Evaluation of the polarity and boiling points of nitrogen-containing heterocyclic compounds by gas chromatography

I. L. Zhuravleva

N. M. Emanuel Institute of Biochemical Physics, Russian Academy of Sciences,
4 ul. Kosygina, 117977 Moscow, Russian Federation.
Fax: +7 (095) 135 4101

Experimental gas-chromatographic data for 55 aromatic and aliphatic N-containing heterocyclic compounds and C_5—C_{13} *n*-alkanes are analyzed. The polar constituents of the boiling points (T_{pol}) were calculated as the difference between the boiling points measured directly and the boiling points calculated from GC data obtained on a nonpolar column. Depending on the number, nature, and position of heteroatoms and alkyl groups in the rings and the structures of the molecules, the T_{pol} values vary from −11° to +82°. The possibility of using T_{pol} values to estimate the physicochemical properties of compounds is discussed.

Key words: gas chromatography, nonpolar stationary phase, boiling points, nitrogen-containing heterocyclic compounds, self-association.

Correlations between the retention parameters and boiling points of compounds are used in gas chromatography (GC) for identification of compounds and in physicochemical strudies.[1—4] The correlations are feasible when columns with nonpolar stationary phases are used. However, in this case, too, boiling points of polar compounds calculated from GC data markedly deviate from experimental values if the correlation plot is constructed using *n*-alkanes. The polar constituents of the boiling points (T_{pol}) have been found as the difference between the boiling points measured directly and those calculated from GC values for compounds with various functional groups: ethers, halides, ketones, aldehydes, *etc.*[1]

The purpose of this work was to determine the polar constituents of the boiling points of nitrogen-containing heterocyclic compounds with various molecular structures and to explore the possibility of using the resulting values for determination of physicochemical properties of compounds.

Experimental

The retention indices of piperidines, morpholines, thiomorpholines,[5] oxazoles, thiazoles,[6] imidazoles (at 150 °C),[7] pyridines,[8] and some aromatic heterocycles with several N atoms in the ring[4,9] were determined previously on a nonpolar glass capillary column with OV-101 at 110 °C. The retention indices of pyrrolidine, *N*-methylpyrrolidine, cyclohexane, and its alkyl derivatives were calculated for a column with OV-101 (50 m × 0.3 mm) at 110 °C in this work. The phase layer thickness was 0.4 μm. A Pye Unicam 104 chromatograph with a flame ionization detector modified for the work with capillary columns was used. The detector and injector temperature was 200 °C, and helium was used as the carrier gas.

The standard compounds used for gas-chromatographic determination of the boiling points were C_5—C_{13} *n*-alkanes. The "*n*-alkane boiling point (T)—retention index (I)" correlation, presented in Fig. 1, is described, with an accuracy of 2 °C, by the equation

$$T_{b.p.} = -148.74 + 0.4135I - 0.00009I^2 = T_{nonpol}. \quad (1)$$

The boiling points of nitrogen-containing compounds, found from Eq. (1) using the I values determined on a column with OV-101 and designated by T_{nonpol}, are presented in Table 1. The polar constituents of boiling points of the sorbates under study (Table 1) were calculated from the equation

$$T_{pol} = T_{b.p.} - T_{nonpol}, \quad (2)$$

where $T_{b.p.}$ are experimental boiling points taken from the literature.[4,5,10,11]

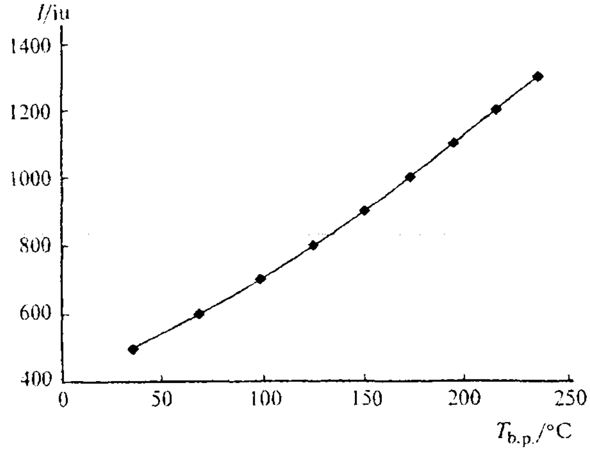

Fig. 1. Retention indices of *n*-alkanes *vs* boiling points.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 2, pp. 323—326, February, 2000.

