Inversion at Trivalent Nitrogen: Application of the MNDO and MINDO/3 Semiempirical Molecular Orbital Methods

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The recently developed MNDO SCF method with full geometry optimization and standard parameterization gives nitrogen inversional barriers in aziridine derivatives which are in close agreement with experimental data (mean deviation 1.7 kcal mol^{-1}). Results for acyclic amino compounds are less accurate (mean deviation 3.5 kcal mol^{-1}). The calculated barriers in some primary NH_2X compounds are too high whereas those in acyclic tertiary amines tend to be too low. The older MINDO/3 method gives better results for ammonia and some primary NH_2X molecules, but seriously underestimates inversional potentials in amines and aziridines. Both rotational and nitrogen inversional potential co-ordinates are calculated for hydroxylamines and methyleneamine.

THE inversional process at trivalent nitrogen has aroused considerable interest and debate among physical and organic chemists during the last few decades.[1] The barriers to inversion have been shown to be remarkably sensitive to structural factors, varying from 0 to over 30 kcal mol^{-1}. These rather subtle structural factors and the rather small energies involved mean that inversional barriers present a formidable challenge to molecular orbital theories. The inversional process is normally intramolecular; therefore entropy and solvent effects are usually small. Accordingly, calculated potential barriers should agree reasonably closely with experimental data obtained for the gas phase or for solution in inert solvents. A detailed n.m.r. investigation[2] of some aziridines has established that nitrogen inversional barriers measured in the gas phase are indeed essentially equivalent to those measured in solution.

The popular CNDO/2 method gives inversional barriers which are two or three time larger than experimental values,[3,4] though Mislow and his co-workers[3] have shown that CNDO/2 can be reparameterized to give good results for nitrogen inversion for a wide range of substrates. Inversional barriers have also been calculated using the INDO, MINDO/1, and MINDO/2′ methods.[4-6] These investigations suffer from the constraint that they used assumed geometries for the ground and transition states. *ab initio* Calculations have provided inversional potentials for some molecules which are in excellent agreement with experimental data.[1] However studies on ammonia and formamide indicate that the choice of basis set is critical if good agreement is to be obtained.[7]

In recent years Dewar and his co-workers have evolved MINDO/3[8] and latterly the MNDO[9] procedures which incorporate efficient geometry optimization routines. These methods (particularly MNDO) generally give a good account of ground-state molecular energetics and geometry, and the MNDO method is based on the less severe NDDO level of approximation. The inclusion of the additional electron repulsion integrals might be expected to improve the results for nitrogen inversion as compared with those given at the CNDO or INDO levels of approximation.

RESULTS AND DISCUSSION

The potential energy barriers to nitrogen inversion in a series of amino-derivatives as calculated by the MNDO and MNDO/3 methods are given in the Table. Experimental barriers and *ab initio* MO results, where available, are also given. In cases where the inversional barrier has not been determined experimentally, data for a closely related derivative, which could reasonably be expected to have a similar barrier, are cited in parentheses. All bond lengths, bond angles, and dihedral angles were automatically optimized to locate the ground state conformation. The inversional transition-state was generally assumed to correspond to coplanar nitrogen (as would be expected), though all other geometrical parameters were optimized. However in several cases (see Table) the transition state was located by calculating the potential co-ordinate as a function of the angle θ between one nitrogen substituent and the trigonal plane containing the nitrogen atom and the other two substituents. In these cases where a potential co-ordinate was determined, the potential maximum, as expected, corresponded with a coplanar nitrogen atom ($\theta \sim 0°$) where the invertomers were enantiomers or topomers, and θ was very close to 0° where the invertomers were diastereoisomers.

Acyclic Amines.—In the case of the parent compound, ammonia (1), the older MINDO/3 method gives a more accurate estimate of the inversional barrier. Both methods incorrectly predict a marked decrease in inversional potential on increasing the number of alkyl substituents on nitrogen [see entries (2)—(4) in the Table]. However the MNDO results for the primary and secondary amines (2) and (3) are in reasonable agreement with experimental data, whereas MINDO/3 grossly underestimates the inversional barriers in alkylamines to the extent that (3) and (4) have planar ground-state geometries, as noted previously by Dewar and his co-workers.[8] MNDO tends to give a too flattened geometry at nitrogen in tertiary amines.

Both methods correctly show that the inversional barriers in the amides (5)—(7) and in aniline (8) are much lower than in ammonia or methylamine, but MINDO/3

incorrectly gives coplanar nitrogen geometry in these compounds. The structure of formamide is particularly contentious and has been the subject of a recent comprehensive *ab initio* investigation.[10] Microwave spectral data have been alternatively interpreted in terms of either a planar structure or a nonplanar nitrogen atom with a low inversional barrier.[11] The MNDO method gives a pyramidal structure, though the angle θ between the N–C(O) bond and the plane containing the NH_2 moiety is only 38° as compared with θ 55° for a regular pyramidal structure.

