Nitrogen Inversion in Cyclic *N*-Chloroamines and *N*-Methylamines

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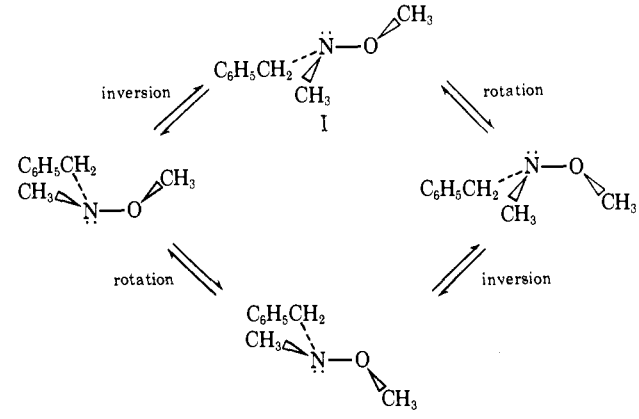
Abstract: Pyramidal inversion about nitrogen has been studied in saturated, cyclic amines containing from four to seven members. Only the nitrogen atom in each ring carries a substituent (chlorine or methyl). The α protons, when decoupled from the β protons, in all cases change from a singlet to an AB quartet at lower temperatures. Complete line-shape analyses are reported for nitrogen inversion in *N*-methylazetidine ($CHClF_2$, E_a = 12.5 kcal/mol; log A = 15.3), *N*-methylpyrrolidine ($CHClF_2$, E_a = 10.2; log A = 15.0), *N*-chloropyrrolidine ($CFCl_3$, E_a = 13.8; log A = 16.4), and *N*-chlorohomopiperidine ($CHCl_2F$, E_a = 11.2; log A = 15.3); coalescence-temperature analyses are given for nitrogen inversion in *N*-chloroazetidine ($CHClF_2$, $\Delta G^{\pm}(-20)$ = 13.4 kcal/mol) and *N*-methylhomopiperidine ($CHClF_2$, $\Delta G^{\pm}(-125)$ = 6.8). The barrier for *N*-chlorohomopiperidine is found to be relatively insensitive to changes in solvent. The methyl-substituted five- and seven-membered rings offer the first unambiguous dynamic nmr examples of nitrogen inversion unhindered by ring strain or electronegative substituents. The observed rate processes in the six-membered rings, *N*-methylpiperidine (reported previously) and *N*-chloropiperidine (CH_2Cl_2, E_a = 17.0 kcal/mol; log A = 15.5), are thought to be ring reversal rather than nitrogen inversion.

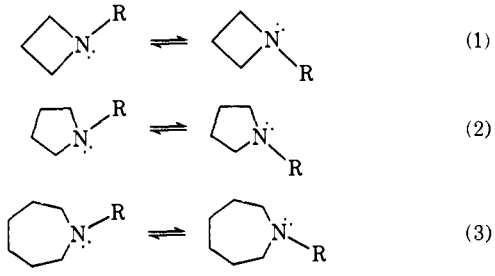
Unimolecular, pyramidal inversion about nitrogen has been the subject of an increasing number of investigations.[2] The rate of nitrogen inversion has frequently proved to be amenable to measurement by the convenient dynamic nuclear magnetic resonance (dnmr) method. The earliest such experiments[3] relied on systems such as aziridines with ring strain to raise the barrier to the more accessible range above 10 kcal/mol. Acyclic systems and rings of larger size were avoided because it was thought that the rates would be too rapid for the method. Bottini and Roberts[4] reported that *N*-alkyl-substituted azetidines, pyrrolidines, piperidines, and morpholines, in contrast to the aziridines, showed temperature-independent nmr spectra down to −77°. We report in the present paper that nitrogen inversion rates may be measured in these saturated nitrogen heterocycles by means of dnmr methods by operation at higher magnetic fields and lower temperatures.

Incorporation of nitrogen into a ring for inversion studies has a particular advantage over open-chain systems. In acyclics, the process of rotation about bonds from nitrogen may not be differentiable from nitrogen inversion by the nmr observables. Thus in the hydroxylamine I, the rate-determining step by which the methylene protons are brought into equivalence may be either N inversion or N–O bond rotation. This mechanistic ambiguity has plagued all studies of acyclic nitrogen systems,[5] and has resulted in



numerous doubtful or even incorrect assignments of the physical process responsible for a particular set of spectral changes.

