Electrochemical Oxidation of Tertiary Amines. The Effect of Structure upon Reversibility

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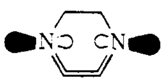
Abstract: Twenty-one tertiary amines containing 1–4 nitrogens, mostly in cage structures, were investigated by cyclic voltammetry. Although most underwent irreversible one-electron oxidations (at scan rates up to 100 V/sec), in addition to Dabco (already known to give a reversible oxidation), 2,2-cyclopentamethylene-1,3-diazaadamantane and tetraazabishomoadamantane (the 2:4 ethylenediamine–formaldehyde condensation product) were discovered to show rereduction waves at 1 and 5 V/sec scan rates, respectively. The results are discussed in terms of lone-pair σ_{CC} interactions.

McKinney and Geske[1] first reported the unusual behavior of 1,4-diazabicyclo[2.2.2]octane (Dabco, **15** in Table I), which demonstrated obvious interaction between the two nitrogens. Evidence for such interaction was found both in the vapor-phase uv spectrum (the maximum occurs at considerably longer wavelength than in simple trialkylamines) and in the oxidation behavior of Dabco. The radical cation of Dabco is formed reversibly at a platinum electrode and is long enough lived to give a well-resolved esr spectrum under slow flow conditions.[1] Dabco is still the only trialkylamine cation radical reported which is sufficiently stable to show a rereduction wave by cyclic voltammetry (cv).[2] In other cases, decomposition (almost surely initiated by α deprotonation from the products isolated[3]) occurs so rapidly that only irreversible waves are observed.

The nature of the interaction in Dabco was studied theoretically by Hoffmann, Imamura, and Hehre[4] who pointed out that a through-space nitrogen–nitrogen interaction would lead to the symmetric lone-pair MO (a_1' or n_+, as shown in I) being lower in energy than the antisymmetric MO (a_2'' or n_-, II). A through-bond interaction would raise the energy of the symmetric MO of I preferentially by mixing with other MO's in the molecule, especially the symmetric σ_{CC} MO made up of the three C–C bonds (represented as III). Extended Hückel calculations[4a] gave the result that the through-bond interaction is by far the most important and predicted that the highest occupied MO of Dabco is the n_+ orbital, which is actually centered 58% on N and 42% on the hydrocarbon framework; the $n_+ - n_-$ splitting was calculated at 1.57 eV. MINDO/2 SCF calculations gave a qualitatively similar result and predicted a 1.36-eV splitting.[4c] These calculations have received striking confirmation in the photoelectron spectroscopy work of Heilbronner and coworkers, who observed an $n_+ - n_-$ splitting of 2.13 eV[5a] and showed that the n_+ orbital was the highest in energy from the vibrational structure of the PS spectrum.[5b]


I


II


III

Our interest in alkylamine lone-pair interactions was stimulated when our naive expectation of stability for the cation from hexamethylenetetramine (**20** in Table I) proved to be incorrect. We had expected that with four equivalent nitrogens held relatively close in space over which to distribute the positive charge, "Dabco-like" stability ought to result. Not only was irreversible oxidation observed for **20**, but the oxidation peak was at an unusually high potential. We initiated a cv study of several aliphatic 1,3- and 1,4-di-, tri-, and tetraamines to elucidate the structural requirements for unusual radical cation stability.

Results and Discussion

The cv data for twenty-one amines were collected and are reported in Table I. All data refer to oxidation at a gold electrode in acetonitrile containing 0.1 *M* sodium perchlorate, using sce as reference electrode. The same apparatus was used as in our hydrazine work;[6] correction was not made for *iR* drop, and some instrumental distortion of our curves is surely present. This should not affect our subsequent arguments, which are semiquantitative at best.

Great caution must clearly be used in interpreting the peak potentials of Table I, since totally irreversible waves were being recorded in all but three examples. The values observed reflect not only the E^0 for the oxidation reaction but also the rate of decomposition of the radical cation. The rate of the following reaction undoubtedly varies rather widely depending on structure, and every factor of 10 increase in decomposition rate should give a 30-mV cathodic shift to E_p^{ox}.[7] Thus although quinuclidine (**2**) shows its E_p^{ox} 500 mV anodic of Dabco (**15**), the wave for Dabco is nearly reversible, and E_p^{ox} is quite close to $E_{1/2}$ (about 0.57 V under our conditions), whereas E_p^{ox} for quinuclidine is doubtless considerably more cathodic than its $E_{1/2}$. Since any inductive effect of introduction of the second nitrogen would be to shift E_p^{ox} to more anodic values, it may be confidently concluded that the second nitrogen in Dabco lowers $E_{1/2}$ substantially by some other effect which, as pointed out above, is now known to be inter-

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[1] T. M. McKinney and D. H. Geske, *J. Amer. Chem. Soc.*, 87, 3013 (1965).

