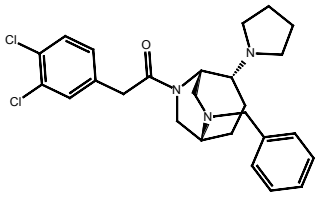
title: Vangveravong:2010p5291:19
pKi: 5.626
model set: 1



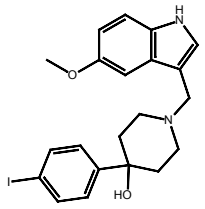
title: Geiger:2007p6144:17
pKi: 5.614
model set: 1



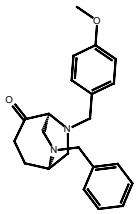
title: Wiedemeyer:2006p2321:22beta
pKi: 5.599
model set: 2



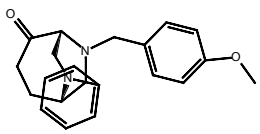
title: Geiger:2010p4212:ent-19
pKi: 5.495
model set: 1



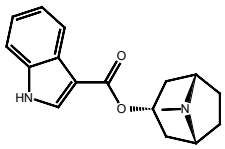
title: Vangveravong:2010p5291:7
pKi: 5.487
model set: 1



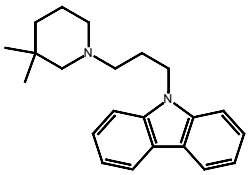
title: Holl:2009p1445:ent-14
pKi: 5.444
model set: 2



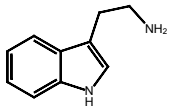
title: Holl:2009p1445:16
pKi: 5.423
model set: 1



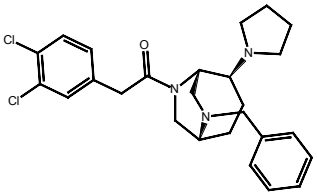
title: Xu:2005p8:3-Tropanylindole-3-c...
pKi: 5.413
model set: 2



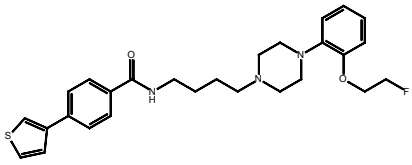
title: Ferorelli:2007p4648:26
pKi: 5.349
model set: 1



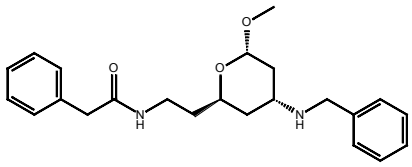
title: Fontanilla:2009p934:tryptamine
pKi: 5.309
model set: 1



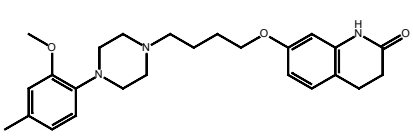
title: Geiger:2010p4212:ent-20
pKi: 5.292
model set: 2



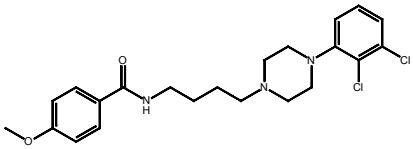
title: Tu:2011p1555:20e
pKi: 5.225
model set: 1



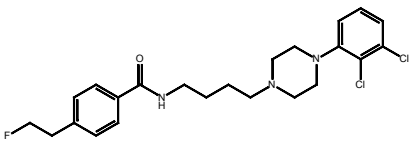
title: Wiedemeyer:2006p2321:29alpha
pKi: 5.213
model set: 1



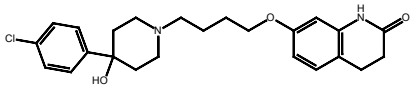
title: Vangveravong:2011p3502:10
pKi: 5.194
model set: 1



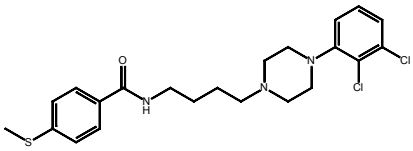
title: Chu:2005p77:13d
pKi: 5.151
model set: 1



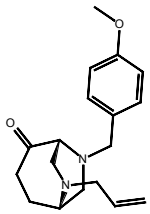
title: Chu:2005p77:13g
pKi: 5.142
model set: 1



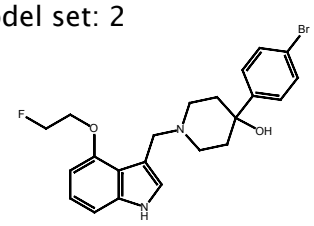
title: Vangveravong:2011p3502:2
pKi: 5.083
model set: 2



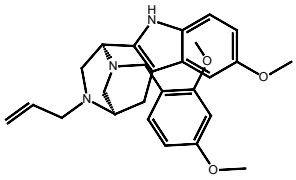
title: Chu:2005p77:13e
pKi: 5.075
model set: 2



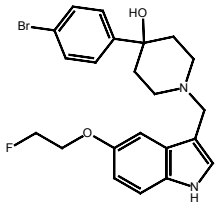
title: Holl:2009p777:12
pKi: 5.041
model set: 1



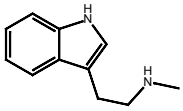
title: Vangveravong:2010p5291:9
pKi: 5.022
model set: 1



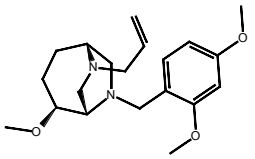
title: Holl:2009p2126:ent-21b
pKi: 4.991
model set: 1



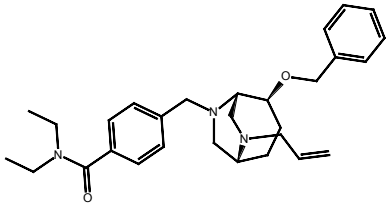
title: Vangveravong:2010p5291:10
pKi: 4.982
model set: 2



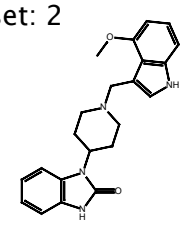
title: Fontanilla:2009p934:N-methyltr...
pKi: 4.892
model set: 2