It is now well established experimentally that a directly bonded nitrogen, oxygen, fluorine, or chlorine atom usually raises the barrier to nitrogen inversion.[1] Both MNDO and MINDO/3 reproduce this effect; *cf.* the calculated barriers for hydrazine (9), hydroxylamine (10),

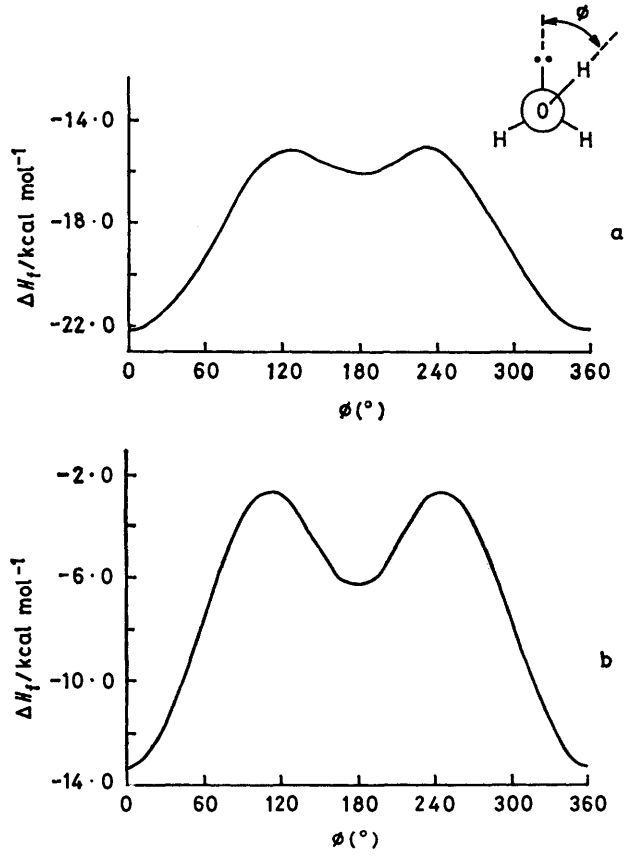
Comparison of calculated and experimental barriers to nitrogen inversion (kcal mol^{-1})

	Compound	Calc. MNDO	Calc. MINDO/3	Expt.	Calc. *ab initio*
(1)	Ammonia	11.5	6.1	5.8 [g]	0.4—11.1 [ee]
(2)	Methylamine	7.6	2.1	4.8 [h]	
(3)	Dimethylamine	4.1	0.0	4.4 [i]	8.6,[ff] 2.6 [gg]
(4)	Trimethylamine	1.7	0.0	(6.7) [j]	
(5)	Formamide	0.8	0.0	1.1, 0.0 [k]	0.04 [ee]
(6)	Cyanamide	5.3 [a]	0.0	2.0 [l]	1.8 [hh]
(7)	Nitramide	4.2	0.0	2.7 [l]	
(8)	Aniline	4.2 [a]	0.0	1.6 [m]	2.7 [ii]
(9)	Hydrazine	13.1 [a,b]	7.6 [a,c]	7.5 [n]	6.1 [jj]
(10)	Hydroxylamine	18.0 [a,d]	15.0 [a,d]		
(11)	Trimethylhydroxylamine	9.3 [a,d]	3.5 [a,d]	(12.3) [o]	
(12)	Fluoramine	17.9			20.2,[hh] 13.0 [gg]
(13)	*N*-Fluoromethylamine	12.9			
(14)	*N*-Fluorodimethylamine	8.1		(15.0) [p]	
(15)	Difluoroamine	29.7			41.7, [gg] 34.4 [gg]
(16)	*NN*-Difluoromethylamine	22.4		(>18) [q]	
(17)	Trifluoroamine	121.2			67.3 [gg]
(18)	Chloramine	17.3		10.0—11.5 [r]	5.0 [kk]
(19)	*N*-Chlorodimethylamine	7.7		(10.2) [s]	
(20)	Aziridine	19.5	9.2 [a]	(19.0) [t]	18.3,[ll] 16.6,[mm] 15.5 [nn]
(21)	1-Methylaziridine	12.0	1.8	19.0 [t]	
(22)	1-Methyl-2-methyleneaziridine	10.6	0.4	10.1 [u]	
(23)	1-(Fluoromethyl)aziridine	9.9			
(24)	1-(Trifluoromethyl)aziridine	7.7		(10.1) [v]	
(25)	1-Aminoaziridine	23.1 [e]		>22 [w]	
(26)	1-Silylaziridine	1.2		(<5.5) [x]	
(27)	1-Phosphinoaziridine	6.5 [a,e]		(<6) [y]	
(28)	1-Methylsulphenylaziridine	15.2 [a,f]		(13.3) [z]	
(29)	1-Chloroaziridine	25.9		(26.7) [aa]	
(30)	Oxaziridine	32.0	21.0	(32.5) [bb]	32.4 [ll]
(31)	7-Azabicyclo[2.2.1]heptadiene	12.3	5.9	(14) [cc]	
(32)	Methyleneamine (CH_2=NH)	26.7	10.3	(28—30) [dd]	27.9 [oo]
(33)	*N*-Methylenemethylamine (CH_2=NMe)	18.8 [a]		(28—30) [dd]	

