

N.m.r. Studies of Rate Processes and Conformations. A Double Rate Process

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N.M.R. SPECTROSCOPY has proved an extremely fruitful method for studying chemical and conformational rate processes.¹ We now report a system which shows a double conformational rate process.

The n.m.r. spectra of the substituted tetrahydropyridazines (I) and (II)² are temperature dependent. At *ca.* 35° c the n.m.r. spectrum of (I) shows two $\cdot\text{CO}_2\text{CH}_3$ peaks of unequal heights, two very well resolved octets for the vinylic protons, two broad unresolved peaks for H-3 and H-6 and a complex broad band for the aromatic protons. Compound (II) shows very unusual features for the resonance signals of the ethyl ester groups: two CH_2 quartets of unequal heights, one sharp triplet and another *very broad* triplet for the methyl groups. The other signals are as for (I). Table I lists the chemical shifts and coupling constants measured.

130° c (see Table I) are in excellent agreement with the mean values calculated from the shifts of the respective pairs of protons at 35° c. Similar results hold for compound (II).

When the temperature is lowered, the upfield $\cdot\text{CO}_2\text{CH}_3$ signal in the spectrum of (I) broadens and then splits (at -3° c) into two signals of unequal intensities at δ 3.50 and 3.54. At the same time the second $\cdot\text{CO}_2\text{CH}_3$ signal is slightly broadened (see Fig. 1). The other signals are as indicated in Table I. Compound (II) gives at -60° c a very complex spectrum containing at least four $\cdot\text{CO}_2\text{CH}_2\text{CH}_3$ triplets of different intensities and widths.

We interpret these changes in the following way. At least three hindered rate processes occur in compounds (I) and (II), two of which can be analysed in the temperature range studied. Two

TABLE

Proton chemical shifts (δ -values in *p.p.m.* from Me_4Si) and coupling constants (*c./sec.*) for Compound (I).^a

Protons	Chemical shifts at -60° c in CDCl_3	Chemical shifts at 35° c in CDCl_3 (TCE) ^b	Chemical shifts at 130° c in TCE ^b	Coupling constants from spectrum at 35° c ^c
$\text{N}\cdot\text{CO}_2\text{CH}_3^d$	3.50 3.54	3.50 (3.38)	3.55 (calc. 3.6)	
$\text{N}'\cdot\text{CO}_2\text{CH}_3^d$	3.87	3.88 (3.80)	3.55 (calc. 3.6)	
H_3	5.28	5.32 (5.18)	5.52 (calc. 5.54)	$J_{3,4} = 2.2$
H_4	5.77	5.79 (5.70)	5.93 (calc. 5.98)	$J_{4,5} = 10.3$
H_5	6.30	6.32 (6.25)	5.93 (calc. 5.98)	$J_{5,6} = 5.1$
H_6	6.00	6.02 (5.90)	5.52 (calc. 5.54)	$J_{3,5} = 1.5$
Aromatic Protons	7.18 7.46	7.22 (7.05) 7.50 (7.40)	7.2 (calc. 7.2)	$J_{4,6} = 1.1$

^a Spectra were measured on a Varian A-60 spectrometer.

^b Tetrachloroethylene.

^c These assignments will be discussed in the final communication.

^d Assignment of these signals to $\cdot\text{CO}_2\text{CH}_3$ on N-1 and N-2 is being studied.

When the temperature is raised, the spectrum of (I) shows coalescence for *all* pairs of similar protons, *i.e.* H-3 and H-6, H-4 and H-5, $\cdot\text{CO}_2\text{CH}_3$ on N-1 and $\cdot\text{CO}_2\text{CH}_3$ on N-2 and phenyl groups at C-3 and C-6. The chemical shifts observed at

of these processes are hindered rotations about $\text{N}\cdot\text{CO}_2\text{R}$ bonds (one of which shows coalescence at $-3 \pm 1^\circ\text{c}$)*; the third one is a ring inversion process between two equivalent conformations and has a coalescence temperature of $+97 \pm 1^\circ\text{c}$. The

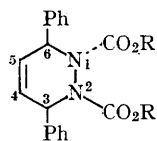
* The coalescence temperature of the other hindered rotation process is being investigated.

