DIPOLE MOMENTS OF INDOLE ANALOGS OF CHALCONES

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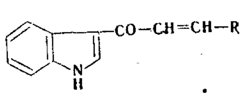
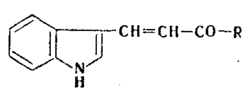
The most probable planar conformations of 22 indole analogs of chalcones were established on the basis of dipole moment measurements. The introduction of substituents into the phenyl ring of 1-(3-indolyl)-3-phenylpropenones causes a change in the dipole moments, which, in the 3-propenone series, correlates with the Hammett σ constants.

It has been previously [1] demonstrated on the basis of the dipole moments and PMR spectra of 3-formylindole, 3-acetylindole, and their N-methyl derivatives that they are all s-trans conformers. In order to ascertain the conformational state of α, β-unsaturated ketones of the indole series, in the present study we have measured the dipole moments of compounds of the type





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According to the IR spectra [2] and PMR spectra [3], chalcone and its heterocyclic analogs are trans isomers with respect to the orientation of the substituents attached to the vinylene group but s-cis conformers with respect to the relative orientation of the aliphatic double bond and the carbonyl group. A comparison of the dipole moments found with the moments calculated via a vector additive scheme for various forms (Table 1), as well as the data from the IR spectra, indicates a similar structure also for indole analogs of chalcones.

The presence of two rotational isomers is possible for each s-cis form. These isomers differ in that the carbonyl group oxygen and the pyrrole ring nitrogen of the indole molecule are situated on the same side of the bond connecting them (syn-s-cis form) or on different sides (anti-s-cis form) (Figs. 1 and 2). It is apparent from a comparison of the experimentally found and calculated dipole moments that the anti-s-cis form is predominant for indole analogs of chalcones. In addition, the presence of the syn-s-cis form is not excluded for 1-(3-indolyl)-3-phenyl-3-propenone and its substituted derivatives, although some steric hindrance exists for this form (Fig. 2). We note that the steric effects for the syn-s-cis form are caused by the hydrogens of the indole ring and the aliphatic double bond and are readily eliminated by deviation of the indole ring from the plane of the molecule.

The considerable difference between the calculated and experimentally obtained μ values in the 1-(3-indolyl)-3-aryl-1-propenone series is apparently due to a considerable degree to conjugation between

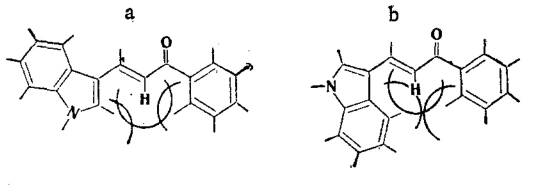

Fig. 1. Conformations of 1-(3-indolyl)-3-phenyl-1-propenone: a) anti-s-cis form; 2) syn-s-cis form.

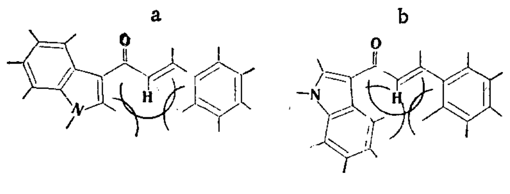

Fig. 2. Conformations of 1-(3-indolyl)-3-phenyl-3-propenone: a) anti-s-cis form; b) syn-s-cis form.

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TABLE 1. Dipole Moments of Indole Analogs of Chalcones

