An Electron Spin Resonance Study of Conformational Inversion in 4-Alkylpiperidine Nitroxides

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Summary Simulation of the e.s.r. spectra of 4-alkylpiperidine nitroxides measured at temperatures in the range +30° to −100° has led to the determination of accurate activation parameters for the ring inversion.

SUBSTITUTED piperidine nitroxides have been studied by e.s.r. spectroscopy, following chemical generation both in aqueous[1] and in non-aqueous solution.[2] The spectra are influenced by ring inversion and to obtain the relevant activation parameters a study over a wide range of temperature is necessary. This has not proved possible using chemical methods of generation. A recent publication by

Windle *et al.*,[3] concerning the generation of piperidine nitroxides by u.v. irradiation of the corresponding hydroxylamines, prompts us to report on our work in this area.

TABLE 1

T	R=H a_2^{ax} (gauss)	R=H $10^8\tau_A$ (sec.)	Me a_2^{ax}	Me $10^8\tau_A$	Me $10^8\tau_B$	Pr^i a_2^{ax}	Pr^i $10^8\tau_A$	Pr^i $10^8\tau_B$	Bu^t a_2^{ax}
+30°	19·57	0·085	19·60	0·58	0·035	19·75	1·0	0·03	19·80
+20	19·75	0·11	19·70	0·70	0·038	19·90*	1·5*	0·04*	19·90
0	20·15	0·18	20·00	2·4	0·095	20·35	5·4	0·10	20·30
−20	20·27	0·80	20·20	10·5	0·30	20·60	32	0·40	20·65
−40	20·72	3·2	20·65	36	0·65	21·05	108	0·90	21·05
−60	21·10	8·0	21·05	150	1·8	21·40	570	3·0	21·65
−80	21·55	22	21·50	1050	7·5	21·95†	*ca.* 14800†	*ca.* 40†	21·85
−100	22·17	200	22·10	*ca.* 19800	*ca.* 60	22·30	—	—	22·45

Conformation A, R equatorial
* At +23°; † at − 84°.

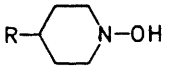
TABLE 2

*Activation parameters**

R	$(\Delta G^{\ddagger}_{298})_A$ kcal.mole^{-1}	$\Delta H^{\ddagger}_B$ kcal.mole^{-1}	$\Delta S^{\ddagger}_A$ e.u.	$(\Delta G^{\ddagger}_{298})_B$	$\Delta H^{\ddagger}_B$	$\Delta S^{\ddagger}_B$
H	5·2 ± 0·4	5·80 ± 0·16	2·2 ± 0·7	—	—	—
Me	6·3 ± 0·3	7·58 ± 0·14	4·2 ± 0·6	4·6 ± 0·2	5·28 ± 0·08	2·3 ± 0·3
Pr^i	6·7 ± 0·5	8·61 ± 0·23	6·3 ± 0·9	4·6 ± 0·4	6·17 ± 0·20	5·3 ± 0·8

* Quoted errors are obtained from the least-squares fit as the probable error defined in ref. 6.

The hydroxylamines (I) were prepared by pyrolysis of the corresponding *N*-ethylpiperidine oxides.[4] Solutions of the hydroxylamines in methylene chloride produced steady state concentrations of the unstable radicals upon continuous u.v. irradiation. The mode of formation of the radical is not apparent but it may be significant that solutions in carbon disulphide gave no signal.



R = H,Me,Pr^i,Bu^t

(I)

Spectra were recorded for the nitroxides generated from (I) over the temperature range +30° to −100°. The spectra of 4-t-butylpiperidine nitroxide did not show alternating line widths, confirming the "locked" nature of this compound. The remaining spectra have been analysed using the Bloch equations with a two-jump model and thereby simulated on a computer. The input parameters for the programme were the coupling constants of each nucleus in each conformation (A and B), the lifetimes (τ_A and τ_B), and a line width parameter which specifies the line width in the absence of inversion. Table I presents those parameters that vary with temperature. Plots of the Eyring equation[5] lead to the activation parameters given in Table 2.

Windle *et al.*[3] obtained values of $\Delta G^{\ddagger}$ for R=H, Me, and Ph at one temperature only due to the approximate treatment of their results. The method used here enables both $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ to be obtained. Thus we calculate, in kcal.mole^{-1}, for R=Me at +80°, $\Delta G^{\ddagger}_A$ as 6·1 and $\Delta G^{\ddagger}_B$ as 4·5 to be compared with 6·9 and 5·3 respectively.[3] It is interesting to note that the conformational preferences at 25° of the methyl and isopropyl groups as given by ($\Delta G^{\ddagger}_A - \Delta G^{\ddagger}_B$) are 1·7 and 2·1 kcal.mole^{-1} respectively. These values are essentially the same as in the analogous cyclohexane systems.[7]

The spectra could only be simulated if a_2^{ax} was allowed to vary with temperature. It can be seen from Table 1 that this variation is similar for all of the compounds studied, including the conformationally locked 4-t-butylpiperidine nitroxide. Thus we infer that this change is independent of the ring inversion and may relate to vibration or inversion of the nitroxide centre.

The spectrum of piperidine nitroxide at −100° shows a small quartet splitting (0·67G), whilst the corresponding spectra for the 4-alkylpiperidine nitroxides contain a triplet with a similar splitting. At low temperatures the 4-substituent will largely occupy the equatorial position and in the 4-t-butyl case will do so exclusively. Hence the proton involved in this coupling from the 4-position must be the equatorial and not the axial. This confirms the observations of Windle *et al.*[3] and is surprising in view of the relative proximities of the protons to the nitroxide centre.

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