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2,3-Dichloro-5,6-dicyano-*p*-benzoquinone as a Mild and Efficient Catalyst for the Tetrahydropyranylation of Alcohols

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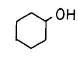
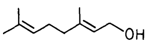
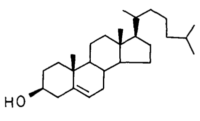
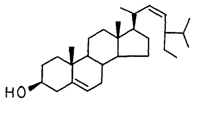
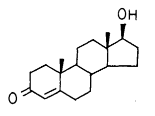
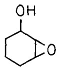
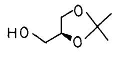
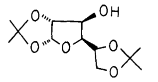
Synopsis. Hydroxy compounds readily add to 3,4-dihydro-2*H*-pyran under neutral conditions in the presence of a catalytic amount of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone, to give high yields of the corresponding tetrahydropyranyl ethers.

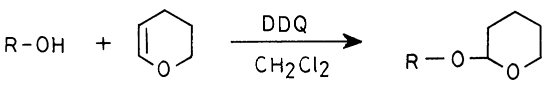
The protection of hydroxyl groups with 3,4-dihydro-2*H*-pyran (DHP) is a useful and representative method in modern synthetic chemistry.[1)] Many catalysts have been already proposed for this purpose. For the tetrahydropyranylation of alcohols, *p*-toluenesulfonic acid[2)] is the most common catalyst and seems to be superior to other catalysts such as hydrochloric acid,[3)] phosphoryl chloride,[4)] and boron trifluoride etherate.[5)] Owing to its strong acidity, however, *p*-toluenesulfonic acid is undesirable for highly acid-sensitive alcohols. Some less acidic catalysts, i.e., pyridinium *p*-toluenesulfonate,[6)] bis(trimethylsilyl) sulfate,[7)] cobalt (II) chloride,[8)] and electrogenerated acid (EG acid)[9)] have been devised for this purpose. For example, pyridinium *p*-toluenesulfonate is a weaker acid (pH 3.0 in 1.0 M aqueous solution)

Table 1. Tetrahydropyranylation of Alcohols **1** with 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone

	Alcohol **1**	Protection with DHP[a)]		Bp[°C/Torr][c,d)] or Mp[°C] (lit,[ref.])
		Reaction time/h	Yield[b)] of **2**/%	
a	$CH_3(CH_2)_{11}OH$	3	92	100—103/1.0 (95—98/0.04[7)])
b	$CH_3(CH_2)_7OH$	3	90	67—70/0.19 (69-72/0.03[9)])
c		3	90	80—84/0.65
d		8	97[e)]	78—81/0.28 (74—77/0.016[9)])
e		6	100	147 (150[11)])
f		6	98	153
g		6	100	100 (101[7)])
h	$C_6H_5CH_2OH$	2	96	105—107/0.40 (120—125/4[7)])
i		5	82	87—89/0.5
j		3	90	72—74/0.4
k		6	98[e)]	110—113/0.47 (103—105/0.019[9)])

a) DDQ (0.1 mmol) was added to a mixture of alcohol **1** (1 mmol) and DHP (1.5 mmol) in CH_2Cl_2 (7.0 ml). b) Isolated yield. c) Bath temperature. d) 1 Torr=133.322 Pa. e) 0.2 mmol of DDQ was used.

than acetic acid (pH 2.4 in 1.0 M aqueous solution) (1 M=1 mol dm^{-3}).⁶⁾ Recently, the tetrahydropyranylation of alcohols using magnesium bromide etherate and 2-(phenylsulfonyl)tetrahydropyran and sodium hydrogencarbonate under mildly basic conditions has been reported.¹⁰⁾ In this paper, we wish to report that 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) can efficiently catalyze the tetrahydropyranylation of alcohols.



1 2

Eleven alcohols **1a**—**k** were treated with DHP in the presence of a catalytic amount of DDQ in dichloromethane to afford the corresponding tetrahydropyranyl (THP) ethers **2a**—**k**. The results are summarized in Table 1. It is worth pointing out that (1) protection using DDQ can be carried out under neutral conditions and is effective for alcohols containing acid-sensitive functional groups such as allylic hydroxyl, acetal, or epoxide (**1d**, **1i**, **1j**, **1k**), (2) THP ethers are obtained in excellent yields (> 90%) for a variety of alcohols, and (3) isolation of the product is remarkably simple (concentration of the reaction mixture and column chromatography of the residue).

In summary, this method constitutes a mild procedure for the preparation of THP ethers under neutral conditions.

Experimental

All boiling points and melting points were uncorrected. IR spectra were recorded on a Jasco IRA-2 spectrophotometer. ^{1}H NMR spectra were measured on a JEOL JNM-FX 90Q or a Hitachi R-24B spectrometer using Me_4Si as an internal standard. Column chromatography was performed on Wacogel C-200 silica gel. Dichloromethane was distilled over P_2O_5 prior to use. DDQ was recrystallized from benzene-hexane.

General Procedure for Protection of Alcohols 1 with DHP. DDQ (23 mg, 0.1 mmol) was added to a mixture of 1-dodecanol (**1a**, 186 mg, 1.0 mmol) and DHP (126 mg, 1.5 mmol) in dry dichloromethane (7.0 ml). The reaction mixture was stirred at room temperature for 3 h. The solvent was evaporated under reduced pressure. Column chromatography (benzene) of the residue gave the corresponding THP ether **2a** (249 mg, 92%) (Table 1).

THP ethers **2e**—**g** and **2i**—**k** were obtained as an inseparable mixture of diastereomers at C-2′.

Compounds **2a**—**h** and **2k** were identified by comparison of their spectroscopic behaviors with those described in the references.⁹˒¹⁰⁾ Analytical data of compounds **2i** and **2j** are as follows. **2i**: IR (Neat) 1260, 911, and 819 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.90—2.10 (m, 12H), 3.12—3.68 (m, 3H), 3.72—4.16 (m, 2H), 4.80 and 4.94 (2×br s, 2×0.5H). Found: C, 66.43; H, 9.17%. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15%. **2j**: ^{1}H NMR ($CDCl_3$) δ=1.37 (s, 3H), 1.42 (s, 3H), 1.37—1.98 (m, 6H), 3.32—4.44 (m, 7H), and 4.64 (br s, 1H). Found: C, 60.79; H, 9.49%. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32%.

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