ORGANIC LETTERS
2011
Vol. 13, No. 2
212–215

Photochemical Heterolysis of 3,5-Bis(dimethylamino)benzyl Alcohols and Esters: Generation of a Benzyl Cation with a Low-Energy Triplet State

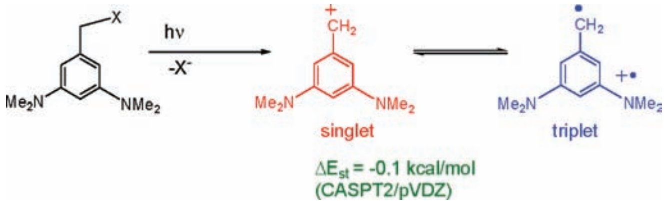
Raffaele R. Perrotta, Arthur H. Winter,[†] and Daniel E. Falvey*

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742-2021, United States

Falvey@umd.edu

Received October 28, 2010

ABSTRACT



An earlier computational study (CASPT2/pVDZ) by Winter et al. predicts the 3,5-bis(dimethylamino)benzyl cation to have nearly degenerate singlet and triplet states. Through product studies it is demonstrated that photolysis of 3,5-bis(dimethylamino)benzyl alcohol and its corresponding acetate and phenylacetate esters in alcoholic solvents produces a solvent incorporated adduct, 3,5-bis(dimethylamino)benzyl ethers, and 3,5-bis(dimethylamino)toluene.

The overwhelming majority of organic molecules have singlet electronic ground states. However it has long been realized that certain classes of molecular fragments, including free radicals, diradicals, carbenes, nitrenium ions, and nitrenes, can possess doublet, triplet, and even higher spin electronic ground states. Such high-spin organic species are interesting from a theoretical point of view but also because, as reactive intermediates, their properties determine the outcomes of numerous synthetically, biologically, and environmentally important reactions.[1] Additional interest in high-spin organic species comes from the long-term goal of developing new materials with interesting bulk magnetic properties.[2] Such materials would presumably be assembled using the aforementioned high-spin intermediates as building blocks. Significant progress in this area has been made using radicals[3] and carbenes.[4] Far less progress has been made employing cationic building blocks although certain phenyl,[5,6] vinyl,[7] and cyclopentadienyl[8,9] cations are known to have triplet ground states.

Some recent computational studies have shown that cationic species bound to a phenyl ring possessing strong π-electron donors in the two *meta* positions (**1**) have low energy triplet states. When sufficiently strong electron donating groups (e.g., NH_2, $(CH_3)_2N$) are coupled with highly electronegative cationic centers (e.g., $X = O^+$, NH^+, $CH_2{}^+$)

[†] Present address: Department of Chemistry, Iowa State University.

(1) Borden, W. T. *Diradicals*; Wiley: New York, 1982.

(2) Lahti, P. M. *Magnetic Properties Of Organic Materials*; Marcel Dekker: New York, 1999.

(3) Rajca, A. *Adv. Phys. Org. Chem.* **2005**, *40*, 153–199.

(4) Hirai, K.; Itoh, T.; Tomioka, H. *Chem. Rev.* **2009**, *109*, 3275–3332.

(5) Lazzanni, S.; Dondi, D.; Fagnomi, M.; Albini, A. J. *J. Org. Chem.* **2009**, *73*, 206–211.

(6) Gasper, S. M.; Devadoss, C.; Schuster, G. B. *J. Org. Chem.* **1995**, *117*, 206–211.

(7) Winter, A. H.; Falvey, D. E. *J. Am. Chem. Soc.* **2010**, *132*, 215–222.

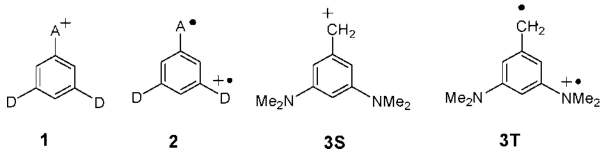
(8) Pincock, J. A.; Speed, A. H. W. *Can. J. Chem.* **2005**, *83*, 1287–1298.

(9) Wörner, H. J.; Merkt, F. *J. Chem. Phys.* **2007**, *127*, 034303.

