# Nuclear Magnetic Resonance Studies of *N*-Nitrosamines. Part 4.† Barriers to Rotation about the N–N Bond for Some Cyclic Compounds

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Information on the barrier to internal rotation about the N-nitroso-bond has been obtained for eight saturated cyclic *N*-nitrosamines by means of variable-temperature proton n.m.r. spectroscopy. Free energies of activation for the process are quoted and are discussed in terms of molecular conformation and group interactions.

STUDIES of the rates of intramolecular processes by n.m.r. spectroscopy are many and varied; they include investigations of hindered rotation around partial double bonds. In particular, rotation of the *N*-nitroso-group around the N–N bond in *NN*-dimethylnitrosamine was among the first of such processes to be studied by n.m.r. spectroscopy.[1]

In this paper we describe n.m.r. studies of the rates of rotation for the *N*-nitroso-group in a series of substituted piperidines and piperazines, a morpholine, and a pyrrolidine. The eight compounds examined were all available following previous work.[2-4] They are *cis*-2,6-dimethyl-1-nitrosopiperidine (I); *cis*-1,3,5-trimethyl-4-nitrosopiperazine (II); γ-2,3,5,6-tetramethyl-1,4-dinitrosopiperazine (III); *cis*-2,6-dimethyl-4-nitrosomorpholine (IV); 2,2,6,6-tetramethyl-1-nitrosopiperidine (V); 2,2,5,5-tetramethyl-1-nitrosopyrrolidine (VI); 1-methyl-4-nitrosopiperazine (VII); and 4-nitrosomorpholine (VIII). The structural formulae are shown in Figure 1. The equilibrium conformations of these compounds have been established previously. At room temperature internal rotation about the N–NO bond is slow on the n.m.r. timescale in every case, and the proton n.m.r. parameters have been reported.[2-4]

In principle the proton spin systems are complex, but in practice the observed methyl proton spectra are relatively simple. For compounds (V) and (VI) at ambient probe temperature two singlets are seen for the methyl protons, whereas for (I), (II), (III), and (IV) the methyl signals consist of two doublets [plus an NMe singlet for (II)], the splittings being essentially due to vicinal coupling to the proximal methine proton. In each case the doubling of the signals is attributable to the orientation of the nitroso-group, the NNO atoms being non-collinear and therefore distinguishing [1] between the ring moieties *cis* and *trans* to the nitroso-oxygen. As the temperature is raised and the rate of internal rotation about the N–N bond increases, the distinction between the ring moieties is lost and the signals merge. Thus at a sufficiently high temperature it is expected that the methyl protons of (V) and (VI) will give rise to a single line whereas those of (I)—(IV) will give one doublet each [plus an NMe singlet for (II)]. The internal rotation for (V) and (VI) may be treated as giving simple uncoupled equally-populated two-site exchange of the A ⇌ X type. Since each $CH_3CH$ group of (I)—(IV) remains coupled throughout the internal rotation process and the X approximation is applicable, the methyl spectra may be described as due to the overlapping of two independent two-site exchange spectra of the A ⇌ X type with a common exchange rate. Computer simulation of such spectra is straightforward. This is not the case for compounds (VII) and (VIII), for which use of ring-proton spectra is enforced (avoidable in the other cases).

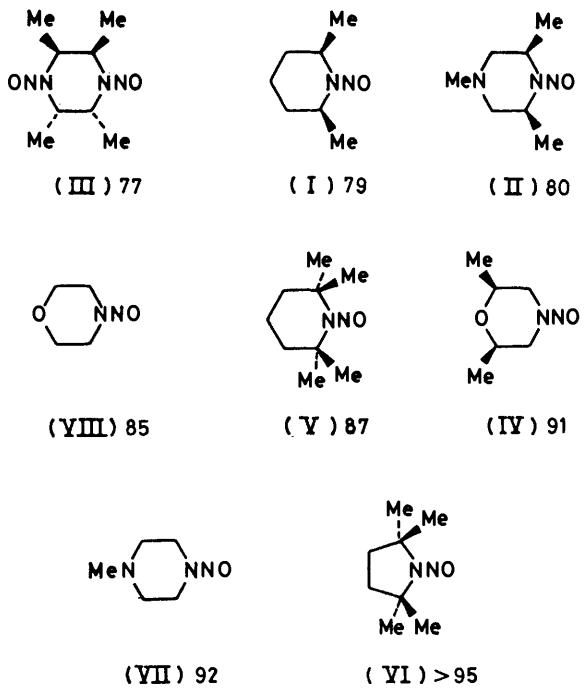



FIGURE 1 Structural formulae of the cyclic *N*-nitrosamines studied. The resulting values of $\Delta G^{\ddagger}(T_c)$ are given (in units of kJ mol$^{-1}$) beneath the structures, and the molecules are arranged in order of increasing $\Delta G^{\ddagger}(T_c)$

