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NMR STUDIES OF RATE PROCESSES AND CONFORMATIONS—IX

CONFORMATIONAL RATE PROCESSES IN BRIDGED BICYCLIC TETRAHYDROPYRIDAZINE AND PIPERIDAZINE SYSTEMS[1]

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Abstract—The NMR spectra of compounds of the bicyclo [2.2.1] heptane and bicyclo [2.2.2] octane types and containing the —N(COOR)—N—(COOR)— fragment have been studied. These spectra are temperature dependent.

Free enthalpies of activation have been obtained from the observed spectral changes. These changes have been related to conformational changes in the molecules studied.

The nitrogen sites are probably nearly planar and none of the observed processes is hindered nitrogen inversion. *Hindered rotation* about the N—COOR bonds is present in both systems. In addition, a "*bridge-flipping*" *process* has been found in the derivatives of the bicyclo [2.2.2] octane type.

The origin of the potential barriers for these processes is discussed.

Résumé—Les spectres de RMN de composés du type bicyclo [2.2.1] heptane et bicyclo [2.2.2] octane et contenant le motif —N(COOR)—N(COOR)—, ont été étudiés. Ces spectres varient en fonction de la température. Les enthalpies libre d'activation ont été calculées à partir des modifications spectrales observées.

Celles-ci ont été reliées à des modifications conformationnelles présentes dans les molécules étudiées: *rotation restreinte* autour des liaisons N—COOR présente dans les deux types de composés; *torsion du pont —N—N—* présente uniquement dans les composés du type bicyclo [2.2.2] octane.

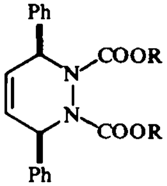
Les atomes d'azote adoptent probablement une configuration presque plane. Les modifications spectrales observées ne peuvent s'expliquer par une inversion empêchée des atomes d'azote.

L'origine des barrières de potentiel calculées est discutée.

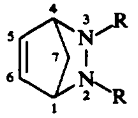
SINCE the initial study[3] of conformational changes in two tetrahydropyridazines (I and II) by means of variable temperature NMR spectroscopy, other reports on these and related systems have appeared in the literature.[4,5] The temperature dependence observed for the NMR signals of I and II has been ascribed to the presence of two rate processes: ring inversion and hindered rotation about the N—COOR bonds.[3] As hindered N-inversion might also give rise to spectral changes in these systems we have undertaken a study of compounds in which these different types of conformational changes may be analysed separately. Firstly in compounds of type A: V, VII, X, XIII and XVI, only one type of rate process has to be considered: N-inversion at the N,N'-dimethylhydrazine site. We have shown that the observed temperature dependence of the NMR spectra of these compounds arises from a *consecutive inversion* process at the two N-sites.[6] Secondly, in compounds of type B: III, IV, VI, VIII, IX, XI, XII, XIV and XV, both N-inversion and hindered rotation processes may be operative.

Finally, the compounds of type C (I, II and analogues) may show the conformational changes present in type B compound as well as ring inversion.

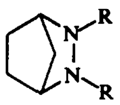
In this paper we report our studies of the conformational rate processes present in bicyclic compounds of type B.[7] Another communication will deal with compounds of type C.[8]



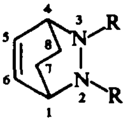
I: R = Me
II: R = Et



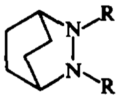
III: R = COOMe
IV: R = COOEt
V: R = Me



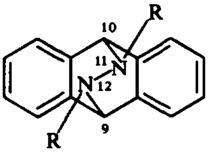
VI: R = COOEt
VII: R = Me



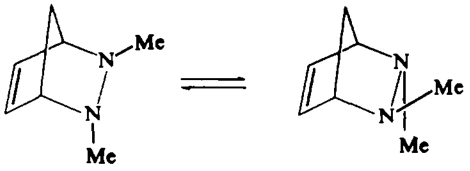
VIII: R = COOMe
IX: R = COOEt
X: R = Me



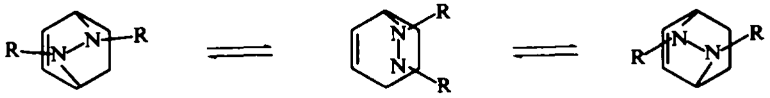
XI: R = COOMe
XII: R = COOEt
XIII: R = Me



XIV: R = COOMe
XV: R = COOEt
XVI: R = Me

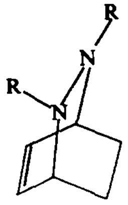


XVII XVIII

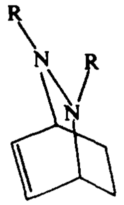


XIX XXI XX

R = COOMe



XIX



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RESULTS

All type B compounds have been prepared by either thermal or photochemical 1,4-addition of methyl or ethyl azodicarboxylate to the corresponding unsaturated system (Experimental).

