Indirect Electrooxidation of Halohydrins by a Double Mediatory System of Ru(VIII)/Ru(IV) and $[Cl^+]/Cl^-$. Optimization for the Oxidation of 1,3-Dichloro-2-propanol to 1,3-Dichloroacetone

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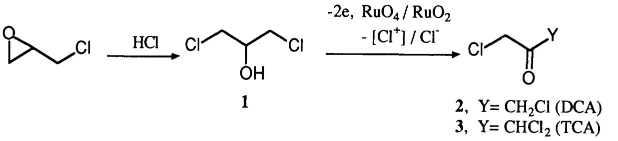
Optimum conditions for the electrooxidation of 1,3-dichloro-2-propanol (**1**) to 1,3-dichloroacetone (**2**) by using a double redox system of Ru(VIII)/Ru(IV) and $[Cl^+]/Cl^-$ are elucidated. The electrolysis of **1** in an AcOEt–aqueous NaCl (2:3 v/v) system buffered at pH 2—4 in a divided cell at 0—5 °C gives **2** in 98% selectivity toward 1,1,3-trichloroacetone (**3**) under the current efficiency of 92%.

1,3-Dichloroacetone (DCA, **2**) constitutes a key segment of a variety of pharmaceutically important heterocycles[1—4] and certain useful agrochemicals.[5] For example, N^2-sulfamoyl-3-[[(2-guanidino-4-thiazolyl)methyl]thio] propionamidine (famotidine), a histamine H_2-receptor and antagonists,[6] is usually synthesized by combining **2** with N''-(thiocarbamoyl)guanidine. The preparation of **2** has conventionally been performed by chlorination of acetone with molecular chlorine in the presence of iodine monochloride.[7] However, the chlorination often faces contamination of inevitable by-products such as mono-, tri-, and perchloroacetones, each of them being unseparable by distillation because of small differences in their boiling points. In contrast, the most clear access to 1,3-dichloroacetone (**2**) must be the oxidation of 1,3-dichloro-2-propanol (**1**)[8] derived from allyl chloride via epichlorohydrin. We applied the indirect electrooxidation procedure with a ruthenium tetraoxide (RuO_4)/active chlorine species $[Cl^+]$ system for the conversion of **1**.[9] With an obligation to meet with demands requested in its purity as fine chemicals, we optimized electrolysis conditions to exclude formation of 1,1,3-trichloroacetone (TCA, **3**) which is produced by chlorination of **2** during the electrolysis of **1**.



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2, Y= CH_2Cl (DCA)
3, Y= $CHCl_2$ (TCA)

Results and Discussion

We first examined a suitable solvent in a two-phase electrolysis system; the results are shown in Table 1. High yields of **2** were obtained in ethyl acetate or dichloroethane when 2 F mol^{-1} of electricity was passed. The yield of **2** increased almost linearly in proportion to charged electricities in ethyl acetate, while the selectivity of **2** in dichloroethane decreased upon passing electricity of more than 2.5 F mol^{-1}. The formation of 1,1,3-trichloroacetone (**3**) tends to increase in dichloromethane and chloroform.

The relationship between the yield and charged electricity with different substrate concentrations in ethyl acetate is shown in Fig. 1. Almost linear lines were obtained in the range of 25—40 wt% concentrations. The yields became flat at about 80% with increasing the by-product **3** when the substrate concentration was 60 wt%.

The correlation between the yields and charged electricity under various amounts of ruthenium dioxide is plotted in Fig. 2. The presence of 2.4—4.8 mol% of ruthenium dioxide provided linear lines in producing 1,3-dichloroacetone (**2**), in good accordance with electricity consumed. The yield of **2** decreased when the amount of ruthenium dioxide was reduced to 0.6 mol% (based on **1**) under a current density of 20—80 mA cm^{-2}. Electrolysis at a lower current density caused a decrease in both the yields and

Table 1. Indirect Oxidation of **1** in Various Organic Solvent–Aqueous Saturated NaCl Systems[a)]

