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Quantitative Structure–Property Relationship: XIII.[1] Properties of Aliphatic Alcohols

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Abstract — A simple quantitative structure–property relationship was used to calculate a set of properties of aliphatic alcohols including the boiling point; enthalpy of vaporization; heat capacity of liquids at constant pressure; entropy, enthalpy, and free energy of formation; free energy of transfer from the gas phase to water; distribution factor in the octanol–water system; dielectric constant; surface tension; viscosity; thermal conductivity; diamagnetic susceptibility; ionization potential; self-association index; distribution factor between the gas and hexadecane; distribution factor between water and dodecyl sulfate mixelles; solubility of HCl in alcohols; and solvatochromic parameter. The rate constants, activation entropies, and activation energies of the Menshutkin reaction in alcohols were also calculated. The calculated values are in good agreement with the experimental data. The suggested relationship well reproduces the proton affinites of a series of alcohols calculated by rigorous methods.

We showed in [1] that relationship (1) reproduces with a good accuracy the properties of saturated hydrocarbons, 1-alkenes, 1-alkynes, carboxylic acid esters, and *n*-alkylbenzenes:

$$P_n = k_1 + k_2 n^{-1/2} + k_3 n^{1/2}, \qquad (1)$$

where P_n is a property of a molecule X–R (X is the residue of an aliphatic or aromatic organic compound, R is a linear substituent C_nH_{2n+1}), n is the number of C atoms in the alkyl radical, and k_i are parameters. Here we show that relationship (1) allows fairly accurate evaluation of virtually any property of aliphatic alcohols of various structures. The choice of aliphatic alcohols as investigation objects was governed by the following facts. On the one hand, a great body of experimental data on diverse properties of alcohols are available, which is important for extending the database concerning the possibilities and limitations of our approach. On the other hand, alcohols are widely used as solvents for chemical reactions, enzyme inhibitors, blockators of ionic channels, pharmaceuticals with various effects, and for other purposes. Therefore, understanding of the structure–“activity” interrelation for alcohols and the possibility of evaluating the activity by a simple relationship are important for chemistry, biochemistry, pharmacology, and other fields.

Using relationship (1), we calculated the following properties of aliphatic alcohols: boiling point, enthalpy of vaporization (ΔH_{vap}), heat capacity of liquids at constant pressure (C_p), entropy of formation (S^0), standard enthalpy of formation (ΔH_f^0), standard free energy of formation (ΔG_f^0) for the hypothetical state of ideal gas at 1 atm and 25°C, standard free energy of transfer from gas to water (ΔG^{0gw}), distribution factor in the octanol–water system ($\log P$), dielectric constant (ε), surface tension (γ), viscosity (η), thermal conductivity (λ), diamagnetic susceptibility (χ_m), ionization potential (I), self-association index (δT_{bp}) [2], distribution factor between the gas and hexadecane ($\log L^{16}$) [3], distribution factor between water and dodecyl sulfate micelles ($\log K_{wm}$) [4], and some other properties.

The boiling points of normal aliphatic alcohols $C_nH_{2n+1}OH$ (n from 1 to 20) are listed as examples in Table 1. To calculate the boiling point (or any other property) of secondary and tertiary alcohols or of primary alcohols with a branched alkyl radical, additional parameters should be introduced to take into account branching, as it was done previously for saturated hydrocarbons [7]. The only difference is that various groups can be located at the branching point: alkyl, hydroxy, or both. The results of calculation of the boiling points of primary, secondary, and tertiary alcohols with branched alkyl radicals are listed in Table 2. The set of alcohols in these and all the other cases was determined by the availability of the corresponding experimental data. Tables 1 and 2 show that

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[1] For communication XII, see [1].

Table 1. Boiling points (°C) of normal aliphatic alcohols

Molecule	Experiment [5, 6]	This work[a]
CH_3OH	64.8	65.7
C_2H_5OH	78.6	76.4
C_3H_7OH	97.2	96.7
C_4H_9OH	117.7	118.0
$C_5H_{11}OH$	137.9	138.7
$C_6H_{13}OH$	158.0	158.5
$C_7H_{15}OH$	176.3	177.4
$C_8H_{17}OH$	195.3	195.5
$C_9H_{19}OH$	213.6	212.9
$C_{10}H_{21}OH$	230.1	229.6
$C_{11}H_{23}OH$	245.9	245.6
$C_{12}H_{25}OH$	260.9	261.1
$C_{13}H_{27}OH$	275.9	276.1
$C_{14}H_{29}OH$	290.9	290.7
$C_{15}H_{31}OH$	304.9	304.8
$C_{16}H_{33}OH$	318.9	318.5
$C_{17}H_{35}OH$	331.9	331.9
$C_{18}H_{37}OH$	344.9	344.9
$C_{19}H_{39}OH$	357.9	357.6
$C_{20}H_{41}OH$	369.9	370.0
		r 1.0000
		s 0.7461

