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ClogP Manual

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CLOGP Reference Manual

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1. Introduction

The CLOGP Reference Manual will help the user understand why the CLOGP program calculates logP(ow) the way it does. Although the procedure cannot be derived from first principles, we have tried to make the rules consistent with solvation theory, if for no other reason than they are more easily remembered. The method simply adds together values for structural parts of a solute molecule and correction factors dependent upon the particular way the parts are put together.

The CLOGP EXAMPLES section contains example CLOGP calculations for a variety of chemicals and is designed as a companion to the CLOGP Reference Manual. An asterisk (*) appears in the CLOGP Reference Manual when one or more examples are provided in *CLOGP Example Calculations* to illustrate aspects of the CLOGP computation. Examples also demonstrate DEPICT (chemical depiction).

Funding for the development of CLOGP was provided by the U.S. Environmental Protection Agency through Cooperative Agreement No. 809295, and we wish to acknowledge the encouragement and support of the project officer, Dr. Gilman Veith of ERL-Duluth.

1.1 Measurement and Past Uses of Partition Coefficients

The partition coefficient is the equilibrium concentration of solute in a non-polar solvent divided by the concentration of the same species in a polar solvent. In this and most other applications, the polar solvent is water. The logarithm of the partition coefficient, log P, has been successfully used as a hydrophobic parameter in 'extrathermo-dynamic' Hammett methodology. 1-octanol has much to recommend it as the choice for the non-polar phase (1) and logP(ow) has been used successfully in Quantitative Structure Activity Relationships (QSAR) in the following special fields: drug and pesticide design (2,3); pharmacokinetics (4); anaesthesiology (5); environmental transport and soil binding (6,7); toxicology (8); bioaccumulation (9); protein folding (10); enzyme binding (11,12); enzymic reactions in non-aqueous solvents (13); and host-guest complexation (14a,b).

In principle, the measurement of the equilibrium concentration of solute in the octanol and water phases, after shaking in a separatory funnel, is very simple, and since good measured values are always to be preferred over calculated ones, it would seem that there should be little need for a procedure to calculate them. As it turns out, reliable shake-flask measurements are time-consuming and often difficult to make. The criteria for high reliability are: measurements over a 10-fold concentration range (with upper concentration no more than 75% of solubility or CMC, or no more than 5% of the aqueous phase, whichever is lower) and standard deviation of 0.03 or less in log terms. This often requires working at sub-micromolar concentrations, and so, with either

UV spectrophotometry or gas chromatography, it means that the standard curves must be established with utmost care. Radiotracer methods seem well-suited for analyses at these low concentrations, but impurities as well as adsorption at phase boundaries (including container walls) can introduce significant errors.

HPLC procedures provide a way around this bottleneck(15,16) and can save time if there is a limited variety of structural types, and the log P values fall in the range of 0.5 to 4.0. Most HPLC procedures which are used to develop log P(ow) values do no use octanol and thus have to be referred to that system by standard curves which can be different depending on whether the solutes do or do not contain certain basic fragments, such as pyridine nitrogen. If the solutes do not absorb well in the UV, difficulties in detecting the elution time eliminates any advantage HPLC may have over the shake-flask method.

Procedures which employ filter probes (17) or solubility columns(18) speed up partition coefficient measurements by eliminating centrifugation as the means of phase separation. However, each has its own set of disadvantages and limit its acceptance as a method for establishing the standard values for a calculation procedure.

More efficient methods of measurement of octanol/water partition coefficients are certain to be developed in the future, but no conceivable 'breakthrough' is likely to eliminate the need for logP calculation. To put the problem in proper prospective, one need only imagine some dedicated synthetic chemist making all possible tri-substituted benzoic acids with the methods commonly available today. When finished, there would be five million analogs for which partition coefficients could be determined. And of course only by calculation is one going to have an estimate of hydrophobicity before synthesis.

The Pomona MedChem Project saw these and other arguments as reason enough to develop a method to calculate log P(ow) from structure by an additive-constitutive procedure. As it turns out, the 'constitutive' portion of the procedure was, by the very nature of the two competing solvation equilibria, very complex, and the manual method required considerable effort before it could be applied with confidence. It is the aim of the second-generation program, CLOGP, to take most of the routine calculation burden from the user but still encourage him to study the interplay of hydrophobic and polar solvation forces which can be so crucial to the design of bioactive chemicals.

1.2 How to Understand CLOGP Calculations

The first published method for calculating log P(ow) from structure (19) was based on a 'substitution' procedure and was developed with substituent pi constants for aromatic rings in mind. Of course this method was limited to deriving a new log P from a 'parent' structure whose log P was already known. Rekker(20) was the first to publish a procedure which was more general in that it assigned 'fragmental constants' to a variety of structural pieces, and the calculated log P was the sum of the values appropriate for the molecule in question. The original pi system can be expressed as:

$$\pi_x = \log P_{C_6H_5X} - \log P_{C_6H_6}$$

while the expression for Rekker's fragment system is:

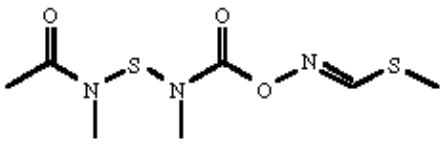
$$\mathrm{LogP} = \sum_{i=1,N} a_i f_i + \sum_{j=1,M} b_j F_j$$

The method developed by Pomona MedChem (21) follows Rekker's general formulation, but there are some important differences in the approach used to derive the actual working constants. Rekker used a 'reductionist' approach - deriving the constants for carbon and hydrogen as well as those for polar fragments from a

statistical treatment of a large body of log P data which contained numerous interaction factors. Both the fragment values (f) and interaction factors (F) had to be identified and evaluated concurrently. Also, Rekker neglected to clearly define just what constitutes a fragment. Instead he provides a table in which the known constants can be found (see footnote). Rekker also treats all correction factors as some multiple of a 'Magic Number' (+0.28), but the selection of multiples was not made clear in his published work. Although his method gained some acceptance for manual calculation, we considered it too seriously flawed to serve as the basis for a computer method.

In order to construct a dependable, verifiable algorithm suitable for log P calculations used in developing QSAR at Pomona College, we first elected to clearly define what constitutes a fragment. Next we chose a 'constructionist' approach to evaluate them; that is, we accepted as axiomatic that the hydrophobic portions of solutes were those most 'hydrocarbon-like', and defined these carbons and hydrogen fragment values as being truly constant. We gave very heavy emphasis to the carefully-measured values for three solutes; molecular hydrogen, methane and ethane, because from these we could derive fragment constants for carbon and hydrogen, which would be free of obscuring interactions. For all hydrocarbon structures more complex than these, whose measured values were NOT the sum of fragment values, we attempted to define the difference in terms of universally-applicable correction factors. It appears that this approach has led not only to a workable algorithm, but has highlighted the importance of certain types of polar solvation forces which have received insufficient attention in the past.

The first attempt to reduce the 'Pomona Method' of log P calculation to computer algorithm was made in collaboration with Dr. Jack Chou and Dr. Peter Jurs of Pennsylvania State University (22). It was called CLOGP. A great deal was learned in the process of developing this first version, and it certainly established the real need for a 'stand-alone' program to make these calculations. Nevertheless, CLOGP was difficult to install and modify, and many well-known correction factors could not be implemented due to programming difficulties. In light of this experience, we deemed it essential to incorporate, in the second generation program, design features which would encourage its continuing evolution. To achieve that objective, the program had to be conceived as a 'modeling system' which could operate from one or more easily-revised 'value files'. As an example of the ease of updating, the largest fragment encountered to date is:



It took less than two minutes to enter it into the database and begin to use it in calculations.

A number of significant improvements have been made to CLOGP over the past few years. The most significant improvement is the ability to estimate a polar fragment value which has not appeared in a solute having a measure log P (oct). This type of estimation is designated as 'calculated'. If the fragment in question has appeared in a measured solute, but in a different bonding environment (e.g., aromatic attached when aliphatic attached is needed), the new 4.0 version allows for all extrapolations and designates the value as 'derived'. The methodology for the 'No Missing Fragments' algorithm is explained in more detail in ref. 23.

Earlier versions of CLOGP were able to assign corrections to polar fragments interacting over two Isolating Carbons (see Section 2. following). In the latest version, this distance has been extended to three I.C.s. A significant improvement in steroid calculations recognizes the unique contribution of polar groups at the 11 position as well as some long-range intramolecular hydrogen bonds. These and a few other minor improvements will be noted in the changed values in the *CLOGP Example Calculations, 6.3* .

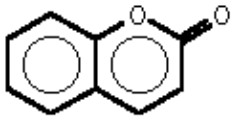
2. Fundamental Fragments

In view of the decision to make alkane carbons and hydrogens the most fundamental fragments in the system, it is necessary to define these very carefully before defining the polar, more hydrophilic fragments.

2.1. Isolating Carbons

An 'Isolating Carbon' (I.C.) atom is carbon which is NOT doubly- or triply- bonded to a hetero atom. An I.C. may be bonded to a hetero atom by a single or an aromatic bond. This definition can be made clearer from the following two examples:

1. pyrimidine



2. coumarin

In an earlier version of the manual calculation procedure (Ref. 21 p. 34) the Kekule structures for pyrimidine was considered; the earlier rule is now superceded. In coumarin, both rings are designated as aromatic, and the only carbon which is not isolating is the one in the carbonyl group, because it is doubly bonded to a hetero outside the ring.

Although the hydrophobic value of an I.C. is constant, several types must still be identified; the degree to which they delocalize electrons in any polar fragments attached to them has a great influence on overall log P. The types of I.C.s presently identified are listed below with appropriate symbols:

Symbol	Type
A	**Aliphatic**
Z	**Benzyl**
V	**Vinyl**
Y	**Styryl**
a	**Aromatic**

To be completely characterized, a polar fragment must have each of its 'valence bonds' designated with one of the above symbols (see section "Fragment Valence Types"). The numerical value of the fragment will increase roughly in the order 'A' to 'a', but must be experimentally determined for high reliability.

All hydrogens bonded to I.C.s are fragments. These two kinds of fundamental fragments are the most important members of the non-polar class. A comparison of their relative values (C = 0.2; H = 0.225) is a reminder that the measure of effective cavity size may not be as simple as using van der Waals radii or CPK models.

2.2. Polar Fragments

A fragment is any atom or group of atoms bounded by Isolating Carbon atoms, and all except hydrogen are considered polar. A fragment may have many internal bonds but those connecting it to I.C.s are called

'valence bonds'. Valence bonds are most often single, but can be aromatic, as in the case of the N fragments in pyrimidine shown above. Each hydrogen in methane is a fragment, but the hydrogens in formaldehyde are not because the carbon to which they are bonded is not isolating. This is very important to remember, for one frequently sees published calculations in which one fragment value is obtained from another by the replacement of a fragment hydrogen with another fragment of known value. At the present time a good rule to follow is: "Never break up a Fragment; estimations can be made from values measured for different bond environments (see below) but a Fragment cannot be constructed from parts." Examples of fragments which cannot be "broken down" further are:

Monovalent:	**-Cl;-CN**
Divalent	**-OC(=O)NH-**
Trivalent:	**-OC(=O)N<**
Tetravalent:	**>NC(=O)N<**

As will become evident in the following sections, polar fragments can interact in various ways. To quantitate this interaction it is necessary to define several types of polar fragments:

> (A) X = any halogen, but for one type of interaction fluorine must be assigned to a special subclass,'F'. (B) Y = all non-X fragments; these are further subdivided according to:

sensitivity to halogen interaction as 'Y-1', 'Y-2', and 'Y-3' containing '-OH' or not.

2.3. Intrinsic Values

Here the term, 'intrinsic' fragment values, means those which would, if summed, yield the correct log P without any correction factors. It is worthwhile to examine some of the accepted hypotheses as to what solvation forces or other phenomena determine these intrinsic values.