[2] C. K. Mann and K. K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, New York, N. Y., 1970.

[3] N. L. Weinberg and H. R. Weinberg, *Chem. Rev.*, 68, 449 (1968).

[4] (a) R. Hoffmann, A. Imamura, and W. J. Hehre, *J. Amer. Chem. Soc.*, 90, 1499 (1968); (b) R. Hoffmann, *Accounts Chem. Res.*, 4, 1 (1971); (c) M. J. S. Dewar and J. S. Wasson, *J. Amer. Chem. Soc.*, 92, 3506 (1970).

[5] (a) P. A. Bischoff, J. A. Hashmall, E. Heilbronner, and V. Hornung, *Tetrahedron Lett.*, 4025 (1969); (b) E. Heilbronner and K. A. Muszkat, *J. Amer. Chem. Soc.*, 92, 3878 (1970).

[6] S. F. Nelsen and P. J. Hintz, 94, 7108 (1972).

[7] (a) R. S. Nicholson and I. Shain, *Anal. Chem.*, 36, 706 (1964); (b) R. S. Nicholson, *ibid.*, 37, 1351 (1965).

action with the C–C σ bonds. Since the :N–C–C–N: interaction is obviously very important in Dabco, one might expect that quinuclidine, with three C–C–N: interactions held in the most favorable geometry, would have a more cathodic E^0 than triethylamine. This may be the case, but cv gave us no evidence for it, the latter having a 320-mV lower E_p^{ox} value. An especially large difference in rates of deprotonation of the radical cations might be involved here, since the CH bond which must break is constrained to be nearly perpendicular to the charge-bearing orbital in the ion from quinuclidine.

There are three σ bonds perfectly aligned for interaction with each lone pair in the azaadamantanes; yet, tetraazaadamantane (**20**) has the highest E_p^{ox} of the compounds studied. One factor is inductive destabilization for the cation, but another could be that the aligned σ bonds are all C–N bonds. Since a C–N bond is lower in energy than a C–C bond and the energy difference of two orbitals appears in the denominator in the equation for the interaction energy,[4b] we suggest that C–N bonds are simply ineffective at mixing with the lone-pair orbitals. Photoelectron spectroscopy measurements on **20**[8] have been interpreted as indicating that the highest occupied MO is essentially localized at the nitrogen lone pairs, which is entirely consistent with the above arrangement.

We therefore investigated bridgehead tri- and diazaadamantanes, which replace geometrically ideal C–N interactions with more favorable C–C ones and also improve the cation inductively. Postulating that the most rapid decomposition reaction for a 1,3-diamine cation radical would be deprotonation between the nitrogens (and certainly not rejecting any possible inductive stabilization), we also prepared the dialkylated diazaadamantane **12** and were rewarded with a stable enough radical cation to allow observance of its rereduction wave at a scan rate of 5 V/sec (Table II). Although $\mathbf{12}\cdot^+$ is not as stable as the Dabco cation radical $\mathbf{15}\cdot^+$ under our conditions, it is qualitatively more stable than the other 11 1,3-diamine radical cations studied. We believe the importance of favorable lone-pair σ_{C-C} alignments is demonstrated by the fact that $\mathbf{8}\cdot^+$, which only differs from $\mathbf{12}\cdot^+$ by lack of the β–β' bridging methylene, lacks the stability of $\mathbf{12}\cdot^+$. The best models we have for the geometry of these systems are the carbocyclic analogs. In bicyclo[3.3.1]nonane derivatives, the C_1–H_1 and C_2–C_3 bonds are not parallel, as they must be in the adamantyl systems since the C_3–C_7 distance would be too small. From an X-ray study of a 1,5-dialkyl-9-hydroxy derivative,[9] the C_2–C_3–C_4 plane intersects the C_1–C_9–C_5 plane at an angle of 17–18° (instead of being parallel). The C_3–C_7 distance observed was 3.06 Å, compared to the 2.52 Å distance expected if the cyclohexane chains were not distorted; there was no evidence for twisting to relieve the C_3–C_7 interaction (*i.e.*, the distances from C_9 to C_2, C_4, C_6, and C_8 were all about the same). Similar conclusions were reached from the X-ray structure of 3-azatricyclo[3.3.1]nonane hydrobromide[10] and from calculations for the parent hydrocarbon.[11] Since the C–C bonds in **12** are not substituted with a nitrogen at each end, the interactions involved are fundamentally different from those in Dabco. The third example of a tertiary amine which gives a radical stable enough to show a rereduction wave and allow measurement of $E_{1/2}$ is that of bishomoadamantane (**21**). Here there are two subunits with only one N–C–C–N Dabco-like linkage apiece, although the two are held close in space by the caged structure. In spite of the poor inductive effect (each nitrogen has two β nitrogens), the $E_{1/2}$ observed is about the same as for Dabco. This surprising result implies that all four nitrogens share the positive charge. The lowering in $E_{1/2}$ upon inserting two methylenes into tetraazaadamantane ($E_{1/2} > E_p^{ox} = 1.37$ V) to give **21** ($E_{1/2} = 0.56$) is impressive and demonstrates the importance of through-bond interaction of the nitrogens in allowing removal of a formally nonbonding electron. We were able to observe a relatively weak esr spectrum upon electrolytic oxidation of **21**, but the steady-state concentration we obtained was low, and the signal was quite slpit up (729 lines assuming the highest possible symmetry); we have been unable to analyze it.

