

# Photoreaction of halomethyl substituted benzocyclic ketones with amines: radical cyclization and ring expansion reactions promoted through photoinduced electron transfer processes

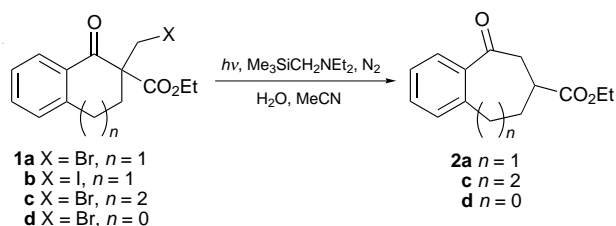
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**Photoreaction of ethyl 2-bromomethyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate **1a** or other related compounds **1b–d** with  $\text{Me}_3\text{SiCH}_2\text{NET}_2$  in aqueous MeCN afforded ethyl 5-oxo-6,7,8,9-tetrahydrobenzocycloheptene-7-carboxylate **2a** or corresponding ring expansion products **2a–d** respectively.**

Irradiation of carbonyl compounds in the presence of electron donors such as amines produces carbonyl anion radicals and donor cation radicals.<sup>1</sup> Apparently proton transfer from donor cation radicals to carbonyl anion radicals is a feasible process. On the other hand, it is also reasonable to expect that carbonyl anion radicals must act as single electron donors. Therefore, generation of carbonyl anion radicals would irreversibly reduce distant carbon–halogen bonds in the same molecules through intramolecular electron transfer.<sup>2</sup> Although photoreactions of a few carbonyl compounds categorized in this group have been explored in the presence of electron donors, the substrates studied were limited to enones and dienones.<sup>3</sup> In this context, photoinduced electron transfer (PET) reaction of haloalkylated benzocycloalkanones such as **1** must be interesting since reductive carbon–halogen bond cleavage should generate carbon radicals followed by radical cyclization and ring expansion pathways.<sup>4</sup> Moreover, the literature observation that the yields of ring expansion products from **1** ( $\text{X} = \text{Br}$ ) were relatively low under ordinary free radical conditions<sup>5</sup> also prompted us to explore photoreaction of **1** with electron donors. We report here the first example of PET promoted radical cyclization and ring expansion reactions of ethyl 2-bromomethyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate **1a** and other related compounds **1b–d** (Scheme 1).

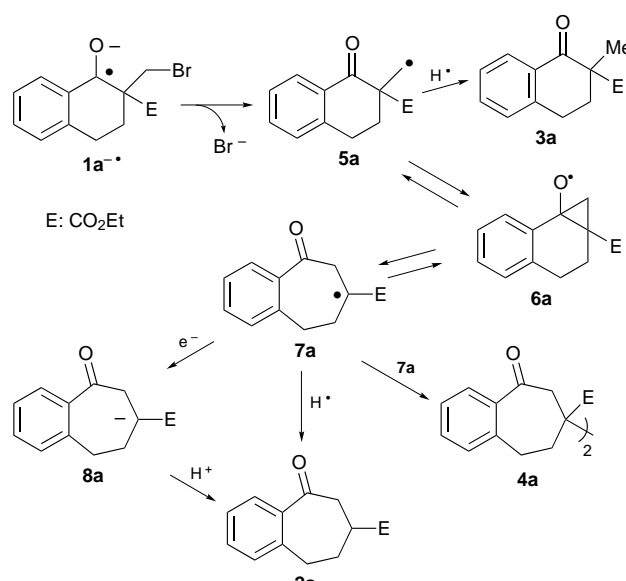
When a  $\text{N}_2$  pre-purged MeCN solution (10 ml) of **1a** ( $\lambda = 295 \text{ nm}$ ,  $\epsilon 820$ ; 0.64 mmol) and  $\text{Me}_3\text{SiCH}_2\text{NET}_2$  (5 equiv.)<sup>6</sup> was irradiated for 1 h with a 500 W Xe–Hg lamp through Pyrex, 50% of the desired benzocycloheptanone **2a**, 10% of the reduced product **3a** and 21% of unexpected dimeric compound **4a** (as a mixture of two diastereomers **4a**<sub>1</sub>:**4a**<sub>2</sub> = 55:45) was isolated together with 35% of unreacted **1a** after chromatographic separation (the product yields are reported on the basis of the conversion of **1a**).<sup>†</sup> Stirring of a similar solution for 2 h in the dark resulted in quantitative recovery of **1a**. Upon irradiation of **1a** for 2 h in the absence of  $\text{Me}_3\text{SiCH}_2\text{NET}_2$ , 92% of **1a** was recovered without formation of **2a**. These control experiments clearly suggest that **2a** is produced through the interaction between the photoexcited **1a** and  $\text{Me}_3\text{SiCH}_2\text{NET}_2$ .



