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Generation and Study of the Reactivity of α-Ammonium Distonic Radical Cations in Solution

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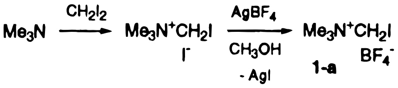
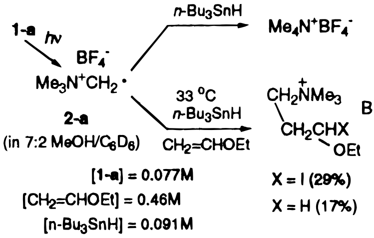
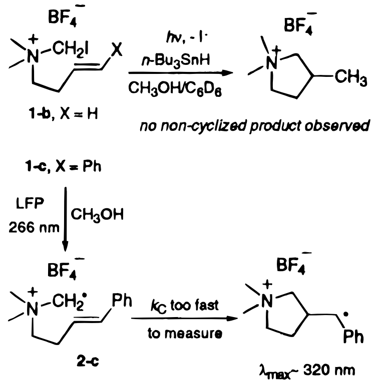
Distonic radical cations, species in which the radical and charged cationic sites are formally separated, continue to attract considerable interest, both experimentally and theoretically.[1−3] Whereas such intermediates have long been accepted as stable and common gas phase species, recent ion−molecule studies, particularly by Kenttämaa, have now demonstrated that α-distonic radical cations, such as $(CH_3)_2S^+CH_2^\bullet$ exhibit gas phase reactivity, including hydrogen abstraction and alkene addition, which is consistent with typical carbon-centered radical behavior.[4,5] This led to their characterization as "reactive radical(s) with an inert charge site".[4]

Nevertheless, α-distonic radical cations have not previously been generated for synthetic purpose nor have they been studied kinetically in solution.[6] Because of our ongoing interest in radical reactivity and because of the potentially unique nature of such radicals, we have initiated a systematic, quantitative examination of the reactivity of α-distonic radical cations in solution. Our initial studies have examined the prototypical, coordinatively saturated α-ammoniomethyl radical system: $R(CH_3)_2N^+CH_2^\bullet$. Such radicals were generated from their readily synthesized iodomethyl precursors by means of irradiative free radical initiation.[10] In preliminary studies of the (trimethylammonio)methyl radical, it was observed that iodomethyl precursor **1-a** in the presence of n-Bu$_3$SnH, underwent rapid light-induced conversion to tetramethylammonium tetrafluoroborate, the reaction expected for a well-behaved free radical chain process involving **2-a**. However, except for its addition to ethyl vinyl ether (depicted above), attempts to observe competitive bimolecular addition of **2-a** to various other olefins, including 1-hexene, styrene, pentafluorostyrene, and α-methylstyrene, were curiously ineffective and led only to formation of tetramethylammonium tetrafluoroborate. Addition of **2-a** to the above styrenes within the time frame of nanosecond laser flash photolysis (LFP) experiments also could not be detected.[13]





In view of the low *bimolecular* alkene addition reactivity exhibited by **2-a**, our attention was shifted to ammonio radical systems which could undergo *unimolecular* cyclization processes. In contrast to the difficulties observed for bimolecular alkene addition, preliminary examination of the unsubstituted 5-hexenyl precursor **1-b** indicated that cyclization of **2-b** was so fast that no competitive reduction could be observed at the maximum possible concentration of n-Bu$_3$SnH (0.18M) in 1:1 MeOH/C_6D_6. This result, coupled with the observation that the 6-phenyl-substituted radical **2-c** underwent cyclization too fast to be measured by nanosecond LFP ($k_C \geq 10^8$ s^{-1} at 25 °C), indicated that kinetic examination of such 5-*exo* cyclizations would not be possible by either LFP or competition methodologies. Because of the approximate 100-fold decrease in rate for 6-*exo* versus 5-*exo* radical cyclizations,[16] the 7-heptenyl analogues **1-d−f** were synthesized and studied.[10]



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[6] Free radical chemistry of related α-sulfinylmethyl and α-sulfonylmethyl radicals has been recently been reported,[7,8] and since submission of this paper, a brief report regarding synthetic use of α-ammoniomethyl radicals has appeared.[9]

[7] Renaud, P.; Moufid, N.; Kuo, L. H.; Curran, D. P. *J. Org. Chem.* **1994**, *59*, 3547−3552.