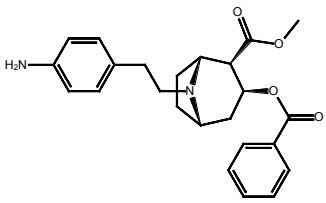
title: Holl:2009p777:ent-16b
pKi: 4.87
model set: 1



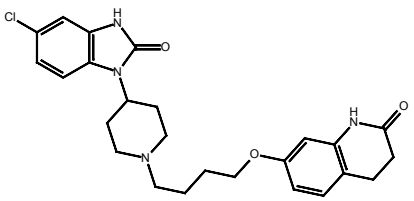
title: Holl:2009p2111:9
pKi: 4.815
model set: 1



title: Vangveravong:2010p5291:11
pKi: 4.792
model set: 2



title: Fontanilla:2008p7205:6
pKi: 4.777
model set: 1



title: Vangveravong:2011p3502:4
pKi: 4.772
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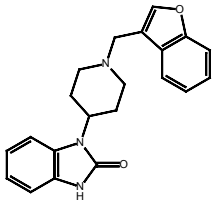

title:
Vangveravong:2010p5291:23
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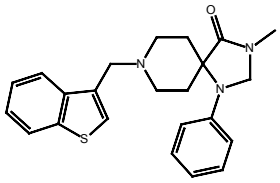
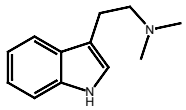
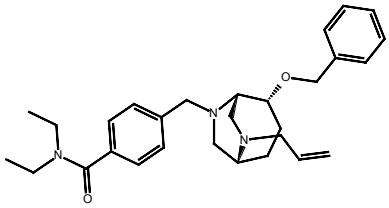
model set: 1



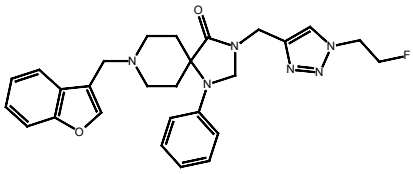
title:
Vangveravong:2010p5291:27
pKi: 4.694
model set: 2



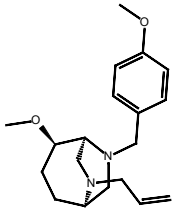
title:
Fontanilla:2009p934:N.N'-dimet...
pKi: 4.663
model set: 1



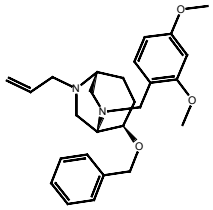
title: Holl:2009p2111:12
pKi: 4.66
model set: 1



title:
Vangveravong:2010p5291:29
pKi: 4.657
model set: 1



title: Holl:2009p777:ent-21a
pKi: 4.65
model set: 2



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Holl:2009p2126:ent-11b
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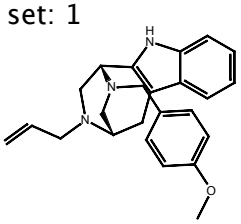
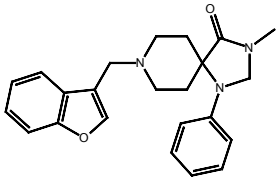
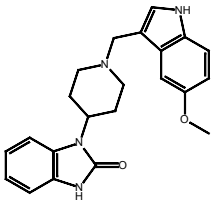


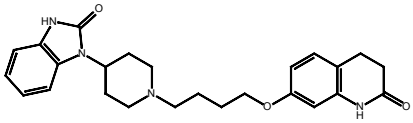
title: Holl:2009p2126:20a
pKi: 4.627
model set: 2



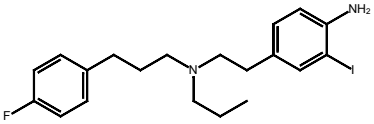
title:
Vangveravong:2010p5291:25
pKi: 4.604
model set: 1



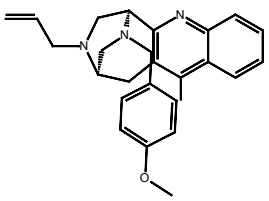
title:
Vangveravong:2010p5291:12
pKi: 4.565
model set: 1



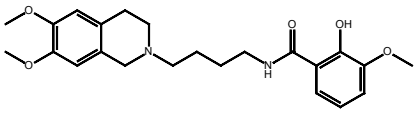
title:
Vangveravong:2011p3502:3
pKi: 4.439
model set: 2



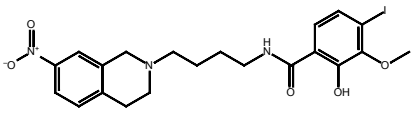
title:
Fontanilla:2008p7205:14
pKi: 4.377
model set: 1



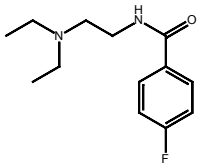
title: Holl:2009p2126:ent-23a
pKi: 4.243
model set: 1



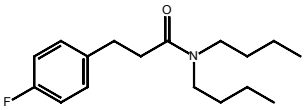
title: Hajipour:2011p7435:5i
pKi: 4.169
model set: 2



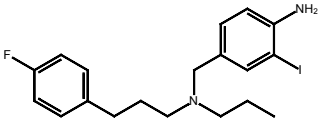
title: Hajipour:2011p7435:5g
pKi: 4.127
model set: 1



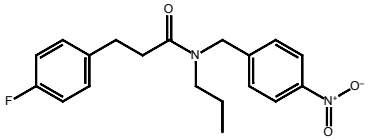
title: Ren:2009p1692:F-FBZA
pKi: 3.921
model set: 1



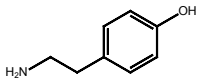
title: Hajipour:2010p4397:4
pKi: 3.898
model set: 2



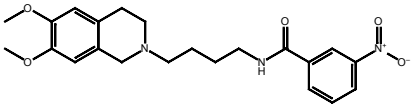
title: Hajipour:2010p4397:16
pKi: 3.875
model set: 1



