Study on Structure-Activity Relationships of Organic Compounds: Three New Topological Indices and Their Applications

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In this paper, three new topological indices, A_{x_1}, A_{x_2}, and A_{x_3}, have been developed for use in multivariate analysis in structure-property relationship (SPR) and structure-activity relationship (SAR) studies. Good results have been obtained by using them to predict the physical and chemical properties and biological activities of some organic compounds.

Quantitative structure-activity relationships (QSAR) have been shown to be a powerful research tool and are being used in many fields. There are two basic kinds of molecular predictors used in QSAR. One of them involves parameters that bear relation to free energy and usually represent some important physicochemical properties of molecules, e.g., hydrophobic, electronic, and steric parameters. The another category of molecular descriptor is the topological index which is produced directly from molecular structure, e.g., the Wiener index W,[1-3] Randic index χ,[4] Hosoya index Z,[5] and Balaban index J.[6] In recent years, the latter type of predictor has gained substantial attention in explaining biological activities and physical and chemical properties of organic compounds. However, there are only a few topological indices which can be used to describe the molecular structures containing multiple bonds and heteroatoms. At present, one of the most popular indices is the molecular connectivity descriptor suggested by Kier and Hall.[7] The index GAI advanced by Xu et al.[8,9] has also been successfully used in QSPR studies of neutral phosphorus extractants and in discrimination of cis/trans isomers.

In this study, three topological indices have been devised to describe the molecular structures not only of alkanes but also molecules containing heteroatoms, multiple bonds, and rings.

METHOD

The three topological indices are generated from path matrices **A**, **B**, and **C**, respectively. These three matrices are defined as follows:

$$\mathbf{A} = (a_{ij}), \quad a_{ij} = \begin{cases} 1 & \text{if there is a path of length } l \text{ between vertices } i \text{ and } j \\ 0 & \text{otherwise} \end{cases}$$

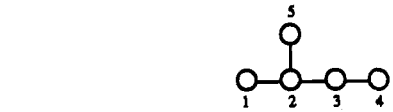
$$\mathbf{B} = (b_{ij}), \quad b_{ij} = \begin{cases} 2 & \text{if there is a path of length 2 between vertices } i \text{ and } j \\ 0 & \text{otherwise} \end{cases}$$

$$\mathbf{C} = (c_{ij}), \quad c_{ij} = \begin{cases} 3 & \text{if there is a path of length 3 between vertices } i \text{ and } j \\ 0 & \text{otherwise} \end{cases}$$

Table I. VDW Radii of Common Atoms

B	0.98	F	1.35	Br	1.95
C	1.80	Si	1.38	I	2.15
N	1.50	P	1.90		
O	1.40	S	1.85		

For instance, the hydrogen-suppressed graph and corresponding matrices **A**, **B**, and **C** of 2-methylbutane are



$$\mathbf{A} = \begin{bmatrix} 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \end{bmatrix} \quad \mathbf{B} = \begin{bmatrix} 0 & 0 & 2 & 0 & 2 \\ 0 & 0 & 0 & 2 & 0 \\ 2 & 0 & 0 & 0 & 2 \\ 0 & 2 & 0 & 0 & 0 \\ 2 & 0 & 2 & 0 & 0 \end{bmatrix} \quad \mathbf{C} = \begin{bmatrix} 0 & 0 & 0 & 3 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 3 & 0 & 0 & 0 & 3 \\ 0 & 0 & 0 & 3 & 0 \end{bmatrix}$$

