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Benzylic Intermolecular Carbon–Carbon Bond Formation by Selective Anodic Oxidation of Dithioacetals

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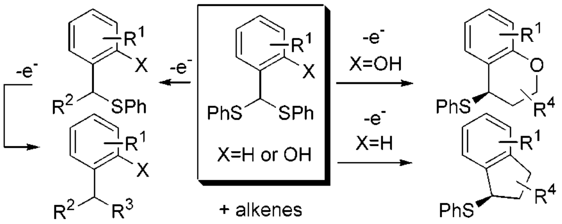
ABSTRACT



Novel anodic intermolecular carbon–carbon bond formation has been accomplished by the oxidative carbon–sulfur bond fission of benzylic dithioacetals to give a wide variety of aromatic compounds. The substitution reaction successfully took place by the selective anodic oxidation of a sulfur atom of a dithioacetal. Stepwise double-substitution reactions were also achieved by the regulation of oxidation potential.

It has recently been shown that electrosynthesis provides an efficient means of inter- and intramolecular carbon−carbon bond formation.[1] The potential of the electrochemical method is used to generate reactive intermediates to construct a wide variety of products under mild conditions. The anodic oxidation of heteroatom compounds often leads to the formation of the carbocation adjacent to the heteroatom, and the cation reacts with the heteroatom or with activated carbon nucleophiles, such as allylsilanes and sily ethers, to give the final products.[2] For example, anodic oxidation of α-heteroatom-substituted organotin compounds gave α-heteroatom-substituted carbocations via carbon−tin bond cleavage. It has been further revealed that the α-heteroatoms assist in lowering oxidation potentials and in cleaving the carbon−tin bonds. Organosulfur compounds have attraction that can also secure anodic intermolecular carbon−carbon bond formation initiated by oxidative carbon−sulfur bond fission. Previously, we accomplished anodic generation of unstable *o*-quinomethanes and *o*-quinodimethanes initiated by benzylic carbon−sulfur bond fission, and these intermediates were successfully trapped by alkenes to give varied polycyclic compounds.[3]

Among those heteroatom compounds that act as precursors of carbocations, dithioacetals have been utilized in chemical reactions because of their high reactivity and ease of preparation. Intermolecular carbon−carbon bond formation using dithioacetal has been primarily accomplished by Lewis acid catalyzed carbon−sulfur bond fission followed by a

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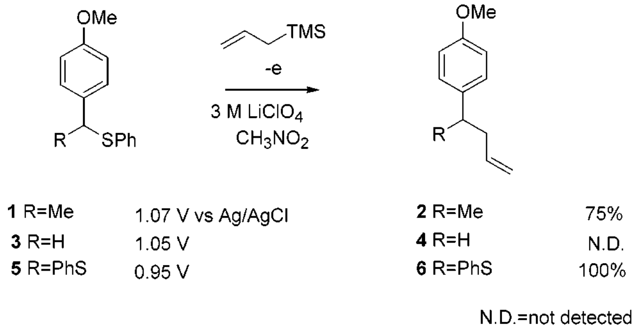
nucleophilic attack by allylsilane or allyltin compounds.[4] Radical-initiated intermolecular cyclization via carbon−sulfur bond fission of dithioacetal has also been achieved.[5] On the other hand, although anodic initiation of carbon−sulfur bond fission of dithioacetal has been applied for efficient partial fluorination reactions,[6] oxidative carbon−sulfur bond fission followed by a nucleophilic attack by the carbon nucleophiles is generally difficult under mild electrolytic conditions. This was disappointing because the neutral electrolysis conditions might allow for the use of a wider variety of olefins as nucleophiles and open the door for sequential reactions to replace both sulfur groups. We therefore planned to introduce dithioacetal moiety as a promising electrolytic substrate for the generation of carbocations. It was expected that the first carbon−sulfur bond fission would take place with the assistance of another α-sulfur atom. Moreover, the electrochemical method was expected to have powerful potential to realize stepwise oxidation, leaving the sulfur atoms under finely controlled oxidation potential to yield double-substituted products.

