

Reduction of a “Cation Pool”: A New Approach to Radical Mediated C–C Bond Formation

Seiji Suga, Shinkiti Suzuki, and Jun-ichi Yoshida*

Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Yoshida Hon-machi, Sakyo-ku, Kyoto 606-8501, Japan

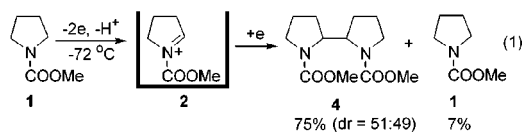
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Carbocations, carbon radicals, and carbanions are important reactive carbon intermediates in organic chemistry, and their interconversions can be carried out by redox processes as shown in Scheme 1. For example, pioneering work of Conant reminded us that one-electron reduction of a carbocation produces a carbon radical.¹ One-electron reduction of a carbon radical produces a carbanion species.² Although, such relationships have been well recognized, experimental work has been limited to analytical studies on highly stabilized intermediates.³ Manipulation of such redox process with complete control, however, still remains as one of the challenging goals of synthetic organic chemistry.

Recently we have developed the “cation pool” method, in which anodic oxidations are employed to generate and accumulate carbocations in relatively high concentrations in the absence of nucleophiles.⁴ We envisioned that such “cation pools” can be utilized for redox-mediated interconversions of reactive carbon species. We wish to report herein the realization of this transformation using acyliminium cation pool as a proof-of-principle of our strategy.

First, we examined the electrochemical reduction of the cation pool in the absence of radical acceptors.⁵ The electrochemical reduction of acyliminium cation **2**,⁶ generated by the low-temperature electrolysis of *N*-(methoxycarbonyl)pyrrolidine (**1**), gave the corresponding homocoupling product **4** as a mixture of two diastereomers (eq 1).⁷

The electrochemical reduction of acyliminium cations produced from other carbamates such as *N*-(methoxycarbonyl)piperidine and *N*-(methoxycarbonyl)diethylamine also gave the corresponding homocoupled products in 39% and 68% yields, respectively.

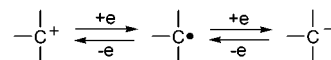


The present result implies that the one-electron reduction of **2** produced carbon-centered radical **3**, which homo-coupled to give dimer **4** (Scheme 2).

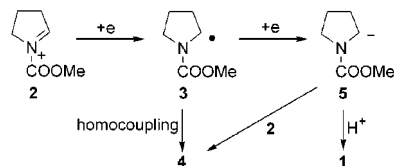
Another possibility to be considered is that two-electron reduction of the acyliminium cation (**2**) took place to give the anion (**5**), which reacted with the original acyliminium cation (**2**) to produce the dimer. As a matter of fact, simply reduced product **1** was also formed probably via protonation of the carbanion intermediate **5**.

The reduction of the acyliminium cation (**2**) with chemical reducing agents such as zinc metal was also examined.⁸ In this case, **1** was obtained as the major product (54%) together with the homocoupled product **4** (16%). Presumably two-electron reduction of the acyliminium cation took place predominantly to produce the corresponding carbanion (**5**), which is trapped by a proton in the reaction media. This result suggests that the radical coupling is the major pathway in the electrochemical reduction.

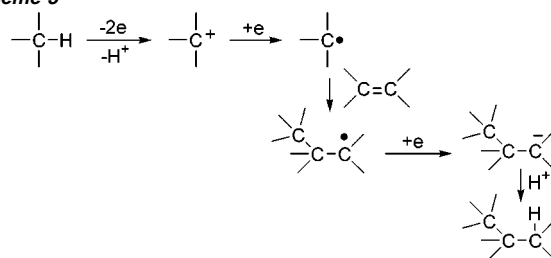
Scheme 1



Scheme 2

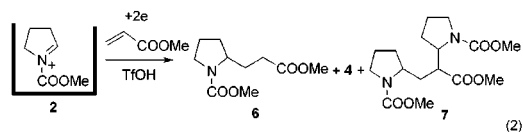


Scheme 3



Next, we focused the reduction of the cation pool in the presence of radical acceptors. The radical that is formed by one-electron reduction of the cation is expected to add to a carbon–carbon double bond as shown in Scheme 3.⁹ We also expected that the resulting radical undergoes subsequent one-electron reduction to generate a carbanion species, which is trapped by protonation. The overall transformation serves as formal addition of C–H to C=C.¹⁰

Thus, we examined the electrochemical reduction of the acyliminium cation pool (**2**) in the presence of methyl acrylate in order to achieve the addition of the radical intermediate to the carbon–carbon double bond.¹¹ The reaction gave the desired product (**6**) together with homocoupled product (**4**) and 2:1 adduct (**7**) as byproduct (eq 2, Table 1).



