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Kolbe Carbon−Carbon Coupling Electrosynthesis Using Solid-Supported Bases

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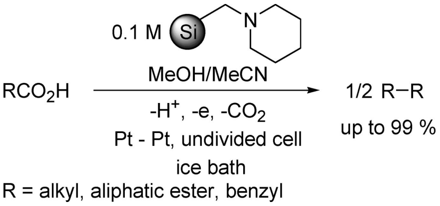
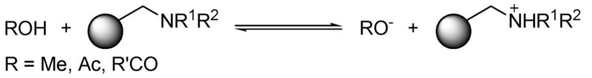


We have developed a novel electrolytic system for Kolbe carbon−carbon coupling electrosynthesis based on the acid−base reaction between carboxylic acids as a substrate and solid-supported bases. On the basis of the electrolytic system, Kolbe electrolysis of various carboxylic acids was successfully carried out to provide the corresponding homocoupling products in moderate to excellent yields.

Organic electrosynthesis has recently attracted much attention as one of the most environmentally friendly methods in organic synthesis, because it is based on the mass-free electron transfer between electrodes and substrates.[1] It can avoid not only the use of conventional redox reagents but also their separation and waste. However, it requires large amounts of supporting electrolytes to provide sufficient ionic conductivity to the solvents for electrolysis.[2] In order to remove the need for supporting electrolytes, we have recently developed a novel electrolytic system for organic electrosynthesis using solid-supported bases.[3] The system is based on the acid−base reactions between protic solvents or carboxylic acid substrates and solid-supported bases, and the conjugate acid−base pairs act as supporting electrolytes (eq 1). With the use of solid-supported bases, it is possible to do electrosynthesis without any additional supporting electrolytes.



(1)

Kolbe electrolysis is the oldest electroorganic reaction[4] and is useful for the synthesis of higher alkanes[5] and 1,*n*-diesters[5a,6] because of its specificity and versatility.[7] In fact, it cannot be achieved by other chemical reactions. Kolbe electrolysis is defined as the electrochemical one-electron oxidation of carboxylate ions with decarboxylation that leads to radicals that dimerize to homocoupling products (Scheme 1). Solid-supported bases may be applied to the Kolbe electrolysis to form carboxylate ions by the acid−base reaction with carboxylic acids as a substrate (eq 1). Furthermore, the conjugate acid−base pair would play the role of supporting electrolytes. Therefore, it should enable us to remove the need for supporting electrolytes in Kolbe electrolysis. We herein report Kolbe carbon−carbon coupling electrosynthesis using solid-supported bases.

First, we measured the cyclic voltammogram of 4,4,4-trifluoro-3,3-dimethoxybutyric acid (**1**) in 0.1 M silica gel supported piperidine (Si-piperidine)/MeOH in order to confirm the acid−base reaction between **1** and Si-piperidine. As shown in Figure 1(a), the background cyclic voltammogram was recorded before the addition of **1**. After the addition of **1**, the oxidation current for MeOH was decreased because of the adsorption of the carboxylate ion derived from **1** on the platinum electrode surface,[8] while the reduction current for H^+ was remarkably increased as shown in Figure 1(b). This electrochemical result is consistent with our previous report.[3c] It should be emphasized that sufficient ionic conductivity was observed without any additional supporting electrolytes. These findings indicate that the acid−base reaction between **1** and Si-piperidine preferentially occurs in MeOH (eq 1), and the conjugate acid−base pair seems to play the role of supporting electrolytes.

Next, we investigated Kolbe electrolysis of **1**[9] as a model reaction using solid-supported bases. It is well-known that the uses of a platinum anode and high current density conditions are favored for Kolbe electrolysis, because they lead to a high concentration of radicals at the platinum anode surface to afford homocoupling products preferentially.[7] With these facts in mind, Kolbe electrolysis of **1** was examined under various conditions to optimize the best reaction conditions as shown in Table 1. The overall experimental