Augmented path matrices $\mathbf{G}_1$-$\mathbf{G}_3$ are obtained by adding two columns into matrices **A**, **B**, and **C**, respectively, so as to reflect the structural traits of the heteroatoms and multiple bonds involved. We also take 2-methylbutane as an example; its augmented path matrices $\mathbf{G}_1$-$\mathbf{G}_3$ are

$$\mathbf{G}_1 = \begin{bmatrix} 1 & 1.34 & 0 & 1 & 0 & 0 & 0 \\ 1.73 & 1.34 & 1 & 0 & 1 & 0 & 1 \\ 1.41 & 1.34 & 0 & 1 & 0 & 1 & 0 \\ 1 & 1.34 & 0 & 0 & 1 & 0 & 0 \\ 1 & 1.34 & 0 & 1 & 0 & 0 & 0 \end{bmatrix}$$

$$\mathbf{G}_2 = \begin{bmatrix} 1 & 1.34 & 0 & 0 & 2 & 0 & 2 \\ 1.73 & 1.34 & 0 & 0 & 0 & 2 & 0 \\ 1.41 & 1.34 & 2 & 0 & 0 & 0 & 2 \\ 1 & 1.34 & 0 & 2 & 0 & 0 & 0 \\ 1 & 1.34 & 2 & 0 & 2 & 0 & 0 \end{bmatrix}$$

$$\mathbf{G}_3 = \begin{bmatrix} 1 & 1.34 & 0 & 0 & 0 & 3 & 0 \\ 1.73 & 1.34 & 0 & 0 & 0 & 0 & 0 \\ 1.41 & 1.34 & 0 & 0 & 0 & 0 & 0 \\ 1 & 1.34 & 3 & 0 & 0 & 0 & 3 \\ 1 & 1.34 & 0 & 0 & 0 & 3 & 0 \end{bmatrix}$$

The elements in the first column of matrices $\mathbf{G}_1$-$\mathbf{G}_3$ are square roots of vertex degrees, and the elements in the second column represent the square roots of the van der Waals (VDW)

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Table II. A_{x_1}–A_{x_3} and Boiling Points of Alkanes

	compound	A_{x_1}	A_{x_2}	A_{x_3}	bp (expt)	bp (calc)
1	ethane	3.3000	2.8000	2.8000	−88.63	−76.14
2	propane	5.6669	6.0459	4.6669	−42.07	−38.63
3	*n*-butane	7.8392	8.5529	9.2097	−0.50	−3.24
4	2-methylpropane	7.9885	13.0764	6.4885	−11.73	−9.71
5	*n*-pentane	9.8972	11.6612	12.2496	36.07	28.79
6	2-methylbutane	10.0455	14.5963	14.8237	27.85	25.55
7	2,2-dimethylpropane	10.2827	24.2755	8.2827	9.50	10.18
8	*n*-hexane	11.8958	14.3288	14.8403	68.74	60.61
9	2-methylpentane	12.0115	17.5400	16.9178	60.27	56.20
10	3-methylpentane	12.0525	16.6500	21.8185	63.28	58.78
11	2,2-dimethylbutane	12.2646	25.3260	20.6586	49.74	45.00
12	2,3-dimethylbutane	12.1542	18.1478	24.8448	57.99	57.62
13	*n*-hexane	13.8625	16.8855	18.8597	98.43	92.06
14	2-methylhexane	13.9503	19.3758	18.8066	90.05	88.60
15	3-methylhexane	13.9874	19.7022	23.5319	91.85	88.63
16	3-ethylpentane	14.0322	19.1897	28.6999	93.48	90.51
17	2,2-dimethylpentane	14.1606	27.6607	22.3396	79.20	75.58
18	2,3-dimethylpentane	14.1070	20.7716	30.7744	89.78	88.67
19	2,4-dimethylpentane	14.0409	22.6454	20.2652	80.50	83.61
20	3,3-dimethylpentane	14.2271	26.6298	31.9429	86.06	78.93
21	2,2,3-trimethylbutane	14.2967	27.0273	35.1277	80.88	79.42
22	*n*-octane	15.8107	19.2375	22.1497	125.67	123.59
23	2-methylheptane	15.8774	21.4680	23.8259	117.65	120.27
24	3-methylheptane	15.9131	21.4806	26.1465	118.93	120.91
25	4-methylheptane	15.9184	22.1710	25.7617	117.71	119.60
26	3-ethylhexane	15.9544	21.8962	30.0869	118.53	120.83
27	2,2-dimethylhexane	16.0469	28.7682	23.7612	106.84	108.50
28	2,3-dimethylhexane	16.0106	23.1371	31.9671	115.61	119.34
29	2,4-dimethylhexane	15.9829	24.2984	25.6591	109.43	116.45
30	2,5-dimethylhexane	15.9436	22.8713	21.7795	109.10	118.63
31	3,3-dimethylhexane	16.1146	29.0337	33.1820	111.97	109.22
32	3,4-dimethylhexane	16.0448	23.2529	35.7401	117.72	119.74
33	2-methyl-3-ethylpentane	16.0504	23.6453	37.0947	115.65	119.04
34	3-methyl-3-ethylpentane	16.5383	28.2243	58.9443	118.26	118.78
35	2,2,3-trimethylpentane	16.2004	29.4635	40.4990	109.23	109.94
36	2,2,4-trimethylpentane	16.1183	31.5374	24.7994	99.23	104.17
37	2,3,3-trimethylpentane	16.2287	28.7363	45.3279	114.76	111.96
38	2,3,4-trimethylpentane	16.1050	25.2149	38.4623	113.46	116.85
39	2,2,3,3-tetramethylbutane	16.3715	31.6124	49.8827	106.47	108.74