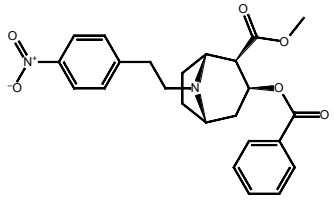
title: Hajipour:2010p4397:6
pKi: 3.627
model set: 2



title: Fontanilla:2009p934:tyramine
pKi: 3.217
model set: 1



title: Hajipour:2011p7435:5a
pKi: 2.917
model set: 1



title: Fontanilla:2008p7205:5
pKi: 2.272
model set: 1

APPENDIX H. SIGMA-1 TRAINING/TEST SETS

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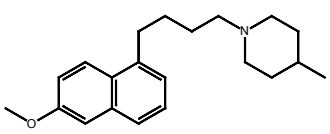
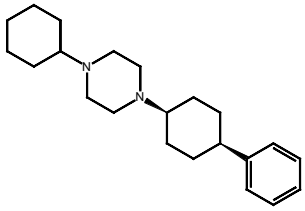
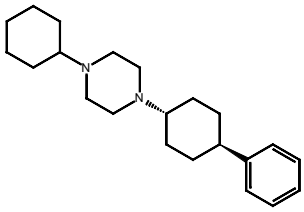


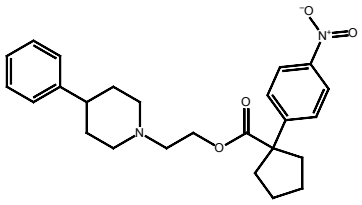
title: Berardi:2005p8237:31
pKi: 10.523
model set: 1



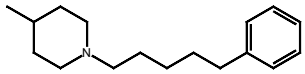
title: Abate:2011p73:cis-7
pKi: 10.377
model set: 1



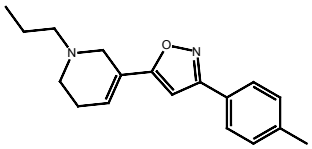
title: Abate:2011p73:trans-7
pKi: 10.347
model set: 2



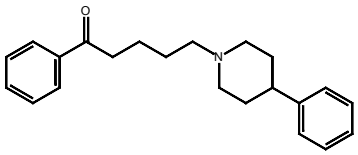
title: Hudkins:1994p1964:15
pKi: 10.301
model set: 1



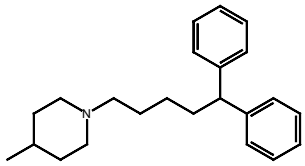
title:
Ablordeppey:2000p2105:9
pKi: 10.155
model set: 1



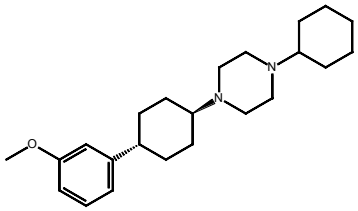
title:
Akunne:1997p51:PD144418
pKi: 10.097
model set: 2



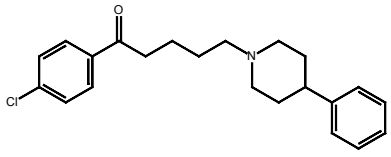
title:
Ablordeppey:1998p625:55
pKi: 10.05
model set: 1



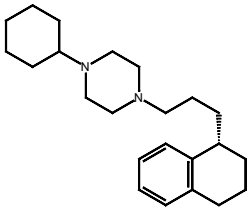
title: Glennon:2004p2217:9
pKi: 10.046
model set: 1



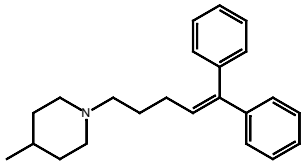
title: Abate:2011p73:trans-9
pKi: 10.0
model set: 2



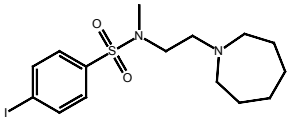
title:
Ablordeppey:1998p625:57
pKi: 9.92
model set: 1



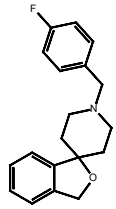
title: Berardi:2009p205:S-3
pKi: 9.886
model set: 1



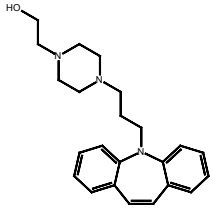
title: Glennon:2004p2217:8
pKi: 9.886
model set: 2



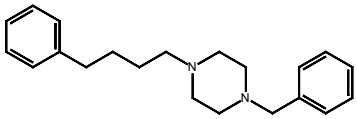
title: John:1998p2445:10
pKi: 9.854
model set: 1



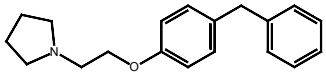
title: Maestrup:2009p3630:2d
pKi: 9.745
model set: 1



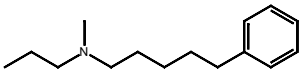
title:
Hanner:1996p8072:Opipramol
pKi: 9.699
model set: 2



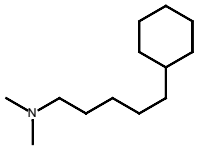
title:
Ablordeppey:2000p2105:3
pKi: 9.699
model set: 1



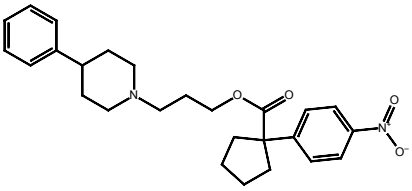
title:
Kedjouar:1999p1927:PBPE
pKi: 9.62
model set: 1



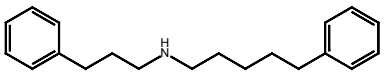
title:
Ablordeppey:2002p2759:5
pKi: 9.602
model set: 2



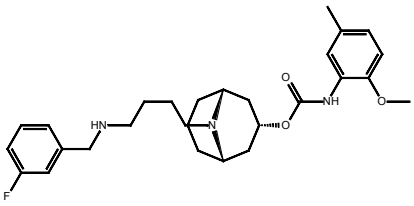
title: Glennon:1994p1214:47
pKi: 9.585
model set: 1



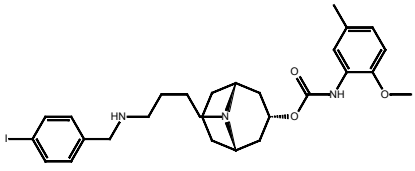
title: Hudkins:1994p1964:25
pKi: 9.569
model set: 1