These may be interpreted in terms of exchange of the equally populated $[AB]_2 \rightleftharpoons [XY]_2$ type, and a more sophisticated approach to computer simulation of the spectra must be used.

For all the compounds studied there are, in principle, complications from long-range coupling, often of the cross-ring type. However, as far as the pertinent parts of the observed spectra are concerned, such coupling merely produces line-broadening [except for compound (II), see below]. Further line-broadening is caused by

† Part 3, ref. 4.

incomplete quadrupolar-induced averaging of coupling to $^{14}N$.

Obtaining accurate exchange rate-constants by fitting n.m.r. bandshapes is well-known to be fraught with difficulties. Allowances must be made for variations of effective chemical shift differences and of 'natural' linewidths with temperature. Attainment of stable uniform temperatures is not easy, and calibration of the temperatures also presents problems. The errors involved get progressively worse at the extremes of the relevant temperature range, *i.e.* measurements near the coalescence temperature give the best results. Moreover, the temperature range available for study is usually rather limited. All these factors make for considerable errors in the thermodynamic parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ if Eyring plots are used. In fact many of the errors are systematic in nature (*i.e.* not reflected in the statistical errors of the Eyring plots), and those resulting for $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are often mutually compensatory, so that $\Delta G^{\ddagger}$ is better defined, particularly in the coalescence region. The problems are aggravated for the present series of compounds because linewidths are rather high (see above) and the spectra are, in principle, complex but do not contain many widely-differing separations to be averaged by the exchange (see ref. 5). Moreover, for most of the compounds studied it was not possible to extend the temperature range [6] far above coalescence [especially for (IV)—(VIII)]. There are many approaches designed to minimise these problems. The best consist of independent methods of determining rate constants in the fast and slow exchange limits. Since such methods were not available to us in the present instances, and since our interest was largely channelled towards discovering the structural factors which qualitatively affect the barriers, we have directed our attention to the use of bandshape fitting as a means of improving the accuracy of $\Delta G^{\ddagger}$ near the coalescence temperatures [simple use of $T_c$ to obtain $\Delta G^{\ddagger}$ being difficult because of the complexity of the spectra, except for compounds (V) and (VI)]. Although values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ were obtained in several cases by our procedures, we put little significance on these for the reasons stated above, and therefore they are not reported herein. For some of the compounds we have not carried out bandshape fitting, or else this has proved to be unsatisfactory, and we only quote $\Delta G^{\ddagger}$ at coalescence.

Similar comments to the above have been made recently by Szymanski *et al.*,[7] who studied N–N internal rotation in *N*-nitroso-*N*-cyanomethylmethylamine in some detail and found values of $\Delta S^{\ddagger}$ differing by as much as 47 J mol$^{-1}$ K$^{-1}$ depending on whether the $CH_2CN$ or the $CH_3$ resonance was studied. They believed systematic errors arose in particular from the variation with temperature of effects of broadening due to spin coupling with quadrupolar $^{14}N$ nuclei. Like us, they treat values of $\Delta S^{\ddagger}$ outside the range $\pm 20$ J mol$^{-1}$ K$^{-1}$ with suspicion.

Barriers to N–N internal rotation for cyclic *N*-nitrosamines have been reported in five previous publications.[8-12] Glidewell [11] has studied nitrosopiperidine, dinitrosohexahydropyrimidine, and trinitrosohexahydro-1,3,5-triazine. Höfner, Stephenson, and Binsch, in work published [12] while our present paper was being prepared, have given very accurate barrier data for the last-mentioned compound and for 1,4-dinitrosopiperazine and some derivatives. Lunazzi *et al.*[10] studied compounds (I) and (V); Chow *et al.*[8] also studied compound (I). Cooney, Brownstein, and ApSimon [9] have reported results for $(CH_2)_nNNO$, with $n = 1$ to 5, and for nitro-3-azabicyclo[3.2.2]nonane and nitrosocamphidine. These authors give [9] full thermodynamic data for four of their compounds, but quote $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ derived at 298 K from Arrhenius parameters. We believe this to be rather unhelpful since this temperature is far below coalescence. The values of $\Delta S^{\ddagger}_{298}$ quoted vary from $-14$ to $+35$ J mol$^{-1}$ K$^{-1}$, but the variations are probably not real. Conversion of their data to 460 K (near coalescence) shows that $\Delta G^{\ddagger}$ values are probably equal within experimental error for all their compounds.

