

Table VIII. Mulliken Orbital Populations of Selected Aromatic Hydrocarbons (electron units)

compound	orbital population			
	1s	2s	2p _x + 2p _y	2p _z
1 C ₃ H ₃ ⁺	1.99232	1.18153	2.04962	0.66667
2 C ₇ H ₇ ⁺	1.99178	1.15295	1.97580	0.85714
3 C ₆ H ₆	1.99178	1.13282	1.92281	1.00000
4 C ₉ H ₉ ⁻	1.99199	1.11693	1.88599	1.11111
5 C ₅ H ₅ ⁻	1.99218	1.11388	1.86741	1.20000
6 C ₈ H ₈ ²⁻	1.99217	1.10775	1.82507	1.25000

Table IX. Optimized Geometries and Scale Factors of Selected Hydrocarbons

compound	r _{CC} (Å)	r _{CH} (Å)	C(1s)	C(2s2p)	H(1s)
1 C ₃ H ₃ ⁺	1.376	1.095	5.702	1.753	1.303
2 C ₇ H ₇ ⁺	1.398	1.089	5.704	1.738	1.247
3 C ₆ H ₆	1.394	1.090	5.704	1.720	1.207
4 C ₉ H ₉ ⁻	1.390	1.085	5.704	1.700	1.174
5 C ₅ H ₅ ⁻	1.394	1.080	5.703	1.676	1.170
6 C ₈ H ₈ ²⁻	1.399	1.089	5.703	1.670	1.132

charge-shift correlations established for a given series of molecules should not be indiscriminately assumed to be valid in all systems. In series of closely related compounds, however, the judicious use of charge-shift correlations can give valuable information about atomic charges. It has been shown, indeed, that the definition of charge (eq 3) satisfying eq 1 is the same as that satisfying molecular energies expressed in terms of electron distributions.²¹ In this manner, charge-shift relationships offer the possibility of studying large molecules of biological interest, which would otherwise lie outside the range of computational feasibility; whether honestly earned from lengthy (and expensive) theoretical calculations, or simply "stolen" from critically established empirical correlations, a charge is a charge and a useful quantity as long as its reliability can be assessed.

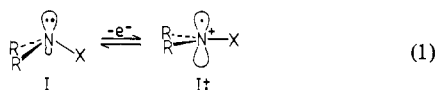
The 3,3-Dimethyl-2-azabicyclo[2.2.2]octyl System as a Bredt's Rule Kinetically Stabilized Dialkylamino Group in Electron-Transfer Studies

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Abstract: PE and CV data are reported for electron removal from 2-substituted 3,3-dimethyl-2-azabicyclo[2.2.2]octyl (2-ADO) derivatives in which the substituent is chloro, dimethylamino, 2-ADO, and —N=N-2-ADO and compared with that for their 9-azabicyclo[3.3.1]nonyl (9-ABN) analogues. The differences observed in both IP₁ and E^{o'} in the two series of compounds are dominated by their steric differences; 2-ADO has *tert,sec*-alkyl substitution at N while 9-ABN has *sec,sec*-alkyl substitution. The E^{o'} values for chloramines and 2-tetrazenes are dominated by the ease of flattening at nitrogen, but RN-N'R interactions dominate the E^{o'} observed for the hydrazines. The 2-ADO dimer (3) has ΔG^o of 18.8 kcal/mol (+63 °C) for methyl interconversion, which is >8.8 kcal/mol greater than twice that of its 2-dimethylamino analogue (5). 3 is argued to have significant flattening at both nitrogens at the transition state, in contrast to all previously studied tetraalkylhydrazines. 3⁺·PF₆⁻ proved isolable.

The principal problem in studying electron removal from dialkylamino-containing compounds¹ (the reaction shown in eq 1)



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Appendix I

The geometries of the compounds indicated in Table VIII were deduced from standard STO-3G calculations, using standard scale factors, i.e., C(1s) = 5.67, C(2s2p) = 1.72, and H(1s) = 1.24. Using the optimized geometries, extensive scale factor optimizations have been carried out, giving the final charge results indicated in Table VIII. The optimized geometries and scale factors are reported in Table IX.

In the evaluation of atomic charges, we have considered that the usual halving of overlap populations implied in Mulliken's scheme¹⁹ may not be appropriate in heteronuclear situations.⁶ For this reason, one should not make comparisons between, say, primary, secondary, etc., carbon atoms using Mulliken charges. In order to avoid this sort of drawbacks, comparisons are made only between atoms engaged in the same type of bonding, e.g., the CH carbon atoms of the compounds indicated in Table VIII, in which case charge differences expressed in terms of Mulliken charges should represent valid estimates.

Registry No. CH₃CHO, 7507-0; C₂H₃CHO, 123-38-6; *i*-C₃H₇CHO, 78-84-2; (CH₃)₂CO, 67-64-1; CH₃COC₂H₅, 78-93-3; CH₃CO-*i*-C₃H₇, 563-80-4; (C₂H₅)₂CO, 96-22-0; C₂H₅CO-*i*-C₃H₇, 565-69-5; (*i*-C₃H₇)₂CO, 565-80-0; CH₄, 74-82-8; CH₂=CH₂, 74-85-1; CH₃CH=C-H₂, 115-07-1; (CH₃)₂C=CH₂, 115-11-7; *trans*-CH₃CH=CHCH₃, 624-64-6; *cis*-CH₃CH=CHCH₃, 590-18-1; (CH₃)₂C=CHCH₃, 513-35-9; (CH₃)₃C=C(CH₃)₂, 563-79-1; CH≡CH, 74-86-2; CH₃C≡CH, 74-99-7; CH₃C≡CCH₃, 503-17-3; cyclopropenium cation, 19553-81-2; cycloheptatriene cation, 26811-28-9; benzene, 71-43-2; cyclononatetraenide anion, 45730-23-2; cyclopentadienide anion, 12127-83-2; cyclooctatetraenide dianion, 34510-09-3; azulene, 275-51-4; ethane, 74-84-0; propane, 74-98-6; isobutane, 75-28-5; neopentane, 463-82-1; cyclohexane, 110-82-7; adamantane, 281-23-2; cyclopentane, 287-92-3; cyclobutane, 287-23-0; cyclopropane, 75-19-4.

is that for most X groups, the radical cation is extremely short-lived because it rapidly loses a proton from a carbon α to the nitrogen atom. This undesired decomposition can be successfully inhibited by "Bredt's rule kinetic stabilization",² by which is meant forcing

(1) For a review, see: Nelsen, S. F. *Isr. J. Chem.* 1979, 18, 45.