[a] Determined by calculating the full inversional co-ordinate (see text). [b] Ground state calculated to be *trans*, see ref. 9. [c] Ground state calculated to be *gauche*. [d] Value quoted is the *trans*—*cis* barrier (see text). [e] Value quoted refers to the cyclic nitrogen atom; the ground state was calculated to have the *trans*-conformation. [f] Value quotes is the *trans*—*cis* barrier; the lowest energy *trans*-conformation has the S–Me bond directed *trans* to the nitrogen lone pair. [g] J. D. Swalen and J. A. Ibers, *J. Chem. Phys.*, 1962, **36**, 1914. [h] M. Tsuboi, A. Y. Hirakawa, and K. Tamagake, *J. Mol. Spectroscopy*, 1967, **22**, 272. [i] J. E. Wollrab and V. W. Laurie, *J. Chem. Phys.*, 1968, **48**, 5058. [j] Value cited is $\Delta G^{\ddagger}$ for dibenzylmethylamine: M. J. S. Dewar and W. B. Jennings, *J. Amer. Chem. Soc.*, 1971, **93**, 401. [k] See ref. 11. [l] D. G. Lister and J. K. Tyler, *Chem. Comm.*, 1966, 152. [m] J. C. D. Brand, D. R. Williams, and J. J. Cook, *J. Mol. Spectroscopy*, 1966, **20**, 359. [n] Y. Hamada, A. Y. Hirakawa, K. Tamagake, and M. Tsuboi, *J. Mol. Spectroscopy*, 1970, **35**, 420. [o] Value cited is $\Delta G^{\ddagger}$ for *N*-benzyl-*NO*-dimethylhydrazine: M. Raban and G. W. J. Kenney, *Tetrahedron Letters*, 1969, 1295. [p] Value cited is $\Delta G^{\ddagger}$ for $PhCH_2NFBu^t$: J. Cantacuzene, J. Leroy, R. Jantzen, and F. Dudtagne, *J. Amer. Chem. Soc.*, 1972, **94**, 7924. [q] Estimated lower limit for the inversional barrier in alkyldifluoroamines: S. K. Brauman and M. E. Hill, *J. Chem. Soc.* (*B*), 1969, 1091. [r] G. Cazzoli and D. G. Lister, *J. Mol. Spectroscopy*, 1973, **45**, 467. [s] Value cited is $\Delta G^{\ddagger}$ for *N*-chlorodiethylamine; W. B. Jennings and R. Spratt, *Chem. Comm.*, 1971, 54. [t] Value cited is $\Delta G^{\ddagger}$ for *N*-methylaziridine in the gas phase; see ref. 2. [u] Value cited is $\Delta G^{\ddagger}$ at −50 °C calculated from the rate constant measured by A. Loewenstein, J. F. Neumer, and J. D. Roberts, *J. Amer. Chem. Soc.*, 1960, **82**, 3599. [v] Value cited is $\Delta G^{\ddagger}$ for 2,2-difluoro-1-(trifluoromethyl)aziridine: A. L. Logothetis, *J. Org. Chem.*, 1964, **29**, 3049. [w] S. J. Brois, *Tetrahedron Letters*, 1968, 5997. [x] Upper limit for $\Delta G^{\ddagger}$ in 2,2-dimethyl-1-trimethylsilylaziridine cited by J. M. Lehn, *Fortschr. Chem. Forsh.*, 1970, **15**, 311. [y] Upper limit for $\Delta G^{\ddagger}$ in 1-(diphenylphosphino)-2,2-dimethylaziridine: A. H. Cowley, M. J. S. Dewar, W. R. Jackson, and W. B. Jennings, *J. Amer. Chem. Soc.*, 1970, **92**, 5206. [z] Value cited is $\Delta G^{\ddagger}$ for 2,2-dimethyl-1-methyl sulphenylaziridine: J. M. Lehn and J. Wagner, *Chem. Comm.*, 1968, 1298. [aa] Value cited is $\Delta G^{\ddagger}$ for 1-chloro-2-methylaziridine, calculated from the rate constant of 2.08×10^{-4} at 80 °C reported by R. G. Kostyanovsky, Z. E. Samojlova, and I. I. Tchervin, *Tetrahedron Letters*, 1969, 719. [bb] Value cited is $\Delta G^{\ddagger}$ for 3-benzyl-2,2-dimethyloxaziridine: A. Mannschreck, J. Linss, and W. Seitz, *Annalen*, 1969, **727**, 224. [cc] See ref. 18. [dd] Estimated from data for substituted imines, see ref. 22. [ee] See ref. 10. [ff] J. M. Lehn and B. Munsch, unpublished result cited by J. M. Lehn, *Fortschr. Chem. Forsh.*, 1970, **15**, 311. [gg] S. Skaarup, L. L. Griffin, and J. E. Boggs, *J. Amer. Chem. Soc.*, 1976, **98**, 3140; A. Schmiedekamp, S. Skaarup, P. Pulay, and J. E. Boggs, *J. Chem. Phys.*, 1977, **66**, 5769. [hh] J. M. Lehn and B. Munsch, *Chem. Comm.*, 1970, 1062. [ii] W. J. Hehre, L. Radom, and J. A. Pople, *J. Amer. Chem. Soc.*, 1972, **94**, 1496. [jj] J. O. Jarvie and A. Rauk, *Canad. J. Chem.*, 1974, **52**, 2785. [kk] G. L. Bendazzoli, D. G. Lister, and P. Palmieri, *J.C.S. Faraday II*, 1973, 791. [ll] J. M. Lehn, B. Munsch, P. Mille, and A. Veillard, *Theor. Chim. Acta*, 1969, **13**, 313. [mm] S. Skaarup, *Acta Chem. Scand.*, 1972, **26**, 4190. [nn] D. T. Clark in 'Proceedings of the Israel Academy of Science and Humanities,' eds. E. D. Bergmann and B. Pullman, Jerusalem Academic Press, 1970, p. 238. [oo] J. M. Lehn and B. Munsch, *Theor. Chim. Acta*, 1968, **12**, 91.

