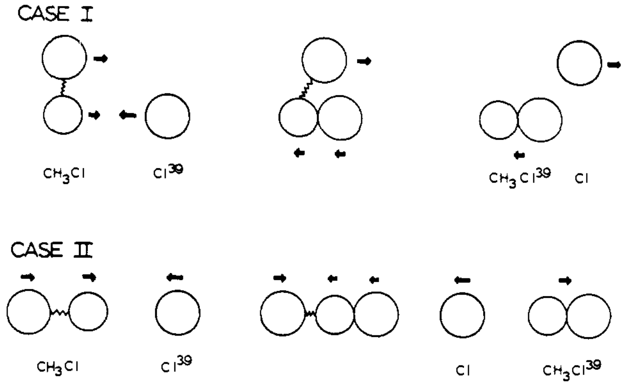

Figure 1. Schematic representation in the center of mass system of extreme cases involving the translational inertial effect on the reaction between Cl^{39} and CH_3Cl. Case I: Approach of Cl^{39} normal to CH_3–Cl bond axis and collision at CH_3 group tend to stretch and thereby to vibrationally excite and weaken the existing C–Cl bond. Case II: Coaxial approach tends to excite existing C–Cl bond by compression. In both cases, rupture of this bond is thereby facilitated.

one-step mechanism,[7] the translational inertial factor predicts preferential replacement of two halogens or a halogen and a hydrogen. The interesting result that displacement of two hydrogen atoms is rare in molecules which also contain halogen is consistent with this expectation.

In summary, it appears that steric and translational-inertial factors can correlate the main features of hot halogen reactions in the gas phase. The fact that in the liquid phase yields are much higher and do not appear to follow the trends observed here is presumably a result of caging effects, known to be important for halogen atoms.[10]

Acknowledgment. The authors wish to thank the staff of the Yale University linear electron accelerator for their help. This work was supported by the U. S. Atomic Energy Commission under Contrast SAR/AT(30-1)1957.

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(7) We do not here discuss the extent to which "double-displacement" products are formed in a single step or by decomposition of an internally excited product of a single replacement reaction. To the extent to which the latter mechanism holds, the product yields measured deviate from the actual primary product yields.[8,9] However, even if all double-displacement products resulted from secondary decomposition, the trend in appropriately corrected single-displacement results would still indicate a strong preference for halogen replacement.

(8) Y. Tang, E. K. C. Lee, and F. S. Rowland, *J. Am. Chem. Soc.*, **86**, 1280 (1964)

(9) Y. N. Tang and F. S. Rowland, *J. Phys. Chem.*, **72**, 707 (1968).

(10) M. Milman, *Radiochim. Acta*, **2**, 180 (1964).

L. Spicer, Richard Wolfgang
Department of Chemistry, Yale University
New Haven, Connecticut
Received November 22, 1967

Macrobicyclic Amines. I. *out–in* Isomerism of 1,(*k* + 2)-Diazabicyclo[*k*.*l*.*m*]alkanes

Sir:

Macrobicyclic diamines with bridgehead nitrogen atoms potentially can exist as conformations in which the lone pairs are both outside and inside the cavity defined by the hydrocarbon bridges. To test this idea, a series of 1,(*k* + 2)-diazabicyclo[*k*.*l*.*m*]alkanes was synthesized with $k, l, m > 6$.

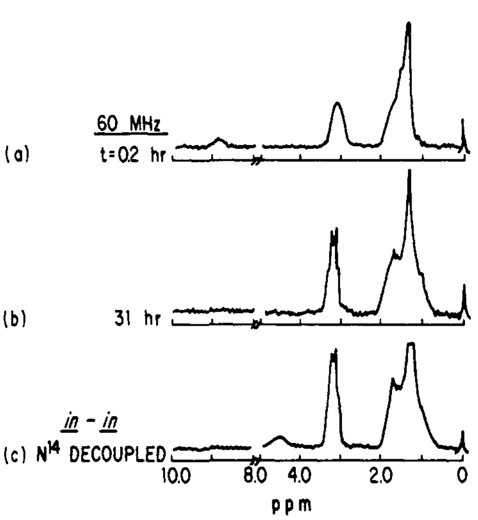


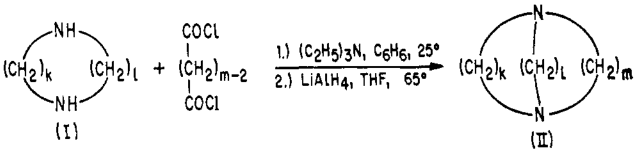
Figure 1. (a, b) Time dependence of the 60-MHz pmr spectrum of 1,10-diazabicyclo[8.8.8]hexacosane bishydrochloride in 50% TFA at 25°. (c) The ^{14}N decoupled spectrum of the i^+i^+ isomer.