Scheme I

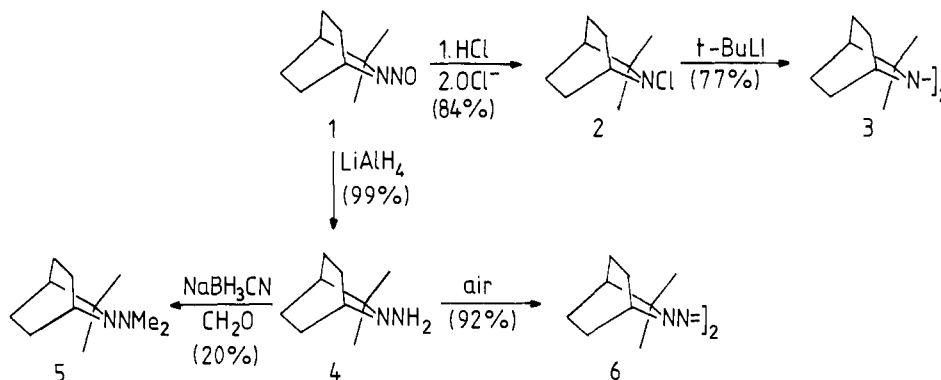
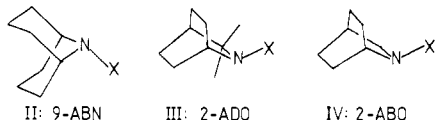


Table I. Formal Oxidation Potentials and Vertical Ionization Potentials for Some Bicyclic Amino Compounds

$R_2N = 2\text{-ADO (II)}$					$R_2N = 9\text{-ABN (III)}^a$			$R_2N = 2\text{-ABO (IV)}$			
example	compd	$E^{\circ'}$ (ΔE_p) ^b	IP, eV ^c	$[E^{\text{ox}}_p]$	compd	$E^{\circ'}$ (ΔE_p) ^b	IP, eV ^c	compd	$E^{\circ'}$ (ΔE_p) ^b	IP, eV ^c	$[E^{\text{ox}}_p]$
R_2NCl	2	1.29 (69)	8.34		7	1.49 (82)	8.55	11	irr [E^{ox}_p 1.32] ^d		[8.6]
$(R_2N)_2$	3	0.26 (83) irr [E^{ox}_p 0.83] ^{d,e}		[7.4, 9.8]	8	-0.01 (62) 1.18 (70) ^e	6.94, 9.07	15	(not studied)	(not studied)	
R_2NNMe_2	5	0.25 (154) ^f		[7.2, 8.0]	9	0.11 (62)	7.53, 8.42, 9.5-9.6	12	0.13 (89)		[7.7, 8.5]
$R_2NN=$	6	0.17 (71) 1.34 (94) ^e	7.04		10	0.40 (72) 1.35 (91) ^e	7.07, 8.54, 9.09	13	0.29 (63) irr [E^{ox}_p 1.28] ^{d,e}		7.05 [8.7, 9.1]

^a Data from ref 2. ^b Cyclic voltammetry conditions = 2.0 mM substrate in acetonitrile containing 0.1 M tetra-*n*-butylammonium perchlorate, 200 mV/s scan rate, 23 ± 1 °C; working electrode, gold for potentials below 1 V, Pt for higher potentials; the same $E^{\circ'}$ values were observed for potentials below 1 V at platinum as at gold. $E^{\circ'}$ reported in V vs. SCE; ΔE_p , the difference in oxidation and reduction peak potentials, is reported in mV. ^c Vertical ionization potentials measured by photoelectron spectroscopy; lone-pair ionizations are reported. ^d Totally irreversible oxidation wave. ^e Data for the second oxidation wave. ^f Obvious heterogeneous electron-transfer rate problems. Even slower electron-transfer rate at platinum, $E^{\text{ox}}_p = 0.53$, $E^{\text{red}}_p = 0.14$, $\Delta E_p = 0.34$, $\Delta E_p = 390$ mV.

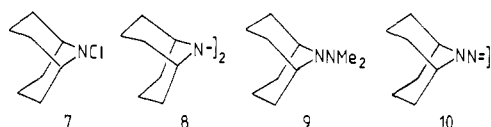
the C_α -H bonds to lie in the nodal plane of the half-filled p orbital on nitrogen of I^+ . When the dialkylamino group is the 9-azabicyclo[3.3.1]nonyl system (9-ABN, II), the radical cation proves



to be conveniently long-lived when X cannot deprotonate rapidly, and relative thermodynamic data have been measured for a number of II and II^+ examples. A large geometry change frequency accompanies electron transfer in dialkylamino compounds, causing these electron transfers to have unusual properties and show strong conformational effects, especially for hydrazine (I , $X = NR_2$) examples.³ Obvious questions are to what extent the results for II are unique to the particular alkyl substituents present and to what extent they may be generalized to other dialkylamino groups. To probe this point, we have studied examples of compounds having another Bredt's rule kinetically stabilized dialkylamino group, the 3,3-dimethyl-2-azabicyclo[2.2.2]octyl system (2-ADO, III). Changing from the *sec,sec*-alkyl substitution of II to the *tert,sec*-alkyl substitution of III causes significant differences in both their electron-transfer and conformational properties.

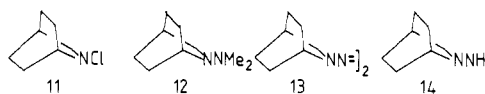
Compound Preparation. The details of the preparation of 2-nitroso-2-ADO (1) from *p*-aminobenzoic acid by catalytic reduction/cyclization to isoquinuclidone, LAH reduction to isoquinuclidine, and dimethylation at C_3 via the deprotonated *N*-nitroso compounds have been previously described.⁴ Conversion

of 1 to the four examples of III studied in this paper is summarized in Scheme I; the reactions are analogous to those used previously in making the II derivatives 7-10. We were pleased to find that

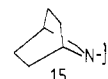


the reductive coupling of 2 to 3 proceeds well, despite the strain present in 3. 2-Amino-2-ADO 4 is notably more air sensitive than typical *N,N*-dialkylhydrazines, and mostly 2-tetrazene 6 was isolated after a normal workup of the LAH reduction of the 2-nitroso compound in air.

As models to consider the effect of the tertiary alkyl substituent of 2-ADO, we have also prepared the 2-azabicyclo[2.2.2]octyl (2-ABO) analogues 11-13 by reactions analogous to Scheme I.



