Tetrahedron. Vol. 28, pp. 5029 to 5036. Pergamon Press 1972. Printed in Great Britain

CONFORMATIONAL ANALYSIS ABOUT THE N—N′ BOND BY NMR SPECTROSCOPY

N′-DERIVATIVES OF N-AMINO[2.2.1]BICYCLO-5-HEPTENE-2,3-*ENDO*DICARBOXIMIDE

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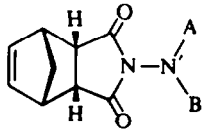
(*Received in the UK* 2 *May* 1972; *Accepted for publication* 29 *June* 1972)

Abstract—A series of N′-derivatives of N-amino[2.2.1]bicyclo-5-heptene-2,3-*endo*-dicarboximide have been prepared and their NMR spectra have been studied. The non-planar 'cage-moiety' structure has been used in the conformational study. Temperature dependent spectral changes have been related to conformational changes about N—N′ and N′-acyl bonds. Free energies of activation ($\Delta G^{\ddagger}$) have been determined for the conformational rate-processes.

Endo-product formation in the Diels–Alder reaction has been demonstrated.

CONFORMATIONAL studies by NMR spectroscopy about N—N′ single bonds are complicated by the possibility of partial-double-bond formation and inversion at the trivalent nitrogen atoms, besides other steric and non-bonding repulsive interactions.[1] Tetra- and hexa-hydropyridazine systems are further complicated by a ring-inversion process.[2,3] Conformations adopted by tetraacyl hydrazines[4] and certain acyclic N,N′-diacyl hydrazine derivatives[5] have been reported to be due to restricted rotation about the open chain N—N′ bonds. The present study reports evidence for the conformations of a series of derivatives of N-amino[2.2.1]bicyclo-5-heptene-2,3-*endo*



I

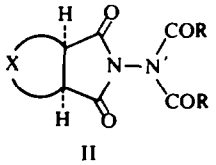
dicarboximide (I). The NMR spectral changes are discussed on the basis of slow rotation about N—N′ and N′-acyl bonds, in the temperature range studied; free energies of activation ($\Delta G^{\ddagger}$) were calculated from the variable temperature spectra using Eyring's rate equation.[6]

In order to make unambiguous assignments for the spectral changes, some simplifications are made in the present system. The 'cage-moiety', i.e. [2.2.1]bicyclo-5-heptene-2,3-*endo* dicarboximidyl part, provides no scope for ring-inversion. Further, the possibility of inversion at the 'cage-moiety' nitrogen, in a planar imide-ring, and also at the *exo*-cyclic nitrogen, when attached to an acyl group, is eliminated. Finally, the 'cage-moiety', with a non-planar structure, would provide a suitable basis for the study of the magnetic environments of N′-substituents.

Tetraacyl hydrazines. Preferred conformations about N—N′ bonds in tetraacyl hydrazines of type II have been rationalized in terms of non-bonded repulsions

between the acyl substituents in the planar transition state; the two acyl groups attached to the *exo*-cyclic nitrogen atom lie above and below the plane of succinimidyl ring.[4] This conformation is in agreement with the crystal-structure of N—N′-bisuccinimidyl.[7] From variable temperature spectral measurements the free energy barriers to rotation about N—N′ bonds have been estimated to be in excess of 18–20 K.cals./mole.[4]

The NMR spectrum of the N′-acetyl-N′-benzoyl compound (IX) shows, along with other proton resonances, two singlets for the acetyl protons and two triplets for the two olefinic protons (Fig. 1; Table 1). Two conformations of compound IX at 44° arising from hindered rotation about N—N′ bond are quite apparent from the spectrum, and could be in the ratio of 2:1. In the more preferred conformation, where the benzoyl group lies *endo*- to the 'cage-moiety' olefinic bond, the phenyl group sits over the olefinic-protons and has a notable shielding effect (internal chemical shift 58 Hz). The downfield signal of the two acetyl singlets (δ 2·6; 2H) would correspond to this