These electrochemical experiments have shown that although Dabco is not unique among tertiary amines in giving a reversible one-electron oxidation, favorable (parallel) alignments for lone-pair σ_{CC} interactions are quite critical in being able to observe such behavior. Our electrochemical data are entirely consistent with favorable through-bond, not through-space, interactions being necessary for observation of low oxidation potentials and radical cation stability. Neither the bridgehead diazabicyclo[3.2.1]octyl (**5**) nor [3.2.2]nonyl (**16**) systems give much evidence of showing either effect, although the nitrogen–nitrogen distance is certainly shorter in the former and not much greater in the latter case. In both cases the angles for lone-pair σ bond interaction are far less favorable than for Dabco.[4b] Similarly, dimethylpiperazine (**14**) is totally irreversible, though it contains the N–CH_2CH_2N linkages.

We believe that inductive effects are clearly shown by these data, and they are certainly expected from the inductive effects observed in hydrazine oxidations,[6] where kinetic complications are not a factor. The α,α'-diamine compounds **17–20** show generally higher E_p^{ox} values than the 1,3-diamines, although **5** admittedly overlaps into their range. The most surprising "inductive" effect is the 300-mV shift between **10** and **11**. It seems very odd that changing from a saturated to a carbonyl carbon at a position γ to the nitrogens could have such a pronounced effect upon $E_{1/2}$, but the 300-mV difference in E_p^{ox} would represent a factor of 10^{10} in relative decomposition rates, so it seems unlikely that the whole difference could be due to this effect alone.

Experimental Section

The electrochemical apparatus and techniques used have been described separately.

Materials. Commercial samples of **1**, **2**, **3**, **13**, **14**, **15**, and **20** were employed.

1,4-Dimethyl-1,4-diazaspiro[4.5]decane (4) was prepared in 50% yield by azeotropic removal of water from a benzene solution of dimethylethylenediamine and cyclohexanone. After distillation of the solvent, the residue was fractionated: bp (25 mm) 100°. Exact mass calcd for $C_{10}H_{20}N_2$, 168.1626, found, 168.1625; nmr and ir consistent with the given structure.

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(8) M. J. S. Dewar and S. G. Worley, *J. Chem. Phys.*, 50, 654 (1969).

(9) W. A. C. Brown, J. Martin, and G. A. Sim, *J. Chem. Soc.*, 1884 (1965).

(10) M. Dobler and V. D. Dunitz, *Helv. Chim. Acta*, 47, 695 (1964).

(11) (a) G. J. Gleicher and P. R. Schleyer, *J. Amer. Chem. Soc.*, **89**, 582 (1967); (b) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. V. Tyminski, and F. A. Van-Catledge, *ibid.*, **90**, 1199 (1968).

