SPATIAL ISOMERISM IN THE N-METHYLISATIN α-ANIL SERIES

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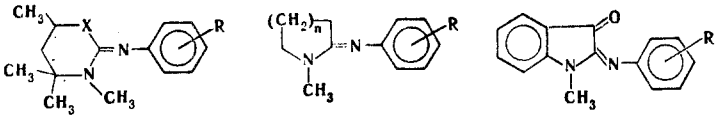
2-Phenylimino derivatives of 1,3-thiazine (I), 1,3-oxazine (I), pyrrolidine (II), piperidine (III), and hexahydroazepine (IV), as well as N-methylisatin α-anils (V), were studied. It is shown on the basis of the PMR spectra that I-IV exist in the anti form. In contrast to them, N-methylisatin α-anils exist in the form of two spatial isomers. The rates and energy barriers of syn–anti isomerization in the molecules of these compounds were determined. On the basis of the data obtained it was established that isomerization at the C=N bond is realized via an inversion mechanism.

In our investigation of the PMR spectra of 2-phenylamino derivatives of 1,3-thiazine and 1,3-oxazine we showed [1, 2] that rotational isomerism relative to the C–N bond, the barrier to rotation of which depends on the character of the solvent, takes place in the molecules of these compounds. In addition, according to the spectral data, this sort of isomerism is not observed in the molecules of the corresponding imino models I, and these compounds exist exclusively in the anti form,* since the syn form cannot be realized because of pronounced steric interaction of the phenyl ring with the ring N-methyl group.



I II-IV V

I X=S, O; II n=1; III n=2; IV n=3

A study of the three-dimensional structures of 2-phenylimino derivatives of pyrrolidine, piperidine, and hexahydroazepine (II-IV) shows that, despite the certain amount of equalization of the steric interactions in the two spatial isomers due to replacement of the oxygen or sulfur atom in I by a methylene group in II-IV, signals corresponding to the syn form do not appear in the PMR spectra of the latter. It may be assumed that the development of this form would be achieved as a result of a further increase in the steric repulsion of any groups in the anti isomer. In this connection, we studied the PMR spectra of N-methylisatin α-anils (V), in which a methylene group is replaced by a carbonyl group. In this case one might have expected a significant increase in the steric interactions in the anti form, since the sum of the length of the C=O bond and the van der Waals radius of the oxygen atom (1.23 + 1.4 = 2.63 Å) in V is greater than the sum of the analogous values of the C–H bond and the hydrogen atom (1.1 + 1.2 = 2.3 Å) in II-IV.

In fact, it was found that two singlet signals with different intensities from the protons of the N–CH_3 group corresponding to the syn and anti forms (Fig. 1, spectrum a) are observed in the low-temperature PMR spectra of N-methylisatin α-anils. Considering that in both isomers because of steric interactions the phenyl ring is not coplanar with the plane of the C=N bond and that the N-methyl group in the syn isomer lies in the region of anisotropic shielding of the benzene ring, the strong-field low-intensity signal was assigned to the syn form.

*The syn and anti designations are relative to the ring nitrogen atom.

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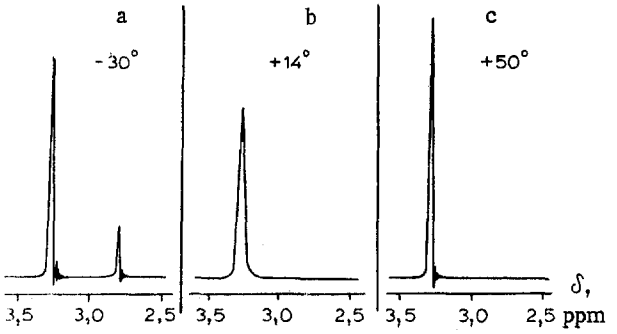

Fig. 1. Change in the signal of the N-methyl group in the PMR spectra of Vb as a function of the temperature.

TABLE 1. Kinetic Parameters of the syn—anti Isomerization in V Molecules

Compound V	R	k, anti/syn	$\Delta G^{\neq}_{a\to c}$, kcal/mole	$\Delta G^{\neq}_{c\to a}$, kcal/mole	$\lg k^{25°}_{a\to c}$	$\lg k^{25°}_{c\to a}$	σ^-
a	*p*-OCH_3	12,2	17,4	15,9	−0,028	1,124	−0,27
b	*p*-CH_3	13,2	17,1	15,6	+0,177	1,343	−0,17
c	*o*-OCH_3	12,0	16,3	14,8			
d	*o*-CH_3	13,0	16,2	14,7			
e	H	15,0	16,5	14,9	+0,654	1,830	0
f	*p*-Cl	17,5	16,0	14,4	+1,032	2.229	+0,23
g	*p*-$COOC_2H_5$	21,6	14,6	13,0	+2,035	3,208	+0,64

As the temperature is raised, and the rate of exchange increases, the two observed signals become broader and merge into one singlet (Fig. 1, spectrum b), which subsequently becomes increasingly narrower (Fig. 1, spectrum c).

syn—anti Isomerization at the C=N bond may take place via both rotational and inversion mechanisms [3]. To determine the mechanism of the isomerization in the molecules of the investigated N-methylisatin α-anils (V) one must study the effect of the position and character of the substituents of the phenyl ring and the nature of the solvent on the rate and activation parameters of the syn—anti transformations.