No such problem exists for studies of four-, five-, and seven-membered azacycles (eq 1–3). Various pseudorotational or ring-puckering processes do occur in these



molecules, but the rates are much too rapid (barriers <5 kcal/mol) to have any influence on the nmr spectra.[6] Six-membered rings, however, do not share this mech-

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(2) For a complete review of the field, see J. B. Lambert, *Top. Stereochem.*, in press; J. M. Lehn, *Fortschr. Chem. Forsch.*, **15**, 311 (1970); A. Rauk, L. C. Allen, and K. Mislow, *Angew. Chem., Int. Ed. Engl.*, **9**, 400 (1970).

(3) A. T. Bottini and J. D. Roberts, *J. Amer. Chem. Soc.*, **78**, 5126 (1956).

(4) A. T. Bottini and J. D. Roberts, *ibid.*, **80**, 5203 (1958).

(5) D. L. Griffith and J. D. Roberts, *ibid.*, **87**, 4089 (1965); A. H. Cowley, M. J. S. Dewar, and W. R. Jackson, *ibid.*, **90**, 4185 (1968); M. J. S. Dewar and B. Jennings, *ibid.*, **91**, 3655 (1969); J. R. Fletcher and I. O. Sutherland, *Chem. Commun.*, 706 (1969); J. E. Anderson, D. L. Griffith, and J. D. Roberts, *J. Amer. Chem. Soc.*, **91**, 6371 (1969); M. Raban and G. W. J. Kenney, Jr., *Tetrahedron Lett.*, 1295 (1969); M. Raban, G. W. J. Kenney, Jr., and F. B. Jones, Jr., *J. Amer. Chem. Soc.*, **91**, 6677 (1969); J. M. Lehn and J. Wagner, *Chem. Commun.*, 1298 (1968); M. G. Barlow and K. W. Cheung, *ibid.*, 870 (1969).

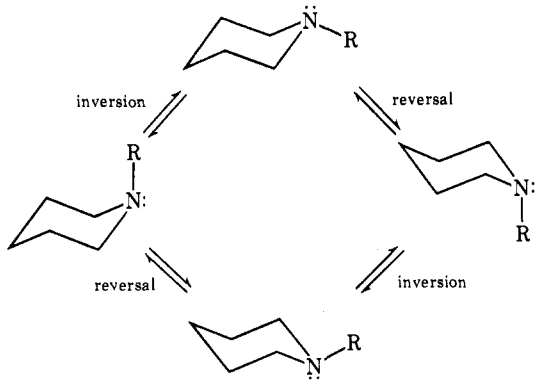
(6) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **83**, 4537 (1961); L. A. Carreira and R. C. Lord, *J. Chem. Phys.*, **51**, 2735 (1969).

Table I. Activation Parameters for Nitrogen Inversion or Ring Reversal in Cyclic *N*-Chloroamines

Compd	Solvent	E_a, kcal/mol	log A	$\Delta H^{\ddagger}$(25°), kcal/mol	$\Delta S^{\ddagger}$(25°), eu	$\Delta G^{\ddagger}$(T_c, °C), kcal/mol	Corr coeff
II[a]	CH_2Cl_2	11.2	15.0	10.6	8.2	9.2 (−86)[b]	0.997
	$CHCl_2F$	11.2	15.3	10.6	9.4	9.0 (−87)[b]	0.995
	CF_2Cl_2					8.8 (−93)[c]	
	CD_3OD					8.9 (−91)[c]	
III[d]	CH_2Cl_2	17.0	15.5	16.4	10.6	13.5 (−1)[b]	0.994
IV[a]	$CFCl_3$	13.8	16.4	13.2	14.5	10.3 (−68)[b]	0.998
V[a]	$CHClF_2$					~13.4 (−20)[c]	

[a] Nitrogen inversion. [b] Complete line-shape analysis. [c] Coalescence-temperature method; at 90 MHz, $\Delta\nu$ for II in either solvent is 36.3 Hz and J = 12.1 Hz, $\Delta\nu$ for V is about 3 Hz. [d] Ring reversal.

