A Variable-temperature Nuclear Magnetic Resonance Study of *N*-Ethoxycarbonylazonin and of Oxonin

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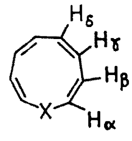
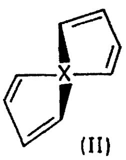
Summary The n.m.r. spectrum of *N*-ethoxycarbonylazonin is strikingly dependent on temperature while that of oxonin is not; evaluation of $\Delta F^{\ddagger}$, at T_c, in various key media allows for a rational explanation of the n.m.r. phenomenon.

IN recent reports dealing with the synthesis and key properties of *N*-ethoxycarbonylazonin[1–3] (Ia) and oxonin[4,5] (Ib) we described the ambient-temperature n.m.r. spectra of these substances and pointed out[6] that the n.m.r. spectrum of (Ia) undergoes very radical changes at temperatures below 0°. Undoubtedly, proper analysis of data derived from temperature-dependent n.m.r. spectra can provide invaluable information concerning structural detail.[7] Hence, we examined, in some detail, the effect of temperature on the n.m.r. spectra of (Ia) and (Ib).



(I)

a; X = NCO_2Et
b; X = O



(II)

Figure 1 shows the n.m.r. spectra of (Ia) taken at three key temperatures. At room temperature (Figure 1A) the spectrum consists of an AB quartet with needle-sharp low-field (τ 3·63) and broad high-field (τ 4·68) doublet components (J 9·5 Hz) arising from the α and β protons, respectively, and a narrow multiplet, situated essentially midway between the two doublets, due to the γ and δ pairs of hydrogens. Upon cooling the sample, all signals broaden and continue to do so until the coalescence point is reached at −10° (Figure 1B). Further cooling beyond this stage serves to sharpen the signals and eventually a pattern emerges (Figure 1C) which is radically different from that observed at room temperature. Thus, the single upfield doublet changes into two well separated doublets, the narrow multiplet splits into two distinct signals and the low-field absorption, while still sharp, appears now as a triplet owing to the fortuitous partial coincidence of two doublets. Clearly, the low-temperature n.m.r. spectrum points to overall loss of molecular symmetry whereby each proton is forced to occupy a unique position in space.

Basically, one or more of three distinct processes may be responsible for the loss of molecular symmetry at low temperatures: (i) the ring assumes a rigid unsymmetrical conformation; (ii) rotation of the ethoxycarbonyl group is hindered; and (iii) inversion of the ring nitrogen is suppressed. The first possibility is readily dismissed upon comparing the ambient-temperature n.m.r. spectrum of oxonin (Ib) with that recorded at −54°. As seen from Figure 2 the two are essentially identical, a fact which, no doubt, requires that oxonin maintain essentially the same conformational features within the temperature range −54°—+25°. Therefore, to the extent that (Ia) and (Ib) share similar conformational requirements, and there is no reason to believe that they do not, we conclude that gross conformational changes are not to any appreciable measure

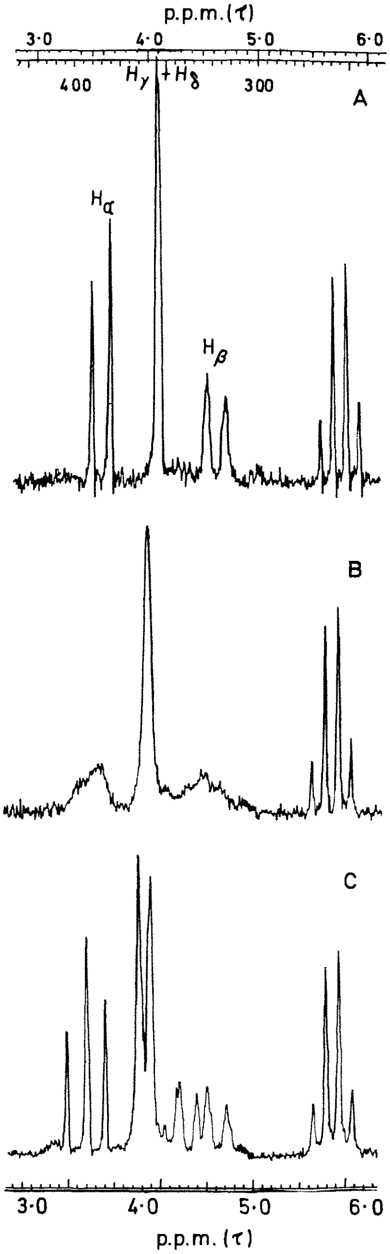


FIGURE 1. 60 *MHz n.m.r. spectra of* (Ia)[a] *determined in* $CDCl_3$ *at:* A, 25°; B, −10°; *and* C −54°.

[a] *The methyl portion of the ethyl absorption serves no purpose in our presentation and has been omitted.*

responsible for the temperature-dependent n.m.r. spectrum of (Ia). Another piece of information that also indicates the non-occurrence of appreciable conformational change in (Ia) is that $J_{\alpha\beta}$ remains entirely constant throughout the temperature range spanned.