No.	Organic solvent–H_2O (satd NaCl) (v/v)	Products, Yield/%[b)]	
		2	**3**
1	CH_3CN–H_2O (1/1.5)	10	1
2	CH_3COCH_3–H_2O (1/1.5)	45	3
3	$ClCH_2CH_2Cl$–H_2O (1/1.5)	62	1
4	CH_2Cl_2–H_2O (1/1.5)	40	3
5	AcOEt–H_2O (1/1.5)	62	1
6	$CHCl_3$–H_2O (1/1.5)	33	10
7	CCl_4–H_2O (1/1.5)	30	26
8	Cyclohexane–H_2O (1/1.5)	40	1

a) Carried out by using **1** (5.0 mmol) in presence of $RuO_2 \cdot 2H_2O$ (0.16 mmol) at 20 mA cm^{-2} by passing 2F mol^{-1} at 5 °C. b) Based on GC analyses. Rest of products was the starting **1**.

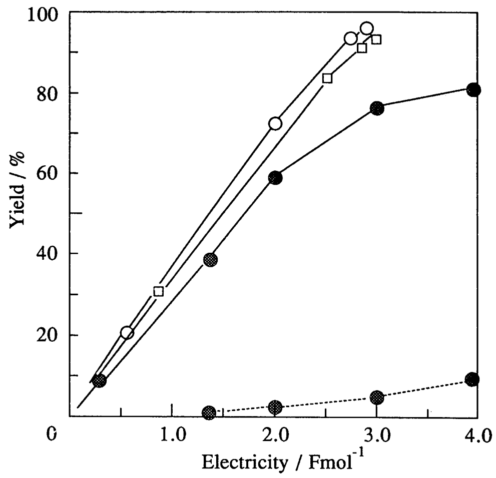


Fig. 1. Effect of the substrate concentration (wt%) in AcOEt. Data points were obtained by electrolysis in AcOEt-saturated NaCl (pH 2, 2:3 v/v) at 40 mA cm^{-2}. Symbols follows: (—); yield of DCA. 25 wt% (○), 40 wt% (□), 60wt% (●). (······); yield of TCA.

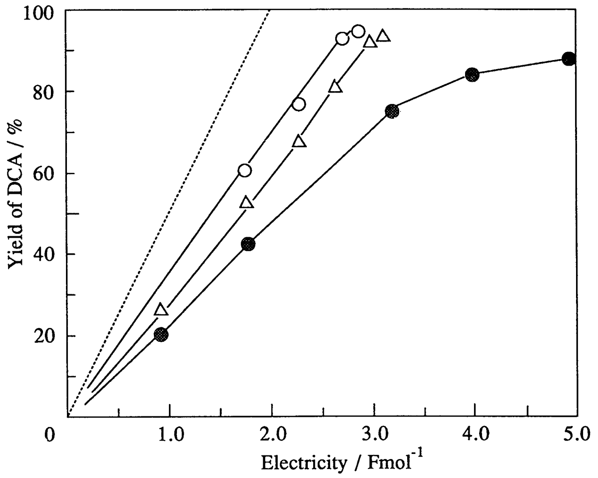


Fig. 2. Relationships between yield and added RuO_2 (mol%). Symbols follows: (—); 0.6 mol% (●), 2.4 mol% (○), 4.8 mol% (△) in AcOEt. (······); theoretical line.

current efficiencies.

In order to know the durability of the ruthenium catalyst for the present oxidation, repeated experiments for a recycle use were examined in the following manner. When electrooxidation was completed, the aqueous layer was separated from an organic layer. The concentration of the organic phase gave the desired ketone and the aqueous layer was combined with the next organic layer containing the starting material **1**. The mixture was subjected to a second electrolysis in a similar manner as before. As shown in Fig. 3, the high reproducibility was found on both yields and current efficiencies in every cases for

