Electrogenerated Acid as an Efficient Catalyst for the Protection and Deprotection of Alcohols with Dihydropyran and Transesterification of Glyceride

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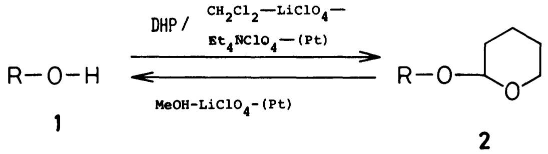
Synopsis. Protection of alcohols with 3,4-dihydro-2*H*-pyran and hydrolysis of the resulting tetrahydropyranyl ethers are cleanly performed by using an electrogenerated acid (EG acid) as a catalyst. Transesterification of glyceride was also achieved with EG acid.

The protection of hydroxyl groups with 3,4-dihydro-2*H*-pyran (DHP) and deprotection of the resulting tetrahydropyranyl (THP) ethers into hydroxyl groups are two essential procedures in modern synthetic chemistry and a variety of catalysts have been already proposed for this purpose.[1] In the course of our study on electrolyses with perchlorate salts, we recently found prominent aspects of acid-catalyzed reactions in an $MeOH-LiClO_4-(Pt)$ electrolysis system, which comprise an acid-catalyzed hemiacetalization of α-hydroxy ketones with methanol and the subsequent oxidative fission of 1,2-diol groups, giving keto esters.[2] As the results of our continuing studies on electrogenerated acid,[3] we disclose here a simple procedure for the protection of alcohol **1** with DHP by using an electrochemically generated acid[4] *in situ* after passing a small amount of electricity in a $CH_2Cl_2-LiClO_4-$(and/or Et_4NClO_4)-platinum electrodes system.



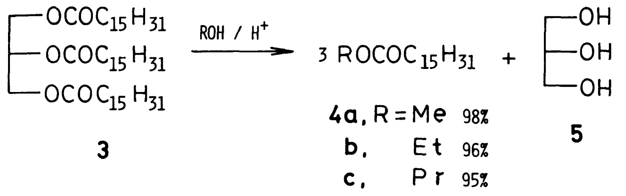
It is noted that *p*-toluenesulfonic acid is frequently used for tetrahydropyranylation of alcohols as a routine catalyst,[5] and it seems to be superior to other catalysts such as hydrochloric acid,[6] phosphoryl chloride,[7] and boron trifluoride etherate.[8] Owing to its strong acidity, however, some milder and more efficient catalysts, *i.e.*, pyridinium *p*-toluenesulfonate (PPTS),[9a] poly(2- or 4-vinylpyridinium *p*-toluenesulfonate),[9b] and bis(trimethylsilyl) sulfate [$(Me_3Si)_2SO_4$],[10] have been devised for this purpose. The present electrochemical procedure for the preparation of THP ether **2** can constitute a facile alternative to reported ones due to its high efficiency (most of the operations complete within several minutes and provide excellent yields).

The electrochemical protection of alcohol **1** (1 mmol) with DHP was carried out using platinum electrodes in a simple undivided cell. Thus, electrolysis of cinnamyl alcohol **1a** and an excess equivalent (1.2—2.0 equiv) of DHP in dichloromethane containing lithium perchlorate ($LiClO_4$, 1 mg) and/or tetraethylammonium perchlorate (Et_4NClO_4, 5 mg) gave the corresponding THP ether **2a** in more than 90% yield only by passing a catalytic quantity of electricity.

Some typical results of the electrochemical tetrahydropyranylation of alcohols are summarized in Table 1.

The acid catalyst generated in the electrolysis medium is also effective for removal of the THP group from **2**. Stirring of **2a** at 55—60 °C for 5 min in methanol containing a small amount of $LiClO_4$ after passing 0.01 F/mol of electricity in the anode compartment of a divided cell gave the parent alcohol **1a** in 95% yield. The results of deprotection experiments are also summarized in Table 1.

In addition to the above results, the electrogenerated acid can be used as a catalyst for the transesterification of glyceride **3**.[11] Heating of **3** with the pre-electrolyzed solution of $LiClO_4$ in either methanol, ethanol, or 1-propanol provided the corresponding palmitates **4a**—**c** in 95—98% yields.