1066-5285/00/4902-0325 $25.00

Table 1. Retention indices on a column with OV-101, and polar (T_{pol}/°C) and gas-chromatographic nonpolar (T_{nonpol}/°C) constituents of boiling points ($T_{b.p.}$/°C) of nitrogen-containing cyclic compounds

Compound	$I_{OV\text{-}101}$	$T_{b.p.}$	T_{nonpol}	T_{pol}
Pyrrole (**1**)*	747	130	110	+20
N-Methylpyrrole (**2**)	731	115—116	105	+11
1,3,5-Trimethylpyrrole	976	173	169	+4
Pyrazole (**3**)	864	187	141	+46
3(5)-Methylpyrazole (**4**)	930	205—206	158	+48
3,5-Dimethylpyrazole	1010	218	177	+41
N-Methylpyrazole	743	127	109	+18
Imidazole (**5**)	1069	256	190	+66
2-Methylimidazole	1050	267—268	186	+82
4(5)-Methylimidazole	1198	263	217	+46
1,2-Dimethylimidazole	1006	204	176	+28
N-Methylimidazole (**6**)	929	195—196	158	+38
1,2,4-Triazole	1116	260	201	+59
Oxazole	580	70	61	+9
2,4-Dimethyloxazole	730	108	105	+3
2,5-Dimethyloxazole	765	117—118	115	+3
2,4,5-Trimethyloxazole	843	133—134	136	−2
Isoxazole (**7**)	590	94	64	+30
3,5-Dimethylisoxazole	801	142—144	125	+18
Thiazole (**8**)	760	117	114	+3
4-Methylthiazole	831	133—134	133	+1
5-Methylthiazole	865	141—142	142	0
2,4-Dimethylthiazole	887	144—145	147	−2
4,5-Dimethylthiazole	941	158	161	−3
Pyridine (**9**)	738	115	107	+8
2-Methylpyridine (**10**)	804	130	126	+4
3-Methylpyridine (**11**)	852	144	138	+6
4-Methylpyridine (**12**)	852	145	138	+7
Pyridazine (**13**)	915	208	154	+54
3-Methylpyridazine	982	214	171	+43
3,6-Dimethylpyridazine	1052	214—215	187	+28
Pyrimidine (**14**)	744	123	109	+14
4-Methylpyrimidine	827	141—142	132	+10
5-Methylpyrimidine	864	152	141	+11
Pyrazine	722	118	103	+15
2-Methylpyrazine	812	135	128	+7
1,3,5-Triazine	663	114	86	+28
Pyrrolidine (**15**)	692	87	94	−7
N-Methylpyrrolidine	680	80	91	−11
Piperidine (**16**)	769	106	116	−10
N-Methylpiperidine (**17**)	766	107	115	−8
N-Ethylpiperidine	850	131	138	−7
N-*n*-Propylpiperidine	930	149—150	158	−8
N-Isopropylpiperidine	933	149—150	159	−9
N-*n*-Butylpiperidine	1025	175—177	180	−4
N-*n*-Pentylpiperidine	1122	201—202	202	0
N-Isopentylpiperidine	1084	188—189	194	−5
N-*n*-Hexylpiperidine	1220	219	222	−3
N-Allylpiperidine	931	155—156	158	−1
Morpholine (**18**)	794	128	123	+5
N-Methylmorpholine	788	116—117	121	−4
N-Ethylmorpholine	878	138—139	145	−6
Thiomorpholine (**19**)	973	169	168	+1
N-Methylthiomorpholine	969	163—164	167	−3
N-Ethylthiomorpholine	1054	184	187	−3
Cyclohexane	668	81	87	−6
Methylcyclohexane	737	101	107	−6
Ethylcyclohexane	846	132	137	−5
n-Propylcyclohexane	938	155	160	−5
Benzene	662**	80	86	−6

* For compounds **1**—**19**, see Fig. 2. ** From the data of Ref. 15.