It takes more energy to form a cavity in water than in octanol. One would predict, therefore, that increasing the size of a solute would increase its log P. Other factors being equal, this appears to be the case. However, other features of the solute can partly or completely override the effect of its size.

Water is much more capable than is octanol of accommodating localized dipoles, and it contains, on a molar basis, more hydrogen bond accepting and donating groups. So it is these three factors -size, localized dipole strength, and H-bonding ability - which largely determine the sign and magnitude of any fragment value.

2.3.1 Halogens

Halogens form an intense localized dipole when bonded to an aliphatic carbon atom.* This intensity is somewhat lessened if the I.C. is benzyl and greatly lessened if it is vinyl, styryl or aromatic.* Fluorine has a negative fragment value when attached to an aliphatic carbon, because the dipole effect outweighs the effect of size. Size is of greater importance with chlorine and bromine, but even bromine is less hydrophobic than a hydrogen in an aliphatic setting. As will become evident in the following section, much of this hydrophilic polar effect can be lost through 'shielding' by other halogens, or by electronic interaction with 'Y' type polar groups.

2.3.2 H-Polar Fragments

H-Polar Fragments ('Y') almost universally form some sort of hydrogen bonds with the donor (H) or acceptor (O) of the aqueous phase. This is thought to interrupt the peculiar 'ice-like' water shell which forms around the non-polar, hydrocarbon-like portions of each solute molecule, and thereby effectively reduces cavity size. As noted above, this should reduce log P.

2.3.3 Ions

Octanol can accept some larger solutes containing a full formal charge in sufficient concentration for measurement. However, one must be careful that the species measured is the same, because water easily supports complete ionization while ion-pairing is the usual condition in octanol except at the very lowest concentrations. Consistent values can be obtained if 'standard conditions' are adhered to: 0.1 M small counter-ion (Na+ or Cl-) and extrapolation to infinite dilution. Measured in this way a carboxylate ion is about 4.1 log units lower than the undissociated acid. No single value can be given to the positive charge on a protonatedamine or quaternary ammonium, because the charge is delocalized along the hydrocarbon chain and thus the effect is dependent on chain-length. It should be emphasized at this point that, except for zwitterions, CLOGP calculates values for the neutral solute only.*

2.3.4 Unsaturations

Double bonds in isolation have a slightly negative effect on log P.* This effect may arise from the polarity of the pi electrons or else it may be due to the shorter bond length reducing cavity size. At any rate, it disappears if the double bonds are conjugated.* Triple bonds are decidedly hydrophilic and require a large negative correction factor.

3. Correction Factors

3.1 Structural Factors

3.1.1 Bonds To properly perform its calculations, CLOGP needs to know the number and types of certain bonds in the solute structure. There is some reason to believe that, for the bonds in question, factors other than bond length affect the size of the solvent cavity needed to contain the hydrophobic portions of the solute molecule.

The effect of all bonds within any fragment is taken care of by the fragment value, and so it is NOT necessary to keep track of them, NOR of any bonds to hydrogen. And, as explained below, it is convenient to allow for the bond effect in aromatic rings by including it in a special aromatic I.C. type, 'aromatic carbon'; therefore, aromatic bonds also are NOT given special attention.

Bonds which DO need to be identified are the following:

3.1.1.1 Chain bonds

Chain bonds are non-ring bonds between I.C.s plus any valence bonds to fragments*.

3.1.1.2 Ring Bonds

Ring bonds are non-aromatic ring bonds between I.C.s plus any valence bonds to fragments*.

3.1.1.3 Branch Bonds

Branch bonds are chain bonds emanating from 'Branched Fragments' (a fragment type presently limited to phosphate esters) and counted to the last I.C. preceding any polar fragment.*

A separate count of each of these bonds types must be made, and a negative correction applied. For chain bonds only, this correction applies to bonds AFTER the first in each chain. For example, there is no net bond correction for ethane but there is one for propane. This suggests that the correction accounts for flexing of the chain which is not possible in methane or ethane. 1,2-diethylbenzene gets only a net of two bond corrections, because each chain is counted separately. Also compatible with a 'flexing' hypothesis is the fact that the correction is greater for chains than for aliphatic rings.

As noted above, an isolated double bond is assigned a negative correction factor (-0.09). This factor actually becomes slightly positive if the double bonds are conjugated in a ring such as benzene. Since it is much more convenient to assign all bonds in large fused ring systems as aromatic type, rather than using the Kekule system of alternating doubles and singles, it is worthwhile to assign a special fragment value to an aromatic carbon and include all the necessary bonding effects therein. The value of aliphatic carbon is +0.20;the value for aromatic carbon which includes all bond effects associated with the aromatic ring system is +0.13.*

3.1.2 Branching at Isolating Carbons

3.1.2.1 Chain Branch

It is well-known that iso-alkanes are more water-soluble than their n-isomers.* This branching evidently does not produce a corresponding solubility increase in the octanol phase in the partitioning process, because the correction required in CLOGP is negative in sign.

In CLOGP, the concept of branching was expanded, and now replaces the earlier use of the 'ring' cluster' correction(21). Fusion carbons in non-aromatic rings are considered as branched and given the same correction factor as chains; i.e., -0.13.* They are designated cluster branches.

3.1.2.2 Group Branch

If an H-Polar group branches from an I.C. the increase in water solubility, compared to the n-isomer, is even greater than with chain branching. Again this carries over to partitioning equilibrium; H-Polar group branching requires a larger correction than does chain branching. For this reason isopropyl alcohol is given one group branch correction and no chain branch is considered.* Tertiary butyl alcohol gets one of each type.*

If a fragment has more than two external(valence) bonds, it could be considered a branching point. However, in all cases except the 'Branched Fragments' noted above (t-amines and phosphate esters), the entire negative branching effect is included in the fragment value itself. Only in the case of the 'Branched Fragments' is the effect chain-length dependent.

3.2 Interaction Factors

3.2.1 Aliphatic Proximity (Measured Topologically)

3.2.1.1 Halogen vs. Halogen (X vs. X)

The positive correction to log P for this interaction is thought to result from dipole shielding and is limited to halogens on the same (geminal) or adjacent (vicinal) I.C.s. The geminal interaction is designated 'X-C-X', and the corrections can be thought to arise as follows: adding a second halogen to an I.C. which already has one creates the first X-C-X pair, and the correction required is +0.60.* Adding the third halogen to the same I.C. creates two more such paintings, each of which requires a correction of +0.5.* If the fourth halogen is added, the dipole is almost completely shielded, and the three additional pairings require corrections of +0.40 each.* For carbon tetrachloride the total geminal halogen correction would be:

EQ on pg. 12

For the vicinal halogen correction, X-C-C-X, the bond between carbons must not be double.* The correction is evaluated by subtracting one from the number of halogens meeting the structural requirement and multiplying by the factor 0.28. (Again Rekker's Magic Constant pops up!)

3.2.1.2 H-Polar vs. H-Polar (Y vs. Y)

As noted in the section on 'Intrinsic Values', the negative sign on the 'Y' fragments is thought to result from their 'structure-breaking' (and thus cavity-reducing) ability in the water phase. 'Y' fragments appear to eliminate the cavity requirement for two or more I.C.s to which they are attached. Obviously if two 'Y' fragments are located on the same or adjacent I.C.s to which they are attached. Obviously if two 'Y' fragments are located on the same or adjacent I.C.s some of this cavity reduction is going to be counted twice. Thus a positive correction factor is called for when the topological separation is less than three I.C.s. The CLOGP algorithm is an improvement over the original Rekker procedure(20) in that, in place of the same correction for every Y-C-Y or Y-C-C-Y, it makes the correction proportional to how much hydrophilic character (negative fragment value) is involved. This proportionality appears to apply even if one of the fragments is charged and has a highly negative value, but as previously noted, the CLOGP algorithm currently does not treat ions.

If one of the 'Y' fragments in a Y-C-Y interaction contains an -OH moiety (e.g. -NHOH, -COOH, or -OH itself), a greater proportion of the hydrophilic character of the pair is lost. The coefficient by which the fragment sum is multiplied increases from 0.32 to 0.42.*

If both the 'Y' fragments and the carbons of Y-C-C-Y are in a ring, the hydrophilicity loss is not as great as if they are all in a chain (coefficient 0.26 vs. 0.20).* If one 'Y' is a substituent on the ring while the other is in the ring, the correction coefficients are averaged (0.23).* If one of the carbons has two 'Y' fragments, the geminal correction is applied first; then, for the (Y-C-C,Y'Y'') correction, both pairings are calculated and averaged.* If both I.C.s have geminal 'Y' fragments, then the vicinal correction is not applicable.* (See penicillin in EXAMPLES).

3.2.1.3 Halogen vs. H-Polar (X vs. Y)

The interaction being considered at this point is limited to that which takes place across single bonds. It is therefore, probably due to an inductive or field effect. (The electronic interaction between fragments on or in aromatic rings is discussed in the following section.) In evaluating the X-C-Y correction factor, all halogens can be treated alike. However, there are at least three levels of sensitivity shown by 'Y' type fragments. In CLOGP the most sensitive class, 'Y-3', is restricted to the structural type: -SO2-R.* 'Y-2' consists of the types: -CONH-R, -O-R, -S-R, and -NH-R; and 'Y-1' of all other, H-polar fragments.* The correction factor for the first alpha-halogen (i.e. X-C-Y) is the same for all three Y-types (+0.9). For 'Y-3' fragments, this correction factor is doubled when there are two alpha halogens (X{2}-C-Y3) and tripled when there are three

(X{3}-C-Y3). For 'Y-2' fragments, the second and third alpha-halogens need much less correction, and for 'Y-1', virtually none. In the case of multiple halogenation, the X-C-X and the X-C-Y corrections are additive.

The CLOGP algorithm makes no separation of 'Y' types to make the X-C-C-Y correction, but needs to distinguish fluorine from the other 'X' halogens.*

3.2.2 Electronic (through Pi-bonds)

3.2.2.1 Fragment Valence Type

As previously noted, all fragments (X or Y type) are assigned the most negative values when bonded to aliphatic I.C.s (designated as 'A'). This can be considered as the 'base' or 'intrinsic' level. If the fragment value when attached to a vinyl I.C. (V) has not been measured it can be estimated as the average of the base and aromatic-bonded (a) values.* Likewise the value for the styryl-attached fragment can be estimated as two-thirds the way from the base to the aromatic value.* CLOGP will only make these estimations when measured values have not been entered in the database.

3.2.2.2 Extension of Aromaticity

The extension of the aromatic ring system through fusion (as in naphthalene or direct substitution (as in biphenyl)) appears to increase log P, especially if the heteroaromatic atom is next to the juncture.* If the ringjoining carbons are attached only to other aromatic carbons, electron delocalization is minimal and so is the correction: +0.10 for each I.C. If the I.C.s are also attached to a polar (fused-in) fragment, such as in quinoline or 2-phenylpyrimidine, the correction is greater, +0.31.*

3.2.2.3 Sigma/Rho Fragment Interaction

When two or more X and/or Y type fragments are attached to an aromatic ring system, the correction factors can be calculated by a method very similar to that used by Hammett(23) to calculate the electronic effects in other equilibria, such as acid ionization.* This requires the assignment of a measure of electronic 'strength' (sigma) and 'susceptibility' (rho). In dealing with electronic effects on partitioning equilibria, a few fragments appear to act 'bidirectionally' and require both sigma and rho values, although they cannot, of course, act upon themselves. Most of the details of sigma and rho assignment to X and Y type fragments can be found elsewhere (24), but it should be pointed out that the latest version of the program (CLOGP) follows a newer procedure for 'fused-in' fragments. Fragments fused in aromatic rings(e.g. -N= or >C=O) may also be assigned both rho and sigma constants and treated together with 'on-ring' fragments instead of requiring a separate treatment.*

Fragments on different rings in an aromatic ring system interact with one another but the effect is attenuated.* If the two rings in the system are fused, as in 5-acetyl-1-naphthylamine, the 'intrinsic' effect is only half the sigma rho product just as it is in the biphenyl system such as in 4-(m-chlorophenyl)aniline.