Variable temperature NMR spectra. Compounds III, IV, VI, VIII, IX, XI, XII, XIV and XV show temperature dependent NMR spectra. These spectra are described in Table 1. We now describe the main spectral features of ($CDCl_3$) solutions of compounds III, VIII, XI, XII and XIV at different temperatures (see also Table 2).

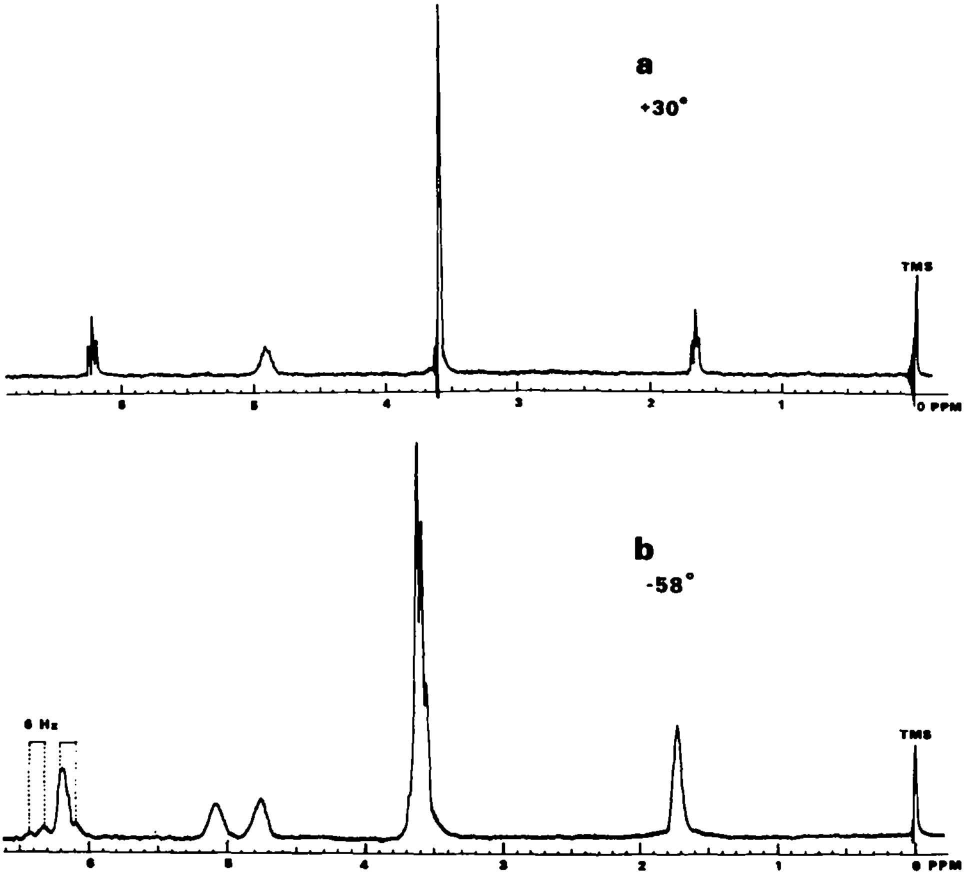

FIG. 1 NMR spectrum of compound III in $CDCl_3$ (a) at +30°, (b) at −58° at 60 MHz. Spectra recorded at different amplifications.

The NMR spectrum of compound III shows at 30° a narrow signal (half-height width: 0·5 Hz) for the COOMe groups. a quintuplet for the bridgehead protons and a triplet (XX' part of an AA'XX' pattern) for the vinylic protons (Fig. 1a). At −58° the spectrum apparently contains three peaks of unequal areas for the COOMe groups, two structure-less broad peaks of unequal areas for the bridgehead protons and a complex pattern for the vinylic protons (Fig. 1b).

Compound VIII shows at 51° a single line for the two COOMe groups, a multiplet for the bridgehead protons, a multiplet (XX' part of an AA'XX' pattern) for the vinylic protons and an AA' BB' pattern for the $—CH_2—CH_2—$ bridge (Fig. 2a). On lowering the temperature the COOMe signal splits at 28° into two lines which remain unchanged from +10° to −8° (Fig. 2b spectrum at +8°). Finally, at −56° four partially overlapping COOMe peaks of unequal intensities are discernable (Fig. 2c), as well as a very broad band for the bridgehead protons, a complex multiplet for the vinylic protons and a complex broad pattern for the $—CH_2—CH_2—$ bridge protons.

