

Conformations of 1,*p*-Diazabicyclo[*n*.2.2]alkanes (Aza-Belted Piperidines)

Stephen F. Nelsen,* J. Thomas Ippoliti, and Peter A. Petillo

S. M. McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706

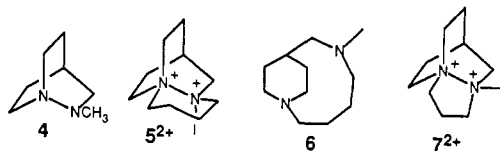
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Reduction of hexaalkylhydrazine dication produced from 2-methyl-1,2-diazabicyclo[2.2.2]octane (4) by alkylation with bis-halides produces diazabicyclo[*n*.2.2] compounds, for which we refer to the nitrogen-containing *n* atom bridge as the "aza-belt" in the title. The compound having a five-atom $[-(\text{CH}_2)_3\text{N}(\text{Me})\text{CH}_2-]$ belt, 13, exists with a boat piperidine ring having an outward paramidized nitrogen (13-1), a conclusion based on comparison of observed ^1H NMR vicinal coupling constants with those calculated using MM2 geometries. MM2 predicts that 13-1 is favored over other conformations by at least 2.6 kcal/mol. ^{13}C NMR chemical shifts suggest a gross conformational change between 13 and the six-atom belt compounds, $[-(\text{CH}_2)_4\text{N}(\text{Me})\text{CH}_2-]$ (6) and $[-\text{CH}_2\text{CH}=\text{CHCH}_2\text{N}(\text{Me})\text{CH}_2-]$ (10), for which MM2 predicts boat piperidine rings having inward pyramidalized nitrogens. PE and optical spectra of 6 and 13 are discussed. 16, the NH analogue of 13, undergoes unusually facile oxidation to give the aminated 1,5-diazatricyclo[6.2.1.0^{5,10}]undecane (19). It is concluded from ^1H NMR vicinal coupling constants and the unusually high-field absorption of H(3e) and C(3) that 19 exists with both its aminated and piperidine six-membered rings in chair conformations, which is also the MM2 prediction.

Introduction

Alder's group developed syntheses of and studied the novel chemistry of an impressive series of propellane-type hexaalkylhydrazine dication and their reduction products, bridgehead bicyclic diamines,¹ which may be conveniently described N(*m.n.p*)N systems. The completely reversible redox chemistry of the example with the longest lived intermediate oxidation state, the N[4.4.4]N compound 1,² is shown in Scheme I. Alder and co-workers have determined X-ray crystallographic structures of all three oxidation states of 1.³ The red cation radical 1^{•+} has an N,N distance of 2.30 Å, 0.77 Å longer than that of the dication, and a CNC angle of 114.0°, 43% of the way from tetrahedral to planar nitrogen atoms; it is the best characterized example of a compound containing a 3e-σ bond. The neutral diamine 1 has inward pyramidalized nitrogens separated by 2.81 Å, and CNC angles of 115.5°, corresponding to 57% of the way from tetrahedral to planar nitrogens. The lifetime of the 3e-σ bonded cation radicals is very dependent upon bridge size. One-electron reduction of the dimethyl bicyclic hydrazine dication 2²⁺, which lacks the third link between the two nitrogens, gives a 3e-σ bonded cation radical which has a lifetime of 5 ms at room temperature,⁴ but the reduction is both electrochemically and chemically irreversible (see Scheme II). Oxidation of the neutral diamine of the "same structure", 3, however, appears not to produce 2^{•+} or 2²⁺, probably because 3 does not exist in a conformation which forms a 3e-σ bond in the cation radical competitively with hydrogen atom transfer.⁵

Our group has been examining the chemistry of compounds derived by bis-alkylation of 2-methyl-1,2-diazabicyclo[2.2.2]octane (4). The (CH₂)₄-bridged hydrazine



(1) For reviews of their extensive work in the area see: (a) Alder, R. W.; Sessions, R. B. *The Chemistry of Amino, Nitroso, and Nitro Compounds*, Part 2; Patai, S., Ed.; Wiley: New York, 1982; pp 762-804. (b) Alder, R. W. *Acc. Chem. Res.* 1983, 16, 321.

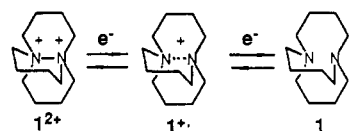
(2) Alder, R. W.; Sessions, R. B. *J. Am. Chem. Soc.* 1979, 101, 3651.

(3) (a) Alder, R. W.; Orpen, A. G.; Sessions, R. B. *J. Chem. Soc., Chem. Commun.* 1983, 999. (b) Alder, R. W.; Orpen, A. G.; White, J. M. *Ibid.* 1985, 949.

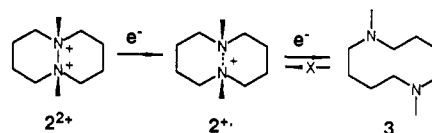
(4) Nelsen, S. F.; Alder, R. W.; Sessions, R. B.; Asmus, K.-D.; Hiller, K.-O.; Göbl, M. *J. Am. Chem. Soc.* 1980, 102, 1429.

(5) Nelsen, S. F.; Ippoliti, J. T. *J. Am. Chem. Soc.* 1986, 108, 4879. Note that we had previously assumed⁴ that the internal decomposition reaction would be proton transfer.

Scheme I



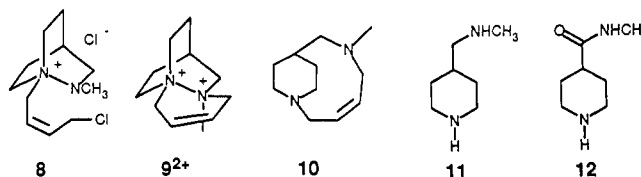
Scheme II



dication 5²⁺ is reduced to diamine 6 (6-methyl-1,6-diazabicyclo[6.2.2]dodecane), which has one bridgehead nitrogen and one in the six-atom "belt" bridging the piperidine ring between positions 1 and 4. 6 is clearly intermediate between 1 and 3 in the conformational restrictions placed on the nitrogens by their bridging substituents. The unusual spectral properties and easy oxidation of 6 led us to suggest in a communication⁶ that it exists in an inside pyramidalized nitrogen boat piperidine ring conformation. This paper focuses on the conformations assumed by the 1,4-aza-belted piperidines produced by reducing 5²⁺, 7²⁺,⁸ and two analogues.

Results: Dication Reduction and Aza-Belted Piperidine Conformations

Reduction of 5²⁺ to 6 is completely chemically and electrochemically irreversible.⁶ The cation radical produced by adding an electron to 5²⁺ does not last the several milliseconds required for observation of a reversible reduction wave by cyclic voltammetry. There is also no evidence that a 3e-σ bonded cation radical is produced upon oxidation of neutral 6. In this work we investigated an unsaturated analogue of 5²⁺ and 6. Alkylation of 4 by *cis*-1,4-dichloro-2-butene gave monoalkylation product 8,



(6) Nelsen, S. F.; Gannett, P. M. *J. Am. Chem. Soc.* 1982, 104, 4698.

(7) Alder, R. W.; Sessions, R. B.; Gmünder, J. O.; Grob, C. A. *J. Chem. Soc., Perkin Trans. 2* 1984, 411.

(8) Nelsen, S. F.; Ippoliti, J. T. *J. Org. Chem.* 1986, 51, 3169.

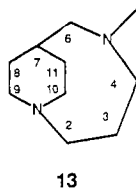
Table I. Irreversible Cyclic Voltammetry Peak Potentials Observed for Diamines and Hexaalkylhydrazine Dications

neutral compd	oxidation waves ^a	dication	dication reduction wave ^{a,b}
3	+0.73 ^c	2 ²⁺	+0.13
6	-0.13, +0.39 ^c	5 ²⁺	+0.09
10	+0.32	9 ²⁺	+0.14
13	+0.31, +0.80	7 ²⁺	-0.05

^a Conditions: 2.0 mM solution in acetonitrile containing 0.1 M *n*-Bu₄NClO₄, scan rate 0.2 V/s, platinum disk electrode unless noted, vs saturated calomel reference electrode. ^b Dication [BF₄]₂ salt. ^c From ref 6; conditions as for *a*, except at a gold electrode.