Table I. Cv Data for Tertiary Amines and Polyamines

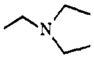
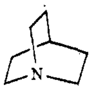
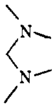
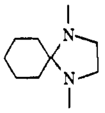
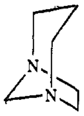
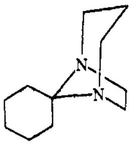
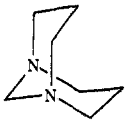
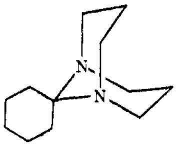
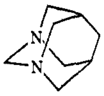
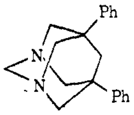
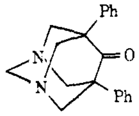
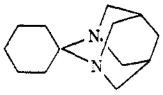
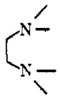
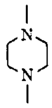
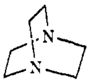
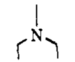
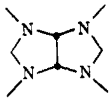
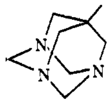
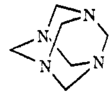
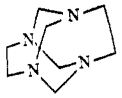
Compound	No.	Concn × 10^3 M	Scan rate, V/sec	E_p^{ox}, V	$E_p^{ox} - E_{p/2}$, mV
Monoamines					
	1	2.77	0.063	0.78	110
	2	4.50	0.096	1.10	260
1,3-Diamines					
	3	3.26	0.071	0.87	120
	4	1.64	0.052	0.85	210
	5	4.64	0.124	1.20	140
	6	3.40	0.051	0.84	200
	7	1.79	0.060	0.69	85
	8	1.35	0.052	0.59	100
	9	0.58	0.080	0.86	80
	10	0.54	0.052	0.85	55
	11	1.26	0.055	1.15	70
	12	0.39	0.050	0.70[a]	95
1,4-Diamines					
	13	4.20	0.054	0.67	100
	14	3.16	0.099	0.75	115
	15	3.11	0.056	0.60[a]	50
	16	1.90	0.066	0.56	90

Table I (*Continued*)

Compound	No.	Concn × 10^3 *M*	Scan rate, V/sec	E_p^{ox}, V	$E_p^{ox} - E_{p/2}$, mV
			Tri- and Tetramines		
	**17**	2.32	0.104	0.94	95
	**18**	2.94	0.092	1.03	140
	**19**	1.38	0.110	1.02	75
	**20**	1.14	0.114	1.37	130
	**21**	0.88	0.060	0.58[a]	55

[a] Rereduction wave observed at faster scan rates. See Table II.

Table II. Cv Data Where Both Oxidation and Reduction Waves Were Observed

Compound	Concn × 10^{-3} *M*	Scan rate, V/sec	$E_{1/2}$, V[a]	ΔE_p, mV[b]
12	0.39	5.05	0.70	70
Dabco (**15**)	3.11	0.11	0.57	85
21	0.88	1.21	0.56	70

[a] *vs.* SCE. [b] Peak to peak separations.

1,5-Diazabicyclo[3.2.1]octane (5) was prepared by a literature method,[12] mp 104–108° (lit.[12] 108–109°).

8,8-Cyclopentamethylene-1,5-diazabicyclo[3.2.1]octane (6) was prepared from homopiperazine and cyclohexanone by azeotropic removal of water with benzene: bp (0.3 mm) 100–101°; exact mass calcd for $C_{11}H_{20}N_2$, 180.1626; found, 180.1624.

1,5-Diazacyclooctane was prepared by hydrogenolysis of 9 g of 1,5-diazabicyclo[3.3.0]octane with 0.5 g of platinum oxide as catalyst instead of the Raney nickel employed in the literature.[13] The hydrogenolysis was run at atmospheric pressure in 40 ml of acetic acid and required 5 days. After removal of solvent, the residue was dissolved in aqueous potassium hydroxide and used directly in subsequent reactions.

1,5-Diazabicyclo[3.3.1]nonane (7) was prepared from an aqueous solution containing 1.0 g (88 m*M*) of 1,5-diazacyclooctane and 0.95 g of formalin. The mixture was stirred with 15 ml of benzene for 12 hr, and the water was removed azeotropically. The product was distilled, bp (125 mm) 125–129°, 0.45 g (36%). It crystallized upon standing: mp 91–92° (sealed capillary); exact mass calcd for $C_7H_{14}N_2$, 126.1157; found, 126.1149.

9,9-Cyclopentamethylene-1,5-diazabicyclo[3.3.1]nonane (8) was prepared in 55% yield using the method employed for **7** but using cyclohexanone. It was separated by distillation, bp (0.15 mm) 84–88°, and crystallized upon standing: mp 58–59° (sealed capillary); exact mass calcd for $C_{12}H_{22}N_2$, 194.1783; found, 194.1796.

