

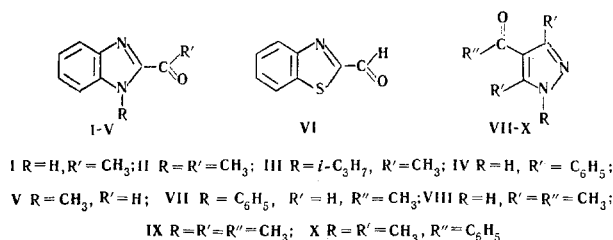
# ACYL GROUP CONFORMATIONS IN AZOLE DERIVATIVES

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The conformations of a number of aldo and keto derivatives of benzimidazole and pyrazole were established from their dipole moments. Several factors which determine the spatial orientation of the carbonyl group are discussed.

In heterocycles I-X, conjugation between the C=O and C=N (or C=C) bonds leads to the substantial manifestation of double bond character of the single bond that links them. Consequently, as in the case of the acyl derivatives of heterocyclic systems with one heteroatom [1-5], the development of *s*-cis-trans isomerism is possible for substituted benzimidazoles I-V, benzothiazoles VI, and pyridazoles VII-X.



We used the dipole moment method to establish the conformations of molecules of I-X.

A comparison of the experimentally obtained ( $\mu_{\text{exp}}$ ) and vector-calculated ( $\mu_{\text{cal}}$ ) moments (Table 1) indicates that a practically plane structure with *s*-trans-situated C=N and C=O bonds is characteristic for I-V and 2-formylbenzothiazole (VI) in solution.

There is currently no single point of view regarding the reasons that determine the conformations of compounds capable of *s*-cis-trans isomerism. Thus, in the case of heterocyclic carbonyl derivatives, analysis of an extensive number of investigations [1-6] indicates that the predominance of one or another plane *s*-isomer is associated with electrostatic repulsion or attraction between the heteroatom and the oxygen atom of the carbonyl group. On the other hand, the determining role of the differences in the energetic

TABLE 1. Dipole Moments of Acylazoles

Compound	Name	$\mu_{\text{exp}}^D$	$\mu_{\text{cal}}^D$	
			<i>s</i> -cis	<i>s</i> -trans
I	2-Acetylbenzimidazole	1,93	6,35	2,29
II	1-Methyl-2-acetylbenzimidazole	2,07	6,35	2,29
III	1-Isopropyl-2-acetylbenzimidazole	2,44	6,35	2,29
IV	2-Benzoylbenzimidazole	1,45	6,61	1,70
V	1-Methyl-2-formylbenzimidazole	3,37	5,96	3,01
VI	2-Formylbenzothiazole	2,84	4,62	3,29
VII	1-Phenyl-4-acetylpyrazole	2,61	0,98	3,80
VIII	3,5-Dimethyl-4-acetylpyrazole	2,26	1,25	3,38
IX	1,3,5-Trimethyl-4-acetylpyrazole	2,79	0,58	3,93
X	1,3,5-Trimethyl-4-benzoylpyrazole	2,80	0,98	4,21

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advantageousness of the s-cis and s-trans isomers was assumed in [7]. Here, the s-trans isomers should predominate for aldehydes and ketones of heterocycles with reduced aromatic properties (furan), while both plane conformers are equally likely for strongly aromatic systems (imidazole, benzimidazole, and others). It should be noted that, in a number of cases, these two points of view lead to the same results. Thus the s-trans conformation of a number of 5-substituted furfurals, as pointed out in [8, 9], is satisfactorily explained by the energetic advantageousness of the trans orientation of the double bonds and by electrostatic attraction between the furan and aldehyde oxygen atoms.

Considering the above and the high aromaticity of the imidazole ring [10], one should expect equilibria between the two possible plane structures for 2-acylbenzimidazoles I-V and VI; however, this contradicts our experimental data. In this connection, it is apparently more accurate to suppose that the reason for the predominant realization of the s-trans form for the acylazoles is repulsion between the negatively charged carbonyl oxygen and the N<sub>3</sub> atom of the heterocycle and attraction of the C=O group to the positive NR and S groups (as occurs in the case of acyl derivatives of pyrrole [1,4] and thiophene [11]). One should also allow for the possibility of stabilization of the plane structure for I and IV by an intermolecular hydrogen bond of the NH . . . O=C type.

As seen from the data in Table 1, introduction of alkyl substituents into the imidazole ring increases  $\mu_{\text{exp}}$  symbatically with respect to the bulk of the substituent (II, R = CH<sub>3</sub>, 2.07 D; III, R = i-C<sub>3</sub>H<sub>7</sub>, 2.44 D). It is well known [12] that this sort of transition in the 1-alkylbenzimidazole series is not accompanied by an appreciable change in the dipole moments. The increase in the dipole moments in the I, II, and III series is therefore really explained by the increased steric hindrance to realization of the s-trans structure.

In contrast to I-VI, for 4-acetylpyrazoles VII-X the  $\mu_{\text{exp}}$  values are intermediate in comparison with those calculated for the two plane structures. While one can again assume an equilibrium between the two plane conformations for 1-phenyl-4-acetylpyrazole (VII), the existence of two plane conformations is sterically impossible for VIII-X, which contain CH<sub>3</sub> groups in the 3 and 5 positions of pyrazole. The observed  $\mu_{\text{exp}}$  values of these compounds may thus correspond to rotation of the keto group about the C<sub>het</sub>-COR bond; this can be estimated vectorially as being 70-100° (assuming a zero value for the angle for the plane s-trans form).

## EXPERIMENTAL

The compounds were synthesized by the methods described in [13-15]. The dipole moments of I-X in benzene were determined at 25° and calculated vectorially, as described in [16].

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