It is assumed throughout this paper, as in previous work,[2,4,13] that nitrosamines contain a planar $C_2NNO$ skeleton. It is likely that, except where there is substantial steric strain, the NO bond will eclipse one of the bonds at each of the α-carbon atoms.[13,14] However, our work would not be greatly affected if there were non-planarity at the amino nitrogen of the nitroso-group, provided this involved inversion at a rate that is rapid on the n.m.r. timescale. The conformations adopted by the rings appear to conform to the hypothesis that for a 6-membered ring an α-methyl group in an equatorial position *syn* to the nitroso-oxygen is strongly destabilising so that stable conformations often involve axial methyl groups. This suggestion, first put forward by Harris and Spragg,[2-4] has been verified for (I) and related compounds by Chow, Colon, and Tam,[8] for *N*-nitroso-2-alkylpiperidines by Forrest, Hooper, and Ray,[15] and (for a corresponding triazene) by Lunazzi *et al.*[16] using *X*-ray diffraction.

## EXPERIMENTAL

$^1H$ N.m.r. spectra were recorded at 100 MHz in the frequency-sweep mode using a Varian HA 100 spectrometer. Typically, sweep widths of 50 or 100 Hz and sweep times of 1 000 s were used. Spectra were calibrated using a Hewlett-Packard 5212A frequency counter. Temperature variation was achieved using the Varian control unit V4343. Temperatures were measured using the standard ethylene glycol sample (calibrated by Varian Associates), both before and after recording each spectrum. Good agreement was found between the two estimates on each occasion, and temperatures are considered accurate to at least $\pm 2$ K. Ambient probe temperature was *ca.* 37 °C. Relevant linewidths in the absence of exchange were *ca.* 0.3 Hz.

Simulations of exchange-affected spectra were carried out using a specially written FORTRAN computer program, based on the theory of Gutowsky *et al.*[17] (as modified by McConnell [18]), for the simple two-site exchanges plus X-

approximation splitting. This program can be used to simulate the A and B regions for AX ⇌ BY with equal populations. In addition it can be used iteratively to yield the four resonance frequencies (equivalent to three separations plus a frequency origin), an intensity scaling factor, a common linewidth factor, and the required exchange lifetime. The program DNMR 3 was used for calculating the $[AB]_2 \rightleftharpoons [XY]_2$ exchange cases.[19,20] An I.C.L. 1905 E computer was used for the calculations.

ane, $Me_3SiOSiMe_3$ (b.p. 171 °C, $\delta_H = 0.06$) or octamethylcyclotetrasiloxane (b.p. 175 °C, $\delta_H = 0.09$ was used for field/frequency locking purposes and for chemical shift measurement. The solutions studied contained between 4.9 and 9.8 mole % of the compound of interest.

In making use of Eyring plots it was assumed that the transmission coefficient, $\kappa$, was unity. There are, of course, possible reasons for departure from unity (*e.g.* rotation of a nitroso-group may occur in two possible directions, though

TABLE 1

Barriers to rotation of the *N*-nitroso-group in a series of piperidine, piperazine, morpholine, and pyrrolidine derivatives

