DIPOLE MOMENTS OF 2- AND 4-SUBSTITUTED 9-ISOTHIOCYANATOACRIDINES

Ivan DANIHEL[a], Gejza SUCHÁR[a], Pavol KRISTIAN[a] and Stanislav BOHM[b]

[a] *Department of Organic Chemistry, Faculty of Natural Sciences, P.J.Safarik University, 014 67 Kosice, Slovak Republic; e-mail: idanihel@kosice.upjs.sk*

[b] *Department of Organic Chemistry, Prague Institute of Chemical Technology, 166 28 Prague 6, Czech Republic; e-mail: bohm@vscht.cz*

Dipole moments of a series of 2- and 4-substituted 9-isothiocyanatoacridines were determined and compared with the values calculated by vector addition using bond and group dipole moments. The results are discussed from the viewpoint of geometrical and conformational structures of the compounds investigated.

Key words: Isothiocyanatoacridines; Dipole moments.

Acridine derivatives possess two important features: broad biological activity[1] and special physicochemical properties such as fluorescence and intercalative effect. These properties inspired us to synthesize 2- and 4-substituted 9-isothiocyanatoacridines[2,3] that represent a suitable combination of the reactive NCS group and the biologically interesting acridine skeleton. In connection with their interaction with biological material and utilization as synthons in organic chemistry, it was of interest to aquire some information on their geometry by means of dipole moments. Dipole moments of acridine[4] and some of its derivatives[5,6] were already determined and discussed. In the present communication we measured the hitherto unknown dipole moments of 2- and 4-substituted 9-isothiocyanatoacridines.

EXPERIMENTAL AND CALCULATIONS

The studied 9-isothiocyanatoacridines were prepared by reaction of the corresponding 9-chloroacridines with AgSCN in anhydrous toluene by a described procedure[2,3]. Their dipole moments were determined in benzene at least at five different concentrations in the region 0.01–0.08 mol dm^{-3}. The benzene used was UV-spectral grade and was distilled on a column (b.p. 80 °C), stored above Nalsit-4 molecular sieve and immediately before the measurement filtered through a column of activated alumina. The permitivities of the compounds were determined on a Dipolmeter DM 01 instrument (Wissenschaftlich-technische Werkstätten, GmbH), accuracy 0.0001. The measurements were carried out at 2 MHz and 20 ± 0.05 °C in 4 ml thermostated cells DFL 2. Density was determined in 10 ml pycnometers for volatile compounds. Dipole moments were calculated according to Halverstadt and

Kumler[7] with corrections to atomic polarization (0 or 10%). Molar refraction R_D was calculated from molar refraction of acridine[4] and the corresponding increments[8,9]. For the theoretical calculations of dipole moments by vector addition, the following standard[10,11] values for bond and group moments (in 10^{-30} C m) were used: C_{ar}–H 0.00, C_{ar}–Cl 5.29, C_{ar}–CH$_3$ 1.23, C_{ar}–OCH$_3$ 4.26 (ϑ 72°), acridine 6.96 (ref.[4]), C_{ar}–NCS 8.1 or 9.7 (ϑ 20°)(ref.[12]). Quantum-chemical calculations were executed by the standard method PM 3 (refs[13,14]).

RESULTS AND DISCUSSION

The dipole moments and the pertinent quantities obtained by the measurements and calculations are given in Table I. In the vector calculations we used for the NCS group the value $9.7 . 10^{-30}$ C m, determined[11] for a series of benzene derivatives, as well as the value $8.1 . 10^{-30}$ C m which affords a better agreement between the calculated and experimentally found dipole moment values in the studied series of acridine derivatives. By analogy, it has been found[16] that for methyl derivatives of pyridine a better fit between the calculated and found dipole moments was obtained by using other value of group dipole moment for the CH$_3$ group than determined for the benzene series. Nevertheless, both the values employed for the NCS group led to practically the same conclusions about the preferred conformations of this group and other substituents.