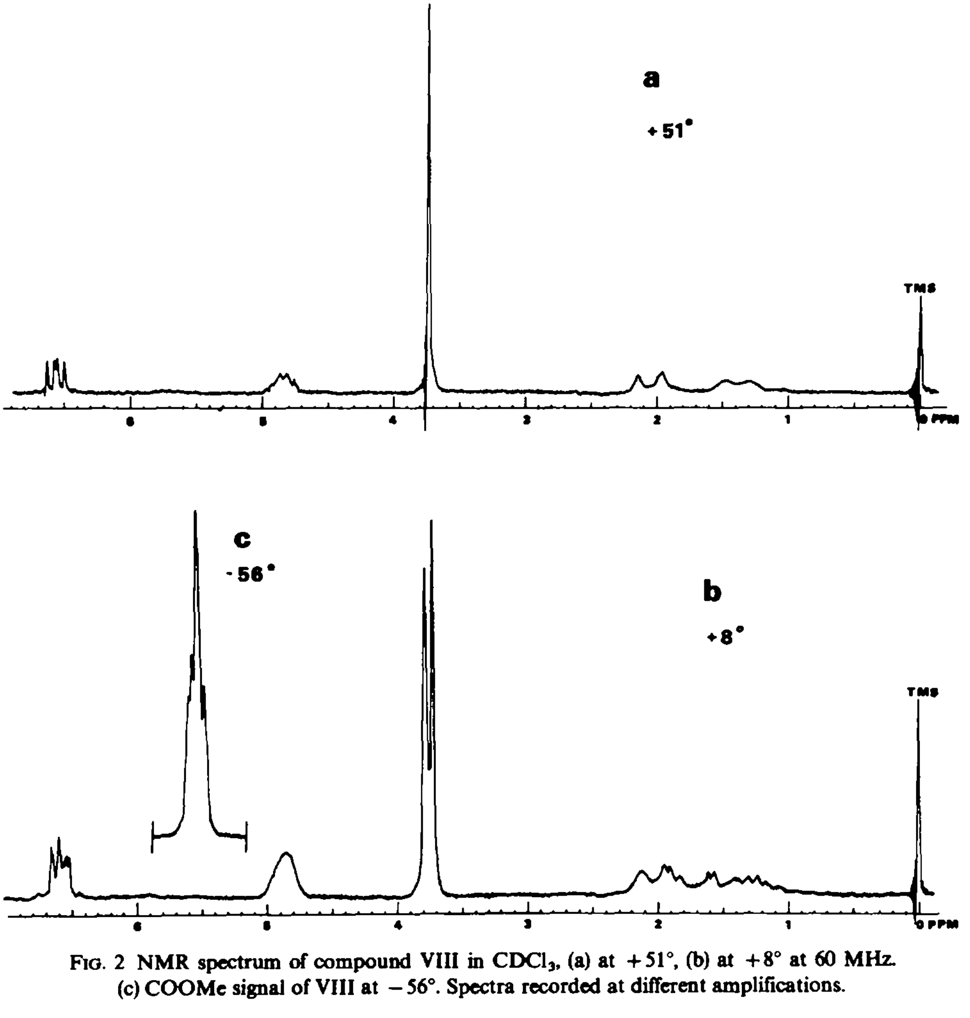

FIG. 2 NMR spectrum of compound VIII in $CDCl_3$, (a) at +51°, (b) at +8° at 60 MHz. (c) COOMe signal of VIII at −56°. Spectra recorded at different amplifications.

The spectrum of compound IX shows at 56° a triplet and a quartet for the COOEt groups; at 16° it shows two triplets for the Me protons and a complex pattern for the CH_2 protons (two overlapping ABC_3 spectra; see below).

The symmetrical compound XI shows the same spectrum from $-10°$ to $+45°$ (single line for the COOMe groups). At $-61°$ all signals are different from those observed at higher temperatures and four partially overlapping COOMe peaks of different intensities may be discerned.

The spectrum of XII contains at 99° a triplet and a quartet for the COOEt groups (A_2B_3 pattern). At 30° it contains a triplet for the Me groups of the esters and a more complex pattern for the CH_2 protons of the COOEt groups. This pattern may be considered as the AB part of an ABC_3 spectrum (Fig. 3), similar to those found for other Et groups in molecules which possess some kind of dissymmetry rendering the CH_2 protons non-equivalent.[9]

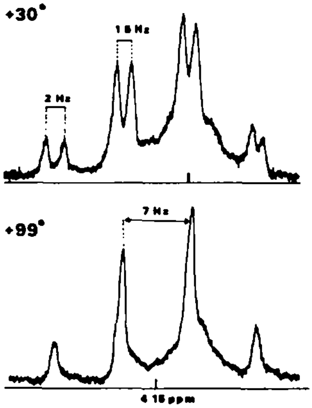

FIG. 3 CH_2 signals of the COOEt groups of compound XII in tetrachloroethylene at 60 MHz. At $+30°$: AB part of ABC_3; at $+99°$: A_2 part of A_2B_3. The broad underlying signal is due to the bridgehead protons.