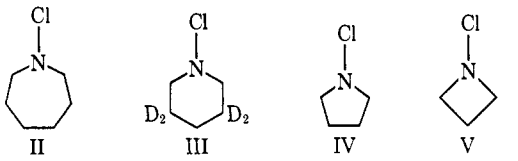
anistic simplicity, since the process of ring reversal is competitive with nitrogen inversion.[7] For the four-, five-, and seven-membered rings, hindered nitrogen inversion may be detected by observation of nonequivalent α protons, and the barrier may be measured by following the conversion of the A_2 spectrum of these protons at room temperature to an AB quartet at low temperatures.[8] For identical spectral changes in six-membered rings, however, either ring reversal or atomic inversion could be rate determining.



Two substituents on nitrogen were utilized in the present study. The methyl group conveys no inductive rate retardation[2] and therefore serves as a useful standard of comparison for all other substituents.[9] *N*-Methylhomopiperidine, which is strain free, should therefore comprise as close a model as possible to "pure" nitrogen inversion in acyclic systems.[10] The chlorine atom is the second substituent studied. The well-known rate-retarding effect of chlorine[11] would be expected to raise the barrier throughout the series. The unsubstituted amines have also been examined for torsional or inversional processes.

Results and Discussion

***N*-Chloroamines.** The *N*-chloroamines were prepared by treatment of the parent amines with *N*-chlorosuccinimide. Various techniques were used to remove the coupling between the α and β protons in order that the simple A_2 to AB change in the α resonance be observed. Double irradiation of the β protons was employed for the seven-membered *N*-chlorohomopiperidine (II). The activation parameters from the complete line-shape analyses for CH_2Cl_2 and $CHCl_2F$ (Freon 21) as solvent are given in Table I, together with coalescence-temperature measurements in CF_2Cl_2 and CD_3OD. The rate data are collected for all systems in the experimental section. For *N*-chloropiperidine (III), the β positions were deuterated; the complete line-shape parameters are given in the table. By way of example, the spectra for III as a function of temperature are presented in Figure 1. Double irradiation was utilized for *N*-chloropyrrolidine (IV),[12] and the kinetic results may be found in the table.



The singlet for the α protons of *N*-chloroazetidine (V), resulting from double irradiation of the β protons at 90 MHz, was found not to change as the temperature was lowered to −80°. Since the coalescence temperature was expected to be about −50°,[13] this result can only be explained by an accidental coincidence, or near coincidence, of chemical shifts. We were surprised to observe, however, that the undecoupled spectra of the α protons were temperature dependent (Figure 2). The highest field component of the triplet reversibly broadens through a coalescence at about −20° to an indistinct doublet at −40°. The center peak broadens only slightly, and the lowest field component remains almost unchanged. Thus, a rate process that is invisible to the two-spin system becomes manifest in the six-spin system. Because of the complex nature of these changes, only coalescence data could be obtained.

Prior to these studies,[7,9] the only reported examples of hindered nitrogen inversion of an *N*-chloroamine, aside from three-membered rings, were 3,3-dimethylazetidine[13,14] and a 7-azabicyclo[2.2.1]heptyl system.[15] The mechanism of interconversion responsible for the spectral changes in II, IV, and V must be nitrogen inversion. The torsional processes that can operate in

(7) J. B. Lambert and W. L. Oliver, Jr., *Tetrahedron Lett.*, 6187 (1968).
(8) G. Binsch, *Top. Stereochem.*, 3, 97 (1968).
(9) J. B. Lambert and W. L. Oliver, Jr., *J. Amer. Chem. Soc.*, 91, 7774 (1969).
(10) M. J. S. Dewar and W. B. Jennings, *Tetrahedron Lett.*, 339 (1970); C. H. Bushweller and J. W. O'Neil, *J. Amer. Chem. Soc.*, 92, 2159 (1970). Low barriers, most probably due to nitrogen inversion, have been observed by these authors, although the acyclic ambiguity formally remains.
(11) S. J. Brois, *ibid.*, 90, 506, 508 (1968); D. Felix and A. Eschenmoser, *Angew. Chem., Int. Ed. Engl.*, 7, 224 (1968).
(12) We are indebted to Mr. Richard Egan of Abbott Laboratories, North Chicago, Ill., for this set of 100-MHz spectra.
(13) J. M. Lehn and J. Wagner, *Chem. Commun.*, 148 (1968).
(14) N-Substituted homopiperidine and an azabicyclo[2.2.2]octane have now also been studied by J. M. Lehn and J. Wagner, *ibid.*, 414 (1970).
(15) V. Rautenstrauch, *ibid.*, 1122 (1969).

