The deprotonation of trialkylamine cation radicals by amines

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On the Deprotonation of Trialkylamine Cation Radicals by Amines

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Contribution from the S. M. McElvain Laboratories of Organic Chemistry, Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. Received November 7, 1985

Abstract: The difference between the formal oxidation potentials of 9-(2-adamantyl)-9-azabicyclo[3.3.1]nonane (7) and the related α-amino radical 6 is 2.67 V, corresponding to a notably large 61-kcal/mol decrease in $C(\alpha)$–H bond strength upon electron removal. Trialkylamine cation radicals must have exceptionally weak $C(\alpha)$–H bonds. Application of one of the equations of Nicholas and Arnold for estimating pK_a of radical cations from electrochemical and bond dissociation energy data gives a value of about 15 for trialkylamine cation radicals, so in contrast to what has often been assumed, these species are not extremely acidic. It is pointed out that amine cation radical deprotonation is probably not a significant mode of their decomposition in many amine oxidation experiments.

Hammerich and Parker have pointed out[1] that the acid strength of trialkylamine cation radicals ($R_3N^{\bullet+}$) has not yet been established. It has often been assumed that $R_3N^{\bullet+}$ species are extremely acidic, a dogma which we have repeated on several occasions.[2-4] It has even been suggested that trifluoroacetate is a strong enough base to deprotonate $R_3N^{\bullet+}$.[5] We reconsider the question here and conclude that $R_3N^{\bullet+}$ does not usually decompose by deprotonation if bases no stronger than R_3N are the only ones present. We suggest that what has really been established by product studies and cyclic voltammetry work is that oxidation of typical R_3N compounds leads to products derived from the α-deprotonated immonium salts[6] and that holding the $C(\alpha)$–H bonds near the nodal plane of $R_3N^{\bullet+}$, either with bicyclic or acyclic alkyl groups (1 has both types[7]),greatly increases the lifetime of $R_3N^{\bullet+}$.


1
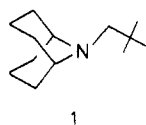
Intramolecular Deprotonation of $R_3N^{\bullet+}$ by $R_3N^{\bullet}$

$R_3N^{\bullet+}$ can be substantially stabilized by through-space interaction with an unoxidized nitrogen lone pair, and these compounds have been important in reaching the conclusions presented here. Alder's group has shown[8] that bridgehead diamines of the type $2[m.n.p]$ which have a nitrogen lone pair in position for σ (end-on) overlap with the half-filled nitrogen p orbital in the radical cation

2[m,n,p]
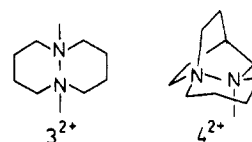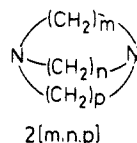
have the positive charge delocalized over both nitrogens. The odd electron is in an NN σ^* orbital, and these species are best described as hexaalkylhydrazine radical cations, $R_6N_2^{\bullet+}$. The lifetime of $R_6N_2^{\bullet+}$ depends greatly on ring size; both $2[3.3.3]^+$ and $2[4.4.4]^+$ are isolable. The X-ray crystal structures of all three oxidation states, neutral, +1, and +2 of 2[4.4.4], have recently been obtained.[9] ICR measurements[10] have shown that the N^+–H bonds of protonated 2[3.3.3] and 2[4.4.4] are 11 kcal/mol weaker than those of the corresponding monoamines. Because the protonated monoamines are estimated to be somewhat more strained than the protonated diamines, the 3e–σ bond strength of the $R_6N_2^{\bullet+}$ species was estimated to be larger than 11 kcal/mol.[10] The 3e–σ bond strength of $3^{\bullet+}$ in solution has been estimated from its lifetime, determined by pulse radiolysis measurements to be 5 ms in water at room temperature.[11] The disappearance of $3^{\bullet+}$ was