Compound XIV shows at 30° a singlet for the COOMe groups and a singlet for the bridgehead protons. At $-65°$ four COOMe peaks of different areas are present, as well as two signals of different areas for the bridgehead protons (Fig. 4).

Compound XV shows for the COOEt groups an ABC_3 pattern $+33°$ and an A_2B_3 pattern at higher temperatures.[6]

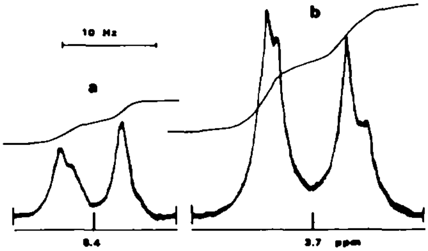

FIG. 4 (a) Bridgehead signals, (b) COOMe signals of compound XIV at $-65°$ in $CDCl_3$ at 60 MHz.

Activation parameters. From the observed spectral changes, activation parameters for the rate processes involved may be calculated. The rate constant at coalescence, k_c, in the case of exchange between two different uncoupled sites A and B of equal populations and lifetimes ($\tau_A = \tau_B = 2\tau$) is given by:[10] $k_c = 1/2\tau_c = \pi\Delta v/\sqrt{2}$ where Δv is the separation of the two signals when exchange is slow. The activation free enthalpy at the coalescence temperature T_c is then:

$$\Delta G_c^* = 4\cdot57\ T_c[9\cdot97 + \log T_c/\Delta v]$$

using Eyring's rate equation and a transmission coefficient of 1.†

In the present systems, however, the accuracy of the ΔG_c^* values is limited as the rate processes observed involve in some cases an exchange between several sites of different populations. This applies specially to ΔG_c^* values obtained from the coalescence of the COOMe or bridgehead proton signal present in the low temperature spectra of III, XI and XIV. With such limitations in mind we have calculated the ΔG_c^* values for the different compounds and for the different rate processes from the spectral parameters. The values of Δv, T_c and ΔG_c^* for the signals considered are listed in Table 1. These approximate ΔG_c^* values are used merely for characterizing the different rate processes and conformational changes involved.

DISCUSSION

From the spectral changes described above it follows that a "low temperature" rate process (T_c below 0°; $\Delta G_{245-270}^* = 13 \pm 1$ kcal/mole; Table 2) is present in *both* the bicyclo [2.2.1] heptane type compounds (e.g. III) and the bicyclo [2.2.2] octane type compounds (VIII, XI, XIV). In addition, the presence of two COOMe signals in the spectrum of VIII between −8° and +10° and of an ABC_3 spectrum for the COOEt groups of XII and XV (at temperatures where the low temperature rate process is fast) indicates the presence of molecular dissymetry, which renders the COOMe groups and the CH_2 protons of the COOEt groups non-equivalent. This dissymmetry disappears at higher temperatures as the COOMe signals of VIII coalesce to a singlet and as the ABC_3 pattern of XII and XV changes over to an A_2B_3 pattern. Therefore a second, "high temperature" conformational rate process (T_c above 0°) is present in the compounds of the bicyclo [2.2.] octane type; it is characterized by a ΔG^* value (at 300–330°K) of 16–19 kcal/mole (Table 2).

Three different types of conformational changes may be responsible for the temperature dependent spectral changes observed in the present compounds:

(i) hindered nitrogen inversion;
(ii) hindered rotation within the NCOOR groups;
(iii) in the bicyclo [2,2,2] octane system some kind of conformational isomerization might occur within the bicyclic framework, due to its much greater flexibility as compared to the bicyclo [2.2.1] heptane system.‡

Nitrogen inversion and the nature of the nitrogen sites. It has been shown that in

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† This seems justified in the present cases as the rate processes involved can probably be represented by a simple potential curve without valley at the top.

‡ This may be easily viewed on molecular models (see also below).

both compounds V and X an exchange of the N—Me groups between *two equally populated* sites via consecutive inversion of the two nitrogens XVII ⇌ XVIII is responsible for the observed spectral changes.[6]

We therefore expect that in the present systems, if hindered N-inversion of the type XVII ⇌ XVIII were one of the observed rate processes, it should:

(i) be present in *both* III and VIII;
(ii) give rise to an exchange process between *two sites of equal populations.*

Considering the two types of changes described above, the low temperature rate process fulfills condition (i) but *not* condition (ii). whereas the high temperature rate process may fulfill condition (ii) but *not* condition (i).

