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A Consideration of the Indirect Electrooxidation of Alkylbenzenes by Metal-Ion Mediators

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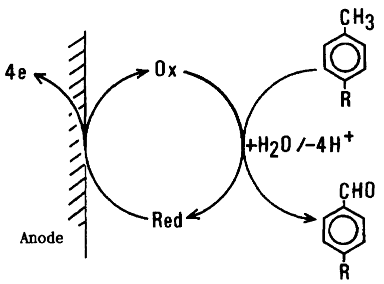
Synopsis. Selective oxidation of substituted alkylbenzenes to the corresponding aromatic aldehydes by metal-ion redox mediators has been investigated. The apparent oxidation potential of the substrate alkylbenzene ($E_{\mathrm{s,ox}}$) measured by voltammetry in an organic medium was used as a measure of the substrate reactivity. The oxidizing power of the mediator was also evaluated based on the apparent reduction potential in the voltammogram (E_{red}). The yields of the experimentally determined reaction products were explained by the mutual relation between $E_{\mathrm{s,ox}}$ of the substrate and E_{red} of the mediator.

Indirect electrooxidation using a redox mediator is an efficient process for functionalization in organic synthesis.[1] There have been many reports on the anodic oxidation of alkylbenzenes to produce aromatic aldehydes and acids.[2,3] Among them, some successful studies have so far been reported on the indirect electrooxidation of alkylbenzenes to aldehydes using redox mediators.[4—7] For example, the cerium(III)/cerium(IV) redox system yields aldehydes from alkylbenzenes to aromatic acids.[2,5,7] Though a number of redox mediator systems have been proposed for this purpose, different substrate/mediator combinations give different results concerning the product yields and distribution. The experimental conditions greatly affect the yields and selectivity of the products, being similar to the cases of conventional organic syntheses. Especially, it is of special importance to clarify the effects of the mediator's properties on the reaction rate or product selectivity, so that one can design an efficient synthetic process. However, few papers have been published concerning the systematic work on the relationship between substrate/mediator combinations and their reaction selectivity, except for kinetic studies on the electron and charge transfers by Kochi's group.[8] In this paper, the selective oxidation of substituted alkylbenzenes to the corresponding aldehydes by a series of metal-ion mediators is examined (Scheme 1). The reaction rate and selectivity generally vary with such synthetic conditions as the solvent, temperature, concentration, and pH. That is, the optimum condition for yielding an objective product differs in each substrate/mediator system. In the present work, however, to determine the importance of the electrochemical potentials of the substances, a uniform condition was employed throughout the entire substrate/mediator system. The product yields are discussed from the viewpoint of the electrochemical congeniality between the organic substrate and the redox mediator.



Scheme 1. Indirect electrochemical oxidation of aromatic compounds by metal-ion mediators.

Experimental

Mediators were generated by anodic oxidation of reduced-form metal salts, iron(II) perchlorate ($Fe(ClO_4)_2$), cerium(III) sulfate ($Ce_2(SO_4)_3$), cerium(III) perchlorate ($Ce(ClO_4)_3$), manganese(II) sulfate ($MnSO_4$), and cobalt(II) sulfate ($CoSO_4$) (Ishizu Pharmaceutical, Hydrated, GR grade). The substrate organic compounds were toluene, *o*-, *m*-, *p*-xylenes, *p*-chlorotoluene, *p*-toluidine, *p*-tolunitrile, *p*-nitrotoluene, and *p*-methylanisole (Ishizu Pharmaceutical, GR grade). These reagents were used as-received.

The redox properties of the mediators were investigated by cyclic voltammetry in aqueous solutions of perchloric or sulfuric acid. The test cell was an H-shape Pyrex-glass cell (100 cm^3) equipped with a glass-filter diaphragm. The working and counter electrodes were Pt sheets with apparent surface areas of 1 and 10 cm^2, respectively. The reference electrode was an SCE connected with the working electrode through a Luggin capillary. A potentiostatic macroelectrolysis was conducted for generating active mediators (oxidized forms of metal ions). The same H-shape cell as the cyclic voltammetry was used in the macro-electrolysis. The electrochemical reactivity of the organic substrate was also evaluated by cyclic voltammetry. In this case, the same apparatus as mentioned above, except for a Pt-wire working electrode (0.19 cm^2), was used. The electrolytic solution was acetonitrile, dissolving 0.05 $\mathrm{mol\,dm^{-3}}$ $NaBF_4$ as a supporting electrolyte.