10.1021/ol102606m

the triplet state is predicted to be the ground state.[10] The explanation for this effect is illustrated by structure **2** wherein an electron is formally transferred from the donor group(s) to the cationic center, creating a diradical cation (Scheme 1). Since the two resulting SOMOs are nondisjoint, similarly to *meta*-xylylene,[11] the triplet state is favored. Of particular relevance to the current study are multireference *ab initio* (CASPT2(10,9)/pVDZ) computations on the 3,5-bis(dimethylamino)benzyl carbenium ion **3** which reveal that this seemingly simple benzylic cation has nearly degenerate singlet and triplet states ($\Delta E_{st} = -0.1$ kcal/mol).[12] Benzylic cations are, of course, very familiar reactive intermediates, which have been known since the early 20th century. Their description is included in almost every advanced organic chemistry textbook in relation to linear free energy relationships.[13] While few studies appear to have addressed the question of their electronic structures, most investigators have implicitly assumed that benzylic cations have singlet ground states. Indeed their reactivity, which appears to consist solely of nucleophilic additions to the exocyclic carbon atom, can be readily understood as occurring via a routine closed-shell singlet state species.[14,15]

Scheme 1. *Meta* Substituted Triplet Diradicals



To our knowledge, triplet state behavior has not been reported for any benzylic carbenium ion despite extensive studies involving such intermediates.[16] This can be attributed to the fact that, unlike the more electronegative oxenium (A $= O^+$) and nitrenium (A $= NR^+$) ions, the carbenium ions show low energy triplet states only when two extremely strong π donating groups are added to the *meta* positions. It was not clear at the outset of this study exactly what chemical reactions would be characteristic of this new class of ion-diradical intermediates, or if these would provide products that are distinct from the reactions of closed-shell singlet carbenium ions.

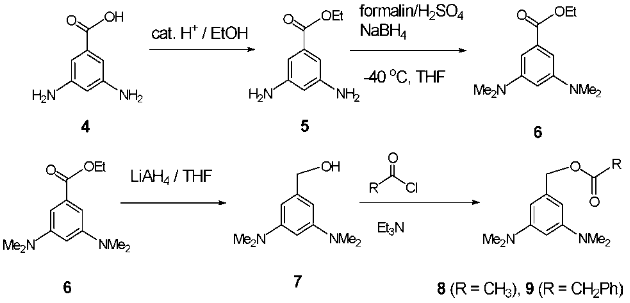
Likewise, inasmuch as the electronic structure of **3** is expected to differ from normal benzylic cations, it was not clear if methods routinely used to generate carbenium ion could be used to cleanly generate these intermediates. The experiments described below show that (1) benzylic cation **3** can be cleanly generated through photoheterolysis of the alcohol or its esters and (2) the cation provides both a solvolysis product, which would be characteristic of the closed-shell singlet state reactions, and a toluene derivative resulting from a net reduction of the C−O bond. On the basis of the earlier high-level computational study, the latter is attributed to the reactions of the open-shell triplet state.

Traditionally, carbenium ions are generated by thermal solvolysis methods wherein a precursor having a very reactive leaving group is decomposed under relatively neutral conditions or a precursor with a relatively weak leaving group is treated under acid or superacid conditions. Neither of these methods was judged to be appropriate for the target species **3**. Reactive leaving groups would be displaced by the (weakly) nucleophilic Me_2N groups. Strong Lewis or Bronsted acids that would be required to activate weak leaving groups (OH, OAc) would coordinate to the Me_2N groups and prevent the formation of the target diradical state.

Coincidentally, Zimmerman,[17−20] Pincock,[21−23] and others have demonstrated that photolysis of *meta*-donor substituted benzyl alcohols and esters forms the corresponding benzylic carbenium ions.[21] There has been considerable discussion of the source of this so-called "*meta* effect". One involves direct formation of an ion pair via a conical intersection joining S_1 of the precursor to the ion pair ground state.[19] An alternative is that the observed ion pairs are formed through an initial homolysis which is followed by an electron transfer reaction of the geminate radical pair.[23,24] For the purposes of our studies, it is sufficient merely to appreciate the well-established empirical evidence that alcohol and esters having this substitution pattern favor photochemical formation of the carbenium ion.