[a] k_1 94.5527 ± 1.9955, k_2 128.0611 ± 2.1095, k_3 116.2703 ± 0.3997.

the calculated values are nicely consistent with the experiment.

Similar accuracy was attained in the calculations of the other properties mentioned above. Therefore, we give in Table 3 only the parameters k_i of Eq. (1) and the statistical criteria of the calculation accuracy. It should be borne in mind that, in most cases, data in Table 3 concern only the first ten representatives of the normal aliphatic alcohol series ($C_nH_{2n+1}OH$, n = 1–10), as for other alcohols systematic experimental data on many properties are lacking. If there were minor “gaps,” the lacking property was calculated in various approximations and the value corresponding to the maximal correlation coefficient and minimal rms deviation was chosen. The experimentally determined properties were taken from [2–11].

Table 2. Boiling points (°C) of primary, secondary, and tertiary alcohols with branched alkyl radicals

No.	Molecule	Experiment [5, 6]	This work[a]
1	$(CH_3)_2CHCH_2OH$	108	109.8
2	$(C_2H_5)(CH_3)CHCH_2OH$	128	129.4
3	$(CH_3)_2CHCH_2CH_2OH$	128.5	129.4
4	$(C_3H_7)(CH_3)CHCH_2OH$	148	148.8
5	$(C_2H_5)(CH_3)CHCH_2CH_2OH$	152.4	148.8
6	$(CH_3)_2CH(CH_2)_2CH_2OH$	151.4	148.8
7	$(CH_3)_2CHOH$	82.4	79.9
8	$(C_2H_5)(CH_3)CHOH$	99.5	99.4
9	$(C_3H_7)(CH_3)CHOH$	118.9	119.0
10	$(C_4H_9)(CH_3)CHOH$	138	138.4
11	$(C_5H_{11})(CH_3)CHOH$	161	157.4
12	$(C_6H_{13})(CH_3)CHOH$	180	175.9
13	$(C_7H_{15})(CH_3)CHOH$	193	193.9
14	$(C_2H_5)_2CHOH$	116.1	119.0
15	$(C_3H_7)(C_2H_5)CHOH$	134	138.4
16	$(C_4H_9)(C_2H_5)CHOH$	157	157.4
17	$(C_5H_{11})(C_2H_5)CHOH$	172	175.9
18	$(C_6H_{13})(C_2H_5)CHOH$	195	193.9
19	$(C_3H_7)_2CHOH$	161	157.4
20	$(C_4H_9)(C_3H_7)CHOH$	176	175.9
21	$(C_5H_{11})(C_3H_7)CHOH$	192	193.9
22	$(C_4H_9)_2CHOH$	193	193.9
23	$(CH_3)_3COH$	82.3	82.2
24	$C_2H_5C(CH_3)_2OH$	102.0	101.8
25	$C_3H_7C(CH_3)_2OH$	120–122	121.2
			r 0.9973
			s 2.6766

[a] Calculated by the relationships $P_n = P_{n,\mathrm{lin}} + \delta^{\perp CH_3}$ (primary alcohols with branched radicals, entries 1–6), $P_n = P_{n,\mathrm{lin}} + \delta^{\perp OH}$ (secondary alcohols, entries 7–22), $P_n = P_{n,\mathrm{lin}} + \delta^{\times CH_3,OH}$ (tertiary alcohols, entries 23–25). The parameters k_1, k_2, and k_3 are the same as for normal alcohols (Table 1). Parameters characterizing branching: $\delta^{\perp CH_3}$ –7.3333 ± 2.0306, $\delta^{\perp OH}$ –17.6714 ± 1.8427, $\delta^{\times CH_3,OH}$ –34.8667 ± 0.2082.