2-Amino-2-ABO 14 is much less air sensitive than 4, and iodine oxidation was employed to generate tetrazene 13. We have failed to prepare 2,2'-bis(2-ABO) 15; the nitrogen is not Bredt's Rule



protected, and neither *tert*-butyllithium treatment of chloroamine 11 nor photolysis of 2-tetrazene 13 generated a significant amount of 15.

Results: CV Studies and Isolation of $3^+\cdot PF_6^-$. Table I contains a summary of the CV formal potential ($E^{\circ'}$) measurements comparing 2-ADO, 9-ABN, and 2-ABO systems. A very large

(2) Nelsen, S. F.; Kessel, C. R.; Brien, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 702.

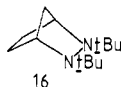
(3) For a review, see: Nelsen, S. F. *Acc. Chem. Res.* **1981**, *14*, 131.

(4) Nelsen, S. F.; Gannett, P. M.; Steffek, D. J. *J. Org. Chem.* **1980**, *45*, 3857.

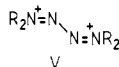
oxidation peak to reduction peak separation (154 mV at 200 mV/s scan rate) was observed for the hydrazine 2-dimethylamino-2-ADO (**5**), implying that electron transfer is unusually slow for this compound. Even greater peak-to-peak separation was observed at platinum (385 mV at 200 mV/s scan rate) than at gold, as expected from previous work.⁵ We suggest that the unusually broad CV is caused by **5** having a very unstable anti lone-pair conformation (lone pair–lone pair dihedral angle 180°) due to steric interference of a dimethylamino methyl group with the C₃ methyl groups. A 1,3-diaxial-like interaction cannot be avoided in the anti conformation. It has been previously established that electron transfer is far faster from anti than from gauche conformations of hydrazines and suggested that prior isomerization to the rapidly oxidizing anti form precedes electron transfer for hydrazines.³ Because of the unusually large peak-to-peak separation in the CV of **5**, its formal potential is significantly less accurate than the other values reported, which should be accurate to ±0.01 V. Another result that should be noted is that no reduction wave could be observed for the second oxidation of bis-2-ADO **3**, even at fast scan rates. This result indicates that 3²⁺, in contrast to 8²⁺, is short-lived on the CV time scale.

Treatment of the 2-ADO dimer **3** with NO⁺PF₆⁻ gave 3⁺·PF₆⁻ as a faintly yellow solid, which was purified by crystallization. Solutions of the solid show the ESR spectrum of 3⁺, similar to that generated by NO⁺PF₆⁻ or (pBrC₆H₄)₃N⁺·SbCl₆⁻ oxidation of **3**: *a*(2N) = 13.5 G, *a*(4H) = 2.5 G (attributed to the anti γ hydrogens) in butyronitrile. The UV spectrum of 3⁺·PF₆⁻ in acetonitrile shows a maximum at 303 nm ($\epsilon = 4.5 \times 10^3$), which we attribute to the π, π^* absorption of the three-electron π bond. This hydrazine radical cation is only the second one reported to be isolable—8⁺ was the first.⁷

Discussion: Effectiveness of 2-ADO as a Bredt's Rule Protected Dialkylamino Group. The CV data of Table I show that 2-ADO does provide an effectively protected R₂N group, since 2-ADO chloride **2** does show reversible oxidation. Chloroamines that are not Bredt's rule protected such as 2-ABO chloride **11** show totally irreversible oxidation, presumably because of rapid radical cation deprotonation. Almost all hydrazines and 2-tetrazenes show reversible first-oxidation waves as do the 2-ADO and 2-ABO derivatives, but the only previously reported hydrazines and 2-tetrazenes having long-lived enough dicationions for observation of reversible second-oxidation waves were those protected as 9-ABN derivatives.² Despite its Bredt's rule protection, bis-2-ADO **3** has a totally irreversible second-oxidation wave, even at -60 °C (in butyronitrile) at a 20 V/s scan rate, so 3²⁺ does not last the several milliseconds required for *E*^{o'} measurement. 3²⁺ is not only strained relative to 8²⁺ (see below) but can cleave off a tertiary alkyl cation, whereas 8²⁺ can only lose a secondary alkyl cation. It has been found previously that cis ditertiary hydrazine radical cations such as that from **16** are unstable on the CV time scale at room tem-



perature and lose the tertiary alkyl group and that their dicationions cleave off a tertiary alkyl group even more rapidly.⁶ 3⁺ is longer lived than such species and is also rather clearly less strained—3⁺ lacks the *cis tert-alkyl-tert-alkyl* interaction, although it has two *tert-alkyl-sec-alkyl* interactions. Both 3²⁺ and 16²⁺ are too short-lived for *E*^{o'} measurement. Strain relief is clearly implied as causing the short lifetime for 3²⁺, because the related tetrazene dication 6²⁺, which has a formal terminal nitrogen charge density of +1 (see V) and is thermodynamically harder to form than is



(5) Evans, D. H.; Kinlen, P. J.; Nelsen, S. F. *J. Electroanal. Chem. Interfacial Electrochem.* **1979**, *97*, 265.

(6) Nelsen, S. F.; Parmelee, W. P. *J. Org. Chem.* **1981**, *46*, 3453.

(7) Nelsen, S. F.; Hollinsed, W. C.; Kessel, C. R.; Calabrese, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 7876.

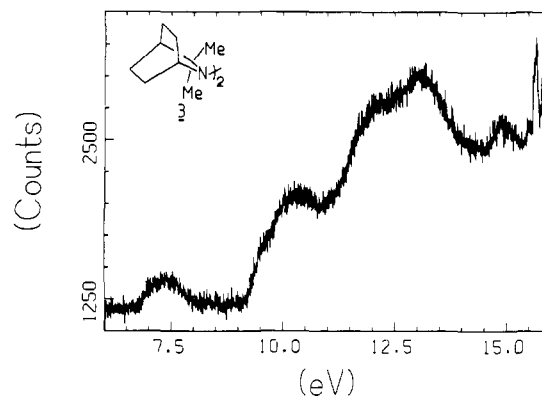


Figure 1. Photoelectron spectrum of **3**.

3²⁺, is long-lived on the CV time scale. 6²⁺ clearly is far less sterically destabilized than 3²⁺. Introducing extra strain and increasing the ease of cleavage by making two of the alkyl groups *tertiary* in **3** decreases the dication lifetime greatly, from decomposition being too slow to observe by CV (in 8²⁺) to being too fast to observe (in 3²⁺).