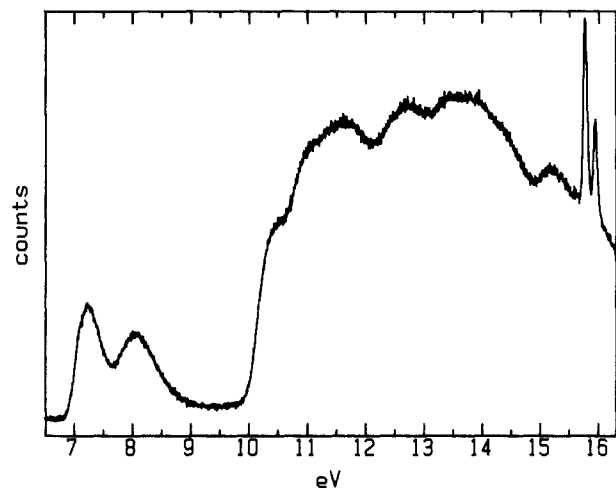
which was cyclized with silver ion to give 9²⁺[BF₄]₂, followed by reduction with sodium in ammonia to give neutral 10. 10 proved to be rather unstable, and cleavage product 11 was detected by NMR in material which had been distilled. 11 was independently prepared by LAH reduction of piperidine derivative 12. The unsaturated compounds 9²⁺ and 10 proved qualitatively similar to their saturated analogues 5²⁺ and 6 in their redox properties; any increase in cation radical lifetime caused by change of shape in the "belt" by the presence of the double bond was too small to affect their electrochemical behavior significantly.

We initially prepared dication 7²⁺ hoping that decreasing the size of the belt would increase the lifetime of 7⁺, and, by forcing the nitrogens in neutral compound 13 to lie



closer in space, perhaps allow the 3e-σ bonded cation radical 7⁺ to be produced upon loss of an electron from 13. Neither hope was realized. As summarized in Table I, the cyclic voltammetry waves for 13 and dication 7²⁺ were also irreversible. All three of the tricyclic diamines 6, 10, and 13 show an oxidation wave substantially below that of the monocyclic compound 3, and our initial hypothesis that removing a methylene group from the belt in going from 6 to 13 would make the nitrogens lie closer together is certainly not supported by the electrochemical data, as the peak potential for oxidation of 13 is significantly more positive than that for 6. Although the waves are irreversible so that they reflect decomposition kinetics as well as thermodynamics for electron removal, it seemed unlikely that the through-space N,N interaction was larger in 13 than in 6. The hexaalkylhydrazine dications reduce in a narrower range,⁹ also irreversibly. Lower temperature experiments showed that they also undergo irreversible reduction at -78 °C, indicating short cation radical lifetimes. Pulse radiolysis experiments showed that one-electron reduction of 5²⁺ and 7²⁺ in water does produce the 3e-σ bonded cations, which give broad visible absorption maxima at 500 ± 10 and 490 ± 10 nm, respectively. Both species are comparable in lifetime to 2⁺,⁴ so, in agreement with the cyclic voltammetry results, introduction of the two-carbon bridge which converts one of the nitrogens of 2⁺ to a bridgehead one in a diazabicyclo[n.2.2] system is not effective at kinetically stabilizing the 3e-σ bonded cation radicals.

(9) The much more negative reduction peak potential originally reported⁶ for 2²⁺ was in error;⁸ the sample had presumably decomposed before the voltammogram was obtained.

**Figure 1.** Photoelectron spectrum of 13.

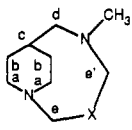
Photoelectron spectroscopy has been important in the characterization of electronic interaction in Alder's N-[*m.n.p*]N diamines,¹⁰ as it is in considering how 3 differs from the bicyclic diamines considered here. 3 gives a single lone-pair ionization in its photoelectron spectrum,⁶ showing that through-space lone-pair, lone-pair mixing is not important. vIP for 3 is 7.81 eV,⁶ 0.24 eV lower than that predicted from the *n*(eff) values¹¹ of its attached alkyl groups, suggesting less pyramidal nitrogens for 3 than for an acyclic trialkylamine. The PE spectrum of 6 has lone-pair vIP values of 7.21 and 7.84 eV,⁶ and that of 13 (see Figure 1) vIP values of 7.23 and 8.05 eV. Because the nitrogens are substantially different in each compound, it is not clear in the absence of other data how much of the difference in vIP values is caused by difference in pyramidal geometry at nitrogen, and whether or not there is significant lone-pair, lone-pair interaction. It will be noted that the first PE band for 13 is noticeably narrower than the second; the half-widths of Gaussians fitting the data are 0.44 and 0.81 eV, respectively. Greater geometry change upon electron removal increases PE band width, so the more easily oxidized nitrogen of 13 (the bridgehead nitrogen; see Discussion) appears likely to be significantly more flattened than the other.

Easily oxidized amines have also been found to show longer wavelength optical absorption than ordinary trialkylamines.¹ For 3, where the nitrogens are only constrained by the diazacyclodecane ring, fairly intense UV end absorption is observed (ϵ [210 nm] 3.0×10^3), but absorption falls off rapidly at longer wavelengths, and ϵ [240] is 3.1×10^2 . The C₄N(Me)C-belted piperidine 6 shows a maximum at 212 nm (ϵ [212] 4.8×10^3) and considerably more intense longer wavelength absorption than 3; it has a shoulder at 245 nm (ϵ [245] 2.5×10^3), indicating that one of the nitrogens is flattened.⁶ The C₃N(Me)C-belted piperidine 13 also exhibits enhanced absorption relative to 3, although definite maxima or shoulders were not resolved; 13 shows ϵ [210] 5.2×10^3 and ϵ [245] 1.9×10^3 .

NMR spectroscopy should provide the most definite information about the conformations assumed by these belted piperidines. We shall consider the far simpler ¹³C

(10) (a) Alder, R. W.; Arrowsmith, R. J.; Casson, A.; Sessions, R. B.; Heilbronner, E.; Kovac, B. Huber, H.; Taagepera, M. *J. Am. Chem. Soc.* 1981, 103, 137. (b) Honegger, E.; Yang, Z.-Z.; Heilbronner, E.; Alder, R. W.; Moss, R. E.; Sessions, R. B. *J. Electron Spectrosc.* 1985, 36, 297.

(11) (a) Nelsen, S. F. *J. Org. Chem.* 1984, 49, 1891. (b) We are assuming that the "through-bond" effect of the 1,5 nitrogens on each other is negligible.

Table II. Comparison of ¹³C NMR Chemical Shifts (δ) of Some Diamines


X = carbon	14 H,H	6 (CH ₂) ₂	10 CH=CH	13 CH ₂
NC(a)H ₂	55.9	47.3	47.9	45.8
C(b)H ₂	31.0	28.7	28.3	28.2
C(c)H	33.5	31.5	31.3	29.7
C(d)H ₂ N	66.3	65.7	66.4	65.7
NCH ₃	46.0 ^a	45.7	46.8	49.5
NC(e,e')H ₂	46.5 ^b	55.8, 57.7	55.6, 55.4	58.9, 58.5
other C		27.9, 23.3	129.6, 131.3 ^c	31.0

^aN(CH₃)₂. ^bN(1)CH₃. ^c=CH.

NMR spectra first. The carbon spectra of **6**, **10**, and **13** are compared with those of unbridged piperidine **14** in

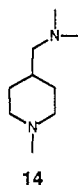
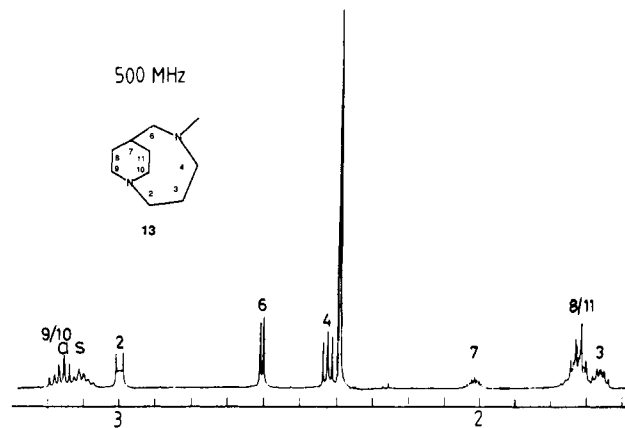
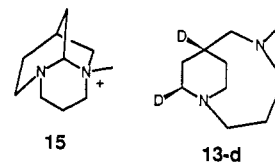


Table II. We believe that the assignments are unambiguous except as noted. Introduction of the double bond in going from **6** to **10** causes rather small changes in shift for the carbons remote from the double bond (see Table II for the definition of the letters used to designate the carbons): +0.6 δ for a, -0.4 for b, -0.2 for c, +0.7 for d, +1.2 for NCH₃, suggesting to us that their conformations are rather similar. Substantially larger changes are seen for deleting one CH₂ carbon from the belt in going from **6** to **13**: -1.6 for a, -0.5 for b, -1.8 for c, 0 for d, +3.8 for NCH₃, and +3.1 and +7.7 for CH₂CH₂CH₂ in the belt (two different such carbons in **6** go to one in **13**). The changes observed suggest to us that the conformation of **13** is likely to be significantly different from those of **6** and **10**. The piperidine ring carbons of **6** are very broad at room temperature, but broadening of those for **13** is not noticeable at 50 MHz. Some broadening for **13** is noticeable at 125 MHz at room temperature, but even at -80 °C, peaks for the "frozen" piperidine ring carbons were not observed.