Distinction between the two remaining possibilities, namely restricted rotation and suppressed nitrogen inversion, is clearly of a more subtle nature. Nevertheless, all the information we have accumulated so far appears to point to the latter (suppressed inversion) as the major cause of the observed n.m.r. temperature-dependence. For example, simple examination of the low-temperature n.m.r. spectrum of (Ia) (Figure IC) reveals the separation of the two low-field, partly coincident, doublets (10 Hz) to be less than that between the two doublet resonances at high field (15 Hz). Obviously the β hydrogens are affected to a greater extent by the induced asymmetry than are the α protons. This is not consistent with the occurrence of restricted rotation, for if this were the case the induced asymmetry would be most heavily felt by the more closely located α protons.[8] On the other hand, examination of a Dreiding molecular model of (Ia) reveals that (i) loss of molecular symmetry due to suppressed nitrogen inversion would most likely manifest itself as a mild twist about the various single bonds of the ring, and (ii) this type of induced asymmetry would affect the β hydrogens quite strongly. Also, it can be argued that if rotation of the ethoxycarbonyl group were to be restricted, the ethyl signals, and especially the quartet among the two, would be expected to undergo detectable broadening at low temperatures. In fact, restricted rotation of the ethoxycarbonyl substituent in *N*-ethoxycarbonylazepineiron tricarbonyl leads to actual splitting within the ethyl resonances.[9] Reference to Figure 1 reveals that the ethyl quartet of (Ia) is neither split nor is it broadened on lowering the temperature to well below the coalescence point.

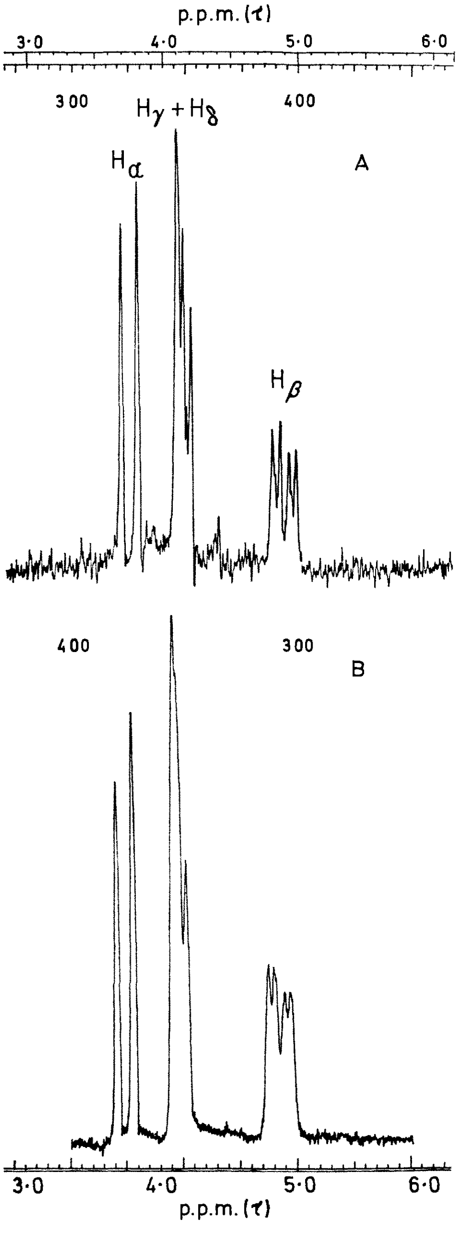


FIGURE 2. *60 MHz n.m.r. spectra of* (Ib) *determined in* $CDCl_3$ *at:* A, 25°; B, −54°.

By far the most compelling evidence in favour of suppressed nitrogen inversion derives from the effect of solvent polarity on the temperature of coalescence (T_c). In this connection Roberts and Griffith[10] have effectively demonstrated that polar solvents ought to facilitate inversion of nitrogen functions bearing electron-withdrawing substituents, *i.e.*, in such cases an increase in the dielectric constant of the medium would invariably *lower* the temperature at which coalescence occurs. Conversely, for obvious electrostatic reasons, we expect rotation to be restricted more effectively in polar than in nonpolar media, *i.e.*, here a polar solvent ought to *raise* the coalescence temperature. Bearing these points in mind we examined the effect of solvent polarity on the n.m.r. spectrum of (Ia) recorded at various temperatures, and calculated various activation parameters and coalescence temperatures. It is abundantly clear from *all* our data in this connection (Table) that an increase in the dielectric constant of the medium invariably leads to a reduced free energy of activation and a lowered coalescence temperature.† This effect, while

Solvent dependence of activation energies and coalescence temperatures for (Ia)

Solvent[a]	ϵ[c]	T_c	$\Delta F^\ddagger$ (kcal/mole)[b]
Chloroform	4·8	−10°	13·7
Acetone	20·7	−22°	13·0
Methanol	32·6	−18°	13·3
Acetonitrile	38·8	−28°	12·6

[a] Fully deuteriated solvent was employed in each case.

[b] Determined at T_c, in the manner described by M. Oki, H. Iwamura, and N. Hayakawa, *Bull. Chem. Soc., Japan*, 1964, **37**, 1865.

[c] Dielectric constant ("Handbook of Chemistry and Physics" 45th Edn., Chemical Rubber Publishing Co., Cleveland, Ohio).

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† The apparent discrepancy in the case where methanol was employed as solvent is not unexpected, since protic solvents are known to reduce substantially the rates of inversion of trigonal nitrogen. See for example, J. D. Roberts, "Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959, p. 76.

obviously inconsistent with the presence of a detectable rotational barrier for the ethoxycarbonyl group, is entirely as expected for an inversion mechanism.

All the information collected herein is most consistently accommodated with the presence of a fairly substantial nitrogen inversion barrier in (Ia). In addition, our data also effectively eliminate a planar geometry for both (Ia) and (Ib) and are entirely consistent with the axisymmetric arrangement, shown in (II) which we have favoured from the start.[1,4]

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[6] Paper 014 presented at the 158th National ACS Meeting, September 7, 1969.
[7] For a comprehensive discussion concerning this subject, see J. D. Roberts, *Chem. in Britain*, 1966, **2**, 529.
[8] For a pertinent example in this context see: T. Matsuo and H. Shosenji, *Chem. Comm.*, 1969, 501.
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