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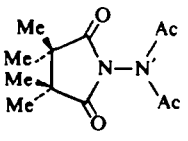

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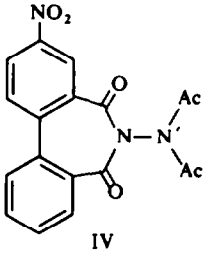
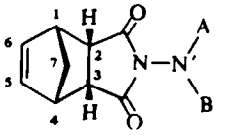


IV

X = a chain with four carbons

more preferred conformation, where the acetyl group would lie *exo*-to the olefinic bond. Molecular models also show acetyl group experiences different magnetic environments in the two different conformations about the N—N′ bond, due to the 'cage-moiety', which has no plane of symmetry in the plane of the succinimidyl ring. In the absence of this property compounds III[4] and IV[8] do not show different signals for the acetyl groups. When both the N′-acyl groups are similar (N′,N′-diacetyl, VII; Table 1) the olefinic protons experience a similar magnetic environment in both conformations and consequently a single normal triplet (2H) is observed, whereas the protons of the two acetyl groups appear as two singlets of equal intensity, with an internal chemical shift of 20 Hz in $CHCl_3$. In the spectrum of the N′-acetyl-N′-ethoxycarbonyl compound (X) two singlets for the acetyl protons, having an intensity ratio of 2:1, are in accordance with the intensity ratio of the interlacing double-triplet for the —$COOCH_2\underline{CH_3}$ methyl protons. The upfield signal of the two acetyl singlets (δ 2·62) would result from shielding of the *endo*-acetyl protons by the olefinic bond in the less preferred conformation. The single quartet for the —$COO\underline{CH_2}CH_3$ methylene protons is not quite sharp, presumably, due to accidental overlapping of two quartets. A similar spectrum for the N′-benzoyl-N′-ethoxycarbonyl compound (XI) has been observed (Fig. 2); the two conformations are of equal population and the benzoyl group, when *endo*- to the olefinic bond, has a direct interaction with the olefinic protons, which appear as two peaks.

All these tetraacyl compounds (VII, IX, X and XI) show temperature dependent NMR spectra. On raising the temperature, the double-triplet of the —$COOCH_2\underline{CH_3}$ methyl protons of compound XI coalesce to a single triplet at 95° ($\Delta G^{\ddagger}$ = 20·29

