THE NATURE OF THE INDUCTIVE EFFECT OF AZINYL GROUPS

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The induction constants of azinyl groups are factored into two components, a σ-induction (σ_χ) and a field (σ_F) component. It is shown that the σ_χ constants of azinyl groups can be thought of as sums of contributions from the phenyl group and the endocyclic nitrogen atoms. A satisfactory correlation is found between the σ_F constants and the size and direction of the dipole moment of the heterocyclic substituents in the framework of the Kirkwood-Westheimer equation.

In previous papers [1-6] we have made a systematic study of the electronic effects of azinyl groups. In it, we have determined a set of various reactivity constants, among them being σ_I (Table 1), which formally characterizes the inductive effect of the azinyl groups. The σ_I constants shown were obtained by averaging values found by different methods. The strengthening of the electron-acceptor properties of the aromatic ring in the presence of endocyclic nitrogen atoms leads to an increase in the induction constants of the corresponding azinyl groups. However, it follows from a comparison of these constants with the induction constant of the phenyl group that the strengthening of the electron-acceptor properties does not follow a simple additivity rule but depends also on the mutual arrangement of the nitrogen atoms in the heteroaromatic ring and their positions relative to the ipso-carbon atom. The purpose of the present work was to establish the quantitative laws for the change in the inductive constants of azinyl groups as a function of the structure of the heteroaromatic ring.

For a number of years, there has been a discussion in the literature concerning the nature of the inductive effect [9-11]. At the present time, the majority of investigators hold the opinion [9, 12-14] that there are two basic mechanisms by which the electronic influence of charged or polar groups is transfered through the σ-skeleton of a molecule. The direct effect (or field effect, F), which is transmitted directly through space to the reaction center or some detectable site, is electrostatic in nature and depends to a substantial degree on the spatial configuration of the molecule. The second effect is due to the successive, and progressively diminishing, polarization of the electrons of the σ-skeleton by the substituent (the σ-induction effect, I_σ). The relative contributions of the two effects to the total inductive effect change depending on many factors, among them the number of σ-bonds in the chain, the geometry of the molecular skeleton, the polarity (μ) and electronegativity (χ) of the substituent, the nature of the reaction center, and the properties of the medium. The existing differences in the treatment of these mechanisms are basically only matters of detail and do not alter the fundamental question. In considering the transmission of the inductive effect through a π-system, moreover, the possibility of the polarization of the π-electrons by the field effect of the substituent (π_F-induction effect) and by direct σ-induction (π_σ-induction effect) is sometimes considered [12, 14]. These additional contributions are difficult to determine experimentally and separate from the resonance effect of the substituent. However, it can be assumed that for weak donor and weak acceptor substituents, aryl and heteroaryl groups among them, the contribution of the π-induction effect (I_π) is quite small.

In comparing the induction constants of azinyl groups, it is convenient to use the induction constant of the phenyl group as a reference point, taking that group as the zeroth member of the entire series of azinyl substituents under consideration. For this, it is important to choose correctly a proper value of the constant for the phenyl group. A col-

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TABLE 1. Induction Constants of Azinyl Groups

Group No.	Group*	σ_I		σ_χ	σ_F Calcd.		μ, D [7]	Angle θ, deg.	μ · cos θ
		found	calc. by Eq. (4)		by (2)	by (3)			
1	Ph	0,13	0,13	0,13	0	0	0	—	0
2	2-Py	0,10	0,12	0,15	−0,05	−0,03	2,20	58	1,17
3	3-Py	0,19	0,18	0,14	0,05	0,04		118,5	−1,05
4	4-Py	0,20	0,20	0,13	0,07	0,07		180	−2,20
5	3-Pyd	0,18	0,16	0,16	0,02	0	3,95	88	0,14
6	4-Pyd	0,24	0,25	0,14	0,10	0,11		150	−3,42
7	2-Pym	0,10	0,10	0,17	−0,07	−0,07	2,23	0	2,23
8	4-Pym	0,18	0,18	0,15	0,03	0,03		116	−0,98
9	5-Pym	0,22	0,22	0,15	0,07	0,07		180	−2,23
10	3-*as*-Tr	0,17	0,15	0,18	−0,01	−0,03	2,40**	63	1,09
11	5-*as*-Tr	0,24	0,24	0,16	0,08	0,08		180	−2,40
12	6-*as*-Tr	0,22	0,20	0,17	0,05	0,03		114	−0,98
13	2-*s*-Tr	0,14	0,17	0,17	−0,03	0	0	—	0

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*Ph — phenyl, Py — pyridyl, Pyd — pyridazinyl, Pym — pyrimidyl, Tr — triazinyl groups.