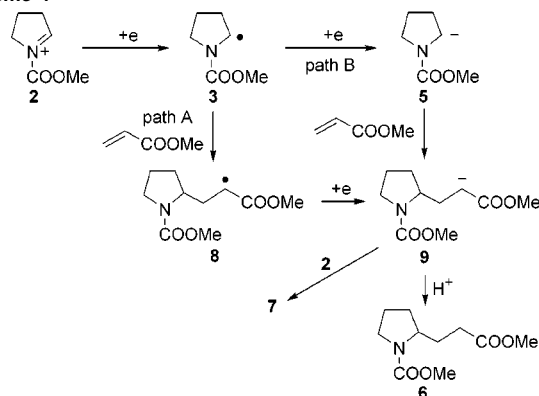
The following mechanism seems to be reasonable (Scheme 4). One-electron reduction of acyliminium cation **2** gives radical **3**. Because **3** is a rather electron-rich radical, it adds to the electron-deficient carbon–carbon double bond of methyl acrylate (path A). The resulting carbon radical (**8**) is an electron-deficient radical and therefore is easily reduced¹² to give the corresponding carbanion (**9**) that is trapped by a proton to give the final product (**6**).

This reaction, however, suffered from the formation of a 2:1 coupling product (**7**), which might be produced by the reaction of **9** with **2**. But, this problem was overcome by the addition of

Table 1. Electrochemical Reduction of **2** in the Presence of Methyl Acrylate^a

TfOH (equiv)	methyl acrylate (equiv)	product (%) ^b			
		6	4	7	1
0	5	34	11	28	2
10	5	66	3	17	1
50	2	78	0	0	4
50	5	88	0	0	0
50	8	83	0	0	0

^a The reactions were carried out in a divided cell using a carbon felt cathode; 0.01 M cation pool was used. ^b GC yields.

Scheme 4

trifluoromethanesulfonic acid (TfOH) as proton source (Table 1).¹³ With 50 equiv of TfOH, the amount of **7** produced was negligible and the yield of **6** increased up to 88%. Presumably, the carbanion

Table 2. Redox-Mediated Coupling of Carbamates and Activated Olefins via Cation Pool^a

carbamate	activated olefin	product	% yield ^b
			84 (88)
			75
			77 dr = 59 : 41 ^c
			32 dr = 64 : 36 ^c
			41 ^d dr = 48 : 52 ^c
			39 dr = 48 : 52 ^c
			71 dr = 73 : 26 ^c
			53
			63

^a The reaction was carried out with 5–8 equiv of an activated olefin and 50 equiv of TfOH. The carbon felt was used as the anode for the generation of the cation pool and as the cathode for the subsequent reduction of the cation pool (0.01 M). ^b Isolated yields. Yield in parentheses was GC yield. ^c Diastereomer ratio. ^d 0.05 M cation pool was used.

intermediate **9** was selectively trapped by proton to give **6**. As for the amount of the radical acceptor, the use of 5 equiv of methyl acrylate gave the best results among the examined.

Two-electron reduction of **2** to generate carbanion **5** followed by the nucleophilic addition to the carbon–carbon double bond to give **9** might be an alternative pathway (path B), but this possibility is denied by the fact that the yield of **1** did not increase by the addition of large excess amount of TfOH, which should trap the carbanion **5** to give **1** (Table 1).

The present reaction is generally applicable to other cyclic and acyclic carbamates, and activated olefins, although yields of the cross-coupled products depend on the structure of the substrates (Table 2).

In summary, we have developed a new strategy for the radical-mediated carbon–carbon bond formation based on the reduction of “cation pool”. The present strategy opens new opportunities to manipulate reactive carbon species using redox processes in organic synthesis.

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Supporting Information Available: Experimental procedures and spectroscopic and analytical data of new compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (6) The acyliminium cation **2** exhibited a reduction wave at -0.85 V vs Ag/AgCl(CH₃CN) in Bu₄NBF₄/CH₂Cl₂ by cyclic voltammetry using a glassy carbon electrode.
- (7) The reduction of cation pool was carried out in a divided cell using a platinum plate cathode under constant current conditions. THF was added to the anodic chamber to facilitate the anodic reaction.
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