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Changeable reactivity of ketyl radicals derived from 2-bromomethyl-2-(3-butenyl)benzocyclic-1-alkanones depending on electron transfer conditions employed

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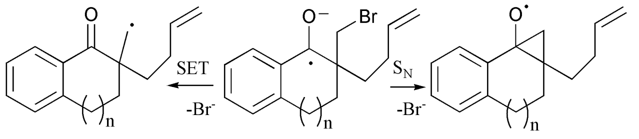
Photoinduced electron transfer reaction of 2-bromomethyl-2-(3-butenyl)benzocyclic-1-alkanones with amines afforded 5-exo radical cyclization products while electron transfer reaction with samarium diiodide produced cyclopropanols.

Carbonyl compounds are known to accept a single electron to become their radical anions (ketyl radicals). Principally, three different modes of reaction are open to these intermediates: (1) bond formation either with electrophiles or with radicals; (2) α- and β-bond cleavages; (3) single electron capture and release.[1] Therefore, ketyl radicals undergo nucleophilic substitution (S_N) as well as single electron transfer (SET) against other functional groups such as carbon–halogen bonds. In this context, investigation of SET reaction of compounds possessing both carbonyls and carbon–halogen bonds provides an interesting opportunity to learn how ketyl radicals of such compounds intramolecularly react with distant carbon–halogen bonds. However, information on the reactivity of such types of ketyl radicals is extremely limited.[2] Thus, in order to investigate this mechanistic problem, we designed 2-bromomethyl-2-(3-butenyl)benzocyclic-1-alkanones **1** as new probe substrates of ketyl radicals[3] which were subjected to photoinduced electron transfer (PET) reaction with amines as well as electron transfer reaction with samarium diiodide (SmI_2).† The primary alkyl radicals, if generated through intramolecular SET in the radical anions of **1**, could rapidly undergo 5-exo radical cyclization[4] while intramolecular S_N could give cyclopropoxy radicals (Scheme 1). Each pathway should lead to the formation of the characteristic products respectively. Here, we communicate preliminary results which suggest that the intramolecular SET mechanism is not operable in the reaction of **1** with SmI_2 but is operable in the PET reaction of **1** (Fig. 1).‡

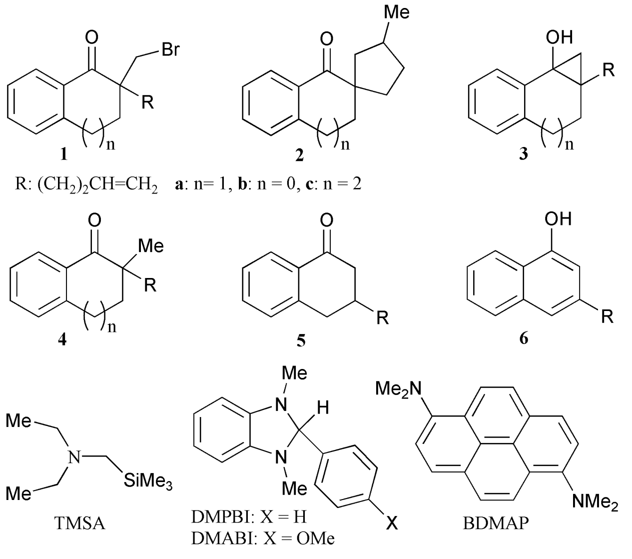
At first, the reaction of **1** with tris(trimethylsilyl)silane (TTMSS) was conducted using triethylborane–air as an initiator to ensure that the primary alkyl radicals derived from **1** undergo 5-exo radical cyclization (**1**: 0.5 mmol, TTMSS: 1.0 equiv. *vs.* **1**, Et_3B: 0.2 equiv. *vs.* **1**, C_6H_6: 10 ml, RT, 6 h). Then, the expected spirocyclic products **2** were obtained in good yields (**2a**: 90%, **2b**: 78%, **2c**: 79%) without the formation of simply debrominated products **4**.§