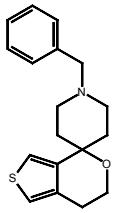
title: Glennon:1994p1214:32
pKi: 9.553
model set: 2



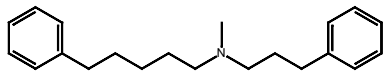
title:
Vangveravong:2006p6988:2b
pKi: 9.523
model set: 1



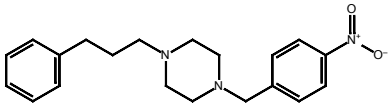
title:
Vangveravong:2006p6988:2f
pKi: 9.469
model set: 1



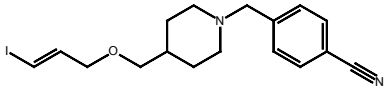
title: Meyer:2010p8016:5
pKi: 9.456
model set: 2



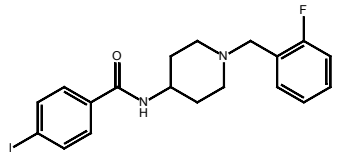
title: Ablordeppey:2002p2759:10b
pKi: 9.444
model set: 1



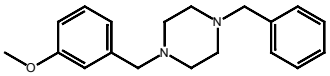
title: Nahas:2008p755:3i
pKi: 9.432
model set: 1



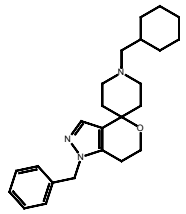
title: Waterhouse:1997p45:1
pKi: 9.42
model set: 2



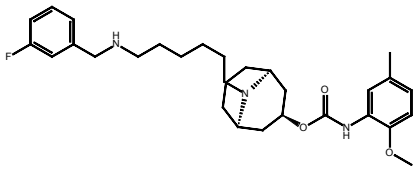
title: Dence:1997p333:2b
pKi: 9.42
model set: 1



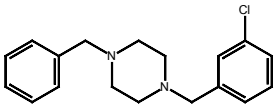
title: Foster:2003p749:4
pKi: 9.409
model set: 1



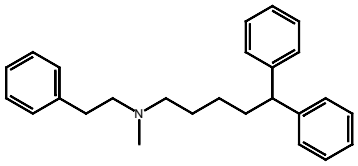
title: Schlager:2011p6704:28d
pKi: 9.367
model set: 2



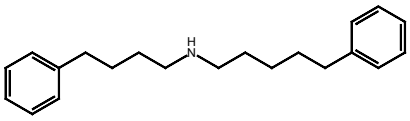
title: Vangveravong:2006p6988:3b
pKi: 9.337
model set: 1



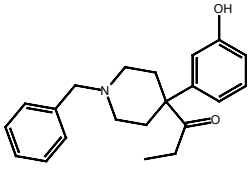
title: Foster:2003p749:7
pKi: 9.337
model set: 1



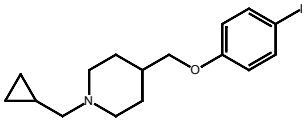
title: Glennon:2004p2217:16a
pKi: 9.319
model set: 2



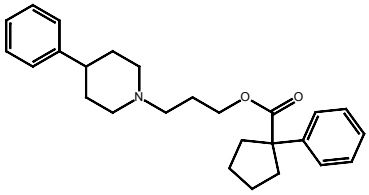
title: Glennon:1994p1214:34
pKi: 9.319
model set: 1



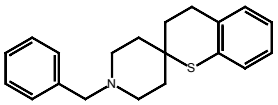
title: May:1998p311:1a
pKi: 9.31
model set: 1



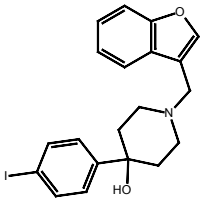
title: Waterhouse:1997p1657:10
pKi: 9.301
model set: 2



title: Hudkins:1994p1964:24
pKi: 9.301
model set: 1



title: Quaglia:1998p1557:2
pKi: 9.301
model set: 1



title: Vangveravong:2010p5291:22
pKi: 9.292
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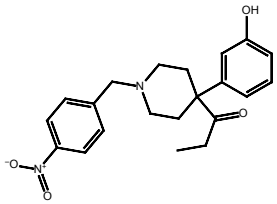
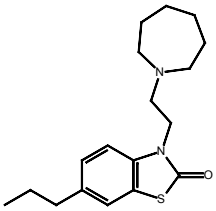
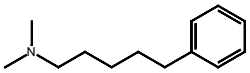


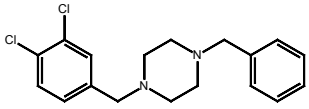
title: May:1998p311:1e
pKi: 9.268
model set: 1



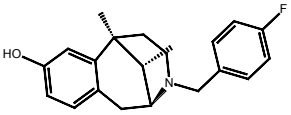
title: Yous:2005p158:9
pKi: 9.252
model set: 1



title: Ablordeppey:1998p625:16
pKi: 9.237
model set: 2



title: Foster:2003p749:9
pKi: 9.237
model set: 1



title: May:1998p311:3d
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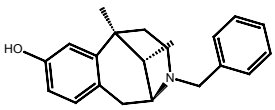

title: May:1998p311:3a
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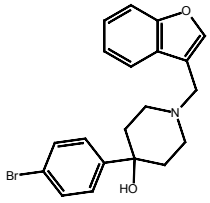
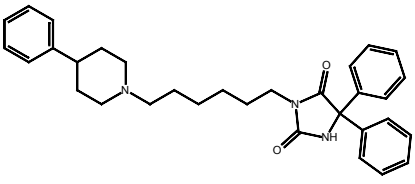
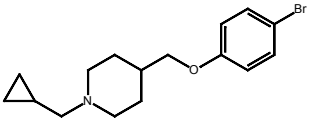
model set: 2



