



An aqueous silica gel disperse electrolysis system. *N*-Oxyl-mediated electrooxidation of alcohols

Hideo Tanaka,* Yusuke Kawakami, Kentaro Goto and Manabu Kuroboshi

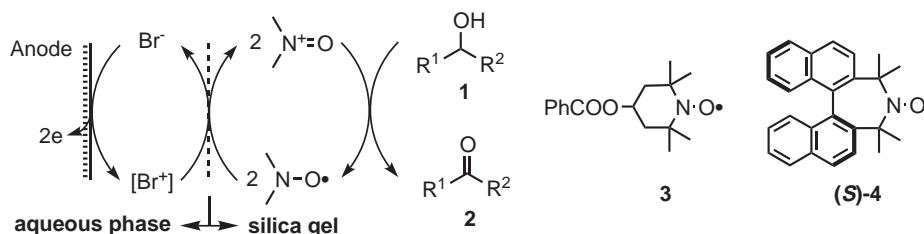
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Abstract—*N*-Oxyl-mediated electrooxidation of alcohols was performed in an aqueous silica gel disperse system. The newly devised electrolysis system offers an organic solvent-free and operationally simple procedure for oxidation of alcohols and could be successfully applied to kinetic resolution of *sec*-alcohol as well as enantioselective oxidation of *meso*-1,4-diol affording optically active γ -lactone. © 2001 Elsevier Science Ltd. All rights reserved.

N-Oxyl-mediated electrooxidation of alcohols has been intensively investigated and many successful applications have been reported.¹ The electrooxidation was mainly carried out in a divided cell under a regulated potential condition and hence polar organic solvents involving a high concentration of the supporting elec-

trolytes were inevitably used to achieve significant current density. Recently, we have reported *N*-oxyl/bromide salt double redox-mediated electrooxidation of alcohols in an H₂O/CH₂Cl₂ two-phase system.² The two-phase electrolysis could be performed by use of a simple beaker-type undivided cell under a constant



Scheme 1. *N*-Oxyl/bromide salt-mediated electrooxidation of alcohols.

Table 1. Electrooxidation of α -phenylethanol **1a** in an undivided cell under a constant current^a

Entry	Electrolysis system	Yield, % ^b	
		2a	1a
1	NaBr-NaHCO ₃ ; H ₂ O (5 ml); silica gel (500 mg)	88	–
2	NaBr-NaHCO ₃ ; H ₂ O/CH ₂ Cl ₂ (4 ml/4 ml)	74	19
3	NaBr-NaHCO ₃ ; H ₂ O/MeCN (4 ml/4 ml)	48	49
4	Lutidine (21 mmol); LiClO ₄ (0.2 mmol); CH ₂ Cl ₂ /MeCN (3 ml/2 ml)	4	76
5	Lutidine (2 mmol); NaClO ₄ (0.5 mmol); H ₂ O/MeCN (1 ml/4 ml)	3	89

^a Carried out in an undivided cell fitted with two platinum electrodes (1.5 × 2 cm²) under a constant current (30 mA, 2.2 F/mol) at room temperature.

^b Isolated yields.

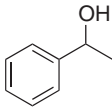
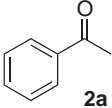
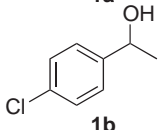
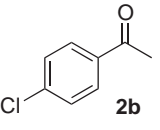
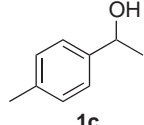
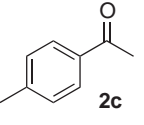
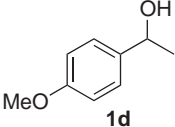
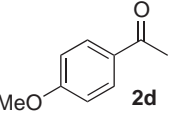
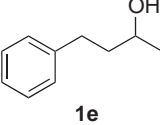
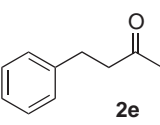
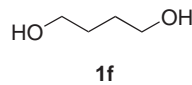
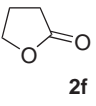
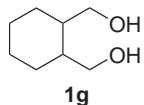
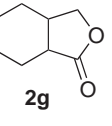
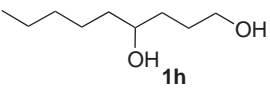
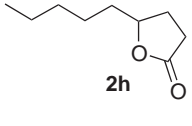
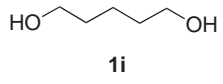
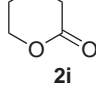
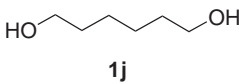
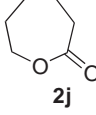
Keywords: electrochemistry; oxidation; alcohols; enantioselective.