Results and Discussion

Chromatographic retention of *n*-alkanes is determined by nonspecific interactions of the dispersion force type with the molecules of the nonpolar stationary phase OV-101. The boiling point found using the correlation (see Fig. 1 and Eq. (1)) corresponds to the boiling point of a hypothetical *n*-alkane with the same retention index as the compound under analysis; hence, it is referred to as the nonpolar constituent of the boiling point (T_{nonpol}). The T_{nonpol} values for compounds with polar functional groups are, as a rule, lower than the experimental boiling points ($T_{b.p.}$) because the latter value is also affected by the polar specific intermolecular interactions in the vaporizing liquid. This type of interaction is reflected in the T_{pol} values calculated from Eq. (2).

It can be seen from Table 1 that the T_{pol} values for the nitrogen-containing heterocyclic compounds vary, depending on the structure of the molecule, from −11 °C to +82 °C. The largest T_{pol} values are observed for aromatic heterocycles with several N atoms in the molecule, namely, pyrazoles, imidazoles, 1,2,4-triazole, pyridazines, and 1,3,5-triazine. The T_{pol} values for some imidazoles prove to be even higher than those for highly polar compounds such as nitro derivatives (T_{pol} = 60 °C[1]). Comparison of the data obtained for diazines and diazoles shows that the T_{pol} values depend substantially on the mutual arrangement of the N atoms in the molecule. The maximum values for diazines are observed with the N atoms occupying vicinal positions; those for diazoles occur when the two N atoms in the ring are separated by a C atom. The T_{pol} values for alkyl-substituted derivatives are usually lower than those for the corresponding unsubstituted compounds, though there are some exceptions. Thus comparison of the 3(5)-methylpyrazole—pyrazole and 2-methylimidazole—imidazole pairs shows that in the case of diazoles that have a free H atom at nitrogen the T_{pol} values increase upon the introduction of a Me group into the α-position with respect to nitrogen. The greatest decrease in T_{pol} occurs upon alkylation of aromatic heterocycles at the N atom. The decrease in T_{pol} caused by methylation at the C atom is insignificant; however, the appearance of several Me groups in the ring decreases substantially the T_{pol} values. Consequently, in terms of T_{pol} some aromatic heterocycles are close to nonpolar substances such as alkyl halides, for which T_{pol} = 7 °C.[1] For the majority of alicyclic nitrogen-containing compounds, negative T_{pol}

values were obtained. We analyzed cyclohexane and its alkylated derivatives on a column with OV-101 under similar GC conditions and found negative T_{pol} values for these compounds (see Table 1). Negative T_{pol} values for cyclohexanes were also found in the case where calculation by Eq. (1) was carried out using the retention indices[12] of these sorbates on nonpolar hydrocarbon stationary phases, $C_{24}H_{50}$ and $C_{30}H_{62}$. Thus, cyclization of an alkyl chain results in negative values of T_{pol}. Ring closure has a greater effect on T_{pol} than the appearance of an N atom in the molecule because the T_{pol} values of piperidines are negative, like those of cyclohexanes.

The main physicochemical parameter characterizing the polarity of a compound is the dipole moment of its molecule (μ). The relationship between the T_{pol} and μ values[4,10,13] for some nitrogen-containing heterocycles, whose dipole moments have been determined, is shown in Fig. 2. It can be seen that there is no clear linear correlation between T_{pol} and μ. Pyrazole and 3(5)-methylpyrazole deviate appreciably from the general plot (see Fig. 2, *3* and *4*), while for the remaining seventeen compounds, a linear dependence is fulfilled with a correlation coefficient of 0.87.

No correlations have been established between T_{pol} and polarizability or the degree of aromaticity of molecules. Pyridine and piperidine, having identical polarizabilities,[14] display T_{pol} with opposite signs. Heteroaromatic compounds are characterized by higher T_{pol} than aliphatic heterocycles, although T_{pol} of benzene (having a high aromaticity degree) is negative.

