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Structure–Property Correlation Equation: VII.[1] Some Properties of Perfluorinated Organic Compounds

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Abstract — The possibilities were demonstrated of using a simple structure–property correlation equation for estimation of physicochemical properties of organofluorine compounds: boiling points, heats of vaporization, factors octanol–water partition, saturated vapor pressures, and also, for the compounds used as blood substitutes, times of half-elimination from body.

Organofluorine compounds are widely used as chemically and thermally stable materials, media for conservation of organs, blood substitutes, etc. Studies in these fields often involve a search for compounds with the required properties. Usually this is done with structure–property correlation equations, which are chosen on the basis of reasonable assumptions for each particular problem. Examples of such approaches are given in [2, 3].

In our previous papers [4, 5] we suggested an approach in terms of which it is possible to approximately estimate any property of molecules of various classes. Here we demonstrate the possibilities of this approach as applied to estimation of various properties of perfluorinated organic compounds.

The expression for a molecular property is as follows:

$$P = \Sigma P_{ii} + \Sigma\Sigma P_{ij}, \tag{1}$$

where P_{ii} is the contribution of the ith fragment to a property of a perfluorocarbon and P_{ij} is the contribution corresponding to interaction of fragments the ith and jth. It is assumed that the molecule is a system of interacting fragments.

If we explicitly take into account all F and C atoms, it is necessary to determine numerous parameters corresponding to different atoms and their interactions. For example, there will be two contributions $P_{i,i+1}$ (P_{CF}, P_{CC}), two contributions corresponding to interactions $P_{i,i+2}$ ($P_{C(C)F}$, $P_{C(C)C}$), etc. To simplify the pattern, let us assume that a perfluorocarbon molecule consists of CF_n fragments with n varying from 3 to 0. Assuming the F atoms to be “erased,” let us represent the perfluorocarbon molecule as a graph with CF_n groups (C centers) as vertices and CC bonds as edges. Following [4], let us assume that all the C centers, CC bonds, and CCC bond angles are equal; then $P_{i,i} = P_{j,j} = \alpha$, $P_{i,i+1} = P_{j,j+1} = \beta$, $P_{i,i+2} = P_{j,j+2} = \gamma$, etc. Then, Eq. (1) for a property of a perfluorocarbon can be rewritten as

$$P = n\alpha + n_{12}\beta + n_{13}\gamma + n_{14}\delta + \ldots \tag{2}$$

Here n is the number of CF_n groups (number of C atoms) and n_{12} is the number of CC bonds. For linear and branched molecules $n_{12} = n - 1$, and for cyclic systems it is higher (e.g., for monocyclic compounds $n_{12} = n$). n_{13} is the number of CCC fragments. For linear molecules it is equal to $n - 2$, and for branched and cyclic molecules it is higher. n_{14} is the number of CCCC fragments, etc. Contributions corresponding to 1–4 and more remote interactions were denoted as δ_{1i} and assumed to be exponential quantities: $\delta_{14} = k_1\exp(-k_2)$, $\delta_{15} = k_1\exp(-2k_2)$, etc., where k_1 and k_2 are certain parameters [5].

We will use this expression for estimating such properties of perfluorinated organic compounds as boiling point (T_b), heat of vaporization (ΔH_v), octanol–water oartition factor ($\log P$), and saturated vapor pressure ($\log P_v$).

The most extensive data are available on the boiling points; therefore, we first try to reproduce these quantities. The boiling points T_b estimated using this approach are listed in Table 1.

It is seen that for cyclic molecules the calculated values of T_b (Table 1) noticeably differ from the experiment. This is due to the fact that the parameters δ_{1i} corresponding to 1–4 and more remote interactions

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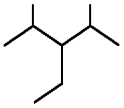
[1] For communication VI, see [1].