In this study, we attempted to achieve novel anodic intermolecular carbon−carbon bond formation by using benzylic dithioacetal as an electrolytic substrate. The reaction has been accomplished, giving varied aromatic compounds by an intermolecular reaction between the electrogenerated benzyl cations and nucleophilic alkenes, including unactivated aliphatic ones.

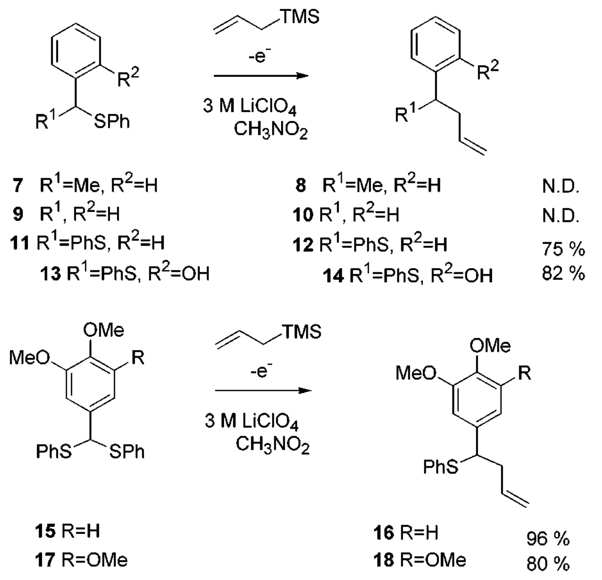
First, compounds **1**, **3**, and **5** were electrochemically oxidized in the presence of 2 equimolar amounts of allyltrimethylsilane in 3 M lithium perchlorate/nitromethane,[7] using a divided cell at their respective peak potential determined by cyclic voltammetry (Scheme 1). Although no desired allylated product was obtained in the anodic oxidation of compound **1** (1.2 F/mol), compound **3** gave the desired allylated product **4** in 75% yield (1.2 F/mol). Furthermore, the oxidation potential of the sulfur atom of dithioacetal **5** was lowered [0.95 V vs Ag|AgCl|KCl(sat)] compared with those of **1** or **3** [1.07 and 1.05 V vs Ag|AgCl|KCl(sat), respectively], and the electrooxidation of **5** in 3 M lithium perchlorate/nitromethane at its peak oxidation potential gave a monoallylated product **6** quantitatively (1.2 F/mol). These results suggested that the benzylic dithioacetal effectively lowered the oxidation potential and further assisted the first oxidative carbon−sulfur bond fission to generate the corresponding benzylic cation intermediate.

Scheme 1

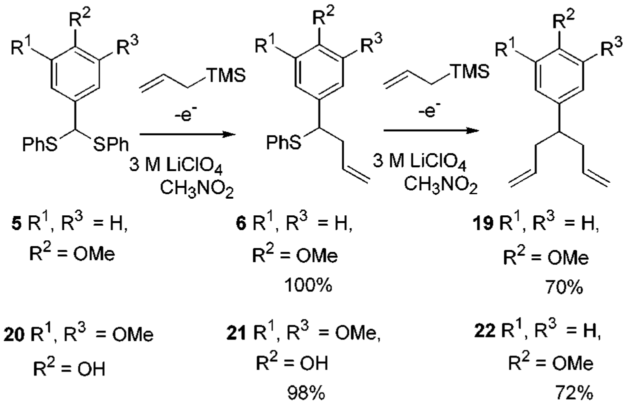


Scheme 2 shows the anodic allylation reaction of benzyl sulfides. Anodic oxidation of primary benzyl sulfides (**7** or **9**) in the presence of allyltrimethylsilane gave corresponding sulfoxides and recovered the starting materials with no desired product. On the other hand, anodic oxidation of corresponding dithioacetals selectively gave monoallylated products (**12**, **14**, **16**, and **18**) in good yields. It was further found that additional allylation of the isolated products (**6** or **21**) by second-step anodic oxidation at a higher potential [1.1 V vs Ag|AgCl|KCl(sat)] gave disubstituted products (Scheme 3, **19** and **22**). These results clearly showed that various combinations of nucleophiles could be introduced

