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Communication

Formation of Carbanions from Carboxylate Ions Bearing Electron-Withdrawing Groups via Photoinduced Decarboxylation: Addition of Generated Carbanions to Benzaldehyde

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The photoinduced decarboxylation of carboxylate ions bearing electron-withdrawing groups using biphenyl and 1,4-dicyanonaphthalene leads to the efficient generation of carbanions under mild conditions. The efficiency of the carbanion generation is strongly dependent on the single-electron transfer from the photogenerated radical anion of the electron-acceptor to the radical. In particular, the cyanomethyl anion formed using this photochemical method can be added to benzaldehydes to give the corresponding adducts.

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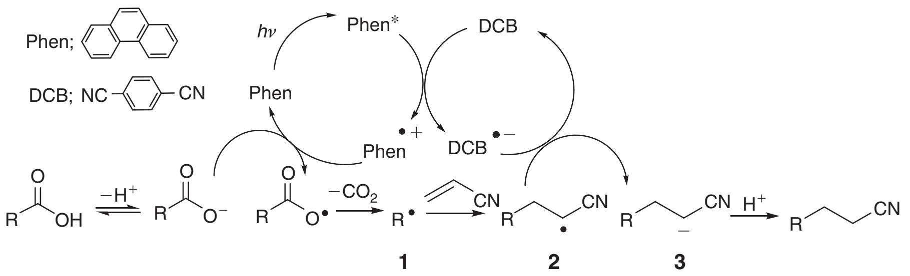
Carbanions are one of the most common and useful reactive intermediates in organic synthesis.[1] For example, carbanions bearing electron-withdrawing groups, such as diethyl malonate ion, are frequently used as valuable components for the preparation of organic molecules.[2] However, the generation of these carbanions typically requires the use of a strong base and heat. Thus, the ability to generate carbanions under mild conditions is desired.

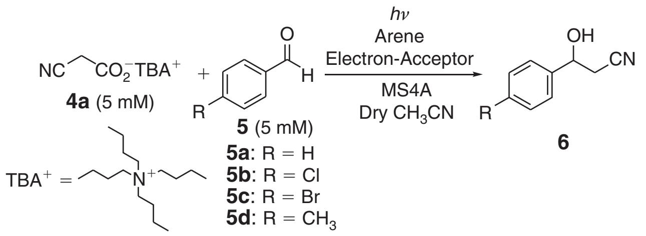
Recently, we reported decarboxylative radical reactions[3] of aliphatic carboxylic acids using phenanthrene (Phen) and 1,4-dicyanobenzene (DCB) via photoinduced electron transfer (PET) (Scheme 1).[4] The process is promoted by a single-electron transfer (SET) from the carboxylate ion to the radical cation of Phen via PET, and leads to the formation of carboxy radicals that rapidly lose CO_2 to produce alkyl radicals **1**. The formed alkyl radicals react with a variety of reagents, such as oxime ethers, thiols, and the radical anion of DCB, to provide the respective addition,[4e] reduction,[4a,f] and substitution[4b] products in high yields. In particular, the addition of generated alkyl radical **1** to an electron-deficient alkene, such as acrylonitrile, proceeds efficiently to form electron-deficient radical **2**.[4c,d,g-i] Subsequently, the SET from the radical anion of DCB to **2** generates carbanion **3**, which upon protonation, gives the corresponding adduct in a high yield. The earlier observation regarding the SET from the radical anion of DCB to electron-deficient radical **2** encouraged us to investigate the photoinduced decarboxylation of carboxylate ions bearing electron-withdrawing groups to form carbanions. Although a laser flash photolysis study of decarboxylative carbanion formation from benzylic carboxylate ions using dicyanoarenes was previously reported,[5] synthetic methodologies based on these reactions have not been reported to date. In this study, we developed a novel, simple process for the generation of carbanions from carboxylate ions bearing electron-withdrawing groups via photoinduced decarboxylation, and addition of the formed cyanomethyl anion to benzaldehydes.