When alcohols are used as solvents, it is important to know their relative basicity, which can be evaluated, e.g., from data on the solubility in alcohols of HCl or such electron-acceptor molecules as I_2 or SO_2. Evaluation of the HCl solubility in normal aliphatic alcohols (from methanol to decanol) by relationship (1) gave the following results (moles of HCl per mole of alcohol at 10°C): 0.86 (methanol), 0.93 (ethanol), 0.96 (propanol), and 0.97 (higher alcohols), at k_1 1.2073 ± 0.0357, k_2 −0.3002 ± 0.0307, and k_3 −0.0452 ± 0.0092. The respective experimental values [12] are 0.86, 0.94, 0.96, 0.97 (butanol to nonanol), and 0.98 (decanol); correlation coefficient 0.9871, rms deviation 0.0065.

One of important characteristics of the solvent polarity is the so-called solvatochromic parameter $E_T(30)$ [13], which efficiently takes into account the polarity and polarizability of solvents and is used in many cases for estimating the solvent effect on the complexation parameters or kinetic parameters of var-

Table 3. Parameters determining the properties of normal aliphatic alcohols $C_nH_{2n+1}OH$ (n = 1–10)

Property	Parameter			Statistical criteria	
	k_1	k_2	k_3	r	s
C_p, J K^{-1} mol^{-1}	-306.9787 ± 27.3128	199.3059 ± 23.4869	192.0918 ± 7.0576	0.9990	4.9553
S^0, J K^{-1} mol^{-1}	-138.4174 ± 43.8747	148.0210 ± 37.7289	214.9634 ± 11.3373	0.9984	7.9600
ΔH^0_f, kJ mol^{-1}	-1.8566 ± 34.3222	-86.1840 ± 29.5144	-166.6541 ± 8.8689	0.9965	6.2270
ΔG^0_f, kJ mol^{-1}	-314.9172 ± 20.3647	95.4502 ± 17.5121	56.6523 ± 5.2623	0.9892	3.6947
ΔG^{0gw}, kJ mol^{-1}	-28.2305 ± 0.5953	3.2957 ± 0.5119	3.5115 ± 0.1538	0.9987	0.1080
$\log P$	-8.9912 ± 0.8275	4.5388 ± 0.7116	3.7828 ± 0.2138	0.9973	0.1501
ε	12.7112 ± 2.3200	23.8764 ± 1.9950	-3.8229 ± 0.5995	0.9988	0.4209
$-\chi_m \times 10^6$	-111.4840 ± 9.1010	66.6182 ± 7.8261	67.4573 ± 2.3517	0.9991	1.6512
I, eV	9.7358 ± 0.1128	1.2684 ± 0.0970	-0.1414 ± 0.0291	0.9988	0.0205
γ, dyne cm^{-1}	11.7060 ± 2.6457	5.3640 ± 2.2751	4.9184 ± 0.6863	0.9852	0.4800
η, cP	-21.5386 ± 3.4343	13.8589 ± 2.9533	8.5999 ± 0.8874	0.9875	0.6231
λ, W K^{-1} m^{-1}	0.0004 ± 0.0145	0.1648 ± 0.0125	0.0352 ± 0.0038	0.9868	0.0026
δT_{bp}, °C	99.1289 ± 26.7704	1.8492 ± 23.0205	-32.0262 ± 6.9175	0.9832	4.8569
$\log L^{16}$	-4.8412 ± 0.3212	2.8476 ± 0.2762	2.9999 ± 0.0830	0.9995	0.0583
$\log K_{wm}$	-5.0136 ± 0.2513	2.5584 ± 0.2161	2.5347 ± 0.0649	0.9995	0.0456

ious chemical reactions [14]. Using relationship (1), we calculated the solvatochromic parameter $E_T(30)$ for aliphatic alcohols $C_nH_{2n+1}OH$ (n = 1–10). As in the case of the other properties, the calculated values (at k_1 44.5509 ± 0.9853, k_2 10.8044 ± 0.8473, k_3 -0.0693 ± 0.2546) are nicely consistent with the experimental data (given in parentheses), taken from [14]: 55.4 (55.3), 51.9 (52.1), 50.7 (50.7), 50.2 (49.9), 49.1 (49.3), 48.8 (48.8), 48.5 (48.5), 48.3 (48.2), 48.0 (48.0), 47.7 (48.0); correlation coefficient 0.9978, rms deviation 0.1788.