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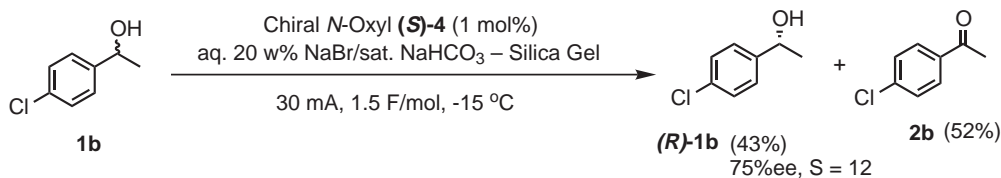
current condition, thereby offering a more beneficial procedure for practical use. The *N*-oxyl-mediated electrooxidation processes reported so far are, however, not necessarily satisfactory in terms of operational simplicity, manufacturing cost, and/or environmental stress arising from the use of organic solvents. In our continuing studies on the *N*-oxyl/bromide

salt-mediated electrooxidation, we found that an aqueous silica gel disperse system could be used successfully for the electrooxidation of alcohols without the use of any organic solvent (Scheme 1). Herein, we describe the first example of an aqueous silica gel disperse electrolysis system for the oxidation of alcohols **1**.

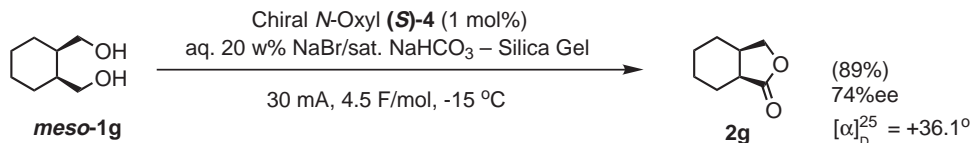
Table 2. Electrooxidation of alcohols in an aqueous silica gel disperse system

Entry	Alcohol	F/mol	Product (Yield, %) ^a
1	 1a	2.2	 2a (88)
2	 1b	2.5	 2b (82)
3	 1c	2.5	 2c (82)
4	 1d	2.5	 2d (42) ^b
5	 1e	2.5	 2e (86)
6	 1f	4.5	 2f (84)
7	 1g	4.5	 2g (92)
8	 1h	4.5	 2h (91)
9	 1i	4.5	 2i (72)
10	 1j	4.5	 2j (–) ^c

^a Isolated yields after column chromatography. ^b *m*-Bromo-*p*-methoxyacetophenone was obtained in 11% yield. ^c Considerable amounts of dimeric esters were obtained.



Scheme 2. Oxidative kinetic resolution of *sec*-alcohol **1b**.



Scheme 3. Enantioselective oxidation of *meso*-diol **1g**.

The electrolysis was carried out in a disperse system with silica gel (Merck Kieselgel 60, 230–400 mesh) as the disperse phase and aqueous 20 w% NaBr saturated with NaHCO₃ as the disperse media. The silica gel (500 mg) was dispersed in an acetone solution of α -phenylethanol **1a** (R¹=Ph, R²=CH₃; 1 mmol) and *N*-oxyl **3** (0.01 mmol) and most of the solvent was evaporated under reduced pressure. The residual solids and aqueous 20 w% NaBr saturated with NaHCO₃ (5 ml) were placed in a beaker-type undivided cell fitted with two platinum foil electrodes (1.5 × 2 cm²). A regulated dc current (30 mA, 2.2 F/mol⁻¹) was supplied (Table 1, Entry 1). The work-up process is quite simple; thus, the disperse phase (silica gel) was freed from the aqueous phase by filtration and rinsed with acetone. The organic filtrate was concentrated in vacuo and the residue was passed through a short column (SiO₂, hexane/AcOEt: 5/1) to afford acetophenone **2a** in 88% yield. Use of NaCl or NaI in place of NaBr could not effectively promote the oxidation, affording only 33% and 11% yields of **2a**, respectively.