1,(*k* + 2)-Diazacycloalkanes (I) were prepared by the procedure of Stetter[1] and converted by an extension of the same method to the crystalline 1,(*k* + 2)-diazabicyclo[*k*.*l*.*m*]alkanes (II) (Table I),[2] which have low solubility in water and alcohol but are soluble in nonpolar solvents. The symmetrical amines II (*k* = *l* = *m*) have simple infrared spectra whose absorptions are much sharper when the chains contain an even number of methylenes.

Table I. Properties of 1,(*k* + 2)-Diazabicyclo[*k*.*l*.*m*]alkanes (II)

II, [*k*.*l*.*m*]	Yield, %[a]	Mp, °C	δ, ppm[b] o^+o^+	o^+i^+	i^+i^+	K_e[b]
7.7.7	20	35	9.2		4.4	0.85
8.8.8	75	120	9.0		4.6	>100
9.9.9	50	32	8.8		4.8	0.41
10.10.10	75	114	8.7	8.5[c]	4.8	3.3
6.6.8	40	45	9.2		4.3	24
6.8.10	60	<0	8.9		4.7	0.70
8.8.10	70	55	8.9		4.5	1.5
[$(C_2H_5)_3N$]			8.2			

[a] Over-all yield based on amines I, which in turn were prepared in 50–70% yields.[1] [b] Chemical shifts of NH^+ and equilibrium constants of the ammonium ions in 50% TFA determined with the 220-MHz pmr spectrometer at 23°; $K_e = [i^+i^+]/[o^+o^+]$. [c] This absorption is presumably due to the *out* proton of the o^+i^+ isomer.



The 100-MHz pmr spectrum of [8.8.8]-II has resonances at 2.20 (12 H) and 1.36 ppm (36 H) in $CFCl_3$ at 25°. Below −95° the α-CH_2 resonance is split into two broad lines (∼3:2) separated by 45 Hz. This observation suggests that a conformational change, possibly nitrogen inversion, occurs with an activation energy of 7.7 kcal/mole and $k = 1.4 \times 10^7$ sec^{-1} at 25°.

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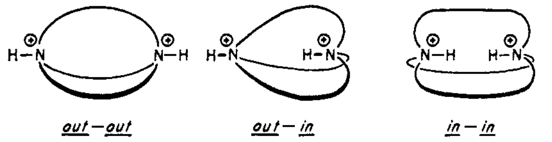
(1) H. Stetter and J. Marx, *Ann.*, **607**, 59 (1957).

(2) New compounds have appropriate elemental analyses, molecular weights, and spectral constants.

The shapes that the macrobicyclic amines assume is revealed by a remarkable isomerization of their ammonium salts. [8.8.8]-II gives a homogeneous, crystalline bishydrochloride from water whose 60-MHz spectrum in 50% aqueous trifluoroacetic acid (TFA) has broad absorptions at 8.9 (2 H), 3.1 (12 H), and 1.0–2.0 ppm (36 H). The N*H*$^+$ resonance at 8.9 ppm is similar to that of $(C_2H_5)_3N \cdot HCl$ (8.2 ppm). The bishydrochloride changed to an isomeric salt over 4 days in this solvent (Figure 1a,b), and addition of NaOH gave quantitative recovery of the amine. In the new ammonium ion, the N*H*$^+$ resonance is too broad to detect, and that of the α-CH_2 is a four-line multiplet centered at 3.2 ppm; the latter band is a sharp triplet (J = 5.5 Hz) in the corresponding bisdeuteriochloride, and the coupling is primarily to the β-CH_2. The lost N*H*$^+$ resonance, when irradiated at the ^{14}N decoupling frequency, appears far upfield at 4.6 ppm (2 H) (Figure 1c). The slow conversion of the initial ammonium ion to the isomer in 50% TFA is virtually complete (K_e > 100), but this equilibrium is established in ~30 min in water (K_e = 1.6). These and other data show that the initial ammonium ion is that isomer in which both NH$^+$ protons are *outside* the cavity, whereas both are *inside* in the new isomer. The 220-MHz spectra of the isomeric bisdeuteriochlorides clearly distinguish them (Figure 2).

We call the stereoisomerism of tetrahedral bridgehead atoms in three-stranded molecules "*out–in*."[3] Three stereoisomers of the bisammonium ions of II can exist when k, l, m > 6.



The $o^+o^+ \rightleftharpoons i^+i^+$ equilibrium has been detected in all amines in Table I, and in some cases crystalline isomers of both configurations have been isolated. For example, in the solid state the bishydrochloride of [8.8.8]-II exists as the o^+o^+ isomer, whereas the bisbifluoride is i^+i^+. Evidently the o^+i^+ isomers are of higher free energy than o^+o^+ or i^+i^+, probably because of torsional and nonbonded repulsion effects. The o^+i^+ ion is detected only when $k = l = m \geq 10$, and then as a fleeting intermediate during establishment of the equilibrium.

