

Enamines. Part XXXVIII.¹ Configurations of 1-Aryl-1-dialkylamino-propenes

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The configurations of several 1-aryl-1-dialkylaminopropenes have been assigned from ¹H n.m.r. data. The olefinic protons of the *E*-isomers resonate at higher field than those of the corresponding *Z*-isomers.

A ¹H n.m.r. study² of several 3-*N*-methylanilino- and dialkylaminopent-2-enes showed that in all cases the *E*- or *Z*-configuration could be assigned from the chemical shifts of the olefinic protons and magnitudes of the allylic coupling constants. All the compounds studied were found to be mixtures of the two configurational isomers, with the thermodynamically more stable one as the major component. In all cases but that of 3-*N*-methylanilino-pent-2-ene the greatest stability is shown by the *E*-isomer. This exception can be explained in terms of steric and electronic effects.

The foregoing results have been shown to apply in general to a large number of enamines of aliphatic ketones, both symmetrical and unsymmetrical and derived from both dialkylamines³ and *N*-alkylanilines.^{4†}

Recently, Sollemberger and Martin⁵ suggested the configuration of some enamines derived from propiophenone and its *p*-substituted derivatives and secondary amines, from examination of molecular models and u.v. spectra. The enamines investigated were all isomerically pure. Also, Duhamel *et al.* have established, by nuclear Overhauser effect studies the configuration of 1-dimethylamino-1-phenylpropene.⁶

We now report a ¹H n.m.r. investigation of the configurations of a homogeneous series of enamines derived from aryl ethyl ketones. In most cases, mixtures containing both *E*- and the *Z*-isomers were studied; thus data for both isomers could be obtained simultaneously.

The enamines listed in Table I were prepared. Configurational assignments were based exclusively on ¹H chemical shifts, coupling constants for each pair of isomers

† In ref. 4 the straightforward application of the Pascual rule to some *N*-methylaniline derivatives led us incorrectly to assign the lower field signal to the *E*-isomer. However this rule, which takes into account only steric features, cannot be applied to enamines, in which electronic factors are also important.

¹ Part XXXVII, D. Pocar and R. Stradi, *Ann. Chim. (Italy)*, 1971, **61**, 181.

being apparently identical. The signals of the olefinic protons and, to a minor extent, of the methyl groups, occurred at higher field for the major form in each pair.

Molecular models showed the complete lack of steric hindrance of the amino-group in the *E*-enamines, conjugation of the nitrogen lone pair with the π -system being easily achieved. In the *Z*-enamine the methyl group hinders the amine residue from assuming the more favourable conformation. This is confirmed by the results obtained with enamines of aliphatic ketones containing very bulky amine residues, where this effect is particularly marked.² Thus one could expect the isomer showing the high-field methyl and olefinic proton signals to have the *E*-configuration. In other words, for all the enamines studied, the *E*-isomer is the major component.

The chemical shifts of the olefinic protons of the *E*-isomers are very similar, whereas those of the *Z*-isomers show a wider range of values. This is in agreement with the above conclusion: the chemical shift of the olefinic proton will be more affected by changes in the aromatic nucleus when the latter lies on the same side of the double bond. Accordingly, in the *Z*-series, the highest δ values are found for compounds (Ih and g) in which the effect of the strongly electronegative heteroatom on the olefinic proton is greatest.

To confirm this effect a series of heterocyclic 1-amino-1-arylethylenes (II) (Table 2) was synthesized. In these compounds the difference between the chemical shifts of the two olefinic protons was in the range 0.27–0.38 p.p.m. when the vinyl group was bonded to the 2-position of the heterocycle, whereas no values greater than 0.16

² R. Stradi and D. Pocar, *Chimica e Industria*, 1971, **53**, 265.

³ G. Bianchetti, unpublished work.

⁴ D. Pocar, R. Stradi, and B. Gioia, *Gazzetta*, 1968, **98**, 959.

⁵ D. Y. Sollemberger and R. B. Martin, *J. Amer. Chem. Soc.*, 1970, **92**, 4261.

⁶ L. Duhamel, P. Duhamel, S. Combrisson, and P. Siret, *Tetrahedron Letters*, 1972, 3603.

p.p.m. were found for the 3- and 4-pyridyl derivatives. Similar behaviour has been found by Coletta *et al.*⁷ for several pyridylethylenes.

The aromatic solvent-induced shift effect in the case of

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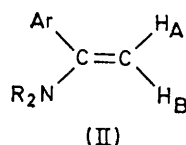
Preparation of Enamines.—The ketone (0.05 mmol) was dissolved in anhydrous hexane or benzene (for the less soluble ketones) (*ca.* 100 ml). The secondary amine (0.30

TABLE 1

(I)