We previously argued² that tetraalkylhydrazine radical cations are typically nonisolable because of the short lifetime of the electron-transfer disproportionation product, a dication, neutral pair. Back electron transfer of this pair is quite exothermic ($K_{\text{disp}} < 10^{-15}$) and presumably fast, so dication decomposition would have to be extremely fast to compete. Despite the instability of 3²⁺ on the CV time scale, which is on the order of tens of milliseconds, 3⁺ is storable as the solid on a time scale of days, proving that precluding proton loss from the dication by Bredt's rule protection successfully prevents dication decomposition competing with back electron transfer in this case.

Results: PE Studies. The ionization potentials recorded in Table I are maxima of least-squares fits of Gaussian peaks to the observed PE data. Overlapping peaks are an especially severe problem for these compounds. One problem is that bicyclo-[2.2.2]octyl derivatives have an overlapping pair of broad peaks near 10 eV that are rather well separated from the rest of the σ -framework ionization bands and obscure other peaks in this region. A second problem is that for the hydrazines **3** (see Figure 1), **5**, and **12**, non-Gaussian peak shapes were seen. Even for the well resolved first-ionization peak of **3**, a single Gaussian peak does not fit the data well because the rise is obviously steeper on the low-ionization-potential side than on the high-IP side. It was reasonably well fit by two half-Gaussian peaks with a half-width ratio of 1.25. The single Gaussian fit gave IP₁ of 7.49 eV, while the two half-Gaussian fits gave 7.37 eV; we report 7.4 eV, in brackets in Table I for IP₁. The second hydrazine lone-pair ionization overlaps badly with σ ionizations; various deconvolution assumptions moved the peak between 9.6 and 9.8 eV. Peaks for which single Gaussian and two half-Gaussian fits gave the same ionization potential to within 0.02 eV are reported to two places and are directly comparable with previous hydrazine PE data we have published.⁸ When the difference was larger, we report the average, rounded to one place, in brackets. Only the first-ionization peak is reported for the 2-ADO tetrazene **6**, because IP₂ and IP₃ overlapped so badly with each other and σ ionizations that we were unable to deconvolute them satisfactorily.

Discussion: PE Spectra. We suggest that the non-Gaussian shape observed for several of these compounds is likely to result from the nitrogen in the bicyclic ring being unusually flattened. For most hydrazines and amines, the lone-pair ionization peaks are Gaussian-shaped envelopes, because the cation radical preferred geometry is flat or nearly flat at nitrogen while the neutral species is strongly pyramidal at nitrogen. When the cation radical is formed in the geometry of the neutral species (which is what

(8) a) Nelsen, S. F.; Buschek, J. M. *J. Am. Chem. Soc.* **1974**, *96*, 6987 and references therein. (b) Nelsen, S. F.; Peacock, V. E.; Weisman, G. R. *Ibid.* **1976**, *98*, 5269. (c) Nelsen, S. F.; Peacock, V. E.; Kessel, C. R. *Ibid.* **1978**, *100*, 7017.

happens in a PE experiment because of its very short time scale), it is formed very high up its energy well, where there is virtually a continuum of closely spaced high vibrational states. The 0-0 absorption band (IP_{ad}) has no intensity, and the first rise observed in the PE spectrum can be much higher than IP_{ad} . In contrast, when an amino nitrogen is nearly planar in the neutral form, little change in geometry occurs upon electron removal and the peak shape is completely different—several sharp vibrational bands are seen, the largest one being the 0-0 band, so $IP_v = IP_{ad}$. This type of PE spectrum is shown by 1-azabicyclo[3.3.3]undecane.⁹ There ought to be an intermediate region of flattening in which vibrational structure is not resolved but the cation radical is formed lower on its potential energy curve and a non-Gaussian peak shape is seen. We presume that the large alkyl groups on these hydrazines force flattening at one nitrogen and cause the non-Gaussian peak shapes.

The PE of **3**, despite the uncertainty in IP_2 , has IP_2-IP_1 of about 2.4 eV and clearly indicates that **3** is in an anti conformation ($\theta = 180^\circ$), which examination of models will quickly convince one is the only possible conformation for this very hindered compound. The nitrogens will clearly be flattened compared to a less strained anti hydrazine like **8**, and we have previously pointed out that flattening at nitrogen significantly lowers amino nitrogen ionization potentials because it increases the p character of the lone pairs.² Increasing p character of the nitrogen lone pairs will increase lone pair-lone pair overlap, and so it is not surprising that **3** has a larger IP_2-IP_1 value than does **8**, which has nitrogens that are bent past tetrahedral.¹⁰ The first ionization potential of **3** is definitely anomalous, however, since **3** undoubtedly has flatter nitrogens and probably a larger IP_2-IP_1 than **8** but still has a 0.4₆-eV higher IP_1 . The different peak shapes indicate that the numbers obtained for **3** and **8** may not be really comparable, but we suggest that the longer N-N bond length probably present in the more strained **3** might also be an important factor.

The PE spectra of **5** and **12** are consistent with the gauche lone-pair conformations that are expected on steric and electronic grounds. Larger IP_2-IP_1 values (0.8 eV) are seen than for less hindered gauche tetraalkylhydrazines, where IP_2-IP_1 values of 0.53 ± 0.03 eV are observed.⁸

Nitrogen Inversion Rates. Bis(2-ADO) hydrazine **3** is conformationally "frozen" on the NMR time scale at room temperature and shows two types of C_3 methyl groups by 1H and ^{13}C NMR. The conformational interconversion barrier for **3** is thus far higher than that for **8**, which shows no evidence for conformational broadening in its ^{13}C NMR spectrum down to $-40^\circ C$, the lowest temperature at which we could obtain spectra because of solubility problems. We were very surprised at the high conformational interconversion barrier for **3** because the C_3 methyl groups were expected to cause flattening at N_2 relative to compounds with smaller gauche interactions and hence lower the nitrogen inversion barrier. 2-Substituted 2-ADO compounds have substantially lower inversion barriers than 2-ABO derivatives when the substituent is small. The 2-ADO chloroamine **2** has a coalescence temperature about $42^\circ C$ lower than that for the 2-ABO chloroamine **11**,¹¹ and its nitrogen inversion barrier is about 2.4 kcal/mol lower at $-50^\circ C$ (see Tables II and III for a summary of the NMR data and Figure 2 for a visual presentation for **2**). The same trend occurs for dimethylamino derivatives **5** and **12**, although their low barriers precluded accurate measurement. The dimethylamino 2-ABO **12** clearly shows conformational broadening of the $C_{6,7}$ signal at $-150^\circ C$, but we could not keep it in solution below $-160^\circ C$ and can only estimate that its nitrogen inversion barrier is under 5.5 kcal/mol. In contrast, we saw no conformational broadening at all for the 2-ADO analogue **5**, so its nitrogen inversion barrier must be significantly below that of