It may be argued that the presence of only one COOMe signal in the spectrum of III at temperatures where VIII shows two such signals might be due to accidental identity of the chemical shifts of the two COOMe groups in III. This seems improbable in view of the following considerations:

(a) The COOMe peak in the spectrum of III remains a sharp singlet (width at half-height: 0·5 Hz) in deuterochloroform, benzene, pyridine and deuterium oxide solution. At the same temperature, VIII shows a doublet in pyridine (3 Hz splitting) and a broad singlet in deuterochloroform (width at half-height ca. 4 Hz).

(b) The chemical shift difference between the two N-Me signals is nearly the same for V and X (16 Hz and 14·9 Hz respectively[6]); one may then expect a chemical shift difference between the COOMe signals of III similar to the one observed for the COOMe signals of VIII (3·5 Hz) in comparable conditions.

(c) Hindered N-inversion should show a higher barrier in the more strained system III than in VIII (as is found in V and X[6]), and should then be easier to observe in III than in VIII.

We are therefore led to the conclusion that *none of the observed rate processes is hindered N-inversion.*

This result is easily rationalized if one considers that the N lone pair is conjugated with the COOR groups. The consequences are a departure of the N from the pure pyramidal state, which leads to a lower barrier to N-inversion, and therefore faster N-inversion than in amines† and an increase of the barrier to rotation about the N—COOR bond due to partial double bond character as in amides.[10]

X-ray analysis of N,N'-diformylhydrazine points to an entirely planar structure for this molecule.[12]

A microwave study of formamide shows that in this molecule the N site retains some pyramidal character although it is much nearer to the planar than to the pure pyramidal state.‡[13]

The high barriers found in amides[10] point to appreciable double bond character for the N—CO bond.

In the present systems we may consider the N-sites as being in a planar or nearly

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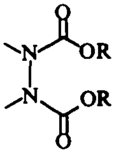
† The effect of conjugation on nitrogen inversion barriers is very strikingly illustrated by the aziridine derivatives. N—Me aziridines have high inversion barriers whereas N—Ph and N—CO—Me derivatives invert much more rapidly.[14] The N—COOMe derivative shows an inversion barrier of 7·6 kcal/mole.[11c] The barrier is expected to be much *lower* in less strained systems.

‡ The inversion barrier of ammonia is ca. 5·8 kcal/mole high. In formamide the barrier is only ca. 1·1 kcal/mole.

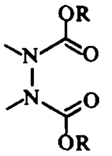
planar state (and in this last case, inverting rapidly on the NMR time scale), the N—COOR bonds having a certain amount of double bond character.

Nature of the "low temperature" rate process ($\Delta G^{\ddagger}_{245-270} = 13 \pm 1$ kcal/mole). This rate process corresponds to exchange between several sites of different populations. Following the above discussion, this process, which is present in both types of compounds (e.g. III . . . and VIII . . .), is then best described as *hindered rotation about the* N—CO *bonds.*† Hindered rotation in amides is well documented[10] and recently, NMR studies of hindered rotation in urethanes[15,16] and in acyclic diacylhydrazines[5] have been reported. The activation energies found in these cases lie in the same range as those found for the present systems.‡

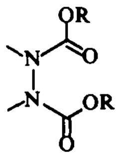
Three different arrangements of the —N(COOR)—N(COOR)— system are possible, giving rise to a maximum of four —COOMe signals: two symmetrical forms S_1 and S_2 (one COOMe signal each) and a dissymmetrical form DS (two COOMe signals):



S_1



S_2



DS

The low temperature spectrum of III (Fig. 1b) may then be explained on the basis of these forms. Three of the four expected COOMe peaks are visible. The pattern obtained for the vinylic protons may be considered as arising from the overlap of two broad A_2 singlets (from the vinylic protons in the S_1 and S_2 forms) and a broadened AB pattern ($J_{AB} \sim 6$ Hz; $\Delta\nu_{AB} \sim 12$ Hz) from the now different vinylic protons in form DS (see also Ref. 5 for similar results). Integration of one half of the AB pattern then leads to the amount of DS form present at −58°. Two signals are observed for the bridgehead protons. Each one arises from two protons of one of the symmetrical forms and from one proton of the DS form. Integrating these signals and using the amount of DS form obtained from the vinylic pattern, we then get the following percentages of the different forms: S_1 (or S_2): ca. 26 ± 3%; S_2 (or S_1): ca. 36 ± 3% and DS: ca. 38 ± 3%. If we assume that the bridgehead proton signal at low field arises from the protons next to the carbonyl group "out" (as in S_1) we find that forms S_2 and DS have the same energies and are slightly more stable than form S_1 ($\Delta G^{\circ}_{215} \sim 125 \pm 50$ cal/mole).