One frequently encounters aromatic ring systems containing several fragments with rho and sigma values assigned, and the potential correction from all cross products of sigma/rho could be very large. Since these multiple effects are NOT additive, some scaling down procedure was indicated. The one chosen for CLOGP takes the following steps:

a) The full potential sigma/rho product for each possible interaction is calculated and placed in descending value order, AFTER considering if the fragment pair are on the same or separate rings.

b) Except for the sigma for a pyridine type nitrogen, each use of sigma or rho causes it to 'age'. The first interaction at the top of the list is entered at full potential because the current age of its sigma and rho components is 'zero' for each. Each use reduces the effective sigma or rho value to 1/2 its previous value, and so if each were at 'age 1', the increment to the correction would only be 1/4 as much as a 'fresh' interaction. The mechanics of this computation are best understood by looking at the detailed output of some complex structures. Two such examples are provided in the example section.*

3.2.3 Special Ortho

As noted in the previous section, aromatic substituent (fragment) pairs, if they have sigma and rho values assigned to them, are given the same correction factor regardless of their relative position on the ring. It is important to keep in mind that if the fragment pair are on adjacent positions (i.e. ortho), an additional correction may be required.

3.2.3.1 Crowding

'Crowding' of certain fragment types can effectively lower their aromatic-attached values. This is most apparent in the case of fragments attached to the aromatic ring through a hetero atom which possesses an electron pair, such as -NHCOCH3.* A reasonable explanation of this observation is that the lone pair can no longer remain in the plane of the ring, making the fragment attachment resemble aliphatic (A) rather than true aromatic (a). The magnitude of the correction appears to depend on both steric and electronic (field) effects(25).

If this explanation is valid, one would expect the correction to vary continuously up to a maximum characteristic of each fragment type. It was surprising, therefore, to find that the rather large data set used in the original evaluation of the 'negative ortho' effect (24) seemed to fit multiples of Rekker's Magic Constant(20). This is handled in CLOGP by assigning integers to a matrix which has generalized fragment types for coordinates.

More recent data provides many examples which do not support this 'quantized' correction. Nevertheless, it is being retained for the present because of simplicity and because its maximum is only 0.14.

3.2.3.2 Intra-Molecular Hydrogen Bonding

Hydrogen bonding is known to occur intramolecularly between two ortho subsituents if one is a donor and the other an acceptor. A classical example of such an H-bond is that in o-nitrophenol. As might be expected, an intramolecular H-bond reduces water's ability to accommodate that solute, and the log P of o-nitrophenol is over two log units higher than the m- and p-isomers in the heptane and carbon tetrachloride solvent systems. One must always keep in mind, however, that the octanol phase possesses both H-donor and H-acceptor capability, not only because it is an alcohol, but because of the 2M water present at saturation. In actuality, the presence of the intramolecular H-bond in o-nitrophenol penalizes solvation in octanol slightly more than it does solvation in water, and its log P is 0.09 log units lower than the m- and p-isomers.

In terms of intramolecular H-bonding between aromatic ortho substituents, the octanol/water system appears to be sensitive to a very restricted class. The only clear-cut cases seem to result from a carbonyl group directly attached to the ring acting as acceptor, and a directly-attached -OH or -NH- acting as donor.* In all of the cases observed so far, the correction is very close to +0.63, and is stored in the same matrix used for the 'negative ortho' corrections. Thus the 'crowding' and H-bonding ortho effects never are applied simultaneously, but a sigma/rho correction cannot be added to either.

4. Summary

The fragment method of calculating log P(ow) has been proved valuable in many fields, including drug design and hazard assessment. However, manual calculations require a great deal of instructions and become very lengthy for complex structures and thus are error-prone. The computer program, CLOGP, enables the method to be applied by non-experts and includes an estimate of error, which is not possible in the future. Regular users can avail themselves of an annual update which will bring them current with all newly measured fragment values and improved correction factors. Versions with the Unified Driver compare the calculation from structure with a measured value from log P(ow) for neutral solutes. Starlist is also included in the annual updating service. We plan to make available in the near future a searching program, GENIE, which will extend the search of Starlist to close analogs.

The current literature contains many examples of QSAR accompanied by calculations of hydrophobicity which have not been made according to a consistent application of the rules they purport to follow. This has caused some confusion and cast doubt upon the entire approach. Perhaps, if the use of CLOGP becomes more widespread, published calculations will become more comparable, especially if reference is made to the program version.

Any prediction of the future is risky, but, judging from the recent past, we can expect an increasing demand for logP(ow) values. It is inconceivable that CLOGP will be perfected to such an extent that it supplants partition coefficient measurement. The two methods should remain as they are now: mutually complimentary.

With the STARLIST module in CLOGP, the user will be able to check the calculated value against an acceptable measured value if the solute structure entered is one of over 4,000 contained in that special file which is limited to non-tautomeric structures measured at a pH where the neutral form predominates.

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6. Example CLOGP Calculations

The calculations shown in the following section illustrate how CLOGP treats the basic fragment types and correction factors discussed in the reference section. No attempt was made to illustrate every fragment in the database, of course. Additional output was generated to illustrate the unusually complex sigma/rho electronic correction factor for atrazine and adenine.

The examples are arranged according to the section number of the CLOGP Reference Manual text which deals with the main feature illustrated. Since some structures illustrate more than one feature, some of these "secondary features" are also indicated by section number in the output.

6.1 Interpretation of Output

6.1.1 Maps

"Verbose" CLOGP output includes a section which shows the input SMILES and assignments of fragments, rings, hydrogen counts, and isolating carbon type. These "maps" are not shown in the example section, but are discussed here. The first line in the "Map Box" gives the SMILES as entered by the user. Fragment ordering, therefore, is NOT unique, and so to completely understand the tabular results, one should become familiar with the map. The second line in the map indicates Isolating Carbon type under their respective SMILES notations. The third line numbers the polar fragments (i.e., all those NOT I.C. or hydrogen) in the order entered. The fourth line shows the locations of hydrogen atoms, including those contained in fragments. The last lines indicate the location of atoms in rings. Even in simple structures these maps can be of help in interpreting the calculations. For example, in the four calculations in section 2.3.1, the value of the -Br fragment varies from 0.2000 to 1.090. The reason is apparent from the maps which show the variation in type of I.C. attachment.

6.1.2 Picture

Each example is accompanied by a picture of the chemical structure as generated by the DEPICT algorithm. DEPICT indicates aromaticity by drawing circles inside aromatic rings and suppressing all aromatic carbons symbols. More information about how aromaticity is defined and how the picture is generated may be found in the SMILES and DEPICT sections of the Daylight Software manual.

6.1.3 Tabular Results

Most of the nomenclature in the "calculation details" is understandable after reading the main body of the CLOGP Reference Manual, but a few terms could use further explanation:

Under Class one may find "SCREEN". This is further documented under the Description section of the CLOGP Reference Manual. For instance, it may note "possibly anomalous steroid". Under Type one may find the ring number for an Ortho interaction, for example, because there may be more than one ring on which such a correction might potentially be applicable. Under Description one finds (ZW-) or (ZW+) after the name of each fragment which can participate in zwitterion formation. However, only when strong enough pairs are present is the correction actually entered (near the bottom of the table). A sulfonic acid is strong enough even if both it and the amine are aromatic; for a carboxylic acid, both it and the amine must be aliphatic. Under "Comment" column the "CLOGP=#" is the version number of the Biobyte algorithm that is being used in the calculation, e.g. CLOGP=3.05. The calculated CLOGP appears in the "Value" column.

6.2 Examples of Anomalies

The final set of calculations illustrate some of the present shortcomings of CLOGP. For the first five of these, some rational explanation can be given for the discrepancy, and even an estimation of the amount.

Adenosine, like 84 other measured purine nucleosides, is underpredicted by CLOGP. There is good evidence that this is due to a long-range intramolecular hydrogen bond between the 5'OH and N3 of the purine. A paper documenting this effect has been submitted for publication, and it is planned to include this correcting in upcoming versions of CLOGP. Cortisone acetate is now well predicted with the special steroid correction factors. Chain overlap is a very difficult situation to identify. The earlier attempt to account for it as a 'Fragment Branch' correction has been abandoned.

7. Appendix - Example Calculations

```
SMILES: CCBr
ATOM #: 123.
ISOC-ID: AA..
FRAG-ID: ..1.
H-COUNT: 32..
```

ethylbromide 2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment Carbon	# 1	Bromide [A] 2 aliphatic isolating carbons 5 hydrogens on isolating carbons 1 chain and 0 alicyclic (net)	Measured	0.200
ExFragment			-	0.390
ExFragment	Hydrog Bonds		-	1.135
			-	-0.120
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.605**

```
logPstar = 1.61
```

```
SMILES: BrCc1ccccc1
ATOM #: 1.23.45678.
ISOC-ID: ..Za.aaaaa.
FRAG-ID: 1.........
H-COUNT: ..2..11111.
RING  1: ...a.aaaaa.
```

benzylbromide 2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Bromide [Z]	Measured	0.480
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780

ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120

RESULT DB=17 All fragments measured CLOGP=4.01 2.924

```
logPstar = 2.92
```

```
SMILES: BrC=C
ATOM #: 1.2.3
ISOC-ID: ..V.V
FRAG-ID: 1....
H-COUNT: ..1.2
```

vinyl bromide 2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Bromide [V]	Measured	0.690
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	3 hydrogens on isolating carbons	-	0.681
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120
ExFragment	Mbonds	1 double, 0 triple (isolated bond)	-	-0.030

RESULT DB=17 All fragments measured CLOGP=4.01 1.611

```
logPstar = 1.57
```

```
SMILES: Brc1ccccc1
ATOM #: 1.2.34567.
ISOC-ID: ..a.aaaaa.
FRAG-ID: 1.........
H-COUNT: ....11111.
RING  1: ..a.aaaaa.
```

bromobenzene 2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Bromide [a]	Measured	1.090
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135

RESULT DB=17 All fragments measured CLOGP=4.01 3.005

```
logPstar = 2.99
```

```
SMILES: NC(Cc1ccccc1)C(O)=O
ATOM #: 12.34.56789..0.1..2
ISOC-ID: ...Za.aaaaa........
FRAG-ID: 11...........1.1..1
H-COUNT: 21.2..11111....1...
RING  1: ....a.aaaaa........
```

phenylalanine 2.3.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	carboxy ZW(+), primary amine ZW(-) [Z]	Measured	-4.000
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120

RESULT DB=17 All fragments measured CLOGP=4.01 -1.556

logPstar = -1.52

SMILES: C=C
ATOM #: 1.2
ISOC-ID: V.V
FRAG-ID: ...
H-COUNT: 2.2

ethylene 2.3.4.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon ExFragment	Hydrog Mbonds	2 aliphatic isolating carbons	-	0.390
		4 hydrogens on isolating carbons	-	0.908
ExFragment		1 double, 0 triple (isolated bond)	-	-0.030

RESULT DB=17 All fragments measured CLOGP=4.01 1.268

logPstar = 1.13

SMILES: C=CC=C
ATOM #: 1.23.4
ISOC-ID: V.VV.V
FRAG-ID: ......
H-COUNT: 2.11.2

1,3-butadiene 2.3.4.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon ExFragment	Hydrog Bonds	4 aliphatic isolating carbons	-	0.780
		6 hydrogens on isolating carbons	-	1.362
ExFragment		2 chain and 0 alicyclic (net)	-	-0.240