For the PET reactions of **1**, *N*,*N*-diethyl-*N*-trimethylsilylmethylamine (TMSA), 1,3-dimethyl-2-phenylbenzimidazoline (DMPBI) and 1,3-dimethyl-2-anisylbenzimidazoline (DMABI) were chosen since these amines are known to act as effective electron donors for various PET reactions.[6,7] When nitrogen pre-purged solutions of **1a** and TMSA in certain solvents such as MeCN, THF and DMF were irradiated with Pyrex filtered light using a 500 W Xe–Hg lamp, **2a** was obtained in 52, 51 and 53% yields, respectively (**1a**: 0.5 mmol, TMSA: 5.0 equiv. *vs.* **1a**, solvent: 5 ml, RT, 4 h). Addition of water (20 equiv. *vs.* **1a**) to the MeCN solution did not much change the yield of **2a** (49%). Photosensitized reaction (λ > 360 nm) of **1a** with TMSA using 1,6-bis(dimethylamino)pyrene (BDMAP)[8] as an electron donor sensitizer similarly led to the formation of **2a** in 58% yield based on 83% conversion of **1a** (**1a**: 0.5 mmol, TMSA: 5.0 equiv. *vs.* **1a**, BDMAP: 0.15 equiv. *vs.* **1a**, DMF: 5 ml, RT, 4 h). Photoreaction of **1a** with DMPBI or DMABI in MeCN produced **2a** in 57 or 60% yield respectively. Irradiation of other **1** with DMABI also produced the corresponding **2** in moderate yields (**2b**: 57% at 85% conversion of **1b**, **2c**: 59% at 79% conversion of **1c**). Interestingly, no **4** were obtained in all the above photoreactions.

On the contrary, when **1a** was treated with SmI_2, cyclopropanol **3a** was obtained in excellent yield (96%) (**1a**: 0.5 mmol, SmI_2: 2.2 equiv. *vs.* **1a**, THF: 12 ml, RT, 30 min). Notably, **3a** was still a major product (97%) for the reaction of **1a** and SmI_2 in the presence of *t*-BuOH (20 equiv. *vs.* **1a**), not giving the ordinary alcohol, 2-bromomethyl-2-(3-butenyl)-1-hydroxy-1,2,3,4-tetrahydronaphthalene. Reaction of **1b** with SmI_2 under the same conditions was rather complicated but interesting. Formation of **3b** (59%) was accompanied with small amounts of byproducts such as **2b** (1%), **5** (7%) and **6** (10%). Although, **5** and **6** are typical radical cyclization-ring expansion products,[9,10] such radical pathways would not exist in this reaction. As described above, **2b** was predominantly obtained under the free radical conditions, which clearly suggests that 5-exo radical cyclization and radical cyclization-ring expansion are not competitive with each other in the primary alkyl radical derived from **1b**. Namely, the involvement of such a radical intermediate is not confirmed by the isolation of **5** and **6** but by that of **2b**.



Scheme 1



R: $(CH_2)_2CH=CH_2$ **a**: n= 1, **b**: n = 0, **c**: n = 2

Fig. 1

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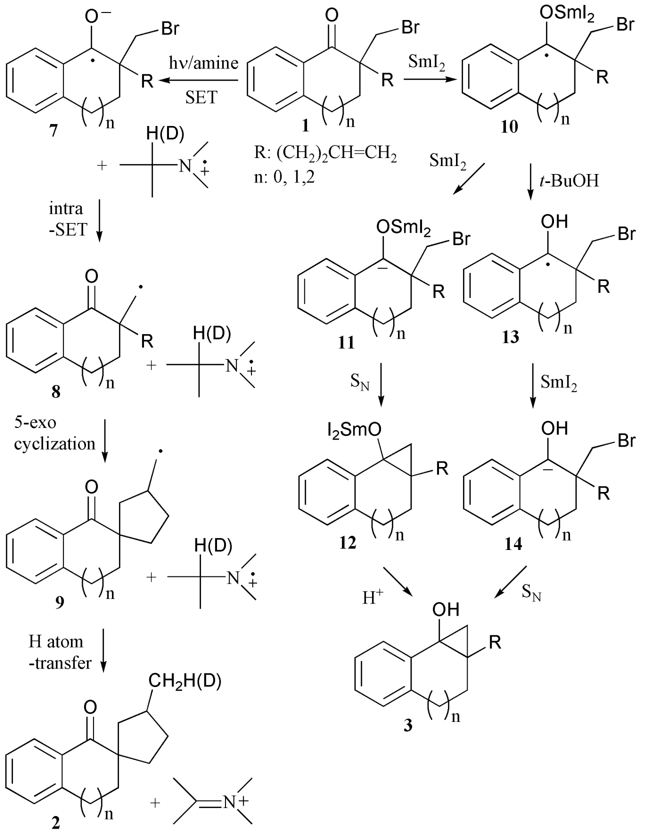
On the basis of the results obtained, plausible reaction pathways are presented in Scheme 2. Photoinduced SET between **1** and amines produced their radical anions and radical cations.¶ Fast intramolecular SET from the ketyl radical parts to the carbon–bromine bonds in **7**, which is not interrupted by the protonation from water, occur to give the primary alkyl radicals **8**. The rearrangement of **8** to **9** should be much faster than the hydrogen atom transfer from the amine radical cations to **8**, which is consistent with no formation of **4**. Hydrogen atom transfer from the amine radical cations to **9** gives **2**. This last step indeed proceeds, although not predominantly, since some deuterium incorporation at the methyl on the cyclopentane ring of **2a** was observed (40%-*d* in MeCN and 53%-*d* in benzene) when 2-deuterio DMPBI (DMPBI-D) was used for the reaction with **1a**. On the other hand, reduction of **1** by SmI_2 produces samarium coordinated ketyl radicals **10**. Intramolecular SET from **10** to the carbon–bromine bonds must be slow, even though such a process exists, because of the extremely low yield of **2b**. Since the reaction of alkyl bromides with SmI_2 is generally low in the absence of activators such as hexamethylphosphorictriamide,[11] the carbon–bromine bonds in **10** are not readily reduced under the conditions employed. Thus, **10** are reduced to become carbanions **11** which undergo S_N against the carbon–bromine bonds to give the samarium cyclopropoxides **12**. The alkoxides **12** are finally protonated to produce **3**. In the presence of proton donors, **10** are protonated to give **13** followed by reduction with another SmI_2 to become **14**. Apparently, intramolecular S_N against the carbon–bromine bonds predominantly proceeds in **14** rather than protonation to produce the corresponding alcohols.