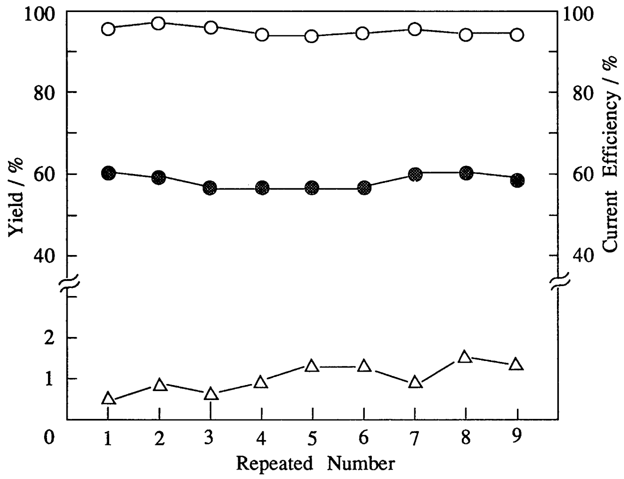


Fig. 3. Repeated experiments for ruthenium catalyst. Symbols follows: yield of DCA (○), current efficiency of DCA (●), yield of TCA (△).

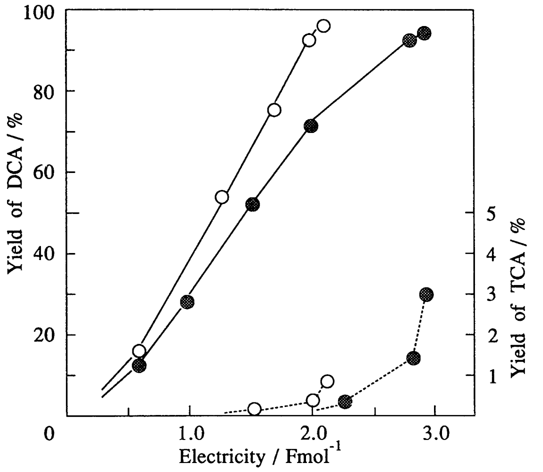
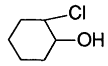
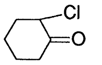


Fig. 4. Yields of DCA and TCA in an undivided and a divided cell. Symbols follows: (—); yield of DCA. (······); yield of TCA. Undivided cell (●), divided cell (○).

10-time repeated experiments.

The following two things remain as unexplored problems for an elaboration of this reaction in a practical sense: one is a complete suppression of the formation of **3** and the second is an improvement in the current efficiency, reaching almost 100%. In order to find such optimized conditions, electrooxidation in a divided cell was investigated as shown in Fig. 4. Furthermore, a suitable adjustment of the pH value in the aqueous phase (Fig. 5) provided 1,3-dichloroacetone (**2**) in excellent current efficiency. Actually, more than 92% of the current efficiency was attained at the range of pH 2—4 in a divided cell. Inferior current efficiency in an undivided cell is presumably due to competitive reductions of a positive chlorine species at the cathode. Scale-up oxidation of 1,3-dichloro-2-

Table 2. Oxidation of Halohydrins[a)]

No.	Substrate	Product[b)]	Selectivity %	Current efficiency/%
1	$PhCH(OH)CH_2Cl$	$PhCOCH_2Cl$	85	82
2	$PhCH(OH)CH_2Br$	$PhCOCH_2Br$	83	80
3	$MeCH(OH)CH_2Cl$	$MeCOCH_2Cl$	98	93
4	$MeCHClCH(OH)Me$	$MeCHClCOMe$	97	94
5			98	95

a) Substrates (1 mmol) were electrolyzed in the presence of $RuO_2 \cdot 2H_2O$ (0.032 mmol) at 20 mA cm^{-2} by passing 2F mol^{-1} at 5 °C in a divided cell. b) All compounds exhibited ^1H NMR and IR spectra which were consistent with the assigned structures.