| Compound | $\Delta\nu$/Hz [a] | $T_c$/K [b] | $\Delta G^{\ddagger}(T_c)$ [b]/kJ mol$^{-1}$ From plot | $\Delta G^{\ddagger}(T_c)$ [b]/kJ mol$^{-1}$ From coalescence |
|---|---|---|---|---|
| γ-2,3,5,6-Tetramethyl-1,4-dinitrosopiperazine (III) | 59.7 | 371 | 77 | 77 |
| *cis*-2,6-Dimethyl-1-nitrosopiperidine (I) | 33.7 | 376 | 79 | 79 [c] |
| *cis*-1,3,5-Trimethyl-4-nitrosopiperazine (II) | 28.4 | 376 | 80 | 80 |
| 4-Nitrosomorpholine (VIII) | 42.6 [d] / 24.4 [e] | 449 | 85 | |
| 2,2,6,6-Tetramethyl-1-nitrosopiperidine (V) | 18.6 | 401 | | 87 [c] |
| *cis*-2,6-Dimethyl-4-nitrosomorpholine (IV) | 8.9 | 407 | | 91 |
| 1-Methyl-4-nitrosopiperazine (VII) | 40.4 [d,g] / 25.2 [e] | 438 | 92 [f] | |
| 2,2,5,5-Tetramethyl-1-nitrosopyrrolidine (VI) | 9.4 [g] | >433 | | >95 |

[a] Chemical-shift differences averaged by the internal rotation (measured at ambient temperature). [b] The values of $T_c$ used are uncorrected for the effects of $T_2$*. [c] Lunazzi *et al.* give [10] $\Delta G^{\ddagger}$ = 82 kJ mol$^{-1}$ for these compounds. Chow *et al.*[8] also obtain $\Delta G^{\ddagger}$ = 82 kJ mol$^{-1}$ for (I). [d] For the protons α to the NO group. [e] For the protons β to the NO group. [f] Only the resonance of the protons α to the NO group was used to derive these values. [g] The value increases with temperature.

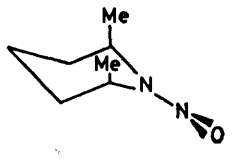
Matching of simulated and experimental spectra was generally carried out by eye, though in certain cases the experimental spectra were digitised using a D-Mac pencil follower, followed by iteration as described above. In the case of merging doublets coalescence temperatures were rather clearly defined, since characteristically flat-topped bands are seen. In the more complex cases, such as for compounds (VII) and (VIII), coalescence is not so well-defined. Therefore, although we quote a value for $T_c$ (to ±2 K) in Table 1 for these cases, we have not used the information to calculate $\Delta G^{\ddagger}$.

The compounds were studied in solution in benzonitrile (b.p. 191 °C), except for *cis*-2,6-dimethyl-1-nitrosopiperidine (I), which was dissolved in 1,1,2,2-tetrachloroethylene (b.p. 121 °C) with a little 1,4-dibromobenzene to act as a linewidth standard. A small amount of 1,1,2,2-tetrachloroethane (b.p. 146 °C) was added in most of the other cases as a linewidth standard. However, for compounds (II) and (VII) the NMe signal was used for this purpose. A check on variations in $T_2$* was therefore possible at each temperature used. In general, the value of $T_2$* used for spectrum simulation was that of the exchanging system itself well below coalescence, but this was corrected where necessary for variations in the resonance width of the linewidth standard with temperature. In practice, little difference arose from this correction. Corrections are also required, in principle, for variation of effective chemical-shift difference with temperature. In most cases we did not carry out such corrections, but we have shown that in the case of *cis*-2,6-dimethyl-4-nitrosomorpholine the resonance frequencies are independent of temperature (within experimental error) below 363 K, as they are for compound (I) between 306 and 379 K. However, the methyl group resonances of compound (VI) did show temperature variation as did the chemical-shift difference between the resonances for the two $CH_2$ groups α to NNO for (VII). In the latter case, computer-fitting of the spectra took the variation into account. In all cases either hexamethyldisiloxthese are not equivalent pathways in most of the cases considered), but since any particular choice may be queried, we chose the most convenient value. Deviations in $\kappa$ from unity may be absorbed in $\Delta S^{\ddagger}$, which, as described above, is difficult to obtain accurately.

## RESULTS

cis-2,6-*Dimethyl*-1-*nitrosopiperidine* (I).—It has been suggested [2] that the six-membered ring for this compound is predominantly in the chair form (IX) with both methyl groups in axial positions, in contrast to the *trans*-isomer, which is in the chair form with the methyl *syn* to the nitroso-group axial and the *anti*-methyl equatorial. However, for (I) in benzonitrile solution (as found earlier [2] for a solution in $CCl_4$), the vicinal coupling constants for the two types of methyl differ by only 0.05 Hz, indicating that there is little differential twisting between the two halves of the ring.