radii of atoms. From matrices $\mathbf{G}_1$–$\mathbf{G}_3$, we can obtain matrices $\mathbf{Z}_1$–$\mathbf{Z}_3$:

$$\mathbf{Z}_1 = \mathbf{G}_1 {}^{*}\mathbf{G}_1; \quad \mathbf{Z}_2 = \mathbf{G}_2 {}^{*}\mathbf{G}_2; \quad \mathbf{Z}_3 = \mathbf{G}_3 {}^{*}\mathbf{G}_3$$

$$\mathbf{Z}_1 = \begin{bmatrix} 3.80 & 3.53 & 4.21 & 2.80 & 3.80 \\ 3.53 & 7.80 & 4.25 & 4.53 & 3.53 \\ 4.21 & 4.25 & 5.80 & 3.21 & 4.21 \\ 2.80 & 4.53 & 3.21 & 3.80 & 2.80 \\ 3.80 & 3.53 & 4.21 & 2.80 & 3.80 \end{bmatrix}$$

$$\mathbf{Z}_2 = \begin{bmatrix} 11.80 & 3.53 & 3.21 & 2.80 & 11.80 \\ 3.53 & 4.80 & 4.25 & 3.53 & 3.53 \\ 3.21 & 4.25 & 3.80 & 3.21 & 3.21 \\ 2.80 & 3.53 & 3.21 & 20.80 & 2.80 \\ 11.80 & 3.53 & 3.21 & 2.80 & 11.80 \end{bmatrix}$$

$$\mathbf{Z}_3 = \begin{bmatrix} 10.80 & 3.53 & 7.21 & 2.80 & 6.80 \\ 3.53 & 8.80 & 4.25 & 3.53 & 3.53 \\ 7.21 & 4.25 & 11.80 & 3.21 & 7.21 \\ 2.80 & 3.53 & 3.21 & 6.80 & 2.80 \\ 6.80 & 3.53 & 7.21 & 2.80 & 10.80 \end{bmatrix}$$

where, $\mathbf{G}_1'$–$\mathbf{G}_3'$ are the tranpose matrices of $\mathbf{G}_1$–$\mathbf{G}_3$. The three new topological indices are defined as

$$A_{x_1} = \lambda_{\max_1}/2; \quad A_{x_2} = \lambda_{\max_2}/2; \quad A_{x_3} = \lambda_{\max_3}/2$$

where $\lambda_{\max_1}$–$\lambda_{\max_3}$ are the largest eigenvalues of matrices $\mathbf{Z}_1$–$\mathbf{Z}_3$. The A_{x_1}–A_{x_3} values of 2-methylbutane are