Equilibrium constants ($o^+o^+ \rightleftharpoons i^+i^+$) for the amines in 50% TFA are given in Table I, and hydrophobic bonding is thought to be important in determining the position of the equilibrium in aqueous media. An alternation effect is evident in the symmetrical ions; even chain lengths favor i^+i^+ isomers and odd, o^+o^+ isomers. The i^+i^+-[8.8.8] ion is particularly stable, and models suggest that it has a beautifully compact structure in which the chains contain a maximum of *trans* arrangements and are oriented for favorable nonbonded and dispersion interactions. It is thought that the o^+o^+ and i^+i^+ ions ($7 \leq k = l = m \leq 10$) have fewer preferred conformations than anticipated from their size and that the i^+i^+ ions exist with ellipsoidal shapes in which the hydrocarbon chains form a closed wall, giving them a sensible interior.

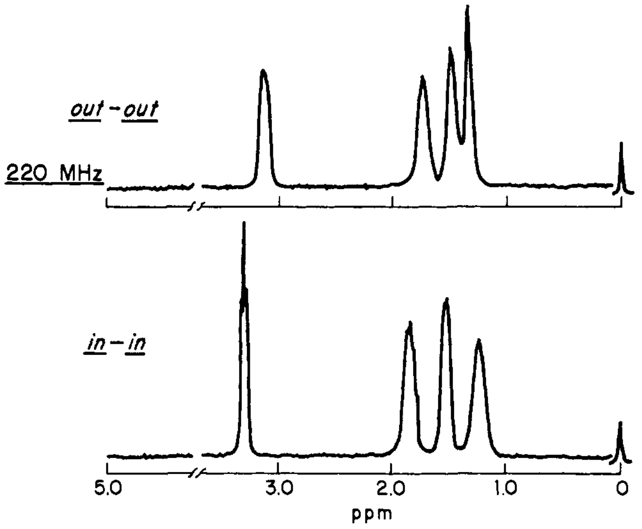


Figure 2. Pmr spectra (220-MHz) of *out,out*- and *in,in*-1,10-diazabicyclo[8.8.8]hexacosane bisdeuteriochloride in 50% CF_3CO_2D at 25°. The α-, β-, γ-, and δ-CH_2 absorptions occur at progressively higher fields.

The chemical shifts of the *out* protons decrease monotonically toward that of a simple tertiary aliphatic ammonium ion, such as $(C_2H_5)_3NH^+$, whereas those of the *in* protons similarly increase as the hydrocarbon chains lengthen (Table I). The unusually large upfield shifts (~4 ppm) of the *in* protons can be accounted for largely in terms of electrostatic effects, diamagnetic anisotropic shielding by the hydrocarbon chains, and less effective solvent hydrogen bonding.

H. E. Simmons, C. H. Park
Contribution No. 1388, Central Research Department
Experimental Station
E. I. du Pont de Nemours and Company
Wilmington, Delaware 19898
Received November 13, 1967

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(3) We suggest names such as *out,out*-1,10-diazabicyclo[8.8.8]hexacosane bishydrochloride, conveniently abbreviated as *out,out*-$[8.8.8]^{2+}$, o^+o^+-[8.8.8], or simply o^+o^+ when the size is clear.

Macrobicyclic Amines. II. *out-out* ⇌ *in-in* Prototropy in 1,(k + 2)-Diazabicyclo[$k.l.m$] alkaneammonium Ions

Sir:

The interconversion of the o^+o^+ and i^+i^+ ammonium ions of 1,(k + 2)-diazabicyclo[$k.l.m$]alkanes[1] in aqueous solvents involves a sequence of prototropic reactions and nitrogen inversions, rather than a homeomorphic isomerization.[2] For example, when *out,out*-1,10-diazabicyclo[8.8.8]hexacosane bishydrochloride (o^+o^+) is dissolved in water at 25°, equilibrium with the *in,in* isomer (i^+i^+) is slowly established.

Our work has been guided strongly by studies of Grunwald[3] on the mechanism of NH$^+$ proton exchange

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(1) H. E. Simmons and C. H. Park, *J. Am. Chem. Soc.*, **90**, 2428 (1968).

(2) Homeomorphic isomerization is used here to mean a conformational change in which three-stranded molecules turn inside out by passage of one chain through the ring defined by the other two chains. Although this process can be demonstrated with Stuart–Briegleb models when $k = l = m \geq 8$, the free-energy barrier is so large that distinct atropisomers can be isolated.

(3) The observed exchange rate is independent of [H$^+$] at pH 1–4 but inversely proportional at pH <1. See E. Grunwald, *J. Phys. Chem.*, **67**, 2208 (1963); **67**, 2211 (1963); E. K. Ralph, III, and E. Grunwald,