**Based on a theoretical calculation of the dipole moments of six-membered heterocycles [8].

TABLE 2. Values of the Induction Constant of the Phenyl Group

σ_I	Method of determination
0,15	p*K*a 4-phenylquinuclidine [15]
0,12	p*K*a $PhCH_2COOH$ [15]
0,11	p*K*a PhC_6H_4OH [16]
0,18	p*K*a $PhC_6H_4\overset{+}{N}H_3$ [16]
0,10	p*K*a PhC_6H_4COOH [16]
0,11	Rate of hydrolysis of $PhC_6H_4COOC_2H_5$ in 60% acetone [16]
0,12	NMR ^{19}F PhC_6H_4F in DMSO [15]
0,14	NMR ^{13}C Ph—Ph in acetone [17]
0,15	NMR ^{13}C Ph—Ph in acetone D_6 [17]
0,12	PMR $PhC_6H_4NH_2$ in DMSO*

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*Calculated from data in [1] from the chemical shifts of amine-group protons in m-aminodiphenyl (5.08 ppm) and p-aminodiphenyl (5.13 ppm) with corrections (0.03 and 0.02 ppm, respectively) for the diamagnetic anisotropy of the phenyl group.

lection of values for the induction constant of the phenyl group found by various methods is presented in reviews [15, 16]. They come primarily from determinations of the ionization constants of the corresponding acids and the rates of hydrolysis of the esters in aqueous solutions (Table 2), processes in which specific solvation effects appear strongly. The determination of the constants of the azinyl groups, however, were carried out in DMSO which is not able to specifically solvate a heterocyclic fragment. Consequently, in considering the value of the induction constant of the phenyl group, we took the values found by the NMR method in solvents that did not contain hydroxyls. Statistical treatment of all of the values considered (Table 2) gives an average value of 0.13 ± 0.03, which agrees well with these last data. A difference in the sensitivities toward medium effects is noted in the values presented for phenyl and azinyl groups. In the case of the phenyl group the values of the constant depend only slightly on the method of determination and the properties of the medium, and the majority of the values shown cluster about the average with little scatter. For azinyl groups, the effects of non-sphericity and special, specific solvation are more substantial because of the polarity of the groups and the presence in the ring of the protophilic aza group [4]. The use of DMSO as the solvent allows the conditions of the determination to be standardized with respect to the medium and the effects of specific solvation of the azinyl groups to be excluded.

In the framework of the mechanisms presented above for the transmission of the inductive effect of a phenyl group, the σ-induction effect appears paramount because of the electronegativity of the sp^2-hybridization of the carbon atoms. To all appearances, the phenyl group has a limited, insignificant dipole moment[*] (compare with data in [8]) and does not show any direct, electrostatic action on the reaction center. For the model structures used, one can also neglect the occurrence of an induced dipole moment in the phenyl group because its π-electronic system has a moderate polarizability [19] and can be polarized to a significant degree only by charged or strongly polar groups at distances that are substantially less than those in the model structures [20]. A theoretical calculation of the σ_F constant of the phenyl group and its translation into the scale of the corresponding empirical constants gives a value close to zero [21]. Consequently, virtually all of the inductive effect of a phenyl group in such compounds can be attributed to the group electronegativity; i.e., $\sigma_F \approx 0$ and $\sigma_\chi \approx \sigma_I = 0.13$. The value obtained for σ_χ is unlikely to be too high. A still higher value (0.20) is given in [22], but this shows the possiblity of overestimating σ_χ-constants because of the contributions of some additional factors.

In the case of azinyl groups, the σ-induction effect of the heteroaromatic ring increases because of the replacement of a methine group by a more electronegative, sp^2-hybridized nitrogen atom. In addition to this, many azinyl groups possessing an appreciable dipole moment can display a direct, electrostatic effect. Its contribution, according to the Kirkwood-Westheimer equation, is determined by the value of the group dipole moment, μ, the radius, L, joining the center of the dipole to the reaction center, and the angle, θ, between the direction of the dipole and radius L, as well as the dielectric permittivity of the medium, D_{eff} [14]:

$$F \sim (\mu \cdot \cos\theta)/(L^2 \cdot D_{eff}). \tag{1}$$

For constant values of L[†] and D_{eff}, contribution F depends only on the quantity $\mu \cdot \cos\theta$, which is the analytical expression for the projection of the dipole moment vector on radius L. The parallelism between σ_I and $\mu \cdot \cos\theta$ (r 0.883, s 0.024) is evidence of a specific contribution by an electrostatic component, characterized by the slope of the regression line (Fig. 1), and of the existence of a contribution by a σ-induction component which corresponds to the section cut off along the ordinate by the line. Proceeding from what has been said above, we attempted to factor the induction constants of the azinyl groups into two components σ_χ and σ_F, reflecting the contributions of σ-induction and direct electrostatic effects, respectively. The σ_χ constants of the azinyl groups can be represented as sums $\sigma_{\chi(Ph)} + \Sigma\sigma_{\chi(N)}$, in which the $\Sigma\sigma_{\chi(N)}$ term characterizes the over-all induction effect of the endocyclic nitrogen atoms of the corresponding azinyl group on the assumption of the additivity of the effect of the nitrogen atoms. In the framework of such an approach, it is possible to calculate the σ_F-component from constant σ_I by Eq. (2), using the values of $\sigma_{\chi(N)}$,

$$\sigma_F = \sigma_I - 0.13 - \Sigma\sigma_{\chi(N)}. \tag{2}$$

The correlation between constant σ_F and the quantity $\mu \cdot \cos\theta$ serves as a criterion of the validity of the calculation. The inverse problem can be solved: to try to find by the best correlation the values of $\sigma_{\chi(N)}$ for nitrogen atoms in the 2, 3, and 4 positions of the heterocycle, relative to the ipso-carbon atom. By an iteration procedure, we have found that for $\sigma_{\chi(2N)} = 0.02$[‡], $\sigma_{\chi(3N)} = 0.01$, and $\sigma_{\chi(4N)} \approx 0$, the correlation of σ_F with the azinyl group dipole moments is substantially improved and the regression line (Fig. 2) passes through reference point No. 1. The values of $\sigma_{\chi(N)}$ were chosen so that their ratio agreed with the assumed coefficient of decay of the σ-induction effect in a chain of sp^2-carbon atoms; i.e., 1/3 [9]. On the basis of Eq. (3) obtained for the regression (r 0.956, s = 0.016), one can give the generalized equation, Eq. (4):

$$\sigma_F = 0.003 - 0.031\mu \cdot \cos\theta; \tag{3}$$

$$\sigma_I = 0.133 + \Sigma\sigma_{\chi(N)} - 0.031\mu \cdot \cos\theta \tag{4}$$

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[*] The dipole moments are practically identical for such pairs of compounds as nitrobenzene and 3-nitrodiphenyl, thiophene and 2-phenylthiophene, indole and 2-phenylindole, etc. [7].

[†] The distance from the Cp-atom of the phenyl group to the center fo the heterocyclic ring in phenylazines varies from 5.51 to 5.67 A.

[‡] For comparison, $\sigma_{\chi(2N)}$ for the sp-hybridized nitrogen atom in a $-C{\equiv}N$ group is 0.03, according to the data in [23].

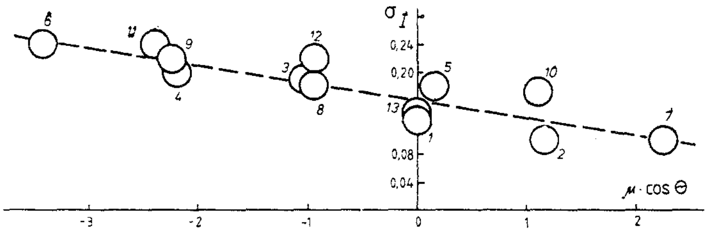

Fig. 1. Correlation between the σ_I-constants of azinyl groups and their dipole moments (points are numbered in accord with the numbering of the groups in Table 1).

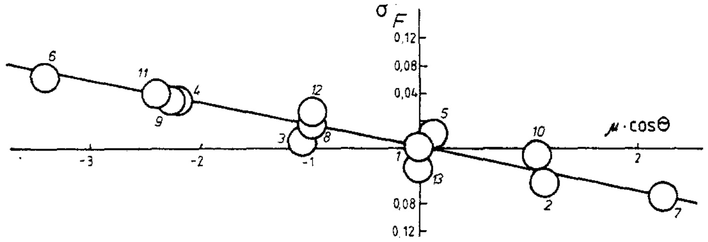

Fig. 2. Correlation of the σ_F components of azinyl groups with their dipole moments (points are numbered in accord with the numbering of the groups in Table 1).

In Table 1, values of σ_I calculated from Eq. (4) are given. The angles θ that are necessary for the calculation were determined graphically from the geometric data for diphenyl, pyridine, sym-triazine [24], pyridazine [25], pyrimidine [26], phenylpyrimidines [27], and chlorophenyl-asym-triazine [28]. The structures of the arylazines were drawn with the C_p atom of the benzene ring or a functional substituent, an amino group for example, in the para position serving as a reference point or reaction center.