An "ex-cell method"[1] was employed for the electrooxidation of the organic substrates by oxidized mediators. This method has a major advantage in that the experimental results exclude any effects caused by direct electrochemical reactions of the organic substrate at the anode.[9] The mediators were first oxidized in the electrochemical cell under a potentiostatic condition. The quantity of electricity passed ranged between 100 and 200C for each electrolysis. After a portion (100 cm^3) of the aqueous solution containing the oxidized mediator was transferred to a glass vessel in a thermostatted bath, the organic substrate dissolved in benzene (0.1 mol dm^{-3}, 10 cm^3) was added to the mediator solution. The organic/aqueous two-phase mixture was stirred for 3.5 h at 25 °C. After this, the mixture was separated into the organic and aqueous phases. The reaction products dissolved in the aqueous phase were extracted by diethylether. The products were quantitatively analyzed by gas chromatography (GC) and high-performance liquid chromatography (HPLC). Redox titration was used for the determination of the recovery of the oxidized mediator.

Results and Discussion

The mechanism of direct electrooxidation of substituted methylbenzenes (R–Ar–CH$_3$; Ar=C$_6$H$_4$) has been widely discussed.[2,10] The oxidation reaction is initiated by one-electron transfer, which forms a cation radical, R–Ar–CH$_3^{+\bullet}$. In a basic medium, the cation radical is attacked by a nucleophile (Nu) to yield a ring-substituted alkylbenzene R–Ar(Nu)–CH$_3$. In another case, the cation radical deprotonates and is then oxidized to form a benzyl cation R–Ar–CH$_2^+$, which reacts with an anion X$^-$, yielding an another product with an oxidized side chain, R–Ar–CH$_2$X.[2]

We first estimated the oxidation potentials of the substituted alkylbenzenes using cyclic voltammetry. Standard oxidation potentials of alkylbenzenes are generally determined by authorized techniques, e. g., using ultra-microelectrodes and an ultra-fast potentiostat.[10,11] However, if one assumes that the electrochemical overvoltage for the one-electron transfer reaction is almost constant through a series of substituted alkylbenzenes, we can use a conventional voltammetric technique to estimate the relative HOMO (Highest Occupied Molecular Orbital) energy of the substrate in question. That is, for example, the first onset potential at which the anodic current increases in the voltammogram for a Pt working electrode, should be a measure of the relative oxidation potential of the substrate. Thus, in this paper we used the onset potential ($E_{\mathrm{s,ox}}$) as a nominal oxidation potential, or a measure of the substrate oxidizeability.

Figure 1 shows the relationship between $E_{\mathrm{s,ox}}$ of the substrate compound and Hammett's constant of the substituent (σ). We used the σ values for the substituent groups at para-position (σ_{para}: open circles), as well as the values corrected for electron-donating effects by the methylene cation (σ^+: closed circles). A linear relation was observed between $E_{\mathrm{s,ox}}$ and σ^+, suggesting that $E_{\mathrm{s,ox}}$ is valid as a measure of the HOMO energy of the substrate compound. Also, compounds with higher HOMO energies show lower $E_{\mathrm{s,ox}}$ values. Similar relations to this, e. g., ionization potential vs. formal oxidation potential, have already been found for a series of alkylbenzenes.[8,12]

A series of alkylbenzenes was oxidized with the Ce(IV) mediator produced by the anodic oxidation of Ce$_2$(SO$_4$)$_3$/H$_2$SO$_4$. Figure 2 shows the yields of aldehydes after a 3.5 h reaction as a function of $E_{\mathrm{s,ox}}$ for each substrate. The current efficiency given in the figure is the coulombic yield of the product based on the quantity of electricity passed for the mediator oxidation, assuming four-electron oxidation for the reactions of alkylbenzenes to yield aldehydes. A high yield was obtained for *p*-anisaldehyde from *p*-methylanisole (substrate no. 2 in Fig. 2). The other alkylbenzenes did not yield any corresponding aldehydes under this oxidation condition. In the cases of substrates with higher $E_{\mathrm{s,ox}}$ val-