3^{2+} 4^{2+}

found to be first order and independent of pH, and it was assumed that 3e–σ bond cleavage was rate-limiting, leading to a bond strength of about 14.5 kcal/mol. It was assumed that bond cleavage would lead to rapid intramolecular deprotonation of the amine radical cation by the unoxidized amine group in the molecule and that this would be faster than the conformational changes leading to re-formation of the 3e–σ bond. This assumption was based on the presumed great acidity of $R_3N^{\bullet+}$. The cyclic voltammogram of 3^{2+} appeared to agree with this assumption,[4] because in contrast to those of 2^{2+} and 4^{2+} no current was observed in the region near 0 V vs. SCE. A rapid enough bond cleavage followed by intramolecular proton or hydrogen atom transfer would give this result, because the transfer product would be an α-amino radical such as 5 and α-amino radicals oxidize at potentials positive of about –1.5.[3b] 5 should therefore rapidly transfer an electron to an electrode at 0 V, and as Feldberg and Jeftic[12]

5
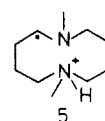
(1) Hammerich, O.; Parker, V. D. *Adv. Phys. Org. Chem.* **1984**, *20*, 129.

(2) (a) Nelsen, S. F. *Free Radicals*; Kochi, J. K., Ed.; Academic Press: New York, 1973; Vol. 2, p 527. (b) Chow, Y. L.; Danen, W. C.; Nelsen, S. F.; Rosenblatt, D. H. *Chem. Rev.* **1978**, *78*, 243.

(3) (a) Nelsen, S. F.; Kessel, C. R. *J. Chem. Soc., Chem. Commun.* **1977**, 490. (b) Nelsen, S. F.; Kessel, C. R.; Brien, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 702.

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

(5) Lindsay Smith, J. P.; Kelly, R. P. *J. Chem. Soc., Chem. Commun.* **1978**, 329.

(6) See, for example, the pioneering electrochemical oxidation work of Mann and co-workers[6a,b] as well as more recent synthetic applications.[6c,d] (a) Smith, P. J.; Mann, C. M. *J. Org. Chem.* **1969**, *34*, 1821. (b) Potis, L. C.; Bhat, V. V.; Mann, C. M. *Ibid.* **1970**, *35*, 2175. (c) Masui, M.; Sayo, H. *J. Chem. Soc. B* **1971**, 1593. (d) Shono, T.; Matsumara, Y.; Inoue, K.; Ohmizu, H.; Kashimura, S. *J. Am. Chem. Soc.* **1982**, *104*, 5753.

(7) Nelsen, S. F.; Cunkle, G. T. *J. Org. Chem.* **1985**, *50*, 3701.

(8) For a review, see: Alder, R. W.; Sessions, R. B. *Chemistry of Amino, Nitroso, and Nitro Compounds and their Derivatives*; Shvo, Y., Ed.; J. Wiley and Sons: New York, 1982; Part 2, Chapter 18, pp 782–804.

(9) The NN bond length of crystalline 1[444]+ is 2.30 Å, 0.77 Å longer than that of the dication: Alder, R. W.; Orpen, A. G.; White, J. M. *J. Chem. Soc., Chem. Commun.* **1985**, 949.

(10) Alder, R. W.; Sessions, R. B.; Gmunder, J. O.; Grob, C. A. *J. Chem. Soc., Perkin Trans. 1* **1984**, 411.

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

(12) Feldberg, S. W.; Jeftic, L. *J. Phys. Chem.* **1972**, *76*, 2439.