In conclusion, PET reaction of 2-bromomethyl-2-(3-butenyl)benzocyclic-1-alkanones with amines afforded 5-exo radical cyclization products while ET reaction with SmI_2 produced cyclopropanols. Such disparate results are due to the difference of the nature of ketyl radicals generated by two distinct methods: a PET method produces free ketyl radicals while a SmI_2 method produces samarium metal coordinated ketyl radicals.



Scheme 2

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Notes and references

† Although samarium diiodide-promoted reduction of haloalkylated ketones has been well investigated (A. Kief, A.-M. Laval, *Chem. Rev.*, 1999, **99**, 745 and references cited therein), there still has been mechanistic controversy regarding whether it is carbonyls or carbon–halogen bonds that are first reduced by SmI_2 in the reaction of these compounds (D. P. Curran, X. Gu, W. Zhang and P. Dowd, *Tetrahedron*, 1997, **53**, 9023). Thus, intramolecular reactivity of samarium coordinated ketyl radicals with carbon–halogen bonds has not been fully understood yet.

‡ Reactants **1**, products **2**, **3**, **5** and **6** were satisfactorily characterized by their ^{1}H-NMR, ^{13}C-NMR and IR data. Compounds **4** were independently synthesized by NaH-promoted α-methylation of 2-(3-butenyl)benzocyclic-1-alkanones.

§ 2,2-Disubstituted 5-hexenyl radicals, which are common structures contained in the primary alkyl radicals in Scheme 1, are known to cyclize ten times faster (3.6×10^6 s^{-1}) than the parent 5-hexenyl radicals (2.3×10^5 s^{-1}): A. L. J. Beckwith, C. J. Easton, T. Lawrence and A. K. Serelis, *Aust. J. Chem.*, 1983, **36**, 545.

¶ Free energy change (ΔG) for single electron transfer (D. Rehm and A. Weller, *Isr. J. Chem.*, 1970, **8**, 259) between the triplet excited state of **1** and amines were estimated to be the range within -21 and -28 kcal mol^{-1} based on the triplet energy of benzocyclic ketones such as 1-tetralone, 72.7 kcal mol^{-1} and 1-indanone, 75.8 kcal mol^{-1} (S. L. Murov, *Handbook of Photochemistry*, Marcel Dekker, New York, 1973), the redox potentials of **1** (E_p^{red}, **1a**: -2.05; **1b**: -2.12; **1c**: -2.28 V *vs.* $Ag/AgNO_3$) and amines (E_p^{ox}, TMSA: +2.07; DMPBI: +0.03; DMABI: +0.01 V *vs.* $Ag/AgNO_3$). Oxidation potential of the singlet excited state of BDMAP (E_p^{ox} = + 0.16 V *vs.* $Ag/AgNO_3$, E_s = 64 kcal mol^{-1} [8]) indicates exothermic SET with **1a** (ΔG = -15 kcal mol^{-1}).

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