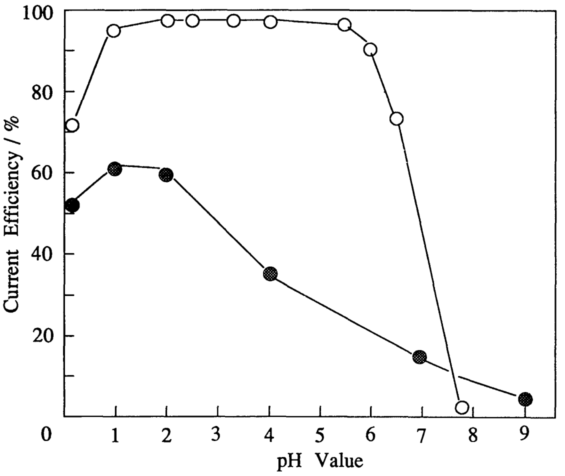


Fig. 5. Relationships between current efficiency and pH. Symbols follows: divided cell (○), undivided cell (●).

propanol (**1**) in about 0.3 mol can afford 1,3-dichloroacetone (**2**) in good yields.

We extended the procedure to the oxidation of other alicyclic and acyclic halohydrins; the results are listed in Table 2. In these conversions, acidic conditions are essential for a selective formation of α-halo ketones.

Our conclusion is that the present ruthenium mediated electrooxidation method, coupled with a previously reported one,[9b)] can be extended in a preparative scale for the oxidation of a wide range of alcohols only by changing electrolysis cell, pH value, and electrolysis medium.

Experimental

Material. $RuO_2 \cdot 2H_2O$ purchased from Nippon Engelhard Co. was used as received. Aqueous buffered solutions were prepared by dissolving appropriate phosphates to aqueous saturated NaCl.

1,3-Dichloro-2-propanol (1). To a solution of aqueous 35% HCl (109.4 g, 1.05 mol) was added dropwise epichlorohydrin (92.5 g, 1.00 mol) by keeping the temperature at 10—40 °C on an ice-water bath. After being stirred for an additional 1 h, the mixture was neutralized at pH 6.5 with aqueous 15% NaOH, and then extracted with AcOEt (100 ml×2). Extracts were washed with brine, dried (Na_2SO_4), and concentrated. Distillation at 85—88 °C/30 Torr (1 Torr≈133.322 Pa) gave 115 g (89%) of **1** (purity was 97% by GC analyses), contaminated with 3% of 2,3-dichloro-1-propanol. **1**: IR (neat) 3330 (OH), 2966, 1433, 1299, 1203, 1149, 1077, 1054, 965, 886, 830, 760, 702 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ=2.50 (br, 1H, OH), 3.68 (d, J=5.3 Hz, 4H, CH_2Cl), 4.05 (quint, J=5.3 Hz, 1H, CH-O); ^{13}C NMR ($CDCl_3$, 50 MHz) δ=45.72, 70.78.

Electrolysis Apparatus. Electrolysis in an undivided cell was carried out in a 30 ml beaker-type cell (2.5 cm diameter and 10 cm height) fitted with a condenser, a stirring bar, a thermometer, and two platinum foil electrodes (3 cm^2) being placed parallel to each other 10 mm apart. An H-type cell separated by a sintered glass diaphragm (5—10 mm porous hole) was used for the electrolysis in a divided cell.

General Procedure for the Electrooxidation in an Undivided Cell. $RuO_2 \cdot 2H_2O$ (85 mg, 0.50 mmol) and a solution of 1,3-dichloro-2-propanol (**1**, 2.0 g, 15.5 mmol) in AcOEt (8 ml) were placed over an aqueous saturated NaCl buffered at pH 2 with 0.2 M NaH_2PO_4 (12 ml; 1 M=1 mol dm^{-3}). The mixture was electrolyzed under a constant current of 40 mA cm^{-2} at about 5 °C with a vigorous stirring. The electrolysis was continued until the organic phase changed to yellow from greenish black. It required about 3 F mol^{-1} of electricity (based on **1**). The mixture was treated with 2-propanol (0.5 ml) to deactivate excess oxidants. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$. Combined extracts were washed with water, dried (Na_2SO_4), and concentrated under vacuum to give 1.92 g of crude crystals. The yield and selectivity of 1,3-dichloroacetone (**2**) were determined by gas chromatography as 94 and 96%, respectively. IR (Nujol) 2986, 2938, 1787, 1736 (CO), 1396, 1321, 1294, 1052, 957, 820, 723 cm^{-1}; ^1H NMR ($CDCl_3$, 60 MHz) δ=4.43 (s, $ClCH_2CO$).

