DIPOLE MOMENTS OF SOME ISOXAZOLE DERIVATIVES

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The dipole moments of isoxazole and 13 of its halo, amino, and nitro derivatives were measured. A method is proposed for vector calculation for estimating the direction of the dipole moment of the isoxazole ring. It is demonstrated that phenyl substituents in the 3 and 5 positions are electron donors with respect to the isoxazole ring. It was found that the dipole moments of 4-substituted 3,5-dimethylisoxazoles correlate satisfactorily with the Hammett constants.

The π-electron distribution in the isoxazole molecule and the interaction of its π system with several substituents (C_6H_5, CH_3, and COOH) have been the subject of a number of theoretical and experimental investigations in which the dipole moments have been examined [1-11]. It has been shown that the introduction of methyl and phenyl substituents has little effect on the polarity of the isoxazole ring [5, 8, 10-12], but a phenyl substituent in the 5 position increases the dipole moment somewhat more than a phenyl group in the 3 position [8]. From the dipole moments of phenyl- and methyl-substituted isoxazole-4-carboxylic acid and its ethyl esters, it was concluded that these molecules are coplanar and that the direction of the moment of the carbonyl group is the opposite of the moment of the isoxazole ring [10, 11].

It follows from Hückel MO calculations [13] and from the reactivity data [14] that the π-electron distribution in the isoxazole aromatic system is extremely irregular and depends substantially on the nature of the substituent. However, until now the dipole moments of isoxazole derivatives with strongly polar substituents have received scarcely any study. The aim of our research was an investigation of the polarizing effect of several polar substituents in various positions of the isoxazole ring on the π-electron system of this ring. For this, we determined the dipole moments of isoxazole (I) and 13 of its derivatives (see Table 1), and the experimental moments (μ_{exp}) were compared with the calculated values (μ_{calc}).

In calculating the dipole moments of molecules with an asymmetrical charge distribution, it is difficult to determine the direction of the moment, but a knowledge of the direction of the moment is essential for the calculation of the moments of more complex molecules. We used two methods to estimate the direction of the vector of the dipole moment of isoxazole.

1. We performed a vector calculation by summation of the dipole moments of the individual fragments of the molecule, in analogy with [15]. Since the valence state of the nitrogen and oxygen atoms in the isoxazole molecule is close to the valence state, respectively, of nitrogen in pyridine and of oxygen in furan, the total dipole moment of the molecule was calculated as the vector sum of the dipole moments of pyridine (2.20 D) [12] and furan (0.71 D) [12] (Fig. 1). The isoxazole ring was considered to be a planar pentagon, and its angular values were taken from [16]. The dipole moment of isoxazole (2.50 D) calculated in this way coincides satisfactorily with the experimental moment (2.82 D) that we and other investigators [12] obtained. The dipole moment of isoxazole is directed away from the ring and forms an angle (θ) of 72° with the N–O bond.

2. The angle between the N–O bond and the vector of the moment of the isoxazole ring ($\theta = 75°$) [8] was calculated from the dipole moments of isoxazole (2.76 D) and its 3-methyl and 5-methyl derivatives (2.86 and 3.13 D, respectively), allowing for the moment of the methyl group (0.37 D).

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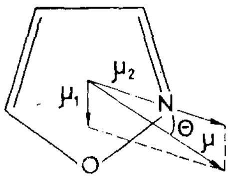


Fig. 1. Diagram of the vector calculation of the direction of the dipole moments of the isoxazole molecule (μ_1 = 0.71 D, μ_2 = 2.20 D, μ = 2.50 D, and θ = 72°).

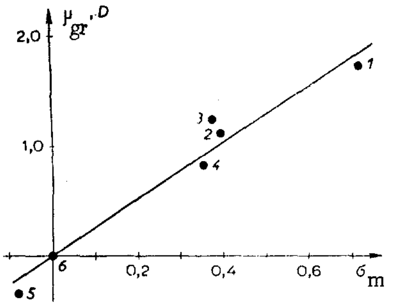
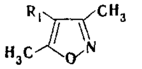


Fig. 2. Correlation of the dipole moments of groups in the 4 position for 4-substituted 3,5-dimethylisoxazoles with the Hammett σ_m substituent constants: 1) NO_2; 2) Br; 3) Cl; 4) I; 5) CH_3; 6) H.

It is seen that the two methods of calculation give results that are in satisfactory agreement, and this made it possible to use the calculated value of θ (72°) in the vector calculation of the moments of isoxazole derivatives. The experimental value of the moment of isoxazole (2.82 D) and the following values of the moments of the substituents were also used in the calculation of the dipole moments of isoxazole derivatives: $\mu_{NH_2} = +1.53$ D, $\mu_{NO_3} = -4.01$ D, $\mu_{Cl} = -1.59$ D, $\mu_{Br} = -1.57$ D, $\mu_I = -1.40$ D, and $\mu_{CH_3} = +0.37$ D [17].