¹ A. Loewenstein and T. M. Connor, *Ber. Bunsen Gesellschaft Phys. Chem.*, 1963, **67**, 280.

² K. Alder and H. Niklas, *Annalen*, 1954, **585**, 81.

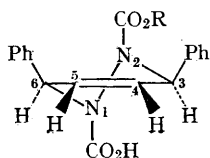
³ J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., New-York, 1959, Ch. 10.

respective free energies of activation³ are ΔG^\ddagger (-3°C) = 14.8 kcal./mole and ΔG^\ddagger ($+97^\circ\text{C}$) = 18.9 kcal./mole.



(I) R=Me

(II) R=Et



(III)

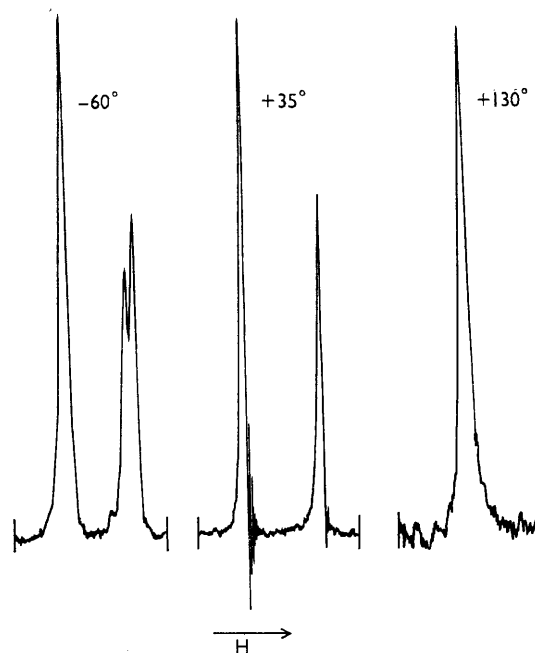
These results are significant for the following reasons:

(1) Hindered rotation is known in several systems $>\text{N}-\text{CO}-\text{X}$ (where X = alkyl, benzyl, phenyl, chloride . . .) with barriers ranging from 7 to 25 kcal./mole.¹ This is the first reported example of hindered rotation in a system where X = O-alkyl.⁴

(2) Cyclohexene-like molecules show ring inversion processes which may be studied by n.m.r. spectroscopy, as do cyclohexane derivatives.⁵

(3) The activation energy for ring inversion of 18.9 kcal./mole (at $+97^\circ\text{C}$) is very high, especially if one considers that the six-membered ring contains four planar sites: the two carbon atoms of the double bond and the two nitrogen atoms (see X-ray study of diformylhydrazine⁶). A large

contribution to this high barrier seems to arise from the two $\text{N}-\text{CO}_2\text{R}$ groups which are coplanar in the transition state and therefore interact strongly. On the basis of the n.m.r. spectrum and of the steric effects involved the two equilibrating conformations of the six-membered ring may be best represented as equivalent half-chair-like conformations (III).



N- CO_2CH_3 signals in the spectrum of Compound (I) at different temperatures.

Further work on these and similar systems is in progress in Strasbourg. A detailed account will be given in due course.

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⁴ Hindered rotation in a vinylogous carbamate has been reported; H. E. A. Kramer and R. Gompper, *Z. phys. Chem. (Frankfurt)*, 1964, **43**, 292.

⁵ Ring inversion in cyclohexene itself has been studied recently; F. A. L. Anet, Private communication.

⁶ Y. Tomiie, C. H. Koo, and I. Nitta, *Acta Cryst.*, 1958, **11**, 774.