Comp.	Name	μ_{exp}, D	μ_{calc}, D			
			anti-s-cis form		syn-s-cis form	
I	1-(3-Indolyl)-3-phenyl-1-propenone	6,05	4,74	1,88		
II	1-(3-Indolyl)-3-phenyl-3-propenone	4,75	4,74	1,88		
III	1-(N-Methyl-3-indolyl)-3-phenyl-1-propenone	6,25	4,78	1,89		
IV	1-(N-Methyl-3-indolyl)-3-phenyl-3-propenone	4,77	4,78	1,89		
V	1-(3-Indolyl)-3-(4-tolyl)-1-propenone	6,05	5,02	1,79		
VI	1-(3-Indolyl)-3-(4-tolyl)-3-propenone	4,63	5,02	1,79		
VII	1-(3-Indolyl)-3-(4-anisyl) 1-propenone	6,80	5,18	3,10		
VIII	1-(3-Indolyl)-3-(4-anisyl) 3-propenone	4,66	5,18	3,10		
IX	1-(3-Indolyl)-3-(4-chlorophenyl)-1-propenone	5,58	3,90	2,80		
X	1-(3-Indolyl)-3-(4-chlorophenyl)-3-propenone	5,57	3,90	2,80		
XI	1-(3-Indolyl)-3-(4-bromophenyl)-3-propenone	5,52	3,91	2,78		
XII	1-(3-Indolyl)-3-(4-nitrophenyl)-3-propenone	7,45	3,69	4,90		
XIII	1-(3-Indolyl)-3-(4-diphenylyl)-3-propenone	5,16	4,74	1,88		
XIV	1-(3-Indolyl)-3-(1-naphthyl)-3-propenone	5,60	4,74	1,88		
XV	1-(3-Indolyl)-3-(2-naphthyl)-3-propenone	5,15	4,74	1,88		
			anti-anti-s-cis form	syn-anti-s-cis form	anti-syn-s-cis form	syn-syn-s-cis form
XVI	1-(3-Indolyl)-3-(2-furyl)-1-propenone	6,15	4,52	1,17	5,41	2,46
XVII	1-(3-Indolyl)-3-(2-furyl)-3-propenone	4,84	4,52	1,17	5,41	2,46
XVIII	1-(3-Indolyl)-3-(2-thienyl)-1-propenone	6,11	4,44	1,36	5,20	2,35
XIX	1-(3-Indolyl)-3-(2-thienyl)-3-propenone	4,84	4,44	1,36	5,20	2,35
XX	1-(3-Indolyl)-3-(2-selenienyl)-3-propenone	4,87	4,50	1,47	5,10	2,24
XXI	1-(3-Indolyl)-3-(3-pyridyl)-3-propenone	5,34	6,90	4,28	4,63	0,12
XXII	1,3-Bis(N-methyl-3-indolyl)propenone	6,42	6,68	3,74	3,74	0,15

the electron-donor indole ring and the electron-acceptor carbonyl group. We have previously pointed out [4] the strong electron-donor effect of the indole ring.

It is interesting that a substantial difference in the dipole moments was also observed in isomeric pyrrole analogs of chalcones [5]. A large dipole moment was observed for 1-(2-pyrrolyl)-3-aryl-3-propenones, in which the anti-s-cis form predominates. The presence of a weak intramolecular hydrogen bond in the isomeric 1-propenones facilitated stabilization of the syn-s-cis form, to which a lower μ value also corresponded. In addition, the furan [6] and thiophene [7] analogs of chalcones (1-propenones) exist in the syn forms. The fact that 1-(3-indolyl)-3-aryl-1-propenones exist in the anti-s-cis conformations, while the pyrrole, furan, and thiophene analogs exist in the syn forms can be explained by the fact that the energetically favorable s-trans orientation of the double bonds [8] of the heteroring and the carbonyl group is realized in all of these cases. In [9] it was proposed that the reason for the preferableness of one or another conformation of the simplest heterocyclic carbonyl compounds is the inclination of the atoms with like charges to be as far apart as possible, as compared with the tendency of atoms with opposite charges to approach one another. This is apparently not the chief reason, since the investigated indole compounds exist in the anti form. The s-trans orientation of the double bond of the heteroring and the exocyclic double bond is also realized for 1-(3-indolyl)-3-aryl-3-propenones in the syn forms. In the latter case, the steric factors are somewhat more favorable for a coplanar anti conformation (Fig. 2), as a consequence of which 3-propenones also exist in both forms.

There is some information [10] that indole contains the undistorted regular ring of pyrrole and that the entire molecule is coplanar. Methylation of indole has an extremely insignificant effect on the dipole moment. This is also observed in our models (compare I and II with III and IV). Consequently, the presence of a bulky methyl group attached to the nitrogen atom does not change the conformational state of the molecules of chalcones that contain an N-methylindole ring.

It is interesting that replacement of a benzene ring by an N-methyl-3-indole ring in the 1-(N-methyl-3-indolyl)-3-phenyl-1-propenone molecule causes an increase of 0.17 D in the dipole moment, while a similar substitution in the isomeric 3-propenone brings about an increase of 1.65 D (compare III and IV with XXII). This may indicate that the 1,3-bis(N-methyl-3-indolyl)propenone molecule exists in a different rotational form than that of the molecules of ketones III and IV.

TABLE 2. Data for Correlation of the Dipole Moments of 1-(3-Indolyl)-3-(4-R-phenyl)-3-propenones

R	$d_R - d_H$	$\mu_R - \mu_H$
CH_3	1,07	−0,12
CH_3O	0,29	−0,09
Cl	0,61	+0,82
Br	0,80	+0,77
NO_2	0,95	+2,70

The introduction of electron-donor and electron-acceptor substituents into the phenyl ring of isomeric 1-(3-indolyl)-3-phenylpropenones leads to a small decrease in the dipole moment (compare I with V and IX and II with VI and VIII).