TABLE 1. M.PS, ELEMENTAL ANALYSES[‡], CHARACTERISTIC IR PEAKS[†] AND NMR SPECTRA[*] OF  ARE RECORDED

No.	Compd.	M.P.	Analysis %C	Analysis %H	IR ν_{max} cm^{-1}	δA	δB	δ(5 + 6)	δ 7	δ(1 + 4 + 2 + 3)
V	A = H B = H	143	60·95	5·82	3334 m, 3270 w, 3220 w, 1768 m, 1700 s	(s, 1H) 4·44	(s, 1H) 4·44	(t, 2H) 6·18	(q, 2H) 1·7	(m, 4H) 3·38
VI	A = H B = Ac	177	59·84	5·22	3540 m, 3420 m, 3180 m, 1780 m, 1734 s, 1686 s	(s, 1H) 7·75	(s, 3H) 2·08	(t, 2H) 6·25	(q, 2H) 1·67	(m, 4H) 3·42
VII	A = Ac B = Ac	123	59·98	5·31	1780 m, 1743 s, 1730 s	(ds, 3H) 2·33 1:1; 20 Hz	(ds, 3H) 2·33 1:1; 20 Hz	(t, 2H) 6·33	(q, 2H) 1·73	(s, 4H) 3·52
VIII	A = H B = COPh	195	67·38	5·23	3440 w, 3265 w, 1790 m, 1725 s, 1668 s, 1600 w	(s, 1H) 2·0	(m, 5H) 7·73	(t, 2H) 6·33	(q, 2H) 1·73	(s, 4H) 3·52
IX	A = Ac B = COPh	157	67·01	4·85	1735 s, 1718 s, 1600 m	(ds, 3H) 2·53 2:1; 7·5 Hz	(s, 5H) 7·6	(dt, 2H) 5·85 1:2; 58 Hz	(q, 2H) 1·53	(m, 4H) 3·25
X	A = Ac B = $COOC_2H_5$	108	57·63	5·68	1690 m, 1755 s, 1740 s, 1730 s	(ds, 3H) 2·63 3:1; 2·5 Hz	(q, 2H) 4·35 (dt, 3H) 1·35 3:1; 2 Hz J = 7 Hz	(m, 2H) 6·25	(q, 2H) 1·7	(m, 4H) 3·5
XI	A = COPh B = $COOC_2H_5$	112	64·34	5·42	1790 m, 1770 s, 1738 s, 1710 s, 1600 w	(m, 5H) 7·7	(q, 2H) 4·21 (dt, 3H) 1·03 1:1; 2 Hz J = 7 Hz	(ds, 2H) 6·3 1:1; 8 Hz	(q, 2H) 1·7	(m, 4H) 3·5
XII	A = H B = CH_3	133	62·46	6·04	3300 m, 3065 w, 1763 m, 1700 s	(s, 1H) 4·3	(s, 3H) 2·63	(t, 2H) 6·22	(q, 2H) 1·7	(m, 2H) 3·48 & (m, 2H) 3·27
XIII	A = Ac B = CH_3	165	61·23	5·72	3068 w, 1780 m, 1730 s, 1683 s	(ts, 3H) 2·03	(ts, 3H) 3·13 1:2:3	(s, 2H) 6·3	(q, 2H) 1·7	(m, 4H) 3·45
XIV	A = COPh B = CH_3	136	69·01	5·57	3065 w, 1788 w, 1725 s, 1683 s, 1600 w, 1580 w	(s, 5H) 7·49	(ds, 3H) 3·2 1:3; 4 Hz	(dt, 2H) 5·74 3:1; 64·5 Hz	(q, 2H) 1·6	(m, 2H) 3·45 & (m, 2H) 2·97
XV	A = H B = Ph	180	70·81	5·59	3280 m, 1770 m, 1710 s, 1600 m, 1500 m	(s, 1H) 6·1	(m, 5H) 7·1	(t, 2H) 6·28	(q, 2H) 1·7	(m, 4H) 3·57
XVI	A = Ac B = Ph	128	68·73	5·12	1780 w, 1730 s, 1693 s, 1682 s, 1595 w	(ds, 3H) 2·0 5:3; 3 Hz	(s, 5H) 7·53	(dt, 2H) 6·05 3:5; 39 Hz	(q, 2H) 1·7	(m, 4H) 3·35
XVII	A = CH_2Ph B = Ph	154	76·85	5·57	3055 w, 1775 w, 1720 s, 1600 m, 1583 w, 1495 m	(s, 2H) 4·81 (m, 5H) 7·2	(m, 5H) 7·2	(Extremely broad, 2H) 6·0	(q, 2H) 1·54	(m, 4H) 3·25

TABLE 1—*contined*

No.	Compd.	M.P.	Analysis %C	Analysis %H	IR ν_{max} cm^{-1}	δA	δB	δ(5 + 6)	δ7	δ(1 + 4 + 2 + 3)
XVIII	A = CH_2Ph B = CH_2Ph	124	77·24	6·19	3055 w, 1770 w, 1710 s, 1600 w, 1583 w, 1493 w	(s, 2H) 4·32 (m, 5H) 7·4	(s, 2H) 4·32 (m, 5H) 7·4	(t, 2H) 5·46	(q, 2H) 1·4	(m, 2H) 3·19 & (m, 2H) 2·8

‡ Carbon and hydrogen analysis results are in good agreement with calculated values.

† IR spectra were recorded in nujol w = weak, m = medium and s = strong.