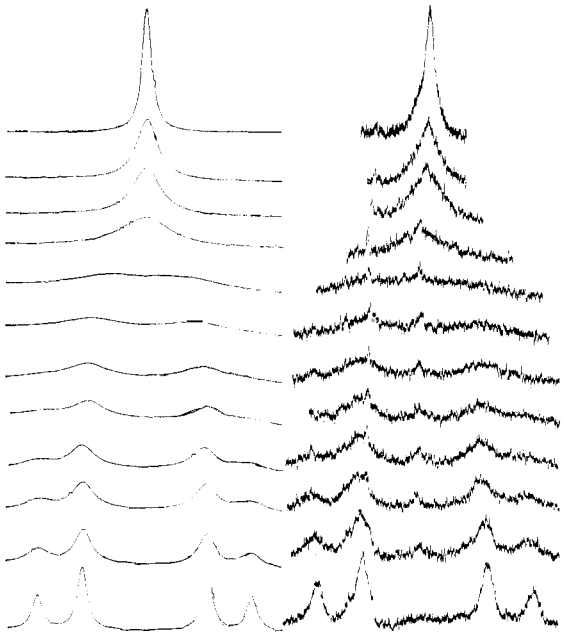


Figure 1. The observed (right) and calculated (left) 60-MHz proton spectra of *N*-chloropiperidine-*3,3,5,5-d*$_4$ (III) as a function of temperature. The spectral parameters are given in Table III. The temperatures for the extreme spectra are −40 and +24°. Small temperature-independent peaks are due to impurities.

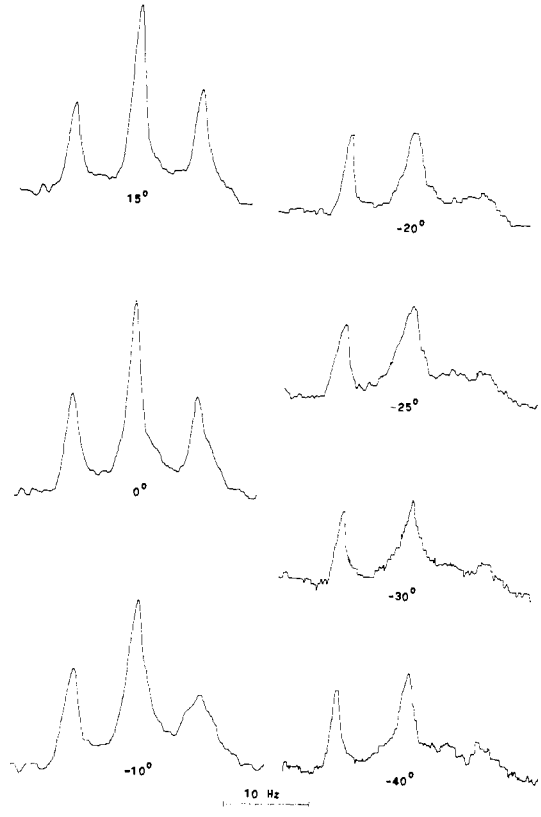


Figure 2. The 90-MHz spectrum of the α proton of *N*-chloroazetidine (V) as a function of temperature.

these rings are of too low a barrier to influence the spectrum. Ring puckering and pseudorotational modes have barriers well below 5 kcal/mol in systems with no more than one substituent.[6] To furnish additional substantiation of this assumption, we examined the spectral properties of the parent amines (azetidine, pyrrolidine, and homopiperidine). Because of rapid intermolecular exchange of the hydrogen on nitrogen, only torsional processes may be observed. In all cases, the spectra remained unchanged down to −150°. Tetrahydrofuran also exhibited a temperature-independent spectrum to −150°.

