Synthesis of Water-Soluble *N*-Oxyl Derivative and It's Application to the Electrooxidation of Alcohols in Water

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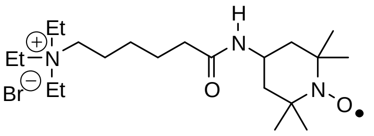
Electrooxidation mediated with *N*-oxyl derivatives has been intensively investigated as a prominent protocol for oxidation of alcohols. Most of the electrooxidation of alcohols were carried out in harmful organic solvents such as acetonitrile and dichloromethane. From the viewpoint of today's environmental concern, on the other hand, the importance of organic reaction in water is now recognized, because water is a cheap, safe, and environmentally benign solvent. Along this line, we have developed the electrooxidation of alcohols in a disperse system with an *N*-oxyl-immobilized silica gel[1)] or polymer particles[2)] as the disperse phase and aqueous saturated $NaHCO_3$ containing 20 wt% NaBr as the disperse media. Both the *N*-oxyl-immobilized disperse phase and the aqueous media could be recovered by simple work-up process and were used repeatedly so that all chemicals could be re-used in this oxidation system; thereby a totally closed system could be performed. In our continuing studies on electrooxidation of alcohol in the *N*-oxyl-mediatory system, we found newly designed water-soluble *N*-oxyl **1** for the electrooxidation of alcohols in water. One of the characteristic points is that *N*-oxyl **1** dissolved in water was remained intact even after extractive workup process, therefore the recovered aqueous solution containing *N*-oxyl **1** was repeatedly used for the electrooxidation of alcohols.



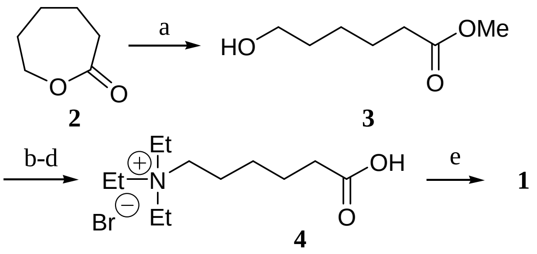
Water-Soluble *N*-Oxyl 1

Synthesis of *N*-oxyl **1** is outlined in **Scheme 1**. ε-Caprolactone **2** was treated with $Mg(OMe)_2$ in methanol at reflux for 1.5 h to afford methyl 6-hydroxyhexanoate **3** in 85% yield. Subsequent bromination, treatment with Et_3N and hydrolysis of compound **3** afforded compound **4**. Finally, compound **4** was treated with 4-amino-TEMPO in the presence of DCC in CH_2Cl_2 to afford the desired *N*-oxyl **1** in 81% yield.

Representative procedure for the electrooxidation of alcohols **5** is as follows: A mixture of 1-(4-chlorophenyl)ethanol **5a**, *N*-oxyl **1**, and ion-exchange water was placed in a beaker-type undivided cell. After stirring the mixture for a few minutes, two platinum foil electrodes were immersed into the reaction mixture and regulated dc current (10 mA/cm^2) was supplied (**Scheme 2**). After passage of 2.5 F/mol of electricity, the reaction mixture was extracted with ethyl acetate, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography to afford *p*-chloroacetophenone **6a** in 69% yield. It is interesting to note that most of the *N*-oxyl **1** was dissolved in the aqueous phase after the extractive workup. The recycle use of the aqueous electrolysis media was successfully performed (**Figure 1, Table 1**).

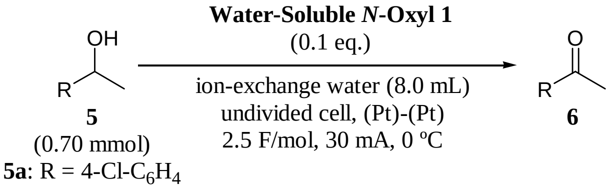
References

1) Tanaka, H.; Kawakami, Y.; Goto, K.; Kuroboshi, M. *Tetrahedron Lett.* **2001**, *42*, 445.
2) Tanaka, H.; Kuroboshi, M.; Kubota, J.; Itogawa, S.; Ido, T.; Uchida, T.; Shimamura, K. Proceeding of 199th Meeting of the Electrochemical Society, Washington D. C., 17-20, (2001).



a) Mg, MeOH, reflux, 1.5 h, 85%; b) CBr_4, Ph_3P, CH_2Cl_2, room temp. (rt), 1.5 h, 78%; c) Et_3N, EtOH, rt, 18 h, quant.; d) 1 M NaOH, MeOH, rt. 24 h, 96%; e) 4-NH_2-TEMPO, DCC, CH_2Cl_2, rt. 6 h, 81%

Scheme 1



Scheme 2

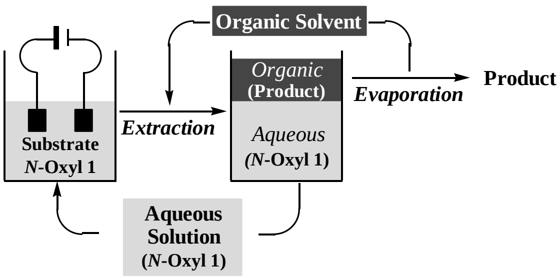


Figure 1. Recycle Use of the Aqueous Solution.

Table 1. Electrooxidation of Alcohol 5a Using Water-Soluble *N*-Oxyl 1 in Water.

Run	Yield **6a** (%)[a]	Recov. **5a** (%)[a]
1st	69	23
2nd	81	9
3rd	78	17
4th	74	16
5th	79	9

[a] The yields were determined by GLPC.