The proton NMR spectrum of **6** is not only complex, but broadened by conformational interconversion dynamics at room temperature. This compound began to decompose when the temperature was raised to 50 °C, and we have not succeeded in extracting useful conformational information from the ¹H NMR of **6**. The 500-MHz ¹H NMR spectrum of **13** (Figure 2) does not show significant conformational broadening at room temperature, and is far more amenable to analysis. A single chemical shift, and no geminal coupling, is observed by ¹H NMR for each of the three CH₂ groups in the belt, showing that **13** is conformationally equilibrating rapidly on the NMR time scale. The C(6)H₂ signal at 2.60 δ is a clean doublet, $J_{6,7av} = 4.4$ Hz. Both NCH₂CH₂CH₂N signals are effectively AA'XX' spin systems because the nonadjacent C(2)H₂ and C(4)H₂ hydrogens are not significantly coupled. The upfield signal (2.42 δ, assigned to C(4)H₂; see Discussion) appears as a slightly distorted triplet, $J_{34} + J_{34'} = 12.3$ Hz, ratio of center to smaller line 1.25; simulations show that J_{34} and $J_{34'}$ differ by about 4 Hz. The downfield AA'XX' signal (3.00 δ, assigned to C(2)H₂; see Discussion) has a most unusual "inverted" appearance, with the outer lines much larger

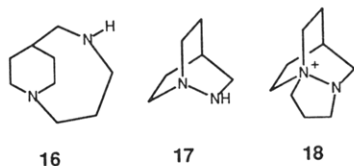
Figure 2. 500-MHz ¹H NMR spectrum of **13**.

than the center lines. The outer-line separation $J_{23} + J_{23'} = 9.9$ Hz and equal-height half-intensity doublets separated by ca. 1.6(2) and 6.0(1) Hz are observed in between. Spectral simulations show that the AA' pattern observed requires a $|J_{23} - J_{23'}|$ value of >8.5 Hz and a significant $|J_{22'} - J_{33'}|$ value (about 3–4 Hz). The piperidine ring signals are far more complex because reorientation of the belt retains different chemical shifts for anti and syn hydrogens and because the chemical shift difference between the C(8/11)H₂ syn and anti hydrogens is small even at 500 MHz. Decoupling of the C(8/11)H₂ region (near 1.7 δ) collapses the C(9/10)H₂ signal to effectively an AB quartet, $J_{9/10s,9/10a} = -13.3$ Hz, $\Delta\nu = 33.2$ Hz. In the coupled spectrum, two five-line patterns which do not overlap are observed; the upfield pattern is clearly broader than the downfield one. Reduction of **15**⁸ with LAD gives a spe-



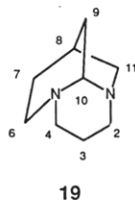
cifically deuterated **13-d** isomer, which we assign as the anti-deuterated isomer illustrated from its synthesis. Integration shows that the deuterium introduced is in the downfield multiplet (which does not change shape, although the upfield multiplet is significantly affected), allowing assignment of the multiplet at 3.17 δ to H(9/10a), and that at 3.10 δ to H(9/10s). Decoupling of the C(9/10)H₂ region collapses the C(8/11)H₂ signal to an ill-resolved XX'YY' pattern; C(7)H at 2.03 δ is still coupled. Simulations show that $\Delta\nu$ for H(8/11)s and H(8/11)a is in the range 6–8 Hz, and that the signal with a larger coupling to H(7) is downfield, which allows assignment (see Discussion) of H(8/11a) at 1.72₈ δ and H(8/11s) at 1.71₂ δ. The greater broadening observed for the H(9/10s) signal is a rather clear indication of a boat piperidine ring conformation, because a boat conformation should have a W plan splitting between the 9s and 10s signals, while a chair would not.

Dication **7**²⁺ shows a remarkable selectivity for loss of hydrogen from the carbons adjacent to N(1) of the bicyclo[2.2.2]octane rings.⁸ Monocation **15** is formed efficiently when **7**²⁺ is allowed to slowly decompose in acetonitrile, upon its treatment with carbonate, or with iodide followed by deprotonation of the product. Under much more strongly basic conditions, decomposition of **7**²⁺ in 3.4 M KOH/D₂O, extraction of the aqueous product mixture with deuteriochloroform reveals the presence of demethylated compound **16**, the expected hydrolysis product resulting



from loss of a methyl proton from 7^{2+} . **16** is more efficiently prepared by bis-alkylating 1,2-diazabicyclo[2.2.2]octane (**17**) with 1,3-dibromopropane to give cation **18**, followed by reduction (H_2/PtO_2 or Na/NH_3). The 1H NMR $NCH_2CH_2CH_2N$ spectral patterns of **16** closely resemble those of **13**. We note that the only proton NMR signals to move significantly between **13** and **16** are the "normal" NCH_2CH_2 pattern, assigned to C(4)H₂, which moves downfield 0.37 δ , and the $HCCH_2N$ signal, C(6)H₂, which moves downfield 0.30 δ upon replacement of NCH_3 by NH.

The presence of a decomposition product when the NMR spectrum of freshly prepared **16** was run in $CDCl_3$ which had not been carefully deaerated showed that this material is surprisingly sensitive to air. Even more surprisingly, **16** appears to autoxidize to a single major product, which proved to be amina **19**. Although at-



tempted kugelrohr distillation of **16** at reduced pressure gave a rather pure sample of **19**, this compound is more reliably prepared by oxidation with I_2 , and an NMR scale experiment showed that **19** is also the major product of quinone oxidation of **16**. We believe that the efficient dehydrogenation of **16** to **19** observed is rather striking. Substantial selectivity for oxidation of the piperidine ring NCH_2 group is observed, although there are four such methylenes in the molecule.

Discussion: 1,4-Aza-Belted Piperidine Conformations

Allinger MM2 calculations¹² have been carried out to test our hypothesis that, based on their oxidation and spectral properties, **6** and **10** exist in similar inside pyramidalized boat piperidine structures,⁶ while **13** exists in a different type of conformation. We did not, however, make substantial progress toward understanding the conformations of these compounds by letting MM2 optimize from what we thought were reasonable idealized input conformations; many minima were missed by this procedure, including the global minimum for **6** and **13**. Saunders kindly provided his stochastic exploration program¹³ which searches for all MM2 minima using random geometry variations, which demonstrated that we had missed minima in several examples.

In agreement with results published by Alder's group,¹⁴ dimethyldiazacyclodecane (**3**) is calculated to be most

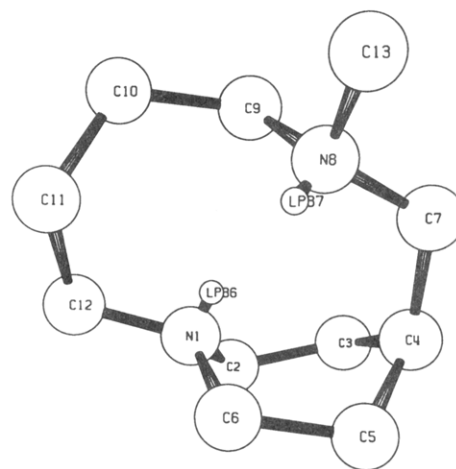


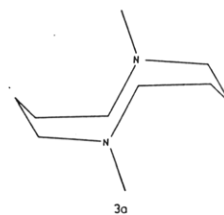
Figure 3. Drawing of conformation 6-1 of Table III.