RESULT DB=17 All fragments measured CLOGP=4.01 1.902

logPstar = 1.99

SMILES: CCCC
ATOM #: 1234
ISOC-ID: AAAA
FRAG-ID: ....
H-COUNT: 3223

butane 3.1.1.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon ExFragment	Hydrog Bonds	4 aliphatic isolating carbons	-	0.780
		10 hydrogens on isolating carbons	-	2.270
ExFragment		2 chain and 0 alicyclic (net)	-	-0.240

RESULT DB=17 All fragments measured CLOGP=4.01 2.810

logPstar = 2.89

SMILES: CCOCC
ATOM #: 12345
ISOC-ID: AA.AA

ethyl ether 3.1.1.1.

```
FRAG-ID: ..1..
H-COUNT: 32.23
```

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Ether [AA]	Measured	-1.820
Carbon		4 aliphatic isolating carbons	-	0.780
ExFragment	Hydrog	10 hydrogens on isolating carbons	-	2.270
ExFragment	Bonds	3 chain and 0 alicyclic (net)	-	-0.360
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.870**

```
logPstar = 0.89
```

```
SMILES: C1CCCCC1
ATOM #: 1.23456.
ISOC-ID: A.AAAAA.
FRAG-ID: ........
H-COUNT: 2.22222.
RING  1: A.AAAAA.
```

cyclohexane 3.1.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon	Hydrog	6 aliphatic isolating carbons	-	1.170
ExFragment		12 hydrogens on isolating carbons	-	2.724
ExFragment	Bonds	0 chain and 6 alicyclic (net)	-	-0.540
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**3.354**

```
logPstar = 3.44
```

```
SMILES: C1CCOC1
ATOM #: 1.2345.
ISOC-ID: A.AR.R.
FRAG-ID: ....1..
H-COUNT: 2.22.2.
RING  1: A.AAAA.
```

tetrahydropyran 3.1.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Ether [RR]	Measured	-1.750
OrthoEther		Ether in a 5-member ring	-	0.130
Carbon		4 aliphatic isolating carbons	-	0.780
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816
ExFragment	Bonds	0 chain and 5 alicyclic (net)	-	-0.450
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.526**

```
logPstar = 0.47
```

```
SMILES: CCN(CC)CC
ATOM #: 123.45.67
ISOC-ID: AA..AA.AA
FRAG-ID: ..1......
H-COUNT: 32..23.23
```

triethylamine 3.1.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Tertiary Amine [AAA]	Measured	-2.370
Carbon		6 aliphatic isolating carbons	-	1.170
ExFragment	Hydrog	15 hydrogens on isolating carbons	-	3.405
ExFragment	Bonds	5 chain and 0 alicyclic (net)	-	-0.600
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.605**

logPstar = 1.45

```
SMILES: CCOP(=O)(OCC)OCC
ATOM #: 1234..5..678.901
ISOC-ID: AA........AA..AA
FRAG-ID: ..11..1..1...1..
H-COUNT: 32........23..23
```

triethylphosphate 3.1.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Phosphate ester [AAA]	Measured	-2.290
Carbon		6 aliphatic isolating carbons	-	1.170
ExFragment	Hydrog	15 hydrogens on isolating carbons	-	3.405
ExFragment	Bonds	5 chain and 0 alicyclic (net)	-	-0.600
Fragbranch	Frag 1	5 net bonds (out of 6) count	-	-1.400
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.285**

logPstar = 0.80

```
SMILES: c1ccccc1
ATOM #: 1.23456.
ISOC-ID: a.aaaaa.
FRAG-ID: ........
H-COUNT: 1.11111.
RING  1: a.aaaaa.
```

benzene 3.1.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon	Hydrog	6 aromatic isolating carbons	-	0.780
ExFragment		6 hydrogens on isolating carbons	-	1.362
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**2.142**

logPstar = 2.13

```
SMILES: CC(C)C
ATOM #: 12.3.4
ISOC-ID: AA.A.A
FRAG-ID: ......
H-COUNT: 31.3.3
```

isobutane 3.1.2.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon	Branch	4 aliphatic isolating carbons	-	0.780
ExFragment	Hydrog	1 chain and 0 cluster branch	Chain	-0.130
ExFragment	Bonds	10 hydrogens on isolating carbons	-	2.270

ExFragment	2 chain and 0 alicyclic (net)	-	-0.240

RESULT DB=17 All fragments measured CLOGP=4.01 2.680

logPstar = 2.76

```
SMILES: CC(=O)C3CCC4C2CCC1=CC(=O)CCC1(C)C2CCC34C
ATOM #: 12..3.4.567.8.901..23..4.567..8.9.012..3
ISOC-ID: A.....A.AAA.A.AAV..W.....RAA..A.A.AAA..A
FRAG-ID: .1..1..............2..2..............
H-COUNT: 3.....1.221.1.22...1.....22...3.1.22...3
RING  1: ......A.AAA.......................A...
RING  2: ..........A.A...................A.AAA...
RING  3: ...............A..AA....AAA............
RING  4: ............A.AAA..........A....A.......
```

progesterone 3.1.2.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carbonyl [AA]	Measured	-1.840
Fragment	# 2	Carbonyl [AV]	Measured	-1.690
Carbon		19 aliphatic isolating carbons	-	3.705
ExFragment	Branch	2 chain and 6 cluster branches	Combined	-1.040
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	30 hydrogens on isolating carbons	-	6.810
ExFragment	Bonds	1 chain and 20 alicyclic (net)	(COMBINED)	-1.920
ExFragment	Mbonds	1 double, 0 triple (isolated bond)	-	-0.030

RESULT DB=17 All fragments measured CLOGP=4.01 3.775

logPstar = 3.87

```
SMILES: CC(C)Cl
ATOM #: 12.3.4.
ISOC-ID: AA.A...
FRAG-ID: .....1.
H-COUNT: 31.3...
```

2-chloropropane 3.1.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [A]	Measured	0.060
Carbon		3 aliphatic isolating carbons	-	0.585
ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240

RESULT DB=17 All fragments measured CLOGP=4.01 1.994

logPstar = 1.90

```
SMILES: ClC1C(Cl)C(Cl)C(Cl)C(Cl)C1Cl
ATOM #: 1.2.3.4..5.6..7.8..9.0..1.2.
ISOC-ID: ..R.R....R....R....R....R...
FRAG-ID: 1.....2....3....4....5....6.
H-COUNT: ..1.1....1....1....1....1...
RING  1: ..A.A....A....A....A....A...
```

hexachlorocyclohexane 3.1.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value

Fragment	# 1	Chloride [A]	Measured	0.060
Fragment	# 2	Chloride [A]	Measured	0.060
Fragment	# 3	Chloride [A]	Measured	0.060
Fragment	# 4	Chloride [A]	Measured	0.060
Fragment	# 5	Chloride [A]	Measured	0.060
Fragment	# 6	Chloride [A]	Measured	0.060
Carbon		6 aliphatic isolating carbons	-	1.170
ExFragment	Hydrog	6 hydrogens on isolating carbons	-	1.362
ExFragment	Bonds	0 chain and 6 alicyclic (net)	-	-0.540
Proximity	XCCX	0 F and 6 non-F fragments; 5 used.	-	1.400

RESULT DB=17 All fragments measured CLOGP=4.01 3.752

logPstar = 3.72

SMILES: CC(C)O
ATOM #: 12.3.4
ISOC-ID: AA.A..
FRAG-ID: 1
H-COUNT: 31.3.1

isopropyl alcohol 3.1.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Carbon		3 aliphatic isolating carbons	-	0.585
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240

RESULT DB=17 All fragments measured CLOGP=4.01 0.074

logPstar = 0.05

SMILES: CC(C)(C)O
ATOM #: 12.3..4.5
ISOC-ID: AA.A..A..
FRAG-ID: 1
H-COUNT: 3..3..3.1

tertiary butyl alcohol 3.1.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Carbon		4 aliphatic isolating carbons	-	0.780
ExFragment	Branch	1 chain and 0 cluster branch	Chain	-0.130
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	9 hydrogens on isolating carbons	-	2.043
ExFragment	Bonds	3 chain and 0 alicyclic (net)	-	-0.360

RESULT DB=17 All fragments measured CLOGP=4.01 0.473

logPstar = 0.35

SMILES: CCl
ATOM #: 12.
ISOC-ID: A..
FRAG-ID: .1.

chloromethane 3.2.1.1.

```
H-COUNT: 3..
```

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [A]	Measured	0.060
Carbon		1 aliphatic isolating carbon	-	0.195
ExFragment	Hydrog	3 hydrogens on isolating carbons	-	0.681
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.936**

```
logPstar = 0.91
```

```
SMILES: ClC(Cl)Cl
ATOM #: 1.2.3..4.
ISOC-ID: ..A......
FRAG-ID: 1...2..3.
H-COUNT: ..1......
```

chloroform 3.2.1.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [A]	Measured	0.060
Fragment	# 2	Chloride [A]	Measured	0.060
Fragment	# 3	Chloride [A]	Measured	0.060
Carbon		1 aliphatic isolating carbon	-	0.195
ExFragment	Hydrog	1 hydrogen on isolating carbon	-	0.227
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Proximity	XCX	3 interacting fragments	-	1.590
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.952**

```
logPstar = 1.97
```

```
SMILES: ClCCl
ATOM #: 1.23.
ISOC-ID: ..A..
FRAG-ID: 1..2.
H-COUNT: ..2..
```

dichloromethane 3.2.1.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [A]	Measured	0.060
Fragment	# 2	Chloride [A]	Measured	0.060
Carbon		1 aliphatic isolating carbon	-	0.195
ExFragment	Hydrog	2 hydrogens on isolating carbons	-	0.454
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120
Proximity	XCX	2 interacting fragments	-	0.600
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.249**

```
logPstar = 1.25
```

```
SMILES: ClC(Cl)(Cl)Cl
ATOM #: 1.2.3...4..5.
ISOC-ID: ..A.........
FRAG-ID: 1...2...3..4.
H-COUNT: ............
```

carbontetrachloride 3.2.1.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [A]	Measured	0.060
Fragment	# 2	Chloride [A]	Measured	0.060
Fragment	# 3	Chloride [A]	Measured	0.060
Fragment	# 4	Chloride [A]	Measured	0.060
Carbon		1 aliphatic isolating carbon	-	0.195
ExFragment	Bonds	3 chain and 0 alicyclic (net)	-	-0.360
Proximity	XCX	4 interacting fragments	-	2.800
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**2.875**

logPstar = 2.83

SMILES: ClCCCl
ATOM #: 1.234.
ISOC-ID: ..AA..
FRAG-ID: 1...2.
H-COUNT: ..22..