It may therefore be considered established that the observed process for II, IV, or V is the configurational inversion about nitrogen. The chlorine atom serves to increase the barrier to inversion[2,11] relative to that for a nitrogen atom with no substituents of electronegativity greater than carbon. As a result, the *N*-chloroamines uniformly invert more slowly than the analogous *N*-methylamines to be discussed in the next section.

Methanol has been said to slow the rate of nitrogen inversion,[16] because a hydrogen bond must be broken and re-formed during the process. In several cases, however, the methanol effect has not been observed.[17] *N*-Chlorohomopiperidine serves as an additional example in which the effect is absent (Table I). Apparently the method does not always furnish a reliable distinction between atomic inversion and torsional processes.

The rate of nitrogen inversion in a homologous series such as II, IV, and V is determined primarily by the magnitude of the C–N–C angle. The sp^2 transition state to inversion has bond angles of about 120°. Therefore, lower barriers will be associated with molecules with ground-state C–N–C angles close to this value.[2] This trend is evident in the *N*-chloro series. In the three-membered ring, the barrier is above the dnmr range[11] (E_a > 24 kcal/mol[18]). We find Arrhenius activation energies of about 16 kcal/mol for *N*-chloroazetidine,[19] 13.8 for *N*-chloropyrrolidine, and 11.2 for *N*-chlorohomopiperidine, with bond angles increasing from about 90° in V to 112° in II.

The spectra for the six-membered ring are much more difficult to interpret because of the ambiguity between atomic inversion and ring reversal. As with the other systems, the α protons of III exhibit an A_2 spectrum that changes to an AB quartet at lower temperatures. Only one AB spectrum is observed, and its chemical-shift difference is invariant from −40 to −80°. The observed barrier of 17 kcal/mol is higher than those in any of the other systems (II, IV, V). If the process responsible for the spectral changes were nitrogen inversion, the barrier for III should have been lower than those for the more strained IV and V. Nitrogen inversion may therefore be excluded as the rate-determining process.[19a] Nonetheless, inversion must undoubtedly be slow on the nmr time scale below −40°, by comparison with the other compounds. The observation of only one AB spectrum can be explained either by the presence of only one conformer, pre-

(16) F. G. Riddell, J. M. Lehn, and J. Wagner, *Chem. Commun.*, 1403 (1968); J. E. Anderson and A. C. Oehlschlager, *ibid.*, 284 (1968); M. Raban, F. B. Jones, Jr., E. H. Carlson, E. Banucci, and N. A. LeBel, *J. Org. Chem.*, **35**, 1496 (1970).

(17) J. E. Anderson, *J. Amer. Chem. Soc.*, **91**, 6374 (1969); J. R. Fletcher and I. O. Sutherland, *Chem. Commun.*, 687 (1970).

(18) M. Jautelat and J. D. Roberts, *J. Amer. Chem. Soc.*, **91**, 642 (1969).

(19) This number is estimated from the observed value of $\Delta G^{\ddagger}$ and the trend between E_a and $\Delta G^{\ddagger}$ for the other entries in Table I.

(19a) Note Added in Proof. This same conclusion has been reached by H. Kessler and D. Leibfritz, *Tetrahedron Lett.*, 4297 (1970).

Table II. Activation Parameters for Nitrogen Inversion or Ring Reversal in Cyclic *N*-Methylamines

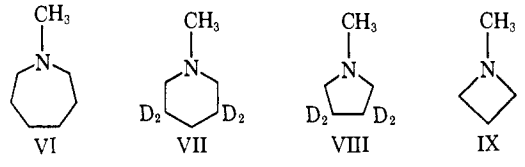
Compd	Solvent	E_a, kcal/mol	log A	$\Delta H^{\ddagger}(25°)$, kcal/mol	$\Delta S^{\ddagger}(25°)$, eu	$\Delta G^{\ddagger}(T_c, °C)$, kcal/mol	Corr coeff
VI[a]	$CHClF_2$					6.8 (−125)[b]	
VII[c]	CD_3OD	14.4[d]	14.8[d]				
VIII[a]	$CDClF_2$	10.2	15.0	9.6	7.9	8.3 (−98)[e]	0.999
IX[a]	$CHClF_2$	12.5	15.3	11.9	9.5	10.0 (−69)[e]	0.998

[a] Nitrogen inversion. [b] Coalescence-temperature method; at 90 MHz, $\Delta\nu$ for VI is 44 Hz. [c] Ring reversal. [d] Data from ref 20. [e] Complete line-shape analysis.

sumably with chlorine equatorial, or by a superposition of the AB spectra from the two conformers.