[8] Mahadevan, A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1995**, *117*, 3272−3273.

[9] Della, E. W.; Knill, A. M.; Smith, P. A. *J. Chem. Soc., Chem. Commun.* **1996**, 1637−1638.

[10] Syntheses of all of the (iodomethyl)ammonium compounds reported in this paper were accomplished by reaction at room temperature of the respective tertiary amines with a 4-fold excess of methylene iodide in acetonitrile.[11,12] All ammonium tetrafluoroborates (**1-a−f**) were fully characterized by ^{1}H and ^{13}C NMR, HRMS, and elemental analysis. All products formed in the competition experiments were isolated and fully characterized in the same manner.

[11] Almarzoqi, B.; George, A. V.; Isaacs, N. S. *Tetrahedron* **1986**, *42*, 601−607.

[12] Laird, T.; Williams, H. *J. Chem. Soc. C* **1971**, 3471−3474.

[13] The $(CH_3)_3N^+CH_2^\bullet$ radical should exhibit somewhat greater electrophilicity than a fluorinated radical of the type $CF_3(CF_2)_nCH_2^\bullet$ (σ_p values of 0.82 versus 0.52 for $(CH_3)_3N^+$ and n-C_4F_9, respectively.)[14] Thus, since we *have* previously been able to obtain second-order rate constants for the addition of the 2,2-difluoropentyl radical to the trio of styrenes by LFP,[15] our inability to observe similar additions with the presumably inherently more reactive **2-a** raises interesting questions concerning the possibility of unique steric problems intervening in the bimolecular addition reactions of **2-a**. These could derive from the presence of the BF_4^- counterion, from the solvent cage surrounding the ammonium substituent, or simply from the neopentyl-like nature of **2-a**. Future studies should allow us to distinguish these possibilities, as well as to indicate why addition to ethyl vinyl ether (IP = 8.8 eV), but not to styrene (IP (ionization potential) = 8.43 eV), was observed to occur.

[14] Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165−195.

[15] Avila, D. V.; Ingold, K. U.; Lusztyk, J.; Dolbier, W. R., Jr.; Pan, H.-Q. *J. Org. Chem.* **1996**, *61*, 2027−2030.

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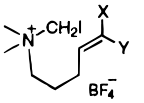
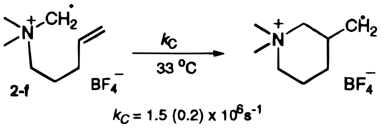


1-d, X = Y = Ph
1-e, X = H, Y = Ph
1-f, X = Y = H

The ensuing LFP study of the 7,7-diphenyl-substituted system **1-d** produced excellent kinetic results for the 6-*exo* cyclization of the instantaneously produced radical **2-d** over a temperature range of −60 to +20 °C.[17] These kinetic data were used to obtain the Arrhenius parameters given in Scheme 1.[19] The cyclization of **2-d** is thus observed to be 60 times faster than that of the related 7,7-diphenyl-6-heptenyl radical (5×10^5 s^{-1})[20] at 25 °C. Limited LFP data for the cyclization of the monophenyl derivative **2-e** was also obtained: ca. 1.7 and 0.21×10^7 s^{-1} at 25 and −61 °C, respectively. The rate constant for cyclization of the monophenyl system is thus approximately half that of the diphenyl system.

Using the **2-d** system as a radical clock, it was possible to obtain the rate constant for H-atom abstraction from n-Bu_3SnH via a series of competition experiments (Scheme 2). This observed rate constant (7.2×10^6 M^{-1} s^{-1} at 33 °C) is seen to be somewhat enhanced in comparison with the analogous value of 2.9×10^6 M^{-1} s^{-1} for H-transfer from n-Bu_3SnH to a primary alkyl radical.[21]

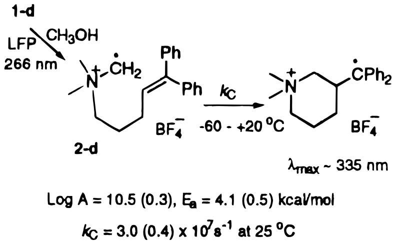
With an H-transfer rate constant now available, the competitive cyclization and reduction of the *unsubstituted* 6-heptenyl system **2-f** was able to be studied. The observed rate constant (1.5×10^6 s^{-1}) for 6-*exo* cyclization of **2-f** at 33 °C, if compared with that for the analogous cyclization of the 6-heptenyl radical (7.6×10^3 s^{-1}),[16] indicates a significantly greater enhancement (∼200-fold) for **2-f** than was observed for the 7,7-diphenyl system **2-d** (60-fold).