1,2-dichloroethane 3.2.1.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [A]	Measured	0.060
Fragment	# 2	Chloride [A]	Measured	0.060
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Proximity	XCCX	0 F and 2 non-F fragments; 1 used.	-	0.280
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.458**

logPstar = 1.47

SMILES: ClC=C(Cl)Cl
ATOM #: 1.2.3.4..5.
ISOC-ID: ..V.V......
FRAG-ID: 1.....2..3.
H-COUNT: ..1........

trichlorethylene 3.2.1.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [V]	Measured	0.600
Fragment	# 2	Chloride [V]	Measured	0.600
Fragment	# 3	Chloride [V]	Measured	0.600
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	1 hydrogen on isolating carbon	-	0.227
ExFragment	Bonds	3 chain and 0 alicyclic (net)	-	-0.360
ExFragment	Mbonds	1 double, 0 triple (isolated bond)	-	-0.030
Proximity	XCX	2 interacting fragments	-	0.600
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**2.627**

logPstar = 2.61

SMILES: ClC(Cl)=C(Cl)Cl
ATOM #: 1.2.3...4.5..6.

tetrachloroethylene 3.2.1.1.

```
ISOC-ID: ..V.....V......
FRAG-ID: 1...2.....3..4.
H-COUNT: ..............
```

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Chloride [V]	Measured	0.600
Fragment	# 2	Chloride [V]	Measured	0.600
Fragment	# 3	Chloride [V]	Measured	0.600
Fragment	# 4	Chloride [V]	Measured	0.600
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
ExFragment	Mbonds	1 double, 0 triple (isolated bond)	-	-0.030
Proximity	XCX	4 interacting fragments	-	1.200
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**3.480**

```
logPstar = 3.40
```

```
SMILES: CCOC(C)OCC
ATOM #: 1234.5.678
ISOC-ID: AA.A.A..AA
FRAG-ID: ..1....2..
H-COUNT: 32.1.3..23
```

diethylacetal 3.2.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Ether [AA]	Measured	-1.820
Fragment	# 2	Ether [AA]	Measured	-1.820
Carbon		6 aliphatic isolating carbons	-	1.170
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	14 hydrogens on isolating carbons	-	3.178
ExFragment	Bonds	6 chain and 0 alicyclic (net)	-	-0.720
Proximity	YCY	Fragments 1 & 2: -.32 (-1.82+-1.82)	-	1.165
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.933**

```
logPstar = 0.84
```

```
SMILES: OC(=O)COc1ccccc1
ATOM #: 12..3.456.78901.
ISOC-ID: ......A.a.aaaaa.
FRAG-ID: 11..1..2........
H-COUNT: 1.....2...11111.
RING  1: ........a.aaaaa.
```

phenoxyacetic acid 3.2.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carboxy (ZW-) [A]	Measured	-1.070
Fragment	# 2	Ether [Aa]	Measured	-0.610
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Proximity	YCY	Fragments 1 & 2: -.42 (-1.07+-0.61)	-	0.706
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.350**

```
logPstar = 1.34
```

```
SMILES: OCCO
ATOM #: 1234
ISOC-ID: .AA.
FRAG-ID: 1..2
H-COUNT: 1221
```

ethylene glycol 3.2.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Alcohol or Hydroxy [A]	Measured	-1.640
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Proximity	YCCY	1 pair over bond 3- 2 (AvWt=-.260)	-	0.853
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**-1.369**

```
logPstar = -1.36
```

```
SMILES: O=NN1CCOCC1
ATOM #: 1.23.45678.
ISOC-ID: .....RR.RR.
FRAG-ID: 1.11...2...
H-COUNT: .....22.22.
RING  1: ...A.AAAAA.
```

N-nitrosomorpholine 3.2.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Nitrosamine [AA]	Measured	-2.250
Fragment	# 2	Ether [RR]	Measured	-1.750
Carbon		4 aliphatic isolating carbons	-	0.780
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816
ExFragment	Bonds	0 chain and 6 alicyclic (net)	-	-0.540
Proximity	YCCY	1 pair over bond 5- 4 (AvWt=-.150)	-	0.600
Proximity	YCCY	1 pair over bond 8- 7 (AvWt=-.150)	-	0.600
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**-0.744**

```
logPstar = -0.44
```

```
SMILES: OC1COC(O)C(O)C1O
ATOM #: 12.345.6.7.8.9.0
ISOC-ID: .R.R.R...R...R..
FRAG-ID: 1...2..3...4...5
H-COUNT: 11.2.1.1.1.1.1.1
RING  1: .A.AAA...A...A..
```

arabinose 3.2.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Ether [RR]	Measured	-1.750
Fragment	# 3	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 4	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 5	Alcohol or Hydroxy [A]	Measured	-1.640

Carbon		5 aliphatic isolating carbons	-	0.975
ExFragment	Branch	4 non-halogen, polar group branches	Group	-0.880
ExFragment	Hydrog	6 hydrogens on isolating carbons	-	1.362
ExFragment	Bonds	0 chain and 6 alicyclic (net)	-	-0.540
Proximity	YCY	Fragments 2 & 3: -.37 (-1.75+-1.64)	-	1.254
Proximity	YCCY	1 pair over bond 3- 2 (AvWt=-.230)	-	0.780
Proximity	YCCY	2 pairs over bond 7- 5 (AvWt=-.245)	-	0.816
Proximity	YCCY	1 pair over bond 9- 7 (AvWt=-.260)	-	0.853
Proximity	YCCY	1 pair over bond 9- 2 (AvWt=-.260)	-	0.853
Proximity	YCCCY	1 pair over bond 7- 2 (AvWt=-.200)	Branch	0.656

RESULT DB=17 All fragments measured CLOGP=4.01 -2.181

logPstar = -2.32

```
SMILES: CC3(C)SC2C(NC(=O)Cc1ccccc1)C(=O)N2C3C(O)=O
ATOM #: 12..3.45.6.78..9.01.23456..7..8.9.0.1.2..3
ISOC-ID: AR..A..R.R.......Za.aaaaa.........R.......
FRAG-ID: ......1....22..2...........3..3.3...4.4..4
H-COUNT: 3...3..1.1.1.....2..11111.........1...1...
RING  1: .......A.A.................A....A.........
RING  2: .A....AA.......................A.A.......
RING  3: ..................a.aaaaa.................
```

benzylpenicillin 3.2.1.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Sulfide [RR]	Derived	-0.700
Fragment	# 2	NH-Amide [AZ/AA]	Adjusted	-2.510
Fragment	# 3	Amide [AAA]	Measured	-3.190
Fragment	# 4	Carboxy (ZW-) [A]	Measured	-1.070
Carbon		7 aliphatic isolating carbons	-	1.365
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	2 chain and 1 cluster branches	Combined	-0.390
ExFragment	Branch	2 non-halogen, polar group branches	Group	-0.440
ExFragment	Hydrog	16 hydrogens on isolating carbons	-	3.632
ExFragment	Bonds	2 chain and 7 alicyclic (net)	(COMBINED)	-0.870
Proximity	YCY	Fragments 1 & 3: -.32 (-0.70+-3.19)	-	1.245
Proximity	YCY	Fragments 2 & 3: -.32 (-2.51+-3.19)	-	1.824
Proximity	YCY	Fragments 3 & 4: -.37 (-3.19+-1.07)	-	1.576
Proximity	YCCY	2 pairs over bond 20- 2 (AvWt=-.190)	-	0.495

RESULT DB=17 Adjusted (1) from measured value CLOGP=4.01 1.747

logPstar = 1.83

```
SMILES: FC(F)(F)S(=O)(=O)Nc1ccccc1
ATOM #: 12.3..4.5..6...7.89.01234.
ISOC-ID: .A..............a.aaaaa.
FRAG-ID: 1..2..3.4..4...4.4........
H-COUNT: ..............1..11111.
RING  1: ..............a.aaaaa.
```

CF3-sulfonanilide 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Fluoride [A]	Measured	-0.380
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	NH-Sulfonamide [aA]	Measured	-1.720

Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	Y3-X3	Effect for Y-fragment # 4	-	2.700

RESULT DB=17 All fragments measured CLOGP=4.01 3.060

logPstar = 3.05

```
SMILES: FC(F)(F)S(=O)(=O)c1ccccc1
ATOM #: 12.3..4.5..6...7.8.90123.
ISOC-ID: .A.............a.aaaaa.
FRAG-ID: 1..2..3.4..4...4.........
H-COUNT: ...................11111.
RING  1: ................a.aaaaa.
```

CF3-phenyl-sulfone 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Fluoride [A]	Measured	-0.380
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	Sulfonyl [Aa]	Measured	-2.170
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	Y3-X3	Effect for Y-fragment # 4	-	2.700

RESULT DB=17 All fragments measured CLOGP=4.01 2.610

logPstar = 2.68

```
SMILES: NC(=O)C(F)(F)F
ATOM #: 12..3.4.5..6.7
ISOC-ID: ......A.......
FRAG-ID: 11..1...2..3.4
H-COUNT: 2.............
```

trifluoroacetamide 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	NH2-Amide [A]	Measured	-1.990
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	Fluoride [A]	Measured	-0.380
Carbon		1 aliphatic isolating carbon	-	0.195
ExFragment	Bonds	3 chain and 0 alicyclic (net)	-	-0.360
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	Y2-X3	Effect for Y-fragment # 1	-	1.700

RESULT DB=17 All fragments measured CLOGP=4.01 -0.005

logPstar = 0.12

```
SMILES: FC(F)(F)C(=O)Nc1ccccc1
ATOM #: 12.3..4.5..6.78.90123.
ISOC-ID: .A...........a.aaaaa.
FRAG-ID: 1..2..3.4..4.4........
H-COUNT: ............1..11111.
RING  1: ............a.aaaaa.
```

trifluoroacetanilide 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Fluoride [A]	Measured	-0.380
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	NH-Amide [aA]	Measured	-1.510
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	Y2-X3	Effect for Y-fragment # 4	-	1.700
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**2.270**

```
logPstar = 2.21
```

```
SMILES: FC(F)(F)Oc1ccccc1
ATOM #: 12.3..4.56.78901.
ISOC-ID: .A.......a.aaaaa.
FRAG-ID: 1..2..3.4........
H-COUNT: ...........11111.
RING  1: .........a.aaaaa.
```

trifluoroanisole 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Fluoride [A]	Measured	-0.380
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	Ether [Aa]	Measured	-0.610
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	Y2-X3	Effect for Y-fragment # 4	-	1.700
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**3.170**

```
logPstar = 3.17
```

```
SMILES: CCOC(=O)C(F)(F)F
ATOM #: 1234..5.6.7..8.9
ISOC-ID: AA......A.......
FRAG-ID: ..11..1...2..3.4
H-COUNT: 32.............
```

trifluoroacetic acid, et.ester 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Ester [AA]	Measured	-1.450

Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	Fluoride [A]	Measured	-0.380
Carbon		3 aliphatic isolating carbons	-	0.585
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
ExFragment	Bonds	5 chain and 0 alicyclic (net)	-	-0.600
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	Y1-X3	Effect for Y-fragment # 1	-	1.150

RESULT DB=17 All fragments measured CLOGP=4.01 1.270

logPstar = 1.18

```
SMILES: NC(=O)CCl
ATOM #: 12..3.45.
ISOC-ID: ......A..
FRAG-ID: 11..1..2.
H-COUNT: 2.....2..
```

chloroacetamide 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	NH2-Amide [A]	Measured	-1.990
Fragment	# 2	Chloride [A]	Measured	0.060
Carbon		1 aliphatic isolating carbon	-	0.195
ExFragment	Hydrog	2 hydrogens on isolating carbons	-	0.454
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120
Proximity	Y2-X1	Effect for Y-fragment # 1	-	0.900

RESULT DB=17 All fragments measured CLOGP=4.01 -0.501

logPstar = -0.53

```
SMILES: CC(=O)NC(CO)C(O)c1ccc(cc1)N(=O)=O
ATOM #: 12..3.45.67.8.9.0.123.45..6..7..8
ISOC-ID: A......A.A..Z...a.aaa.aa.........
FRAG-ID: .1..1.1...2...3...........4..4..4
H-COUNT: 3.....11.21.1.1...11..11.........
RING  1: ...............a.aaa.aa.........
```

parent amphenicol 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	NH-Amide [AA]	Measured	-2.710
Fragment	# 2	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 3	Alcohol or Hydroxy [Z]	Measured	-1.340
Fragment	# 4	Nitro [a]	Measured	-0.030
Carbon		4 aliphatic isolating carbons	-	0.780
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	2 non-halogen, polar group branches	Group	-0.440
ExFragment	Hydrog	11 hydrogens on isolating carbons	-	2.497
ExFragment	Bonds	6 chain and 0 alicyclic (net)	-	-0.720
Proximity	YCCY	1 pair over bond 6- 5 (AvWt=-.260)	-	1.131
Proximity	YCCY	1 pair over bond 8- 5 (AvWt=-.260)	-	1.053
Proximity	YCCCY	1 pair over bond 8- 6 (AvWt=-.200)	Branch	0.596