Table III. Optimized Conformations for **6**, **10**, **13**, and **16** as Calculated by MM2, and in Italics, by AM1 Starting from the MM2 Geometry

comp	conf no.	SE ^a	$d(N,N)$, Å	$\alpha(av)$ N(1)	$\alpha(av)$ N(Me)	$\angle N1C$, CC, °	$\angle CC$, ^b CNMe, deg
6	1	0.00 ^c	2.78	114.2	111.5	+62.3	-49.0
	<i>1AM</i>	<i>0.00^g</i>	<i>3.29</i>	<i>118.4</i>	<i>113.0</i>	<i>+77.9</i>	<i>-50.7</i>
	2	0.01	2.73	113.8	111.3	-54.7	-94.9
	3	1.70	2.91	113.7	111.6	+54.2	+57.8
10	4	5.23	3.46	113.8	113.0	+45.4	+129.9
	1	0.00 ^d	2.87	114.1	111.5	-22.5	+82.0
	2	2.42	4.48	112.3	112.0	+99.9	-110.7
	3	2.44	4.53	112.9	111.2	+92.3	+40.6
13	1	0.00 ^e	3.43	114.2	111.5	-80.5	+62.0
	<i>1AM</i>	<i>0.00^h</i>	<i>3.35</i>	<i>114.6</i>	<i>114.2</i>	<i>-83.9</i>	<i>+61.2</i>
	2	2.63	3.55	113.0	111.6	+67.1	+41.4
	<i>2AM</i>	<i>2.54</i>	<i>3.45</i>	<i>114.0</i>	<i>114.3</i>	<i>+59.2</i>	<i>+39.9</i>
	3	3.99	3.53	114.4	111.8	+61.2	-89.4
16	<i>3AM</i>	<i>1.01</i>	<i>3.47</i>	<i>115.3</i>	<i>114.1</i>	<i>+58.9</i>	<i>-91.1</i>
	1	0.00 ^f	3.41	114.3	110.9	+79.6	-61.6
	2	2.32	3.53	113.0	110.8	+67.5	+36.9
	3	3.00	3.55	114.3	112.8	-83.6	+64.1

^a Difference in MM2 steric energy (difference in heat of formation for the AM1 calculations in italics) in kcal/mol relative to the least strained conformation for each compound. ^b C(3)C(4),C(5)N(6) for **6** and **10**, C(2)C(3),C(4)N(5) for **13** and **16**. ^c SE 43.31 kcal/mol. ^d SE 38.24 kcal/mol. ^e SE 46.29 kcal/mol. ^f SE 41.64 kcal/mol. ^g $\Delta H_f = -1.32$ kcal/mol. ^h $\Delta H_f = 0.30$ kcal/mol.

stable (MM2 steric energy 25.59 kcal/mol) in the Dale¹⁵ [2323] "boat,chair,boat" conformation illustrated as **3a**,



which minimizes cross-ring interactions and has $d(NN)$ 3.248 Å, with $\alpha(av)$ at N 111.5°. The next lowest energy conformations found are slightly twisted "boat,chair,chair" types, 3.77 kcal/mol higher in energy, $d(NN)$ 2.921, $\alpha(av)$ at N 111.2 and 112.3°. Even if electron loss from the lowest energy conformation of **3** did give a $3e-\sigma$ bonded cation, it would be formed in the destabilized boat,boat conformation, which might be expected to be even shorter lived than the chair,chair species derived by addition of an electron to 2^{2+} .

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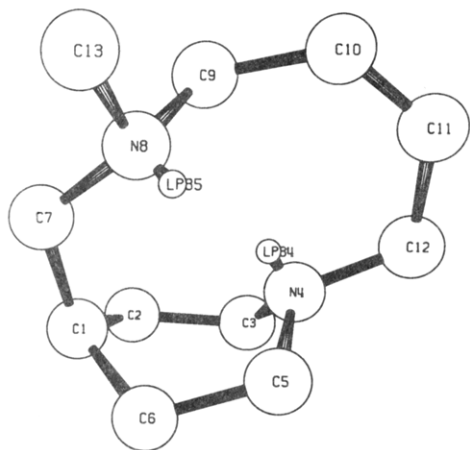


Figure 4. Drawing of conformation 10-1 of Table III.

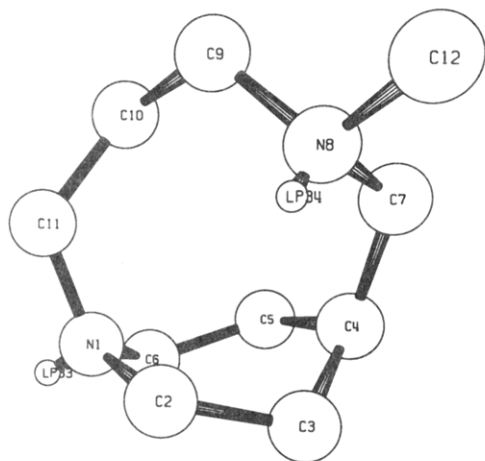


Figure 5. Drawing of conformation 13-1 of Table III.

Conformational information for the lowest energy conformations found for the aza-belted piperidine compounds 6, 10, 13, and 16 are summarized in Table III. The low steric energy conformations 6-1 (Figure 3) to 6-4 of Table III all have inward pyramidalized twist boat piperidine rings, which differ in the disposition of the belt and the amount of twist in the boat. 10-1 (Figure 4) displays a rather similar inward pyramidalized twist-boat conformation, but the next lowest steric energy conformations, 10-2 and 10-3, are very different outward pyramidalized conformations with the five piperidine ring carbons nearly planar, and large NN distances. These and other conformations are calculated to be >2.4 kcal/mol higher in energy than 10-1, in qualitative agreement with the great similarity of the ^{13}C NMR chemical shifts of 6 and 10. Both 13 and 16 are calculated to be more stable in outward pyramidalized twist-boat piperidine ring conformations which have the nitrogens 3.4–3.6 Å apart. Our naive idea of removing a CH_2 group from the belt of 6 to draw the nitrogens together does not work because, although the inward pyramidalized twist-boat conformation of 13 would indeed have the nitrogens somewhat closer together, the lowest energy such conformation is calculated to be 7.5 kcal/mol higher in energy than 13-1. The lowest energy conformations 13-1 (Figure 5) and 16-1 (Figure 6) are calculated to be >2.3 kcal/mol more stable than other conformations of these compounds, and to have nearly identical folding of the belt relative to the piperidine ring. This agrees with the very similar ^1H NMR splitting patterns observed for the belt protons of these compounds.

The ^1H NMR spectrum of 13 is favorable to determine whether the predicted conformation is that observed.

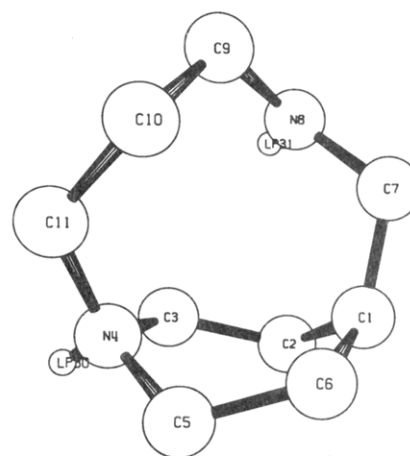
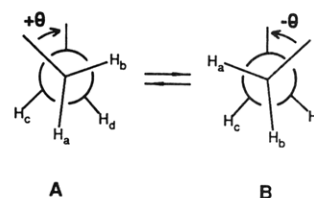


Figure 6. Drawing of conformation 16-1 of Table III.

Allinger and Profetta's parameters¹² are excellent for "ordinary" amines, but aza-belted piperidines have some unusual structural features not present in the amines with which the MM2 force field was parameterized. Testing to see whether MM2 gives the proper conformation of 13 is important to establish whether the calculations give responsible predictions for these compounds. Because of the symmetry of the piperidine ring, 13 equilibrates rapidly on the NMR time scale between equal energy conformations related by inverting the signs of all of the internal dihedral angles and flipping the nitrogen of the belt. Such equilibration causes pairwise exchange of a $\text{CH}_a\text{H}_b\text{CH}_c\text{H}_d$ unit, interchanging the roles of H_a and H_b simultaneously with those of H_c and H_d , as illustrated below on structures A and B.



