Double Rate Processes in Substituted Tetrahydropyridazines

By C. HACKETT BUSHWELLER

(*Department of Chemistry, University of California, Berkeley 4, California*)

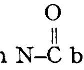
IN a recent Communication,[1] evidence for at least three distinct rate processes occurring in the substituted tetrahydropyridazines (I) and (II) was presented.

At 130°c in tetrachloroethylene, the nuclear magnetic resonance (n.m.r.) signal due to the methyl protons of (I) is a singlet. Below 97° c, the methyl resonance has split into two peaks of distinctly different intensities, the upfield peak at δ3·50 and downfield peak at δ3·88 in deuterochloroform. The area ratio of downfield to upfield peaks is approximately 1·5 : 1·0. Below −3° c, the peak δ3·88 broadens slightly and the peak at δ3·50 separates into two peaks at δ3·50 and δ3·54.

Compound (II) exhibits essentially the same behaviour. At 35° c, the methylene protons' n.m.r. signal consists of two quartets of unequal intensities. Below −3° c, the two quartets separate into at least four quartets.

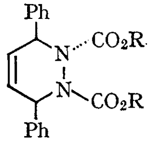
The authors[1] attribute the first observed transition at 97° c to a slowing of ring inversion as illustrated [(III) $\rightleftharpoons$ (IV)]. However, examination of models of the two conformers (III) and (IV) shows that they are mirror images and, therefore, equivalent in all respects. Consequently, a slowing of the rate of ring interconversion would result in the methyl protons' resonance splitting into two peaks of equal intensities. Since the observed spectrum at 35° c shows two peaks of distinctly different areas, this spectrum is clearly inconsistent with "frozen" ring inversion as in (III) $\rightleftharpoons$ (IV).

With regard to the corresponding ethyl ester, if a slowing of the rate of ring inversion occurs at 97° C, at 35° C one should see two quartets of equal intensities for the methylene protons, and not the observed variation in intensities.

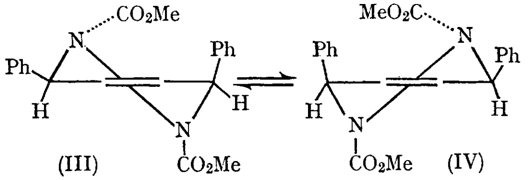
A more reasonable interpretation of the observed spectrum of the methyl ester at 35° C is that the ring inversion rate is still fast on the n.m.r. time scale, but rotation about the N–CO_2Me bond has been slowed. It has been observed that the energy barrier ($\Delta F^{\ddagger}$) to rotation about an  $\mathrm{N{-}\overset{\overset{O}{\|}}{C}}$ bond is of the order of 15—20 kcal./mole.[2] The observed differences in intensities for the methyl and methylene protons of (I) and (II) would be more consistent with a conformational preference of the methoxy- or ethoxy-carbonyl groups. As illustrated in canonical structures (V) and (VI), it would not be unlikely that such a conformational preference would exist, and that a significant chemical shift would occur between the methyl groups in two different environments.

Examination of a model of (I) indicates that in the event of ring interconversion at a rate fast with respect to the n.m.r. time scale and "frozen" rotation about the N–CO_2Me bond, four different methyl resonances are possible. In the event of "frozen" ring inversion and "frozen" N–CO_2Me rotation, it is possible that eight different methyl peaks would be observed because the two phenyl groups are not exactly symmetrically placed with respect to one another in a given conformer. However, it appears from the spectral data that not all conformers are present or that the chemical shifts of some of them coincide.

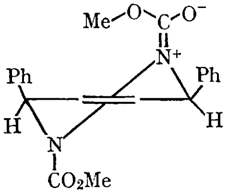
Concerning the spectral behaviour at −3° C and lower, it is possible that ring inversion has been slowed to a measurable rate. This would require the energy barrier ($\Delta F^{\ddagger}$) for ring inversion to be tremendously higher than that observed for cyclohexene and its derivatives ($\Delta F^{\ddagger} = 5{\cdot}2$—$5{\cdot}9$ kcal./mole).[3] At −60° C, four of the eight possible peaks are seen for methyl groups in four different environments. Two of the peaks are not resolved. If indeed ring inversion has been "frozen", the higher barrier may be due to eclipsing of the methoxycarbonyl groups in the boat configuration, a necessary intermediate in the interconversion.



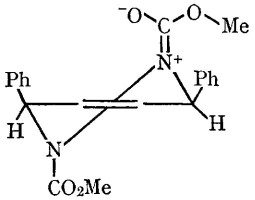
(I) R = Me
(II) R = Et



(III) (IV)



(V)



(VI)

(*Received, January 11th,* 1966; *Com.* 018.)

---

[1] J. C. Breliere and J. M. Lehn, *Chem. Comm.*, 1965, 426.

[2] W. D. Phillips, *J. Chem. Phys.*, 1955, **23**, 1363.

[3] F. A. L. Anet and M. Z. Haq, *J. Amer. Chem. Soc.*, 1965, **87**, 3147; F. R. Jensen and C. H. Bushweller, *ibid.*, p. 3285.