TABLE I
Dipole moments ($\mu . 10^{30}$ C m) and molar refractions R_D (cm^3 mol^{-1}) for 2- and 4-substituted 9-isothiocyanatoacridines in benzene at 20 °C

| Compound | X | | | α^a | β^b | R_D | μ_{exp} | | $\mu_a{}^c$ | |
	2-	4-	9-				$\mu_{0\%}$	$\mu_{10\%}$	A	B
1	H	H	NCS	0.93	–0.37	79.69	2.8	1.9	2.8	
2	CH$_3$	H	NCS	1.36	–0.69	84.34	2.6	1.5	1.7	3.8
3	OCH$_3$	H	NCS	0.91	–0.49	86.10	2.3	0.9	6.3^d	2.3^e
									5.1^f	6.0^g
4	Cl	H	NCS	1.74	–0.50	84.53	5.5	5.0	8.0	3.8
5	H	CH$_3$	NCS	1.01	–0.39	84.34	3.1	2.2	3.3	
6	H	OCH$_3$	NCS	2.11	–0.29	86.10	6.8	6.4	6.8^h	1.5^i
									1.5^j	6.8^k
7	H	H	Cl	0.78	–0.45	69.92	1.7	0.0	1.7	

^{a} Slope of relationships ε_{12} vs weight fractions w_2. ^{b} Slope of relationships $1/d_{12}$ vs weight fractions w_2. ^{c} Dipole moments, calculated by vector addition of group dipole moments. ^{d} Conformation $\mathbf{A}_1^a$. ^{e} Conformation $\mathbf{B}_1^a$. ^{f} Conformation $\mathbf{A}_1^b$. ^{g} Conformation $\mathbf{B}_1^b$. ^{h} Conformation $\mathbf{A}_2^a$. ^{i} Conformation $\mathbf{B}_2^a$. ^{j} Conformation $\mathbf{A}_2^b$. ^{k} Conformation $\mathbf{B}_2^b$.

We have been interested in preferred conformations arising by rotation of the NCS or OCH_3 groups around the C3–N, C2–O or C4–O bonds. The conformational analysis was carried out by comparison of found dipole moments with the values for individual rotamers, calculated by the vector addition method. We started with planar arrangement of group and bond dipole moments in the 2- and 4-substituted 9-isothiocyanatoacridines. For substituents with zero angle group dipole moment (X = CH_3 or Cl), this arrangement corresponds to conformers A_1 and B_1 or A_2 and B_2, for nonzero angle dipole moment substituent (X = OCH_3) the corresponding conformers are A_1^a, A_1^b, B_1^a, B_1^b, and A_2^a, A_2^b, B_2^a, B_2^b (Scheme 1).
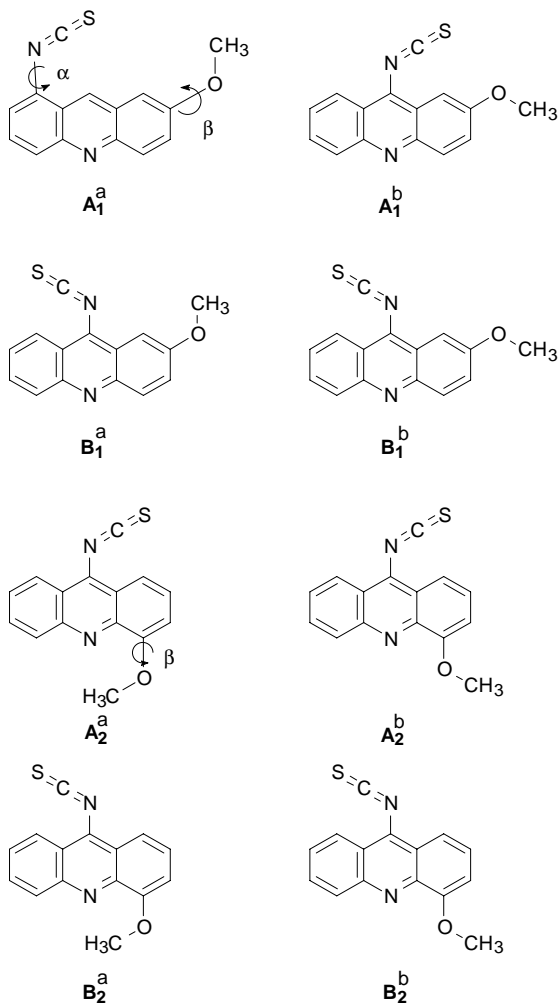
SCHEME 1

Substituents with Zero Angle Dipole Moment

From comparison in Table I it follows that in the case of X = 2-CH$_3$ the NCS group is not coplanar with the acridine system. From the graphic dependence of dipole moments calculated by vector addition, μ_a, on the angle of rotation of the NCS group about the C9–N bond (Scheme 1, angle α) it follows that the experimental value of the dipole moment, μ_{exp}, corresponds to $\alpha = 110°$. Quantum chemical calculations (PM 3) led to an energy minimum for the rotamer with $\alpha = 147°$. The calculated barrier to rotation is very small.

