Reduction of "Cation Pool". A New Approach to Radical Mediated C-C Bond Formation

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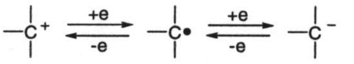
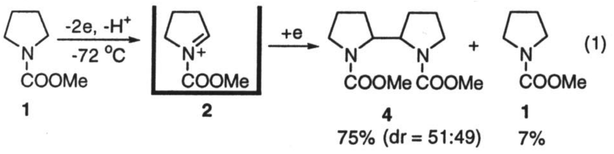
Carbocations, carbon radicals, and carbanions are important reactive carbon intermediates in organic chemistry and their interconversions can be accomplished by redox processes as shown in Scheme 1. Although, such relationships have been well recognized, experimental work has been limited to analytical studies on highly stabilized intermediates. Manipulation of such redox process with complete control is, however, still remaining as one of the challenging goals of organic synthesis.

Scheme 1.



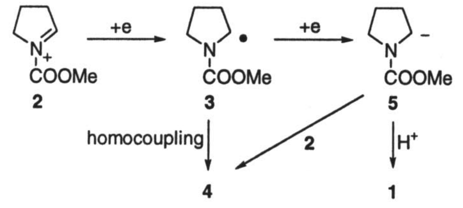
Recently we have developed "cation pool" method,[1] in which carbocations are generated and accumulated in relatively high concentrations by the low temperature electrolysis in the absence of nucleophiles. We envisioned that such "cation pools" can be utilized for redox-mediated interconversions of reactive carbon species. We wish to report herein the realization of this transformation using acyliminium cation pool as a proof-of-principle of our strategy.[2]

First, we examined the electrochemical reduction of the cation pool in the absence of radical acceptors. The electrochemical reduction of acyliminium cation **2**,[3] generated by the low temperature electrolysis of *N*-(methoxycarbonyl)pyrrolidine (**1**), gave the corresponding homocoupling product **4** (eq 1).



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).

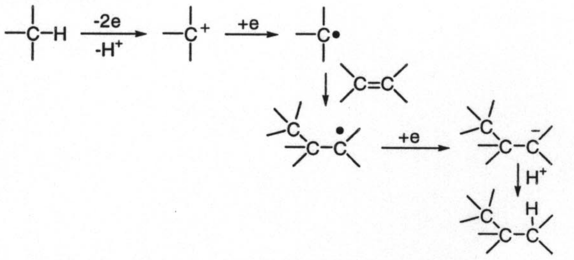
Scheme 2.



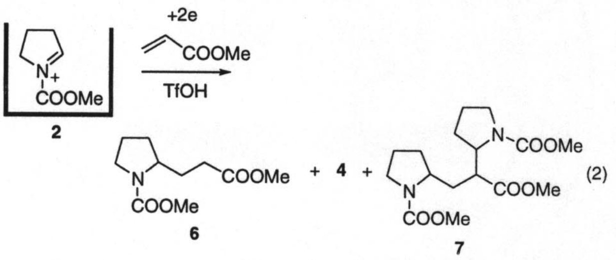
The reduction of the acyliminium cation (**2**) with chemical reducing agents such as zinc metal was also examined. In this case, **1** was obtained as the major product (54%) together with the homocoupled product **4** (16%). Presumably two-electron reduction of the acyliminium cation took place predominantly 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 2).

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. The resulting radical may undergo subsequent one-electron reduction takes to generate a carbanion species, which is trapped by protonation. The overall transformation serves as formal addition of C-H to C=C.

Scheme 3.



Thus, the electrochemical reduction of the acyliminium cation pool (**2**) was carried out in the presence of methyl acrylate in order to achieve the addition of the radical intermediate to the carbon-carbon double bond.[4] The reaction gave the desired product (**6**) together with homocoupled prodct (**4**) and 2:1 adduct (**7**) as byproducts (eq 2). Under the optimized conditions, compound **6** was obtained in 88% with negligible amounts of **4** and **7**.



In summary, we have developed a new strategy for the radical-mediated carbon-carbon bond formation based on the electrochemical 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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[1] (a) Yoshida, J.; Suga, S.; Suzuki, S.; Kinomura, N.; Yamamoto, A.; Fujiwara, K. *J. Am. Chem. Soc.* **1999**, *121*, 9546. (b) Suga, S.; Suzuki, S.; Yamamoto, A.; Yoshida, J. *J. Am. Chem. Soc.* **2000**, *122*, 10244. (c) Suga, S.; Okajima, M.; Yoshida, J. *Tetrahedron Lett.* **2001**, *42*, 2173. See also (d) Suga, S.; Okajima, M.; Fujiwara, K.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 7941.

[2] Suga, S.; Suzuki, S.; Yoshida, J. *J. Am. Chem. Soc.* in press.

[3] Although the reductive coupling of acyliminium cation was unknown, the reductive coupling of iminium cation was reported in the literature. (a) Andrieux, C. P.; Savéant, J. M. *Bull. Soc. Chim. France* **1968**, 4671. (b) Andrieux, C. P.; Savéant, J. M. *J. Electroanal. Chem.* **1970**, *26*, 223. (c) Andrieux, C. P.; Savéant, J. M. *J. Electroanal. Chem.* **1970**, *28*, 446. (d) Kerr, J. B.; Iversen, P. E. *Acta. Chem. Scand. B* **1978**, *32*, 405.

[4] Electroreductive cross-coupling reaction of α-hydroxycarbamates with activated olefins has been reported. (a) Ohmizu, H.; Takahashi, M.; Ohtsuki, O. *Stud. Org. Chem.* **1987**, *30*, 241.

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