Table 1. Boiling points of some perfluorocarbons

Molecule[a]	T_b, K			
	experiment [6, 7]	this work		
		b	c	d
CF_4	145.25	144.79	144.79	144.79
C_2F_6	194.95	195.04	195.04	195.04
C_3F_8	235.25	237.73	237.73	237.73
C_4F_{10}	271.55	273.65	273.65	273.65
C_5F_{12}	302.55	304.43	304.43	304.43
C_6F_{14}	329.55	331.30	331.30	331.30
C_7F_{16}	355.65	355.20	355.20	355.20
C_9F_{20}	396.25	396.80	396.80	396.80
$C_{10}F_{22}$	419.25	415.43	415.43	415.43
$C_{12}F_{26}$	448.25	450.00	450.00	450.00
$C_{16}F_{34}$	513.25	513.11	513.11	513.11
iso-C_4F_{10}	276.25	272.86	272.86	272.86
neo-C_5F_{12}	299.15	300.43	300.43	300.43
iso-C_5F_{12}	303.45	315.55	315.55	315.55
cyclo-C_5F_{10}	296.25	213.45	327.20	308.5
CF_3-*cyclo*-C_6F_{11}	349.55	252.32	366.03	361.5
1,2-CF_3,CF_3-*cyclo*-C_6F_{10}	375.85	262.03	375.71	382.5
1,3-CF_3,CF_3-*cyclo*-C_6F_{10}	375.37	263.65	377.33	382.5
1,4-CF_3,CF_3-*cyclo*-C_6F_{10}	374.22	264.89	378.57	382.5
C_2F_5-*cyclo*-C_6F_{11}	370.75	267.31	380.99	382.5
C_3F_7-*cyclo*-C_6F_{11}	390.75	285.15	398.81	402.2
C_9F_{16} **(IX)**	391.05	188.30	415.72	402.2
C_9F_{18} **(X)**	398.45	285.15	398.81	402.2
$C_{10}F_{18}$ **(III)**	413.25	182.34	409.71	425.2
$C_{11}F_{20}$ **(V)**	434.25	177.87	405.20	446.1
$C_{13}F_{22}$ **(XI)**	463.25	103.75	444.80	475.06
C_9F_{20} **(I)**	–	362.35	362.35	402.2
C_9F_{20} **(II)**	–	356.68	356.68	402.2
$C_{10}F_{18}$ **(IV)**	–	175.58	402.94	425.2
$C_{12}F_{22}$ **(VI)**	–	194.20	421.51	454.2
$C_{12}F_{20}$ **(VII)**	–	645.25	405.59	454.2
$C_{12}F_{20}$ **(VIII)**	–	793.51	420.40	454.2

[a] For structural formulas of **I**–**XI**, see below. [b] Calculated by relation (2): α 144.79±3.11, β –94.54±3.98, γ –7.56±0.70, k_1 –6.77±0.55, k_2 0.275±0.113, correlation factor *r* 0.3858. [c] Calculated by relation (2) with the additional parameter allowing for ring closure, Δ_{cycl} 113.75±4.61; correlation factor *r* 0.9908, rms deviations 2.25. [d] Calculated by relation (3); Δ_{cycl} 5.95±0.4, correlation factor *r* 0.9981.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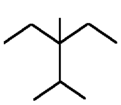
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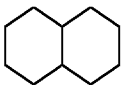
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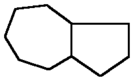
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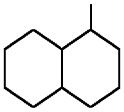
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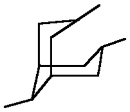
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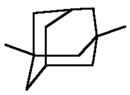
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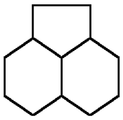
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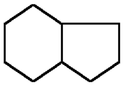
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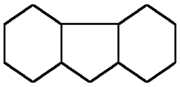
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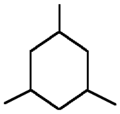

XI

depend on the conformations of the corresponding fragments, and this dependence was not taken into account because of the lack of the required experimental data. These problems can be circumvented by introducing additional parameters as it was done, e.g., in [5]. For example, we can supplement Eq. (2) with an additional parameter for ring formation (the corresponding values are given in the fourth column of Table 1) or assume that a property of a cyclic molecule can be estimated from data on a linear molecule with the same number of atoms in the chain:

$$P_{\text{cycl}\,C_n} = P_{n\text{-}C_n} + \Delta_{\text{cycl}}. \qquad (3)$$

The corresponding data are given in the fifth column of Table 1. This approach ensures a good agreement of the calculated boiling points with the experiment.