Using the same dependence of μ_a on α for X = 2-Cl, the experimental dipole moment, μ_{exp}, corresponds to $\alpha = 68°$. Quantum chemical calculations (PM 3) for rotation of the NCS group from the acridine plane lead to $\alpha = 145°$, the calculated energy barrier being again very low (0.21 kcal/mol).

For derivative **5** (X = 4-CH$_3$) the experimental and calculated dipole moments agree well (Table I).

Substituents with Nonzero Angle Dipole Moment

The assumed planar conformers of derivative **3** (X = 2-OCH$_3$) are given in Scheme 1. As follows from Table I, the planar conformation $\mathbf{B}_1^a$ is preferred. This is in good accord with the PM 3 calculations (Fig. 1), where the isoenergetic map shows minimum for $\alpha = 180°$ (for rotation of NCS group) and $\beta = 165°$ (for OCH$_3$), the calculation being based on the conformation $\mathbf{A}_1^b$.
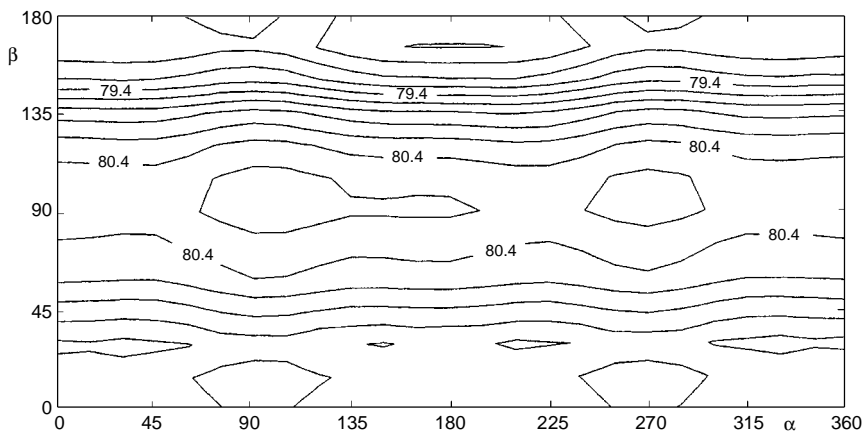

FIG. 1

Isoenergetic map of heats of formation calculated by method PM 3 for rotation of the NCS group in 2-methoxy-9-isothiocyanatoacridine. Angles α and β are described in Scheme 1

For derivative **6** with the OCH$_3$ group in position 4, the planar rotamers **A**$_2^a$ and **B**$_2^b$ are preferred (Scheme 1). Comparison of the moments μ_{exp} and μ_a indicates that both conformations are of about the same energy, the "quasi-*trans*" arrangement of the 9-NCS and 4-OCH$_3$ groups being the decisive factor. However, judging from the ^{1}H NMR data[11], conformation **A**$_2^a$ with the possible interaction between the OCH$_3$ hydrogen atoms and the acridine nitrogen seems to be more probable (4-OCH$_3$: δ(OCH$_3$) = 4.14 ppm; 2-OCH$_3$: δ(OCH$_3$) = 3.95 ppm). A relationship similar to that in Fig. 1 affords for the 4-OCH$_3$ derivative two energetically very close minima at $\alpha = 150°$ and $\beta = 170°$, and at $\alpha = 210°$ and $\beta = 170°$. As for the 2-OCH$_3$ derivative, the barriers to rotation are very small.

We were also interested in the published[5] zero dipole moment of 9-chloroacridine which does not correspond to the value $1.7 \cdot 10^{-30}$ C m, obtained by vector addition of group dipole moments. The value for 9-chloroacridine obtained by us without correction for atomic polarization, agrees very well with the calculated value (Table I).

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