In the spectrum of XIV at −65° all four COOMe signals are visible, as well as two signals for the bridgehead protons (Fig. 4). From the areas of these latter signals one finds that there is 12% more of one symmetrical form than of the other, in

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† Hindered rotation about the CO—OR bonds might also be considered. Such a process in unlikely to be the one observed here as shown by data from ultrasonic relaxation measurements.[14] These measurements indicate that the barrier to rotation about the CO—OEt bond in ethyl acetate is 8·7 kcal/mole high (ΔH^*) and that the rotamers have very different energies ($\Delta H^{\circ} \sim 3$ kcal/mole); this is not the case in the present systems. A detailed discussion of N—CO versus CO—OR bond rotation is in preparation.

‡ Direct comparison is difficult as the ΔG^* values reported are for different temperatures; the entropy terms may also be different for the various types of compounds.

agreement with that found for III. If one tries to decompose the upfield COOMe signal into its components one obtains an abundance of 25 ± 4% for the less stable symmetrical form. It follows that the percentages of the other forms are 37% ± 4% for the more stable symmetrical form and 38 ± 4% for the DS form.

Nature of the "high temperature" rate process ($\Delta G^*_{300-330}$ = 16–19 kcal/mole). From the spectral changes described above it follows that a second rate process, with a higher activation energy, is present in the compounds of the bicyclo [2.2.2] octane type (VIII, IX, XI, XII, XIV, XV). As such a process could not be detected in the compounds of the bicyclo [2,2,1] heptane type (III. IV. VI),† we are led to the conclusion that this process is characteristic of a property present in the first type of systems but not in the second. Furthermore, this property belongs to the bicyclic framework itself. The obvious difference is that systems of the bicyclo [2.2.1] heptane type are much more strained and rigid[17] than systems of the bicyclo [2.2.2] octane type. In these systems some twisting of the bridges is possible and this partially removes eclipsed non-bonded interactions without appreciable angle strain. Such a twisting is even more probable if substituents bulkier than hydrogen are present as is the case here. Compound VIII may then be represented as in XIX–XX. The presence of a double bond or of fused benzene rings in VIII or in XIV renders the system somewhat more rigid than in XI and XII.

The spectral changes observed for VIII, XII and XV require that the molecules be non-symmetrical at lower temperatures, and that at higher temperatures there be present a species having in effect a plane of symmetry. This may be accounted for by a conformational rate process of the type XIX ⇌ XX, which we may call a *"bridge flipping" process.* This process interconverts two conformers of the type XIX and XX, which possess a twisted —N(COOR)—N(COOR)— bridge, the two nitrogens being near to the planar state (see above). When the interconversion is slow (on the NMR time scale) the two COOMe groups of VIII are different and the COOEt groups of XII and XV display an ABC_3 pattern. When it becomes fast the COOMe groups collapse into a single line and the ABC_3 pattern changes over into an A_2B_3 pattern (i.e. the CH_2 protons become equivalent).

Solvent effects. If this process were N-inversion, one would expect a strong change in ΔG^* on changing from a $CDCl_3$ solution to a D_2O solution, as has been shown in cases where nitrogen inversion is indeed the observed rate process.[6, 11a] In fact the value of ΔG^*_c for the present process remains unchanged in $CDCl_3$ and in D_2O (Table 2) solutions. This confirms that it is *not* a N-inversion process (see above).

Origin of the potential barrier

Hindered rotation process. The ΔG^* values found for this process may contain an entropy barrier ΔS^* as well as an enthalpy barrier ΔH^*. So it is difficult to compare quantitatively these systems with others in the literature, The hindrance to N—CO bond rotation may be said to arise from partial double bond character of this bond due to conjugation of the N lone pair with the CO group. Assuming a similar ΔS^* value as that in amides,[10] the barriers (ΔH^*) in urethanes[15] and in the present di-urethanes (see also Ref. 5) seem lower than in amides[10] as might be expected from the electronic effects of the OMe groups.

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† See Discussion above.

‡ Temperature dependent changes in rotamer populations may also influence the chemical shift difference between the CH_2 protons of the COOEt groups.