In summary, we believe that for III ring reversal is rate determining, but a synchronous process involving both ring reversal and nitrogen inversion cannot be excluded. The value of E_a for ring reversal in *N*-chloropiperidine is about 3 kcal/mol higher than those for piperidine or *N*-alkylpiperidines.[20] Harris and Spragg[21] correlated the free energy of activation for ring reversal in some morpholines and piperazines with the torsional barriers in model acyclic compounds. It may be that the high barrier in III reflects a high torsional barrier for the $NCl-CH_2$ bond, although it may also be due to increased difficulty in deforming the C–NCl–C valence angle.

***N*-Methylamines.** *N*-Methylhomopiperidine (VI) and *N*-methylazetidine (IX) were prepared from the corresponding unsubstituted amines. *N*-Methylpyrrolidine (VIII) was produced by the reaction of 1,4-dibromobutane with methylamine. *N*-Methylpiperidine (VII) was prepared for an earlier study.[20] Double



VI VII VIII IX

irradiation of the β protons of the azetidine IX provided a typical set of spectra (A_2 to AB) from which rates could be determined (Table II). This technique failed for both VI and VIII, since the chemical-shift separations at 90 MHz coincided precisely with the 60-Hz beat from the decoupler. Consequently, only coalescence kinetics are listed in Table II for the homopiperidine VI. The pyrrolidine VIII, however, was prepared fully deuterated in the β position by the method outlined below. The α protons of the deu-

$$CH_3O_2CCH_2CH_2CO_2CH_3 \xrightarrow[NaOCH_3]{CH_3OD}$$

$$CH_3O_2CCD_2CD_2CO_2CH_3 \xrightarrow{LiAlH_4}$$

$$HOCH_2CD_2CD_2CH_2OH \xrightarrow{PBr_3}$$

$$BrCH_2CD_2CD_2CH_2Br \xrightarrow[2.\ KOH]{1.\ CH_3NH_2} \text{VIII}$$

terated derivative produce the expected A_2 to AB change, which could be analyzed by the complete line-shape method (Table II). The kinetics for *N*-methylpiperidine-*3,3,5,5-d*$_4$ (VII) have been reported previously.[20] A coalescence phenomenon produces an AB spectrum for both the α and the γ protons at −50°. We examined the spectrum in cyclopropane down to −150° and observed no further changes. Specifically, the *N*-methyl resonance remains an unsplit singlet.

In the previous section, we showed that hindered nitrogen inversion is not restricted to highly strained rings but may be readily observed in four-, five-, and seven-membered cyclic *N*-chloroamines. The observations with the *N*-methylamines in this section prove that the rate-retarding chlorine substituent is not necessary to place nitrogen inversion in the observable dnmr range. *N*-Methylhomopiperidine furnishes the simplest unambiguous example of nitrogen inversion in a trialkylamine yet observed.[10,14] The molecule has none of the constraints (electronegative substituents, ring strain) previously placed on nitrogen inversion to permit the observation of atomic inversion by dynamic nmr spectroscopy.

The trend in barrier height for this series parallels that for the *N*-chloroamines. As ring strain diminishes and the C–N–C bond angle opens up, the barrier decreases. In 1,2,2-trimethylaziridine, the Arrhenius energy of activation is 24 kcal/mol.[18] For *N*-methylazetidine, we observe 12.5;[13] for *N*-methylpyrrolidine, 10.2; and for *N*-methylhomopiperidine, about 9 kcal/mol.[19] By comparison with the figures in Table I, it may be seen that replacement of methyl by chlorine raises the barrier by 2–4 kcal/mol.