Initial exploratory studies were carried out regarding the photoinduced decarboxylative addition of tetra-*n*-butylammonium cyanoacetate (**4a**) with benzaldehydes **5** in dry CH_3CN using molecular sieves (MS4A) because water and the acidic proton of the carboxy group quenched the photogenerated carbanion (Table 1). Irradiation of a dry CH_3CN solution (30 mL) containing **4a** (5 mM, 48.9 mg), benzaldehyde **5a** (5 mM, 15.9 mg), Phen (20 mM, 106 mg) as an arene, DCB (20 mM, 76.8 mg) as an electron-acceptor, and MS4A (6 g) in two Pyrex vessels (>280 nm, 15 × 180 mm) under an argon atmosphere using a 100 W high-pressure mercury lamp for 10 h at room temperature led to formation of adduct **6a** in 46 % yield (Entry 1). In addition to Phen and DCB, biphenyl (BP) and 1,4-dicyanonaphthalene (DCN) served as a viable arene and electron-acceptor, respectively, in the photoreaction, and significantly increased the yield of **6a** (88 %) (Entry 2).[6] As we previously reported,[3f,4h] the SET from the radical anion of DCN to radical intermediate **1** occurs more smoothly than the SET from the radical anion of DCB to **1** because of the relatively long lifetime of the radical anion of DCN. A similar trend in the SET from the radical anion of DCN to the generated cyanomethyl radical was observed, and led to an increase in the yield of **6a**. In addition, lower concentrations of BP and DCN led to a decrease in the yield of **6a**, likely due to the lower concentration of the radical anion of DCN (Entries 3 and 4). These results indicated that the efficiency of carbanion generation was



Scheme 1. Decarboxylative radical addition of aliphatic carboxylic acids to acrylonitrile by the photogenerated radical cation of Phen.

Table 1. Photoinduced decarboxylative addition of 4a with 5[A]



Entry	Arene	Electron-Acceptor	**5**	Irradiation. time [h]	Yield of **6** [%][B]
1	Phen (20 mM)	DCB (20 mM)	**5a**	10	46
2	BP (20 mM)	DCN (20 mM)	**5a**	10	88
3	BP (10 mM)	DCN (10 mM)	**5a**	10	63
4	BP (5 mM)	DCN (5 mM)	**5a**	10	36
5	BP (20 mM)	DCN (20 mM)	**5b**	6	67
6	BP (20 mM)	DCN (20 mM)	**5c**	8	39
7	BP (20 mM)	DCN (20 mM)	**5d**	10	16

[A] Dry acetonitrile solutions containing **4a** (5 mM), **5** (5 mM), arene, electron-acceptor, and MS4A under an Ar atmosphere were irradiated at room temperature. TBA^{+} = tetra-*n*-butylammonium cation.

[B] Isolated yield.

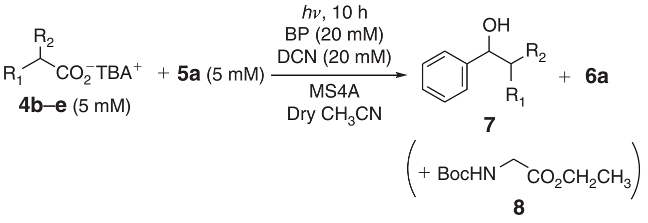
strongly dependent on the SET from the radical anion of the electron-acceptor to the generated radical. When 4-substituted benzaldehydes **5b–d** were subjected to the photoreaction, corresponding adducts **6b–d** were obtained in moderate or low yields because products **6b–d** decomposed under the reaction conditions employed (Entries 5–7). In fact, the photoreaction of **6c** (5 mM) for 3 h under the aforementioned conditions (BP: 20 mM; DCN: 20 mM) led to the recovery of **6c** in only 58 % yield. In contrast, similar photoreactions with 4-methoxy or 4-cyano-benzaldehydes did not give adduct **6**, possibly because methoxy and cyano-benzaldehydes disturb the PET process.

Subsequently, the effects of substituents on the carboxylate ion on the photoreaction were explored (Table 2). The photoinduced decarboxylative addition of monoethyl malonate ion **4b**, alkylcyanoacetate ions **4c** and **4d**, and monoethyl aminomalonate ion **4e** to **5a** did not take place, but gave **6a**. In the case of **4e**, the decarboxylative reduction product **8** was also obtained (76 %).[7] These results indicated that the carbanions generated from **4b–e** via photoinduced decarboxylation did not attack the carbonyl group of aldehyde **5a**, but abstracted a proton from the solvent, acetonitrile, to form a cyanomethyl anion, which led to the formation of **6a** because the anions generated from **4b–e** are more basic than the cyanomethyl anion.[8] In order to overcome this problem, other solvents were examined. Instead of acetonitrile, propionitrile, isobutyronitrile, cyanobenzene, and a 1 : 1 mixture of cyanobenzene and THF were evaluated; however, they were not suitable for this photoreaction because the low polarity of the solvents retarded the formation of the radical cation of BP via PET to recover the starting materials.[4d] Improvement of the reaction conditions to facilitate the use of other carboxylate ions such as **4b–e** in this photoreaction is in progress in our laboratory.