RESULT DB=17 All fragments measured CLOGP=4.01 -0.043

logPstar = -0.03

```
SMILES: OCC(NC(=O)CCl)C(O)c1ccc(cc1)N(=O)=O
ATOM #: 123.45..6.78..9.0.1.234.56..7..8..9
ISOC-ID: .AA.......A...Z...a.aaa.aa.........
FRAG-ID: 1...22..2..3....4...........5..5..5
H-COUNT: 121.1.....2...1.1...11..11.........
RING  1: ..................a.aaa.aa.........
```

monochloramphenicol 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	NH-Amide [AA]	Measured	-2.710
Fragment	# 3	Chloride [A]	Measured	0.060
Fragment	# 4	Alcohol or Hydroxy [Z]	Measured	-1.340
Fragment	# 5	Nitro [a]	Measured	-0.030
Carbon		4 aliphatic isolating carbons	-	0.780
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	2 non-halogen, polar group branches	Group	-0.440
ExFragment	Hydrog	10 hydrogens on isolating carbons	-	2.270
ExFragment	Bonds	7 chain and 0 alicyclic (net)	-	-0.840
Proximity	Y2-X1	Effect for Y-fragment # 2	-	0.900
Proximity	YCCY	1 pair over bond 3- 2 (AvWt=-.260)	-	1.131
Proximity	YCCY	1 pair over bond 9- 3 (AvWt=-.260)	-	1.053
Proximity	YCCCY	1 pair over bond 9- 2 (AvWt=-.200)	Branch	0.596
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.570**

```
logPstar = 0.59
```

```
SMILES: OCC(NC(=O)C(Cl)Cl)C(O)c1ccc(cc1)N(=O)=O
ATOM #: 123.45..6.7.8..9..0.1.2.345.67..8..9..0
ISOC-ID: .AA.......A.......Z...a.aaa.aa.........
FRAG-ID: 1...22..2...3..4....5...........6..6..6
H-COUNT: 121.1.....1.......1.1...11..11.........
RING  1: ......................a.aaa.aa.........
```

chloramphenicol 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	NH-Amide [AA]	Measured	-2.710
Fragment	# 3	Chloride [A]	Measured	0.060
Fragment	# 4	Chloride [A]	Measured	0.060
Fragment	# 5	Alcohol or Hydroxy [Z]	Measured	-1.340
Fragment	# 6	Nitro [a]	Measured	-0.030
Carbon		4 aliphatic isolating carbons	-	0.780
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	2 non-halogen, polar group branches	Group	-0.440
ExFragment	Hydrog	9 hydrogens on isolating carbons	-	2.043
ExFragment	Bonds	8 chain and 0 alicyclic (net)	-	-0.960
Proximity	XCX	2 interacting fragments	-	0.600
Proximity	Y2-X2	Effect for Y-fragment # 2	-	1.300
Proximity	YCCY	1 pair over bond 3- 2 (AvWt=-.260)	-	1.131
Proximity	YCCY	1 pair over bond 10- 3 (AvWt=-.260)	-	1.053
Proximity	YCCCY	1 pair over bond 10- 2 (AvWt=-.200)	Branch	0.596
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.283**

```
logPstar = 1.14
```

```
SMILES: OCC(NC(=O)C(Cl)(Cl)Cl)C(O)c1ccc(cc1)N(=O)=O
ATOM #: 123.45..6.7.8...9..0..1.2.3.456.78..9..0..1
ISOC-ID: .AA.......A..........Z...a.aaa.aa.........
FRAG-ID: 1...22..2...3...4..5....6..........7..7..7
H-COUNT: 121.1.................1.1...11..11.........
RING  1: ........................a.aaa.aa.........
```

trichloramphenicol 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	NH-Amide [AA]	Measured	-2.710
Fragment	# 3	Chloride [A]	Measured	0.060
Fragment	# 4	Chloride [A]	Measured	0.060
Fragment	# 5	Chloride [A]	Measured	0.060
Fragment	# 6	Alcohol or Hydroxy [Z]	Measured	-1.340
Fragment	# 7	Nitro [a]	Measured	-0.030
Carbon		4 aliphatic isolating carbons	-	0.780
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	2 non-halogen, polar group branches	Group	-0.440
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816
ExFragment	Bonds	9 chain and 0 alicyclic (net)	-	-1.080
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	Y2-X3	Effect for Y-fragment # 2	-	1.700
Proximity	YCCY	1 pair over bond 3- 2 (AvWt=-.260)	-	1.131
Proximity	YCCY	1 pair over bond 11- 3 (AvWt=-.260)	-	1.053
Proximity	YCCCY	1 pair over bond 11- 2 (AvWt=-.200)	Branch	0.596
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**2.386**

```
logPstar = 1.97
```

```
SMILES: OCC(Cl)Cl
ATOM #: 123.4..5.
ISOC-ID: .AA......
FRAG-ID: 1...2..3.
H-COUNT: 121......
```

2,2-dichloroethanol 3.2.1.3

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Chloride [A]	Measured	0.060
Fragment	# 3	Chloride [A]	Measured	0.060
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	3 hydrogens on isolating carbons	-	0.681
ExFragment	Bonds	3 chain and 0 alicyclic (net)	-	-0.360
Proximity	XCX	2 interacting fragments	-	0.600
Proximity	XCCY	0 F and 2 non-F interactions	-	0.700
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.491**

```
logPstar = 0.37
```

```
SMILES: OCC(Cl)(Cl)Cl
ATOM #: 123.4...5..6.
ISOC-ID: .AA.........
FRAG-ID: 1...2...3..4.
H-COUNT: 12..........
```

2,2,2-trichloroethanol 3.2.1.3

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Chloride [A]	Measured	0.060
Fragment	# 3	Chloride [A]	Measured	0.060
Fragment	# 4	Chloride [A]	Measured	0.060
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	2 hydrogens on isolating carbons	-	0.454
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	XCCY	0 F and 3 non-F interactions	-	1.050
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.544**

logPstar = 1.42

SMILES: OCC(F)(F)F
ATOM #: 123.4..5.6
ISOC-ID: .AA.......
FRAG-ID: 1...2..3.4
H-COUNT: 12........

2,2,2-trifluoroethanol 3.2.1.3

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	Fluoride [A]	Measured	-0.380
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	2 hydrogens on isolating carbons	-	0.454
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCX	3 interacting fragments	-	1.590
Proximity	XCCY	3 F and 0 non-F interactions	-	1.350
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.524**

logPstar = 0.41

SMILES: OCCCl
ATOM #: 1234.
ISOC-ID: .AA..
FRAG-ID: 1..2.
H-COUNT: 122..

2-chloroethanol 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Chloride [A]	Measured	0.060
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Proximity	XCCY	0 F and 1 non-F interactions	-	0.350
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**-0.172**

logPstar = -0.06

```
SMILES: OCCF
ATOM #: 1234
ISOC-ID: .AA.
FRAG-ID: 1..2
H-COUNT: 122.
```

2-fluoroethanol 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Fluoride [A]	Measured	-0.380
Carbon		2 aliphatic isolating carbons	-	0.390
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Proximity	XCCY	1 F and 0 non-F interactions	-	0.450
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**-0.512**

```
logPstar = -0.76
```

```
SMILES: OC(CF)CF
ATOM #: 12.34.56
ISOC-ID: .A.A..A.
FRAG-ID: 1...2..3
H-COUNT: 11.2..2.
```

1,3-difluoro-2-propanol 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Carbon		3 aliphatic isolating carbons	-	0.585
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCCY	2 F and 0 non-F interactions	-	0.900
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**-0.480**

```
logPstar = -0.36
```

```
SMILES: FC(F)(F)CN(CC(F)(F)F)N=O
ATOM #: 12.3..4.56.78.9..0.1.2.3
ISOC-ID: .A......A..AA..........
FRAG-ID: 1..2..3..4....5..6.7.4.4
H-COUNT: ........2..2...........
```

n-NO-bis(2,2,2-triflet)amine 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Fluoride [A]	Measured	-0.380
Fragment	# 2	Fluoride [A]	Measured	-0.380
Fragment	# 3	Fluoride [A]	Measured	-0.380
Fragment	# 4	Nitrosamine [AA]	Measured	-2.250
Fragment	# 5	Fluoride [A]	Measured	-0.380
Fragment	# 6	Fluoride [A]	Measured	-0.380
Fragment	# 7	Fluoride [A]	Measured	-0.380
Carbon		4 aliphatic isolating carbons	-	0.780
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908

ExFragment	Bonds	9 chain and 0 alicyclic (net)	-	-1.080
Proximity	XCX	6 interacting fragments	-	3.180
Proximity	XCCY	6 F and 0 non-F interactions	-	2.700

RESULT DB=17 All fragments measured CLOGP=4.01 1.958

logPstar = 2.15

SMILES: CCOCCCl
ATOM #: 123456.
ISOC-ID: AA.AA..
FRAG-ID: ..1..2.
H-COUNT: 32.22..

2-chloroethylether 3.2.1.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Ether [AA]	Measured	-1.820
Fragment	# 2	Chloride [A]	Measured	0.060
Carbon		4 aliphatic isolating carbons	-	0.780
ExFragment	Hydrog	9 hydrogens on isolating carbons	-	2.043
ExFragment	Bonds	4 chain and 0 alicyclic (net)	-	-0.480
Proximity	XCCY	0 F and 1 non-F interactions	-	0.350

RESULT DB=17 All fragments measured CLOGP=4.01 0.933

logPstar = 0.98

SMILES: CCCC(O)=O
ATOM #: 1234.5..6
ISOC-ID: AAA......
FRAG-ID: ...1.1..1
H-COUNT: 322..1...

butyric acid 3.2.2.1

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carboxy (ZW-) [A]	Measured	-1.070
Carbon		3 aliphatic isolating carbons	-	0.585
ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240

RESULT DB=17 All fragments measured CLOGP=4.01 0.864

logPstar = 0.79

SMILES: OC(=O)Cc1ccccc1
ATOM #: 12..3.45.67890.
ISOC-ID: ......Za.aaaaa.
FRAG-ID: 11..1.........
H-COUNT: 1.....2..11111.
RING 1: ....a.aaaaa.

phenylacetic acid 3.2.2.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carboxy (ZW-) [Z]	Measured	-1.030
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780

ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120

RESULT DB=17 All fragments measured CLOGP=4.01 1.414

logPstar = 1.41

```
SMILES: CC=CC(O)=O
ATOM #: 12.34.5..6
ISOC-ID: AV.V......
FRAG-ID: ....1.1..1
H-COUNT: 31.1..1...
```

crotonic acid 3.2.2.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carboxy (ZW-) [V]	Measured	-0.570
Carbon		3 aliphatic isolating carbons	-	0.585
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
ExFragment	Mbonds	1 double, 0 triple (isolated bond)	-	-0.030

RESULT DB=17 All fragments measured CLOGP=4.01 0.880

logPstar = 0.72

```
SMILES: OC(=O)C=Cc1ccccc1
ATOM #: 12..3.4.56.78901.
ISOC-ID: ......Y.Ya.aaaaa.
FRAG-ID: 11..1...........
H-COUNT: 1.....1.1..11111.
RING  1: .........a.aaaaa.
```

cinnamic acid 3.2.2.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carboxy (ZW-) [Y]	Measured	-0.430
Carbon		2 aliphatic isolating carbons	-	0.390
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Proximity	PCCY	1 phenyl-fragment pair	-	0.150

RESULT DB=17 All fragments measured CLOGP=4.01 2.239

logPstar = 2.13

```
SMILES: OC(=O)c1ccccc1
ATOM #: 12..3.4.56789.
ISOC-ID: ......a.aaaaa.
FRAG-ID: 11..1.........
H-COUNT: 1.......11111.
RING  1: ......a.aaaaa.
```

benzoic acid 3.2.2.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carboxy (ZW-) [a]	Measured	-0.030
Carbon		6 aromatic isolating carbons	-	0.780

ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135

RESULT DB=17 All fragments measured CLOGP=4.01 1.885

logPstar = 1.87

```
SMILES: c2ccc1ccccc1c2
ATOM #: 1.234.56789.0.
ISOC-ID: a.aaa.aaaaa.a.
FRAG-ID: ..............
H-COUNT: 1.11..1111..1.
RING  1: ....a.aaaaa...
RING  2: a.aaa.....a.a.
```

naphthalene 3.2.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon	Carbon	10 aromatic isolating carbons	-	1.300
Fusion	Carbon	2 extended aromatic iso-C's	-	0.200
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816

RESULT DB=17 All fragments measured CLOGP=4.01 3.316

logPstar = 3.30

```
SMILES: c1ccc(cc1)c2ccccc2
ATOM #: 1.234.56..7.89012.
ISOC-ID: a.aaa.aa..a.aaaaa.
FRAG-ID: ..................
H-COUNT: 1.11..11....11111.
RING  1: ..........a.aaaaa.
RING  2: a.aaa.aa..........
```

biphenyl 3.2.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Carbon	Carbon	12 aromatic isolating carbons	-	1.560
Fusion	Carbon	2 extended aromatic iso-C's	-	0.200
ExFragment	Hydrog	10 hydrogens on isolating carbons	-	2.270

RESULT DB=17 All fragments measured CLOGP=4.01 4.030

logPstar = 4.01

```
SMILES: c2ccc1ncccc1c2
ATOM #: 1.234.56789.0.
ISOC-ID: a.aaa..aaaa.a.
FRAG-ID: ......1.......
H-COUNT: 1.11...111..1.
RING  1: ....a.aaaaa...
RING  2: a.aaa.....a.a.
```

quinoline 3.2.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Carbon		9 aromatic isolating carbons	-	1.170
Fusion	Carbon	1 extended aromatic iso-C	-	0.100
Fusion	Carbon	1 extended hetero-aromatic iso-C	-	0.310

```
ExFragment    Hydrog     7 hydrogens on isolating carbons    -                1.589
```

RESULT DB=17 All fragments measured CLOGP=4.01 2.029

```
logPstar = 2.03
```

```
SMILES: c3ccc2nc1ccccc1nc2c3
ATOM #: 1.234.56.78901.23.4.
ISOC-ID: a.aaa..a.aaaaa..a.a.
FRAG-ID: ......1........2....
H-COUNT: 1.11.....1111.....1.
RING  1: .......a.aaaaa......
RING  2: ....a.aa.....a.aa...
RING  3: a.aaa...........a.a.
```

phenazine 3.2.2.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 2	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Carbon		12 aromatic isolating carbons	-	1.560
Fusion	Carbon	4 extended hetero-aromatic iso-C's	-	1.240
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816
Electronic	SigRho	2 potential interactions; 2.00 used	WithinRing	0.540

RESULT DB=17 All fragments measured CLOGP=4.01 2.876

```
logPstar = 2.84
```

```
SMILES: Nc1cccc(c1)N(=O)=O
ATOM #: 12.3456.7..8..9..0
ISOC-ID: .a.aaaa.a.........
FRAG-ID: 1..........2..2..2
H-COUNT: 2..111..1.........
RING  1: .a.aaaa.a.........
```

m-nitroaniline 3.2.2.3

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Primary Amine [a]	Measured	-1.000
Fragment	# 2	Nitro [a]	Measured	-0.030
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908
Electronic	SigRho	1 potential interaction; 1.00 used	WithinRing	0.600

RESULT DB=17 All fragments measured CLOGP=4.01 1.258

```
logPstar = 1.37
```

```
SMILES: Nc1nc(N)nc(n1)c2ccccc2
ATOM #: 12.34.5.67.8..9.01234.
ISOC-ID: .a..a....a....a.aaaaa.
FRAG-ID: 1..2..3.4..5..........
H-COUNT: 2.....2.........11111.
RING  1: ..............a.aaaaa.
RING  2: .a.aa...aa.a..........
```

benzoguanamine 3.2.2.3.

Class	Type	Log(P) Contribution Description	Comment	Value

Fragment	# 1	Primary Amine [a]	Measured	-1.000
Fragment	# 2	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 3	Primary Amine [a]	Measured	-1.000
Fragment	# 4	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 5	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Carbon		9 aromatic isolating carbons	-	1.170
Fusion	Carbon	1 extended aromatic iso-C	-	0.100
Fusion	Carbon	1 extended hetero-aromatic iso-C	-	0.310
ExFragment	Hydrog	5 hydrogens on isolating carbons	-	1.135
Electronic	SigRho	12 potential interactions; 6.99 used	WithinRing	3.744

RESULT DB=17 All fragments measured CLOGP=4.01 1.039

logPstar = 1.36

```
SMILES: CCNc1nc(Cl)nc(NC(C)C)n1
ATOM #: 1234.56.7..89.01.2.3.4.
ISOC-ID: AA.a..a.....a..A.A.A...
FRAG-ID: ..1..2..3..4..5......6.
H-COUNT: 321..........11.3.3...
RING  1: ...a.aa....aa........a.
```

atrazine 3.2.2.3.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Secondary amine [Aa]	Measured	-1.030
Fragment	# 2	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 3	Chloride [a]	Measured	0.940
Fragment	# 4	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 5	Secondary amine [Aa]	Measured	-1.030
Fragment	# 6	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Carbon		5 aliphatic isolating carbons	-	0.975
Carbon		3 aromatic isolating carbons	-	0.390
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	12 hydrogens on isolating carbons	-	2.724
ExFragment	Bonds	5 chain and 0 alicyclic (net)	-	-0.600
Electronic	SigRho	17 potential interactions; 7.07 used	WithinRing	3.974

RESULT DB=17 All fragments measured CLOGP=4.01 2.703

logPstar = 2.61

```
SMILES: CN(C)c1cccc2c(cccc12)S(N)(=O)=O
ATOM #: 12.3.4.5678.9.0123...4.5...6..7
ISOC-ID: A..A.a.aaaa.a.aaaa.............
FRAG-ID: .1...................2.2...2..2
H-COUNT: 3..3...111....111......2.......
RING  1: ..........a.a.aaaa.............
RING  2: .....a.aaaa......a.............
```

1-dimeam-5-SO2NH2-naphth 3.2.2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Tertiary Amine [AAa]	Measured	-1.120
Fragment	# 2	NH2-Sulfonamide [a]	Measured	-1.610
Carbon		2 aliphatic isolating carbons	-	0.390
Carbon		10 aromatic isolating carbons	-	1.300
Fusion	Carbon	2 extended aromatic iso-C's	-	0.200
ExFragment	Hydrog	12 hydrogens on isolating carbons	-	2.724
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240

Electronic	SigRho	1 potential interaction; 1.00 used	FusedRings	0.160

RESULT DB=17 All fragments measured CLOGP=4.01 1.804

logPstar = 2.01

```
SMILES: CCOc2ccc1sc(nc1c2)S(N)(=O)=O
ATOM #: 1234.567.89.01.2..3.4...5..6
ISOC-ID: AA.a.aaa..a..a.a...........
FRAG-ID: ..1......2..3.....4.4...4..4
H-COUNT: 32...11........1....2.......
RING  1: .......a.aa.aa..............
RING  2: ...a.aaa.....a.a............
```

ethoxyzolamide 3.2.2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Ether [Aa]	Measured	-0.610
Fragment	# 2	Thiophenyl [aa]	Measured	0.360
Fragment	# 3	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 4	NH2-Sulfonamide [a]	Measured	-1.610
Carbon		2 aliphatic isolating carbons	-	0.390
Carbon		7 aromatic isolating carbons	-	0.910
Fusion	Carbon	2 extended hetero-aromatic iso-C's	-	0.620
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816
ExFragment	Bonds	2 chain and 0 alicyclic (net)	-	-0.240
Electronic	SigRho	6 potential interactions; 3.03 used	WithinRing	1.043
Electronic	SigRho	6 potential interactions; 1.64 used	FusedRings	0.408
H-bonding	Ring 1	Frag-pair: 4 & 3	-	0.100

RESULT DB=17 All fragments measured CLOGP=4.01 2.047

```
SMILES: Nc1ncnc2nc[nH]c12
ATOM #: 12.3456.78.9..0..
ISOC-ID: .a..a.a..a....a..
FRAG-ID: 1..2.3..4..5.....
H-COUNT: 2...1....1.1.....
RING  1: ......a.aa.a..a..
RING  2: .a.aaaa.......a..
```

adenine 3.2.2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Primary Amine [a]	Measured	-1.000
Fragment	# 2	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 3	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 4	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 5	Aromatic NH [aa]	Measured	-0.680
Carbon		5 aromatic isolating carbons	-	0.650
Fusion	Carbon	2 extended hetero-aromatic iso-C's	-	0.620
ExFragment	Hydrog	2 hydrogens on isolating carbons	-	0.454
Electronic	SigRho	5 potential interactions; 4.35 used	WithinRing	2.475
Electronic	SigRho	7 potential interactions; 2.64 used	FusedRings	0.753

RESULT DB=17 All fragments measured CLOGP=4.01 -0.148

```
SMILES: CC(=O)Nc1ccccc1C
ATOM #: 12..3.45.67890.1
```

```
ISOC-ID: A......a.aaaaa.Z
FRAG-ID: .1..1.1.........
H-COUNT: 3.....1..1111..3
RING  1: .......a.aaaaa..
```

ortho-methylacetanilide 3.2.3.1. (m=0.85)

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	NH-Amide [aA]	Measured	-1.510
Carbon		2 aliphatic isolating carbons	-	0.390
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	10 hydrogens on isolating carbons	-	2.270
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120
Benzylbond	Simple	1 benzyl bond to simple aromatic	-	-0.150
Ortho	Ring 1	1 normal ortho interaction	-	-0.650
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**1.010**

```
logPstar = 0.86
```

```
SMILES: NC(=O)c1ccccc1C(N)=O
ATOM #: 12..3.4.56789.0.1..2
ISOC-ID: ......a.aaaaa.......
FRAG-ID: 11..1.........2.2..2
H-COUNT: 2.......1111....2...
RING  1: ......a.aaaaa.......
```

o-phthalamide 3.2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	NH2-Amide [a]	Measured	-1.260
Fragment	# 2	NH2-Amide [a]	Measured	-1.260
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908
Electronic	SigRho	2 potential interactions; 2.00 used	WithinRing	0.384
Ortho	Ring 1	1 normal ortho interaction	-	-1.360
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**-1.808**

```
logPstar = -1.73
```

```
SMILES: CC(=O)Nc1ccccc1Cl
ATOM #: 12..3.45.67890.1.
ISOC-ID: A......a.aaaaa...
FRAG-ID: .1..1.1........2.
H-COUNT: 3.....1..1111....
RING  1: .......a.aaaaa...
```

o-chloroacetanilide 3.2.3.1.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	NH-Amide [aA]	Measured	-1.510
Fragment	# 2	Chloride [a]	Measured	0.940
Carbon		1 aliphatic isolating carbon	-	0.195
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	7 hydrogens on isolating carbons	-	1.589
ExFragment	Bonds	1 chain and 0 alicyclic (net)	-	-0.120
Electronic	SigRho	1 potential interaction; 1.00 used	WithinRing	0.258
Ortho	Ring 1	1 normal ortho interaction	-	-0.850

