Electroreduction of *m*-Hydroxybenzoic Acid.[1] Preparation of *m*-Phenoxybenzyl Alcohol for the New Insecticide Ethofenprox

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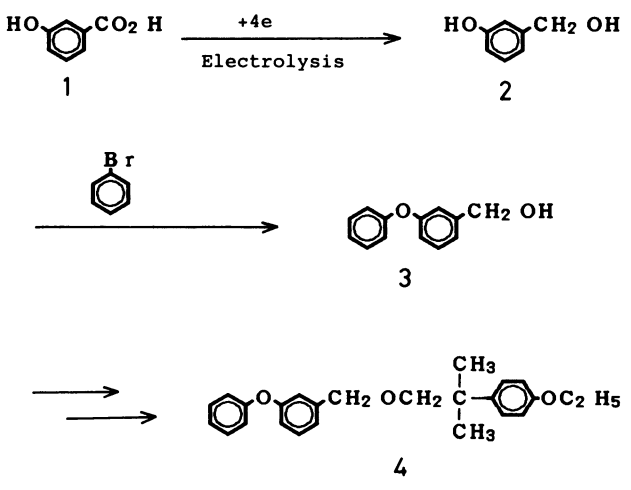
Synopsis. The electroreduction of *m*-hydroxybenzoic acid was examined from both mechanistic and technical points of view, and a practical route to *m*-phenoxybenzyl alcohol has been developed.

Recently, various kinds of artificial pyrethroids having *m*-phenoxybenzyloxy group have been developed and their characteristic features have received much attention in the insecticide chemistry. Among these pyrethroids, due to low toxicity to fish as well as to mammals and excellent pesticidal activity, the exceptional potency of ethofenprox (**4**)[2] has opened up an important market, especially in agriculture for pest control. In our research project on the development of a commercially feasible procedure for the synthesis of **4**, we needed an efficient procedure for producing *m*-phenoxybenzyl alcohol (**3**) (Scheme 1).

Many attempts have been made to prepare **3**; majority of the hitherto disclosed procedures relies upon partial oxidation of *m*-phenoxytoluene (**5**). For example, the halogenation of **5** followed by hydrolysis[3] has been intensively investigated, but the product selectivity is not necessarily satisfactory. On the other hand, alternative route to **3** has been performed by the air-oxidation of **5** followed by the electroreduction.[4] However, there still remain some difficulties in operating in the industrial practice, since the air-oxidation requires vigorous conditions, e.g., high temperature and high pressure, and the substrate concentration in the electrolysis is impractically low.

Herewith, we describe a new efficient procedure for the synthesis of **3** (Scheme 1) involving electroreduction of *m*-hydroxybenzoic acid (**1**), which is easily available on a commercial basis, and subsequent condensation of hydroxybenzyl alcohol **2** with bromobenzene.[5]



Scheme 1.

The merit of this approach strongly depends upon ease of the operation and high yield of the electrochemical reduction step (**1**→**2**). Reduction of the carboxylic acid **1** to alcohol **2** has been performed by the chemical reduction with borane–dimethyl sulfide,[6] but the use of a stoichiometric amount of the expensive reduction agent is impractical. As a potential tool for the catalytic hydrogenation of **1**, electroreduction has received some attention.[7] The yield of **2** reported so far, however, is insufficient (44%), and the commercial application of the electrolysis procedure has been out of consideration.

In order to improve the yield of **2** sufficient for practical use, we reinvestigated the electrochemical reduction of **1** from both mechanistic and technical points of view.

Electroreduction was carried out with two lead electrodes using an H-shaped two compartment cell divided by ion-exchange membrane in aqueous H_2SO_4 solution. The results under various electrolysis conditions are summarized in Table 1. Satisfactory current efficiency was attained in the aqueous acidic media (Entries 1—4), while in neutral conditions (Entry 8), the reduction was very slow, and no appreciable amount of **2** was detected in basic conditions (Entry 9). A lead cathode gave better results than mercury one (Entries 3 and 6). Attempts were made to assess the relative importance of acids in this reduction by influences of current efficiency upon several different H_2SO_4 concentrations (Table 1, Entries 1—4). Better results were obtained at higher H^+ concentrations, but decomposition of product **2** was promoted at the same time.

