Electrochemical Investigation of the Behavior of Solid-supported Bases in Aprotic Organic Solvents Using Anodic Oxidation of *p*-Methoxybenzyl Alcohol as a Model Reaction

Toshiki Tajima,[*1] Rieko Oba,[2] and Atsushi Nakajima[1]
[1]*Global Edge Institute, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 226-8502*
[2]*Department of Electronic Chemistry, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 226-8502*

The behavior of solid-supported bases in aprotic organic solvents was investigated by cyclic voltammetry as well as preparative electrolyses using anodic oxidation of *p*-methoxybenzyl alcohol as a model reaction.

About 30 years ago, Cohen et al. demonstrated one-pot multistep reactions with the concept of site isolation, which was defined as the attachment of opposing reagents to the respective insoluble polymers suppresses their mutual destruction.[1] Since the pioneering work of Cohen et al., sol–gel materials,[2] layered clays,[3] star polymers,[4] magnetic particles,[5] and microcapsules[6] have been applied to site-isolated heterogeneous catalysts toward one-pot multistep reactions.[7] On the other hand, electrodes in electrochemical reactions are inherently site-isolated heterogeneous redox reagents. Therefore, site isolation between electrodes and solid-supported reagents would also be achieved. We have recently developed a novel electrolytic system for organic electrosynthesis based on the acid–base reactions between protic solvents[8] or carboxylic acid substrates[9] and solid-supported bases. In a series of studies, it was found that solid-supported bases are electrochemically stable and thus reusable for many times. We can regard their electrochemical stability as site isolation in electrochemical reactions. It may be defined as solid-supported reagents, which can not enter the electric double layer, are not subject to electrochemical destruction at electrodes. On the basis of the concept of site isolation in electrochemical reactions, we have most recently demonstrated that solid-supported bases accelerate the deprotonation step in anodic methoxylation of fluoroethyl phenyl sulfides without oxidative destruction at the anode.[10] In the work, it was suggested that not solid-supported bases but methoxide ion, which is derived from the acid–base reaction between methanol as a solvent and solid-supported bases, acts as a base to accelerate the deprotonation of the cationic intermediates generated at the anode surface. This prompted us to investigate the behavior of solid-supported bases in aprotic organic solvents.

It has been reported that anodic oxidation of benzyl alcohols generally affords the corresponding benzaldehydes.[11] However, anodic oxidation of *p*-methoxybenzyl alcohol (**1**) gives a polymeric product because the methoxy group stabilizes the radical cation intermediate to inhibit its deprotonation (Scheme 1, path A). On the other hand, the deprotonation can be promoted by bases to form *p*-methoxybenzaldehyde (**2**) (Scheme 1, path B).[12] With these facts in mind, we chose anodic oxidation of **1** as a model reaction to investigate the behavior of solid-supported bases in aprotic organic solvents.

First of all, we measured the cyclic voltammograms of **1** in MeCN in the absence and presence of solid-supported bases. As shown in Figure 1a, two oxidation waves were observed at ca.
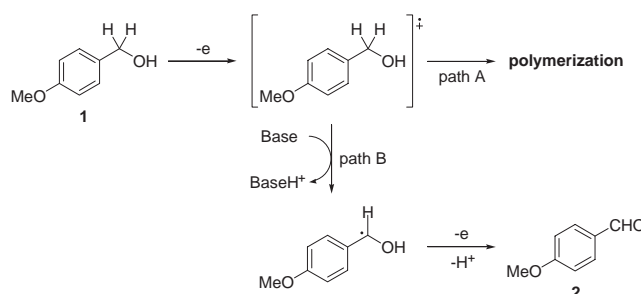
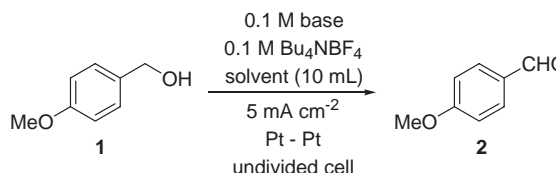**Scheme 1.** Anodic oxidation of *p*-methoxybenzyl alcohol.
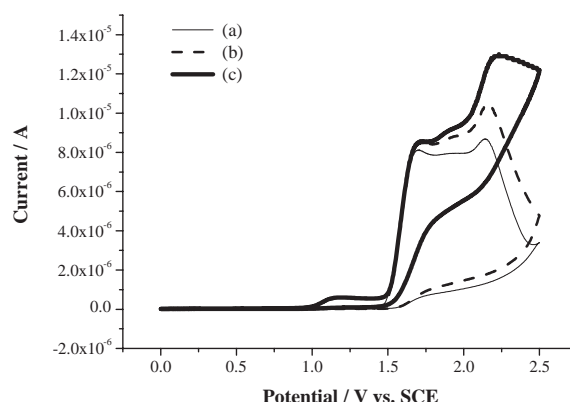
Figure 1. Cyclic voltammograms of (a) **1** (0.05 M), (b) **1** (0.05 M) in the presence of 0.1 M Si–piperidine, and (c) **1** (0.05 M) in the presence of 0.1 M Si–TBD in 0.1 M Bu$_4$NBF$_4$/ MeCN, recorded at a Pt disk electrode ($\phi = 100\,\mu$m). The scan rate was 500 mV s^{-1}.