fluoramine (12), and chloramine (18) with that for ammonia (1). However the MNDO method seems to overestimate the inversional barriers in these NH_2X compounds by *ca.* 5 kcal mol^{-1}. The MNDO barriers increase considerably along the series NH_3 (1), NH_2F (12), NHF_2 (15), NF_3 (17) as expected, but the introduction of methyl substitution into fluoramine or chloramine is associated with a marked decrease in the calculated barrier [see entries (12)—(19) in the Table]. The available experimental data (Table) indicate that the effect of methyl substitution is probably an artefact of the MNDO method.

There has been considerable discussion in the literature whether the experimental stereodynamic barriers of *ca.* 12 kcal mol^{-1} in alkylhydroxylamines, measured by n.m.r. spectroscopy, refer to nitrogen inversion or N–O bond torsion.[12] The MNDO method gave energy minima for hydroxylamine and trimethylhydroxylamine corresponding to both *cis*- and *trans*-conformations around the N–O bond (Figure), though the *trans*-forms were more stable than *cis* by 6.0 and 7.2 kcal mol^{-1}

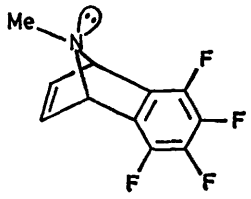


Heat of formation (ΔH_f) calculated by MNDO for (*a*) NH_2OH and (*b*) Me_2NOMe as a function of the dihedral angle (ϕ) between the O–H bond and the nitrogen lone pair axis

respectively. The *trans* ⟶ *cis* rotational barriers were determined to be 6.8 and 10.7 kcal mol^{-1}, respectively. The general form of the rotational potentials (Figure) are similar to those calculated previously for hydroxylamine, *N*-methylhydroxylamine, and *O*-methylhydroxylamine using *ab initio* methods.[13-15] The latter calculations also gave the energy of the *cis*-form to be 7—8 kcal mol^{-1} above the *trans*, and differ from CNDO/2 results[16] for dimethylhydroxylamine which give a *trans* — *cis* energy difference of only 1.2 kcal mol^{-1} and a rotational barrier of 2.8 kcal mol^{-1}. It has recently been claimed that electron diffraction data for alkylhydroxylamines show that the *cis* form is only *ca.* 0.6 kcal mol^{-1} less stable than the *trans*.[17]