Scheme 2



Scheme 3



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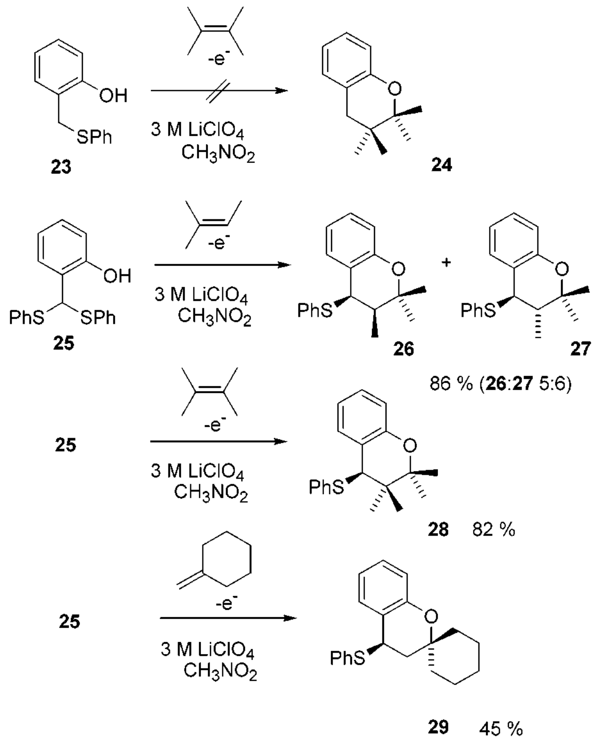
[5] Trost, B. M.; Sato, T.; *J. Am. Chem. Soc.* **1985**, *107*, 719.

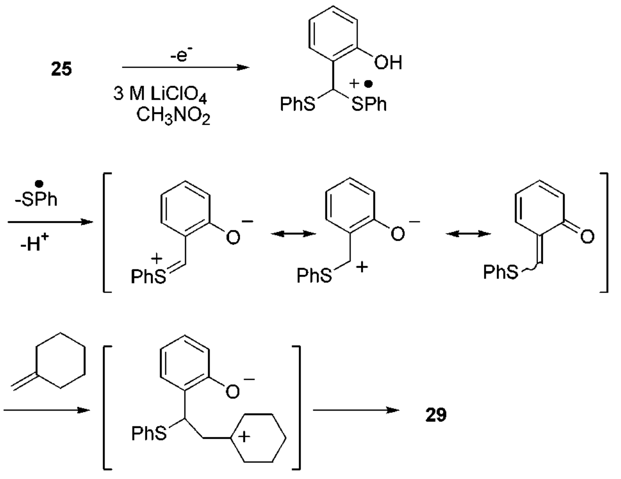
by the potential-regulated stepwise electrolysis of the dithioacetals provided the aryl ring was electron-rich.

Furthermore, even unactivated alkenes such as aliphatic olefins gave cyclized products with electrogenerated intermediates. For example, electrooxidation of the dithioacetals having *o*-hydroxyl groups gave corresponding chromans by a cyclization reaction with various unactivated alkenes (Scheme 4). The reaction was accomplished via a formal hetero-Diels−Alder reaction between anodically generated corresponding *o*-quinomethanes and alkenes (Scheme 5). It is generally difficult to form chromans by an intermolecular formal [4 + 2] cycloaddition reaction between unactivated alkenes and in-situ generated *o*-quinomethanes with no electron-donating groups.[8] However, these reactions were successfully achieved by the anodically induced reaction of the dithioacetals, and no rearrangement or polymerization reaction was observed. Under this reaction condition, dithioacetal assisted the oxidative generation of corresponding *o*-quinomethanes even under such a moderate electrolytic condition.