As indicated above, the effect of the internal rotation on




(IX)

methyl proton signals is to cause the merging of two doublets into one, in the fashion shown in Figure 2. Thus there are simultaneous mutual exchanges A ⇌ X and B ⇌ Y. Comparison of computer-simulated spectra with the experimental ones resulted in the value for $\Delta G^{\ddagger}(T_c)$ given in Table 1, which also gives information derived from visual estimation of the coalescence temperature (376 ± 2 K).

cis-1,3,5-*Trimethyl*-4-*nitrosopiperazine* (II).—This compound is closely similar to the preceding one both in its

assumed conformation and in the way in which the internal rotation influences the spectrum. The chemical-shift difference between the methyl groups is 28.4 Hz. Cross-ring coupling is large enough (*ca.* 0.5 Hz) to cause an observable additional splitting of the methyl signals (poorly resolved) at ambient probe temperature, but this was

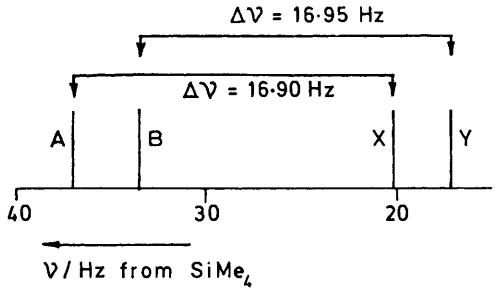
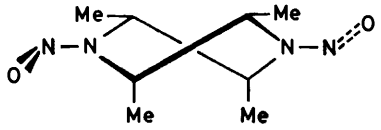



FIGURE 2 The exchange situation for *cis*-2,6-dimethyl-1-nitrosopiperidine (I). The doublet at high frequency is due to the *anti*-methyl protons; that to low frequency is due to the *syn*-methyl protons

ignored in our analysis of the exchange. Our approach was similar to that for (I), and the barrier results are reported in Table 1.

*γ*-2,3,5,6-*Tetramethyl*-1,4-*dinitrosopiperazine* (III).—A twist-boat structure (X) has been assigned [4] to this compound, with methyls *syn* to the nitroso-oxygens in axial positions whereas those *anti* are in equatorial positions. The nitroso-oxygens are mutually *transoid* and the methyl groups are equivalent in pairs. Thus the room temperature spectrum of the methyl protons consists of two doublets, and the effects of internal rotation may be treated in the same way as for (I) and (II). The results are listed in Table 1.




(X)

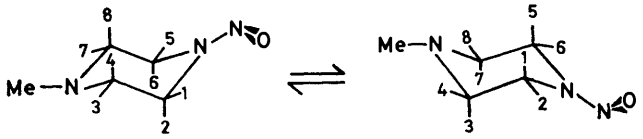
cis-2,6-*Dimethyl*-4-*nitrosomorpholine* (IV).—Treatment of the spectrum of this compound was not straightforward as the sample was a mixture [2] of the *cis*- and *trans*-isomers in the approximate concentration ratio 3 : 1. Attempts were made to either separate the isomers or enrich the quantity of the *cis*-isomer by fractional distillation under reduced pressure. These were not successful, and the distillate was found to contain almost the same amounts of the *trans*-form as before distillation. The distillate was used for the present investigation. The *cis*-isomer exists [2] in the chair form with both methyl groups equatorial. The doublets for this isomer could be clearly distinguished. Band-shape fitting was not feasible, but coalescence was observed. The coalescence temperature is substantially higher (407 K) than for compounds (I)—(III) (see Table 1).

2,2,6,6-*Tetramethyl*-1-*nitrosopiperidine* (V).—The chemical-shift difference between the two methyl proton signals for this compound was found to be 18.6 Hz at the lower end of the temperature range, where exchange is absent, and was assumed to be invariant with temperature. The activation energy was obtained from the coalescence temperature (the exchange process is of the simple A ⇌ X type) and is given in Table 1.