The free energy of activation ($\Delta G^{\neq}$) of the syn—anti isomerization was determined from the Eyring equation (Table 1), and the lifetimes (τ) of the isomers were calculated by the method presented in [4]. The reaction constants (ρ) of 2.23 and 2.27, which were close to the corresponding ρ constants of other imines in which isomerization at the C=N bond proceeds via an inversion mechanism [3], were determined from the correlation dependence of the logarithms of the isomerization rate constants calculated for 25°C with the Hammett σ^- constants of R substituents (correlation coefficient r = 0.997).

The introduction of ortho substituents in the phenyl ring has only a slight effect on the stabilities of the two isomers. In addition, a decrease in the barrier of the syn—anti transformations is observed on passing from p-OCH_3- and p-CH_3-substituted Va,b to the corresponding ortho derivatives Vc,d (Table 1). This pattern is in agreement with an inversion mechanism for syn—anti isomerization [3].

In the case of inversion an increase in the polarity of the solvent should not have affected the $\Delta G^{\neq}$ value. However, transition to more polar (as compared with chloroform) solvents (pyridine, alcohol, acetonitrile, acetone, and dimethylformamide) is accompanied by an almost complete shift of the equilibrium to favor the anti form; this is evidently due to stabilization of the more polar anti structure in a polar medium. For this reason the determination of the mechanism of the isomerization on the basis of a study of the effects of the medium on the rate of this process is impossible in this case.

Thus, in contrast to I-IV, N-methylisatin α-anils display the ability to exist in the form of a mixture of syn and anti isomers; this is due to the presence in the 3 position of the heteroring of a C=O group, which has a greater volume than the oxygen and sulfur atoms and the methylene group. In this case syn–anti isomerization at the C=N bond in the V molecules is realized via an inversion mechanism.

EXPERIMENTAL

The PMR spectra of deuterochloroform solutions of the compounds were recorded with a Jeol C-60HL spectrometer with tetramethylsilane as the standard. In the calculations of the kinetic parameters the temperature was determined with respect to a standard sample of methanol. The accuracy in the determination of the temperatures was ±1°C, and the isomer ratio ranged from 3 to 5%. With allowance for these errors, the accuracy in the determination of the $\Delta G^{\neq}$ values was ±0.3 kcal/mole.

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SPECTROSCOPIC AND QUANTUM-CHEMICAL STUDY OF 5-ALKOXYPYRIDINE-2- AND 6-ALKOXYPYRIDINE-3-CARBOXYLIC ACIDS

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The peculiarities of the structures of 5-alkoxypyridine-2- and 6-alkoxypyridine-3-carboxylic acids were studyed by experimental (IR, UV, and PMR spectroscopy) and quantum-chemical methods. It was established that both types of compounds exist in the form of dimers in the crystalline state, whereas in CCl_4 the first type exist in the form of monomers, while the second type exist in the form of dimers and monomers in dynamic equilibrium. The ability to form an intramolecular hydrogen bond and the interaction of the unshared pairs of electrons of the ring nitrogen atom and the oxygen atom of the C=O group are among the reasons for the absence of liquid-crystal properties in 5-alkoxypyridine-2-carboxylic acids as compared with 6-alkoxypyridine-3-carboxylic acids, which have such properties. From the point of view of the electronic structures, 6-alkoxypyridine-3-carboxylic acids differ from 5-alkoxypyridine-2-carboxylic acids in that in the former the ring nitrogen atom and the COOH and OAlk groups have an identical effect on the sign of the π-electron charges of the ring carbon atoms, and their π-dipole moments are directed virtually along the longitudinal axis of the molecule.

In liquid-crystal compounds replacement of a benzene ring by a pyridine ring in a number of cases leads to a substantial change in the mesomorphic properties [1]. Of the simplest potentially mesomorphic 5-alkoxypyridine-2- (I) and 6-alkoxypyridine-3-carboxylic acid (II) derivatives that we synthesized, which can be regarded as analogs of liquid-crystal p-alkoxybenzoic acids (III), only II have liquid-crystal properties. At the same time, a decrease in the melting point as compared with the corresponding III is observed for both series I and II. It is known that the liquid-crystal properties of aromatic carboxylic acids are due to the formation of dimers through intermolecular hydrogen bonds of the carbonyl groups [2].

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