When the *N*-oxyl/NaBr-mediated electrooxidation of **1a** was carried out in a two-phase system comprising CH₂Cl₂ and aqueous NaBr/NaHCO₃ (Entry 2)² or in a homogeneous system (aqueous acetonitrile) (Entry 3), a similar reaction occurred but less effectively, affording 74 and 48% yields of **2a**, respectively. The presence of a bromide salt (NaBr) is indispensable for the electrooxidation of **1a** in an undivided cell, since no appreciable reaction occurred in the absence of the bromide salt; see for example entries 4 and 5. Notably, both electrolysis systems have been frequently used for *N*-oxyl-mediated electrooxidation of alcohols in a divided cell, affording good to excellent yields of the corresponding carbonyl compounds.^{1a}

The newly devised silica gel disperse electrolysis system was successfully applied to the electrooxidation of various alcohols. The representative results are summarized in Table 2. Oxidation of *sec*-alcohols **1** proceeded smoothly to afford the corresponding ketones **2** (Entries 1–3, and 5), while α -(*p*-methoxyphenyl)ethanol **1d** partially suffered bromination on the *p*-methoxypheny

moiety to afford a mixture of the ketone **2d** and its *m*-bromo-substituted product (Entry 4). 1,4-Diols and 1,5-diols were selectively converted to γ -lactones and δ -lactone, respectively, after passage of 4.5 F/mol⁻¹ of electricity (Entries 6–9). Under similar conditions, 1,5-diol **1j** afforded no detectable amount of the corresponding lactone **2j**, yielding a mixture of esters resulting from intermolecular reactions³ (Entry 7).

Kinetic resolution of secondary alcohol **1b** with chiral *N*-oxyl (**S**)-**4**⁴ was carried out in a similar silica gel disperse electrolysis system (Scheme 2). Passage of 1.5 F/mol⁻¹ of electricity at –15°C afforded the corresponding ketone **2b** in 52% yield and recovered alcohol **1b** in 43% yield, 75% ee⁵ (*S* = 12). Enantioselective oxidation of *meso*-1,4-diol **1g** was achieved in a similar manner, affording bicyclic lactone **2g**⁶ in 89% yield, 74% ee⁵ (Scheme 3).

The characteristic features of the silica gel-disperse electrolysis system are summarized as follows:

1. Electrolysis can be performed in an undivided cell under a constant current condition (self-controlled potential) without the use of organic solvents.
2. The work-up process is exceptionally simple; just filtration, extraction of silica gel with acetone, evaporation, and short column chromatography.
3. High current efficiency and good to excellent yields of products can be achieved.

References

1. (a) Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4492. (b) Bobbit, J. M.; Hung, Q. T.; Ma, Z. *J. Org. Chem.* **1993**, *58*, 4837. (c) Yanagisawa, Y.; Kashiwagi, Y.; Kurashima, F.; Anzai, J.; Osa, T.; Bobbit, J. M. *Chem. Lett.* **1996**, 1043. (d) Kashiwagi, Y.; Yanagisawa, Y.; Kurashima, F.; Anzai, J.; Osa, T.; Bobbit, J. M. *J. Chem. Soc., Chem. Commun.* **1996**, 2745. (e) Kashiwagi, Y.; Yanagisawa, Y.; Kurashima, F.; Anzai, J.; Osa, T. *Tetrahedron Lett.* **1999**, *40*, 6469.

2. (a) Inokuchi, T.; Matsumoto, S.; Nishiyama, T.; Torii, S. *J. Org. Chem.* **1990**, *55*, 462. (b) Torii, S.; Inokuchi, T.; Matsumoto, S.; Saeki, T.; Oki, T. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 852. (c) Inokuchi, T.; Matsumoto, S.; Torii, S. *J. Org. Chem.* **1991**, *56*, 2416. (d) Inokuchi, T.; Liu, P.; Torii, S. *Chem. Lett.* **1994**, 1411. (e) Kuroboshi, M.; Yoshihisa, H.; Cortona, M. N.; Kawakami, Y.; Gao, Z.; Tanaka, H. *Tetrahedron Lett.* **2000**, *41*, 8131–8135.
3. Involving HO(CH₂)₄CO₂(CH₂)₄CO₂H, HO₂C(CH₂)₄CO₂-(CH₂)₅OH, etc.
4. Rychnovsky, S. D.; McLernon, T. L.; Rajapakse, H. *J. Org. Chem.* **1996**, *61*, 1194.
5. Determined by HPLC, column: CHIRALCEL-OD (4.6 mm ϕ , 50 mm), mobile phase: hexane/2-propanol (90/1), flow rate: 0.5 ml min⁻¹.
6. Ishikawa, T.; Oku, Y.; Kotake, K.-I. *Tetrahedron* **1997**, *53*, 14915–14928.