$$A_{x_1} = 10.0455, \quad A_{x_2} = 14.8963, \quad A_{x_3} = 14.8237$$

Table III. Results of Correlation Analysis between Various Combinations of A_{x_1}–A_{x_3} and Boiling Points of Alkanes

descriptor	*r*	*s*	*F*	*n*
A_{x_1}	0.9846	8.7251		39
A_{x_2}	0.7537	32.7660		39
A_{x_3}	0.7421	33.4201		39
A_{x_1}, A_{x_2}	0.9959	4.5841	2170.30	39
A_{x_1}, A_{x_3}	0.9855	8.5664	608.49	39
A_{x_2}, A_{x_3}	0.7979	30.4698	31.53	39
A_{x_1}, A_{x_2}, A_{x_3}	0.9959	4.6490	1406.74	39

Used to facilitate the computation of the three indices, the van der Waals radii of the common atoms are shown in Table I.

APPLICATIONS OF TOPOLOGICAL INDICES A_{X_1}–A_{X_3}

1. Alkanes. It is of interest to test methods on data for alkanes because good data are generally available for complete isomer sets. In this paper A_{x_1}–A_{x_3} values of 39 alkanes containing 2–8 carbon atoms were calculated and are listed in Table II.

Table III shows a summary of the correlation coefficients, *r*, standard deviations, *s*, and *F*-test values by various combinations of A_{x_1}–A_{x_3}.

It can be seen from Table III that the best individual descriptor is A_{x_1} with $r = 0.9846$ and $s = 8.7251$. Better results have been achieved by using the combination of A_{x_1}

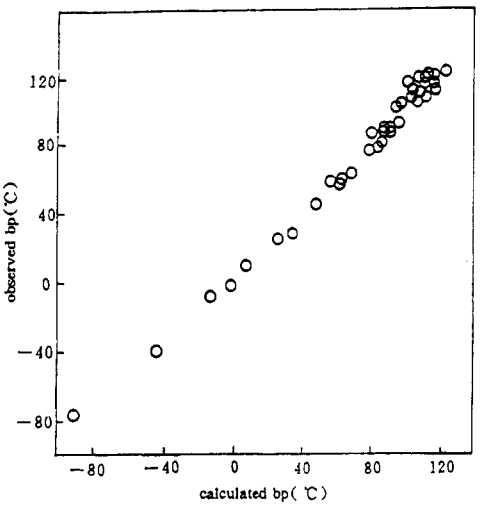


Figure 1. Plot of observed boiling points vs calculated boiling points of alkanes.