RESULT DB=17 All fragments measured CLOGP=4.01 1.282

```
logPstar = 1.28
```

```
SMILES: OC(=O)c1ccccc1O
ATOM #: 12..3.4.56789.0
ISOC-ID: ......a.aaaaa..
FRAG-ID: 11..1.........2
H-COUNT: 1.......1111..1
RING  1: ......a.aaaaa..
```

salicylic acid 3.2.3.2.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Carboxy (ZW-) [a]	Measured	-0.030
Fragment	# 2	Alcohol or Hydroxy [a]	Measured	-0.440
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Hydrog	4 hydrogens on isolating carbons	-	0.908
Electronic	SigRho	1 potential interaction; 1.00 used	WithinRing	0.339
H-bonding	Ring 1	Frag-pair: 1 & 2	-	0.630

RESULT DB=17 All fragments measured CLOGP=4.01 2.187

```
logPstar = 2.26
```

```
SMILES: Nc1ncnc2n(cnc12)C3OC(CO)C(O)C3O
ATOM #: 12.3456.7.890...1.23.45.6.7.8.9
ISOC-ID: .a..a.a...a.a...R..R.A..R...R..
FRAG-ID: 1..2.3..4..5......6...7...8...9
H-COUNT: 2...1.....1.....1..1.21.1.1.1.1
RING  1: ..............A.AA....A...A..
RING  2: ......a.a.aaa..................
RING  3: .a.aaaa.....a..................
```

adenosine

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Primary Amine [a]	Measured	-1.000
Fragment	# 2	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 3	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 4	1-Pyrrole [Aaa]	Measured	-1.090
Fragment	# 5	Aromatic nitrogen (TYPE 2) [aa]	Measured	-1.140
Fragment	# 6	Ether [RR]	Measured	-1.750
Fragment	# 7	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 8	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 9	Alcohol or Hydroxy [A]	Measured	-1.640
OrthoEther		Ether in a 5-member ring	-	0.130
Carbon		5 aliphatic isolating carbons	-	0.975
Carbon		5 aromatic isolating carbons	-	0.650
Fusion	Carbon	2 extended hetero-aromatic iso-C's	-	0.620
ExFragment	Branch	1 chain and 0 cluster branch	Chain	-0.130
ExFragment	Branch	3 non-halogen, polar group branches	Group	-0.660
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816
ExFragment	Bonds	1 chain and 5 alicyclic (net)	(COMBINED)	-0.570
Proximity	YCY	Fragments 4 & 6: -.32 (-1.09+-1.75)	-	0.909
Proximity	YCCY	1 pair over bond 14-13 (AvWt=-.230)	-	0.780
Proximity	YCCY	1 pair over bond 16-13 (AvWt=-.230)	-	0.780
Proximity	YCCY	1 pair over bond 18-16 (AvWt=-.260)	-	0.853
Proximity	YCCY	2 pairs over bond 18-11 (AvWt=-.230)	-	0.704
Proximity	YCCCY	1 pair over bond 16-14 (AvWt=-.200)	Branch	0.656

Electronic	SigRho	6 potential interactions; 4.39 used	WithinRing	1.938
Electronic	SigRho	10 potential interactions; 2.70 used	FusedRings	0.572

RESULT DB=17 All fragments measured CLOGP=4.01 -2.158

logPstar = -1.05

```
SMILES: CC(=O)OCC(=O)C3(O)CCC4C2CCC1=CC(=O)CCC1(C)C2C(=O)CC34C
ATOM #: 12..3.456..7.8..9.012.3.456..78..9.012..3.4.5..6.78..9
ISOC-ID: A......A.....R....AAA.A.AAV..W.....RAA..A.R......RA..A
FRAG-ID: .1..1.1.2..2....3.............4..4.........5..5......
H-COUNT: 3......2........1.221.1.22...1.....22...3.1......2...3
RING  1: ............A....AAA............................A...
RING  2: ..................A.A..................A.A....AA...
RING  3: ........................A..AA....AAA...............
RING  4: ....................A.AAA..........A....A...........
```

cortisone ac.

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Ester [AA]	Measured	-1.450
Fragment	# 2	Carbonyl [AA]	Measured	-1.840
Fragment	# 3	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 4	Carbonyl [AV]	Measured	-1.690
Fragment	# 5	Carbonyl [AA]	Measured	-1.840
Carbon		19 aliphatic isolating carbons	-	3.705
ExFragment	Branch	2 chain and 6 cluster branches	Combined	-1.040
ExFragment	Branch	2 non-halogen, polar group branches	Group	-0.440
ExFragment	Hydrog	29 hydrogens on isolating carbons	-	6.583
ExFragment	Bonds	3 chain and 20 alicyclic (net)	(COMBINED)	-2.160
ExFragment	Mbonds	1 double, 0 triple (isolated bond)	-	-0.030
Proximity	YCY	Fragments 1 & 2: -.32 (-1.45+-1.84)	-	1.053
Proximity	YCY	Fragments 2 & 3: -.42 (-1.84+-1.64)	-	1.462
STEROID	STRONG	11-keto steroid	-	1.160

RESULT DB=17 All fragments measured CLOGP=4.01 1.832

logPstar = 2.10

```
SMILES: CCCCCN(CCCCC)CC(O)c1ccccc1
ATOM #: 123456.78901.23.4.5.67890.
ISOC-ID: AAAAA..AAAAA.AZ...a.aaaaa.
FRAG-ID: .....1.........2.........
H-COUNT: 32222..22223.21.1...11111.
RING  1: ..................a.aaaaa.
```

2(N,N-dipentam)1-phenylethanol

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Tertiary Amine [AAA]	Measured	-2.370
Fragment	# 2	Alcohol or Hydroxy [Z]	Measured	-1.340
Carbon		12 aliphatic isolating carbons	-	2.340
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	30 hydrogens on isolating carbons	-	6.810
ExFragment	Bonds	13 chain and 0 alicyclic (net)	-	-1.560
Proximity	YCCY	1 pair over bond 13-12 (AvWt=-.260)	-	0.965

RESULT DB=17 All fragments measured CLOGP=4.01 5.405

```
logPstar = 2.86
```

```
SMILES: CCN(CC)CC(O)c1ccccc1
ATOM #: 123.45.67.8.9.01234.
ISOC-ID: AA..AA.AZ...a.aaaaa.
FRAG-ID: ..1.......2.........
H-COUNT: 32..23.21.1...11111.
RING  1: ............a.aaaaa.
```

2(N,N-dietam)1-phenylethanol

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Tertiary Amine [AAA]	Measured	-2.370
Fragment	# 2	Alcohol or Hydroxy [Z]	Measured	-1.340
Carbon		6 aliphatic isolating carbons	-	1.170
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	18 hydrogens on isolating carbons	-	4.086
ExFragment	Bonds	7 chain and 0 alicyclic (net)	-	-0.840
Proximity	YCCY	1 pair over bond 7- 6 (AvWt=-.260)	-	0.965
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**2.231**

```
logPstar = 2.02
```

```
SMILES: CN1CCC24C3Oc5c(O)ccc(CC1C2C=CC3O)c45
ATOM #: 12.345..6.78.9.0.123.45.6.7.89.0.1..
ISOC-ID: A..RAZ..A..a.a...aaa.ZR.A.V.VR...a..
FRAG-ID: .1........2....3..............4....
H-COUNT: 3..22...1......1.11..21.1.1.11.1....
RING  1: .....A..A.AA.....................A..
RING  2: .....A..A..............A.A.AA......
RING  3: .A.AAA................A.A...........
RING  4: .....A.............A.AA.A........A..
RING  5: ...........a.a...aaa.............a..
```

morphine

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Tertiary Amine [ARR]	Measured	-2.200
Fragment	# 2	Ether [Aa]	Measured	-0.610
Fragment	# 3	Alcohol or Hydroxy [a]	Measured	-0.440
Fragment	# 4	Alcohol or Hydroxy [A]	Measured	-1.640
Carbon		11 aliphatic isolating carbons	-	2.145
Carbon		6 aromatic isolating carbons	-	0.780
ExFragment	Branch	0 chain and 5 cluster branches	Cluster	-0.650
ExFragment	Branch	1 non-halogen, polar group branch	Group	-0.220
ExFragment	Hydrog	17 hydrogens on isolating carbons	-	3.859
ExFragment	Bonds	0 chain and 13 alicyclic (net)	-	-1.170
ExFragment	Mbonds	1 double, 0 triple (isolated bond)	-	-0.030
Benzylbond	Simple	2 benzyl bonds to simple aromatics	-	-0.300
Proximity	YCC=C	1 allylic structure	-	0.200
Proximity	PCCY	1 phenyl-fragment pair	-	0.150
Proximity	YCCY	1 pair over bond 19- 6 (AvWt=-.230)	-	0.517
Electronic	SigRho	1 potential interaction; 1.00 used	WithinRing	0.180
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.572**

```
logPstar = 0.76
```

```
SMILES: OC(CBr)C(O)C(O)C(O)CBr
ATOM #: 12.34..5.6.7.8.9.0.12.
ISOC-ID: .A.A...A...A...A...A..
FRAG-ID: 1...2....3...4...5..6.
H-COUNT: 11.2...1.1.1.1.1.1.2..
```

dibromodeoxymannitol

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Bromide [A]	Measured	0.200
Fragment	# 3	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 4	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 5	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 6	Bromide [A]	Measured	0.200
Carbon		6 aliphatic isolating carbons	-	1.170
ExFragment	Branch	4 non-halogen, polar group branches	Group	-0.880
ExFragment	Hydrog	8 hydrogens on isolating carbons	-	1.816
ExFragment	Bonds	10 chain and 0 alicyclic (net)	-	-1.200
Proximity	XCCY	0 F and 2 non-F interactions	-	0.700
Proximity	YCCY	1 pair over bond 5- 2 (AvWt=-.260)	-	0.853
Proximity	YCCY	1 pair over bond 7- 5 (AvWt=-.260)	-	0.853
Proximity	YCCY	1 pair over bond 9- 7 (AvWt=-.260)	-	0.853
Proximity	XCCCY	2 unbranched XCCCY adjustments (0.15)	-	0.300
Proximity	YCCCY	1 pair over bond 7- 2 (AvWt=-.200)	Branch	0.656
Proximity	YCCCY	1 pair over bond 9- 5 (AvWt=-.200)	Branch	0.656
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**-0.384**

```
logPstar = -0.29
```

```
SMILES: CC2C1CCC4C(O)C1(CC(O)C3(O)C2CC(O)C3(C)C)CC4(C)O
ATOM #: 12.3.456.7.8.9..01.2.3..4.5.67.8.9..0.1.23..4.5
ISOC-ID: AA.A.AAA.R...A..AR...R....A.AR...A..A.A.AR..A..
FRAG-ID: ..........1.......2....3......4.............5
H-COUNT: 31.1.221.1.1....21.1....1.1.21.1....3.3.2...3.1
RING  1: .......A.A...A.........................AA.....
RING  2: ..................A....A.AA...A.............
RING  3: ...A.AAA.A...A..............................
RING  4: .A.A.........A..AA...A....A.................
```

dihydrograyanotoxin

Class	Type	Log(P) Contribution Description	Comment	Value
Fragment	# 1	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 2	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 3	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 4	Alcohol or Hydroxy [A]	Measured	-1.640
Fragment	# 5	Alcohol or Hydroxy [A]	Measured	-1.640
Carbon		20 aliphatic isolating carbons	-	3.900
ExFragment	Branch	4 chain and 6 cluster branches	Combined	-1.300
ExFragment	Branch	5 non-halogen, polar group branches	Group	-1.100
ExFragment	Hydrog	29 hydrogens on isolating carbons	-	6.583
ExFragment	Bonds	0 chain and 19 alicyclic (net)	-	-1.710
Proximity	YCCY	1 pair over bond 13-11 (AvWt=-.260)	-	0.853
Proximity	YCCCY	1 pair over bond 17-13 (AvWt=-.200)	-	0.656
Proximity	YCCCY	1 pair over bond 23- 7 (AvWt=-.200)	-	0.656
RESULT	**DB=17**	**All fragments measured**	**CLOGP=4.01**	**0.338**

```
logPstar = 1.51
```