Several precursors to benzylic cation **3** were synthesized starting with 3,5-diaminobenzoic acid **4** as indicated in Scheme 2. Esterfication of **3** followed by methylation of the amino groups and subsequent reduction of the ester provides the benzyl alcohol **7**. The latter along with esters **8** and **9** can all be used as photoprecursors to cation **3**.

Scheme 2. Synthesis of Benzyl Cation Precursors **7**−**9**



---

(10) Winter, A.; Falvey, D.; Cramer, C. *J. Am. Chem. Soc.* **2004**, *126*, 9661–9668.

(11) Wright, B. B.; Platz, M. S. *J. Am. Chem. Soc.* **1983**, *105*, 628–630.

(12) Winter, A.; Falvey, D.; Cramer, C.; Gherman, B. F. *J. Am. Chem. Soc.* **2007**, *129*, 10113–10119.

(13) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York, 1981.

(14) Finneman, J. I.; Fishbein, J. C. *J. Am. Chem. Soc.* **1995**, *117*, 4228–4239.

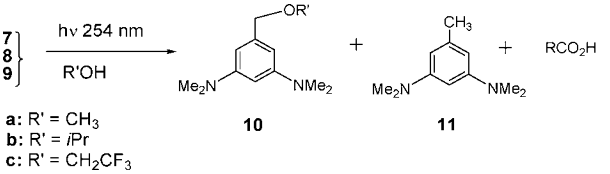
(15) Bentley, T. W.; Koo, I. S.; Choi, H.; Llewellyn, G. *J. Phys. Org. Chem.* **2008**, *21* (3), 251–256.

(16) Several important excited state reactions appear to involve adiabatic formation of triplet benzylic cations. For example. Rajesh, C. S.; Givens, R. S.; Wirz, J. *J. Am. Chem. Soc.* **2000**, *122*, 611–618.

(17) Zimmermann, H. E.; Sandel, V. R. *J. Am. Chem. Soc.* **1963**, *85*, 915–922.

Photolysis (254 nm) of (**7**−**9**) in CH_3OH, $(CH_3)_2CHOH$, and CF_3CH_2OH provides two significant products: the major product is an ether **10** derived from addition of the solvent to the benzylic carbon. The minor product is a toluene derivative **11** that is formed from a formal substitution of a hydride for the leaving group (Scheme 3). Product **11** is not expected to arise from typical benzyl cation chemistry, and several possibilities for its origin are considered below. The solvent-based origin of the benzylic hydrogen atom in **11** is confirmed by isotopic labeling experiments. Photolysis of **8** and **9** in CD_3OD provides **11** with a single deuterium on the benzylic carbon as seen by ^1H NMR (see Supporting Information).

Scheme 3. Photoproducts from **7**−**9**



The photoproducts were analyzed by GC, and their identities were confirmed by GC/MS and coinjection of authentic standards. Product ratios with the different photoprecursors in different solvents were determined by GC and corrected for detector response (Table 1). In several cases further support for these products was obtained through ^1H NMR analysis of the photoproduct mixtures.

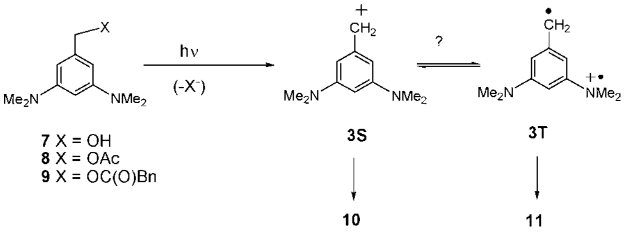
Table 1. Product Ratios (**10**/**11**) from Photolysis of **7**−**9**

solvent/additive	**7**	**8**	**9**
MeOH	6.7	3.7	3.5
i-PrOH	2.8	5.3	2.7
CF_3CH_2OH	2.8	5.3	3.2
CF_3CH_2OH/CHD	2	2	nd

There are some quantitative variations in the product ratios, but we can discern no obvious pattern. For example, in CH_3OH, the highest ratio of solvolysis product **10** is seen with the OH leaving group. In TFE, however, that trend is reversed and the OH leaving group provides the lowest proportion of **10**. Addition of 1,4-cyclohexadiene (CHD), a strong H-atom donor to the reaction, results in a modest increase. This result suggests that the reduction product forms through H-atom transfer. Two possible origins for the formation of the reduction product **11** were considered. The first possibility, which we favor for reasons discussed below, is that **11** reflects formation of the predicted triplet carbenium ion diradical **3T**.

