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MUTAROTATION AND ISOMERIZATION OF IMINES. SUBSTITUTED N-(1-PHENYLETHYL)-1-BENZOYLBENZYLIDENEIMINES.

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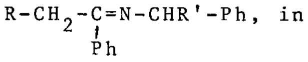
Summary: The mutarotation observed for several benzilmonoimines, having a chiral center, is atributed to the equilibration between two stereoisomers which differ in configuration around the single bond OC-CN which, due to restricted rotation, becomes a chiral axis of the imines.

In a previous paper[1], the synthesis of (+)-N-(1-phenylethyl)-1-benzoylbenzylideneimine (I) and the mutarotation shown by this imine in various solvents have been reported. Mutarotation, either in solution or in pure liquid compound, had previously been described for various imines derived from monocarbonyl compounds, ArRC=NCHR'Ar'. In these cases, variations observed in the IR and, particularly, ^{1}H-NMR spectra with time, suggested the establishment of an equilibrium between both geometrical isomers of imine as responsible for the optical change[2,3,4]. However, in the benzilmonoimine, I, the structural changes responsible for the variation of optical rotation with time are undetectable by IR, ^{1}H-NMR, ^{13}C-NMR and UV. This rules out the Z-E isomerization around C=N bond and also an imine-enamine tautomerization as the origin of the mutarotation in imine I.

By using as model compounds, simple imines of the type  $R\text{-}CH_2\text{-}\underset{\text{Ph}}{C}\text{=N-CHR'-Ph}$, in which both geometrical isomers were detectable, it was possible, from ^{13}C-NMR studies, to assign the Z configuration around the C=N bond to compound I and to establish that the planes containing CO and CN groups (conjugated with the phenyl groups bonded to them) are very nearly orthogonal[5]. X-ray diffraction studies of compound I[6], are in whole agreement with the foregoing conclusions and allowed the establishment of its absolute configuration (I_A in Fig. 1; S-center-R-axis). A similar structure has been found for other benzilmonoimines in which the amine residue has been changed (Ph-CHR-N=)[7].

A kinetic study of mutarotation has been carried out, on the basis of equations /1/ and /2/, in which α_o, α_e and α stand, as usual, for the values of specific rotation of compound I at the start, at equilibrium and at time t. Equation /1/ is the kinetic expression for a first order process of the type $A \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} B$. Plotting of ln $(\alpha-\alpha_e)$ versus time (in acetone, at 30°) yields a straight line with a slope of $16.10^{-5}\ s^{-1}$ (r=0.997); according to this, mutarotation should have its origin in the establishment of an equilibrium between only two species. This leaves also out the possibility, pointed out previously[1], that restricted rotation around =N-C single bond could give rise to the change in rotatory power. Equation /2/, corresponding to kinetics of a process $A \xrightarrow{k_1} B$, is applied only to the earlier ten minutes of equilibrium (<5 per cent of the total time). At this early stage, it is supposed that A is the only species present, as it happens in the crystalline state[8,9]. Then, values for k_1 and k_{-1} were determined.

$$\ln(\alpha-\alpha_e) = -(k_1 + k_{-1})\,t + \ln(\alpha_o-\alpha_e) \qquad /1/$$

$$\ln\alpha = -k_1 t + \ln\alpha_o \qquad /2/$$

Study of mutarotation has been extended to monoimines resulting from reaction of (-)-1-phenylethylamine with m,m'-dinitrobenzil (II), m,m'-dichlorobenzil (III), m,m'-dimethylbenzil (IV) and p,p'-dimethoxybenzil (V), (see Fig. 1), the synthesis of which have been reported elsewere[1,10]. All of them show a polarimetric behaviour and structural characteristics which are wholly referable to those of monoimine I[11]. Kinetic analysis of mutarotation data obtained for these compounds in acetone at 30°, by using equations /1/ and /2/, yields the values of k_1 collected in table 1[12].

Table 1

Specific rates of mutarotation for substituted benzilmonoimines in acetone at 30°.

Imine	I	II	III	IV	V
R (see Fig. 1)	H	m-NO_2	m-Cl	m-Me	p-MeO
$10^5\ k_1\ (s^{-1})$	3.53	6.64	3.71	2.46	0.8

For the origin of mutarotation in this particular type of monoimines it is suggested the establishment of an equilibrium between the two stereoisomers which results from rotation around the OC-CN single bond, as seen in Fig. 1. Then, restricted rotation endows this type of structures with a chiral axis in the direction of the bond linking both functional groups.

The structural resemblance of both stereoisomers may explain that no variation could be detected by spectroscopic techniques. This, together with the analysis of kinetics data and with the exclusion of other alternatives pointed out before, are the basis of the foregoing hypothesis.