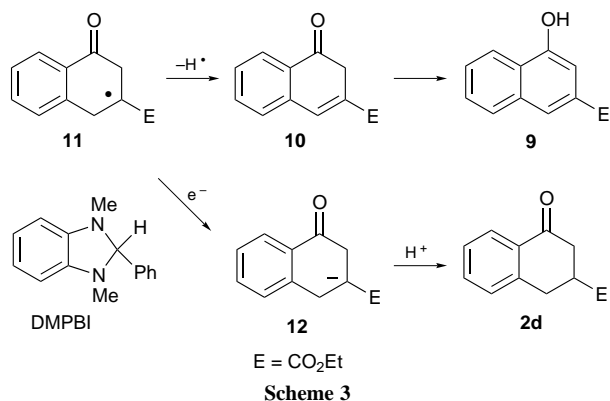
Scheme 1

It was also found that water significantly affects the product ratio when the reactions were conducted for 1 h in MeCN containing various amounts of water: 61% of **2a**, 10% of **3a**, 20% of **4a** and 24% of **1a** in 5% aq. MeCN; 68, 7, 16 and 25% in 10% aq. MeCN; 75, 6, 10 and 25% in 30% aq. MeCN. While addition of water increased the yield of **2a** and decreased the yields of **3a** and **4a**, the total yield of the products remained almost constant at about 90%. This would suggest that the observed products are formed through common intermediates. In order to obtain information on the nature of the intermediates, a deuterium labeling experiment was performed. Thus, when irradiation of **1a** for 2 h were conducted in 5%  $\text{D}_2\text{O}$  as well as 5%  $\text{H}_2\text{O}$  containing MeCN solutions, similar conversions (90 and 90%) as well as product yields (**2a**: 60 and 59%; **3a**: 7 and 7%) were observed, respectively. NMR analyses of the isolated products revealed that *ca.* 82% of hydrogen at  $\text{C}_3$  in **2a** was substituted by deuterium and no deuterium was incorporated in **3a**. Therefore, **2a** is mainly formed through an ionic route in which its precursor is protonated. On the other hand, **3a** is formed through hydrogen abstraction by the radical intermediate.

On the basis of the above results, the reaction mechanism in Scheme 2 is proposed. Single electron transfer to the photoexcited state of **1a** from  $\text{Me}_3\text{SiCH}_2\text{NET}_2$  produces the anion radical of **1a** and the cation radical of  $\text{Me}_3\text{SiCH}_2\text{NET}_2$ .<sup>‡</sup> The resulting anion radical of **1a** rapidly reacts,<sup>§</sup> undergoing carbon–bromine bond cleavage through intramolecular electron transfer to give the carbon radical **5a**. The radical **5a** abstracts hydrogen to produce **3a**, which is consistent with the deuterium labeling experiment. On the other hand, **5a** cyclizes to give the oxy radical **6a** followed by the ring opening to the ethoxy



Scheme 2



carbonyl substituted carbon radical **7a**. Apparently, **7a** has a long enough lifetime to dimerize, giving **4a**. Cyclization of the carbon radical on the carbonyl group and ring opening would be a reversible process (**5a** → **6a** → **7a**).<sup>7</sup> If **7a** abstracts hydrogen, **2a** should be formed. However, the deuterium labeling experiment suggests that this is a minor route, even though it exists. Instead, **7a** is reduced to its anion **8a** followed by protonation to give the formation of **2a**.

In the proposed reaction mechanism, the most plausible candidate for the reducing agent of **7a** must be the  $\alpha$ -amino radical formed through desilylation of the cation radical of Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>. Thus, effective formation of the  $\alpha$ -amino radical is required for the formation of **2a**. Indeed, when **1a** was irradiated with 1,4-diazabicyclo[2.2.2]octane (DABCO) for 5 h in MeCN, no formation of **2a** was observed. Although DABCO is a strong enough electron donor,<sup>‡</sup> its cation radical is known to be stable, so that the efficient formation of the  $\alpha$ -amino radical by deprotonation cannot be expected.<sup>8</sup> In the reaction system of **1a** and Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>, water would act as a silophile to generate the  $\alpha$ -amino radical by desilylation of the cation radical of Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>.<sup>9</sup> On the other hand, water would not be a strong enough base for  $\alpha$ -deprotonation of an amine cation radical.<sup>10</sup> This was confirmed by the observation that photo-reactions of **1a** with triethylamine<sup>‡</sup> in dry as well as wet MeCN reveal no significant water effect on the product ratio. Another notable observation was made when the reactions were conducted for 1 h with addition of various quantities of Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub> in 10% aq. MeCN: 56% of **2a**, 7% of **3a**, 24% of **4a** and 39% of **1a** with 1.5 equiv. of Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>; 68, 7, 16 and 25 with 5 equiv.; 73, 10, 12 and 27 with 10 equiv. Increasing the quantity of Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub> increased the yield of **2a** as well as **3a** and decreased that of **4a**, which would suggest that excess Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub> donates a hydrogen to the radical intermediates, leading to the formation of **2a** and **3a**, and eventually decreasing the yield of **4a**.