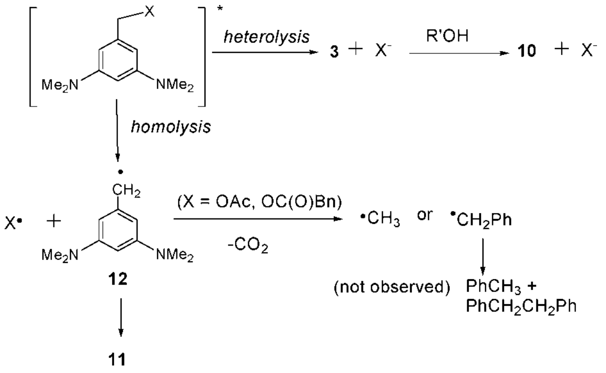
As described in Scheme 4, photoheterolysis of the alcohol **7** or ester **8** and **9** produces the carbenium ion **3**. The CASPT2 calculations indicate that the singlet state and triplet state are nearly degenerate. Consequently reaction from both states is possible. The current data are not sufficient to distinguish whether the product-determining reaction steps are occurring from rapidly equilibrating singlet and triplet states or if these trapping steps are fast relative to intersystem crossing.

Scheme 4. Photoheterolysis Mechanism



The second possibility is that **11** reflects formation of a radical **12**. This would entail a homolytic C−O bond scission in the excited state of **7**, **8**, and **9** which competes with the heterolytic bond scission leading to **10**. This alternative mechanism is illustrated in Scheme 5.

Scheme 5. Competing Photoheterolysis and Photohomolysis



We favor the first mechanism for the following reasons.

(1) Lack of Radical Products from the Leaving Groups. Following Scheme 5 formation of radical **12** would necessarily be accompanied by formation of the acetoxy or phenylacetoxy radicals, respectively, from photoprecursors **8** and **9**. The latter intermediates are known to decarboxylate on a subnanosecond time scale—Hilborn and Pincock[25] report rate constants of ca. 1.3 × 10^9 s^{-1} for acetoxy and 5 × 10^9 s^{-1} for phenylacetoxy making it unlikely that these species would be trapped in simple alcohol solvents. In the case of **9**, we expect that any radical reactions would result in

---

(18) Zimmerman, H. E. *J. Am. Chem. Soc.* **1995**, *117*, 8988–8991.
(19) Zimmerman, H. E. *J. Phys. Chem. A* **1998**, *102*, 5616–5621.
(20) Zimmerman, H. E. *J. Phys. Chem. A* **1998**, *102*, 7725–7725.
(21) Hilborn, J. W.; Macknight, E.; Pincock, J. A.; Wedge, P. J. *J. Am. Chem. Soc.* **1994**, *116*, 3337–3346.
(22) Pincock, J. A.; Wedge, P. J. *J. Org. Chem.* **1994**, *59*, 5587–5595.
(23) Pincock, J. A. *Acc. Chem. Res.* **1997**, *30*, 43–49.
(24) Those studies focused on the 3,5-dimethoxy derivatives, and according to our DFT calculations the resulting benzylic cation would still have a singlet ground state.

formation of significant quantities of bibenzyl ($PhCH_2CH_2Ph$) and/or toluene. Standard addition of these potential products to the GC analysates established that they were not formed (<1%). Also, no heterocoupling products ($PhCH_{2*}$ + solvent radicals or **12**) could be detected by GC-MS. Furthermore, formation of acetic acid and phenylacetic acid was confirmed by ^1H NMR analysis of the photolysis mixtures. Peak integrations showed that these byproducts accounted for all of the consumed ester, within the experimental uncertainty.

