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We recently reported the novel electrolyte combination of alkali-metal fluoride (MF) and poly(ethylene glycol) (PEG) for effective anodic reactions of organic compounds. 1,3 The electrolytic solution consisting of MF and PEG is highly conductive and could be used in electroorganic synthesis. Particularly, anodic halogenation of organic compounds has been achieved using MF and PEG. 2

In this study, we further report on the use of MF and PEG for anodic reactions of organic compounds. MF and PEG have been used individually for anodic reactions of organic compounds. MF has been used for halogenation of organic compounds, while PEG has been used for anodic coupling reactions of organic compounds. However, the use of MF and PEG in combination has not been reported before.

We herein report the extended studies of the new electrolytic system using MF and PEG for anodic reactions of organic compounds. We recently reported the novel electrolyte combination of alkali-metal fluoride (MF) and poly(ethylene glycol) (PEG) for effective anodic reactions of organic compounds. 1,3 The electrolytic solution consisting of MF and PEG is highly conductive and could be used in electroorganic synthesis. Particularly, anodic halogenation of organic compounds has been achieved using MF and PEG. 2

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produce a large amount of waste after use in a large scale (poor atom economy). Thus milder, selective, non-hazardous and inexpensive reagents are still in demand. Electrochemical reactions using sodium halides such as sodium chloride (NaCl) and sodium bromide (NaBr) are potential candidates to fulfill the requirements if they are soluble in electrolytic solvent. Our strategy using PEG additive seems to be effective to solubilize such sodium halides in aprotic organic solvents.

First, cyclic voltammetry measurements of NaBr only (Fig. 1, line a) and NaBr in the presence of 0.3 M PEG (Fig. 1, line b) were carried out in anhydrous MeCN. As shown in Fig. 1, line a, a faradaic current was not observed due to the insolubility of NaBr in MeCN. In sharp contrast, the oxidation current for Br\(^+\) around +0.9 V vs. SCE and the reduction current for cationic species of Br (ca. +0.3 V vs. SCE) were clearly observed, indicating that the sufficient ionic conductivity appeared. Under these conditions, PEG seemed to work as solubilizing agent for NaBr because the oxidation onset potential of PEG was observed at +1.4 V (vs. SCE) in our previous report.\(^{10}\) Next investigation is the reaction of the anodically generated cationic species of Br and electron-rich aromatic substrate such as aniline derivatives. In the cyclic voltammogram of NaBr in the presence of PEG and \(N,N\)-dimethylaniline (1a) (Fig. 1, line c), the oxidation current for Br\(^+\) appeared, while the reduction current for the cationic species of Br completely disappeared. The generated cationic species of Br seemed to be consumed for electrophilic substitution on 1a. These results indicated that the ionic dissociation of NaBr was promoted with the support of PEG in MeCN, and that the resulting ions acted as ionic charge carriers and bromine source.

We then investigated the macro-scale anodic halogenation of 1a in the presence of NaX (\(X = Br, Cl\)) with PEG in MeCN (Table 1). In Entry 1, the anodic bromination using NaBr in the absence of PEG did not take place at all, while the reaction proceeded efficiently with PEG to give brominated product 2a in excellent yield (Entry 2). The anodic bromination of other derivatives like 1b–1d was similarly achieved (Entries 3–5) by passing 4 F/mol of charge. In the undivided cell, the generated cationic species of Br may be re-reduced at the cathode to form Br\(^-\); this cycle requires additional electricity to the theoretical one (2 F/mol). The anodic chlorination of 1d was also successful to give chlorinated product 2d\(^+\) in high yield (Entry 6). In Entries 5 and 6, the halogenation at the benzylic position did not take place at all. In addition, catechol (1e) and 2-methoxynaphthalene (1f) were brominated similarly in excellent yields (Entries 7 and 8). To our best knowledge, conventional electrolysis using alkali-metal halides in MeCN requires a large amount of quaternary ammonium salts to impart sufficient ionic conductivity, and the electrolysis proceeds in suspension of hardly soluble alkali-metal halides.\(^{16}\) The two-phase (chloroform/water) anodic bromination of aromatic compounds\(^{17}\) requires a large amount of water, in which water-sensitive reactions cannot be carried out. Moreover, chloroform is harmful. These facts indicated that the use of PEG as an additive markedly enhanced the inorganic salt-based anodic halogenation under mild and safe conditions for the first time.