The deviations of the GC-calculated boiling points are specific to highly associated liquids.[1] Based on this fact, the difference between the experimental and calculated boiling points was termed as the GC indicator ($\delta T_{b.p.}$), characterizing the capacity of substances as pure liquids for self-association.[4] The gas-chromatographic boiling points were found using linear correlation equations, the coefficients for which were determined for each pair of neighboring *n*-alkanes. To calculate the GC boiling points, we constructed the "retention index—boiling point" correlation common for the whole series of *n*-alkanes. Generally, it appears to be nonlinear, although the values for each pair of neighboring *n*-alkanes are close to a straight line (see Fig. 1). The boiling points calculated using the dependence shown in Fig. 1 as well as the T_{pol} and $\delta T_{b.p.}$ values coincide with those determined by the previously published method[4] to within 1—2 °C, which corresponds to the experimental accuracy of determination of the boiling points of the nitrogen-containing heterocycles.[4,5,10,11]

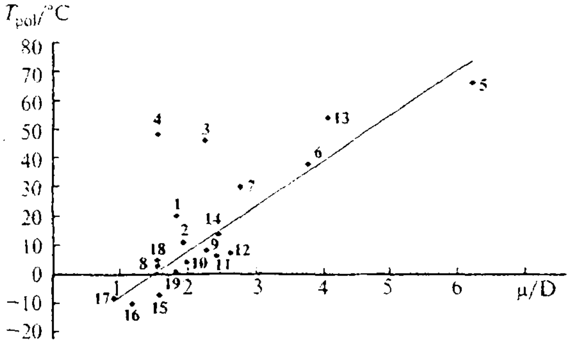

Fig. 2. Relationship between T_{pol} and dipole moments μ (benzene, ~20 °C)[4,10,13] for compounds **1—19** from Table 1.

The nitrogen-containing compounds studied can form self-associates through hydrogen bonds, especially when they have a free H atom at nitrogen. In the case of aromatic compounds, π—π interactions between the electronic systems of two molecules are possible. The types of self-associates existing in aromatic nitrogenous heterocycles have been discussed previously.[4] For imidazole, *N*-methylimidazole, and 1,2-dimethylimidazole, the T_{pol} values (see Table 1) correlate with the enthalpies of self-association determined by measuring osmotic coefficients in THF, CCl_4, and H_2O.[16] However, discussion of self-association of molecules in a pure liquid based on the data obtained for solutions is not completely justified. The short-range forces acting between molecules in liquids differ from those acting in solutions of the same substances. This might account for the absence of a clear-cut correlation between T_{pol} and dipole moments (see Fig. 2). The μ values used in Fig. 2 were determined in benzene, whose properties differ substantially from those of pure liquid nitrogen-containing bases.

Since the T_{pol} values are related to the degree of association of molecules in pure liquids, an explanation can be offered for the appearance of negative values. The reference (standard) compounds taken for the GC calculation of boiling points are *n*-alkanes, for which T_{pol} = 0, according to Eq. (2). However, *n*-alkanes are also associated in pure liquids. There are no liquids, except for liquid helium, that do not give self-associates of one or another nature. It is clear that some liquids can be less associated than *n*-alkanes. This is just the case for liquid alicyclic compounds, apparently, because their molecules are compact in shape, while those of *n*-alkanes are elongated.

The method for determination of the polar constituents of boiling points used in this study supplements the known GC and NMR and IR spectroscopy methods[17—20] for estimation of the polarity and degree of association of substances based on the values of excess thermodynamic functions of dissolution in nonpolar solvents. Extensive published data on retention indices make it possible to compare the polarity and capacity for self-association of various organic compounds in the liquid state.

The author is grateful to T. E. Kuz'menko for determination of the retention indices of pyrrolidines and cyclohexanes.