Table IV. A_{x_1}–A_{x_3} and Boiling Points of Alcohol Compounds

	compound	A_{x_1}	A_{x_2}	A_{x_3}	bp (expt)	bp (calc)
1	methanol	3.0976	2.5976	2.5976	64.7	52.5
2	ethanol	5.4746	5.8284	4.4752	78.3	76.1
3	1-propanol	7.6573	8.3661	8.9686	97.2	97.2
4	2-propanol	7.8007	12.8538	6.3016	82.3	88.4
5	1-butanol	9.7202	11.4583	12.0534	117.7	115.9
6	2-butanol	9.8628	14.3690	14.5873	99.6	108.3
7	2-methyl-1-propanol	9.8714	14.4825	14.5899	107.9	108.0
8	2-methyl-2-propanol	10.0976	24.0559	8.0986	82.4	88.7
9	1-pentanol	11.7211	14.1407	14.6582	137.8	135.1
10	2-pentanol	11.8314	17.3099	16.6930	119.0	126.6
11	3-pentanol	11.8720	16.4279	21.5494	115.3	126.6
12	2-methyl-1-butanol	11.8804	16.5067	21.6088	128.7	126.5
13	3-methyl-1-butanol	11.8396	17.3667	16.7766	131.2	126.5
14	2-methyl-2-butanol	12.0821	25.0985	20.4278	102.0	106.2
15	3-methyl-2-butanol	11.9766	17.9546	24.6156	111.5	122.0
16	2,2-dimethyl-1-propanol	12.0961	25.2581	20.4315	113.1	105.9
17	1-hexanol	13.6890	16.7056	18.6384	157.0	153.4
18	2-hexanol	13.7717	19.1464	18.5853	139.9	147.8
19	3-hexanol	13.8120	19.2870	23.1430	135.4	145.2
20	2-methyl-1-pentanol	13.8193	19.3742	23.1899	148.0	145.0
21	3-methyl-1-pentanol	13.8203	19.3374	23.3000	152.4	145.1
22	4-methyl-1-pentanol	13.7788	19.2329	18.6568	151.8	147.7
23	2-methyl-2-pentanol	13.9792	27.4254	22.1120	121.4	125.6
24	3-methyl-2-pentanol	13.9309	20.5661	30.5531	134.2	138.7
25	4-methyl-2-pentanol	13.8644	22.4374	20.0744	131.7	139.1
26	2-methyl-3-pentanol	13.9297	20.5904	30.5076	126.5	138.6
27	3-methyl-3-pentanol	14.0459	26.3955	31.5904	122.4	123.4
28	2-ethyl-1-butanol	13.8610	19.0234	28.5027	146.5	143.3
29	2,2-dimethyl-1-butanol	14.0590	26.5469	31.7318	136.8	123.1
30	2,3-dimethyl-1-butanol	13.9376	20.6108	30.5913	149.0	138.6
31	3,3-dimethyl-1-butanol	13.9930	27.5317	22.2290	143.0	125.4
32	2,3-dimethyl-2-butanol	14.1176	26.7931	34.9025	118.6	121.3
33	3,3-dimethyl-2-butanol	14.1238	26.9196	34.9036	120.0	121.0
34	1-heptanol	15.6377	19.0644	21.9498	176.3	172.4
35	1-octanol	17.5745	21.3351	24.8307	195.2	191.7
36	1-nonanol	19.5034	23.5232	27.8040	213.1	211.1
37	1-decanol	21.4266	25.6519	30.5163	230.2	230.8

and A_{x_2}. Statistical analysis yields the following result.

$$\text{bp °C} = -131.9603 + 18.6511A_{x_1} - 2.0450A_{x_2} \quad (1)$$

$$r = 0.9959, \quad F = 217.3047, \quad s = 4.5841, \quad n = 39$$

The boiling points calculated by eq 1 are also listed in Table II. Figure 1 shows the relationship between the observed boiling points of alkanes and boiling points calculated by eq 1.

Table V. Results of Correlation Analysis between Various Combinations of A_{x_1}–A_{x_3} and Boiling Points of Alcohols

descriptor	r	s	F	n
A_{x_1}	0.9052	14.8387		37
A_{x_2}	0.4418	31.3306		37
A_{x_3}	0.5723	28.6396		37
A_{x_1}, A_{x_2}	0.9743	7.9806	318.12	37
A_{x_1}, A_{x_3}	0.9332	12.7377	114.85	37
A_{x_2}, A_{x_3}	0.5724	28.6398	8.28	37
A_{x_1}, A_{x_2}, A_{x_3}	0.9780	7.4988	242.04	37

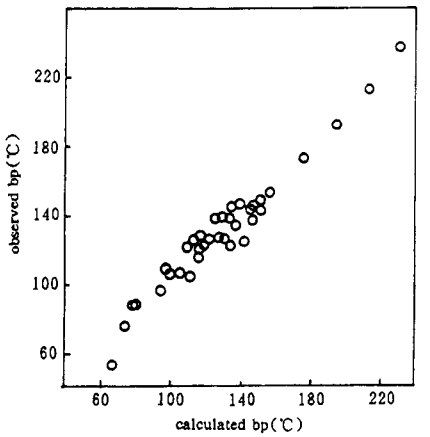


Figure 2. Plot of observed boiling points vs calculated boiling points of alcohols.