As already noted, alcohols are often used as solvents for chemical reactions, affecting their kinetics and mechanism. It was interesting to examine the possibility of using relationship (1) for calculating the rate constants and other parameters of chemical reactions occurring in alcohols. As example we used the Menshutkin reaction:

$$C_6H_5\text{–}N(C_2H_5)_2 + C_2H_5\text{–}Br \rightleftharpoons [C_6H_5\text{–}N(C_2H_5)_3]Br.$$

For this reaction, Stepukhovich *et al.* [15] determined the rate constants (K), activation entropy ($\Delta S^{\neq}$), and activation energy ($\Delta E^{\neq}$) in normal aliphatic alcohols C_nH_{2n+1} (n = 1–8). We were able to reproduce the experimental data from [15] fairly accurately using relationship (1) (Table 4); the most accurate estimates were obtained for the activation energy. However, with higher alkanols (n > 10), the estimated $\Delta E^{\neq}$ becomes negative, which is senseless from the physicochemical viewpoint. This may be due either to large errors in the experimental $\Delta E^{\neq}$ values or to bad choice of the structure–property relationship. At a smooth decrease in $\Delta E^{\neq}$, the first differences between the $\Delta E^{\neq}$ values should decrease, whereas the experiment gives the opposite pattern. Apparently, the errors in experimental determination of $\Delta E^{\neq}$ are large, being responsible for the result obtained. To circumvent this problem, we assumed that the asymptotic behavior of $\Delta E^{\neq}$ should be close to exponential, e.g., at $n \to \infty$, $\Delta E^{\neq} \to 0$. This means that the expression for $\Delta E^{\neq}$ should be written as follows:

$$P_n = e^{f(n)}. \qquad (2)$$

Having chosen $f(n) = k_1 + k_2 n^{-1/2} + k_3 n^{1/2}$, we obtained the $\Delta E^{\neq}$ values listed in the last column of Table 4.

Finally, let us consider how relationship (1) reproduces the results of more rigorous calculations. Ligon [16] calculated by the B3LYP/6–31+G(d,p) the gas-phase proton affinity of alcohols as the negative enthalpy ($-\Delta H$) of the reaction ROH + $H^+ \to R\text{–}OH_2^+$. Our calculation results and Ligon's data [16] are listed in Table 5. It is seen that relationship (1) reproduces the results of more rigorous calculations with a good accuracy.

Thus, we have applied simple relationship (1) to calculation of diverse properties of aliphatic alcohols; in all cases, the results were nicely consistent with the

Table 4. Rate constant, activation entropy, and activation energy of the Menshutkin reaction in normal aliphatic alcohols

Molecule	$\ln(K \times 10^6$, mol^{-1} l s^{-1})		$\Delta S^{\neq}$, J K^{-1} mol^{-1}		$\Delta E^{\neq}$, kJ mol^{-1}		
	experiment [15]	this work[a]	experiment [15]	this work[b]	experiment [15]	this work	
						c	d
CH_3OH	2.04	1.97	–255.64	–256.29	27.45	27.44	26.18
C_2H_5OH	2.16	2.23	–264.01	–263.27	24.27	24.28	27.12
C_3H_7OH	2.32	2.63	–274.05	–270.69	20.29	20.53	21.59
C_4H_9OH	3.11	3.04	–275.73	–277.66	17.36	16.92	16.35
$C_5H_{11}OH$	3.77	3.43	–280.33	–284.13	13.85	13.53	12.28
$C_6H_{13}OH$	3.97	3.80	–290.79	–290.17	9.67	10.34	9.26
$C_7H_{15}OH$	4.12	4.16	–296.23	–295.85	7.11	7.33	7.04
$C_8H_{17}OH$	4.26	4.49	–302.50	–301.22	4.85	4.48	5.40
r		0.9742		0.9908		0.9989	0.9852
s		0.2496		2.5540		0.4471	1.7526

[a] k_1 –2.2496 ± 1.7962, k_2 2.0939 ± 1.4519, k_3 2.1220 ± 0.05010. [b] k_1 –202.1157 ± 18.3797, k_2 –21.8706 ± 14.8573, k_3 –32.3038 ± 5.1270. [c] k_1 58.8066 ± 3.2173, k_2 –13.8938 ± 2.6007, k_3 –17.4700 ± 0.8975. [d] Calculated by Eq. (2), k_1 7.7592 ± 0.7173, k_2 –2.6825 ± 0.5798, k_3 –1.8118 ± 0.2001.