In order to determine the generality of this PET reaction, photoreactions of other halo ketones **1b–d** were briefly conducted (product yields were not optimized). Irradiation of the iodide **1b** with Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub> produced 46% of **2a**. The moderate yield of **2c** (41%) from **1c** is still encouraging since thermal reaction of **1c** with tributyltin hydride produced **2c** only as a minor product.<sup>5</sup> More interestingly, it turned out that the major product from **1d** was ethyl 1-hydroxynaphthalene-3-carboxylate **9** (52%) instead of **2d**, which was isolated in 14% yield in the photoreaction of **1d** with Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>. As shown in Scheme 3, naphthol **9** is considered to be an enol form of ketone **10**, which is probably formed *via* hydrogen abstraction from the ethoxy carbonyl substituted carbon radical **11**. If so, the relative yield of **2d** vs. **9** should increase under the conditions in which **11** is efficiently reduced to its anion **12**. This was actually the case when Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub> was replaced by 1,3-dimethyl-2-phenylbenzimidazole (DMPBI),<sup>11</sup> which gave 47% of **2d** and 11% of **9**.<sup>¶</sup> Since the  $\alpha$ -amino radical

derived from the cation radical of DMPBI is readily oxidized to a stable imidazolium ion, it would act as a stronger reductant than that from the cation radical of Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>.

As described above, we have discovered that a PET process can promote the conversion of certain halomethyl substituted benzocyclic ketones to ring expanded ketones. Further studies focused on designing substrates as well as electron donors are now in progress, with the aim of providing a thorough mechanistic understanding and an expansion of the synthetic versatility of this unique PET reaction.

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## Footnotes and References

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† Ring expansion products **2a,c** and the reduced product **3a** are known compounds (ref. 5). The structure of unknown **2d** was determined by direct comparison of its spectral data with that of the compound independently prepared by reaction of **1d** with tributyltin hydride. Compounds **4a** and **9** were satisfactorily characterized by their NMR and IR spectroscopic data.

‡ Free energy changes ( $\Delta G$ ) for single electron transfer between the triplet excited state of **1a** and amines were estimated (D. Rehm and A. Weller, *Isr. J. Chem.*, 1970, **8**, 259) from the triplet energy of 1,2,3,4-tetrahydronaphthalen-1-one (72.7 kcal mol<sup>-1</sup>; S. L. Murov, *Handbook of Photochemistry*, Marcel Dekker, New York, 1973) and the redox potentials of **1a** (−1.85 V vs. SCE) and amines<sup>3</sup> (−19 kcal mol<sup>-1</sup> for Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>, −15 kcal mol<sup>-1</sup> for DABCO, −11 kcal mol<sup>-1</sup> for NEt<sub>3</sub>).

§ Pulsed laser photolysis (355 nm) of **1a** in nitrogen-saturated MeCN resulted in a transient absorption around 370 nm which was assigned as the T–T absorption. In the presence of Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub>, the T–T absorption was replaced by a new shoulder absorption ranging from 400 to 500 nm, which decayed with a rate constant of ca. 3 × 10<sup>6</sup> s<sup>-1</sup>. A plausible explanation for these observations is that the triplet excited state of **1a** is quenched by Me<sub>3</sub>SiCH<sub>2</sub>NEt<sub>2</sub> to generate the anion radical of **1a**, which decays rapidly owing to its high intramolecular reactivity. The cyclic voltammetric behaviour of **1a** is also consistent with the above explanation: the redox process of **1a** is totally irreversible (100 mV s<sup>-1</sup> in MeCN).

¶ An alternative explanation for this phenomenon would be the occurrence of direct hydrogen transfer from the cation radical of DMPBI or its neutral form to the radical **11** to give **2d** (Note added in proof).

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