Based on the obtained results, a plausible mechanism for the photoreaction is shown in Scheme 2. First, absorption of light (>280 nm) by electron-acceptor DCN produces the excited state of DCN (DCN*). PET between BP and DCN* generates the radical cation of BP and the radical anion of DCN. Subsequently, the SET from the carboxylate ion bearing an electron-withdrawing group to the radical cation of BP leads to the formation of an electron-deficient radical via decarboxylation. The third electron transfer from the radical anion of DCN to the electron-deficient radical generates the carbanion. With the cyanomethyl anion (R = CN), the formed anion reacts with benzaldehydes **5** to give adduct **6**. In contrast, other carbanions derived from **4b–e** abstract a proton from acetonitrile to form the cyanomethyl anion, which yields **6a** due to the higher basicity.

In conclusion, we have described the development of a new and mild method for the generation of carbanion intermediates via the PET-promoted decarboxylation of carboxylate ions bearing electron-withdrawing groups. The efficiency of the

Table 2. Substituent effect of carboxylate ions 4b–e on photoreaction[A]



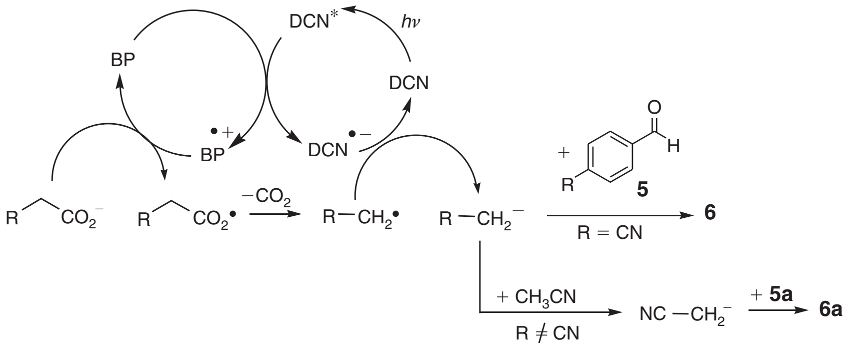
Entry	4	R_1	R_2	Yield of **7** [%][B]	Yield of **6a** [%][B]
1	**4b**	$CO_2CH_2CH_3$	H	0	39
2	**4c**	CN	CH_2CH_3	0	24
3	**4d**	CN	$CH_2CH_2CH_3$	0	10
4	**4e**	$CO_2CH_2CH_3$	NHBoc[C]	0 (76)[D]	42

[A] Dry acetonitrile solutions containing **4** (5 mM), **5a** (5 mM), BP (20 mM), DCN (20 mM), and 4AMS under an Ar atmosphere were irradiated for 10 h at room temperature.

[B] Isolated yield.

[C] Boc = *t*-butoxycarbonyl.

[D] Yield of **8**.



Scheme 2. Plausible mechanism for the photoinduced carbanion generation from carboxylate ion using BP and DCN.

carbanion generation in this photoreaction is strongly influenced by the SET from the radical anion of the electron-acceptor to the electron-deficient radical. Although the addition to benzaldehydes is only achieved with the use of cyanoacetate ion **4a**, we found that a variety of carbanions from **4b–e** can be generated using this method. Further investigations regarding the applicability of this methodology in reactions involving the photogenerated carbanions are underway in our laboratory.

Supplementary Material

^{1}H and ^{13}C NMR spectral data of **4**, **6**, and **8** are available on the Journal's website.

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[6] Typical experimental procedure for the photoreaction of **4a** with **5a**: A dry CH_3CN solution (30 mL) containing **4a** (0.15 mmol, 5 mM), **5a** (0.15 mmol, 5 mM), BP (0.6 mmol, 20 mM), DCN (0.6 mmol, 20 mM), and 4A molecular sieves (6 g) in two Pyrex vessels (15 mm × 180 mm) were purged with argon for 10 min. The mixture was irradiated with a 100 W high-pressure mercury lamp for 10 h, and filtered. Then, the filtrate was evaporated. The product was purified by silica gel column chromatography using hexane and ethyl acetate as eluents to give adduct **6a**.

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