Not only would useful topological indices be easy to derive, but also they would possess high structure selectivity, i.e. indices will differ in value whenever they characterize two graphs that are not isomorphic. A comparative study of several topological indices by Razinger et al.[10] confirmed that the discriminating power of Balaban's J index is remarkable and reaches its initial degenerate value with alkane isomers containing 11 carbon atoms. In the present work, it has been found that both A_{x_2} and A_{x_3} are able to distinguish all the isomers of alkanes up to 11 carbon atoms, and among 159 undecanes there is one duplicate value of index A_{x_1}.

2. Alcohols. Because the most interesting structures possessing activity are rather complex molecules with multiple bonds and/or heteroatoms, it is quite important that topological indices are able to characterize these kinds of molecules. Alcohol contains one heteroatom, oxygen, whose VDW radius is 1.40 (Table I).

The significant correlation between boiling point and the topological indices A_{x_1}–A_{x_3} and high structure selectivities of these three indices has been found for alcohols. The supporting data are presented in Table IV.

The results of the correlation analysis are listed in Table V.

It is clear that the best result can be obtained with the combination of all three indices. The regression equation, correlation coefficient, F-test value, and standard deviation are

$$\text{bp °C} = 17.4838 + 14.1708A_{x_1} - 2.7805A_{x_2} - 0.6229A_{x_3} \quad (2)$$

$$r = 0.9780, \quad F = 242.0399, \quad s = 7.4988, \quad n = 37$$

The plot of the observed boiling points versus boiling points calculated by eq 2 is shown in Figure 2.

3. Barbiturates. Barbiturates were thought to be nonspecific narcotic agents principally because log P (P = partition coefficient in octanol–water) correlates very well with their

Table VI. log P and Topological Indices A_{x_1}–A_{x_3} for Barbiturates with Structure I

	R_1	R_2	A_{x_1}	A_{x_2}	A_{x_3}	log P exptl	log P calc
1	methyl	1-methyl, 1-propenyl	31.9219	51.8177	97.0396	0.65	0.55
2	ethyl	1-methyl, 1-propenyl	33.8157	54.3626	107.4888	1.15	0.96
3	propyl	1-methyl, 1-propenyl	35.6742	56.2542	108.7299	1.65	1.50
4	allyl	1-methyl, 1-propenyl	37.5330	57.7404	111.1818	2.15	2.02
5	methyl	1-methylvinyl	31.0761	50.8345	95.2211	0.15	0.32
6	ethyl	1-methylvinyl	32.9670	53.3982	105.9361	0.65	0.72
7	propyl	1-methylvinyl	34.8206	55.8622	107.0816	1.15	1.27
8	butyl	1-methylvinyl	36.6749	56.7721	109.5384	1.65	1.64
9	isobutyl	1-methylvinyl	36.6896	58.5235	119.6529	1.45	1.64
10	amyl	1-methylvinyl	38.5335	58.1687	111.2351	2.15	2.33
11	isoamyl	1-methylvinyl	38.5381	60.0193	121.5974	1.95	2.17

Table VII. log P and Topological Indices A_{x_1}–A_{x_3} for Barbiturates with Structure II