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SCHEME 1. Reaction Mechanism of Kolbe Electrolysis

$$RCO_2^- \xrightarrow[-CO_2]{-e} R\cdot \xrightarrow{R\cdot} R{-}R$$

procedure is illustrated in Figure 2. The reactions were run in an undivided cell and the cathodic reaction involved the reduction of H^+. The use of polystyrene-supported piperidine (PS-piperidine) and Si-piperidine gave the almost same yields of the corresponding homocoupling product **2** (entries 1 and 2). However, the cell voltage in entry 1 was extremely high (more than 100 V) because PS-piperidine did not swell in MeOH. This means that the piperidine group, which is inside the polystyrene particle, does not interact with **1** and hence inhibits the acid–base reaction (eq 1), thereby affording a low concentration of the conjugate acid–base pair. Therefore, it results in greater cell resistance and the need for the higher cell voltage. In contrast, Si-piperidine has high solvent compatibility,[10] because the piperidine group is covalently immobilized on the porous silica gel surface. Therefore, Kolbe electrolysis of **1** using Si-piperidine was smoothly conducted with a lower cell voltage (60–70 V) in entry 2. Next, MeCN was used as a cosolvent in order to suppress the oxidation of MeOH (entry 3). As expected, the current efficiency of **2** in entry 3 was remarkably increased about twice compared to that in entry 2. As shown in entries 3–7, Kolbe electrolysis of **1** was carried out using several silica gel supported bases. When silica gel supported pyridine was used, the cell voltage was too high to conduct the constant current electrolysis (entry 4). Although **2** was obtained in high to excellent yields by using silica gel supported imidazole and morpholine in entries 5 and 6, the cell voltages were higher than that in entry 3. These results (entries 4–6) indicate that the concentrations of the conjugate acid–base pairs in eq 1 are insufficient for the constant current electrolysis owing to the low basicities of pyridine, imidazole, and morpholine. When silica gel supported 1,5,7-triazabicyclo[4.4.0]dec-5-ene (Si-TBD) was used, a large amount of **1** was recovered (entry 7). In this case, the methoxide ion (MeO^-) derived from the acid–base reaction between MeOH as a solvent and Si-TBD seems to be mainly oxidized at the anode, because Si-TBD is a strong base. From entries 3–7, we selected Si-piperidine as the most suitable solid-supported base for Kolbe electrolysis. To compare it with a conventional method,[7] we next used NaOMe (1 equiv to **1**) as a supporting electrolyte (entry 8). However, 60% of **1** was recovered. In this case, MeO^- should be mainly oxidized at the anode.

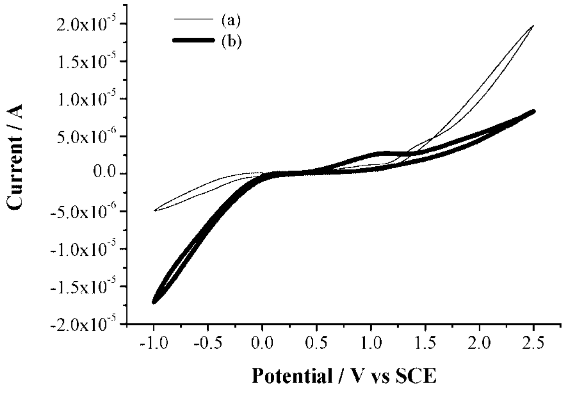
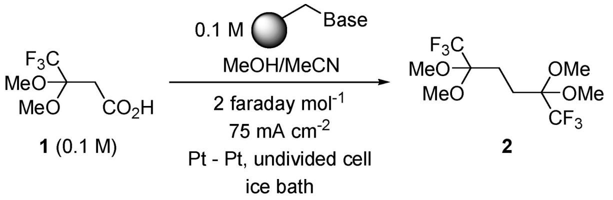


FIGURE 1. Cyclic voltammograms of (a) 0.1 M Si-piperidine/MeOH and (b) **1** (0.1 M) in 0.1 M Si-piperidine/MeOH, recorded at a Pt disk electrode ($\phi = 0.8$ mm). The scan rate was 100 mV s^{-1}.