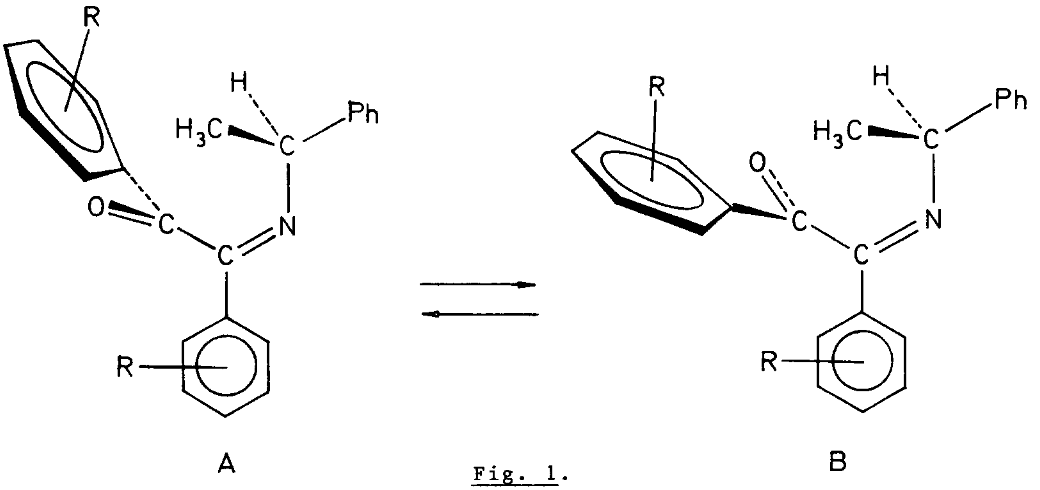
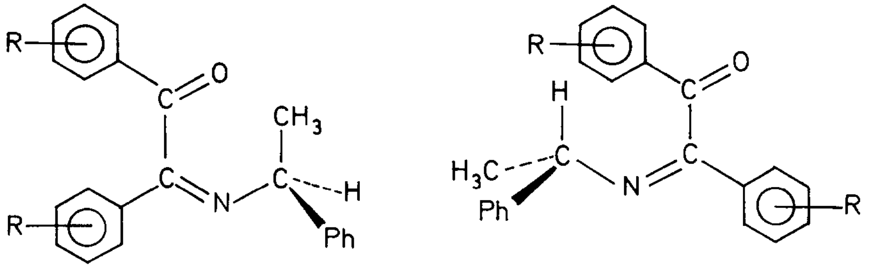


Fig. 1.

I, R = H; II, R= m-NO_2; III, R = m-Cl; IV, R = m-Me; V, R = p-OMe

The two possible transition states for the process are shown in Fig. 2. The large dipolar unstabilisation in T.S. 1 and the steric effects in T.S. 2 mayjustify the restriction of rotation around the single bond OC-CN to a point that the process can be followed in the polarimeter.



1 Fig.2 2

Plotting of 5 + log k_1 values versus Hammett substituent constants yields a straight line (r=0.987), with a positive slope (+ 0.6)[13];then, the process is favoured by electron withdrawing substituents. For monoimine V (R=p-OMe) a good correlation is obtained with the constant σ^+; by using σ a large deviation is observed. This suggests an extensive delocalization involving substituent and reaction center that requires that conjugation between CO and CN groups with their respective rings does not change significantly on reaching the transition state. Since electron-withdrawing substituents should minimize dipolar repulsions in T.S. 1 and also the planarity of conjugated carbonyl and imine systems will be greatly altered in T.S. 2, it seems that isomerization goes through T.S.1.

To verify this assumption a study of kinetics of mutarotation of imine I in solvents of varying polarity at 40° has been carried out (table 2).

Table 2

Specific rates of mutarotation of imine I in various solvents at 40°.

Solvent	CH_3CN	CH_3COCH_3	$CHCl_3$	C_6H_6	$C_6H_5CH_3$	CCl_4
$10^5\ k_1\ (s^{-1})$	14.35	11.52	9.02	6.16	4.09	5.11

Plotting of 5 + log k_1 versus the solvent ε_T parameter[14] yields a straight line (r=0.964) with a positive slope (+ 0.035); this shows that the rate of the process increases with solvent polarity. Since dipolar interactions decrease on increasing solvent ε_T, transition state **1** becomes the more acceptable.

The study of mutarotation of substituted benzilmonoimines at different temperatures is now being carried out in order to establish the activation parameters of the process involved which will contribute to the elucidation of the -- problem.

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12. Experimental data were linearly adjusted by the method of least squares (datasets >20); correlation coefficient were >0.99. Verification and optimization of results were performed by analysis of data obtained at least at two wavelengths (λ=578 and 546 nm); differences in the values of k_1 < 4% were found. Then values of k_1 in Table 1 are average values.
13. It seems reasonable that the effect of each substituent on the phenylimino and benzoyl groups to which they are directly attached will be, in first approximation, not very different. Thus the obtained slope may represent $\rho_{CO}+\rho_{CN}$.
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