Another model [29] for estimating the electrostatic effect of a substituent considers the dipole-dipole interaction of the polar substituent with the polar or polarizing bond and requires using trigonometric function not only of angle θ but also of a second angle, θ, between radius L and the polar bond under consideration. It also uses the value L^3. For the model structures chosen this function also leads to a $\mu\cdot\cos\theta$ term, inasmuch as angle θ is very small and the change in L is insignificant. The use of L^2 or L^3 in the calculations does not improve the correlation.

The separation of the inductive effect of the azinyl groups into two components allows one to explain the unexpectedly small induction constants of the 2-pyridyl, 2-pyrimidyl, and 3-asym-triazinyl groups, for which these components have opposite signs.

LITERATURE CITED

1. O. P. Shkurko and V. P. Mamaev, Zh. Org. Khim., 15, 1737 (1979).
2. O. P. Shkurko, L. L. Gogin, S. G. Baram, and V. P. Mamaev, Izv. Sibir. Otdel. Akad. Nauk SSSR, Ser. Khim. Nauk, No. 2, 95 (1980).
3. S. G. Baram, O. P. Shkurko, and V. P. Mamaev, Izv. Sibir. Otdel. Akad. Nauk SSSR, Ser. Khim. Nauk, No. 4, 135 (1982).
4. O. P. Shkurko, S. G. Baram, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 1, 66 (1983).
5. O. P. Shkurko, S. A. Kuznetsov, A. Yu. Denisov, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 7, 951 (1986).
6. O. P. Shkurko, L. L. Gogin, S. G. Baram, and V. P. Mamaev, Khim. Geterotsikl. Soedin., No. 2, 257 (1987).
7. O. A. Osipov, V. I. Minkin, and A. D. Garnovskii, Handbook on Dipole Moments [in Russian], Vyssh. Shkola, Moscow, 1971.

8. M. H. Palmer, R. H. Findlay, and A. J. Gaskell, J. Chem. Soc., Perkin, 2, No. 4, 420 (1974).
9. Yu. A. Zhdanov and V. I. Minkin, Correlation Analysis in Organic Chemistry [in Russian], Izd. Rost. Univ., Rostov-na-Donu, 1966.
10. A. J. Hoefnagel, M. A. Hoefnagel, and B. M. Wepster, J. Org. Chem., 43, 4721 (1978).
11. O. Exner and P. Fiedler, Coll. Czech. Chem. Comm., 45, 1251 (1980).
12. R. D. Topsom, Prog. Phys. Org. Chem., 12, 1 (1976).
13. M. Charton, Prog. Phys. Org. Chem., 13, 119 (1981).
14. W. Reynolds, Prog. Phys. Org. Chem., 14, 165 (1983).
15. O. Exner, in: Correlation Analysis in Chemistry. Recent Advances, N. B. Chapman and J. Shorter, eds., Plenum, New York, 1978, p. 439.
16. S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, Prog. Phys. Org. Chem., 10, 1 (1973).
17. S. G. Baram, O. P. Shkurko, and V. P. Mamaev, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 294 (1983).
18. S. P. Fradkina, I. Ya. Kvitko, and I. N. Vasil'eva, Zh. Org. Khim., 19, 190 (1983).
19. S. Marriott and R. D. Topsom, J. Chem. Soc., Perkin 2, No. 1, 113 (1984).
20. A. N. Vereshchagin and S. G. Vul'fson, Izv. Akad. Nauk SSSR, Ser. Khim., No. 6, 1231 (1967).
21. S. Marriott and R. D. Topsom, J. Am. Chem. Soc., 106, 7 (1984).
22. R. Knorr, Tetrahedron, 37, 929 (1981).
23. S. Marriott, W. Reynolds, R. W. Taft, and R. D. Topsom, J. Org. Chem., 49, 959 (1984).
24. L. E. Sutton, ed., Tables of Interatomic Distances and Configuration in Molecules and Ions, Chem. Soc., London, 1958.
25. A. Almenningen, G. Bjoernsen, T. Ottersen, R. Seip, and T. G. Strand, Acta. Chem. Scand., A31, 63 (1971).
26. P. J. Wheatley, Acta Cryst., 13, 80 (1960).
27. S. G. Baram, Dissertation for Candidate in Chemical Sciences Degree, Novosibirsk, 1983.
28. J. L. Atwood, D. K. Krass, and W. W. Paudler, J. Heterocycl. Chem., 11, 743 (1974).
29. R. D. Topsom, J. Am. Chem. Soc., 103, 39 (1981).