Cpd.	Ar	R ₂ N	E/Z	E				Z				B. range (°C) (at 1 ± 0.5 Torr)
				δ ^{CCl₄} CH ₃	δ ^{C₆D₆} CH ₃	δ ^{CCl₄} H	δ ^{C₆D₆} H	δ ^{CCl₄} CH ₃	δ ^{C₆D₆} CH ₃	δ ^{CCl₄} H	δ ^{C₆D₆} H	
(Ia)	Ph	Morpholino	100/0	1.55	1.63	4.61	4.62					95—103
(Ib)	Ph	Et ₂ N	90/10	1.52	1.64	4.51	4.62	1.76	1.75	5.07	5.17	93—102
(Ic)	C ₆ H ₄ ·OMe(-4)	Morpholino	100/0	1.56	1.67	4.57	4.60					135—145
(Id)	C ₆ H ₄ ·OMe(-4)	Et ₂ N	92/8	1.57	1.70	4.44	4.61	1.73	1.78	4.95	5.13	112—120
(Ie)	C ₆ H ₄ ·NO ₂ (-4)	Morpholino	100/0	1.58	1.43	4.80	4.55					(m.p. 71)
(If)	C ₆ H ₄ ·NO ₂ (-4)	Et ₂ N	80/20	1.55	1.49	4.68	4.62	1.82	1.68	5.30	5.13	145—156
(Ig)	2-Pyridyl	Morpholino	87/13	1.61	1.78	4.80	4.80	1.87	1.78	5.61	5.75	80—90
(Ih)	2-Pyridyl	Et ₂ N	70/30	1.56	1.82	4.70	4.82	1.85	1.82	6.00	6.27	75—85
(Ii)	4-Pyridyl	Morpholino	92/8	1.58	1.49	4.75	4.58	1.86	1.65	5.11	4.99	87—95
(Ij)	4-Pyridyl	Et ₂ N	78/22	1.57	1.54	4.64	4.62	1.82	1.67	5.35	5.26	75—85
(Ik)	3-Pyridyl	Morpholino	95/5	1.58	1.52	4.78	4.64	1.85	1.70	4.97	4.89	88—96
(Il)	3-Pyridyl	Et ₂ N	90/10	1.54	1.54	4.64	4.61	1.79	1.67	5.14	5.06	75—85
(Im)	2-Thienyl	Morpholino	96/4	1.74	1.74	4.75	4.68	1.80	1.67	5.22	5.28	70—80
(In)	2-Thienyl	Et ₂ N	85/15	1.71	1.76	4.72	4.75	1.78	1.70	5.45	5.56	67—75
(Io)	2-Furyl	Morpholino	78/22	1.73	1.77	4.74	4.70	1.80	1.70	5.46	5.57	67—75
(Ip)	2-Furyl	Et ₂ N	70/30	1.70	1.80	4.70	4.76	1.80	1.76	5.75	5.90	58—65

TABLE 2



Cpd.	Ar	R ₂ N	δ ^{CDCl₃} H _A	δ ^{CDCl₃} H _B	B. range (°C) (at 1 ± 0.5 Torr)
(IIa)	2-Pyridyl	Morpholino	4.75	4.40	80—100
(IIb)	2-Pyridyl	Et ₂ N	4.50	4.23	82—90
(IIc)	3-Pyridyl	Piperidino	4.27 or 4.23	4.23 or 4.27	86—95
(IId)	3-Pyridyl	Et ₂ N	4.19 or 4.16	4.16 or 4.19	85—94
(IIe)	4-Pyridyl	Morpholino	4.45	4.29	90—102
(IIf)	4-Pyridyl	Piperidino	4.40	4.28	86—100
(IIg)	4-Pyridyl	Et ₂ N	4.33	4.20	85—93
(IIh)	2-Furyl	Et ₂ N	4.50	4.12	59—70
(IIi)	2-Thienyl	Morpholino	4.53	4.20	92—100
(IIj)	2-Thienyl	Et ₂ N	4.44	4.12	63—70

the enamines (I) is very strong (see Table 1), but not readily explicable; however the magnitudes of the induced shifts are quite different for the two sets of isomers.

The foregoing results, obtained on mixtures of *E*- and *Z*-isomers, are in accord with those described by Duhamel⁶ in relation to isomerically pure 1-dimethyl-amino-1-phenylpropene. Moreover, in this homogeneous series, the differences in chemical shifts of the olefinic protons of the *E*- and *Z*-isomers are great enough to allow assignment of configuration even when only one isomer is present.

* Birkhofer *et al.*⁸ obtained *o*-aminophenols by reactions of acylfurans and with secondary amines and interpreted the reaction in terms of an intermediate enamine. However, we found the furyl enamines (Io and p) and (IIh) to be stable and easily distilled.

mmol) was then added, followed dropwise with stirring, under nitrogen, by a solution of titanium tetrachloride (0.028 mmol) in anhydrous hexane (25 ml). After 24 h the mixture was filtered or centrifuged and the filtrate was evaporated. The crude enamine was distilled in a microapparatus at 1—2 Torr.* Only the enamine (Ie) was isolated directly, as a crystalline solid, m.p. 71 °C (from hexane). G.l.c. confirmed the purity of all the products, the only impurity being *ca.* 1—2% of the starting ketone.

The ¹H n.m.r. spectra were recorded with a Varian A-60 spectrometer operating at 60 MHz with Me₄Si as internal standard.

[4/176 Received, 28th January, 1974]

⁷ F. Coletta, A. Gambaro, and L. Pasimeni, *Gazzetta*, 1973, **103**, 265.

⁸ L. Birkhofer and G. Daum, *Chem. Ber.*, 1962, **95**, 183.