

RESTRICTED ROTATION ABOUT N-N SINGLE BONDS. THE
CONFORMATION OF TETRAHYDROPYRIDAZINE RINGS

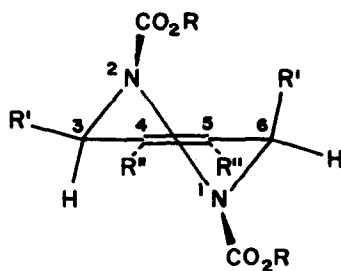
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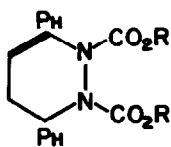
In agreement with recent publications (1-3) we interpret asymmetry in the p.m.r. spectra of diene-azodicarboxylic ester adducts of type I in CDCl_3 at 40° to mean that ring-inversion at this temperature is slow compared with the difference of resonance frequencies within the pairs of chemically equivalent groups. Signals for Ia are assigned as H6, $\delta 6.00$; H5, $\delta 6.30$; H4, $\delta 5.72$; H3, $\delta 5.25$; on the grounds that equatorial proton H6 will be more deshielded than axial proton H3 by the olefinic system and,



	R	R'	R''
Ia:	Et	Ph	H
Ib:	Me	Ph	H
Ic:	Me	Me	H
Id:	Et	Ph	Me
IIa:	Interchange R' and H at C3 in Ia		

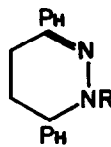
assuming Karplus-type relations govern these coupling constants, more strongly coupled to the adjacent olefinic proton ($J_{56} = 5.0$, $J_{34} = 2.0$). Slow interchange of the ester group between axial and equatorial positions about a non-planar nitrogen center as suggested for Ic (2) seems less likely than hindered rotation about the N-CO bond in these amidic systems (1,3) to account for the greater breadth of the upfield ester methyl signals. These are of the same integrated intensity as the downfield signals. The criticism (4), based only on peak heights, and suggestion that the ring is freely inverting at 35° would require that magnetic non-equivalence of chemically equivalent protons in these esters (I) arises from hindered rotation in the spatially remote carbamic ester groups. Evidence that this is unlikely follows.

The adduct (Ia) on mild treatment with methanolic potassium hydroxide yields the trans-isomer (IIa), m.p. 147° , showing, like the adduct (Ia), only benzenoid absorption in the ultraviolet, and isomer IIIa, m.p. $108-9^\circ$,



IIIa: R = Et

IIIb: R = Me



IVa: R = H

IVb: R = CO₂Me

showing high-intensity absorption at 251 m μ . More vigorous treatment of Ia with alkali gives the cyclic hydrazone (IVa), m.p. $158-9^\circ$. P.m.r. spectra are in accord with these assignments, those of IIIa and IVa being irrelevant to the present discussion. That of the trans-isomer (IIa) at 40° shows only one methyl triplet (60.68) but two interlacing methylene quartets (63.64, 3.72, of equal intensities as judged by peak heights). Whether the ring conformation is fixed or inverting, there is restricted

rotation about the N-CO bonds. The ring protons nevertheless give rise to an A_2B_2 multiplet ($\delta_A \sim 6.2$, $\delta_B \sim 6.0$). These signals are centered near the corresponding downfield signals for Ia, so the ring conformation is probably fixed with both phenyl groups axial. In this position they appear to suffer less non-bonded interactions than in the equatorial position (c.f. the similar conclusion for 6-substituted 1-phenylcyclohexenes (5)). One may also plausibly relate the upfield shift of the ethoxyl signals for IIa (0.3-0.6 p.p.m. from those for Ia) to likely orientations of the axial and equatorial phenyl groups in the isomers. Attempts to isomerize the dimethyl ester (Ib) have given 1,4-diphenylbutadiene, isomer IIIb, and hydrazone ester IVb. Ester Id was unchanged under the same conditions.