* NMR spectra were recorded in $CDCl_3$ at 44°. Total number of protons and the multiplicity of the bands are indicated in brackets. In the case of multiplicity due to slow rotations, the ratio of the intensity of the downfielded signal to the upfielded and the separation (in Hz) are indicated.
s = singlet, t = triplet, q = quartet, ds = double singlet, dt = double triplet, ts = triple singlet, m = multiplet. TMS as internal reference.

TABLE 2. VARIABLE TEMPERATURE SPECTRAL DATA AND FREE ENERGIES OF ACTIVATION ($\Delta G^{\ddagger}$) IN NITROBENZENE

Compd.	Spectral change studied	$\Delta\nu$ at $T_1^\circ C$ Hz	$\Delta\nu$ at $T_2^\circ C$ Hz	Coalescence temp. $Tc^\circ C$	$\Delta G^{\ddagger}$ at T_2 or T_c K.Cals./mole.	Conformational change
VII	Decrease in $\Delta\nu$ of acetyl signals	10·10 (44°)	8·50 (110°)	—	20·83 (110°)	Rotation about N—N′ bond
IX	Decrease in $\Delta\nu$ of acetyl signals	7·20 (44°)	5·49 (110°)	—	20·95 (110°)	Rotation about N—N′ bond
XI	Collapse of the double-triplet of $-COOCH_2\underline{CH_3}$ into a single triplet	3·70 (44°)	—	95°	20·29 (95°)	Rotation about N—N′ bond
XIII	Collapse of the three N′—CH_3 signals to two signals	4·70 (44°)	—	70°	18·64 (70°)	Rotation about N′—CO bond
	Collapse of the two N′—CH_3 signals to one singlet	5·40 (70°)	—	110°	20·86 (110°)	Rotation about N—N′ bond
XIV	Collapse of the two N′—CH_3 singlets to one singlet	3·60 (44°)	—	85°	19·74 (85°)	Rotation about N—N′ bond

$\Delta\nu$ = Internal chemical shift of temperature dependent signals.

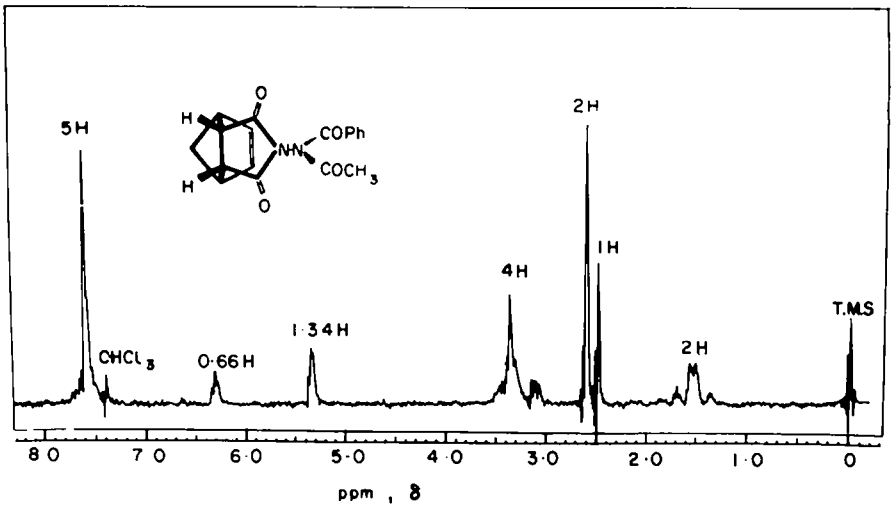


FIG 1. 60 MHz NMR spectrum of N′-acetyl-N′-benzoyl-N-amino[2.2.1]bicyclo-5-heptene-2,3-*endo* dicarboximide (IX) in $CDCl_3$ at 44°.