TABLE 1. VARIABLE TEMPERATURE NMR SPECTRA OF COMPOUNDS III, IV, VI, VIII, IX, XI, XII, XIV, XV[a]

Compound	Temperature (Solvent)	N—COOR	H-1, H-4	H-5, H-6	H-7 or H-7, H-8	Others
III	30° ($CDCl_3$)	3·60 (s; 6H)	4·92 (m; 2H)	6·23 (t, splitting 1·7 Hz; 2H)	1·65 (t, splitting 1·5 Hz; 2H)	—
	−58° ($CDCl_3$)	ca. 3·6 (3 peaks; 6H)	4·75 (bp; 1·04H) 5·07 (bp; 0·96H)	6–6·5 (A_2 + AB; $J = 6$ Hz; 2H)	1·73 (bp; 2H)	—
IV	30° ($CDCl_3$)	1·30 (t: 7·2 Hz; 6H) 4·20 (q: 7·2 Hz; 4H)	5·15 (m; 2H)	6·52 (t, splitting 1·8 Hz: 2H)	1·73 (t, splitting 1·6 Hz; 2H)	—
VI	30° ($CDCl_3$)	1·25 (t: 7 Hz; 6H) 4·15 (q: 7 Hz; 4H)	4·42 (bp; 2H)	1·70 (bp; 4H)	1·70 (bp; 2H)	—
VIII	51° ($CDCl_3$)	3·74 (sharp s; 6H)	4·85 (m; 2H)	6·55 (XX′ of AA′XX′; 2H)	2·1 (bd; 2H) 1·4 (bd; 2H)	—
	8° ($CDCl_3$)	3·72 (s; 3H) 3·78 (s; 3H)	4·85 (bp; 2H)	6·55 (m; 2H)	1–2·2 (broad multiplet; 4H)	—
	−56° ($CDCl_3$)	3·85 (four p; 6H)	5·0 (bp; 2H)	6·65 (bm; 2H)	1–2 (broad m; 4H)	—
IX	56° ($CDCl_3$)	1·25 (t: 7 Hz; 6H) 4·25 (q: 7Hz; 4H)	4·9 (bp; 2H)	6·60 (XX′ of AA′XX′; 2H)	1·5 (bd; 2H) 2·1 (bd; 2H)	—
	16° ($CDCl_3$)	1·25 (t: 7 Hz; 3H) 1·27 (t: 7 Hz; 3H) 4·2 (several q; 4H)	4·9 (bp; 2H)	6·6 (bm; 2H)	1·5–2·3 (bm; 4H)	—
XI	+45° ($CDCl_3$)	3·78 (s; 6H)	4·25 (bp; 2H)	1·5–2 (bm; for H-5, H-6, H-7, H-8; 8H)		
	−10° ($CDCl_3$)	Same spectral data as at +45°				
	−61° ($CDCl_3$)	3·85 (four p; 6H)	4·25 (bp; 2H)	1·4–2 (bm; for H-5, H-6, H-7, H-8; 8H)		
XII	99° (TCE)	1·25 (t: 7 Hz; 6H) 4·15 (q: 7 Hz; A_2 of A_2B_3; 4H)	4·10 (bp; 2H)	1·5–2 (bm; for H-5, H-6, H-7, H-8; 8H)		—
	30° (TCE)	1·25 (t: 7 Hz; 6H) 4·20 (AB of ABC_3; 4H)	4·15 (bp; 2H)	1·4–2 (bm; for H-5, H-6, H-7, H-8; 8H)		—

TABLE 1—*continued*

XIV	30° ($CDCl_3$)	3·65 (sharp s; 6H)	6·25 (sharp s; 2H)	—	—	7–7·5 (bm; 8H)
	−65° ($CDCl_3$)	3·70 (4 peaks; 6H)	6·40 (2 peaks; 2H)	—	—	7·1–7·6 (bm; 8H)
XV	30° (CCl_4)	1·1 (t: 7 Hz; 6H) 3·9 (AB of ABC_3; 4H)	6·0 (sharp s; 2H)	—	—	7–7·5 (bm; 8H)

[a] Shifts are in ppm downfield from internal TMS. Coupling constants are in Hertz (= c/s) Hz.
s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; b: broad; p: peak; TCE: tetrachloroethylene; signal integral is last term in parentheses.

TABLE 2. SPECTRAL DATA AND $\Delta G_c^{\neq}$ VALUES

Compound	Signals and spectral changes studied	$\Delta\nu$ (at $T°$) Hz	T_c (solvent)	$\Delta G_c^{\neq}$ kcal/mole	Conformational change
III	Collapse of low temperature signals from bridgehead protons,	20·0 (−58°)	−5° ($CDCl_3$)	13·7 ± 0·5?[a]	Rotation about N—COOMe bond
VIII	Collapse of COOMe doublet present between −8° and +10°	3·5 (8°)	27·5° ($CDCl_3$)	16·4 ± 0·3	Bridge flipping
	id.	3·5 (2°)	32° (D_2O)	16·6 ± 0·3	Bridge flipping
IX	Collapse of two COOEt CH_3 triplets present at 16°	1·15 (16°)	28° ($CDCl_3$)	17·0 ± 0·4	Bridge flipping
XII	Collapse of AB part of ABC_3 from COOEt to A_2 (Fig. 3)	2·0 (30°)	70° (TCE)[b]	19·0 ± 0·5	Bridge flipping
		1·5 (30°)	60° (TCE)[b]	18·7 ± 0·5	Bridge flipping
XIV	Collapse of COOMe signals (Fig. 4)	8·5 (−65°)	−28° ($CDCl_3$)	12·6 ± 0·5?[a]	Rotation about N—COOMe bond
	Collapse of signals from bridgehead protons (Fig. 4)	7·7 (−65°)	−30° ($CDCl_3$)	12·7 ± 0·5?[a]	Rotation about N—COOMe bond