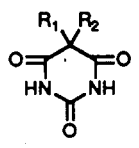
	R_1	R_2	R_3	A_{x_1}	A_{x_2}	A_{x_3}	log P exptl	log P calc
12	methyl	ethyl	methyl	33.9096	53.4735	99.0809	1.15	1.12
13	ethyl	ethyl	methyl	35.7997	56.0127	109.6860	1.65	1.53
14	propyl	ethyl	methyl	37.6555	57.9238	110.9629	2.15	2.07
15	isopropyl	ethyl	methyl	37.6737	59.2067	120.9469	1.95	1.92
16	methyl	methyl	ethyl	33.9286	53.9510	100.2572	1.15	1.11
17	ethyl	methyl	ethyl	35.8177	56.4716	110.4755	1.65	1.52
18	propyl	methyl	ethyl	37.6724	58.3897	111.8534	2.15	2.06
19	isopropyl	methyl	ethyl	37.6908	59.6247	121.3889	1.95	1.91
20	methyl	propyl	methyl	35.7597	54.8940	100.9102	1.65	1.65
21	ethyl	propyl	methyl	37.6523	57.4307	111.4127	2.15	2.06
22	methyl	isopropyl	methyl	35.7572	55.5639	101.2083	1.45	1.65
23	methyl	butyl	methyl	37.6131	56.2789	101.9917	2.15	2.20
24	propyl	butyl	methyl	39.5086	58.8191	112.4071	2.65	2.61
25	ethyl	ethyl	propyl	39.5344	59.7796	114.8177	2.65	2.59

Table VIII. Results of the Correlation Analysis between A_{x_1}–A_{x_3} and log P of Barbiturates

descriptor	r	s	F	n
A_{x_1}	0.9700	0.1530		25
A_{x_2}	0.8780	0.3011		25
A_{x_3}	0.6224	0.4923		25
A_{x_1}, A_{x_2}	0.9786	0.1324	248.50	25
A_{x_1}, A_{x_3}	0.9790	0.1311	253.73	25
A_{x_2}, A_{x_3}	0.9599	0.1803	128.91	25
A_{x_1}, A_{x_2}, A_{x_3}	0.9791	0.1339	162.07	25

biological potency.[11] Other studies[12] show a dependence of the action of barbiturates upon chemical structure. Therefore, it was of interest to carry out a correlation analysis of log P and topological parameters. Correlations between the topological indices A_{x_1}–A_{x_3} and log P for barbiturates have been revealed by this investigation.

The topological indices A_{x_1}–A_{x_3} and log P of 25 barbiturate acid derivatives with structure I and structure II are listed in Table VI and Table VII, respectively.



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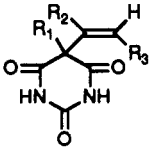

II

Table VIII shows the results of the correlation analysis between various combinations of A_{x_1}–A_{x_3} and log P values of these compounds.

It is clear from Table VII that the combination of A_{x_1} and A_{x_3} gives the best result. The regression equation, correlation coefficient, F-test value, and standard deviation are

$$\log P = -7.5991 + 0.3042A_{x_1} - 0.0161A_{x_3} \quad (3)$$

$$r = 0.9790, \quad s = 0.1311, \quad F = 253.73, \quad n = 25$$

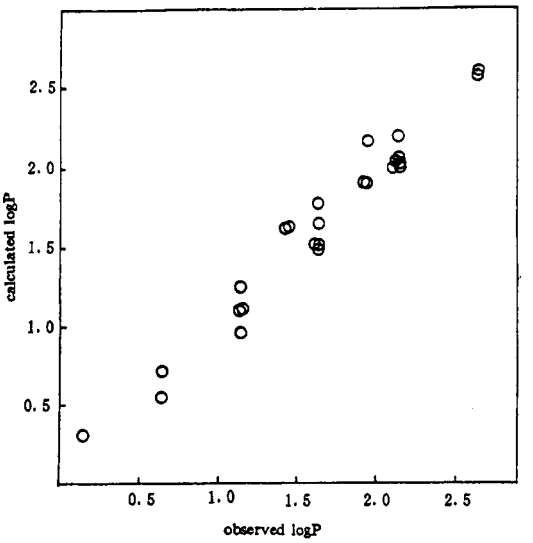

Figure 3. Plot of calculated log P values vs observed log P values of barbitures.

The plot of the observed log P versus the calculated log P based on eq 3 is shown in Figure 3.