In order to extend the generality of the electrolytic system, we next focused on other anodic reactions using sodium tetrafluoroborate (NaBF\(_4\)) as a supporting electrolyte. Since NaBF\(_4\) has a wider potential window and higher chemical stability than sodium halides, a variety of anodic organic reactions can be performed only when it dissolves in aprotic organic electrolytic solution. As expected, NaBF\(_4\) was found to be soluble in MeCN in the presence of PEG enough to supply sufficient ionic conductivity to the solution, and the onset potential of NaBF\(_4\) was observed at much higher potential (+2.1 V vs. SCE) than that of NaBr (+0.5 V vs. SCE).

Then we investigated the anodic deprotection of cyclic dithioacetals (3) and thioester (5) together with the coupling reaction of 1,2,4-trimethoxybenzene (7) in NaBF\(_4\)-PEG/MeCN

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**Figure 1.** Cyclic voltammograms of (a) NaBr (0.1 M), (b) NaBr (0.1 M) in the presence of PEG (0.3 M), and (c) NaBr (0.1 M) with \(N,N\)-dimethylaniline (1a) (0.02 M) in the presence of PEG (0.3 M), measured in MeCN with Pt disk (\(\phi = 1.6 \text{ mm}\)) as a working electrode, SCE as a reference electrode at a scan rate of 50 mV/s.

**Table 1.** Anodic halogenation of aromatic compounds in NaX-PEG/MeCN system.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>NaX</th>
<th>Electricity (F/mol)</th>
<th>Product</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^c)</td>
<td>1a</td>
<td>NaBr</td>
<td>—</td>
<td>2a</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
<td>NaBr</td>
<td>4</td>
<td>2a</td>
<td>97</td>
</tr>
<tr>
<td>3</td>
<td>1b</td>
<td>NaBr</td>
<td>4</td>
<td>2b</td>
<td>67(^d)</td>
</tr>
<tr>
<td>4</td>
<td>1c</td>
<td>NaBr</td>
<td>4</td>
<td>2c</td>
<td>68(^d)</td>
</tr>
<tr>
<td>5</td>
<td>1d</td>
<td>NaBr</td>
<td>4</td>
<td>2d</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>1d</td>
<td>NaCl</td>
<td>6</td>
<td>2d(^e)</td>
<td>86</td>
</tr>
<tr>
<td>7</td>
<td>1e</td>
<td>NaBr</td>
<td>4</td>
<td>2e</td>
<td>94</td>
</tr>
<tr>
<td>8</td>
<td>1f</td>
<td>NaBr</td>
<td>20</td>
<td>2f</td>
<td>92</td>
</tr>
</tbody>
</table>

\(^{0.3}\text{M PEG (}M_0 \sim 200)\).\(^{d}\) Determined by GC-MS. \(^{b}\)In the absence of PEG. \(^{d}\)Dibrominated byproduct was also detected.
The conventional deprotection of cyclic dithioacetals usually requires hazardous and polluting heavy metal salts, which cause waste disposal problem. We successfully carried out the deprotection of $3$ and $5$ by using this new electrolytic system (Schemes 1 and 2). The deprotection method has advantages such as extremely low toxicity, mildness and high efficiency. Moreover, the anodic oxidation of $7$ was successfully performed in the same protocol to afford the corresponding homo-coupling product quantitatively (Scheme 3).

4. Conclusions

In conclusion, we have developed the novel electrolytic system for anodic halogenation, deprotection of dithioacetal and thionoester together with anodic coupling reaction using alkali-metal salt-PEG/MeCN system. The PEG seems to be an excellent additive to solubilize inorganic salts in aprotic solvents such as MeCN, which makes it possible to perform various electrochemical oxidation reactions of organic compounds under mild and environmentally friendly conditions. The scope and limitations of this new electrolytic system are now under investigation.

Acknowledgments

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