TABLE 1. Kolbe Electrolysis of 1 Using Solid-Supported Bases



entry	solid	base (0.1 M)	MeOH/MeCN (v/v%)	yield[a] (%)
1	PS[b]	piperidine (11.2)[c]	100/0	50 [25][d]
2	SiO_2[e]	piperidine	100/0	47 [24]
3	SiO_2	piperidine	50/50	85 [43]
4	SiO_2	pyridine (5.2)	50/50	
5	SiO_2	imidazole (7.2)	50/50	96 [48]
6	SiO_2	morpholine (9.0)	50/50	83 [42]
7	SiO_2	TBD (14.5)	50/50	44[f] [22]
8		NaOMe	100/0	34[g] [17]
9[h]	SiO_2	piperidine	50/50	93[i]

[a] ^{19}F NMR yield based on the CF_3 group using monofluorobenzene as an internal standard. [b] Polystyrene. [c] pK_a value of the conjugate acid in parantheses. [d] Current efficiency in brackets. [e] Silica gel. [f] A large amount of **1** was recovered. [g] 60% of **1** was recovered. [h] 3 faraday mol^{-1} was passed. [i] Isolated yield.

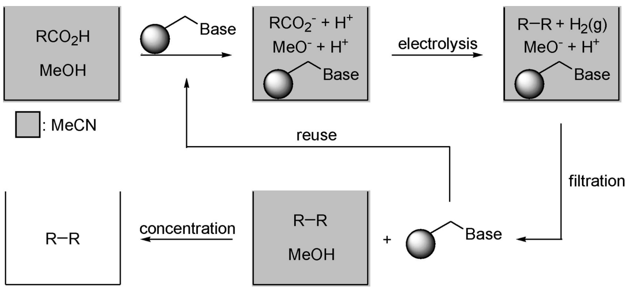


FIGURE 2. Experimental procedure.

According to the comparison, it is clear that the use of Si-piperidine (entry 3) is superior to the conventional method in Kolbe electrolysis of **1**. Finally, Kolbe electrolysis of **1** using Si-piperidine was carried out until the complete consumption of **1** (3 faraday mol^{-1}) to provide **2** in excellent yield (entry 9). It is notable that Si-piperidine was simply separated by only filtration after the electrolysis and the pure product **2** was readily isolated by concentration of the filtrate (Figure 2).

We next examined the reusability of Si-piperidine in Kolbe electrolysis of **1**. Kolbe electrolysis of **1** was carried out 10 times under the conditions of entry 3 (6 faraday mol^{-1}) in Table 1 by the reuse of Si-piperidine as shown in Figure 2. As shown in Figure 3, the yield of **2** was always more than 90% and did not decrease at all. This clearly suggests that Si-piperidine is electrochemically stable to even high current consumption and thus reusable for many times.

To demonstrate the scope of the reactions, we carried out Kolbe electrolysis of various carboxylic acids using Si-piperidine as shown in Table 2. The higher alkanes **4** and **6** were synthesized from open-chain carboxylic acids **3** and **5** in excellent yields, respectively (entries 1 and 2). In the same manner, 1,4- and 1,8-diesters **8** and **10** were obtained in high to excellent yields (entries 3 and 4). Furthermore, Kolbe

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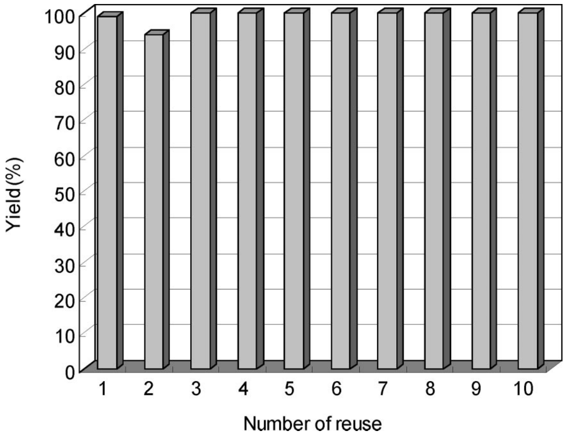
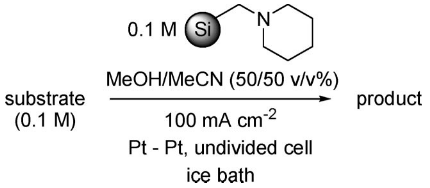
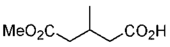
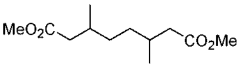
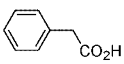
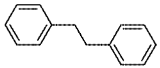
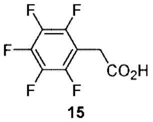
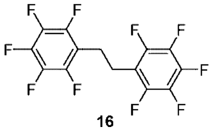


FIGURE 3. Yield of **2** in the reuse of Si-piperidine.