Information on the chemical shift difference between H_a and H_b and between H_c and H_d is averaged away in the process, which converts an ABXY spin system into an AA'XX' spin system. The crucial conformational information on the magnitude of θ is not lost by the averaging, but retained in the $J(\text{AX})$ and $J(\text{AX}')$ values,¹⁶ so that conformations with significantly different θ values will show significantly different ^1H NMR spectra. As for "frozen" spectra, however, the approximately $\cos^2 \theta$ angle dependence of vicinal splittings causes very similar spectra to be observed for equal deviations of θ from the value which gives equal $J(\text{AX})$ and $J(\text{AX}')$ for a given system. Averaged vicinal splittings for the MM2 geometry-optimized structures were calculated using Haasnoot, de Leeuw, and Altona's generalized Karplus equation which includes electronegativity effects,^{17a} and we compare the vicinal coupling constants calculated from the MM2 optimized conformations of 13 with the data available from its NMR spectrum in Table IV. Large coupling constant differences are not predicted for the piperidine ring protons, which

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Table IV. Comparison of Vicinal NMR Splittings (Hz) with Calculated Values for 13^a

signal shift, δ	H(6)	H(4)	H(2)	H(7)	H(8/11)	H(9/10)
	2.60	2.42	3.00	2.03	1.72	3.10(s) 3.17(a)
quantity obs, Hz	J_{67av} 4.4	$J_{34}, J_{34'}$ sum 12.3, diff ~ 4	$J_{23}, J_{23'}$ sum 9.9 diff > 8	J_{78a}, J_{78b} diff > 4	J_{869a}, J_{869b} 6-8	J_{8a9a}, J_{8a9b} 6-8
calc for:						
13-1	4.4	7.5, 2.6	8.4, 0.7	7.3, 1.9	7.3, 5.6	5.3, 7.3
13-1AM	4.3	7.4, 2.7	8.4, 0.5	7.0, 1.7	7.9, 5.4	4.8, 8.0
13-2	2.9	7.8, 1.2	6.1, 2.4	8.7, 2.1	8.1, 4.0	6.2, 7.8
13-2AM	2.9	6.3, 5.8	7.3, 3.0	8.6, 1.8	8.5, 3.9	6.0, 8.3
13-3	3.2	8.2, 0.5	7.3, 4.4	7.9, 2.5	5.9, 5.9	6.0, 6.0
13-3AM	3.2	8.2, 0.5	7.3, 3.0	6.7, 3.5	6.5, 5.9	5.6, 6.5

^aFor MM2 optimized structures, and in italics, values calculated at AM1 optima obtained starting from the MM2 geometry.

is not surprising because all three conformations correspond to outside pyramidalized twist-boat piperidine rings. Significantly different predictions are made for the belt hydrogens H(2), H(4), and H(6), because the dihedral angles of the belt are very different for the three conformations (see Table III). Although the NCH_2CH_2 J values are predicted by Haasnoot, de Leeuw, and Altona's method to be lower than those observed for all three low-energy conformations, it will be noted that the MM2 lowest energy conformation 13-1 fits the observed spectrum best. 13-2 gives poor fit because neither the N(1)C(2), C(3)C(4) nor the N(5)C(4), C(3)C(2) dihedral angle is close enough to 90° to produce the "inverted" pattern with largest outer lines observed for one of the NCH_2CH_2 signals. Although 13-3 does have these two dihedral similar in size to those of 13-1, the assignments of the "normal" and "inverted" AA'XX' patterns would have to be switched. The fact that the δ value for the "inverted" pattern does not move between 13 and 16, but both the "normal" pattern and the unambiguously assigned H(6) doublet more > 0.3 δ units downfield when N(5)CH₃ is replaced by N(5)H, makes it clear that the "normal" pattern must be assigned to the hydrogens at C(4), and that 13-1 dominates the conformational mixture, as predicted by MM2.

We do not have sufficient proton NMR data to properly test the MM2 result that 6 and 10 are in inside-pyramidalized boat conformations. The ¹³C NMR results suggest substantially different conformations for 13 and 6, and similar ones for 10 and 6, which is entirely consistent with the MM2 calculations.

Although ¹H NMR is excellent for estimating heavy-atom dihedral angles in these compounds, it is essentially useless for consideration of how pyramidal the nitrogen atoms are. Pyramidalization at nitrogen is of great importance in determining how easy it is to remove an electron from nitrogen, and PE spectroscopy provides a convenient quantitative experimental determination of vIP values. We will now consider nitrogen pyramidalization for 3, 6, and 13 using their PE spectra. The lowering of vIP for a tris-primary alkyl trialkylamine caused by increasing the size of alkyl groups in the absence of pyramidalization effects is linear with an "inductive" parameter $n(\text{eff})$ for the alkyl groups, available data are fit by eq 1, and the lowering due to flattening at nitrogen may be estimated from the value of $\Delta I(\alpha)$, which is defined in eq 2.¹¹ Because the lowering

$$I(\text{calc}) = 8.92 - 0.12 \sum n(\text{eff}) \quad (1)$$

$$\Delta I(\alpha) = [\alpha(\text{av}) - 110.8][0.88/9.2] \quad (2)$$

$$\text{vIP}(\text{est}) = I(\text{calc}) - \Delta I(\alpha) \quad (3)$$

in vIP caused by flattening at nitrogen is calculated to be linear with $\alpha(\text{av})$, and 1-azamanxane (HC[3.3.3]N) is accepted as having a planar nitrogen atom and has a vIP value 0.88 eV lower than its $I(\text{calc})$ value, eq 2 and 3 were

Table V. Comparison of PE Data with Estimated Values for Lone-Pair Ionizations

	3	13	6
experimental data			
av lp vIP, eV	7.81	7.64	7.53
Δ vIP, eV	unobs	0.82	0.63
at MM2 optimized geometry	3-1	13-1	6-1
est av lp vIP, eV ^a	8.00	7.78	7.77
est Δ vIP, eV ^a	[0]	0.32	0.31
Koopmans' AM1 Δ vIP, eV ^b	0.16	0.42	0.25
at AM1 optimized geometry			
est av lp vIP, eV ^a	7.89	7.64	7.51
est Δ vIP, eV ^a	[0]	0.10	0.57
Koopmans' AM1 Δ vIP, eV ^b	0.17	0.25	0.79

^aCalculated using eq 1-3, that is, ignoring any possible through-space interaction. ^bObtained from the difference in eigenvalues for the two highest occupied orbitals in an AM1 calculation at the indicated geometry.

suggested (in slightly different form) for estimation of pyramidalization at nitrogen.¹¹ An additional factor, lone-pair, lone-pair interaction, affects the vIP values for diamines. If the interaction is assumed to cause symmetrical splitting, the average lone-pair ionization potential, vIP(av), would not be affected by lp,lp interaction. The availability of the X-ray crystallographic $\alpha(\text{av})$ value of 115.5° for 1³ allows testing the applicability of eq 1-3 for this diamine, which has in,in pyramidalized nitrogens, causing a through-space lp,lp splitting of 1.10 eV.² For 1, $I(\text{calc})$ is 7.86 eV, and $\Delta I(\alpha)$ is 0.45 eV, so the average vIP(est) using eq 1-3 is 7.41 eV, which is 0.1 eV higher than the observed value of 7.31 eV.²

The observed PE spectral parameters for 3, 13, and 6 appear in Table V, along with values estimated from eq 1-3 at two geometries, the MM2 geometry optimum, and the semiempirical molecular orbital AM1¹⁸ geometry optimum obtained starting from this point. AM1 optimization of 3 starting from the MM2 minimum gives a similar boat,chair,boat conformation, with $d(\text{N},\text{N})$ 3.237 Å and $\alpha(\text{av})$ 112.7°. As indicated in Table V, the slightly flatter nitrogens of the AM1 structure are more consistent with the vIP observed, when eq 1-3 are used to estimate vIP. It is worth noting that MM2 calculations on 1 get the nitrogens too pyramidal,¹⁰ obtaining $\alpha(\text{av})$ at 113.8°, which is 1.7° smaller than that of the X-ray structure. An inability of MM2 to flatten the nitrogens of 1 and other medium-ring amines enough is not surprising because MM2 treats the lone-pair electrons as a small, soft atom. Because the piperidine nitrogens of the compounds considered here are calculated to be flatter than those of 1, it is likely that the $\alpha(\text{av})$ values calculated for them by MM2 are at least as much in error. The AM1 optimized

geometries of starting from 13-1 to -3 geometries were also calculated. Although the nitrogens at the AM1 optimum geometry are somewhat less pyramidal, otherwise the molecular shape obtained is very similar to that obtained by MM2, as demonstrated by the geometrical information in Table III and the vicinal NMR hydrogen splittings in Table IV. It will be noted that AM1 gets less energy difference between the conformations shown than does MM2, and also inverts the order of the second and third lowest energy conformation relative to the most stable. We believe that it is very interesting that such similar geometries and relative energies are obtained by calculations as different in principle as molecular mechanics and a semiempirical molecular orbital method for these compounds. This increases our confidence that the calculated geometries are reasonable close to experimental ones.