The barrier observed for the *N*-methyl six-membered ring (14.4 kcal/mol) again exceeds those for the more highly strained four- and five-membered rings. We may therefore confirm[20] that the rate-determining process for this system must be ring reversal rather than atomic inversion.[19a] The fact that only one AB spectrum for the α protons and one peak for the methyl protons are observed down to −150° again requires either that the equatorial conformer predominate (>95%) or that there be an accidental coincidence of resonances.

Experimental Section

Nmr spectra were measured on Varian A-60 and T-60 spectrometers and the Bruker 90-MHz HFX-10 spectrometer.[22] Infrared spectra were recorded on Beckman IR-5 and IR-10 spectrometers. Kinetic analyses were performed on CDC 3400 and 6400 computers equipped with the Calcomp plotting accessory.

***N*-Chloropiperidine-*3,3,5,5-d*$_4$ (III).** A mixture of 1.0 g of 1,5-dibromopentane-*2,2,4,4-d*$_4$[23] and 5.0 g of methanol saturated with ammonia was heated in a sealed tube for 5 hr. The methanol and excess ammonia were removed by bulb-to-bulb distillation, and the remaining solid was dissolved in the minimum amount of water. Pellets of KOH were added until crude piperidine-*d*$_4$ floated to the top of the solution. After purification by bulb-to-bulb distillation, the deuterated piperidine was dissolved in ether and added

(20) J. B. Lambert, R. G. Keske, R. E. Carhart, and A. P. Jovanovich, *J. Amer. Chem. Soc.*, **89**, 3761 (1967).
(21) R. K. Harris and R. A. Spragg, *J. Chem. Soc. B*, 684 (1968).
(22) We are grateful to the National Science Foundation for a grant that made possible the purchase of this instrument.
(23) J. B. Lambert and R. G. Keske, *J. Org. Chem.*, **31**, 3429 (1966).

to an ethereal solution of 0.15 g of *N*-chlorosuccinimide. After stirring for 1 hr at room temperature, the solution was washed twice with water and once with dilute H_2SO_4 and dried over sodium sulfate. The ether was removed leaving the lachrymatory product.

N-Chloropyrrolidine (IV). To 1.0 g of *N*-chlorosuccinimide in ether was added 2.0 g of pyrrolidine (Aldrich Chemical Co.). After stirring for 2 hr, the ether solution was washed with water and dilute acid and dried over sodium sulfate. After removal of the ether, the product was purified by bulb-to-bulb distillation.

N-Chlorohomopiperidine (II). To 2.0 g of *N*-chlorosuccinimide in ether was added 1.0 g of homopiperidine (Aldrich Chemical Co.). The mixture was stirred for 1 hr, washed with water and dilute acid, and dried over sodium sulfate. Removal of the ether and bulb-to-bulb distillation yielded the pure product.

Azetidine was prepared by the method of Wadsworth.[24]

N-Chloroazetidine (V). To 0.3 g of *N*-chlorosuccinimide in ether was added 0.15 g of azetidine. The mixture was stirred for 1 hr, washed with water and dilute acid, and dried over sodium sulfate. The product was purified by bulb-to-bulb distillation.

N-Methylhomopiperidine (VI).[25] To 13 ml of formic acid was added 11.2 g of homopiperidine (Aldrich) with cooling from running water. This mixture was added to 12 g of 36% formaldehyde solution and the resulting solution heated to 95–100°. When CO_2 began to evolve, the flask was removed from the oil bath. After gas evolution had ceased, the mixture was heated for 7 hr at 95–100°. The mixture was allowed to cool and 50 ml of 2 *N* HCl was added. The water was removed by distillation *in vacuo*. leaving a yellow oil that was dissolved in 40 ml of water. To this solution, 50 ml of saturated aqueous KOH was added, causing the amine to separate. The crude product was distilled to give 5.1 g of VI, bp 140–141°.

N-Methylazetidine (IX). To 0.15 g of azetidine in refluxing methanol was added 0.2 g of methyl iodide. Ten minutes after the addition was completed, the mixture was cooled and 70 ml of ether was added to precipitate the salt, which was isolated by filtration. The solid was dissolved in the minimum amount of water, and KOH pellets were added until the amine floated to the top of the solution.