Table II. Carbon NMR Shifts^a for 2-Azabicyclo[2.2.2]octane Derivatives

compd	frozen spectrum	equilibrating spectrum	assignment
3 ^b	59.15	58.46	C_3
	52.56	51.78	C_1
	37.79	36.86	C_4
	30.55	unobservable	$C_{6,7}$
	24.90		
	29.06	unobservable	$C_{5,8}$
	25.91		
	22.63	21.39	Me
	22.50		
	22.43	62.45	C_3
2 ^c	62.49	61.72	C_1
	39.97	36.56	C_4
	27.44	26.54	Me
	28.03		
	20.86	23.46	$C_{6,7}$
11 ^d	21.99	21.18	$C_{5,8}$
	65.79	65.512	C_3
	59.48	58.63	C_1
	27.84	27.34	C_4
	30.44	24.33	$C_{6,7}$
	21.47		
	25.23	23.79	$C_{5,8}$
23.11			

^a ppm downfield from internal Me_4Si . ^b Frozen spectrum at $+32^\circ C$ in Me_2SO-d_6 (0.22 M); equilibrating at $+104.5^\circ C$ in Me_2SO-d_6 . ^c Equilibrating spectrum at $-18^\circ C$ in CD_2Cl_2 (2.31 M); frozen at $-116.3^\circ C$ in 2:1 CF_3Cl_2/CD_2Cl_2 . ^d Equilibrating spectrum at $-22^\circ C$ in CD_2Cl_2 (2.0 M); frozen at $-84.0^\circ C$ in CD_2Cl_2 .

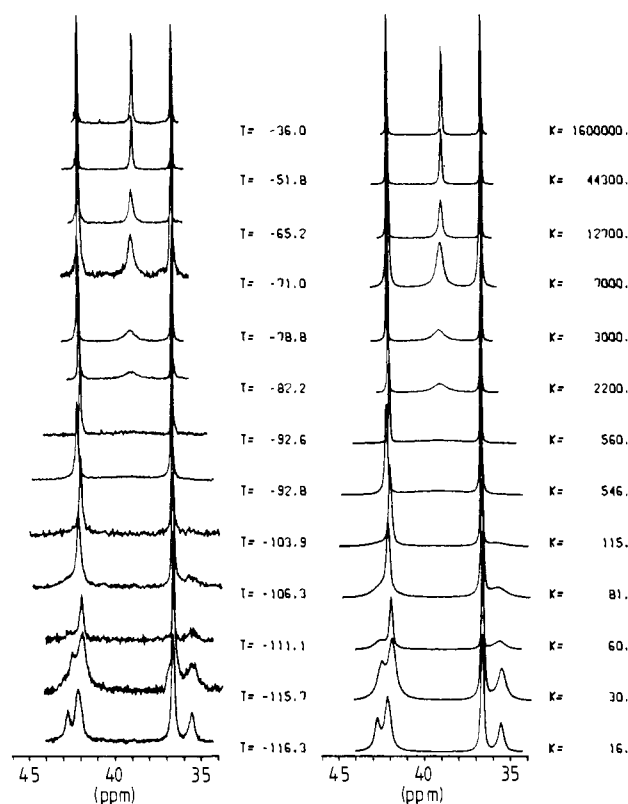


Figure 2. Comparison of experimental ^{13}C NMR spectra of **2** between -36 and $-116^\circ C$ (left) with simulations having the rate constants shown (right). The portion of the spectrum shown includes C_3Me_2 , $C_{5,8}$, and $C_{6,7}$.

12. There is a huge barrier increase on going from the dimethylamino 2-ADO **5** to the bis(2-ADO) derivative **3**. As summarized in Table III, ΔG^\ddagger for methyl interconversion in **3** is 18.8 kcal/mol ($+63^\circ C$), at least 3.5 times as high as that for **5**. This large methyl interconversion barrier is a result of the great

(9) Aue, D. H.; Webb, H. M.; Bowers, M. T. *J. Am. Chem. Soc.* **1976**, *98*, 311.

(10) Nelsen, S. F.; Hollinsed, W. C.; Calabrese, J. C. *J. Am. Chem. Soc.* **1977**, *99*, 4461.

(11) Our ^{13}C NMR measurements on **11** agree completely with the earlier 1H NMR measurement of the nitrogen inversion barrier for this compound: Wagner, J.; Lehn, J. M. *J. Chem. Soc., Chem. Commun.* **1970**, 414.

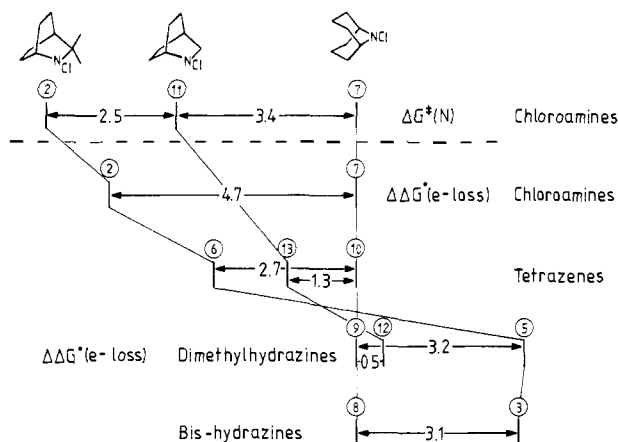
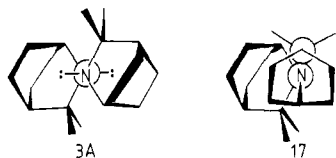


Figure 3. Comparison of changes in ΔG^* for nitrogen inversion (top) with $\Delta\Delta G^\circ$ for electron loss in solution (below the dotted line) for changing the 9-ABN group to the 2-ADO and 2-ABO groups. Data are quoted in kilocalories per mole on a per dialkylamino group basis.

steric crowding in **3**. Anderson and Lehn pointed out fifteen years ago¹² that overall double nitrogen inversion is necessary to interconvert conformations in cyclic hydrazines and that this proceeds by sequential nitrogen inversions (accompanied by pseudorotations) because the energy required to flatten at a single nitrogen is rather large, and it is clearly less costly in energy to invert the nitrogens one at a time than to flatten both at once. We argue that flattening at a single nitrogen is not the lowest energy pathway for conformational interconversion in **3** but that both nitrogens must flatten substantially at the transition state.