1.7 and 2.2 V vs. SCE in the absence of solid-supported bases. These waves correspond to the oxidation of **1** and the resulting product **2**, respectively. In the presence of silica gel-supported piperidine (Si–piperidine), the oxidation wave for **2** became larger as shown in Figure 1b. Furthermore, the oxidation wave for **2** became the largest in the presence of silica gel-supported 1,3,5-triazabicyclo[4.4.0]dec-5-ene (Si–TBD) as shown in Figure 1c. These results suggest that solid-supported bases promote the deprotonation of the radical cation intermediate of **1** to generate **2** preferentially.

Next, we investigated anodic oxidation of **1** in MeCN in the absence and presence of solid-supported bases as shown in Table 1.[13] In the absence of solid-supported bases, anodic oxidation of **1** was attempted, however, the corresponding aldehyde **2** was formed in low yield and a polymeric product was deposited on the anode surface (Entry 1). On the other hand, **2** was obtained in good yield in the presence of Si–piperidine (Entry 2). Furthermore, the yield increased to 89% with the use of Si–

Table 1. Anodic oxidation of **1** in the absence and presence of solid-supported bases

Entry	Base	Solvent	Electricity /F mol^{-1}	Yield/%[a]
1	—	MeCN	5	12[b]
2	Si–piperidine	MeCN	3	73
3	Si–TBD	MeCN	2.5	89
4	MTBD	MeCN	9	10[b]
5	—	CH$_2$Cl$_2$	4	0
6	Si–TBD	CH$_2$Cl$_2$	3.5	12[b]
7	Si–TBD	MeCN/CH$_2$Cl$_2$[c]	3.5	93
8	Si–TBD	CH$_2$Cl$_2$[d]	3.5	53

[a]Isolated yield. [b] ^{1}H NMR yield based on the CHO group using CH$_3$NO$_2$ as an internal standard. [c]The volume ratio of MeCN/CH$_2$Cl$_2$ was 10/90 v/v%. [d]A small amount of water (0.5 mmol) was added.

TBD as a strong base (Entry 3). In contrast, when 7-methyl-1,3,5-triazabicyclo[4.4.0]dec-5-ene (MTBD) was used instead of Si–TBD, **2** was formed in only 10% yield (Entry 4). In this case, a large amount of electricity (9 F mol^{-1}) was required until the complete consumption of **1**. This indicates that MTBD suffered oxidative destruction at the anode during the early stage electrolysis. These results suggest that solid-supported bases promote the deprotonation of the radical cation intermediate of **1** without oxidative destruction at the anode. However, the lifetime of the radical cation intermediate generated at the anode surface seems to be too short for it to be affected directly by solid-supported bases, because site isolation between the anode and solid-supported bases is concluded.[10] Therefore, a small amount of a contaminant such as water in MeCN might participate in promoting the deprotonation.

In order to further investigate the behavior of solid-supported bases in aprotic organic solvents, we next used CH$_2$Cl$_2$ as a water-immiscible solvent. In the absence of solid-supported bases, **2** was not formed at all (Entry 5). Furthermore, **2** was formed in only 12% yield even in the presence of Si–TBD (Entry 6). This finding indicates that Si–TBD did not promote the deprotonation of the radical cation intermediate of **1** in CH$_2$Cl$_2$. Therefore, it is suggested that Si–TBD does not act directly on the radical cation intermediate generated at the anode surface. In sharp contrast, when MeCN was used as a cosolvent, **2** was obtained in excellent yield (Entry 7). These results suggest that a conjugate base, which is generated from the acid–base reaction between a small amount of a contaminant such as water in MeCN and Si–TBD, acts as a base to promote the deprotonation of the radical cation intermediate at the neighborhood of the anode surface. We then carried out the reaction in CH$_2$Cl$_2$ in the presence of a small amount of water. As shown in Entry 8, the yield of **2** obviously increased about 5 times compared to that in the absence of water (Entry 6), which supports our suggestion. In addition, MeCN might affect the miscibility of water in CH$_2$Cl$_2$ from the comparison of Entries 7 and 8.

In summary, we have demonstrated that site isolation between solid-supported bases and cationic active species generated at the anode surface is concluded in aprotic organic solvents such as CH$_2$Cl$_2$. Furthermore, it was found that the site isolation is dissolved by the presence of a small amount of water, which mediates between them.

References and Notes
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13 General procedure for anodic oxidation of **1**: Anodic oxidation of **1** (1 mmol) was carried out with platinum plate electrodes (2 × 2 cm^2) in 0.1 M Bu$_4$NBF$_4$/solvent (dehydrated MeCN and/or CH$_2$Cl$_2$, 10 mL) in the presence of 0.1 M solid-supported bases (based on the concentration of the bases) using an undivided cell. Constant current electrolysis (5 mA cm^{-2}) was conducted with magnetic stirring at room temperature. After the electricity was passed until the complete consumption of **1**, the electrolytic solution was filtered by a glass filter (pore size: 5–10 μm) to remove solid-supported bases. The filtrate was concentrated under reduced pressure and the residue was passed through a short column of silica gel eluting with ether (150 mL) to remove Bu$_4$NBF$_4$. The filtrate was concentrated under reduced pressure to give the product **2**, which was identified by an authentic sample using ^{1}H NMR and mass spectrometry.