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MUTAROTATION AND ISOMERIZATION OF IMINES

R. Perez Ossorio and V. Sanchez del Olmo
Departamento de Quimica Organica
Instituto de Quimica "Alonso Barba"
Madrid 6, Spain

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CURTIN and HAUSSER,[1] have recently reported the interconversion of stereoisomeric N-methyl and N-aryl-imines derived from p-substituted benzophenones. The changes take place on standing or in solution in cyclohexane and at rates which vary greatly with the nature of the N-substituent. According to these authors "there seem to be no (previous) cases where true steroisomerism (of imines) has been demonstrated unequivocally". In this connexion we wish to report further data on the behaviour of N-(1-phenylalkyl)-1-phenylakylidenimines,[2] for which two tentative explanations have been advanced, including a cis-trans (sin-anti) isomerization similar to that proposed by Curtin and Hausser.

We have been studying for several years the ethoxide ion catalyzed prototropic change of N-benzyl-benzylidenimine and its alkylderivatives in ethanol-dioxane:

$$\underset{A}{\text{Ph-CHR-N=CR'-Ph}} \rightleftharpoons \underset{B}{\text{Ph-CR=N-CHR'-Ph}}$$

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[1] D.Y. Curtin and J.W. Hausser, J.Amer.Chem.Soc. 83, 3474 (1961).

[2] R. Perez Ossorio and V. Sanchez del Olmo, An.Real.Soc.Espan.Fis. y Quim. 56-B, 921 (1960).

(R, R' = H or alkyl)[3]. When in A, R = alkyl and R' = H, the rate of the forward change $A \rightarrow B$ was followed, in some instances[3a,j] by the loss of optical activity of the system starting with optically active A[4]. As A looses its activity on tautomerization to racemic B which, in turn, reverts to racemic A, the optical activity of the system approaches zero. However, when the tautomerization of N-(1-phenylethyl)-1-phenylethylidenimine (A = B, R = R' = Me) was attempted, the optical activity of the solution decreased slightly and approached a limiting value. It was subsequently shown that imines in which both R and R' were alkyl groups did not give the prototropic change, under the conditions in which N-benzyl-benzylidenimine and its monoalkylderivatives do. The treated dialkylimine behave under polarimetric observations in the same manner as the untreated compound. Therefore rotation changes must be attributed to another origin.[3k]

The optically active imines recorded in Table 1 were next examined: II, III and VII, when polarimetrically observed without solvent, showed mutarotation which was apparently absent in the remaining compounds. In ethanol solution, mutarotation was observed in the same cases as for the pure imines but its direction was reversed: thus, in the dimethyl derivative

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[3a] R. Perez Ossorio and F. Gomez Herrera, An.Real Soc.Espan.Fis. y Quim. 50-B, 875 (1954); [b] R. Perez Ossorio, F. Gomez Herrera and A. Hidalgo, Ibid. 52-B, 123 (1956); [c] R. Perez Ossorio, F. Gomez Herrera and R.M. Ultrilla, Nature.Lond. 179, 40 (1957); [d] R. Perez Ossorio, J.M. Gamboa and R.M. Utrilla, An.Real Soc.Espan.Fis. y Quim. 53-B, 17 (1957); [e] R. Perez Ossorio and A. Alemany, Ibid. 54-B, 471 (1958); [f] R. Perez Ossorio, F. Gomez Herrera, R.M. Utrilla, A. Hidalgo and J.M. Gamboa, Ibid. 54-B, 481 (1958); [g] R.M. Utrilla, Ibid. 54-B, 487 (1958); [h] J.M. Gamboa, R.M. Utrilla and R. Perez Ossorio, Radioisotopes in Scientific Research Vol. II, Proc. First p. 57. UNESCO Int. Conf. Paris, 1957. Pergamon Press, London (1958); [i] F. Gomez Herrera and A. Hidalgo, An.Real Soc.Espan.Fis. y Quim. 55-B, 617 (1959); [j] F. Gomez Herrera, Ibid. 56-B, 909 (1960); [k] R. Perez Ossorio and V. Sanchez del Olmo, Ibid. 56-B, 915 (1960).

[4] See R. Perez Ossorio and E.D. Hughes, J.Chem.Soc. 426 (1952) and references given there.

the rotation increased when observed without solvent and decreased when in, ethanol solution.

Table 1

Mutarotation of N-(1-Phenylalkyl)-1-phenylalkylidenimines

Ph-CHR-N=CR'-Ph

Compound	R	R'	Net[a]	Ethanol sol.[a,b]	Ref.
I	Me	H	+34.47 + 34.54	+1.32 + 1.42[c]	3j
II	Me	Me	-35.16 - 39.62	+9.31 + 6.32	2
III	Et	Et	+46.95 - 15.65	+0.72 + 5.05	2
IV	Pr^i	Pr^i	-10.24 - 10.24	-1.88 - 1.87	2
V	Bu^t	Bu^t	+18.15 + 18.14	+3.68 + 3.92[d]	2
VI	Me	Pr^i	-42.94 - 43.05	-	5
VII	Pr^i	Me	- 6.04 - 9.76	-	5
VIII	Me	Ph	+8(±4) + 7.90	+1.24 + 1.21[e]	2

[a] Initial and final observed rotations at constant temperatures are given.

[b] [imine] = 0.61-0.68 M, T = 32.3o C, α for ℓ = 1 dm.

[c] The small change may be due to solvent evaporation or solvolysis since observations were taken for 1024 hr.

[d] See c; observations taken for 337 hr.

[e] [imine] = 0.39 M, for ℓ = 2 dm.