Scheme I
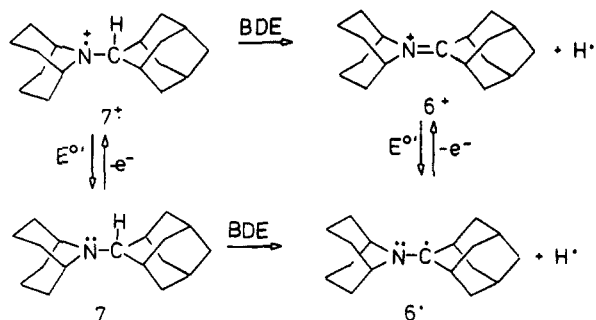
pointed out in their discussion of $\overline{\text{ECE}}$ electrochemical mechanisms, the current near 0 V would drop to a vanishingly small value. We recently discovered that the sample of 3^{2+} used for the cyclic voltammetry experiment discussed above obviously had decomposed, because a reinvestigation[13] showed that authentic 3^{2+} has a CV which closely resembles that of 4^{2+}. Both dications show completely irreversible reduction waves near 0 V, and neither shows the sharply diminished reduction current which would be seen if the reduction mechanism were $\overline{\text{ECE}}$. Species which are oxidized very rapidly at 0 V are in fact not being formed extremely rapidly in either case. Neither $3^{\bullet+}$ nor $4^{\bullet+}$ survives for milliseconds at the electrode surface, but intramolecular hydrogen transfer is not likely to be the reason.

$C(\alpha)$–H Bond Strength in $R_3N^{\bullet+}$

Alder, Bonafacic, and Asmus[14] have recently shown by pulse radiolysis experiments that even rather unreactive free radicals abstract hydrogen quite rapidly from $2[4.4.4]^{\bullet+}$. The second-order rate constants for hydrogen atom abstraction were found to be 3.2×10^9 with *tert*-butylS$^\bullet$ and 1.7×10^8 with $I_2^{\bullet-}$. Their results are only consistent with an unusually low $C(\alpha)$–H bond strength for $2[4.4.4]^{\bullet+}$. This presumably results from unusually large mixing for its aligned $C(\alpha)$–H bonds with the half-filled $\sigma^*(NN)$ orbital. As discussed elsewhere,[13] reaction of 3^{2+} with iodide leads to significantly higher selectivity for attack at the aligned NCH_2 hydrogens than at the NCH_3 hydrogens than does reaction with bases. This behavior is consistent with the mechanism in the case of iodide decomposition involving electron transfer, followed by hydrogen atom abstraction from $3^{\bullet+}$ by $I^\bullet$.

The half-filled orbital of $R^3N^{\bullet+}$ ought to be even lower lying than the $\sigma^*(NN)$ orbital of $R_6N_2^{\bullet+}$, implying that $C(\alpha)$–H bond weakening ought to be even greater. The amount of $C(\alpha)$–H bond weakening which occurs upon electron removal from a trialkylamine can now be rather accurately estimated in one case. The Bredt's rule protected immonium cation 6^+ is reversibly reduced to the unusually long-lived α-amino radical $6^\bullet$ at $E^{\circ\prime} = -1.77$ V vs. SCE.[3b] The $E^{\circ\prime}$ value for oxidation of the related amine 7 has been roughly measured in the same solvent at $+0.9_0$ V.[7] As indicated in Scheme I, because these compounds differ by homolytic cleavage of their $C(\alpha)$–H bonds, the difference in their $E^{\circ\prime}$ values reflects the difference in their bond dissociation energies: $\text{BDE}(7^{\bullet+}) - \text{BDE}(7) = -1.77 - (0.9_0) = 2.6_7$ V, or about 61 kcal/mol. Lossing, Griller, and co-workers[15] have estimated the $C(\alpha)$–H bond strength of H_2NCH_2–H at 94 kcal/mol, which drops to 89 kcal/mol in H_2NCMe_2–H and 84 kcal/mol in Me_2NCH_2–H. This leads to a reasonable estimate of the $C(\alpha)$–H bond strength in 7 of on the order of 79 kcal/mol, implying a $C(\alpha)$–H bond strength of only about 18 kcal/mol for $7^{\bullet+}$. Bond weakening will depend upon the ability to line up the $C(\alpha)$–H bond with the half-filled p orbital, but this alignment is enforced by the bulky bicyclic alkyl groups for 7. The great $C(\alpha)$–H bond weakening which must be present for typical amine radical cations