Scheme 4

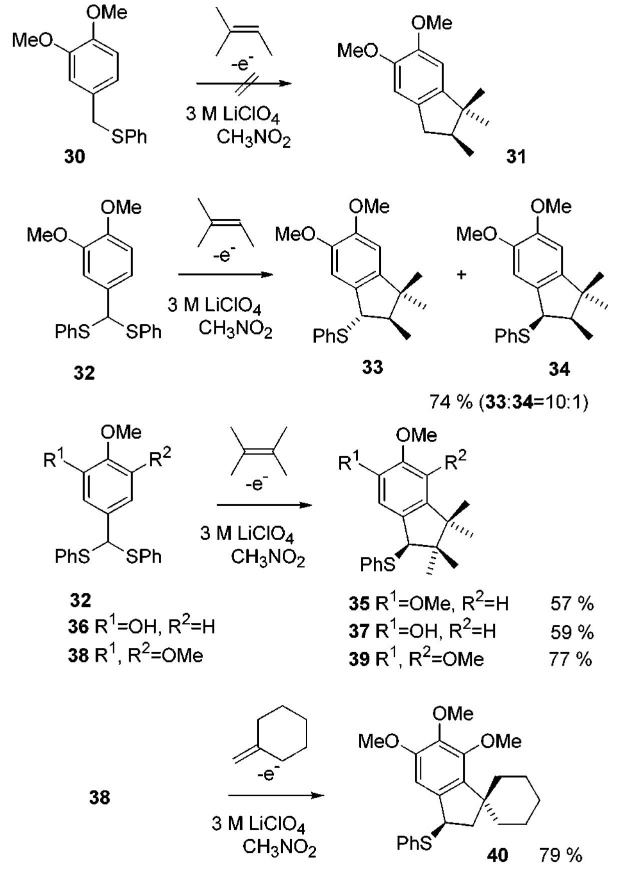


Scheme 5



Scheme 6 shows a direct indan synthesis by formal [3 + 2] cycloaddition between electrogenerated benzyl cations and aliphatic alkenes. The electron-donating groups on the benzene rings of benzylic dithioacetal must have enhanced their nucleophilicity to accomplish the formation of the five-membered ring. Dimethoxy and trimethoxy derivatives

Scheme 6



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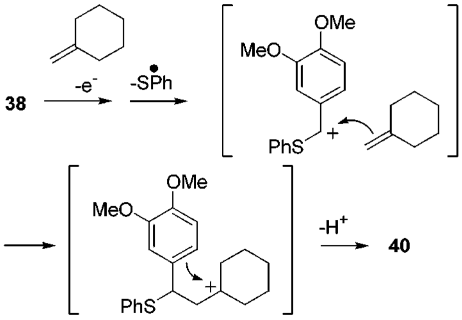
therefore led to the formation of the indan skeleton, including a sterically hindered spiro-indan, in good yield. In addition, no rearranged product was obtained even in the synthesis of the spiro-indan **40** using an unstable terminal olefin (Scheme 7).

Scheme 7



In conclusion, anodic oxidation of benzylic dithioacetals gave varied aromatic derivatives with both activated and unactivated alkenes in the lithium perchlorate/nitromethane system. The reaction scarcely took place in other usual electrolytic media, such as lithium perchlorate/acetonitrile and tetralkylammonium perchlorate/acetonitrile, and only the lithium perchlorate/nitromethane solution efficiently gave the desired reaction. The dithioacetal group effectively increased the reactivity for the anodically induced reaction, and corresponding benzyl cation was generated even in the absence of an electron-donating group on the benzene ring. Furthermore, it is noteworthy that the oxidative carbon−sulfur bond fission under potential-regulated electrolytic conditions in a moderate medium could furnish these sequential stepwise substitution reactions.

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Supporting Information Available: Experimental procedures and spectroscopic data for compounds **6**, **12**, **14**, **16**, **18**, **19**, **21**, **22**, **26**−**29**, **33**, **35**, **37**, **39**, and **40**. This material is available free of charge via the Internet at http://pubs.acs.org.

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