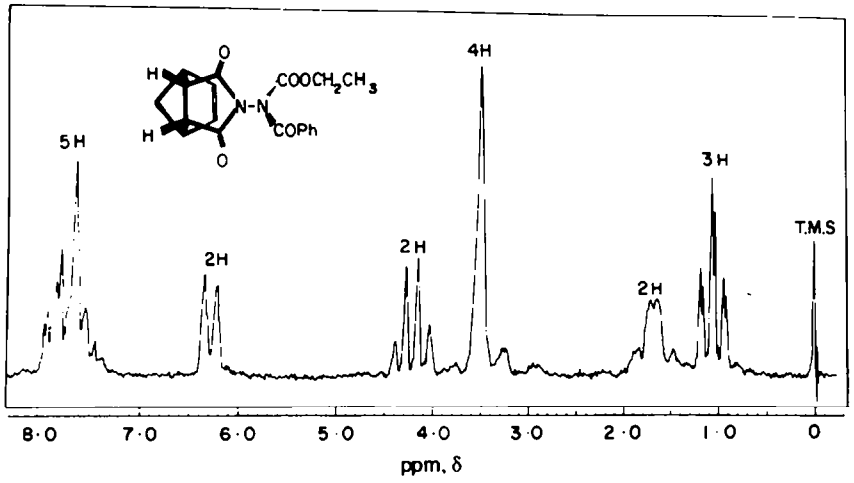


FIG 2. 60 MHz NMR spectrum of N′-benzoyl-N′-ethoxycarbonyl-N-amino[2.2.1]bicyclo-5-heptene-2,3-*endo* dicarboximide (XI) in $CDCl_3$ at 44°.

K.Cals./mole.), but compounds VII and IX do not show coalescence up to 110° and the minimum values of free energies of activation ($\Delta G^{\ddagger}$) at 110° are of the order of 21 K.Cals./mole. (Table 2).

Triacyl hydrazines. The N′-methyl-N′-benzoyl compound (XIV) shows a typical spectrum for triacyl compounds (Fig. 3; Table 1); two singlets for the N′-methyl protons and two triplets for the olefinic protons were observed. This is strong evidence for two conformations, due to hindered rotation about N—N′ bond. The benzoyl group *endo*- to the 'cage-moiety' olefinic bond seems to be the less-preferred conformation, because the shielded component of the two triplets of the olefinic protons

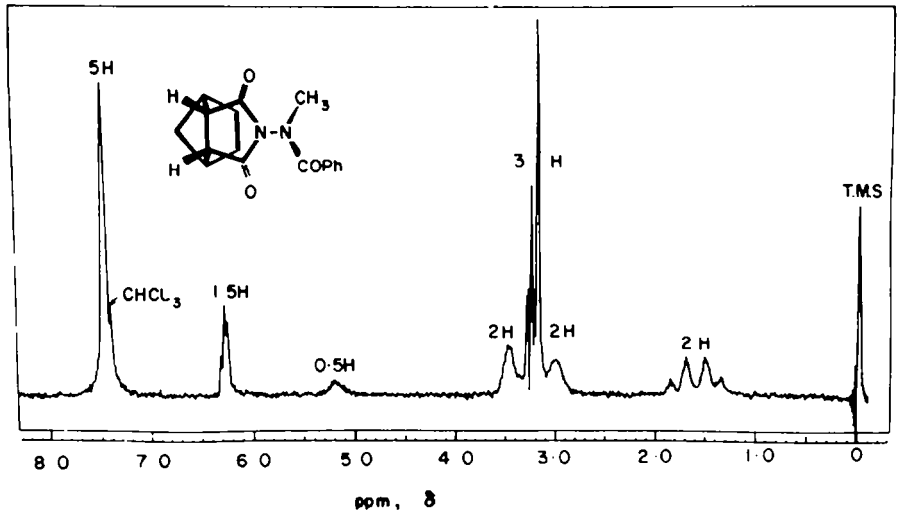


FIG 3. 60 MHz NMR spectrum of N′-methyl-N′-benzoyl-N-amino[2.2.1]bicyclo-5-heptene-2,3-*endo* dicarboximide (XIV) in $CDCl_3$ at 44°.