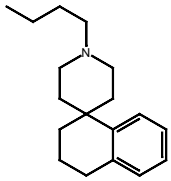
title: Vangveravong:2010p5291:21
pKi: 9.229
model set: 1



title: Hudkins:1994p2185:13
pKi: 9.229
model set: 1



title: Waterhouse:1997p1657:14
pKi: 9.222
model set: 2



title:
Moebius:1997p1:L-609404
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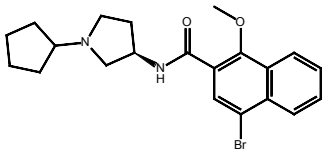
model set: 1



title: Huang:2001p1815:14
pKi: 9.155
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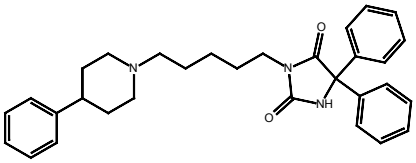
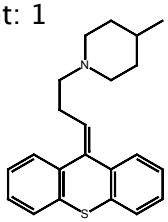
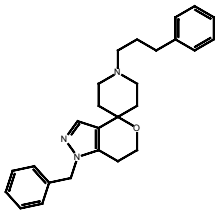


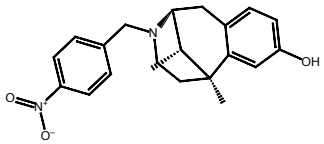
title: Hudkins:1994p2185:12
pKi: 9.155
model set: 2



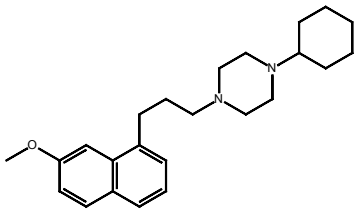
title: Glennon:2004p2217:5
pKi: 9.097
model set: 1



title: Schlager:2011p6704:28c
pKi: 9.092
model set: 1



title: May:1998p311:3e
pKi: 9.081
model set: 2



title: Ferorelli:2007p4648:16
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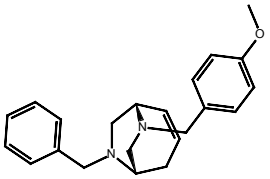
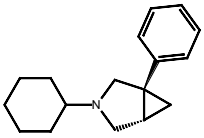
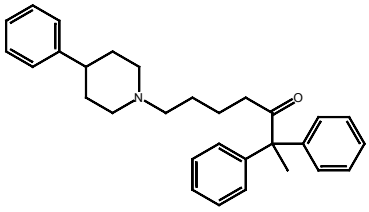


title: Holl:2009p220:3
pKi: 9.041
model set: 1



title: Marrazzo:2004p156:
(+)-(1R.2S)-14
pKi: 9.041
model set: 2



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pKi: 9.018
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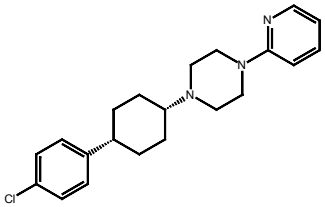

title:
Berardi:2008p7523:cis-31
pKi: 5.963
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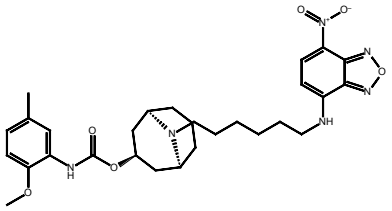

title:
Zeng:2007p6708:K05-138
pKi: 5.959
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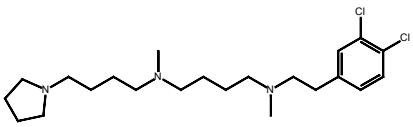

title: deCosta:1994p314:13
pKi: 5.95
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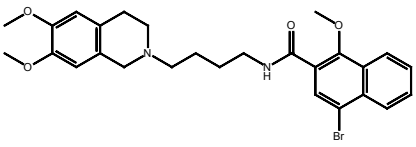

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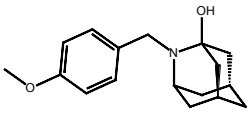
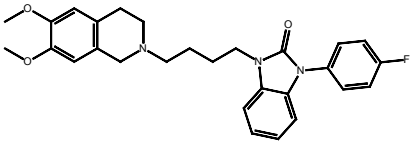
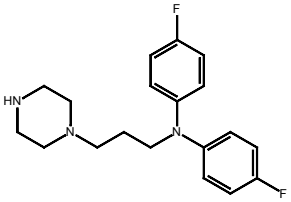
pKi: 5.936
model set: 1



title: Banister:2011p5289:13
pKi: 5.907
model set: 2



title: CM353
pKi: 5.903
model set: 1



title: Cao:2003p2589:15
pKi: 5.857
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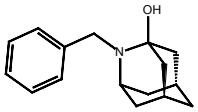
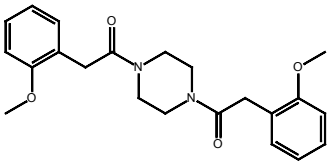
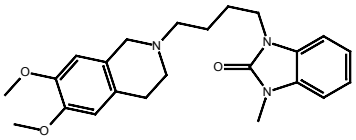


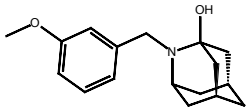
title: Banister:2011p5289:9
pKi: 5.839
model set: 2



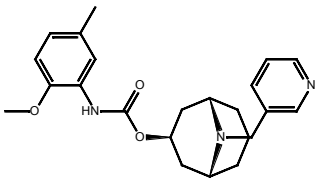
title: Zhang:1998p4950:18
pKi: 5.834
model set: 1



title: CM398
pKi: 5.821
model set: 1



title: Banister:2011p5289:12
pKi: 5.71
model set: 2



title: Chu:2009p1222:11d
pKi: 5.63
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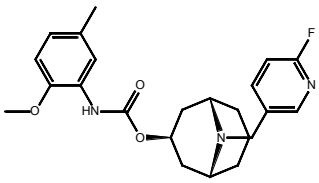
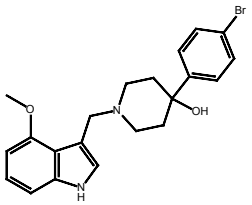
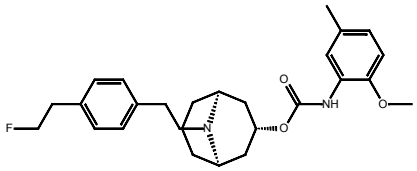