[a] Approximate values due to the presence of an exchange between several sites of different populations.
[b] TCE: tetrachloroethylene

Bridge flipping process. This process shows quite high ΔG^* values (Table 2). The transition state of the interconversion XIX $\rightleftharpoons$ XX corresponds to a planar arrangement of the di-urethane system (e.g. as in XXI), in which relief of the non-bonded interactions between the COOR groups by some rotation around the N—CO bond leads to loss of conjugation energy.

Among the factors contributing to the barrier to bridge flipping and to the preference of the diaza-bridge for a twisted zig-zag, arrangement (as in XIX and XX) the following may play an important role:

(i) The presence of bulky substituents on the N atoms (rendered presumably much bulkier by their preference for a planar arrangement which allows conjugation as shown by the presence of hindered rotation about the N—CO bonds) may force the ground state conformation of the bridge into a twisted arrangement. These substituents will interact strongly in the transition state XXI and may therefore contribute significantly to the flipping barrier.

(ii) Bridge flipping necessarily involves rotation about the N—N bond. An SCF calculation of the potential curve for rotation about the N—N bond in the hydrazine molecule[18] leads to an energy barrier of 11·5 kcal/mole for the eclipsed form. This is much higher than the barrier to rotation about the C—C bond in ethane (ca. 3 kcal/mole[22]). Although the electronic structure of the present system is very different from that of hydrazine, it might be possible that a significant contribution to the high barriers observed arises from a high torsional energy for the planar *cis* arrangement of the transition state XXI.

(iii) In addition to the ΔH^* barrier, the greater symmetry of the transition state may lead to an entropy barrier (negative ΔS^*) which may raise ΔG^* above ΔH^*.

For the ring inversion process of I an entropy barrier $\Delta S^* = -7$ eu is found.[8] As this process is related to the bridge flipping one[8] a ΔS^* barrier of a similar magnitude may be operative in the interconversion XIX $\rightleftharpoons$ XX.

These three factors, steric, electronic and entropic are probably also operative in determining the high barriers (of the order of 20–21 kcal/mole) to rotation about the N—N bond in tetraacylhydrazine derivatives.[19]

Furthermore, a recent X-Ray analysis in N,N′-bisuccinimidyl indicates that the ring planes make a dihedral angle of 65°.[20]

These latter results confirm that, as discussed above, a very important contribution to the bridge flipping barrier arises from energy terms inherent to the di-urethane system (see also Discussion in the following communication), which seems to show a strong preference for a non-eclipsed arrangement about the N—N bond, leading to a high barrier to rotation about this bond.

EXPERIMENTAL

The spectra were recorded on a Varian A-60 spectrometer equipped with the variable temp accessory. The general recording conditions are as given in Ref. 6. Shifts are in ppm downfield from TMS; coupling constants are in Hz and have been obtained by a first order analysis.

Preparation of the compounds. Compounds III,[21] IV,[22] IX,[23] XII,[23] XIV[24] and XV[24] have been prepared by established methods and had physical constants and spectral data in agreement with their structures.

2,3-*Diaza-bicyclo* [2.2.2] 5-*octene*-2,3-*dicarboxylic acid dimethyl ester* (VIII). Prepared by the method of Askani[23] from cyclohexadiene and diazodicarboxylic acid dimethyl ester, using twice the amount of solvent (cyclohexane): yield ca. 70%; b.p. 98°/0·04 mm. (Found: C, 53·07; H, 6·42; N, 12·36. $C_{10}H_{14}N_2O_4$ requires: C, 53·09; H, 6·24; N, 12·38%.) n_D^{24}: 1·499.

2,3-*Diaza-bicyclo* [2.2.2] *octane-2,3-dicarboxylic acid dimethyl ester* (XI). Obtained by hydrogenation of VIII in accordance with the hydrogenating IX;[23] b.p. 103°/0·17 mm. (Found: C, 52·48; H, 7·21; N, 12·31. $C_{10}H_{16}N_2O_4$ requires: C, 52·62; H, 7·07; N, 12·77%.) $n_D^{24} = 1{\cdot}492_2$.

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