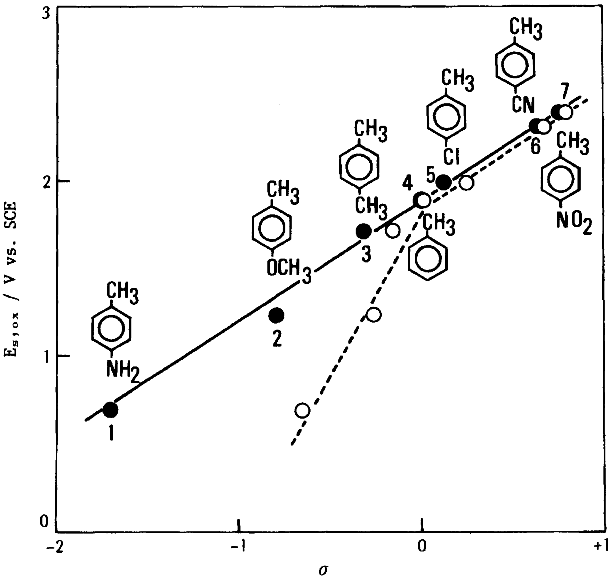


Fig. 1. Relation between the oxidation potential of the substrate ($E_{\mathrm{s,ox}}$) and Hammett's constant of the substituent (σ). ○ : σ_{para}, ● : σ^+.

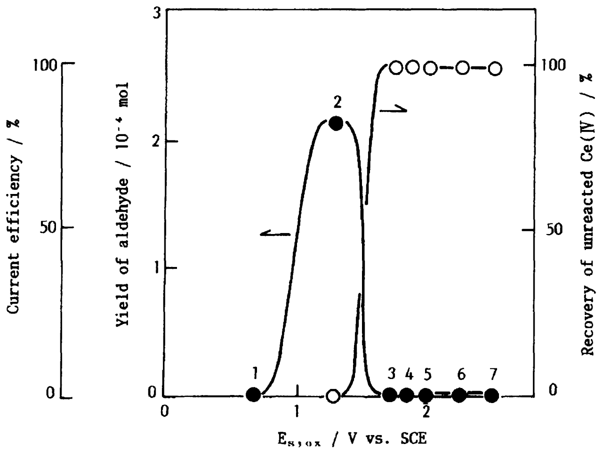


Fig. 2. Yield of aldehyde and current efficiency as a function of the oxidation potential of the substrate ($E_{\mathrm{s,ox}}$), by Ce$_2$(SO$_4$)$_3$/H$_2$SO$_4$. Organic phase: 0.1 mol dm^{-3} substrate in 10 cm^3 benzene, Aqueous phase 0.05 mol dm^{-3} Ce$_2$(SO$_4$)$_3$ in 2.0 mol dm^{-3} H$_2$SO$_4$, Reaction time: 3.5 h, Quantity of electricity passed: 100 C.

ues (substrate nos. 3—7), the recovery of unreacted Ce(IV) was about 100%. *p*-Toluidine (substrate no. 1) gave neither the corresponding aldehyde nor the high recovery of unreacted Ce(IV). Because of the high reactivity of the amino group, *p*-toluidine would be highly oxidized to yield some polymeric compound.

Figure 3 summarizes the results of similar reactions of alkylbenzenes using the Mn(III) mediator produced by the oxidation of $MnSO_4$ in H_2SO_4. In this case the highest yield was obtained for the oxidation of *p*-xylene (substrate no. 3) to *p*-tolualdehyde. The yield of *p*-anisaldehyde from *p*-methylanisole using Mn(III) was lower than that using the Ce(IV) mediator in H_2SO_4. The recovery of unreacted Mn(III), being almost 0% for the oxidation of *p*-methylanisole, suggests that the reaction with Mn(III) yielded highly oxidized products, such as carboxyl acids. On the other hand, high Mn(III) recoveries for the reactions of higher $E_{\mathrm{s,ox}}$ substrates (nos. 4—7) mean that the lower yields of aldehydes are due to the low reaction rates by the Mn(III) mediator.

The Ce(IV) mediator formed by the oxidation of $Ce(ClO_4)_3$ in $HClO_4$, being a mediator with a higher E_{red}, yielded arylaldehydes from corresponding alkylbenzenes with higher $E_{\mathrm{s,ox}}$'s. A higher yield of *p*-tolualdehyde (no. 3) was observed for the oxidation of *p*-xylene by Ce(IV) in $HClO_4$. Although benzaldehyde and *p*-chlorobenzaldehyde were obtained by the oxidation of toluene and *p*-chlorotoluene, respectively, their yields were relatively low. These results suggest that although the Ce(IV) mediator in $HClO_4$ can oxidize toluene and *p*-chlorotoluene thermodynamically, their reaction rates would be low at ambient temperature.