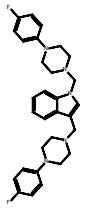
title: Chu:2009p1222:11e
pKi: 5.6
model set: 1



title: Vangveravong:2006p815:8
pKi: 5.592
model set: 2



title: Chu:2009p1222:11i
pKi: 5.579
model set: 1



title: Yarim:2011p869:2a
pKi: 5.57
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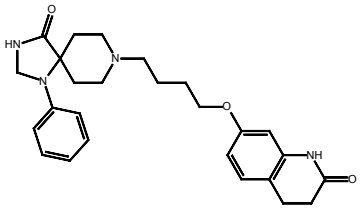
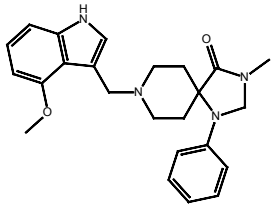


title: Vangveravong:2011p3502:5
pKi: 5.51
model set: 2



title: Vangveravong:2006p815:14
pKi: 5.502
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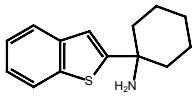
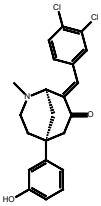
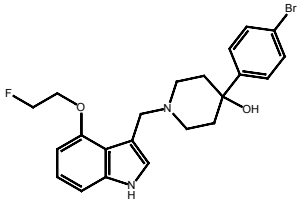


title: He:1993p1188:4
pKi: 5.499
model set: 1



title: Bertha:1994p3163:(+)-(1R.5R)-6
pKi: 5.495
model set: 2



title: Vangveravong:2010p5291:9
pKi: 5.492
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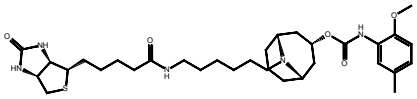

title: Vangveravong:2006p6988:5
pKi: 5.468
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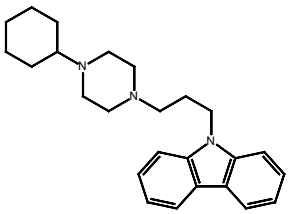
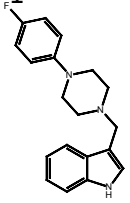
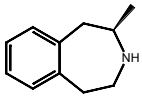


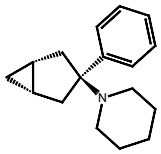
title: Ferorelli:2007p4648:29
pKi: 5.462
model set: 2



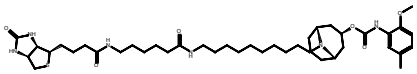
title: Yarim:2011p869:1a
pKi: 5.439
model set: 1



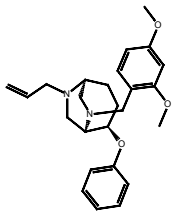
title: Husain:2009p2788:12a
pKi: 5.435
model set: 1



title: deCosta:1992p4704:6
pKi: 5.429
model set: 2



title: Vangveravong:2006p6988:8
pKi: 5.418
model set: 1



title: Holl:2009p2126:13b
pKi: 5.393
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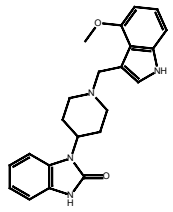
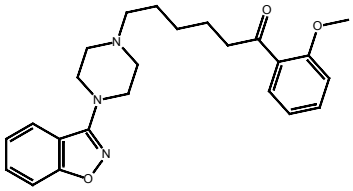


title: Vangveravong:2010p5291:11
pKi: 5.384
model set: 2



title: Perrone:2003p646:43
pKi: 5.367
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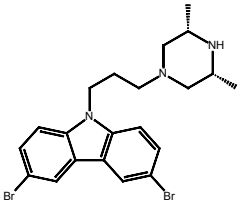

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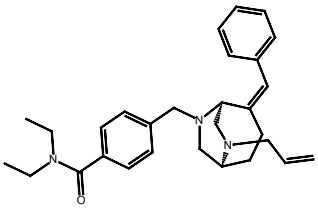

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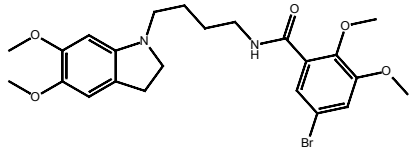

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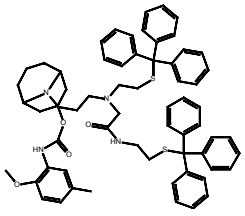

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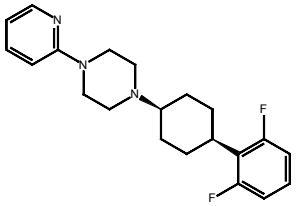

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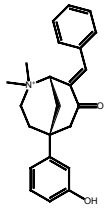

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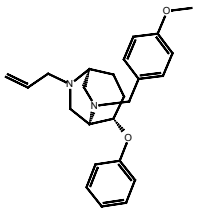

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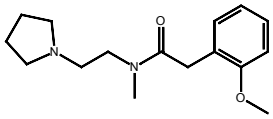

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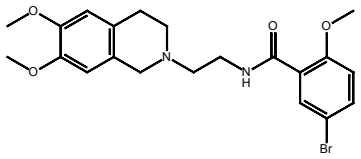

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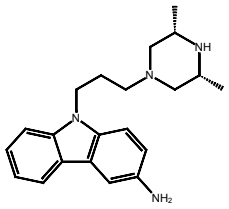

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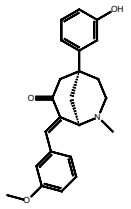

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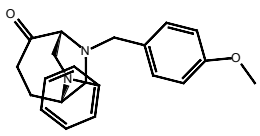

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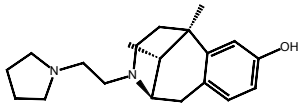

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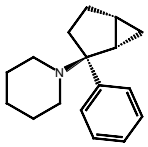

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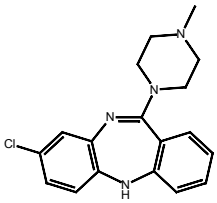