The stable form of **3** is shown by Newman projection down the NN bond in structure **3A**, and **17** shows a hypothetical **3** molecule



that has been flattened at the front nitrogen. This flattening would introduce enormous nonbonded interactions, and we note that **17** is not going to be a transition state for single nitrogen inversion. Continuing inversion of the front nitrogen would probably not lower the energy but raise it. The nonbonded interactions in **17** would be decreased if the back nitrogen were flattened at the same time as the front one. We contend that double nitrogen inversion of **3**, in contrast to that for hydrazines previously studied, really does involve substantial flattening of both nitrogens at once.

Discussion: Alkyl Group Effects on Solution Oxidation Potentials. Table I shows that there is essentially no correlation between vertical IP and E° (and therefore ΔG° (e^- loss) in solution) as one might have expected because of the difference in preferred geometry between the neutral form (pyramidal N) and cation radical (planar N). We will argue that $\Delta\Delta G^\circ$ (e^- loss) for replacing one bicyclic alkyl group with another is dominated by the strain energy required to flatten at nitrogen when the third attached substituent is small. The relative ease in flattening at nitrogen in the chloroamines has been experimentally determined by the NMR measurements for **2** and **11** (Table III). Unfortunately for this discussion, only the crude estimate of $\Delta G_c^*(N) = 14 \pm 1$ kcal/mol, $T_c = 0 \pm 10$ °C is available for **7**,¹³ and this number has been used in constructing Figure 3, which shows the relative $\Delta G^*(N)$ values at the top. The higher barrier for 9-ABN inversion than for the bicyclooctanes presumably reflects both greater alkyl-chlorine strain in the pyramidal form of the bicyclooctanes and greater angle strain in the planar transition state

for 9-ABN derivatives. Below the dotted line in Figure 3, the E° data are displayed in the form of $\Delta\Delta G^\circ$ (e^- loss) values, also in kilocalories per mole. For the chloroamines, changing the dialkylamino group from 9-ABN to 2-ADO lowers $\Delta\Delta G^\circ$ (e^- loss) 4.7 kcal/mol, almost all of the 5.9 (± 1) kcal/mol $\Delta G^*(N)$ for the nitrogen flattening that occurs upon electron loss. The pattern of $\Delta\Delta G^\circ$ (e^- loss) values is similar for 2-tetrazenes **6**, **13**, and **10**, but the differences are smaller, which is reasonable because 2-tetrazenes are substantially easier to flatten than chloroamines. For these dialkylamine derivatives that have a small third substituent at nitrogen, the ease of oxidation appears to be dominated by the relative ease of flattening at nitrogen, a process that accompanies oxidation. It appears as if $\Delta G^*(N)$ values from NMR will be useful to assess the relative flattening strain energies, which appear to be an important component of the observed E° , and this idea will be developed more fully in future work. As noted above, IP_v does not correlate at all with $\Delta\Delta G^\circ$. We suggest that because the dialkylamino groups contain 7–9 carbon atoms, their ability to stabilize the positive charge at nitrogen are very similar in solution, and any residual electronic differences are outweighed by steric considerations.¹⁴ The variation in IP_v values probably reflects, among other things, differences in bending at nitrogen that are sterically imposed; lone-pair ionizations prove to be quite sensitive to bending effects.²

For the hydrazines, flattening at nitrogen is accompanied by NN rotation to give the eclipsed CNN'C geometry in the radical cations coupled with a substantial decrease in NN bond length (15% for **8** in the solids⁷); this is found to lead to a reversal in the order of oxidation ease to 9-ABN > 2-ABO > 2-ADO. The opposing effect of N flattening must still be present, but alkyl-alkyl eclipsing effects are so large they dominate. Because flattening at nitrogen in hydrazines is substantially more difficult than in 2-tetrazenes but easier than in chloroamines, the effect on replacing 9-ABN by 2-ADO must be between the 2.7 and 4.7 observed for tetrazenes and chloroamines, leading to an estimate for the alkyl-alkyl interaction increase when a 9-ABN group in a hydrazine is replaced by a 2-ADO group of (3.1 + ~3.7), of about 7 kcal/mol. Thus **3**²⁺ is estimated to have on the order of 14 kcal/mol more alkyl-alkyl steric interaction than **8**²⁺ (since we expect little geometry change upon removal of a second electron, to the extent the NN bondlength does shorten the 14 kcal/mol estimate is too small). The increased steric strain coupled with greater stability for alkyl cleavage product (tertiary instead of secondary cation) are observed to lead to very short lifetimes for **3**²⁺, in contrast to **8**²⁺.

Conclusions

The 2-ADO system is a successful "Bredt's Rule kinetically stabilizing" dialkylamino group. Not only are **2**⁺ and **6**²⁺ long-lived on the CV time scale but **3**⁺·PF₆⁻ proved isolable, despite its severe strain. The dimer hydrazine dication, **3**²⁺, decomposes rapidly on a time scale of milliseconds, in contrast to its 9-ABN analogue **8**²⁺. Strain effects dominate the changes in both vertical ionization potential and adiabatic oxidation potential when 2-ADO and 9-ABN compounds of like substitution are compared. Flattening at nitrogen caused by the flanking methyl groups of the tertiary C₃ of 2-ADO causes electron removal to be easier when small substituents are attached, but other steric effects cause electron removal to be more difficult in the dimeric 2-ADO hydrazine (**3**) than in dimeric 9-ABN (**8**). Although **3** doubtless has flatter nitrogens than less hindered hydrazines, methyl group equilibration is surprising slow, having an activation energy at least 8.8 kcal/mol higher than twice that of 2-dimethylamino-2-ADO (**5**). The high activation energy is attributed to maximized lone-pair-lone-pair repulsion at the transition state, which requires

(12) Anderson, J. E.; Lehn, J. M. *J. Am. Chem. Soc.* **1967**, *89*, 81.

(13) Noted as an "unpublished result" in: Lehn, J. M. *Top. Curr. Chem.* **1970**, *15*, 311.

(14) We note that the second oxidations of tetrazenes **6** and **10** occur at the same E° , though their first oxidations differ by 5.3 kcal/mol in $\Delta\Delta G^\circ$ (e^- loss). Flattening at nitrogen has been argued to be responsible for the E° difference. $E_{2^\circ} - E_{1^\circ}$ values should reflect differences in the ability of 2-ADO and 9-ABN to stabilize the increased positive charge at N in the dications. The difference in ΔE° observed corresponds to 2.5 kcal/mol per 2-ADO for 9-ABN substitution.