Along with perfluorocarbons, we will also consider some other perfluorinated organic compounds, e.g., amines and ethers. The contributions P_{ii} and P_{ij} for heteroatoms differ from those for CF_n groups, and, reasoning in terms of the perturbation theory, we can qualitatively explain the available experimental data and make predictions. Since, e.g., perfluoro amines contain one tertiary N atom, the expression for P will always include one contribution Δα and three contributions Δβ, which can naturally be combined in one parameter $\Delta\alpha_N$. The number of contributions Δγ is equal to the number of contributions δ_{CCN}, which is different for molecules of different structures, and this will be the second additional parameter. Perfluoro ethers can be considered similarly. The expression for a property of a molecule containing heteroatom X can be written as follows:

$$P = n\alpha + n_{12}\beta + n_{13}\gamma + ... + n'_{1\Delta}\gamma_{CCX} + \Delta\alpha_X. \qquad (4)$$

The estimated boiling points of perfluorinated organic compounds of various classes are given in Table 2.

Table 2. Boiling points of some perfluorinated ethers[a] and amines[b]

Molecule (F atoms are omitted)	T_b, K		Molecule (F atoms are omitted)	T_b, K	
	experiment [3]	calculation by relation (4)		experiment [3]	calculation by relation (4)
COC	214.25	214.94	$CO(C_2O)_3C$	378.00	367.61
C_2OC_2	283.55	284.57	$CO(C_2O)_3C$	391.00	385.41
COC_4	309.25	309.97	$CO(C_2O)_4C$	411.00	395.55
C_3OC_3	329.25	335.35	$CO(C_2O)_4C$	420.00	412.34
COC_6	354.25	355.53	$CO(C_2O)_5C$	437.00	421.13
C_3OC_4	352.25	357.00	$CO(C_2O)_5C$	447.00	437.48
COC_7	379.25	374.00	$CO(C_2O)_6C$	459.00	445.67
C_4OC_4	374.85	376.94	$CO(C_2O)_6C$	466.50	461.83
C_4OC_5	393.25	395.58	$C_2O(C_2O)_2C$	371.00	373.51
C_5OC_5	407.25	398.11	$NC_1C_1C_1$	262.35	252.48
COC_{10}	427.25	428.66	$NC_1C_1C_2$	293.75	300.56
C_6OC_6	452.25	446.47	$NC_1C_2C_2$	319.25	329.96
C_7OC_8	488.25	493.26	$NC_2C_2C_2$	343.85	360.98
COC_4-*tert*	309.25	304.43	$NC_2C_2C_3$	362.25	373.66
C_3-*iso*-OC_3-*iso*	329.25	328.81	$NC_1C_3C_4$	387.25	388.20
COCOC	263.00	260.30	$NC_2C_2C_4$	391.25	387.58
COC_2OC	289.70	288.64	$NC_2C_3C_3$	388.25	393.66
$C_2OC_2OC_2$	349.00	335.67	$NC_1C_3C_5$	400.25	408.19
$C_2OC_3OC_2$	354.00	357.08	$NC_3C_3C_3$	403.25	398.78
$CO(C_2O)_2C$	334.50	352.91	$NC_2C_2C_6$	425.25	428.24
$(C_2OC_2)_2$	379.00	375.71	$NC_3C_3C_4$	420.25	418.08
$CO(C_{20})_2C$	358.00	354.38	$NC_4C_4C_4$	452.25	437.99
$C_2OC_5OC_2$	393.60	393.37	$NC_5C_5C_5$	498.25	472.21

[a] Parameters of relation (4): α 144.79±3.11, β –94.54±3.98, γ –7.56±0.70, k_1 –6.77±0.55, k_2 0.275±0.113, $\Delta\alpha_O$ –24.27±1.36, $\Delta\gamma_O$ 1.47±0.50, correlation factor *r* 0.9938, rms deviation σ 1.23. [b] Parameters of relation (4): α 144.79±3.11, β –94.54±3.98, γ –7.56±0.70, k_1 –6.77±0.55, k_2 0.275±0.113, $\Delta\alpha_N$ –56.86±10.43, $\Delta\alpha_N$ 12.16±1.86, correlation factor *r* 0.9851, rms deviation σ 2.95.