Figure 4 summarizes the results for the oxidation of *p*-methylanisole (substrate no. 2), *p*-xylene (no. 3) and toluene (no. 4) as a function of the oxidation power of the mediator (E_{red}). The highest yield of *p*-anisaldehyde was obtained in the case of using the Ce(IV) mediator in H_2SO_4. The E_{red} value of the Fe(III) mediator is too low to oxidize *p*-methylanisole, and the oxidation powers of the other mediators (Ce(IV) in $HClO_4$, Mn(III), and Co(III)) are too strong to yield the aldehyde effectively. On the other hand, the yield of *p*-tolualdehyde was higher in the case of using $MnSO_4$ or $Ce(ClO_4)_3$ than using other mediators. For the oxidation of toluene to yield benzaldehyde, mediators with higher oxidation potentials than that of $CoSO_4$ might be suitable. Concerning an oxidation by Co(III), however, the major cause for the low current efficiency was the oxidation of the solvent benzene by the active mediator. Thus, higher yields of benzaldehyde may be obtained if more stable solvents are used for the reaction.

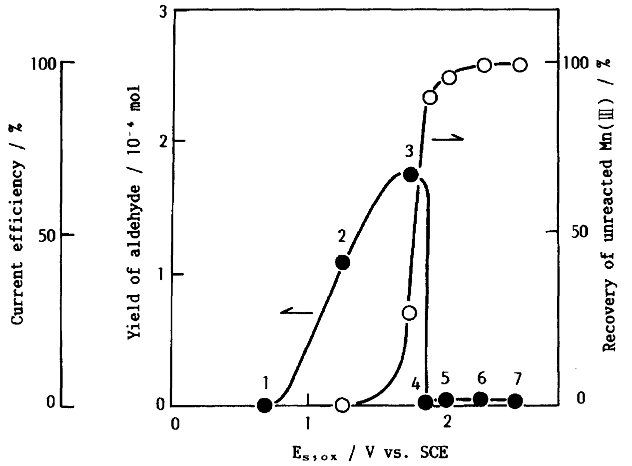


Fig. 3. Yield of aldehyde and current efficiency as a function of the oxidation potential of the substrate ($E_{\mathrm{s,ox}}$), by $MnSO_4/H_2SO_4$. Organic phase: 0.1 mol dm^{-3} substrate in 10 cm^3 benzene, Aqueous phase 0.05 mol dm^{-3} $MnSO_4$ in 8.0 mol dm^{-3} H_2SO_4, Reaction time: 3.5 h, Quantity of electricity passed: 100 C.

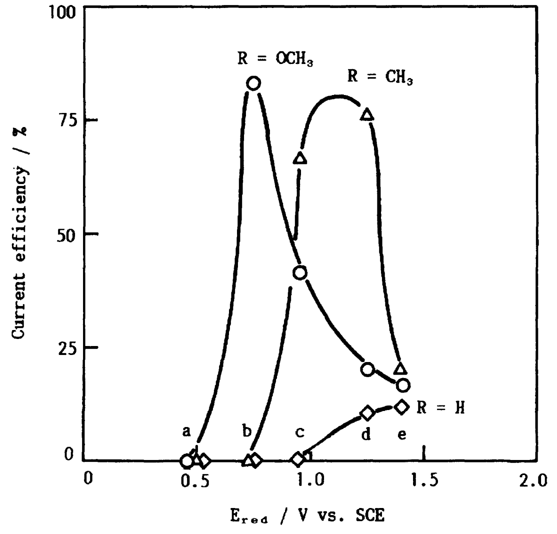


Fig. 4. Relation between current efficiency for aldehyde formation and E_{red} of the mediator. a: $Fe(ClO_4)_2$, b: $Ce_2(SO_4)_3$, c: $MnSO_4$, d: $Ce(ClO_4)_3$, e: $CoSO_4$.

In conclusion, we wish to emphasize two issues concerning the indirect electrooxidation of toluene derivatives to arylaldehydes. First, the oxidizing power of the mediator can be estimated by its apparent redox potential (E_{red}), and the reactivity of the substrate can be evaluated by the anodic oxidation potential ($E_{\mathrm{s,ox}}$), both of which are obtained experimentally in aqueous or non-aqueous media. Second, the product yields are determined by matching the mediator's E_{red} and the reactivity of the substrate ($E_{\mathrm{s,ox}}$) if a certain common synthetic condition is employed.

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