2,2,5,5-*Tetramethyl*-1-*nitrosopyrrolidine* (VI).—As for compound (V), the pyrrolidine gives rise to two singlets for the methyl proton spectrum at room temperature, and the exchange is of the simple A ⇌ X type. The resonances broadened on raising the temperature, but coalescence had not occurred by 403 K, when boiling in the sealed tube became a problem. A new sealed tube was made with the

TABLE 2

Chemical shifts and coupling constants for 1-methyl-4-nitrosopiperazine (VII) in benzonitrile solution



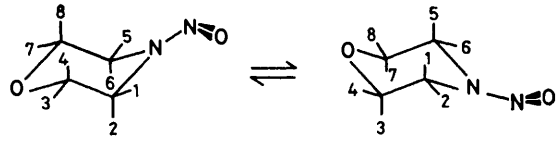

| | *syn* | *anti* |
|---|---|---|
| δ(α)/p.p.m. | 3.804 | 4.208 |
| δ(β)/p.p.m. | 2.237 | 2.489 |
| $J_{12}$,$J_{34}$/Hz [a] | 11.11, 9.51 | |
| $J_{56}$,$J_{78}$/Hz [a] | 11.86, 9.74 | |
| $J_{13} = J_{24}$, $J_{57} = J_{68}$/Hz | 6.81, 6.89 | |
| $J_{14} = J_{23}$, $J_{58} = J_{67}$/Hz | 3.60, 4.01 | |

[a] The values of $J_{12}$ and $J_{34}$ are not distinguished by the analysis, and their difference is more accurately determined than their sum. Similar remarks apply to $J_{56}$ and $J_{78}$.

introduction of 200 mmHg pressure of nitrogen gas, and this extended the accessible range by 26 °C. However even this proved to be inadequate to observe coalescence. An attempt was made to estimate the barrier using the line-width method of Piette and Anderson.[21] The rate constants obtained showed considerable scatter, but it could be concluded that the free-energy barrier to rotation was higher than 95 kJ mol$^{-1}$. Unfortunately the chemical shifts of the methyl groups were somewhat temperature

TABLE 3

Chemical shifts and coupling constants for 4-nitrosomorpholine (VIII) in benzonitrile solution




| | *syn* | *anti* |
|---|---|---|
| δ(α)/p.p.m. | 3.648 | 4.074 |
| δ(β)/p.p.m. | 3.413 | 3.657 |
| $J_{12}$, $J_{34}$/Hz [a] | 11.04, 8.80 | |
| $J_{56}$, $J_{78}$/Hz [a] | 10.91, 9.10 | |
| $J_{13} = J_{24}$, $J_{57} = J_{68}$/Hz | 6.41, 6.50 | |
| $J_{14} = J_{23}$, $J_{58} = J_{67}$/Hz | 4.25, 3.39 | |

[a] The values of $J_{12}$ and $J_{34}$ are not distinguished by the analysis, and their difference is more accurately determined than their sum. Similar remarks apply to $J_{56}$ and $J_{78}$.

dependent (increasing from 9.4 Hz at 35 °C to 13.4 Hz at 156 °C), which introduces complications.

1-*Methyl*-4-*nitrosopiperazine* (VII).—The room-temperature proton spectrum of this compound consists [2,3] of a pair of $[AB]_2$-type sub-spectra (from the two $CH_2CH_2$ moieties), plus a singlet for the NMe group. Spectral analysis yields the chemical shifts and coupling constants reported in Table 2; the coupling constants agree well with previously

reported values [2,3] for a $CCl_4$ solution. The computer program DNMR 3 was used to simulate spectra ($\alpha$-$CH_2$ region only) obtained at higher temperatures and hence to obtain rate data which were used to give $\Delta G^{\ddagger}$ as reported in Table 1.

*4-Nitrosomorpholine* (VIII).—In principle, this compound is of the same exchange type as (VII), and the chemical shifts and coupling constants obtained from the spectrum at ambient probe temperature are given in Table 3; the latter parameters agree well with those found [2,3] for a $CCl_4$ solution. However, linewidths were rather high and the data are unlikely to be very accurate. Simulation of exchange-affected spectra ($\alpha$-$CH_2$ region only) using DNMR 3 did not lead to good exchange-rate data but the value of $\Delta G^{\ddagger}$ in the region of coalescence, which we quote in Table 1, should be reasonably accurate.