Electrolysis in a Divided Cell, a General Procedure. A solution of **1** (2.0 g, 15.5 mmol) in AcOEt (8 ml), $RuO_2 \cdot 2H_2O$ (85 mg, 0.50 mmol), and an aqueous saturated NaCl (12 ml) were placed in the anodic compartment of a divided cell. The cathodic compartment was filled with an aqueous saturated NaCl (20 ml). The anolyte was maintained at pH 3—4 by adding aqueous saturated Na_2CO_3 during electrolysis. Electrolysis under a constant current of 40 mA cm^{-2} was continued until the organic layer changed from greenish black to slightly yellow. It required about 2.08 F mol^{-1} of electricity (based on **1**). The mixture was treated with 2-propanol (0.5 ml) and worked up in the manner described above. The crude crystalline products (1.92 g) were analyzed by gas chromatography and the yield and selectivity of **2** were determined to be 96 and 98%, respectively.

Analysis.[10] Starting 1,3-dichloro-2-propanol (**1**) and products (**2** and **3**) were analyzed by GC on a Shimadzu Model GC7AG with a packed column of 10% PEG 20 M supported on CW-HP (80/100 mesh). Carrier: N_2 (30 ml min^{-1}), Column temp: 130 °C. Retention times (R_t, min) were as follows: DCA (**2**); 14.9, TCA (**3**); 19.0, **1**; 25.3.

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References

1) D. C. Bigg, Eur. Pat. Appl. 2400; *Chem. Abstr.*, **92**, 22501r (1980).

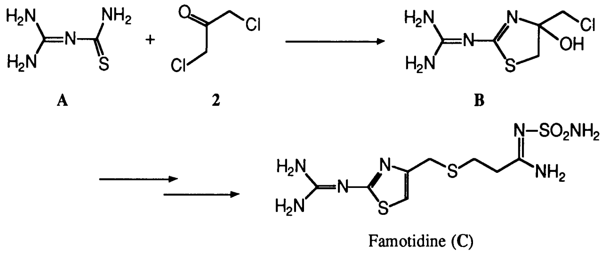
2) I. Ueda, D. Morino, and K. Takimoto, Eur. Pat. Appl. 32058 (1981); *Chem. Abstr.*, **95**, 169217y (1981).

3) Lilly Industries Ltd., Brit. 1328549 (1970); *Chem. Abstr.*, **79**, 137130t (1973).

4) R. R. Crenshaw and A. A. Algieri, Ger. Offen. 3033169 (1981); *Chem. Abstr.*, **95**, 62220s (1981).

5) S. Narayanaswami and K. Richardson, Eur. Pat. Appl. EP 96569 (1982); *Chem. Abstr.*, **100**, 139122t (1984).

6) Y. Hirata, I. Yanagisawa, Y. Ishii, and M. Takeda, Ger. Offen. 3008056 (1980); *Chem. Abstr.*, **94**, 139794w (1981).



7) V. P. Kurkov, Jpn. Kokai Tokkyo Koho 130511 (1979).

8) a) Oxidation by chromate: K. E. Matsumoto, J. H. -H. Chan, and D. R. Baker, Ger. Offen. 2703370 (1977); *Chem. Abstr.*, **87**, 133896q (1977); b) Bromine-oxidation: P. J. Turner, V. I. Routledge, and M. Jeff, Eur. Pat. Appl. EP 260054 (1988); *Chem. Abstr.*, **109**, 109863d (1988).

9) a) S. Torii, T. Inokuchi, and T. Sugiura, *J. Org. Chem.*, **51**, 155 (1986); b) S. Torii, T. Inokuchi, S. Matsumoto, T. Saeki, and T. Oki, *Bull. Chem. Soc. Jpn.*, **62**, 2108 (1989).

10) Since 1,3-dichloroacetone is highly corrosive, the analyses of the reactions were carried out by use of GC.