suggests that even if these species are quite acidic, their decomposition by hydrogen atom abstraction might be more rapid under the conditions in which they are often formed. For example, electrochemical oxidation of amines forms the amine radical cations at relatively high concentration at the electrode surface. Hydrogen atom transfer disproportionation might well be expected to be an important decomposition mode under these conditions. The rate constant for second-order disappearance of $Me_2NH^{\bullet+}$ by self-reaction has been measured by Malatesta and Ingold[16] to be on the order of 10^6 M^{-1} s^{-1} with an activation energy of only 5 kcal/mol. They suggested $C(\alpha)$–H hydrogen atom transfer disproportionation as one of several mechanistic possibilities between which their experiments could not distinguish. Given the extreme $C(\alpha)$–H bond weakening expected for $R_3N^{\bullet+}$, we suggest that hydrogen atom transfer disproportionation is rapid even for this reaction of two cations, which is completely consistent with the activation parameters found. Such facile disproportionation would give the observed electrochemically irreversible oxidation of trialkylamines even in the absence of extremely rapid proton loss from the radical cation, and without the oxidation current being sharply decreased. Steric bulk should slow down approach of two $R_3N^{\bullet+}$ species, and the bulk introduced by groups which keep the $C(\alpha)$–H bonds from being well aligned with the spin-bearing p orbital at nitrogen in species like 1 may well be as important as the alignment factor which our previous discussions have emphasized in causing such cation radicals to be long-lived.

Acidity of Amine Radical Cations

If very weak $C(\alpha)$–H bonds for $R_3N^{\bullet+}$ species are accepted, should not $R_3N^{\bullet+}$ also be extremely acidic? Maybe not, because deprotonation leads to an α-amino radical. α-Amino radicals do have significant resonance stabilization, which Griller and Lossing[17] have estimated for a tetraalkyl-α-amino radical at 20 kcal/mol from mass spectroscopic appearance potential measurements. Hydrogen atom loss leads to an immonium cation, which has a full C=N bond, and obviously has far more resonance stabilization. The difference in resonance energy for the two products is substantial, and $R_3N^{\bullet+}$ might not be strongly acidic.

Nicholas and Arnold[18] have discussed the question of how to estimate radical cation acidity from bond strengths and electrochemical data. Using their eq 19 with the constants in footnote 8, we obtain the following relation:

$$pK_a(R_3N^{\bullet+}) =$$
$$(\text{BDE}(R_3N)_g - 37.6)/1.36 - E^{\circ\prime}(R_3N)/0.05916$$

where $\text{BDE}(R_3N)_g$ is the bond dissociation energy of the $C(\alpha)$–H bond in kcal/mol and $E^{\circ\prime}$ is the formal potential for oxidation in V vs. SCE in acetonitrile. By using the numbers discussed above of 79 kcal/mol and 0.9 V for 7, the pK_a of $7^{\bullet+}$ is estimated at 15. Although pK_a values in acetonitrile are considerably more positive than those in water,[19] this estimate indicates that aminium cations are not extremely acidic at all, and suggests that proton transfer to neutral amine might not, in fact, be fast in solution. This hypothesis is also consistent with the CIDNP studies of Gardini and Bargon[20] on $R_3N^{\bullet+}$ generated by amine quenching of photoexcited naphthalene. They have shown that although the C-(α)–H hydrogens of simple trialkylamine cation radicals exchange rapidly with the acidic protons of water, alcohols, and even β-diketones, the polarizations observed for triethylamine are inconsistent with the α-amino radical being an intermediate in the exchange. Because these experiments were conducted at 0.2 M amine concentration, extremely rapid deprotonation of $Et_3N^{\bullet+}$ by Et_3N apparently does not occur. It is clear that simple $R_3N^{\bullet+}$ species can be deprotonated rapidly by sufficiently strong bases, as is discussed by Lewis and co-workers[21] for other photogenerated

(13) Nelsen, S. F.; Ippoliti, J. T. *J. Org. Chem.*, in press.

(14) Alder, R. W.; Bonafaič, M.; Asmus, K.-D. *J. Chem. Soc., Perkin Trans. 2* **1986**, 277.

(15) Burkey, T. J.; Castelhano, A. L.; Griller, D.; Lossing, F. P. *J. Am. Chem. Soc.* **1983**, *105*, 4701.