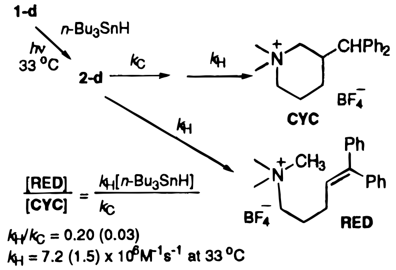
One would expect that the kinetic impact of the *electrophilicity* of such ammoniomethyl radicals should be greater in addition situations which manifest a smaller enthalpic driving force. This certainly was what was observed in alkene additions of the even more electrophilic perfluoro-n-alkyl radicals. In our recent studies of the reactivity of n-$C_3F_7^{\bullet}$, we found that addition to styrene was enhanced (relative to addition of n-alkyl radical) by a factor of ∼350, whereas addition to 1-hexene was enhanced by a factor of >30 000.[22]

The enhanced reactivities which are observed for the cyclizations of **2-d**−**f**, and in the H-transfer reaction of **2-d**, derive from some combination of three factors: electrophilicity, enthalpic effects, and the *gem*-dimethyl effect. The two nitrogen-bound methyl groups of the alkenyl ammoniomethyl radical systems **2-d**−**f** will certainly have a significant impact on their rate constants of cyclization, due to the *gem*-dimethyl effect. Beckwith has found that *gem*-dimethyl substituents at the 2-position lead to a ∼16-fold rate enhancement for 5-*exo*-hexenyl cyclizations.[16] Assuming that a similar enhancement can be expected for 6-*exo*-heptenyl cyclizations, the net enhancements due to the ammonio substituent in the cyclizations of **2-d**,**f** would be reduced to factors of ∼4 and ∼12, respectively.

Scheme 1



Scheme 2



These small, but significant, net enhancements most likely derive largely from the electrophilicity of the ammoniomethyl system, as discussed earlier, although enthalpic factors could also be contributing since, according to Bordwell's and Pasto's estimation of bond dissociation energies, the (trimethylammonio)methyl radical, $(CH_3)_3N^+CH_2^{\bullet}$, should be destabilized by ∼4 kcal/mol.[23−25]

In conclusion, α-ammonium distonic radical cations have for the first time been purposefully generated and their reactivity studied in solution. Such ylidions have been found to exhibit behavior which is typical for a carbon-bound radical. Moreover, they are electrophilic and somewhat more reactive in H-atom abstractions and cyclization reactions than analogous hydrocarbon radicals, but are not nearly so reactive as their conventional dialkylaminium cation radical counterparts (i.e., $RNHCH_3^{+\bullet}$).[26]

The ease with which the α-halo ammonium precursors can be made, combined with the observed high efficiency of the 5-*exo* and 6-*exo* cyclizations of the intermediate ammoniomethyl radicals, should give the cyclization processes of α-ammonium distonic radical cations considerable synthetic potential.

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Supporting Information Available: Experimental details (17 pages). See any current masthead page for ordering and Internet access instructions.

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(17) Distonic radical cations **2-c**−**e** were generated upon 266 nm photolysis of the corresponding iodides in methanol using a Lumonics HY-750 Nd:YAG laser (8 ns pulse width; ca. 45 mJ/pulse). The UV-vis computer-controlled detection system has been described previously.[18] The kinetics of the ring closure reactions of **2-d**,**e** were studied at 320 and 335 nm, repectively (formation of products). The temperature was varied from ca. −60 to +20 °C.

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(19) All stated errors correspond to 2σ. They include both random and propagated errors, as appropriate.

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