Table V also includes estimations of vIP(av) and lp ionization separation in the absence of through-space lp,lp interaction at the AM1 optimized geometries of the lowest energy conformations of 6 and 13. The average lp vIP is considerably closer to experiment using AM1. In addition to generally flatter nitrogens, the principal difference between the AM1 and MM2 optimized geometries is that AM1 gets the piperidine nitrogen of 6-1 as flatter than that of 13-1, but MM2 gets their pyramidalities almost the same. In contrast to MM2, which gets the nitrogens to be too pyramidal, AM1 might be expected to get them to be too flat; AM1 obtains $\alpha(\text{av})$ of 112.8° for trimethylamine,¹⁸ about 2° too large. It seems to us likely that the pyramidalities at nitrogen actually present for these compounds is between the values predicted by MM2 and by AM1 calculations. We note that the lone-pair, lone-pair PE splittings observed (Table V) do not increase as the N,N distance decreases, if the geometries obtained by MM2 and AM1 are reasonably accurate, as we believe they are. No splitting is observed for 3, despite the N,N distance being estimated to be about 0.2 Å smaller than for 13, and 13 exhibits a 0.19 eV larger splitting than 6, although its N,N distance is estimated to be 0.6 Å larger than that of 6. We suggest that these initially puzzling data are a result of the relative orientation of the lone pairs. The lone-pair axes of the lowest energy conformation of 3 are calculated by MM2 to be tilted significantly from a line connecting the nitrogens ($\angle(\text{lpNN})$ 47.6°), and directed away from each other (dihedral $\angle(\text{lpN}, \text{Nlp})$ 180.0°), a geometry which leads to small overlap. The lone pairs of 13 are calculated to have $\angle(\text{lpN}_1, \text{N}_5)$ 152°, $\angle(\text{N}_1, \text{N}_5, \text{lp})$ 46°, $\text{dih}\angle(\text{lpN}_1, \text{N}_5, \text{lp})$ 41°, and those of 6 $\angle(\text{lpN}_1, \text{N}_6)$ 23°, $\angle(\text{N}_1, \text{N}_6, \text{lp})$ 45°, $\text{dih}\angle(\text{lpN}_1, \text{N}_6, \text{lp})$ 151°, so lp,lp overlap is substantially affected by geometrical parameters other than distance in comparing these compounds. The lone pairs of 6 are directed to cause small overlap despite the smaller NN distance of 6 than 13. Although AM1 calculations on pairs of NH₃ molecules held in various orientations at fixed distances do show large differences in calculated Koopmans' lp splittings, the Koopmans' lp splittings calculated by AM1 are significantly smaller than the experimental ones for both 6 and 13 (and for other calculated energy minima of these molecules); this approximation appears to us to be too crude to give useful information about relative N,N geometry in molecules of this sort. Both 6 and 13 are predicted to have substantially flattened nitrogens, which is sufficient to lead to the unusually long wavelength optical absorption observed for these diamines. The long wavelength absorption cannot be used as an experimental indication of through-space N,N overlap.

The ¹H NMR spectrum of the tricyclic aminal 19 exhibits both unusual chemical shifts and couplings. H(3e)

appears at 0.84 δ , 1.36 δ upfield of the H(3a) signal at 2.20 δ , and ¹³C(3) appears at 11.5 δ , also unusually far upfield. These features are associated with the alignment of the lone pairs, and the N(1) methylated cation 15 has considerably less unusual chemical shifts; here H(3e) appears at 1.74 δ , H(3a) at 2.26 δ , and C(3) at 16.4 δ .⁸ Decoupling experiments established the couplings and assignments shown in the Experimental Section, which correspond to the aminal ring being an only slightly flattened chair (Buys *R* value^{19a} 1.52, corresponding to significantly less flattening than that for 1,5-diazabicyclo[3.3.1]nonane, *R* value 1.17^{19b}). The piperidine ring is assigned as greatly flattened chair (*J* values at C(6,7) 11.1 (aa), 7.4 (ea and ae), and 1.6 (ee) Hz, *R* value 0.86). MM2 calculations completely agree with the above assignments. They obtain an aminal chair, flattened piperidine chair conformation (steric energy 35.42 kcal/mol) as substantially the most stable one, with the next most stable conformation having a boat aminal ring (clearly ruled out as a significant contributor to the conformational mixture by the couplings at C(3)) 3.0 kcal/mol higher in energy, and the third lowest energy conformation, which has a boat piperidine ring and chair aminal ring, as lying 4.2 kcal/mol higher in energy. For the more stable conformation, H(3e) is aligned in a nearly perfect W plan with both nitrogen lone pairs (the H(3e)-C(3) bond has dihedral angles of -3 and +3° with the lone-pair axes, and lpN,CC(3) dihedral angles of 174 and 165°). The coupling constants at C(6,7) are calculated at 11.0 (aa), 6.2 (ae), 7.2 (ea), and 0.4 (ee) Hz, *R* value 0.85, in excellent agreement with the experimental values, resulting from an N(5)C(6),C(7)C(8) dihedral angle of 38°.

Conclusion

The use of MM2¹² in conjunction with Saunders's stochastic (random movement) search for conformational minima¹³ leads to predicted conformations which rationalize both the NMR and PE spectral data for the compounds under discussion. Semiempirical MO AM1 calculations give rather similar geometries for these compounds, although the nitrogens are predicted to be flatter, in better agreement with the PE spectral data. We note that a stochastic search for conformational minima using semiempirical calculations would not only be prohibitively expensive, but would not work because the "jumps" break bonds. Generating a series of starting structures using molecular mechanics appears to provide a reasonable entry to finding structures for semiempirical calculations on flexible molecules. None of the compounds studied are predicted to have their lone pairs directed toward each other in a manner that electron loss can smoothly lead to a 3e- σ bonded cation radical, rationalizing the observed lack of dication formation upon oxidation of the neutral compounds.

Experimental Section

1-(4-Chlorobut-2-enyl)-2-methyl-1-azonia-2-azabicyclo[2.2.2]octane Chloride (8). A mixture of 4 (0.50 g, 3.97 mmol) in CH₃CN (5 mL) and 1,4-dichloro-2-butene (0.496 g, 3.97 mmol) was refluxed for 15 min and allowed to stand at room temperature overnight. The white precipitate formed was filtered under N₂ to yield 8 (0.24 g, 0.956 mmol, 24%) as hygroscopic white crystalline needles. Concentration of the mother liquors showed a mixture of 8 with what appeared from its NMR spectrum to be bis-aminated 2-butene, but their separation was not achieved. For 8: ¹H NMR (CDCl₃) δ 6.10 (m, 1 H), 5.68 (m, 1 H), 4.83 (d, 2 H), 4.56 (m, 2 H), 4.48 (d, 2 H), 3.95 (m, 2 H), 3.20 (d, 2 H), 2.85 (s,

(19) (a) For discussion of *R* values, see: Lambert, J. B. *Acc. Chem. Res.* 1971, 4, 87. (b) Nelsen, S. F.; Hintz, P. J.; Landis, R. T., III *J. Am. Chem. Soc.* 1972, 94, 7105.

3 H), 1.9–2.4 (m, 6 H); ^{13}C NMR (CDCl_3) δ 21.7 (CH), 23.3 (CH_2 , 2 C), 39.1 (CH_2), 40.98 (CH_3), 54.78 (CH_2 , 2 C), 57.4 (CH_2), 59.3 (CH_2), 119.8 (CH), 135.8 (CH); mp >270 °C dec. Anal. (micro). Calcd for $\text{C}_{11}\text{H}_{20}\text{N}_2\text{Cl}_2$: C, 52.57; H, 8.03; N, 11.16; Cl, 28.24. Found:²⁰ C, 52.38; H, 8.01; N, 11.04; Cl, 28.16.

6-Methyl-1,6-diazoniatricyclo[6.2.2.0^{1,6}]dodec-3-cis-ene Bis(tetrafluoroborate) ($9^{2+}[\text{BF}_4^-]_2$). A sample of 8 (80 mg, 0.32 mmol) was added via solid addition funnel to a stirred solution of Ag_2O (74 mg, 0.32 mmol) in 48% HBF_4 (1.0 mL); the mixture was stirred at room temperature under N_2 for 12 h. The gray precipitate which formed was filtered off through a medium-glass fritted filter and washed with 0.5 mL of 48% aq HBF_4 . To this filtered solution was added a 60/40 EtOH/Et₂O solution dropwise until a precipitate formed. The precipitate was collected to give $9^{2+}[\text{BF}_4^-]_2$ (60 mg, 0.16 mmol, 53%) as a white powder, mp 170–171.5 °C dec: ^1H NMR (D_2O) δ 6.01 (m), 5.5–5.8 (m), 4.0–4.9 (m), 3.75 (s), 2.25 (m). This powder is extremely base sensitive and decomposes slowly in D_2O ; it was used without further characterization.