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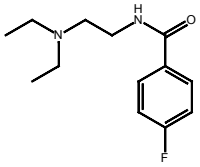

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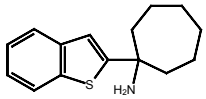

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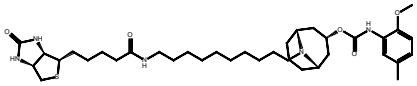

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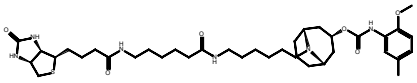

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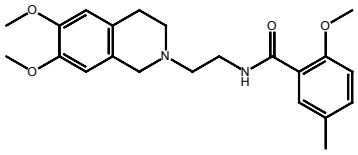

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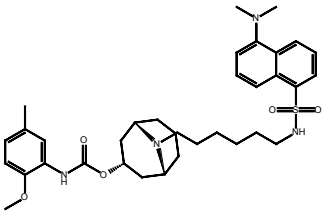

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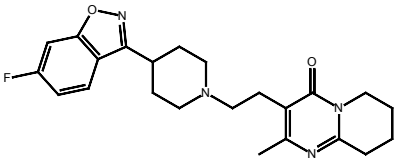

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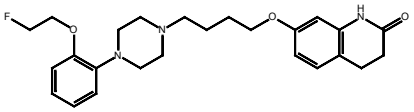

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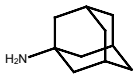

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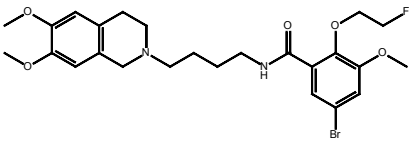

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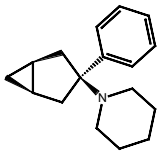

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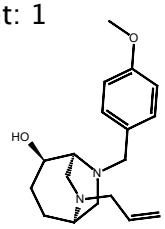

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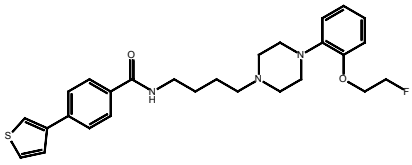

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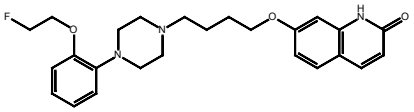

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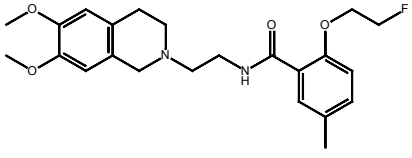

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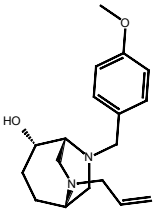

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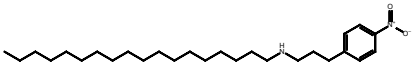

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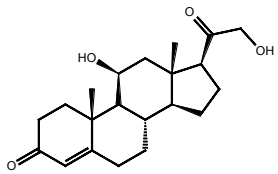

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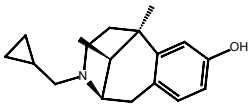

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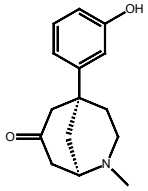

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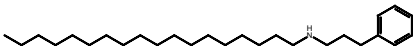

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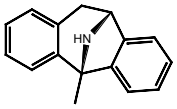

title: Linders:1993p2499: (+)-3
pKi: 4.228
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APPENDIX I. COPYRIGHT PERMISSIONS RELEASES

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Medicinal Chemistry
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Email: dewatson@go.olemiss.edu

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Article title: Structural Features Important for .sigma.1 Receptor Binding
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Article title: Synthesis and Structure−Activity Relationships ofN-(1-Benzylpiperidin-4-yl)arylacetamide Analogues as Potent σ1Receptor Ligands
Author(s): Huang, Yunsheng ; et al
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Article title: Novel (4-Phenylpiperidinyl)- and (4-Phenylpiperazinyl)alkyl-Spaced Esters of 1-Phenylcyclopentanecarboxylic Acids as Potent .sigma.-Selective Compounds
Author(s): Hudkins, Robert L. ; Mailman, Richard B. ; DeHaven-Hudkins, Diane L.
DOI: 10.1021/JM00039A008
Date: Jun 1, 1994
Volume: 37
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Article title: Discovery of High-Affinity Ligands of σ1Receptor, ERG2, and Emopamil Binding Protein by Pharmacophore Modeling and Virtual Screening
Author(s): Laggner, Christian ; et al
DOI: 10.1021/JM049073+
Date: Jul 1, 2005
Volume: 48
Issue: 15

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Article title: Synthesis, Biological Evaluation, and Three-Dimensional in Silico Pharmacophore Model for σ1Receptor Ligands Based on a Series of Substituted Benzo[d]oxazol-2(3H)-one Derivatives
Author(s): Zampieri, Daniele ; et al
DOI: 10.1021/JM900366Z
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From: <kenneth.domino@domemtech.com>
Subject: RE: Permissions request for dissertation
Date: May 16, 2012 8:26:14 AM CDT
To: "David Watson" <dewatson@go.olemiss.edu>

Hi David,

Of course, you can use the figures for your dissertation. At the moment, I don't have easy access to the original figures, so you will probably need to scan the figures from the books. If I find them, I will forward them to you.