References

1. A. V. Kiselev, A. V. Ioginsen, K. I. Sakodynskii, V. M. Sakharov, Ya. I. Yashin, A. P. Karnaukhov, N. E. Buyanova, and G. A. Kurkchi, *Fiziko-khimicheskoe primenenie gazovoi khromatografii* [*Physicochemical Use of Gas Chromatography*], Khimiya, Moscow, 1973, 103, 234 (in Russian).
2. M. S. Vigdergauz, L. V. Semenchenko, V. A. Ezrets, and Yu. N. Bogoslovskii, *Kachestvennyi gazokhromatograficheskii analiz* [*Qualitative Gas-Chromatographic Analysis*], Nauka, Moscow, 1978, 105 (in Russian).
3. A. N. Beresnev, I. N. Stan'kov, V. A. Yarova, K. I. Sakodynskii, and S. P. Leonova, *Zh. Fiz. Khim.*, 1990, **64**, 2148 [*Russ. J. Phys. Chem.*, 1990, **64** (Engl. Transl.)].
4. R. V. Golovnya, T. E. Kuz'menko, and I. L. Zhuravleva, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 730 [*Russ. Chem. Bull.*, 1999, **48**, 726 (Engl. Transl.)].
5. M. B. Terenina, I. L. Zhuravleva, and R. V. Golovnya, *Zh. Anal. Khim.*, 1991, **46**, 2228 [*Russ. J. Anal. Chem.*, 1991, **46** (Engl. Transl.)].
6. I. L. Zhuravleva, V. V. Shenderyuk, E. V. Yakush, and R. V. Golovnya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1990, 1338 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1990, **39**, 1204 (Engl. Transl.)].
7. R. V. Golovnya, I. L. Zhuravleva, and M. A. Sal'kova, *Zh. Anal. Khim.*, 1992, **47**, 1269 [*Russ. J. Anal. Chem.*, 1992, **47** (Engl. Transl.)].
8. R. V. Golovnya, A. L. Samusenko, and L. B. Dmitriev, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1987, 2234 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1987, **36**, 2069 (Engl. Transl.)].
9. I. L. Zhuravleva and T. E. Kuz'menko, *Izv. Akad. Nauk, Ser. Khim.*, 1999, 1955 [*Russ. Chem. Bull.*, 1999, **48**, 1931 (Engl. Transl.)].
10. M. A. Kuznetsov, L. M. Kuznetsova, R. L. Plechko, A. A. Potekhin, V. P. Semenov, and B. V. Stolyarov, *Svoistva organicheskikh soedinenii* [*Properties of Organic Compounds*], Khimiya, Leningrad, 1984, 518 pp. (in Russian).
11. *Handbook of Fine Chemicals, Catalog*, Aldrich Chemical Company, Millwaukee, 1996—1997, 509, 997, 1026, 1027, 1034, 1270, 1416, 1487, 1490.
12. V. M. Nabivach and A. V. Kirilenko, *Chromatographia*, 1980, **13**, 93.
13. A. E. Lutskii and V. V. Prezhdo, *Zh. Fiz. Khim.*, 1971, **45**, 1273 [*Russ. J. Phys. Chem.*, 1971, **45** (Engl. Transl.)].
14. *Spravochnik khimika* [*Chemist's Handbook*], Vol. 1, Khimiya, Moscow—Leningrad, 1966, 384 (in Russian).
15. A. L. Samusenko and R. V. Golovnya, *Chromatographia*, 1988, **25**, 531.
16. Yu. A. Teterin, L. N. Talanova, L. N. Nikolenko, and A. A. Popov, *Zh. Obshch. Khim.*, 1976, **46**, 1427 [*J. Gen. Chem. USSR*, 1976, **46** (Engl. Transl.)].
17. F. Smith, *Aust. J. Chem.*, 1977, **30**, 23, 43.
18. G. DiPaola-Baranyi, J. E. Guillet, H.-E. Jeberien, and J. Klein, *Macromol. Chemie*, 1980, **181**, 215.
19. U. Domanski, K. Domanski, C. Klofutar, and S. Paljk, *Thermochim. Acta*, 1990, **173**, 273; *Chem. Abstrs.*, 1991, **114**, 130496z.
20. A. J. Treszczanowicz, G. C. Benson, and T. Treszczanowicz, *Bull. Pol. Acad. Sci., Chem.*, 1990, **38**, 59; *Chem. Abstrs.*, 1991, **114**, 12947z.

Received April 29, 1999;
in revised form October 4, 1999