is less intense than the downfield component (Table 1). The N′-methyl-N′-acetyl compound (XIII) shows three singlets for N′-methyl and also for N′-acetyl protons with relative intensities of 1:2:3 (Table 1). Hindered rotation about N—N′ bond could yield two signals for each of these groups. Further multiplicity, as observed for this compound, could arise from hindered rotation about the N′—CO bond,[9] which would yield four signals for each group; only three being observed presumably due to accidental overlapping of two. The N′-methyl group increases the N′—CO double-bond character and hence a high torsional barrier could be expected. The N′-methyl signals coalesce to two singlets (intensity ratio 1:1) in nitrobenzene at 70° ($\Delta G^{\ddagger} = 18{\cdot}64$ K.Cals./mole), which could be due to increased rotation about the N′—CO bond. Finally the two singlets coalesce to one singlet at 110°, which could be due to increased rotation about N—N′ bond. In the case of compound XIV, N′—CO bond rotation seems to be fast in the temperature range studied. N′-Phenyl-N′-acetyl compound (XVI) shows two singlets for the acetyl protons and two triplets for the olefinic protons (Table 1), indicating slow rotation about the N—N′ bond.

The triacyl compounds show complete coalescence for the chemically equivalent proton signals below 120° (Table 2) and free energies of activation ($\Delta G^{\ddagger}$) for the rotation about the N—N′ bonds are of the order of 20 K.Cals./mole.

All N′-mono-acyl-, alkyl-, and aryl- substituted compounds (VI, VIII, XII and XV), N′,N′-dibenzyl compound (XVIII) and N′-phenyl-N′-benzyl compound (XVII)* show normal peaks for the chemically equivalent protons (Table 1). This could be due to fast rotation about the N—N′ and N′—R bonds, where R is an acyl group.

The direct interaction of the N-substituents with the cage-moiety olefinic protons, but not with the cage-moiety methylene protons, is strong evidence for *endo*- product formation in the Diels–Alder addition of maleic anhydride to cyclopentadiene.[10]

* Cage-moiety olefinic protons signal is quite broad.

EXPERIMENTAL

NMR spectra were recorded on a Varian A-60D spectrometer equipped with a variable temperature controller (Model No. V-6040). IR spectra were recorded on a Perkin–Elmer-257 Spectrophotometer. Chemical analyses, spectral data and m.ps of all compounds are in Table 1.

N-Amino[2.2.1]*bicyclo-5-heptene-2,3-endo-dicarboximide* (V). This was prepared by condensing [2.2.1]-bicyclo-5-heptene-2,3-*endo*-dicarboxylic anhydride[10] with hydrazine hydrate in equimolecular proportions at 25° in alcohol. (yield 90%) m.p. 143°. It was soluble in water.

Compound V formed a benzal derivative with benzaldehyde in dioxane: m.p. 104°. (Found: C, 72·09; H, 5·14; Required for $C_{16}H_{14}N_2O_2$: C, 72·18; H, 5·26). ν_{max} 1710 s, 1610 w, 1600 w, 1573 w cm^{-1}. δ ($CDCl_3$) 9·0 (1H, s).

N-Methylamino- and N-anilino[2.2.1]*bicyclo-5-heptene*-2,3-endo-*dicarboximides* (XII and XV). These were obtained by condensing the anhydride with methyl- and phenyl-hydrazines, respectively as described for V. The N-methylamino compound is soluble in water while the N-anilino compound is soluble in HCl aq.

Compounds X *and* XI. Compound V was reacted with an equimolecular quantity of ethyl chloroformate in dry benzene in the presence of $NaHCO_3$ and the product yielded compounds X and XI respectively on acetylation and benzoylation.

Compounds VI to IX, XIII, XIV and XVI to XVIII were derived from compounds V, XII and XV by the usual preparative methods.

Acknowledgement—We thank Prof. G. B. Singh for his keen interest and the C.S.I.R. for the award of a Research Fellowship (to C.K.R.).

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