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Oxidative Deprotection of Tetrahydropyranyl Ethers to Carbonyl Compounds with 4-(Dimethylamino)pyridinium and 2,2′-Bipyridinium Chlorochromates under Non-aqueous Conditions†

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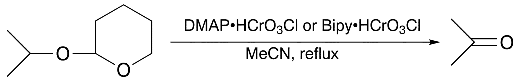
An efficient oxidation of tetrahydropyranyl ethers to their carbonyl compounds using 4-(dimethylamino)pyridinium and 2,2′-bipyridinium chlorochromates is described.

The tetrahydropyranyl group is one of the most useful protective groups for alcohols in multi-step organic syntheses.[1] Many catalysts have already been proposed for the tetrahydropyranylation of alcohols and deprotection of tetrahydropyranyl ethers to the parent alcohols.[2–17] But there are only a few reports dealing with the direct oxidation of tetrahydropyranyl ethers to their carbonyl compounds.[18,19] Consequently, there is a need to develop and introduce new methods and reagents for such functional group transformations.

We now report a new and efficient oxidative deprotection of tetrahydropyranyl ethers to their carbonyl compounds in high yields using 4-(dimethylamino)pyridinium and 2,2′-bipyridinium chlorochromates.[20,21] As shown in Table 1 these reagents are able to convert primary and secondary tetrahydropyranyl ethers **1** to their corresponding aldehydes and ketones **2** efficiently in refluxing acetonitrile. Oxidation of THP ethers in which a conjugated benzylic double bond exists, in addition to the desired product is usually accompanied with cleavage of the double bond to produce the corresponding carbonyl compounds in 20–25% yield (entries 9 and 10).



1 **2**

In order to investigate whether THP ethers are directly oxidized or initially cleaved to the corresponding alcohols and then oxidized to carbonyl compounds, we attempted to oxidize some corresponding alcohols under the same reaction conditions. We found that the oxidation of alcohols is very fast compared to THP ethers. Therefore, it was not feasible to observe such alcohol intermediates in the oxidation. It is worth mentioning that such intermediates were not observed by TLC or GLC. It is possible that THP ethers are first cleaved to alcohols and then converted, *via* very fast reactions, to the final products.

In summary, the present methodology offers an attractive and efficient method for the direct oxidation of tetrahydropyranyl ethers to their carbonyl compounds.

Experimental

4-(Dimethylamino)pyridinium and 2,2′-bipyridinium chlorochromates were prepared by reported methods.[20,21] Yields refer to isolated products. All oxidation products were identified by comparison of their physical data, IR and NMR spectra with those of authentic samples. THP ethers were prepared according to described procedures.[3,12]

General Procedure for the Oxidative Deprotection of THP Ethers with 4-(*Dimethylamino*)*pyridinium Chlorochromate*.—In a round-bottomed flask (50 ml) equipped with a condenser and a magnetic stirrer, a solution of THP ether (1 mmol) in MeCN (15 ml) was prepared, 4-(Dimethylamino)pyridinium chlorochromate (0.775 g, 3 mmol) was added to this solution and refluxed for 25–50 min. The progress of the reaction was monitored by GLC or TLC (eluent: n-hexane–ethyl acetate, 20:1). After completion of the reaction, silica gel (2 g) was added and the mixture was stirred at room temperature for 5 min. The reaction mixture was filtered and the solid material was washed with MeCN (15 ml). The filtrates were combined and evaporated. The resulting crude material was purified on a silica-gel plate or silica-gel column with appropriate eluent. Evaporation of the solvent afforded pure carbonyl compound; yield 65–96% (Table 1).

Table 1 Oxidative deprotection of THP ethers with DMAP · HCrO$_3$Cl and Bipy · HCrO$_3$Cl

			Yield (%) (*t*/min)		Mp/°C [bp/°C/Torr]	
Entry	Substrate	Product	DMAP · HCrO$_3$Cl	Bipy · HCrO$_3$Cl	Found	Reported
1	PhCH$_2$OTHP (**1a**)	PhCHO (**2a**)	90 (25)	93 (20)	176–178	178–179
2	3-MeOC$_6$H$_4$CH$_2$OTHP (**1b**)	3-MeOC$_6$H$_4$CHO (**2b**)	92 (30)	94 (25)	141–143/50	143/50
3	4-MeOC$_6$H$_4$CH$_2$OTHP (**1c**)	4-MeOC$_6$H$_4$CHO (**2c**)	90 (30)	90 (15)	247–248	248
4	3-O$_2$NC$_6$H$_4$CH$_2$OTHP (**1d**)	3-O$_2$NC$_6$H$_4$CHO (**2d**)	72 (50)	85 (35)	57–59	57–59
5	4-O$_2$NC$_6$H$_4$CH$_2$OTHP (**1e**)	4-O$_2$NC$_6$H$_4$CHO (**2e**)	90 (40)	93 (35)	106–108	105–108
6	PhCH$_2$CH$_2$CH$_2$OTHP (**1f**)	PhCH$_2$CH$_2$CHO (**2f**)	93 (30)	91 (25)	96–98/12	97–98/12
7	PhCH(Me)OTHP (**1g**)	PhCOMe (**2g**)	94 (30)	92 (30)	200–202	202
8	4-ClC$_6$H$_4$CH(Me)OTHP (**1h**)	4-ClC$_6$H$_4$COMe (**2h**)	95 (30)	95 (30)	231–232	232
9	PhCH=CHCH$_2$OTHP (**1i**)	PhCH=CHCHO (**2i**)	68 (30)	70 (20)	246–248	248
		PhCHO (**2a**)	23	20		
10	3-O$_2$NC$_6$H$_4$CH=CHCH(Ph)OTHP (**1j**)	3-O$_2$NC$_6$H$_4$CH=CHCOPh (**2j**)	65 (30)	68 (30)	145–146	144–146
		3-O$_2$NC$_6$H$_4$CHO (**2d**)	25	25	106–108	105–108
11	4-PhC$_6$H$_4$CH(Me)OTHP (**1k**)	4-PhC$_6$H$_4$COMe (**2k**)	96 (35)	98 (30)	117–118	116–118
12	α-Tetralol tetrahydropyranyl ether (**1 l**)	α-Tetralone (**2 l**)	90 (40)	96 (25)	114–116	113–116/6
13	Cyclohexanol tetrahydropyranyl ether (**1m**)	Cyclohexanone (**2m**)	80 (30)	85 (30)	153–155	155
14	(−)-Menthol tetrahydropyranyl ether (**1n**)	(−)-Menthone (**2n**)	85 (40)	87 (30)	208–210	207–210
15	Cholesterol tetrahydropyranyl ether (**1o**)	Cholest-5-en-3-one (**2o**)	80 (40)	83 (30)	124–126	125–127

General Procedure for the Oxidative Deprotection of THP Ethers with 2,2′-*Bipyridinium Chlorochromate*.—To a solution of THP ether

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†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

(1 mmol) in MeCN (15 ml) was added 2,2′-bipyridinium chlorochromate (0.438 g, 1.5 mmol) and the mixture was stirred magnetically under reflux conditions for 15–35 min. The progress of the reaction was monitored by GLC or TLC (eluent: n-hexane-ethyl acetate, 20:1). After completion of the reaction, silica gel (2 g) was added and the mixture was stirred at room temperature for 5 min. The reaction mixture was filtered and the solid material was washed with MeCN (15 ml). The combined filtrates were evaporated on a rotary evaporator and the resulting crude material was purified on a silica-gel plate or silica-gel column with appropriate eluent. Evaporation of the solvent afforded pure carbonyl compound; yield 68–98% (Table 1).

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