Next, we studied this phenomenon from voltammetric viewpoint. In the acidic electrolysis systems, reduction of **1** competes with the hydrogen evolution reaction. Therefore, particular attention should be paid to the relative reduction potential of **1** against hydrogen overvoltage. It is of interest to note that in spite of the fact that no appreciable shifts of hydrogen overvoltage of lead electrode were observed with the variation of H_2SO_4 concentration (−1.73—1.75 V vs. Hg/Hg_2SO_4), reduction wave of **1** appeared more clearly at higher H_2SO_4 concentrations. The reduction wave shifts to ca. −1.66 V from −1.71 V by increasing the H_2SO_4 concentration from 5% up to 17.5%, while no appreciable change of the potential was observed over 17.5% (Table 1, Entries 1—4). These results are good in accordance with the variation of the current efficiency. These remarkable effects of the concentration of H_2SO_4 are well understood by assuming the four electron reduction mechanism[8] involving protonated aromatic carboxylic acid as a

Table 1. Electroreduction of *m*-Hydroxybenzoic Acid (**1**)[a]

Entry	Solvent electrolyte	Conversion of **1**[b,c] %	Current efficiency[c] %	Yield of **2**[c] %	Reduction potential of **1**[d]
1	5% aq H_2SO_4	10.5	4.2	8.7	−1.71
2	10% aq H_2SO_4	51.0	20.4	48.1	−1.69
3	17.5% aq H_2SO_4	99.9	40.0	91.5 (90)[h]	−1.66
4	25% aq H_2SO_4	100.0	40.0	86.4 (85)[h]	−1.66
5[e]	17.5% aq H_2SO_4	25.1	10.0	21.4	
6[f]	17.5% aq H_2SO_4	81.2	32.5	75.1	
7[g]	17.5% aq H_2SO_4	99.9	40.0	31.6	
8	15% aq Et_4NOTs	3.3	1.3	2.9	
9	15% aq NaOH	—	—	—	

a) The electroreduction was curried out under constant current of 16 A dm^{-2} with an H-shaped devided cell fitted with two lead electrodes at 50 °C. The amount of each 15% of **1**(vs. solvent) was added portionwise. b) Electricity was passed up to 10 F mol^{-1}. c) Analyzed by HPLC based on **1**. d) V vs. Hg/Hg_2SO_4. e) **1** was added all at once at the beginning. f) A Hg pool cathode was used. g) Carried out at 80 °C. h) Isolated yield based on **1**.

reactive species. Thus, in more acidic solutions, a greater proportion of activated **1** by protonation may contribute to move the reduction potential in positive direction and to improve the current efficiency.

In a practical sense, it is important to operate the electrolysis at a high substrate concentration, since the concentration is directly related to the production efficiency and economy. Unfortunately, carboxylic acid **1** has a low solubility in the water, and when **1** was added beyond its solubility, deposits of insoluble parts of **1** covered the surface of the cathode to disturb the desired reduction (Table 1, Entry 5). In order to obtain a 10% homogeneous solubility of **1**, reaction temperature must be raised above 80 °C. However, product **2** is easily decomposed in the acidic solution, and the decomposition rate undesirably increases as the temperature rises. Lower yield of **2** at 80 °C (Table 1, Entry 7) compared with that at 50 °C (Entry 3) seems to be ascribed to thermal decomposition of **2**.

The contradictory problems can be solved by portionwise addition of **1**. When the electrolysis was carried out at 50 °C by adding **1** little by little during the course of electrolysis with a gradual generation of the product, reduction of significant amount of the carboxylic acid could be achieved and finally concentration of the product reached to 15%. This can be ascribed to the fact that in contrast to the poor solubility of starting **1**, product **2** is very soluble in the water, and the presence of **2** improves the solubility of **1** significantly. Due to these investigations, this electrochemical reduction has successfully gone through pilot plant test and is being studied for the commercial production.