1,3-Diazatricyclo[3.3.1.1^{3,7}]decane (9) was prepared by the method of Galovinsky and Langer,[13] mp 262° (sealed capillary) (lit. mp 264–265°).

2,2-Cyclopentamethylene-1,3-diazatricyclo[3.3.1.1^{3,7}]decane (12) was prepared from 3,7-diazabicyclo[3.3.1]nonane and cyclohexanone by azeotropic removal of water with benzene. The residue was sublimed at 65 (0.2 mm), giving **10** as a crystalline solid: mp 123–124.5° (sealed capillary); exact mass calcd for $C_{13}H_{22}N_2$, 206.1783; found, 206.1770.

1,3-Diphenyl-5,7-diazatricyclo[3.3.1.1^{3,7}]decane-2-one (11) was prepared by the method of Stetter, Schafer, and Dieminger:[14] mp 257–259° (lit. mp 257°); nmr ($CDCl_3$) τ 2.72 (m, 10 H), 5.74 (5, 2 H), 6.17 (5, 8 H); ir 5.88 μ.

1,3-Diphenyl-5,7-diazatricyclo[3.3.1.1^{3,7}]decane (10) was also prepared by the literature method:[14] mp 212–216°; nmr ($CDCl_3$) τ 2.69 (m, 10 H), 5.83 (5, 2 H), 6.60 (AB quartet, *J* = 12.5 Hz, $\Delta\nu$ = 30 Hz, 8 H), 7.57 (8, 2 H); ir, on NH or C═O.

1,5-Diazabicyclo[3.2.2]nonane (16) was prepared by the method of McElvain and Bannister[15] except for the work-up of the pyrolysis mixture. We dissolved the crude mixture in concentrated aqueous KOH, extracted with methylene chloride, dried over sodium carbonate, and distilled the amines, bp (100 mm) 50–60°. The mixture of products was separated by vpc at 90° (XF 1150 column) and gave **16**: mp 91–19.5° (sealed capillary) (lit. 89–92°); nmr ($CDCl_3$) τ 6.92 (t, 4 H), 7.10 (5, 8 H), 8.17 (approx quintet, 2 H); ir, no NH or C═O.

1,3,5-Trimethylhexahydro-1,3,5-triazine (17) was prepared by the method of Graymore,[16] bp (25 mm) 64–65° (lit. 160–164°).

2,4,6,8-Tetramethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane-2,5-dione was prepared by the method of Franchimont and Klobbie:[17] mp 227–229° (lit. mp 215°); nmr ($CDCl_3$) τ 5.06 (s, 2 H), 7.04 (s, 12 H).

2,4,6,8-Tetramethyl-2,4,6,8-tetraazabicyclo[3.3.0]octane (18) was prepared by addition of 50 m*M* of the above dione to 3.8 g (100 m*M*) of $LiAlH_4$ in 500 ml of ether and refluxing for 6 hr. After work-up, the residue was distilled: bp (42 mm) 107–111°; 3.4 g (40%); nmr ($CDCl_3$) τ 6.23 (s, 2 H), 6.34 (d, *J* = 5.5 Hz, 2 H), 6.92 (d, *J* = 5.5 Hz, 2 H), 7.60 (s, 12 H); ir, no NH or C═O; exact mass calcd for $C_8H_{18}N_4$, 170.1531; found, 170.1531.

1-Methyl-3,5,7-triazatricyclo[3.3.1.1^{3,7}]decane (19) was prepared by the method of Stetter and Bockmann:[18] mp 174–175° (sealed tube) (lit. 175°); nmr (CCl_4) τ 5.68 (d, *J* = 12.5 Hz, 3 H), 6.11 (d of m, *J* = 12.5 Hz, 3 H), 6.91 (s, 6 H), 9.48 (s, 3 H); ir, no NH or C═O.

1,3,6,8-Tetraazatricyclo[4.4.1.1^{3,8}]dodecane (21) was prepared by the method of Riddell and Murray-Rust:[19] mp 196–200° (lit. mp 196°); nmr ($CDCl_3$) τ 6.01 (s, 8 H), 6.76 (s, 8 H); ir, no NH or C═O.

Acknowledgment. We thank Professors T. Whitesides and D. Evans for helpful discussions throughout the course of this work and Mr. A. Jacobs for the preparation of **16**. This work was supported by the National Science Foundation, the Petroleum Research Fund, administered by the American Chemical Society, and the Sloan Foundation.

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