Table 5. Proton affinity of normal aliphatic alcohols

Molecule	$-\Delta H$, kJ mol^{-1}		
	experiment [16]	calculation [16]	this work[a]
CH_3OH	754.3	753.5	753.3
C_2H_5OH	776.4	776.0	776.0
C_3H_7OH	786.5	785.2	785.9
C_4H_9OH	789.2	791.4	791.7
$C_5H_{11}OH$		795.7	795.6
$C_6H_{13}OH$		799.1	798.5
$C_8H_{17}OH$		802.6	802.5
$C_{10}H_{21}OH$		805.3	805.1
$C_{12}H_{25}OH$		807.2	807.0
$C_{14}H_{29}OH$		808.5	808.4
$C_{16}H_{33}OH$		809.4	809.6
$C_{18}H_{37}OH$		810.2	810.5
			r 0.9998
			s 0.3525

[a] k_1 832.7831 ± 1.1585, k_2 –78.5747 ± 1.1536, k_3 –0.8930 ± 0.2473.

experiment. We have already noted previously [17] that various properties of *n*-alkylbenzenes described by the same relationship are mutually correlated. Such a correlation is observed with aliphatic alcohols also; the correlation coefficients are given in Table 6. This is not surprising; it merely means that the properties of alcohols (and of any other compounds) are governed by the same intermolecular interactions. Indeed, the boiling point, enthalpy of vaporization, heat capacity at constant pressure, and other properties are determined by the energy of intermolecular interactions; the stronger the interactions, the higher these values, as boiling, vaporization, or simply increase in the molecular mobility in a condensed medium require at least partial break of bonds with the surrounding.

Thus, our simple approach allows estimation of diverse properties of primary, secondary, and tertiary

Table 6. Coefficients of mutual correlation of properties of normal aliphatic alcohols

Property	T_b	ΔH_{vap}	C_p	S^0	ΔH_f^0	ΔG_f^0	ΔG^{0gw}	$\log P$
T_b	1.0000	0.9994	0.9995	0.9967	–0.9956	0.9764	0.9979	0.9978
ΔH_{vap}		1.0000	0.9998	0.9986	–0.9973	0.9725	0.9971	0.9977
C_p			1.0000	0.9981	–0.9970	0.9739	0.9969	0.9981
S^0				1.0000	–0.9987	0.9608	0.9955	0.9944
ΔH_f^0					1.0000	–0.9535	–0.9955	–0.9956
ΔG_f^0						1.0000	0.9667	0.9713
ΔG^{0gw}							1.0000	0.9944
$\log P$								1.0000

Property	ε	γ	η	λ	χ_m	I	$E_T(30)$
T_b	–0.9290	0.9845	0.9812	–0.4357	0.9994	–0.9186	–0.8829
ΔH_{vap}	–0.9352	0.9839	0.9814	–0.4523	1.0000	–0.9247	–0.8922
C_p	–0.9319	0.9856	0.9835	–0.4452	0.9998	–0.9212	–0.8874
S^0	–0.9508	0.9810	0.9745	–0.4966	0.9986	–0.9412	–0.9133
ΔH_f^0	0.9481	–0.9805	–0.9770	0.4930	–0.9973	0.9361	0.9100
ΔG_f^0	–0.8487	0.9636	0.9687	–0.2806	0.9725	–0.8420	–0.7868
ΔG^{0gw}	–0.9402	0.9837	0.9728	–0.4636	0.9971	–0.9286	–0.8962
$\log P$	–0.9184	0.9858	0.9889	–0.4175	0.9977	–0.9057	–0.8711
ε	1.0000	–0.9184	–0.8625	0.7297	–0.9352	0.9967	0.9916
γ		1.0000	0.9708	–0.4398	0.9839	–0.9086	–0.8657
ν			1.0000	–0.3175	0.9814	–0.8455	–0.8074
λ				1.0000	–0.4523	0.7487	0.7975
χ_m					1.0000	–0.9247	–0.8922
I						1.0000	0.9902
$E_T(30)$							1.0000

alcohols with linear and branched alkyl radicals, including parameters of chemical reactions and complexation. It should be emphasized that, although in the majority of tables we give only data for the first 8–10 homologs, this limitation is exclusively due to the lack of systematic experimental data for other alcohols. In cases when such data (boiling points and some thermodynamic functions) were available, good agreement with the experiment was obtained with the other alcohols also. Since the choice of relationship (1) involved no assumptions concerning the structure of molecular fragment X, it is logical to expect that this relationship will be applicable to other classes of organic compounds also.

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