The change in the dipole moments on introduction of substituents into the phenyl ring of 1-(3-indolyl)-3-phenyl-3-propenone correlates satisfactorily ($r = 0.98$) with the σ constants of McDaniel and Brown [11] according to the equation [12] $(\mu_R - \mu_H)/(d_R - d_H) = 1.62\sigma$, where μ is the dipole moment, and d_R is the distance from the center of the aromatic ring to the center of the substituent (Table 2).

The considerable difference in the dipole moments of 1-(3-indolyl)-3-(α-naphthyl)-3-propenone and 1-(3-indolyl)-3-(β-naphthyl)-3-propenone is probably a consequence of the better conjugation of the α-naphthyl group with the chalcone system.

Replacement of the phenyl group in the molecules of the isomeric 1-(3-indolyl)-3-phenylpropenones by furyl, thienyl, and selenienyl groups leads to an insignificant increase in the dipole moment. Several rotational isomers that differ with respect to the orientation of the five-membered heterorings are possible for such compounds. It is seen from the data in Table 1 that the anti-syn form is most probable for XVI and XVIII, while the anti-anti form is most probable for XVII, XIX, and XX.

EXPERIMENTAL

The measurements were made at 25 ± 0.01°C by the Debye dilute-solution method [7]. The synthesis of the compounds is described in [4]. Schemes of the possible planar conformations with allowance for van der Waals and covalent radii (Figs. 1 and 2) were constructed for a qualitative estimate of the steric effects. The dipole moments of indole (2.11 D) [13] and N-methylindole (2.16 D) [14] were assumed to be directed at an angle of 43° to the internal bisector of the CNC angle of the pyrrole ring. The bond lengths and angles in the indole ring and in the aliphatic chain were taken from [15, 16]. The dipole moments of the carbonyl, methyl, methoxy, nitro, chloro, and bromo groups were taken from [17], while the dipole moments of furan, thiophene, and pyridine were taken from [18]. The dipole moment of selenophene was taken as 0.41 D [7].

LITERATURE CITED

1. S. V. Tsukerman, N. S. Pivnenko, A. I. Bugai, and V. F. Lavrushin, Zh. Strukt. Khim., 12, 443 (1971).
2. S. V. Tsukerman, Yu. N. Surov, and V. F. Lavrushin, Zh. Obshch. Khim., 38, 524 (1968).
3. S. V. Tsukerman, A. I. Yatsenko, V. D. Orlov, and V. F. Lavrushin, Teor. i Éksperim. Khim., 6, 67 (1970).
4. S. V. Tsukerman, V. M. Nikitchenko, A. I. Bugai, and V. F. Lavrushin, Khim. Geterotsikl. Soedin., 268 (1969); 399 (1970).
5. S. V. Tsukerman, V. P. Izvekov, and V. F. Lavrushin, Zh. Fiz. Khim., 42, 2159 (1968).
6. S. V. Tsukerman, A. I. Artemenko, and V. F. Lavrushin, Zh. Obshch. Khim., 34, 3591 (1964).
7. S. V. Tsukerman, V. D. Orlov, and V. F. Lavrushin, Zh. Strukt. Khim., 9, 67 (1968); 10, 263 (1969); Khim. Geterotsikl. Soedin., 232 (1967).
8. G. Del Re, J. Chem. Soc., 3324 (1962).
9. V. I. Minkin, O. A. Osipov, and Yu. A. Zhdanov, Dipole Moments in Organic Chemistry [in Russian], Khimiya, Leningrad (1968), p. 120.
10. H. Kofod, L. E. Sutton, and J. Jackson, J. Chem. Soc., 1467 (1952).
11. D. H. McDaniel and H. C. Brown, J. Org. Chem., 23, 420 (1958).

12. S. V. Tsukerman, Chang Kuok Shuon, and V. F. Lavrushin, Zh. Fiz. Khim., 40, 160 (1966).
13. H. Lumbroso and G. Pappalardo, Bull. Soc. Chim. France, 1131 (1960).
14. E. F. Janetzky and M. C. Lebret, Rec. Trav. Chim., 63, 123 (1944).
15. L. I. Karle, K. Britts, and P. Gum, Acta Cryst., 17, 496 (1964).
16. R. Bramly and R. J. Le Fevre, J. Chem. Soc., 56 (1962).
17. C. P. Smyth, Dielectric Behaviour and Structure, New York (1956).
18. O. A. Osipov and V. I. Minkin, Handbook of Dipole Moments [in Russian], Moscow (1965).