Concerning the Protonation of 1,2-Diazepines

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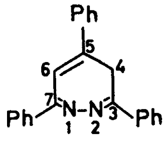
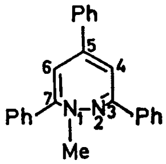
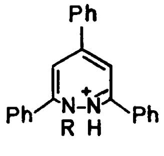
Summary Protonation of 3,5,7-triphenyl-4*H*-1,2-diazepine, (**1**), previously believed to give cation (**3**), has been shown by n.m.r. study to give (**5**) or (**6**).



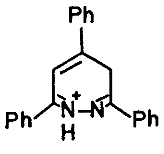
(1)



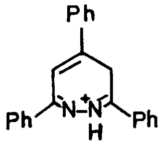
(2)



(3) R=H
(4) R=Me



(5)



(6)

It has been reported that the 3,5,7-triphenyl-1,2-diazepines (**1**) and (**2**) have different u.v. absorptions, but that their protonated derivatives resemble each other closely (see Table). To account for this resemblance, and for the bathochromic effect of protonation, planar structures (**3**) and (**4**) were suggested for the respective cations.[1]†

N.m.r. examination of the protonated form of (**1**) has now shown, however, that a methylene group is still present. The resemblance to the two cations in the u.v. is fortuitous, and structure (**3**) must be replaced by (**5**) or (**6**), which are non-planar; this is confirmed by *X*-ray crystallographic examination of the picrate.[3]

The n.m.r. spectrum of (**1**) in $CDCl_3$ shows an ABX pattern, with the AB methylene protons at τ 5·6 and 7·4.[4] The spectrum is similar in acetic acid, but an acidic solution in $CDCl_3$, prepared with dry HCl, shows only a broad singlet, representing two protons, at τ 6·1. Similar methylene signals are given by solutions of (**1**) in CF_3CO_2H or H_2SO_4, or of its hydroperchlorate‡ in CD_3CN. The protonated form is evidently the same in all cases, and gives the same u.v. spectrum under these varied conditions.

U.v. absorption spectra

	In EtOH λ_{max} (ϵ)	In 0·1N-ethanolic HCl[a] λ_{max} (ϵ)
(**1**)	258 (30,800), 293 (22,600)	253 (15,100), 343 (28,600)
(**2**)	270 (25,900)	260 (16,600) 333 (18,000)

[a] Spectra in 5N-ethanolic HCl were similar.

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† These results have been widely quoted, see ref. 2.

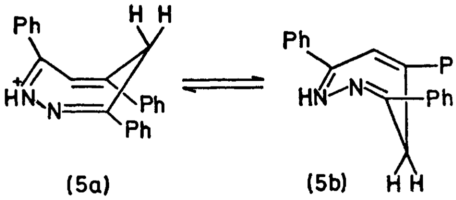
‡ Prepared under standard conditions; it showed m.p. 227—229° and correct analytical data. Attempts to prepare a crystalline hydrochloride failed.

The base (**1**) is recoverable in high yield from the acidic solutions even after prolonged standing.

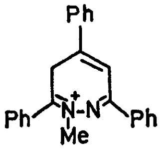
The temperature variable n.m.r. spectrum of (**1**) in $CDCl_3$–HCl solution was recorded at 100 MHz. The broad singlet at τ 6·1 ($w_{\frac{1}{2}}$ 14 Hz) observed at 31° coalesced into a sharp spike at 60°. On cooling, the broad singlet was resolved at −24° into an exchange-broadened doublet and at −40° into two distinct but broad AB doublets (τ 4·7 and 7·55, J 10 Hz). The coalescence temperature, T_c 8 ± 3°, corresponds to a free energy of activation, $\Delta G_c^{\ddagger}$ 10·2 ±0·2 kcal mol^{-1} for the inversion process.§ This compares favourably with a previous estimate of 12 kcal mol,$^{-1}$ recorded without comment for (**1**) in CF_3CO_2H.[4] On the other hand, $\Delta G_c^{\ddagger}$ for unprotonated (**1**) has been reported to be 17—18 kcal mol^{-1} in various solvents.[4,6] Evidently protonation lowers the energy barrier for the interconversion of the two conformations (*e.g.*, **5a** and **5b**), possibly because it eliminates repulsion between the N-1 and N-2 electron lone pairs in the planar transition state.

When a solution of (**1**) in CF_3CO_2D–D_2O was stirred at room temperature for 24 h, the recovered diazepine showed incorporation of deuterium (11·5% $^2H_0$, 29·5% $^2H_1$, 42·5% $^2H_2$, 16·5% $^2H_3$) by mass spectroscopy. Integration of the appropriate peaks in its n.m.r. spectrum indicated that 75% of the deuterium was located at C-4 and 22% at C-6. This exchange can be attributed to tautomerism between (**5**) or (**6**) and low concentrations of (**3**).

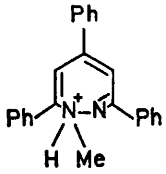
The n.m.r. spectrum of the *N*-methyl derivative (**2**) in $CDCl_3$–HCl exhibited absorptions at τ 2·04—2·75 (m, 16H, ArH, 4-H), 3·1 (s, 1H, 6-H), and 5·87 (s, 3H, Me). The *N*-methyl and 6-H signals are far downfield (Δ p.p.m. 1·24 and 1·01 respectively) from those observed in the base.[7] The lack of broad high-field absorption indicates that *C*-protonated species (*e.g.*, **7**) is not present in significant amounts, and (**2**) was indeed recovered unchanged from the conditions that effected deuteriation of (**1**). The similar u.v. spectra exhibited by (**2**) in EtOH–HCl, $CDCl_3$–HCl, and CF_3CO_2H indicate that the same protonated species is present throughout; this may be (**4**) as originally suggested,[1] although the large *N*-methyl downfield shift perhaps points to (**8**).



(**5a**) (**5b**)



(**7**)



(**8**)

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§ Calculated according to ref. 5, which gives a method for obtaining a reliable estimate of k_c from the AB portion of an ABX spin system in which $\Delta\nu > J$.

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