For the ring-inversion process in Ib, $\Delta G^\ddagger = 18.9$ kcal/mole at 97° (1); for Ic, $\Delta G^\ddagger = 17.9 \pm 0.2$ kcal/mole in the range $53-84^\circ$ (calcd. from data in (2)). These values are much larger than those for cyclohexene (6) and 4-bromocyclohexene (7), probably as a result of eclipsing of the ester groups in the transition state (1,4). The following observations appear relevant.

Tetramethylsuccinic anhydride, unlike the parent, reacts with hydrazine in hot ethanol to give the N-aminosuccinimide (Va), m.p. $56-7^\circ$, $\nu_{\max}^{\text{Nujol}}$ 1779s, 1694vs, 1626s cm^{-1} (succinhydrazide has $\nu_{\max}^{\text{Nujol}}$ 1695 m, 1605s cm^{-1}), whose structure is shown by its reaction with benzaldehyde in cold ethanol to give the tetramethylsuccinylhydrazone, m.p. $97-8^\circ$. Boiling glacial acetic acid converts Va into N-(acetamido)tetramethylsuccinimide (Vb), m.p. 108° , $\nu_{\max}^{\text{Nujol}}$ 1799w, 1736vs, 1721vs, 1686s cm^{-1} , whereas acetic anhydride in pyridine gives N-(diacetylamino)tetramethylsuccinimide (Vc), m.p. $79-80^\circ$, $\nu_{\max}^{\text{Nujol}}$ 1799m, 1745vs, 1727vs cm^{-1} . The

p.m.r. spectrum of Vb in deuteriochloroform at 40° shows a singlet at δ 2.09 for the acetyl protons and a singlet of four times the intensity at δ 1.22 for the four equivalent methyl groups. The corresponding signals for Vc are singlets of relative intensity 1:2 at δ 2.37 and δ 1.31, respectively. In these compounds at 40° therefore there is probably free rotation about the N-Ac bonds. If however the acetyl groups adopt preferred orientations exclusively, both acetyl-methyl groups in Vc must be syn or both anti with respect to the other acetyl group on the same nitrogen atom, unless the chemical shifts are negligibly different. Cyclohexene-cis-4,5-dicarboxylic anhydride, its dihydro derivative, and 9,10-endo-dihydroanthracenesuccinic anhydride may be converted into analogous N-aminosuccinimides (VIa, VIIa, VIIIa, respectively), N'-acetyl derivatives (VIb, VIIb, VIIIb, respectively), and N',N'-diacetyl derivatives (VIc, VIIc, VIIIc, respectively). The p.m.r. spectra (Table 1) of the diacetyl compounds each show two singlets of equal intensity for the acetyl protons. Those of VIc and VIIc taken alone could be interpreted on the basis of hindered rotation about the N-Ac bonds (with more or less fortuitously equal populations of conformers with the appropriate chemical shifts), the tetraacylhydrazine system being either coplanar or freely rotating about the N-N bond. The spectrum of the endo-dihydroanthracene derivative (VIIIc), however, shows one of the acetyl signals shifted ca 1.5 p.p.m. to high field from the other. This remarkable shielding is in our opinion only compatible with a preferred conformation in which the C-N-C plane of the diacetyl amino group is at right angles to the plane of the succinimide ring so that one of the acetyl groups lies in the shielding region immediately above one of the aromatic rings; a projection of this conformation onto the plane of the diacetyl amino group is shown in IX. The separation of the acetyl signals in hexadeuterodimethylsulphoxide at

TABLE 1

P.m.r. Spectra of Some *N*-(Diacylamino)succinimides δ in p.p.m. from Internal T.M.S. ReferenceAcetyl Proton Signals^a

	CDCl ₃ at 40°	DMSO at 40°	DMSO (at T°)
VIc	2.13, 2.47	2.21, 2.34	2.17, 2.27 (120°)
VIIc	--	2.24, 2.44	2.20, 2.37 (100°)
VIIIc	0.92, 2.48	0.93, 2.39	0.96, 2.37 (80°)
VId	2.46, 2.62 ^b	2.29, 2.51 ^b	2.25, 2.39 (120°)
VIIId	--	2.40	--