## DISCUSSION

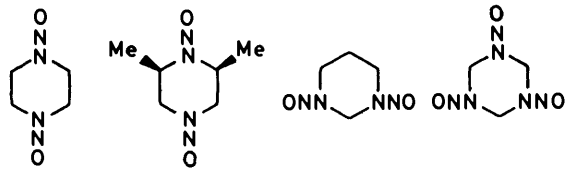
Band-shape fitting methods are likely to yield reasonably accurate values of $\Delta G^{\ddagger}$ in the vicinity of the coalescence temperature. Table 1 gives values of $\Delta G^{\ddagger}$ at $T_c$, obtained both by bandshape fitting and directly from observation of coalescence, for internal rotation about the *N*-nitroso-bond. It is encouraging to note that where both methods have been used the agreement is good. The data for $\Delta G^{\ddagger}$ are summarised in Figure 1, in order of increasing magnitude (in most cases this is the same order as $T_c$). The variations are quite substantial and clearly reflect real chemical effects; they will be discussed in terms of energetics, ignoring possible variations in the entropy contributions to $\Delta G^{\ddagger}$ (such neglect is also implicit in the attempt to compare data obtained from different coalescence temperatures).

Incorporation of the amino-nitrogen of a nitroso-group into a six-membered ring does not appear, of itself, to influence $\Delta G^{\ddagger}$ substantially. Thus the value for (VII) is 92 kJ mol$^{-1}$ at 438 K, which is closely similar to the result of Glidewell [11] for nitrosopiperidine (93.0 kJ mol$^{-1}$ at 450 K); these values may be compared to that for $Me_2NNO$, which is given as 97.0 kJ mol$^{-1}$ at 450 K in the most accurate determination [11] to date. Our result for nitrosomorpholine (85 kJ mol$^{-1}$ at 449 K) is appreciably lower, and it is not clear why this is so. The value for (IV) is substantially higher than that for (VIII), which can perhaps be accounted for by the additional rigidity of the ring for (IV) (the methyl groups being constrained to be equatorial).

The remaining data may be rationalised by considering the likely influences on the energy of the equilibrium conformation relative to that of the transition state. Thus it is known [2] that both (I) and (II) exist with the ring approximately in the chair form but with the methyl groups axial because of strong steric interactions between the oxygen and the *syn*-methyl group when the latter is equatorial. However, such conformations introduce 1,3-diaxial interactions which must destabilise the ground state. On the other hand, in the transition state the interaction between the nitroso and the *syn*-methyl groups is removed and the ring is no longer constrained to the form with methyl groups axial. Therefore a lowered barrier to N–N internal rotation is to be expected, as is found in practice. In fact our data indicate that the 1,3-diaxial interaction between axial methyl groups must be of the order of or greater than 11 kJ mol$^{-1}$, which compares well with other estimates [22] for related compounds. A similar situation has been found [12] for 1,4-dinitrosopiperazine (XI) and its *cis*-2,6-dimethyl derivative (XII). The barrier, $\Delta G^{\ddagger}$, for the 1-nitroso-group in the latter compound is 17 kJ mol$^{-1}$ below that for the former at 400 K whereas the 4-nitroso-group in (XII) has a higher barrier. Analogous conclusions for related systems have also been reported (see Lunazzi *et al.*[16] and refs. therein). It should be noted that $\Delta G^{\ddagger}$ has been reported [8,16] as 82 kJ mol$^{-1}$ for (I). The difference of 3 kJ mol$^{-1}$ from our value may be due to experimental errors or perhaps solvent effects (ref. 8 used *ortho*-dichlorobenzene as a solvent and obtained a methyl chemical shift difference of only 17.2 Hz; ref. 16 used nitrobenzene as a solvent).

The situation for (III), which gives $\Delta G^{\ddagger} = 77$ kJ mol$^{-1}$ at 371 K, is somewhat similar, though in this case the steric strain caused by the proximity of the nitroso-oxygen and a *syn*-methyl group results in the adoption of a twist-boat conformation for the ring, as shown in (X). Once more, the strain would be relieved in the transition state, so that a lowered barrier results.

A rather different reason for the lower barrier in (III) could be suggested, namely the fact that it is a *di*-nitroso-compound. The existence of a barrier implies a contribution from resonance structures involving a N=N double bond and a formal positive charge on the amino-nitrogen. For (III) this would mean two formal positive charges in proximity across the ring, resulting in destabilisation and a consequent decrease in $\Delta G^{\ddagger}$. Such reasoning is invoked by Glidewell [11] for the lowered barriers in (XIII) * ($\Delta G^{\ddagger} = 84$ kJ mol$^{-1}$ at 450 K) and (XIV) ($\Delta G^{\ddagger} = 72$ kJ mol$^{-1}$ at 450 K). However, this is less likely to be important for 1,4-dinitroso-compounds, and Höfner, Stephenson, and Binsch [12] find $\Delta G^{\ddagger} = 93.4$ kJ mol$^{-1}$ at 400 K for 1,4-dinitrosopiperazine (XI) itself,