(16) Ingold, K. U.; Malatesta, V. J. *J. Am. Chem. Soc.* **1973**, *95*, 6400.

(17) Griller, D.; Lossing, F. P. *J. Am. Chem. Soc.* **1981**, *103*, 1586.

(18) Nicholas, A. M. de P.; Arnold, D. R. *Can. J. Chem.* **1982**, *60*, 2165.

(19) See, for example: Kolthoff, I. M.; Coetzee, J. F. *J. Am. Chem. Soc.* **1956**, *78*, 870.

(20) Gardini, G. P.; Bargon, J. *J. Chem. Soc., Chem. Commun.* **1980**, 757.

radical ion pairs. There is also cyclic voltammetry evidence for rather slow deprotonation of the far longer lived **1**⁺ by (dimethylamino)phthalimide.[7] We believe that the above discussion suggests very strongly that R₃N is usually not a strong enough base to lead to extremely rapid deprotonation of its radical cation in competition with other modes of decomposition. Because the α-amino radical is so much more easily oxidized than the parent amine, it would seem impossible to devise conditions under which R₃N•⁺ and the α-amino radical derived from it by deprotonation could be equilibrated, which would be necessary for experimental determination of the thermodynamic acidity of R₃N•⁺. Hydrogen atom abstraction by R₃N•⁺ is known to be a fast process,[2] and abstraction from a neutral amine with the same R groups gives the same products as does proton transfer, but the hydrogen ends

up on the other partner in the reaction. Sorting out electron, hydrogen atom, and proton transfer in an unsymmetrical case would be a most formidable task! Whitten and co-workers have very recently shown[22] that cleavage of weak CC bonds α to nitrogen occurs upon photooxidation of some tertiary amines, which fits in well with the great bond weakening for CH bonds α to nitrogen discussed above. **Note Added in Proof**: We thank Prof. von Sonntag for informing us of his recent pulse radiolytic determination of the pK_a of Me₃N as 8.0 in water, which agrees with the conclusions of this paper.[23]

(21) (a) Lewis, F. D.; Ho, T.-I.; Simpson, J. T. *J. Am. Chem. Soc.* **1982,** *104,* 1924 and references therein. (b) Lewis, F. D.; Zebrowski, B. E.; Correa, P. E. *Ibid.* **1984,** *106,* 187. (c) Lewis, F. D.; Correa, P. E. *Ibid.* **1984,** *106,* 194. (d) Hub, W.; Schneider, S.; Dörr, F.; Oxman, J. D.; Lewis, F. D. *Ibid.* **1984,** *106,* 701, 708.

(22) Lee, L. Y. C.; Ci, X.; Giannotti, C.; Whitten, D. G. *J. Am. Chem. Soc.* **1986,** *108,* 175.

(23) Das, S.; von Sonntag, C. *Z. Naturforsch.* **1986,** *41a,* 50S.

Irradiation-Induced Transformations of Homoconjugated Dienones.[1] Highly Selective Photorearrangements in the Spiro[5.5]undeca-1,3-dien-7-one System[2]
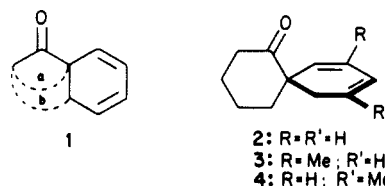
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Contribution from the School of Chemistry, Tel-Aviv University, Ramat-Aviv, 69978 Tel-Aviv, Israel. Received November 26, 1985