Experimental

Melting points are uncorrected and were determined in open-ended capillaries. IR spectra were recorded on a Hitachi 285 grating spectrometer, and ^1H NMR spectra were measured at 90 MHz with a Nippon Denshi FX-90Q spectrometer. Chemical shifts are quoted in parts par million downfield from Me_4Si used as an internal reference. Cyclic voltammetric experiments were performed by using Hokuto Denko Ltd. Model HA-303 potentio-galvanostat, HB-104 function generator and Riken Denshi Co., Ltd. Model F-3 X-Y plotter.

Consumption of the starting material and purity of products were checked on a Shimazu HPLC system (Model LC-5A pump, SPD-2A spectrophotometric detector) using *p*-nitrophenol as an internal standard. For reverse-phase chromatography, Dupont Zorvax ODS column (a 4.6 mm diameter, 25 cm length stainless steel) was used. An eluent solvent of 40/60 MeCN–H_2O was buffered with 0.3 mmol dm^{-3} AcOH and 3 mmol dm^{-3} AcONa. The flow rate was 0.5 ml min^{-1} and fixed-wavelength detection (266 nm) was used.

Materials. *m*-Hydroxybenzoic acid (**1**) was available as a commercial product of our company. *m*-Hydroxybenzyl alcohol (**2**) was purchased from Aldrich Chemicals Co. as authentic sample.

Apparatus. An H-shaped cell divided with ion-exchange membrane (Asahi Glass Co., Ltd. Selemion CMV) was used, which was equipped with two lead plate electrodes (50 cm^2, 12 cm apart), stirring bars, and a thermometer. A vessel was immersed in a hot water bath at 50 °C and regulated dc power was supplied by Kikusui Electronics Co. Model PAD 35—60L.LP.

General Procedures. Electrochemical Reduction of *m*-Hydroxybenzoic Acid (1). Into both the anode and cathode compartments was placed a 17.5% water solution of H_2SO_4 (200 g each). After regulated dc power (16 A dm^{-2}) was supplied at 50 °C, to the catholytes was portionwise added *m*-hydroxybenzoic acid (**1**; 6.85 g h^{-1}, total 35.0 g, 0.253 mol) during the first 6 F mol^{-1} (5.1 h). After being electrolyzed (10 F mol^{-1}, 8.5 h) at 50 °C, the catholytes were extracted with diethyl ether. The extract was washed with brine, dried (Na_2SO_4) and concentrated in vacuo, giving a brown oil (29.3 g). The rapidly crystallized at room temperature, giving tan crystals, mp 68—70 °C (lit,[7] mp 73 °C), with IR and ^1H NMR spectrums identical with that reported for the authentic material.[9] The crystals were checked on HPLC and purity of *m*-hydroxybenzyl alcohol (**2**) was 96.5% (90.0% yield based on **1**), along with 0.1% of starting material **1** by using an internal standard.

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References

1) S. Takenaka, R. Oi, C. Shimakawa, and Y. Shimokawa, 7th Electroorganic Chemistry Symposium, Kyoto, June 1986, Abstr., No. 25, p. 53; *idem*, International Symposium on Electroorganic Synthesis, Kurashiki, Oct. 1986, Abstr., No. PI04.

2) S. Numata, "Seibutsu Kassei Bussitsu no Bunshi Sekkei," ed by H. Yoshioka and K. Shutoh, Soft Science Co., Tokyo (1986), Chap. 9, p. 338.

3) For example, Nippon Oils and Fats Co., Ltd. Jpn. Patent Kokai 81-166142 (1981); *Chem. Abstr.*, **96**, 162334w (1982).

4) A. Chaintreau, G. Adrian, and Couturier, *Synth. Commun.*, **11**, 439 (1981).

5) S. Takenaka and R. Oi, Jpn. Patent Kokai 86-186339 (1986); *Chem. Abstr.*, **105**, 226022g (1986).

6) C. F. Lane, H. Mayatt, J. Daniels, and H. B. J. Hopps, *J. Org. Chem.*, **39**, 3052 (1974).

7) C. Mettler, *Ber.*, **38**, 1743 (1905).

8) M. Brikett and A. T. Kuhn, *Electrochim. Acta*, **21**, 991 (1976).

9) "Standard Proton NMR Spectra Collection," Sadter Research Laboratories, a division of Bio-Rad Laboratories, Inc., (1980), IR: No. 18817, ^{1}H NMR: No. 13297.