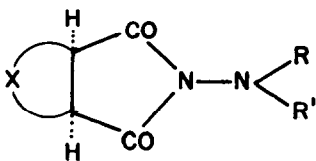
Other signals at 40° (proton count in parentheses)

VIc in CDCl₃: 2.3-3.0 (4), 3.2-3.4 (2), 5.9-6.2 (2)

VIIc in DMSO: 1.3-2.2 (8), 3.2-3.5 (2)

VIIIc in CDCl₃: 3.38 (2)^c, 4.88 (2)^c, 7.0-7.5 (8)VId in CDCl₃: 2.0-3.2 (6), 5.3-5.5 (4/3), 5.8-6.1 (2/3), 7.2-7.7 (5)

VIIId in DMSO: 0.8-2.0 (8), 2.5-3.3 (2), 7.56 (sharp, 5)

^aEach of intensity for three protons except b.^bRelative intensities approximately 1:2.^cIdentical triplets, splitting ca 3 c/s, of A₂X₂ system.

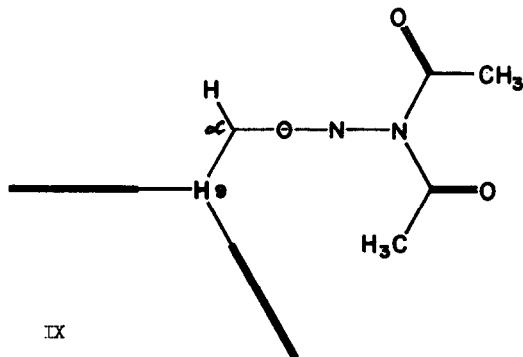
a: R = R' = H

b: R = H; R' = Ac

c: R = R' = Ac

VIII: X = 9,10-endodihydroanthracene d: R = Ac; R' = Bz

40° and 80° suggest (8, and Eyring's equation) a free energy of activation for interchange of the acetyl groups in excess of 18 kcal/mole.



Corresponding conformations are likely for the other compounds in Table 1 and for the tetramethylsuccinimide derivatives (Vb and Vc). For the N'-acetyl-N'-benzoyl derivatives (VIId and VIIId), prepared either by benzoylation of the monoacetyl derivatives (VIb and VIIb, respectively) or by acetylation of the N-benzamidossuccinimides, two non-equivalent conformations are possible. Two are present in VIId in the approximate ratio 1:2 (from the relative intensities of acetyl signals, or of olefinic-proton multiplets), whereas VIIId apparently adopts one conformation exclusively. The corresponding endodihydroanthracene derivative (VIIIId) could not be prepared: the N'-acetyl derivative (VIIIb) was recovered from mixtures with benzoyl chloride and pyridine on the steambath, and the corresponding N'-benzoyl derivative with acetic anhydride and pyridine yielded the diacetyl derivative (VIIIc). For VIc, VIIc, and VIId in hexadeuterodimethylsulphoxide at the highest temperature (120°) so far available to us, free energies of activation for the rotation process about the N-N bond of the order of 20-21 kcal/mole are indicated. We have not yet checked whether polar or "pure" steric forces are dominant by

comparative high-temperature measurements in non-polar solvents; the small differences in separation of the acetyl signals at 40° are not significant.

For the tetrahydropyridazines (I), a contribution somewhat smaller than 20 kcal/mole to the free energy of activation for ring inversion may be expected from hindered rotation about the N-N bond because the planes of the carbamic ester groups are in the ground state already partly twisted toward the eclipsed conformation of the transition state and because only one pair of ester groups becomes eclipsed.

P.m.r. spectra were measured on the Varian A-60 spectrometer at the University of Sydney by Mr. D. C. Dehlsen and Mr. W. J. Davidson under the supervision of Dr. A. V. Robertson and Dr. S. Sternhell, and we gratefully acknowledge their kind cooperation.

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