Table III. Conformational Barriers for 2-Azabicyclo[2.2.2]octane Derivatives Determined by Dynamic ^{13}C NMR

compd	signals anal.	temp range, $^{\circ}\text{C}$	ΔG^{\ddagger} , kcal/mol ^a [T_c , $^{\circ}\text{C}$]	ΔH^{\ddagger} , ^a kcal/mol	ΔS^{\ddagger} , eu ^a	ΔG^{\ddagger} , kcal/mol. ^a 25 $^{\circ}\text{C}$
3	$\text{C}_3(\text{Me})_2$	49–108 ^b	18.79 (5) [+63]	17.5 (9)	-3.9 (27)	18.64 (13)
2	$\text{C}_{6,7}$	-36 to -116 ^c	8.08 (4) [-95]	7.8 (3)	-1.4 (16)	8.25 (19)
11	$\text{C}_{5,8}$ and $\text{C}_{6,7}$	-22 to -84 ^d	10.61 (3) [-44] ^e 10.59 (3) [-52] ^f	10.0 (3)	-2.5 (14)	10.79 (10)

^a Calculated with $\kappa = 1$. Numbers in parentheses are statistical uncertainties in the last place quoted, calculated at the 95% confidence level. ^b In $\text{Me}_2\text{SO}-d_6$, 11 data points. ^c In CD_2Cl_2 with CF_2Cl_2 added below -70°C , 13 data points. ^d In CD_2Cl_2 , 13 data points. ^e For $\text{C}_{5,8}$. ^f For $\text{C}_{6,7}$.

flattening at both nitrogens at once for **3**, in contrast to other known hydrazines.

Experimental Section

2-Chloro-3,3-dimethyl-2-azabicyclo[2.2.2]octane (2). A solution of 0.19 g (1.13 mmol) of *N*-nitroso compound **1**⁴ in 60 mL of benzene was heated to reflux while HCl (g) was bubbled in through a gas dispersion tube for 1 h. After the solution was cooled to room temperature, N_2 , HCl, and N_2 were bubbled through for 0.5 h each, and the benzene was removed in vacuo to give 0.192 g (97%) of residue, which was dissolved in 2 mL of H_2O , and 3 mL of Chlorox and 2 mL of diethyl ether were added at 0°C . After the solution was stirred for 1.5 h at 0°C , the layers were separated, the aqueous layer was extracted with 3×5 mL ether, and the combined ether layers were dried (MgSO_4) and concentrated. The residue was sublimed (0.1 mm, 80°C) to give 156 mg (84%) of **2** as a colorless solid: mp 122–124 $^{\circ}\text{C}$; ^1H NMR (CD_3CN) δ 3.0 (m, 1 H), 1.8–2.3 (m, 4 H), 1.26 (s, 6 H), 1.1–1.7 (m, 5 H); ^{13}C NMR ($\text{C}-\text{D}_3\text{CN}$) δ 21.2 (t), 23.5 (t), 26.5 (q), 36.6 (d), 61.7 (d), 62.5 (s). Empirical formula $\text{C}_9\text{H}_{16}\text{ClN}$ established by high-resolution MS.

2,2'-Bi(3,3-dimethyl-2-azabicyclo[2.2.2]octane) (3). A solution of 1.9 M *tert*-butyllithium in pentane (0.64 mL, 1.22 mmol, 0.5 eq^{15}) was added dropwise to 0.205 g (1.22 mmol) of **2** in 5 mL of THF at -78°C . After 1 h at -78°C and 17 h at ambient temperature, concentration of the solution, TLC of the residue (silica, 9:1 $\text{CCl}_4/\text{Et}_2\text{O}$), and sublimation gave 120 mg (77%) of **3** as colorless leaves: mp 79–80 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 3.03 (m, 2 H), 1.98 (m, 4 H), 1.92 (m, 4 H), 1.2–1.5 (m, 10 H), 1.18 (s, 6 H); ^{13}C NMR (CDCl_3) δ 22.5 (t), 22.6 (t), 24.9 (q), 25.9 (t), 29.0 (t), 30.6 (q), 37.8 (d), 52.6 (d), 59.2 (s). Empirical formula $\text{C}_{18}\text{H}_{32}\text{N}_2$ established by high-resolution MS.

2-Amino-3,3-dimethyl-2-azabicyclo[2.2.2]octane (4). An ether solution of LAH (11 mL of 1.0 M, 11 mmol) was added dropwise to 1.0 g (5.95 mmol) of **1**⁴ in 60 mL of ether, the mixture refluxed 7 h, cooled to ambient temperature, and treated with 0.5 mL of H_2O , 0.5 mL of 15% aqueous NaOH, and 0.5 mL of H_2O . After filtration and concentration (venting to N_2), 0.91 g (99%) of **4** was obtained as a white, flocculent solid: mp 79–80 $^{\circ}\text{C}$ (sealed tube); ^1H NMR (CDCl_3) δ 3.0 (br s, 2 H), 2.6–2.7 (m, 1 H), 1.82–2.0 (m, 4 H), 1.25–1.6 (m, 5 H), 1.24 (s, 6 H); ^{13}C NMR (CDCl_3) δ 22.1 (t), 25.4 (q), 36.3 (d), 59.9 (d), 66.1 (s); IR (CCl_4) cm^{-1} 3350 (NH), 2940, 1470 (CH). Empirical formula $\text{C}_9\text{H}_{18}\text{N}_2$ established by high-resolution MS.

Azo-2,2'-bis(3,3-dimethyl-2-azabicyclo[2.2.2]octane) (6). A solution of 0.9 g (5.9 mmol) of **4** in 50 mL of Et_2O was allowed to stand in the presence of air until TLC (alumina, CHCl_3) no longer showed the presence of **4**. Concentration and crystallization from hexane gave 0.85 g (92%) of **6** as colorless needles: mp 131–133 $^{\circ}\text{C}$ (rapid decoloration and gas evolution from 145 $^{\circ}\text{C}$); ^1H NMR (CDCl_3) δ 4.25 (m, 2 H), 1.75–2.2 (m, 1 H), 1.2–1.7 (m, 8 H), 1.32 (s, 6 H); ^{13}C NMR (CDCl_3) 22.4 (t), 24.1 (t), 27.7 (q), 37.4 (d), 44.9 (d), 59.0 (s); IR (CCl_4) cm^{-1} 2940, 1460 (CH), 1110 (CN); UV (CH_3CN) 295 nm (ϵ 1.22×10^4). Empirical formula $\text{C}_{18}\text{H}_{32}\text{N}_4$ established by high-resolution MS.