Ken Domino

> -------- Original Message --------
> Subject: Permissions request for dissertation
> From: David Watson <dewatson@go.olemiss.edu>
> Date: Tue, May 15, 2012 3:34 pm
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>
> Dr. Domino,
>
> I am requesting permission to use Figs. 1 from pages 40 and 56 of "Multiple Sigma and PCP Receptor Ligands: Mechanisms for Neuromodulation and Neuroprotection?" in my dissertation titled "Quasi-comprehensive scaffold perception, pharmacophore development, and structure--affinity relationships of sigma site ligands".
>
> The references for the pertinent selections are:
> Carroll, F. I.; Abraham, P.; Parham, K.; Bai, X.; Zhang, X.; Brine, G. A.; Mascarella, S. W. In Mul- tiple Sigma and PCP Receptor Ligands: Mechanisms for Neuromodulation and Neuroprotection?; Ka- menka, J.-M., Domino, E. F., Eds.; NPP Books: Ann Arbor, MI, 1992; pp 33–44.
>
> Gund, T. M.; Shukla, K.; Su, T.-P.; Parish, D. In Multiple Sigma and PCP Receptor Ligands: Mechanisms for Neuromodulation and Neuroprotection?; Kamenka, J.-M., Domino, E. F., Eds.; NPP Books: Ann Arbor, MI, 1992; pp 53–59.
>
> Sincerely,
> David Watson
>
> --
> David Watson
> Ph.D. Candidate
> Medicinal Chemistry
> 425 Faser Hall
> University MS 38677
> 662 915 16 63

Stephen Cutler <cutler@olemiss.edu> June 5, 2012 9:45 AM
To: David Watson <dewatson@go.olemiss.edu>, "Straalen van, Berendina, Springer SBM NL" <B.vanStraalen@springer.com>
Cc: "Honour, Carolyn, Springer US" <Carolyn.Honour@springer.com>
RE: MCRE - Permissions request...

Thank you!

S.

Stephen J. Cutler, Ph.D.
Chair & Professor
Director NIH COBRE CORE-NPN
Editor, Medicinal Chemistry Research
Department of Medicinal Chemistry
School of Pharmacy
University of Mississippi
University, MS 38677
662-915-7101
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From: David Watson [mailto:dewatson@go.olemiss.edu]
Sent: Tuesday, June 05, 2012 2:34 AM
To: Straalen van, Berendina, Springer SBM NL
Cc: Honour, Carolyn, Springer US; Stephen Cutler
Subject: Re: MCRE - Permissions request...

Thank you all very much for clarifying the matter for me, and for providing the permissions to use the selected figures in my dissertation.

On Jun 5, 2012, at 1:56 AM, Straalen van, Berendina, Springer SBM NL wrote:

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The permission is also granted for UMI dissertations.

From: Honour, Carolyn, Springer US
Sent: maandag 4 juni 2012 19:19
To: Straalen van, Berendina, Springer SBM NL
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Carolyn

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Subject: FW: MCRE - Permissions request...

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From: David Watson [mailto:dewatson@olemiss.edu]
Sent: Monday, June 04, 2012 10:07 AM

VITA

David E. Watson

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Education

Ph.D. Pharmaceutical Sciences, University of Mississippi, School of Pharmacy, Department of Medicinal Chemistry, *expected* 2013.
Dissertation Advisor: Christopher R. McCurdy; Dissertation Title: "Quasi-comprehensive scaffold perception, pharmacophore development, and structure–affinity relationships of sigma site ligands"

B.S. Chemistry, University of Mississippi, School of Liberal Arts, Department of Chemistry, 1999. *Minor:* German.

Scientific Appointments/Experience

Graduate Research Assistant, Department of Medicinal Chemistry, School of Pharmacy, University of Mississippi, University, MS. Advisor: Christopher McCurdy, January 2008–Present.

Certifying Scientist and Laboratory Technician, ElSohly Laboratories, Oxford, MS. Fall 2000–Present.

Student and Technician Supervision

Emily Carrell, 05/2012–08/2012

Andrew Mullen, 06/2010–08/2011

Scientific Associations

American Chemical Society, Member, 2008–2013
Medicinal Chemistry Division, Member, 2008–2013
Computers in Chemistry Division, Member, 2008–2013

American Association of Pharmaceutical Scientists UM Student Chapter, Member, 2010–2012

University of Mississippi Medicinal Chemistry Journal Club, Member, 2009-2013

Honors and Awards

Rho Chi Society, University of Mississippi, 2009

Phi Eta Sigma, University of Mississippi, 1993

Service as Scientific Referee

Invited National Institutes of Health Referee (ad hoc)

NIH-NCRR COBRE CORE-NPN Predoctoral Fellowship ad hoc Study Section, 2010.

NIH-NCRR COBRE CORE-NPN Predoctoral Fellowship ad hoc Study Section, 2009.

Invited Journal Referee

Journal of Natural Products, 2011–Present

Professional Service

American Association of Pharmaceutical Scientists Student Chapter, University of Mississippi.
Chair, 2011
Chair Elect, 2010

University Committees, and Service

University of Mississippi, School of Pharmacy

Information, Resources and Computing Committee, Graduate Student at Large, 2009-2010.

Presentations

Regional Presentations

Watson, D.E. Comparative modeling of prolylcarboxypeptidase to elucidate factors responsible for the selective hydrolysis of kinins. 38th Annual MALTO Medicinal Chemistry and Pharmacognosy meeting, Houston, TX, May 23, 2011

Local Presentations

Watson, D.E. Voltage Gated Sodium Channel Ligands: Opportunities and Challenges. Department of Medicinal Chemistry, School of Pharmacy, University, MS, November 3, 2009

Watson, D.E. Hot or not? Selective TRPV1 antagonists. Department of Medicinal Chemistry, School of Pharmacy, University, MS, September 30, 2008

Watson, D.E. Using BibTeX to Manage References for Scientific Publications. Mississippi Center for Supercomputing Research, University, MS, May 6, 2008

Watson, D.E. Typesetting with LaTeX. Mississippi Center for Supercomputing Research, University, MS, April 10, 2008

Bibliography

Peer-reviewed scientific research

Chajkowski, S. M.; Mallela, J.; Watson, D. E.; Wang, J.; McCurdy, C. R.; Rimoldi, J.; Shariat-Madar, Z. Highly selective hydrolysis of kinins by recombinant prolylcarboxypeptidase. *Biochem. Biophys. Res. Commun.* **2011**, *405:* 338-343.

Brenneisen, R.; Elsohly, M. A.; Murphy, T. P.; Passarelli, J.; Russmann, S.; Salamone S. J.; Watson, D. E. Pharmacokinetics and excretion of gamma-hydroxybutyrate (GHB) in healthy subjects. *J. Anal. Toxicol.* **2004**, *28*: 625–30.

Editor

MALTO Thirty-seventh Annual Medicinal Chemistry and Pharmacognosy Meeting-in-Miniature Organizing Committee Book of Abstracts, University of Mississippi, 2010.