_N_-Oxyl-Mediated Electro-oxidation of Alcohols in Silica Gel-Water Disperse System. Column-Flow System

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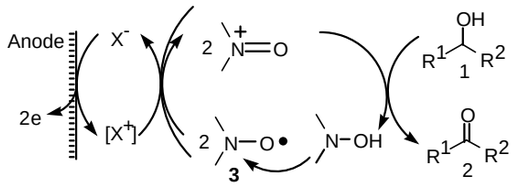
Electro-oxidation mediated with *N*-oxyl compounds has been intensively investigated as a prominent tool for oxidation of alcohols. So far reported *N*-oxyl mediated electro-oxidation processes are, however, not necessarily satisfactory in terms of operational simplicity, manufacturing cost, and environmental stress mainly arising from use of polar organic solvents containing supporting electrolytes. To overcome these problems, we developed electro-oxidation of alcohols in a silica gel or polymer disperse-water system without using troublesome organic solvents, wherein water-insoluble organic substrates and mediators were supported on the disperse phase (Scheme 1).[1,2] Recycle use of the mediator could be performed by using *N*-oxyl-immobilized silica gel and polymers,[3] thereby offering a completely closed system for oxidation. In this connection, *N*-oxyl mediated oxidation of alcohols using water-soluble electrochemically generable/ regenerable oxidants, such as NaOCl, as a terminal oxidant was also investigated. This paper describes the fundamental studies on the oxidation system as well as column-flow system for a new devices directed towards automated oxidation process.



aqueous phase silica gel/polymer adsorption layer

Scheme 1. N-Oxyl/X⁻-Double Mediatory System

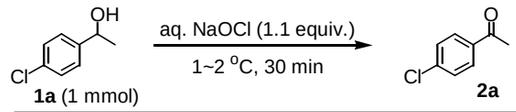
N-Oxyl/aq. NaOCl promoted oxidation of alcohols in a silica gel-disperse water system was carried out as follows. A mixture of alcohol **1a** (1 mmol), silica gel (1 g), *N*-oxyl **3** (1 mol%), and aq. NaOCl (1.1 mmol, 5 mL) was stirred at 0 ºC for 30 min to afford the corresponding ketone **2a** in good yield (Table 1, Entry 1). To be noticed, Br^- mediator is not necessary for this system, which is indispensable in a CH_2Cl_2-H_2O two-phase system (Entries 3, 4). Oxidation of **1a** also proceeded in an *N*-oxyl-immobilized silica gel[2] disperse-water system (Entry 2). The *N*-oxyl-immobilized silica gel can be recovered and used repeatedly without significant change of the yield of **2a** (Table 2). Representative results of oxidation of alcohols in this system are shown in Table 3.

Next, we investigated a column-flow reactor as illustrated in Fig. 1 with a view to obtaining a new access to automated synthesis. *N*-Oxyl immobilized silica gel was packed in the column, and acetone solution of **1a** and aq. NaOCl (0.7 M, 3 mL) were loaded successively. Finally, the silica gel was rinsed with acetone to afford the corresponding ketone **2a** in good yield.

The aq. NaOCl can be regenerated electrochemically; therefore, this protocol would be a potent Ex-Cell method, offering a new closed system for oxidation of alcohols. Details on the column-flow oxidation system will be discussed.

1) H. Tanaka, *et al*. The 197th Meeting of ECS, Abstr. No. 1087.
2) H. Tanaka, *et al*. The 199th Meeting of ECS, Abstr. No. 959.
3) H. Tanaka, *et al*. 2001 Joint International Meeting, Abstr. No. 1207.

Table 1. Oxidation of Alcohol 1a with Aqueous NaOCl

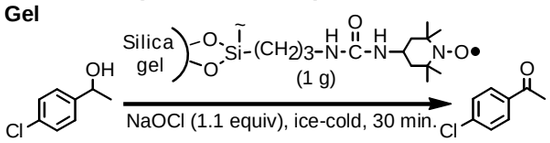


1a (1 mmol) **2a**

Entry	Oxidation Media	*N*-Oxyl mol%	KBr equiv.	Yield, %[a] 2a	1a
1	SiO_2–H_2O	1	—	96	—
2	SiO_2–N*N*-Oxyl[b]–H_2O	—	—	97	—
3	CH_2Cl_2–H_2O	1	—	1	>99
4	CH_2Cl_2–H_2O	1	0.1	89	11

[a] Determined by glpc. [b] *N*-Oxyl-immobilized silica gel

Table 2. Recycle use of N-Oxyl-Immobilized Silica Gel

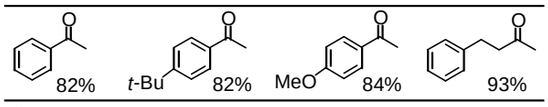


1a (1 mmol) 2a

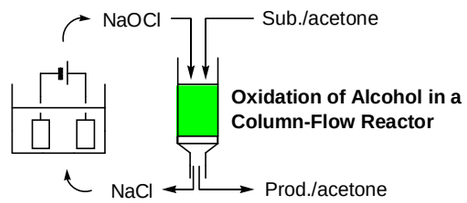
Entry	1	2	3	4	5	6	7	8	9
Yield (%)[a]	95	100	98	98	96	97	95	92	98

[a] Based on glpc analysis.

Table 3. *N*-Oxyl Mediated Oxidation of Alcohols in a Silica/aq. NaOCl Disperse System[a]



[a] Determined by glpc



Electro-Regeneration of NaOCl

Fig. 1. A Column-Flow Reactor System