2-(Dimethylamino)-3,3-dimethyl-2-azabicyclo[2.2.2]octane (5). An excess (3.5 g, 43 mmol) of 37% aqueous formaldehyde was added to 0.91 g (5.94 mmol) of **4** and 1.28 g (20.6 mmol) of NaBH_3CN in 25 mL of acetonitrile, and HOAc was added at 15-min intervals to maintain a pH near 6. After 18 h, 12 mL of water and solid NaOH pellets were added, and the mixture was extracted with 3×50 mL of pentane. After the residue was dried (Na_2SO_4) and concentrated, it was chromatographed (silica gel, 2:3 $\text{Et}_2\text{O}/\text{CHCl}_3$) to give 0.22 g (20%) of **5** as a colorless oil: ^1H NMR (CDCl_3) δ 3.0 (7, 1 H), 2.4 (s, 6 H), 1.5–2.1 (m, 5 H), 1.15 (s, 6 H); ^{13}C NMR (CDCl_3) δ 22.6 (t), 25.7 (q), 26.4 (t), 36.2 (d), 40.7 (d), 45.4 (q). Empirical formula $\text{C}_{11}\text{H}_{22}\text{N}_2$ established by high-resolution MS.

2-Chloro-2-azabicyclo[2.2.2]octane (11) was made by the literature method.¹⁶

2-(Dimethylamino)-2-azabicyclo[2.2.2]octane (12) was prepared by reductive alkylation of **14** (1.2 g) by using the same method employed for **4**. The fraction boiling at 89–90 $^{\circ}\text{C}$ (30-mm Hg), 0.35 g, was impure, and this material was chromatographed on silica, eluting with 1:1 $\text{Et}_2\text{O}/\text{CHCl}_3$ followed by Et_2O ; redistillation gave only 0.156 g (10.5%) of pure **12** as a colorless oil: ^1H NMR (CDCl_3) δ 2.95 (m, 2 H), 2.4 (s, 6 H), 1.3–2.2 (complex, 10 H); ^{13}C NMR (CDCl_3) δ 24.7 (t), 26.8 (d), 41.8 (q), 44.5 (d), 51.3 (t). Empirical formula $\text{C}_9\text{H}_{18}\text{N}_2$ determined by high-resolution MS.

Azo-2,2'-bis(2-azabicyclo[2.2.2]octane) (13). A solution of iodine (1.71 g, 6.79 mmol) in 55 mL of ether was added dropwise over 30 min to a solution of 2-amino-2-azabicyclo[2.2.2]octane (0.85 g, 6.75 mmol) in 70 mL of ether that was cooled in an ice bath. After about 40 mL of iodine solution had been added, the color of iodine persisted and addition was stopped. After stirring the solution for 0.5 h at 0°C , 60 mL of 10% aqueous $\text{Na}_2\text{S}_2\text{O}_3$ was added and the ether layer was separated and washed with 60 mL of H_2O . After the residue was dried and (MgSO_4), concentrated it gave 0.57 g of residue. Sublimation of this residue (1.5 mm, 100°C) gave 0.28 g (33%) of **13** as a colorless solid: mp 176–178 $^{\circ}\text{C}$ dec; ^1H NMR (CDCl_3) δ 3.76 (m, 1 H), 3.42 (m, 2 H), 1.45–2.15 (complex, 9 H); ^{13}C NMR (CDCl_3) δ 25.2 (t), 26.0 (t), 26.6 (d), 51.1 (d), 54.2 (t); UV (absolute EtOH) 295 nm (ϵ $1.1 \times 10^4 \text{ cm}^{-1} \text{ M}^{-1}$); IR (CCl_4) cm^{-1} 2920, 2850, 1455. Empirical formula $\text{C}_{14}\text{H}_{24}\text{N}_4$ established by high-resolution MS.

2-Amino-2-azabicyclo[2.2.2]octane (14) was prepared by LAH reduction of the 2-nitroso compound² by using the same method as for the preparation of **4** and obtained as an extremely hygroscopic white solid (78% yield); mp 110–112 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 3.68 (br s, 2 H), 2.94 (m, 2 H), 2.7 (m, 1 H), 2.0 (m, 1 H), 1.3–1.9 (complex, 8 H); IR (CCl_4) cm^{-1} 2970, 2860, 1450. Empirical formula $\text{C}_7\text{H}_{14}\text{N}_2$ determined by high-resolution MS.

2,2'-Bi(3,3-dimethyl-2-azabicyclo[2.2.1]octane)lithium Hexafluorophosphate (3^+PF_6^-). To a solution of 67 mg (0.25 mmol) of **3** in 10 mL of CH_2Cl_2 at -78°C was added in one portion 44 mg (0.25 mmol) of NOPF₆. After the solution was stirred for 1 h at -78°C and 1 h at room temperature, the precipitate that formed was filtered and washed with several portions of ether. Pumping off the last traces of ether yielded 52 mg (49% yield) of 3^+PF_6^- : mp 202–203 $^{\circ}\text{C}$ dec; IR (KBr) 2930, 1465 cm^{-1} ; UV and ESR reported in text. Anal. for 3^+PF_6^- . Calcd for $\text{C}_{18}\text{H}_{32}\text{N}_2\text{PF}_6$: C, 51.28; H, 7.66; N, 6.65. Found: C, 51.13; H, 7.63; N, 6.68.

Physical Measurements. The PE,⁸ CV,⁸ and ^{13}C NMR¹³ measurements were made on equipment previously described. PE data analysis employed program GFIT, written for the Harris computer by W. Erhard and modified by D. Anderson. ^{13}C NMR line-shape analysis employed visual comparison of the data with curves generated by program NMRSIM, written by M. Chen and modified by P. M. Gannett. A stacking program displaying the NMR results in NMRPL, written by P. M. Gannett. Activation parameters were calculated by program DEEJAY, written by G. R. Weisman. All computations were carried out on a Harris Slash 7 computer.

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Supplementary Material Available: The PE curves for **2**, **5**, **6**, **11**, **12**, and **13** and the ^{13}C NMR variable-temperature experimental and calculated curves for **2** and **11** (8 pages). Ordering information is given on any current masthead page.

(15) A 1:1 molar ratio is required because metal-halogen exchange generates *tert*-butyl chloride, which rapidly consumes *tert*-butyllithium.

(16) Gassman, P. G.; Fox, B. L. *J. Am. Chem. Soc.* **1967**, *89*, 338.