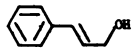
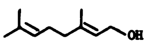
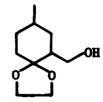
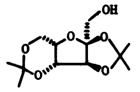
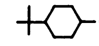
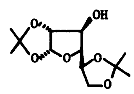
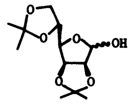
Experimental

General Procedure for Protection of Alcohol 1 with Dihydropyran. A mixture of cinnamyl alcohol (**1a**, 134 mg, 1.0 mmol), 3,4-dihydro-2*H*-pyran (101 mg, 1.2 mmol), and $LiClO_4$[12] (1 mg, 0.009 mmol) was dissolved in CH_2Cl_2[13] (5 ml) in an undivided cell. Two platinum foil electrodes were immersed in the solution and voltage of 10 V (current: 0.4 mA) was applied. TLC monitoring revealed that the reaction has terminated after passage of about 0.0002 F/mol of electricity (it took about 1 min) based on **1a**. Pyridine (45 mg, 0.57 mmol) was then added. Evaporation of volatile material and column chromatography (SiO_2, hexane-AcOEt 15:1) of the residue gave the corresponding THP ether **2a** in 92% yield (Table 1).

Spectral data along with elemental analyses of the THP ether of carbohydrates **1e**, **1g**, and **1h** are as follows. **2e**: IR (neat) 1450, 1385, 1375, 1335, 1285, 1250, 1205, 1165, 1127, 1080, 972, 915, 870, 786, 733 cm^{-1}; ^1H NMR (60 MHz) δ 1.30—1.80 (m, 6, CH_2), 1.35, 1.40 (s, 6, CH_3), 1.41 (s, 6, CH_3), 3.30—4.95 (m, 10, CH_2O, CH-O). Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.29; H, 8.19. Found: C, 59.36; H, 8.20. **2g**: IR (neat) 1450, 1435, 1375, 1365, 1245, 1207, 1148, 1118, 1068, 965, 840, 760 cm^{-1}; ^1H NMR (100 MHz) δ 1.30—2.00 (m, 6, CH_2), 1.35 (s, 6, CH_3), 1.45, 1.52 (s, 6, CH_3), 3.44—4.96 (m, 9, CH_2O, CH-O), 5.96 (d, J=4 Hz, 1, CH-O). Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.29; H, 8.19. Found: C, 59.27; H, 8.11. **2h**: IR (neat) 1446, 1435, 1375, 1366, 1255, 1200, 1155, 1060, 1005, 955, 845, 810 cm^{-1}; ^1H NMR δ 1.20—1.90 (m, 6, CH_2), 1.36, 1.40 (s, 6, CH_3), 1.51 (s, 6, CH_3), 3.50—5.08 (m, 9, CH_2O, CH-O), 5.80 (s, 1, CH-O). Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.29; H, 8.19. Found: C, 59.25; H, 8.18.

General Procedure for Deprotection of 2. An MeOH solution (6 ml) containing $LiClO_4$ (12 mg) was placed in each compartment of the electrolysis cell. Electric current was

TABLE 1. ELECTROCHEMICAL PROTECTION AND DEPROTECTION OF ALCOHOLS **1**

	Alcohol **1**	Protection with DHP[a]				Deprotection[b]	
		electrolyte[c]	F/mol (min)	yield[d] of **2**/%	bp [°C/Torr][e] mp [°C]([ref.]lit,)	F/mol (min)	yield[d] of **1**/%
a		A	0.0002 (1)	92	95—96°/0.02 ([10]125—130°/1)	0.01 (5)	95
b	$CH_3(CH_2)_6CH_2OH$	A	0.0003 (10)	98	69—72°/0.03	0.01 (5)	95
c		A	0.037 (5)	85	74—77°/0.016 ([10]78—85°/1)	0.01 (150)	96
d		A	0.024 (12)	72	90—92°/0.02	0.01 (90)	90
e		A	0.0005 (1)	94	113—116°/0.03	f)	
f		B	0.015 (12)	97	81—82°/0.022 ([10]82—89°/0.04)	0.01 (5)	98
g		B	0.021 (10)	96	103—105°/0.019	f)	
h		B	0.0189 (15)	87	109—114°/0.016	f)	

a) Carried out using **1** (1.0 mmol) and DHP (1.2—2.0 mmol) in CH_2Cl_2 (5 ml) at 20 °C. b) Carried out using **2** (1.0 mmol) in MeOH (6 ml)-$LiClO_4$ (12 mg) at 55 °C. c) A: $LiClO_4$ (1 mg); B: $LiClO_4$ (1 mg)-Et_4NClO_4 (5 mg). d) Isolated yield. e) Air bath temperature. f) Unsatisfactory for selective hydrolysis of tetrahydropyranyl moiety.

passed under an applied voltage of 10 V (current: 8 mA) using platinum electrodes. After the passage of 0.01 F/mol of electricity (based on the THP ether **2f**) for two minutes, the anolyte was transfered to **2f** (240 mg, 1.0 mmol) placed in another flask. The mixture was heated at 55—60 °C for 5 min while stirring and quenched with pyridine (0.2 ml). Usual workup and chromatography (SiO_2, hexane-AcOEt 10:1) gave 153 mg (98%) of 4-*t*-butylcyclohexanol (**1f**): mp 64—68 °C.