Table 3. Heats of vaporization of some perfluorinated organic compounds[a]

Molecule	ΔH_v, kcal mol^{-1}	
	experiment [6]	calculation by relation (2)
CF_4	2.86	2.46
C_2F_6	3.86	3.45
C_3F_8	4.69	4.55
C_4F_{10}	6.10	5.47
C_5F_{12}	6.24	6.24
C_6F_{14}	7.64	6.92
iso-C_5F_{12}	6.49	6.49
cyclo-C_5F_{10}	6.30	6.15
cyclo-C_6F_{12}	6.51	6.67

[a] Parameters of relation (2): α 2.460±0.38, β –1.469±0.70, γ 0.114±0.387, k_1 –0.195±0.226, k_2 0.355±0.176, Δ_{cycl} 0.62±0.86, correlation factor *r* 0.9812, rms deviation σ 0.1276.

By a similar procedure we estimated the heats of vaporization ΔH_v. The results are listed in Table 3; agreement with the experiment is good. It should be noted that the Trouton rule $\Delta H_v = kT_b$ is obeyed with a high accuracy, with *k* 0.021, which is close to the Trouton constant.

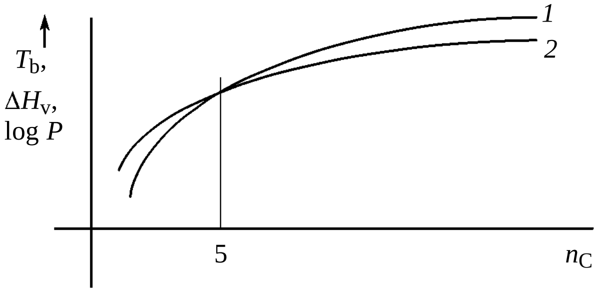
For many applications it is necessary to estimate the partition factors *P* of perfluorinated organic compounds between an organic phase (usually octanol is considered) and water. However, experimental data on partition factors of perfluorinated organic compounds are very few. All the data available to us and data for the corresponding hydrocarbons are listed in Table 4. Experimental data on perfluorocarbons are insufficient to estimate the parameters of Eq. (2); to circumvent these problems, we proceeded from the fact that various properties of perfluorocarbons and hydrocarbons vary similarly depending on the number of C atoms (see figure). We assumed that the log*P*

Table 4. Logarithms of the partition factors (log *P*) of some saturated hydrocarbons and perfluorocarbons in the octanol–water system

Molecule	log *P* [8]	
	X = H	X = F
CX_4	1.09	1.18
C_2X_6	1.81	2.0
C_3X_8	2.36	–
C_4X_{10}	2.89	–
C_5X_{12}	3.39	–
C_6X_{14}	3.90	–
cyclo-C_6X_{12}	3.44	2.91

values for perfluorocarbons *n*-C_4, *n*-C_5, and *n*-C_6 are close to those for the corresponding hydrocarbons and that for larger *n* these values should be lower than for hydrocarbons (for *n*-C_{12} log *P* should be about 6.5). With these assumptions, we obtained the parameters of Eq. (2) and estimated log *P* for perfluorocarbon molecules. The results are listed in Table 5. It is reasonable to assume that at $n > 5$ the log *P* values for hydrocarbons give the upper limits of the log *P* values for the corresponding perfluorocarbons. Therefore, the results in Table 5 seem quite reasonable. Available experimental data are reproduced with a good accuracy. Here and hereinafter, in expression (2) for a property we restricted the consideration to the contributions δ_{15}, and the parameters δ_{14} and δ_{15} corresponding to interactions 1–4 and 1–5 were chosen independently.

Equation (2) was also used for estimating the saturated vapor pressure of perfluorinated organic compounds of various classes. The results are listed in Table 6. In this case, too, the experimental data are reproduced with a good accuracy.



Correlation of the properties of linear (*1*) saturated hydrocarbons and (*2*) perfluorocarbons with the number of carbon atoms.