(2) Weak or No Dependence of the Product Ratio on the Solvent. In Scheme 5 the products are determined by the nature of two competing bond-breaking processes. The heterolytic process, which creates two ions from a neutral excited state, should be accelerated in polar solvents and inhibited in less polar solvents. By contrast, the homolytic fragmentation (Scheme 5) is expected to show little or no solvent dependence. Thus we would have anticipated consistently higher yields of the solvolysis product in TFE ($E_T(30) = 61.1$ kcal/mol) than in *i*PrOH ($E_T(30) = 48.6$ kcal/mol); MeOH ($E_T(30) = 55.5$ kcal/mol) would have intermediate values.[26]

(3) Precedent for the Photochemical *Meta* Effect. Previous studies of the photochemical *meta* effect show that benzylic esters having a single moderately electron-donating group (MeO) do, in fact, give a mixture of heterolytic and homolytic fragmentation. However substitution with two *meta* MeO goups is sufficient to provide for clean heterolysis.[16] Extrapolating from this example, it would seem that increasing the potency of the donors should further favor heterolysis. While it is conceivable that Me_2N[27] substitution could reverse the observed trend and again allow for competitive homolysis reactions, we view this as improbable.

Also considered was the possibility that the reduction product originates from a direct hydride abstraction from the solvent by **3S**. However, such a reaction pathway would be unprecedented for any simple benzylic cation. Moreover, it is extremely unlikely that TFE, with a strong electron-withdrawing CF_3 group, would provide rates of hydride donation that are comparable to that of *i*PrOH, which has two electron-donating methyl groups.

These experiments establish that the 3,5-bis(dimethylamino)benzyl cation **3** can be generated through photolysis of the corresponding esters and alcohol. Independent of any conclusions regarding the origin of the reduction product **11**, detection of the solvolysis products **10** make it clear that the targeted carbenium ion **3** is formed in these photochemical reactions. This finding should allow for additional experimental studies using laser flash photolysis and low temperature matrix methods.

The formation of reduction product **11** provides some evidence that the theoretically predicted triplet diradical state **3T** is sufficiently low in energy that it can be chemically trapped. It should be acknowledged that this evidence is indirect, and none of the arguments 1−3 listed above are completely irrefutable. For example while solvent effects on heterolysis/homolysis partitioning tend to be profound in ground state chemistry, excited state reactions should have smaller barriers and thus could exhibit a much more modest dependence on solvent polarity. Likewise the *meta* effect is well precedented for alkoxy groups, but there is far less empirical evidence that amino groups will provide the same degree of photoheterolysis. While the quantitative formation of carboxylic acids provides strong evidence against homolysis, it is possible, although not likely, that identification of several unknown trace products seen by GC and NMR could change our view of the mechanism. Finally, the variations in product ratios with the leaving group is not fully understood at this time and could indicate a more complex mechanism than that considered here. However taken as a whole, we consider the formation of **11** through photohomolysis (Scheme 5) very unlikely and that its formation through a low energy triplet diradical **3T** as the more plausible interpretation of the current data.

Acknowledgment. We thank Mr. William Coldren (University of Maryland) for preliminary calculations on the 3,5-dimethoxybenzylcation and the Chemistry Division of the National Science Foundation for support. R.R.P. is supported by the U.S. Department of Education through a GAANN fellowship.

Supporting Information Available: Detailed synthesis and characterization data of benzyl cation precursors **7**−**9** and GC standards **10a**, **10c**, and **11** are provided. ^1H NMR data of the photolysis mixtures are also provided, as well as standard GC calibration curves. This material is available free of charge via the Internet at http://pubs.acs.org.

OL102606M

---

[25] Hilborn, J. W.; Pincock, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 2683–2686.

[26] Reichardt, C.; Schafer, G. *Liebigs Ann.* **1995**, (8), 1579–1582.

[27] The one example where **3** is generated photochemically is complicated by competition between heterolysis to form the targeted cation and fragmentation within the diazeniumdiolate leaving group itself. Ruane, P. H.; Bushan, K. M.; Pavlos, C. M.; D'Sa, R. A.; Toscano, J. P. *J. Am. Chem. Soc.* **2002**, *124*, 9806–9811.