6-Methyl-1,6-diazabicyclo[6.2.2]dodec-3-cis-ene (10). To a blue stirring solution of Na (0.2 g, 8.8 mmol) in ammonia (15 mL) in a three-necked 25-mL round-bottomed flask was added $9^{2+}[\text{BF}_4^-]_2$ (0.311 g, 0.88 mmol) via solid addition funnel. The solution was stirred at reflux for 2 h and methanol was added dropwise until the blue color disappeared; the solvent was evaporated at room temperature with a stream of N_2 . After addition of 5 mL of water to the residue and extraction with 3 \times 20 mL portions of ether, drying over K_2CO_3 , and filtration, solvent removal by rotary evaporation (warm-water bath) gave 10 (40 mg, 0.22 mmol, 25%) as a clear oil: ^1H NMR (CDCl_3) δ (ppm) 5.7 (qt, $J = 11.0$ Hz, 1 H), 5.45 (dt, $J = 11.0$, 3.3 Hz, 1 H), 3.23 (m, 4 H), 2.99 (td, 2 H), 2.5 (m, 4 H), 2.30 (s, 3 H), 1.9 (m, 3 H), 1.7 (m, 2 H); ^{13}C NMR (CDCl_3) δ 131.32 (CH), 129.57 (CH), 66.37 (CH_2), 55.57 (CH_2), 55.42 (CH_2), 47.88 (CH_2 , 2 C), 46.84 (CH_3), 31.27 (CH_2), 28.301 (CH_2 , 2 C). Empirical formula $\text{C}_{11}\text{H}_{20}\text{N}_2$ was determined by high resolution mass spectroscopy; IR (neat) 2770, 1645 cm^{-1} .

4-(*N*-Methylaminomethyl)piperidine (11). A heterogeneous mixture of 11 (160 mg, 1.12 mmol) in anhydrous ether (50 mL) and benzene (50 mL) was added to a solution of LAH (430 mg, 11.2 mmol) in ether (50 mL) and stirred at reflux under N_2 for 24 h. After standing at room temperature for 48 h, the mixture was worked up by the 1:1:3 method and filtered through a layer of Celite; the resulting clear solution was dried over K_2CO_3 . The solvent was removed by rotary evaporation to give a crude yellow oil which was Kugelrohr distilled to give 11 (110 mg, 0.86 mmol, 77%) as a colorless viscous oil. Empirical formula $\text{C}_7\text{H}_{16}\text{N}_2$ determined by high resolution mass spectroscopy. ^1H NMR (CDCl_3) δ 3.09 (bd, 2 H), 2.6 (dt, 2 H), 2.45 (m, 5 H, CH_3 singlet), 1.7 (bd), 1.55 (m), 1.15 (m).

4-(*N*-Methylcarbamoyl)piperidine (12). A 50-mL Parr bottle was charged with 4-(*N*-methylcarbamoyl)piperidine (2.0 g, 14.6 mmol, prepared from the ethyl ester and methylamine in a sealed tube, mp 109–111 °C, lit.^{21a} 110 °C), 15 mL of acetic acid, and PtO_2 (300 mg). This mixture was shaken under H_2 (30–40 psi) until hydrogen consumption had ceased. The reaction mixture was filtered through a layer of Celite and rinsed with AcOH; most of the acetic acid was removed by rotary evaporation. To this viscous solution were added 50 mL of H_2O and KOH until the solution was basic. After extraction with 8 \times 25 mL portions of ether to remove impurities, the aqueous solution was extracted with ethyl acetate (8 \times 25 mL and then 6 \times 50 mL), the extract dried with K_2CO_3 , and solvent removed by rotary evaporation to give 12 (0.94 g, 6.6 mmol, 45%) as a white solid, mp 123–125 °C (lit.^{21b} 117–121 °C): ^1H NMR (CDCl_3 , 200 MHz) δ 5.42 (bs, 1 H), 3.15 (dt, 2 H), 2.82 (d, 3 H), 2.61 (td, 2 H), 2.33 (tt, 1 H), 1.83 (bd, 2 H), 1.58 (qd, 2 H).

5-Methyl-9-*exo*-deuterio-1,5-diazabicyclo[5.2.2]undecane (13-d). Anhydrous ether (25 mL) was added via cannula to a flame-dried, N_2 -flushed 50-mL round-bottomed flask containing a stirring bar, and 137 mg (3.26 mmol) of lithium aluminum

deuteride was added to the stirred solution, followed by addition of solid 15⁸ (100 mg, 0.34 mmol) in small portions. After the addition was complete, the reaction mixture was stirred at room temperature under N_2 for 21 h and quenched using the 1:1:3 method (0.15 mL of H_2O , 0.15 mL of 15% aqueous NaOH, and 0.45 mL H_2O). The salts were stirred vigorously in ether and then filtered, rinsing several times with ether. The extracts were dried (K_2CO_3), filtered, and concentrated by rotary evaporation to give 13-d (40 mg, 0.24 mmol, 70%) as a clear colorless oil. Empirical formula $\text{C}_{10}\text{H}_{19}\text{DN}_2$ was determined by high resolution mass spectroscopy. ^1H NMR (CDCl_3 , 500 MHz) 3.17 (m, H[10-anti]), 3.10 (m, 2 H[9,10-syn]), 3.00 (m, outer peak separation 10 Hz, 2 H[2]), 2.60 (d, $J = 4.4$ Hz, 2 H[6]), 2.42 (approx t, $J = 6.1$ Hz, 2 H[4]), 2.39 (s, 3 H[Me]), 2.03 (m, 1 H[7]), 1.72 (m, 4 H[8,11]), 1.68 (m, 2 H[3]).

4-(*N,N*-Dimethylaminomethyl)-*N*-methylpiperidine (14). Formic acid (88%, 1.0 mL) was cooled to 0 °C and added to neat 11 (124.2 mg, 0.97 mmol), followed by the immediate addition of 40% formaldehyde (1.08 g, 14.4 mmol). After stirring at ambient temperature for 30 min, the mixture was heated on a steam bath for 6 h. After cooling to room temperature, the solution was basified with 10 mL of saturated KOH and extracted with pentane (5 \times 7 mL). The organic phases were combined, dried (K_2CO_3), and concentrated under reduced pressure to produce a clear oil which was Kugelrohr distilled to yield 116.7 mg (0.74 mmol, 77%) of 14. Empirical formula $\text{C}_9\text{H}_{20}\text{N}_2$ was determined by high resolution mass spectroscopy. ^1H NMR (CDCl_3) δ 2.85 (bd, 2 H), 2.28 (s, 3 H), 2.21 (s, 6 H), 2.1 (d, 2 H), 1.9 (bt, 2 H), 1.72 (bd), 1.4 (bm, 1 H), 1.25 (btd, 2 H). See Table II for the ^{13}C NMR. The same Table II for the ^{13}C NMR. The same material was prepared in 26% yield by reduction of 1,2,2-trimethyl-1,2-diazoniabicyclo[2.2.2]octane bis(fluoroborate) (bis-methylated 4) with sodium in ammonia.

1-Azonias-5-azatricyclo[5.2.2.0^{1,5}]undecane Bromide (18). To a solution of 17 (0.73 g, 6.52 mmol) in absolute ethanol (20 mL) was added 1,3-dibromopropane (6.58 g, 32.6 mmol, 5 equiv), and the mixture was stirred at reflux under N_2 for 48 h. After solvent removal by rotary evaporation under aspirator pressure, excess 1,3-dibromopropane was removed at 1 Torr. The brown residue was recrystallized from chloroform to give 18 (0.486 g, 2.1 mmol, 32%) as small white plates, mp 246–252 °C dec: ^1H NMR (CDCl_3) δ 4.7 (m, 2 H), 3.98 (t, $J = 7.7$ Hz, 2 H), 3.7 (m, 2 H), 3.33 (t, $J = 7.3$ Hz, 2 H), 3.26 (d, $J = 2.9$ Hz, 2 H), 2.41 (quintet, $J = 7.7$ Hz, 2 H), 2.31 (quintet, $J = 3.0$ Hz, 1 H), 2.12 (td, $J = 3.4$, 8.4 Hz, 4 H); ^{13}C NMR (CDCl_3) δ 63.25 (CH_2), 57.16 (CH_2 , 2 C), 55.88 (CH_2), 51.72 (CH_2), 23.98 (CH_2 , 2 C), 22.35 (CH_2), 22.28 (CH). Anal. (micro):²⁰ Calcd for $\text{C}_9\text{H}_{17}\text{N}_2\text{Br}$: C, 46.34; H, 7.35; N, 12.05; Br, 33.94. Found: C, 46.21; H, 7.30; N, 11.96; Br, 34.06. Note: The yield in the above reaction can be improved by adding 2 molar equiv of K_2CO_3 to the reaction and filtering it off before evaporation of the solvent.