TABLE 2. Kolbe Electrolysis of Various Carboxylic Acids Using Si-Piperidine



entry	substrate	electricity (faraday mol^{-1})	product	yield[a] (%)
1	$C_7H_{15}CO_2H$ **3**	3	$C_{14}H_{30}$ **4**	90
2	$C_9H_{19}CO_2H$ **5**	3	$C_{18}H_{38}$ **6**	99
3	$MeO_2C(CH_2)_2CO_2H$ **7**	4	$MeO_2C(CH_2)_4CO_2Me$ **8**	91
4	$MeO_2C(CH_2)_4CO_2H$ **9**	4.5	$MeO_2C(CH_2)_8CO_2Me$ **10**	88
5	 **11**	2.5	 **12**	91
6	 **13**	1.5	 **14**	44[b]
7	 **15**	2	 **16**	52[b]

[a] Isolated yield. [b] The benzylic methoxylated product (non-Kolbe product) was also formed.

electrolysis of a β-branched carboxylic acid **11** also proceeded smoothly to provide the corresponding homocoupling product **12** in excellent yield (entry 5). In entries 1−5, Si-piperidine was simply separated by filtration after the electrolysis and the desired pure products were readily isolated by concentration of the filtrates. On the other hand, Kolbe electrolysis of phenyl acetic acid (**13**) and its derivative **15** gave the corresponding homocoupling products **14** and **16** in only moderate yields, respectively (entries 6 and 7). In these cases, the benzylic methoxylated products (non-Kolbe products) were also formed, because the two-electron oxidation of **13** and **15** with decarboxylation generates their corresponding stable benzyl cations, which react with MeOH as a solvent. This reaction selectivity is similar to that of the conventional method.[7] These results indicate that the electrolytic system based on the acid−base reaction between carboxylic acids as a substrate and solid-supported bases is available for the wide range of Kolbe carbon−carbon coupling electrosynthesis, especially the synthesis of higher alkanes and 1,*n*-diesters.

In summary, we have developed a novel electrolytic system for Kolbe carbon−carbon coupling electrosynthesis based on the acid−base reaction between carboxylic acids as a substrate and solid-supported bases. On the basis of the electrolytic system, Kolbe electrolysis of various carboxylic acids was successfully carried out to provide the corresponding homocoupling products in moderate to excellent yields. This system has some practical advantages: (a) no need for any additional supporting electrolytes, (b) simple separation of solid-supported bases by only filtration, and (c) reusability of solid-supported bases. It is expected that this system will make a significant contribution to green chemistry and open a new aspect of organic electrosynthesis.

Experimental Section

General Procedure for Kolbe Electrolysis of 4,4,4-Trifluoro-3,3-dimethoxybutyric Acid (1). Kolbe electrolysis of **1** (202 mg, 1 mmol) was carried out with platinum plate electrodes (2 × 2 cm^2; distance between electrodes, 1 mm) in 0.1 M Si-piperidine/MeOH/MeCN (10 mL; MeOH/MeCN = 50/50 v/v%) using an undivided cell. Constant current electrolysis (75 mA cm^{-2}) was conducted with magnetic stirring in an ice bath. The conversion of **1** was monitored by TLC. After the electricity was passed until the complete consumption of **1**, the electrolytic solution was passed through a glass filter (pore size, 40−60 μm) to remove Si-piperidine. The filtrate was concentrated to provide the corresponding homocoupling product **2**. The yield of **2** was calculated by means of ^{19}F NMR by using a known amount of monofluorobenzene (96 mg, 1 mmol) as an internal standard. The product **2** was identified by comparison with the literature values[9] using ^1H and ^{19}F NMR and mass spectroscopy.

1,1,1,6,6,6-Hexafluoro-2,2,4,4-tetramethoxyhexane (2). ^1H NMR (270 MHz, $CDCl_3$) δ 1.96 (s, 4H), 3.36 (s, 12H); ^{19}F NMR (254 MHz, $CDCl_3$) δ 1.06 (s); MS (EI, *m/z*) 314 (M^+), 283 (M^+-OMe), 251, 231, 213.

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Supporting Information Available: Electrochemical cell and experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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