Transesterification of Tripalmitate (3). A solution of MeOH (10 ml) containing $LiClO_4$ (10 mg) was electrolyzed under a constant current of 5 mA in the anode compartment of the electrolysis cell. After the passage of 1.0 F/mol of electricity (based on **3**), the anolyte was added to **3** (204 mg, 0.25 mmol) placed in another flask. The mixture was heated to reflux for 3 h and quenched with pyridine (0.1 ml). Concentration and chromatography (SiO_2, hexane-AcOEt 20:1) gave 202 mg (98%) of **4a** (R=Me): mp 28—29 °C (lit,[14] 28 °C); bp 115—117 °C (3 mm).

Similarly, **4b** (R=Et) and **4c** (R=Pr) were obtained in 96% and 95% yields by heating for 4—7 h. **4b**:[14] bp 117—119 °C (2 mm). **4c**:[14] bp 120—123 °C (2 mm).

References

1) a) T. W. Green, "Protective Group in Organic Synthesis," John Wiley & Sons, New York (1981); b) J. F. McOmie, "Protective Groups in Organic Chemistry," Plenum Press, London (1973).

2) a) S. Torii, T. Inokuchi, and R. Oi, *J. Org. Chem.*, **47**, 47 (1982); b) S. Torii, T. Inokuchi, and R. Oi, *ibid*, **48**, 1944 (1983).

3) For another use of the electrogenerated acid as a catalyst, see a) K. Uneyama, A. Ishimura, K. Fujii, and S. Torii, *Tetrahedron Lett.*, **24**, 2853 (1983); b) K. Uneyama, N. Nishiyama, and S. Torii, *Tetrahedron Lett.*, **25**, 4137 (1984); c) K. Uneyama, Y. Masatsugu, T. Ueda, and S. Torii, *Chem. Lett.*, **1984**, 529; d) S. Torii and T. Inokuchi, *ibid.*, **1983**, 1349; e) S. Torii, T. Inokuchi, and T. Kobayashi, *ibid.*, **1984**, 897.

4) a) R. Kossai, J. Simonet, and D. Dauphin, *Tetrahedron Lett.*, **21**, 3575 (1980); b) J. Delaunay, A. Lebouc, A. Tallec, and J. Simonet, *J. Chem. Soc., Chem. Commun.*, **1982**, 387; c) J. Y. Becker and B. Zinger, *J. Am. Chem. Soc.*, **104**, 2327 (1982); d) *idem, J. Chem. Soc., Perkin Trans. 2*, **1983**, 395.

5) a) A. C. Ott, M. F. Murray, and R. L. Pederson, *J. Am. Chem. Soc.*, **74**, 1239 (1952); Ion-exchange resin containing SO_3H groups (Amberlyst H-15) can be used as a catalyst; b) A. Bongini, G. Cardillo, M. Orena, and S. Sandri, *Synthesis*, **1979**, 618.

6) R. G. Jones and M. J. Mann, *J. Am. Chem. Soc.*, **75**, 4048 (1953).

7) C. W. Creenhalgh, H. B. Henbest, and E. R. H. Jones, *J. Chem. Soc.*, **1951**, 1190.

8) H. Alper and L. Dinkes, *Synthesis*, **1973**, 81.

9) a) M. Miyashita, A. Yoshikoshi, and P. A. Grieco, *J. Org. Chem.*, **42**, 3772 (1977); b) F. M. Menger and C. H. Chu, *ibid*, **46**, 5044 (1981).

10) Y. Morizawa, I. Mori, T. Hiyama, and H. Nozaki, *Synthesis*, **1981**, 899.

11) a) C. E. Rehberg, *Org. Synth. Coll. Vol. III*, **1955**, 146. b) J. C. Sauer, B. E. Hain, and P. W. Boutwell, *ibid*, **1955**, 605.

12) Commercially available, anhydrous $LiClO_4$ was dried before use in an oven at about 110 °C for 12 h.

13) Dichloromethane was once distilled over P_2O_5.

14) H. Pyan and T. Dillon, *J. Chem. Soc.*, *I*, **1913**, 583.