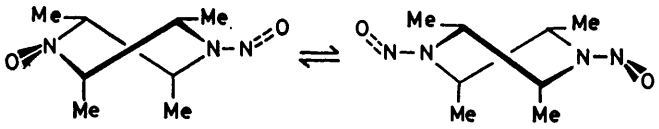

(XI) (XII) (XIII) (XIV)

very close to the values for (VII) and for nitrosopiperidine.[11] Thus the two nitroso-groups in (XI) appear to behave independently, and this is confirmed by the fact that concerted double rotations appear [12] to be absent in (XI) and related compounds.

Among the eight compounds studied (III) is actually unique since interconversion between equivalent con-

* Ref. 12 gives values of $\Delta G^{\ddagger} = 76.1$, 75.5, and 76.9 kJ mol$^{-1}$ for the three different single internal rotations for this compound at 340 K.

formations necessarily involves not just one process (internal rotation about one N–N bond), but three, *viz.* internal rotation about *both* N–N bonds plus ring inversion, as shown in (XV) (the processes may be con-



(XV)

certed, or consecutive—the former appears likely to minimise the barrier). In principle, this situation affects the meaning of the barrier to the process, but we do not believe it invalidates the above discussion.

On such arguments it might be anticipated that an even lower barrier should be found for (V), which is not the case. The ground-state conformation of this compound is said [23] to be essentially 'coplanar' and we feel it is unlikely that the strain due to interaction between the nitroso-group and a *syn*-equatorial methyl can be relieved by such conformational changes as occur for (I) or (III). Yet clearly the ring must be twisted in some way. Lunazzi *et al.*[16] suggest a twist-boat form for a related triazene and quote data for $^{13}C$ chemical shifts to support their conclusion. An alternative possibility is that twisting might occur so as to lock the nitroso-oxygen between the two *syn*-methyl groups (this may be regarded as a partial rotation of the nitroso-group) so that although the ground-state energy is raised by steric strain (or by the partial rotation), the full internal rotation involves the nitroso-oxygen brushing past methyl groups, thus also raising the energy of the transition state. The resulting barrier depends on a balance between these two effects. In this context it may be noted that for (I), (II), and (III) there exists in each case a pathway for internal rotation which does *not* involve the nitroso-oxygen brushing past a methyl group. It should be noted, however, that Lunazzi *et al.*[10] find *equal* barriers ($\Delta G^{\ddagger} = 82$ kJ mol$^{-1}$) for (I) and (V); this result is not completely in agreement with our own.*

If such reasoning is applied to (VI), which has a high barrier, it is clear that the steric effect on the transition state must predominate over that in the ground state. We believe this to be reasonable, in spite of the fact that the ring geometry implies a somewhat greater distance of closest approach between the nitroso-oxygen and a methyl group during the internal rotation. This belief is based on the difference in geometry between a 5-membered and a 6-membered ring. For the latter some strain is necessary for the nitroso-oxygen to lie between the *syn*-methyls whereas for the former such a situation is a natural consequence of the ring geometry. Cooney, Brownstein, and ApSimon [9] have shown that the barriers to N–N internal rotation for nitrosopyrrolidine and nitrosopiperidine are very similar, so that the mere involvement of a 5-membered ring has little effect, and our observations can only be accounted for by the presence of the methyl groups.

During the above discussion it has been assumed that other dynamic processes such as ring inversion and nitrogen inversion [for the NMe of (II) and (VII)] are fast compared to N–N internal rotation, and that consequently conformation of the ring and at NMe will adjust so as to relieve strain in the transition state where possible, thus minimising the barriers. We do not regard N–N internal rotation and ring inversion, for instance, as necessarily *consecutive* processes.

For all the compounds studied, the internal rotation process (when suitably combined with ring and NMe inversion where necessary) involves interconversion of equivalent conformations. There are thus no parameters describing relative populations that need to be taken into account. However, in several cases there may be metastable intermediates. We have neglected such possibilities in our bandshape simulation. Ahrens and Strehlow [24] discuss the criteria for validity of such an approach.

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* Dr. Lunazzi informs us that he has confirmed both his own results and our for (V); it may be concluded that the discrepancies are due to solvent effects.

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