Dimethyl Succinate-*2,2,3,3-d*$_4$. Dimethyl succinate (Aldrich Chemical Co., 73 g, 0.5 mol) was refluxed with 82 ml (4 mol) of methanol-d_1,[23] to which 1 g of sodium had been added. After 1 day the exchanged methanol was removed by distillation. After five such exchanges, 8 ml of D_2O was added to the remaining material, which was extracted with ether. The organics were washed twice with 2-ml portions of D_2O. The solution was dried over magnesium sulfate, the ether removed, and the product distilled under vacuum to yield 67.1 g (92%) of 90% deuterated diester.

1,4-Butanediol-*2,2,3,3-d*$_4$. To 22 g (0.615 mol) of lithium aluminum hydride in dry ether, 67 g (0.507 mol) of diester was added cautiously over 6 hr and the mixture was refluxed overnight. To this mixture, 84 ml of 5% aqueous NaOH was added. The ester was decanted, tetrahydrofuran was added to the solid, and the mixture was refluxed overnight. The solution was filtered and the combined organics were stripped of solvent and distilled to yield 26.0 g (49%) of diol.

1,4-Dibromobutane-*2,2,3,3-d*$_4$. Phosphorus tribromide (80 g) was added to 26 g of deuterated diol. The solution was refluxed overnight, water was added, and the mixture was extracted with CH_2Cl_2. The product was distilled to yield 53 g (0.238 mol, 93%) of deuterated dibromide.

N-Methylpyrrolidine-*3,3,4,4-d*$_4$ (VIII). Methylamine (1.0 g of 40% aqueous solution), 1,4-dibromobutane-*2,2,3,3-d*$_4$ (1.0 g), and 5 ml of methanol were placed in a sealed tube and heated to 110° for 4 hr. The solvent and the cyclic amine were bulb-to-bulb distilled from the methylamine hydrobromide. Dry HCl gas was passed through the distillate, which was then redistilled to leave methylpyrrolidine hydrochloride. This solid was taken up in the minimum amount of water, and the amine was freed by the addition of KOH pellets. The product was purified by bulb-to-bulb distillation. The nmr spectrum showed that the product was 90% deuterated.

Kinetic Measurements. Complete line-shape analyses were carried out for *N*-chloropiperidine-*3,3,5,5-d*$_4$ (III) in CH_2Cl_2, *N*-chloropyrrolidine (IV) in $CFCl_3$, *N*-chlorohomopiperidine (II) in CH_2Cl_2 and $CHCl_2F$, *N*-methylpyrrolidine-*3,3,4,4-d*$_4$ (VIII) in $CHClF_2$, and *N*-methylazetidine (IX) in $CHClF_2$. The spectra of the α protons were examined as a function of temperature. In each case an A_2 singlet at room temperature became an AB quartet at low temperatures. Rates were measured at intermediate temperatures by fitting the observed spectra with line shapes obtained from trial-and-error values of the mean lifetime ($\tau = 1/k$). The error in τ is about 10%. Appropriate corrections were made when the relaxation time (T_2) was temperature dependent. The spectral parameters are given in Table III. The derived activation parameters are presented in Tables I and II.

Table III. Spectral Parameters

Compd	$\Delta\nu_{AB}$, Hz	J_{AB}, Hz	T_c, °C	$\Delta G_c^{\ddagger}$, kcal/mol[a]
II-CH_2Cl_2	36.3[b]	12.1	−86[b]	9.3
II-$CHCl_2F$	36.3[b]	12.1	−87[b]	9.2
III	37.2[c,d]	10.2	−1[c]	13.7
IV	26.3[e]	10.0	−68[e]	10.3
VIII	94.4[b]	8.8	−98[b]	8.4
IX	41.0[b]	4.5	−69[b]	10.2

[a] These figures are calculated from the rate at T_c, $k = [\pi(\Delta\nu^2 + 6J^2)/2]^{1/2}$; they compare very favorably with the values for $\Delta G^{\ddagger}$ calculated from the CLS rates and listed in Tables I and II. [b] 90 MHz. [c] 60 MHz. [d] The data are for the α protons; for the γ protons, $\Delta\nu$ = 23.7 Hz[c] and J = 12.0 Hz. [e] 100 MHz; see ref 12.

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