An examination of the experimental and calculated dipole moments reveals a peculiar phenomenon when phenyl groups are introduced into the 3 and 5 positions. When there is no substituent in the 4 position, the moment of 3,5-dimethylisoxazole is 3.08 D [12], which is 0.25 D lower than the dipole moment of 3,5-diphenylisoxazole (3.33 D) [12]. Quilico and co-workers [5] have pointed out the electron-donor action of phenyl groups with respect to the isoxazole ring. A comparison of 4-halo-3,5-dimethyl derivatives of isoxazole (IX-XI) with 4-halo-3,5-diphenyl derivatives of isoxazole (XII-XIV) demonstrates that μ_{exp} for 3,5-dimethyl-4-chloroisoxazole (IX) and 3,5-dimethyl-4-bromoisoxazole (X) practically coincide with μ_{exp} for 3,5-diphenyl-4-chloroisoxazole (XII) and 3,5-diphenyl-4-bromoisoxazole (XIII), respectively. The coincidence of the μ_{exp} values of the corresponding 3,5-dimethyl and 3,5-diphenyl derivatives is probably due to a shift in the electron density to the electron-acceptor substituent in the 4 position. However, in this case, the phenyl substituents in the 3 and 5 positions display electron-donor properties, since, according to the vector calculations, the coincidence of the μ_{exp} values of 4-halo-3,5-diphenylisoxazoles with the moments of the corresponding 3,5-dimethyl derivatives is possible only if the vectors of the group moments of both the phenyl and methyl groups are directed identically, i.e., from the substituent to the isoxazole ring. The pK_a values also indicate the positive effect of conjugation of the phenyl groups in the 3 and 5 positions of the isoxazole ring [18].

In contrast to the 4-chloro and 4-bromo derivatives (compare IX and X with XII and XIII), μ_{exp} of 3,5-dimethyl-4-iodoisoxazole (2.28 D) differs by 0.20 D from μ_{exp} of 3,5-diphenyl-4-iodoisoxazole (2.49 D). This can be explained by the considerable steric hindrance between the iodine atom and the phenyl groups, as a consequence of which, conjugation of the benzene ring with the isoxazole ring is disrupted.

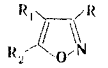


VIII-XI $R_1 = NO_2$, Cl, Br, I

We made an attempt to correlate the dipole moments of the groups in the 4-position with the Hammett σ constants of these same groups for VIII-XI.

The dipole moment of a group was determined as the vector difference between the experimental dipole moments of 3,5-dimethylisoxazole and 3,5-dimethyl-4-substituted isoxazole. The dipole moments of 3,4,5-trimethylisoxazole ($R_1 = CH_3$) and 3,5-dimethylisoxazole (R_1 = H) [8] (3.42 and 3.18 D, respectively) were also used in the correlation. Since the 4 position of the isoxazole ring is equivalent to the m position of the benzene ring with respect to the heteroatoms of the ring, we used the Hammett σ_m constants [19]. As seen from Fig. 2, a satisfactory linear correlation with correlation coefficient r = 0.982 is obtained. A similar linear correlation for the same compounds was obtained on comparing the pK_a values with the σ_m constants [18].

TABLE 1. Dipole Moments of Isoxazoles



Comp.	R	R_1	R_2	α	β	P_∞	MR_D	μ_{exp}, D	μ_{calc}, D
I	H	H	H	4,8658	0,1416	181,769	16,482	2,82±0,05	2,50
II	H	H	p-$NO_2C_6H_4$	8,8643	0,8892	336,257	47,526	3,72	3,35
III	NH_2	H	C_6H_5	6,5375	0,5498	257,590	44,223	3,20	3,23
IV	p-$NO_2C_6H_4$	H	H	12,7049	0,4840	474,916	47,526	4,53	4,87
V	C_6H_5	H	NH_2	8,1444	0,6019	309,715	44,223	3,57	3,90
VI	C_6H_5	H	Cl	5,5306	0,5898	229,613	45,629	2,97	2,32
VII	C_6H_5	NO_2	H	0,8789	0,8353	71,776	46,498	1,10	1,55
VIII	CH_3	NO_2	CH_3	1,1071	0,5635	71,611	31,417	1,39	1,36
IX	CH_3	Cl	CH_3	2,1023	0,3819	104,625	30,588	1,89	1,57
X	CH_3	Br	CH_3	2,4181	0,9421	115,376	33,445	1,99	1,59
XI	CH_3	I	CH_3	3,1960	1,3315	146,925	33,658	2,28	1,73
XII	C_6H_5	Cl	C_6H_5	2,6181	1,1834	142,734	69,960	1,87	1,33
XIII	C_6H_5	Br	C_6H_5	3,0056	1,8158	153,958	72,857	1,99	1,40
XIV	C_6H_5	I	C_6H_5	4,1889	1,7533	211,013	78,070	2,49	1,54

EXPERIMENTAL

The dipole moments were determined in benzene at 25 ± 0.1° with a Dipol' apparatus. Four to six solutions of different concentration from $7 \cdot 10^{-4}$ to $5 \cdot 10^{-3}$ mole fraction were prepared for each compound. The molecular polarization at infinite dilution (P_∞) was calculated as in [20], while $\mu_{exp} = 0.2192 \times \sqrt{P_\infty - (P_e + P_a)}$, where $P_e + P_a$ was assumed to be equal to MR_D (MR_D is the molar refraction calculated via an additive scheme). The resulting α, β, P_∞, MR_D, and μ_{exp} coefficients are presented in Table 1. All of the investigated substances were analytically pure. Chemically pure-grade benzene was dried over calcium chloride and sodium metal and distilled.

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