The *trans–cis* interconversion can also be accomplished by nitrogen inversion, and an inversional potential co-ordinate calculated using MNDO gave *trans* ⟶ *cis* barriers of 18.0 and 9.3 kcal mol^{-1} for hydroxylamine and trimethylhydroxylamine, respectively. The barrier to oxygen inversion in hydroxylamine was calculated to be 57.6 and 31.5 kcal mol^{-1} by MNDO and MINDO/3, respectively. Evidently this is a higher energy process than either N–O bond rotation or nitrogen inversion.

Aziridines.—Aziridines have long been favourite substrates for dynamic n.m.r. studies of the nitrogen inversion process as ring strain effects slow down the inversional process. The strained nature of the aziridine ring might be expected to pose additional problems for molecular orbital methods. It is therefore particularly noteworthy that the MNDO results for nitrogen inversion in the aziridine derivatives (20)—(30) are generally in good agreement with the available experimental data (Table). The barrier-lowering effects of silyl (26), phosphino (27), sulphenyl (28), and fluoroalkyl (23) and (24) substituents are quantitatively reproduced as are the barrier-raising effects of amino (25), oxy (30), and chloro (29) substituents.



(34)

It has been reported that the 7-azabicyclo[2.2.1]-heptadiene derivative (34) has an unusually high barrier to nitrogen inversion ($\Delta G^{\dagger}$ *ca.* 14 kcal mol^{-1})[18] as compared with say *N*-methylpyrrolidine ($\Delta G^{\dagger}$ 7.9 kcal mol^{-1}).[19] MNDO calculations on the parent compound (31) gave a nitrogen barrier of 12.3 kcal mol^{-1} which is close to the experimental result for the derivative (34) and is considerably larger than the barrier in dimethylamine.

The MINDO/3 method gives very poor results for aziridines (Table). This failure is probably connected with the known tendency of this older method to seriously underestimate strain effects in three-membered rings.[8]

Imines.—Imines can isomerize or topomerize either by nitrogen inversion or by rotation through 180° about the

C=N bond.[20-22] An intermediate pathway is also possible.[21] The barrier to nitrogen inversion in the parent compound (32) of 26.7 kcal mol^{-1} calculated by MNDO (Table) is very close to experimental estimates of 28—30 kcal mol^{-1} based on data for alkyl-substituted analogues.[22] Previous molecular orbital calculations on methyleneamine have given inversional barriers of 31.1 (CNDO/2),[21] 14.7 (MINDO/1),[23] and 27.9 kcal mol^{-1} (*ab initio*).[24] The MINDO/3 estimate of 10.3 kcal mol^{-1} for this process is much too low.

The C=N bond rotational co-ordinate was also investigated by MNDO and MINDO/3, but it was found to be necessary to fix the C=N–H bond angle at its optimized ground-state value of 114.5 or 117.5°, respectively, otherwise this angle opened out to 180° and a nitrogen inversional co-ordinate was obtained. The resulting rotational barriers of 45.6 (MNDO) and 27.3 kcal mol^{-1} (MINDO/3) appreciably lower than the rotational barriers of 61.1 and 57.5 kcal mol^{-1} calculated previously by CNDO/2 and *ab initio* procedures, respectively.[21,24] The present calculations do not provide any support for an intermediate pathway since the energy of such a process is calculated to be greater than that for planar nitrogen inversion.

Calculations were also performed on the *N*-methyl derivative (33), but the MNDO inversional barrier is too low by nearly 10 kcal mol^{-1}. It would appear that MNDO results for nitrogen inversion are generally more reliable for amino compounds containing an N–H linkage. Thus, full *N*-alkyl substitution leads to low MNDO and MINDO/3 estimates for nitrogen inversional barriers as found for example in *N*-methylimine (33), trimethylamine (4), and *N*-methylaziridine (21). Possibly these calculations overestimate alkyl–alkyl repulsion in the more sterically congested pyramidal ground states.[8,9]

EXPERIMENTAL

The molecular orbital calculations were performed on the CDC 7600 computer at the Manchester University Regional Centre *via* the Swan link to Birmingham University, and on the IBM 370/158 at Auburn University Computer Centre. The MNDO and MINDO/3 programs (QCPE nos. 252 and 279) incorporated the standard parameters for first-row elements, though MNDO was modified to include the parameters for second-row elements recently proposed by Dewar and his co-workers.[25] Neither of these programs explicitly include *d*-orbitals.

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