Table 5. Values of log *P* of some perfluorinated organic compounds in the octanol–water system[a]

Molecule	log *P*	
	experiment [8][b]	calculation by relation (2)
CF_4	1.18	1.27
C_2F_6	2.0	1.95
C_3F_8	(2.45)	2.47
C_4F_{10}	(2.9)	2.93
$CF(CF_3)_3$	–	2.85
C_5F_{12}	(3.4)	3.39
$C(CF_3)_4$	–	3.07
C_6F_{14}	(3.9)	3.85
C_7F_{16}	–	4.31
C_9F_{20}	–	5.23
$C_{12}F_{26}$	–	6.60
cyclo-C_5F_{10}	2.91	2.96
C_9F_{20} **(I)**	–	4.51
C_9F_{20} **(II)**	–	4.24
$C_{10}F_{18}$ **(III)**	–	3.28
$C_{10}F_{18}$ **(IV)**	–	3.21
$C_{11}F_{20}$ **(V)**	–	3.44
$C_{12}F_{20}$ **(VI)**	–	3.48
$C_{12}F_{20}$ **(VII)**	–	2.13
$C_{12}F_{20}$ **(VIII)**	–	2.72

[a] Parameters of relation (2): α 1.270±0.095, β −0.593±0.178, γ −0.151±0.056, δ_{14} −1.809±0.133, δ_1 −0.037±0.113.

[b] In parentheses are given the “recommended” values of log *P* of perfluorocarbons, close to those of the corresponding hydrocarbons.

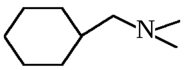
Some perfluorinated organic compounds are used as blood substitutes. One of their properties determining the possibility of using perfluorocarbon emulsions as blood substitutes is the half-elimination time $t_{1/2}$, since foreign compounds introduced intravenously should not reside in a body for a long time even if they are chemically inert. Blood substitutes are emulsions of perfluorocarbons which can schematically be considered as drops of perfluorocarbons coated with a shell of emulsifier molecules. Elimination of such emulsions consists of two stages: (1) breakdown of the shell and formation of a “drop” of a pure perfluorocarbon; (2) elimination of perfluorocarbon molecules from the body. The breakdown of the shell is poorly understood, and we can roughly take into account this process by introducing into Eq. (1) a special term *K*:

$$P = \Sigma P_{ii} + \Sigma\Sigma P_{ij} + K. \tag{5}$$

Table 6. Saturated vapor pressure ($\log P_v$) of some perfluorinated organic compounds[a]

Molecule[b]	$\log P_v$	
	experiment [2]	this work
$(C_3F_7)_3N$	1.27	1.220
$(C_4F_9)_2NCF_3$	1.20	1.162
$(C_3F_7)_2N(tert\text{-}C_4F_9)$	0.845	0.829
$(iso\text{-}C_4F_9)_2N(C_3F_7)$	0.362	0.426
$(C_4F_9)_3N$	0.041	0.169
C_9F_{20} (**I**)	1.351	1.313
C_9F_{20} (**II**)	1.235	1.293
$C_{10}F_{18}$ (**III**)	1.103	1.117
$C_{10}F_{18}$ (**IV**)	1.130	1.139
$C_{11}F_{20}$ (**V**)	0.681	0.772
$C_{12}F_{22}$ (**VI**)	0.462	0.355
$C_{12}F_{20}$ (**VII**)	0.230	0.319
$C_{12}F_{20}$ (**VIII**)	0.623	0.496
$C_9F_{19}N$ (**XII**)	1.225	1.196
$C_{10}F_{21}N$ (**XIII**)	0.939	0.924
$C_9F_{17}N$ (**XIV**)	1.240	1.379
$C_9F_{17}N$ (**XV**)	1.315	1.401
$C_{10}F_{19}N$ (**XVI**)	1.029	1.053
$C_9F_{19}N$ (**XVII**)	1.434	1.297
$C_9F_{19}N$ (**XVIII**)	1.376	1.330
$C_{10}F_{21}N$ (**XIX**)	0.991	0.929
$C_{10}F_{19}N$ (**XX**)	0.934	0.984
$C_{10}F_{19}N$ (**XXI**)	0.977	0.984
$C_{11}F_{21}N$ (**XXII**)	0.707	0.660
$C_9F_{17}N$ (**XXIII**)	1.378	1.320
$C_{10}F_{19}N$ (**XXIV**)	0.973	0.966

[a] Parameters of relation (4): α 4.288 ± 0.082, β −4.648 ± 0.096, γ −0.0379 ± 0.006, δ_{14} 0.022 ± 0.006, δ_{15} 0.0086 ± 0.006, $\Delta\gamma$ 0.18 ± 0.008, $\Delta\alpha$ 0.187 ± 0.040, Δ_{cycl} 4.793 ± 0.100, correlation factor r 0.9810, rms deviation s 0.0141. [b] For structural formulas of **XII**–**XXIV**, see below.