4. Nitrogen-Containing Aromatic Molecules. The 18 nitrogen-containing aromatic molecules given in Table IX have activities of inhibition to the population growth of tetrahymena that are applied in this paper. The molecular

Table IX. Nitrogen-Containing Molecules and Their Activities

	molecule	A_{x_1}	A_{x_2}	A_{x_3}	log (IGC50)
1	pyridine	16.2462	22.2459	18.7464	1.1853
2	3-picoline	18.2208	27.0819	26.7527	1.0175
3	4-picoline	18.2212	27.0499	26.8258	0.8921
4	3,4-lutidine	20.1810	30.8706	38.8383	0.5051
5	quinoline	27.3730	41.8459	52.8343	−0.0132
6	4-phenylpyridine	32.0861	45.3290	57.8735	−0.6576
7	acridine	38.1744	57.1935	81.2076	−1.3979
8	aniline	18.2630	27.0741	26.7617	0.2201
9	3-toluidine	20.2034	31.9202	33.9390	0.4133
10	4-toluidine	20.2008	30.8119	33.0246	0.1271
11	3,4-xylidine	22.1347	35.0104	44.2257	0.2878
12	1-naphthylamine	29.2913	45.5792	62.7174	−0.2218
13	4-aminobiphenyl	33.9767	48.1754	64.4747	−0.8239
14	nitrobenzene	22.7907	33.4581	42.0925	0.0645
15	3-nitrotoluene	24.6856	37.4021	46.5200	−0.3098
16	4-nitrotoluene	24.6829	36.9886	50.7205	−0.2366
17	4-nitro-*o*-xylene	26.5796	40.5718	58.3159	−0.6383
18	4-nitrobiphenyl	33.7190	51.1373	72.9092	−1.0000

Table X. Results of Correlation Analysis between A_{x_1}–A_{x_3} and the Activities of Nitrogen-Containing Compounds

descriptor	r	s	n
A_{x_1}	−0.9320	0.2638	18
A_{x_2}	−0.9336	0.2606	18
A_{x_3}	−0.9363	0.2542	18

structures of these compounds are more complex than the molecules mentioned above.

In this study the correlations between the topological indices A_{x_1}–A_{x_3} and acute toxicities (the concentration which inhibits 50% growth IGC50) are observed for the 18 selected compounds. Table X shows that satisfactory results can be obtained by using only a single index, so no combination of A_{x_1}–A_{x_3} was used. The best regression analysis is

$$\log (\mathrm{IGC50}) = 1.7292 - 0.0378A_{x_3} \qquad (4)$$

$$r = -0.9363, \quad s = 0.2542, \quad n = 18$$

A plot of the log (IGC50) values versus A_{x_3} shows a direct linear correlation (Figure 4). These results based on indices A_{x_1}–A_{x_3} are quite similar to that obtained by Schultz et al.[13] using a hydrophobic parameter.

CONCLUSION

The A_{x_1}–A_{x_3} indices, suggested in this paper, correlate significantly with a number of physicochemical properties and biological activities. The study also indicates that the three topological indices have high structural selectivity. All

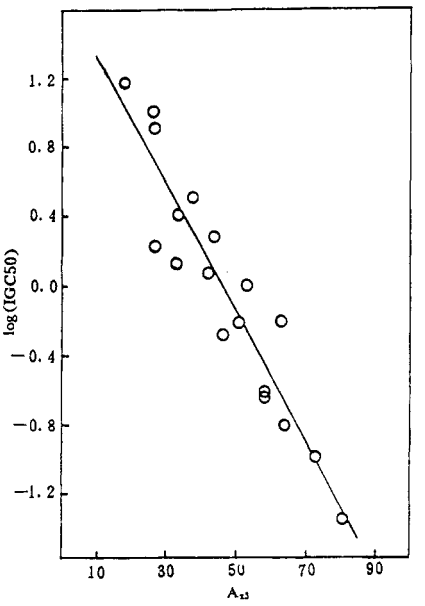

Figure 4. Plot of activities of nitrogen-containing compounds vs topological index A_{x_3}.

of the results obtained in this paper demonstrate convincingly that the A_{x_1}–A_{x_3} proposed here are useful topological indices.

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