The next step was the study of mutarotation of II, III, IV and V in different solvents. Some results obtained with II and III are recorded in Table 2; III and IV were tested in four alcohols and no significant change of rotation could be detected.

The observed mutarotations are then dependent of structure and medium

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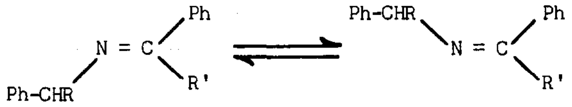
[5] To be published.

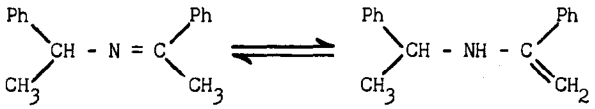
It may be argued that the lack of mutarotation can be attributed to the rapid attainement of equilibrium. So with benzene no change was observed with II and III (Table 2) but to decide between an unmeasurably small change and a very rapid one, a recently distilled sample of II, (α_D = + 16.29) and another sample for which equilibrium had been attained, (α_D = + 19.13) were dissolved in benzene and immediately observed under the polarimeter; values of $[\alpha]_D$, + 15.81 and + 15.79 were obtained. With III the recently distilled sample (α_D = + 24.07) gave in benzene $[\alpha]_D$ = - 1.25 and the sample in equilibrium (α_D = - 8.08) gave in benzene solution $[\alpha]_D$ = - 1.01. A rapidly attained equilibrium is suggested. The equilibrium, in other non hydroxylic solvents, was also reached very rapidly.

Two possible interpretations have been contemplated: a cis-trans isomerization:



As III changes much more slowly than II, both without solvent and in the alcohols, IV and V might change at an unobservable slow rate due to steric reasons. Furthermore VI would behave as IV and VII as II. I might change very rapidly. VIII was tested as control, since no cis-trans isomerism is possible; in spite of experimental difficulties for the polarimetric observation it appears to show no mutarotation. N-(1-phenylethyl)-cyclohexylidenimine and cyclopentylidenimine could also be used as controls; but attempts to isolate these imines in pure condition failed.

The possibility of an imine-enamine tautomerism, which does not affect the asymmetric carbon atom, was also considered:



This is in agreement with the lack of mutarotation of the ditert-butyl-derivative but does not explain the behaviour of the di-isopropylimine. Some data about this tautomerism can be found in the literature.[6] However, attempts to isolate derivatives of enamine failed or yielded no clear-cut results.

Table 2

Mutarotation of N-(1-Phenylakyl)-1-phenylaklylidenimines in Different Solvents

Solvent	Compound II[a]	Compound III[a]
MeOH	-3.92[b] - 2.22	-2.35[d] - 4.58
EtOH	+9.31 + 6.32	-0.83[d] - 3.58
Pr^iOH	-6.39[b] - 4.20	-0.51[d] - 5.13
Bu^tOH	-7.86[b] --6.03	+1.13[d] - 0.71
C_6H_6	+2.10 + 2.08	-0.16 - 0.17
$CHCl_3$	+3.19[c] + 2.98	-0.28[e] - 0.85
C_5H_5N	+4.01[c] + 3.90	+1.20[e] + 2.21
CCl_4	+3.40[c] + 3.10	+0.90[e] - 0.50
CH_3CO_2Et	+2.35[c] + 2.21	+1.50[e] + 0.64

[a] Initial and final rotations at constant temperatures are given: [imine] 10%, α for ℓ = 1 or 2 dm.

[b] Solutions prepared from a sample of II which, after mutarotation without solvent gave α = -26.96.

[c] See b; α = +13.30 for pure imine.

[d] See b; α = +10.01 for pure imine.

[e] See b; α = + 8.19 for imine.

[6a] A. Seher, Arch.Pharm. 284, 371 (1951); Chem.Abstr. 2124 (1953);

[b] W. Krabbe, E. Polzin and A. Seher, Ber.Dtsch.Chem.Ges. 74-B, 1892 (1941).

The mutarotation of II is slow enough to allow spectroscopic observation long before equilibrium is reached. The infra-red spectrum of recently distilled II and that of II in equilibrium show the same bands, but small differences in intensity are apparent at 1660, 1035 and 928 cm^{-1} among others; no frequency asignable to the NH group could be detected. II was then disolved in ethanol and the ultra-violet spectrum of the solution was taken both immediately and after a time long enough for the equilibrium in solution be attained; the maximum at λ,238mμ gave, respectively, log ε,3.98 and 3.95; the small change in intensity could be reproduced.

Table 3

Ultra-violet Spectra of N-(1-Phenylalkyl)-1-phenyl-alkylidenimines,
Ph-CHR-N=CR'-Ph

Compound	R	R	λ_{max}(mμ)	log ε
IX	H	H	248	4,28
I	Me	H	248	4,28
X	H	Me	241	4,11
II	Me	Me	240	4,10
III	Et	Et	238	3,98
IV	Pr^i	Pr^i	(238)[a]	(3,56)

[a] No maximum. Absorption taken at the recorded λ.

Finally, assignment of the <u>predominant</u> configuration of imines in ethanol may tentatively be based on their ultra-violet spectra. These spectra show a single maximum recorded in Table 3. In the series N-benzylbenzylidenimine IX, and its dialkylderivatives II, III, IV, the bathochromic shift and specially the decrease in intensity may be attributed to increasing steric inhibition of the resonance between the C = N bond and the attached phenyl group. The identity of spectra of IX and I (and of X and II) may mean that a trans configuration is predominant in the ethanol solution.

All these results which are still being completed, and will be published in more detail elsewhere, suggest that a case of stereoisomerism, similar to that described by Curtin and Hausser may be under observation.

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