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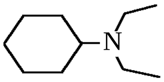

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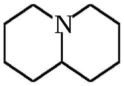

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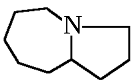
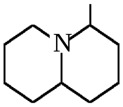


XV



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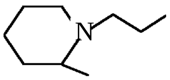

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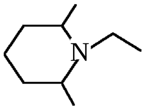

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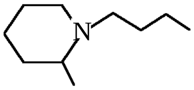

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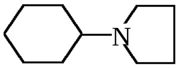

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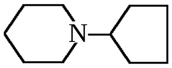

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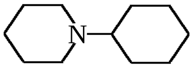

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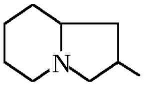

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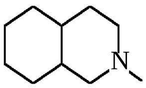

XXIV

Table 7. Estimated half-elimination times of perfluorinated organic blood substitutes

Molecule	$\log t_{1/2}$		
	experiment [2]	this work	
		a	b
$(C_3F_7)_3N$	1.812	1.724	1.726
$(C_4F_9)_2NCF_3$	1.361	1.747	1.726
$(C_3F_7)_2N(tert\text{-}C_4F_9)$	2.078	2.076	2.065
$(iso\text{-}C_4F_9)_2N(C_3F_7)$	2.537	2.641	2.547
$(C_4F_9)_3N$	2.950	2.959	3.066
$C_9F_{19}N$ (**XII**)	1.476	1.224	1.182
$C_{10}F_{21}N$ (**XIII**)	1.731	1.695	1.628
$C_9F_{17}N$ (**XIV**)	0.672	0.642	0.674
$C_9F_{17}N$ (**XV**)	0.301	0.575	0.674
$C_{10}F_{19}N$ (**XVI**)	0.827	0.998	1.084
$C_9F_{19}N$ (**XVII**)	1.476	1.151	1.182
$C_9F_{19}N$ (**XVIII**)	1.079	1.042	1.146
$C_{10}F_{21}N$ (**XIX**)	1.777	1.603	1.628
$C_{10}F_{19}N$ (**XX**)	1.175	1.254	1.120
$C_{10}F_{19}N$ (**XXI**)	1.161	1.254	1.120
$C_{11}F_{21}N$ (**XXII**)	1.795	1.572	1.567
$C_9F_{17}N$ (**XXIII**)	0.699	0.703	0.638
$C_{10}F_{19}N$ (**XXIV**)	0.944	0.992	1.084

[a] Calculation by relation (5) taking into account all the parameters: α 0.929 ± 0.063, β −0.415 ± 0.074, γ −0.0066 ± 0.030, δ_{14} −0.067 ± 0.020, δ_{15} 0.012 ± 0.011, $(K + \Delta\alpha_N)$ −3.342 ± 0.294, $\Delta\gamma_N$ −0.020 ± 0.023, r 0.9641, s 0.041. [b] Only α, β, γ, and K were taken into account; α 0.919 ± 0.047, β −0.436 ± 0.068, γ −0.0360 ± 0.029, K −3.215 ± 0.289, r 0.9569, s 0.045.

The contribution K is assumed to be equal for all perfluorocarbons.

We have estimated the $\log t_{1/2}$ values for various classes of perfluorinated organic compounds (hydrocarbons, amines, ethers); data for a series of amines are given as example in Table 7.

Since the parameters β and γ are negative, the value of $t_{1/2}$ will be the lower, the more contributions β and γ are included in Eq. (4) for $\log t_{1/2}$, i.e., it will be lower for cyclic and branched compounds. Indeed, in linear compounds the number of contributions β is $n - 1$ (where n is the number of C centers), whereas in cyclic compounds it is equal to n. The number of contributions γ in a linear structure is $n - 2$, whereas in a branched structure containing a $C(CF_3)_3$ group, with the same number of C centers, the number of contributions γ is by 3 larger. Apparently, this approach opens prospects for predicting the half-elimination time $t_{1/2}$ of perfluorinated organic compounds suggested for use as blood substitutes.

As seen, relation (2) (with additions obvious for each specific problem) allows estimation with a good accuracy of various properties of perfluorocarbon molecules solely from data on their structure, using parameters that are estimated from a limited set of experimental data.

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