1,5-Diazabicyclo[5.2.2]undecane (16). (a) **By H_2 Reduction.** A 25-mL Parr bottle was charged with 18 (200 mg, 0.858 mmol), platinum oxide (25 mg), 4 mL of ethanol, and acetic acid (1 mL). The mixture was shaken under 5–40 psi of hydrogen until uptake of H_2 had ceased, the catalyst filtered off through a layer of Celite, and the solvent removed by rotary evaporation. The slightly brown solid residue was dissolved in H_2O (2 mL), basified with KOH, and extracted with ether (3 \times 10 mL). The ether extract was dried (K_2CO_3), and filtered. The solvent was removed by rotary evaporation to give 16 (30 mg, 0.2 mmol, 23%) as a yellowish oil: ^1H NMR (CDCl_3) δ 3.15 (m, 4 H[9,10]), 3.0 ("inv. t", 2 H[2]), 2.9 (d, 2 H[6]), 2.8 (t, 2 H[4]), 2.1 (m, 1 H[7]), 1.7 (m, 6 H[8,11,3]), ^{13}C NMR (CDCl_3) 58.49 (CH_2), 57.40 (CH_2), 49.42 (CH_2), 45.50 (CH_2 , 2 C), 31.25 (CH_2), 29.52 (CH), 27.34 (CH_2 , 2 C). Empirical formula $\text{C}_9\text{H}_{18}\text{N}_2$ was established by high resolution mass spectroscopy.

(b) **By Na Reduction.** Solid 18 (71 mg, 0.305 mmol) was added to a blue stirred solution of Na (0.7 g, 30.5 mmol) in NH_3 (15 mL) in a three-necked 25-mL round-bottomed flask equipped with solid addition funnel, dry ice reflux condenser, and rubber septum. The mixture refluxed for 3 h, methanol was added dropwise until the blue color was dissipated, ammonia was then allowed to evaporate by warming to room temperature under N_2 , and methanol was removed under vacuum, warming the flask slightly with a heat gun. The product was bulb-to-bulb distilled under

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vacuum by heating with a heat gun, giving 20 mg (43%) **16** as an oil.

1,5-Diazatricyclo[6.2.1.0^{5,10}]undecane (19). (a) **By I₂ Oxidation of 16.** A solution of I₂ (41 mg, 0.16 mmol) in CDCl₃ (1.0 mL) was added dropwise to a solution of **16** (18 mg, 0.12 mmol) in CDCl₃ until an orange color persisted. Examination of the solution by ¹H NMR showed protonated **19** to be present. The solution was washed with aq KOH, the chloroform layer dried (K₂CO₃) and filtered, the solvent removed by rotary evaporation. Bulb-to-bulb distillation under high vacuum using a heat gun gave **19** as a clear colorless oil: ¹H NMR (CDCl₃, 500 MHz) δ 4.01 [d, *J* = 4.2 Hz, H(10)], 3.36 [td, 13.2, 4.6, H(2/4a)], 3.22 [dd, 9.6, 5.9, H(11x)], 3.1 [m, 2H H(2/4e), H(4/2a)], 3.03 [td, 11.7, 7.4, H(6a)], 2.90 [m, H(4/2e)], 2.88 [ddd, 12.3, 7.4, 1.6, H(6e)], 2.63 [d, 9.6, H(11n)], 2.39 (br m, H(8)), 2.20 [dt, 14.1, 12.2, 5.2, H(3a)], 1.91 [m, H(9a), H(7e)], 1.75 [m, H(7a)], 1.59 [d, 11.1, H(9b)], 0.84 [dt, 14.2, 4.3, 2.2, H(3e)]; ¹³C NMR (CDCl₃) δ 74.5 (CH[10]), 52.8 (CH₂), 51.2 (CH₂), 46.5 (CH₂), 42.6 (CH₂), 38.4 (CH₂), 32.3 (CH[8]), 31.8 (CH₂), 11.5 (CH₂[3]).

(b) **By Autoxidation.** O₂ was bubbled in to a solution of **16** in CDCl₃ (10.0 mg/0.5 mL, 0.13 M) for 1 min. **19** was detectable, although **16** was still the major product.

(c) **By Quinone Oxidation.** A solution of **16** (0.0073 g, 0.047 mmol) in CDCl₃ (0.40) was prepared and examined by ¹H NMR. To this solution was added a solution of benzoquinone (5.0 mg, 0.047 mmol) in CDCl₃ (0.1 mL). Analysis by ¹H NMR showed **19** to be present; no **16** remained.

Equipment. Bruker AM.500 and EM.270 NMR spectrometers, a Varian IEE-15 PE spectrometer modified as previously described,²² and PAR electrochemical equipment were employed. Pulse radiolysis experiments were conducted using the 1.55-MeV Van de Graaf generator at the Hahn-Meitner-Institut, Berlin, using N₂-saturated water containing 0.1 M *tert*-butyl alcohol to scavenge hydroxyl radicals and 1–2 × 10⁻⁴ M dication.

Calculations. Calculations were carried out on a VAX 8650. MM2 calculations used a modified version of QCPE Program No.

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395. It should be noted that early QCPE versions of MM2 have a mistake in the amine parameters,^{12b} and give different answers as a result. Vicinal H,H couplings were calculated using a modified version of Program 3JHH. Osawa and Jaime's implementation^{17b} of Haasnoot, de Leeuw, and Altona's generalized Karplus equation.^{17a} The most important modification^{17c} was fixing a bug in subroutine HCOREC of ref 17b in which the CH₂ symmetry correction recommended in ref 17b was improperly handled and sometimes gave wildly incorrect couplings. AM1 calculations used the AMPAC 1.00 package (*QCPE Bull.*, 1986, 506, 24a).

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Registry No. 2²⁺[BF₄⁻]₂, 73843-85-3; 3, 82415-33-6; 4, 6523-29-1; 5²⁺[BF₄⁻]₂, 82415-32-5; 6, 82415-30-3; 7²⁺[BF₄⁻]₂, 103094-95-7; 8, 126579-23-5; 9²⁺[BF₄⁻]₂, 126579-25-7; 10, 126579-21-3; 11, 126579-26-8; 12, 1903-69-1; 13, 103094-97-9; 13-*d*, 126579-27-9; 14, 126579-28-0; 15, 103094-84-4; 16, 103671-59-6; 17, 329-94-2; 18, 126579-29-1; 19, 126579-22-4; ClCH₂CH=CHCH₂Cl, 764-41-0; Br(CH₂)₃Br, 109-64-8; 4-(*N*-methylcarbamoyl)pyridine, 6843-37-4.

Supplementary Material Available: Illustrations of the ¹H NMR spectra of **10**, **11**, **13-d**, **14**, **16**, and **19**, and ¹³C NMR spectra of **10** and **14** (8 pages). Ordering information is given on any current masthead page.

Estimating Entropies and Enthalpies of Fusion of Hydrocarbons

James S. Chickos* and Donald G. Hesse

Department of Chemistry, University of Missouri—St. Louis, St. Louis, Missouri 63121

Joel F. Liebman

Department of Chemistry and Biochemistry, University of Maryland—Baltimore County, Baltimore, Maryland 21228

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A group additivity method for estimating fusion entropies and fusion enthalpies is described. The method is based on experimental fusion enthalpies of 191 hydrocarbons. Group values are provided for most structural environments. Applications of the technique are described, and comparisons with literature values and other estimation techniques are also included. The average deviation between experimental and calculated fusion entropies and enthalpies is ±1.85 eu and ±0.56 kcal/mol, respectively.

Fusion, vaporization, and sublimation enthalpies are important physical properties of the condensed phase. A variety of studies including those that reference the gas phase as a standard state require accurate values for these quantities.^{1,2} The vast number of new organic compounds

prepared annually far exceeds the relatively few number of thermochemical measurements reported in this same period. This divergence in numbers has directed our interest toward the development of simple empirical relationships that can be used to estimate these enthalpies.³

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