Abstract: We present a study of the photorearrangements in the homoconjugated (β,γ,δ,ε-unsaturated) ketone **1a** system, viz., derivatives of spiro[5.5]undeca-1,3-dien-7-one (**2, 3, 4**) which are of mechanistic interest and considerable synthetic potential because of their high *wavelength selectivity, regioselectivity, and diastereoselectivity.* Thus, in direct irradiation of **2–4** at 254 nm, electrocyclic opening of the cyclohexadiene ring to trienone products (**5, 9**) occurs, along with some α-cleavage and β-H abstraction to give aromatic aldehydes (**10, 11**). These are the main products at λ ≥ 300 nm while at λ ≥ 340 nm an oxa-di-π-methane (ODPM) rearrangement takes place to give exclusively the *trans*-tricyclo[5.4.0.0⁷,¹¹]undeca-9-en-2-ones (**12t, 13t,** and **14t**). Sensitized irradiation of **2, 3,** and **4** yielded the latter along with 1,2-acyl shift products of a second kind: *cis*- and *trans*-tricyclo[5.4.0.0⁷,⁹]undeca-10-en-2-ones (**15–17**). Quantum yields, triplet sensitizer energy, quenching, and solvent effects were studied. The involvement of multiple excited states is inferred, and mechanistic models are discussed.

We have recently initiated a systematic investigation of homoconjugated dienones featuring fixed s-cis 1,3-dienes in judiciously directed geometry of juxtaposition to the homoconjugated carbonyl group (see below for a rationalization of this approach in the context of the well-documented β,γ-unsaturated carbonyl photochemistry[3]). After a relatively disappointing, even if eventful investigation of fused systems (**1b**),[5] we report now on the unusually interesting photochemical behavior of an **1a** type system, namely spiro[5.5]undeca-1,3-dien-7-one (**2**) and two of its

methyl-substituted derivatives (**3** and **4**). Their synthesis recently has been described.[6]

1

2: R=R'=H
3: R=Me; R'=H
4: R=H; R'=Me

Photochemistry: Product Isolation and Characterization

The first striking feature of their photochemical behavior is the high wavelength selectively on direct irradiation; this is generally depicted in Scheme I. Thus, as a rule, low wavelength (254 nm) irradiation induces electrocyclic opening of the cyclohexadiene ring, the isolated end products being substitution dependent: while the parent compound (**2**) yields the linear conjugated trienone (**6**), the 2-methyl derivative (**3**) leads to a mixture of isomeric cross-conjugated trienones (**8** and **9**), most likely following an initial (thermal or photochemical) 1,7-sigmatropic hydrogen shift in **5** to **7**. The reason for the diverse secondary reaction paths is believed to be the steric influence of the methyl group which

(1) Photochemical Studies. 26. Part 25: Oren, J.; Viskin, R.; Fuchs, B. *Tetrahedron Lett.* **1985,** *26,* 2365.

(2) (a) Taken in part from the Ph.D. Thesis of J.O., Tel Aviv University 1984. (b) Presented in part at the Sendai Symposium on Organic Photochemistry, August 1985. (c) Some of the present results have been included in a preliminary communication: Zizuashvili, J.; Abramson, S.; Fuchs, B., *J. Chem. Soc., Chem. Commun.* **1982,** 1375.

(3) (a) de Mayo, P., *Rearrangement in Ground and Excited States*, Wiley: New York, 1980; Vol. 3. (b) Schuster, D. I. In ref 3a, p 232. (c) Houk, K. N. *Chem. Rev.* **1976,** *76,* 1. (d) Schaffner, K. *Tetrahedron* **1976,** *32,* 641. (e) Dauben, W. G.; Lodder, G.; Ipaktschi, J. *Top. Curr. Chem.* **1975,** *54,* 73. (f) Hixson, S. S.; Mariano, P. S.; Zimmerman, H. E. *Chem. Rev.* **1973,** *73,* 531.

(4) (a) Dauben, W. G.; Kellog, M. S.; Seeman, J. I.; Spitzer, W. A. *J. Am. Chem. Soc.* **1970,** *92,* 1786. (b) Givens, R. S.; Oettle, W. F. *J. Am. Chem. Soc.* **1970,** *93,* 3963 (*Chem. Commun.* **1969,** 1066).

(5) Abramson, S.; Fuchs, B. *Tetrahedron Lett.* **1980,** *21,* 1165; **1982,** *23,* 1377.

(6) Zizuashvili, J.; Abramson, S.; Fuchs, B. *J. Org. Chem.* **1982,** *47,* 3473.