3-Carboxypyridinium Chlorochromate (CPCC):[1] A Mild, Efficient and Inexpensive Reagent for Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers under Non-Aqueous Conditions

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Primary and secondary trimethylsilyl and tetrahydropyranyl (THP) ethers are converted to their carbonyl compounds efficiently using 3-carboxypyridinium chlorochromate. Trimethylsilyl ethers are oxidized selectively in the presence of tetrahydropyranyl ethers.

Direct oxidation of trimethylsilyl ethers to the corresponding carbonyl compounds has found considerable attention during recent years.[1-15] However, some of the reported methods show limitations such as the requirement for aqueous reaction conditions,[5,8] use of expensive reagents,[10,14,15] long reaction times,[7,9] low yields of the products[13] and tedious workup.[8] Therefore, introduction of new methods and inexpensive reagents for such functional group transformations is still in demand.

Tetrahydropyranyl (THP) is a useful protecting group for alcohols in organic synthesis. Many catalysts have been proposed for the tetrahydropyranylation of alcohols and the cleavage of tetrahydropyranyl ethers to the parent alcohols.[16-26] Direct oxidation of tetrahydropyranyl ethers to their carbonyl compounds is a useful practical achievement. This oxidation is rather rare in the literature and only few reports are available.[27,28]

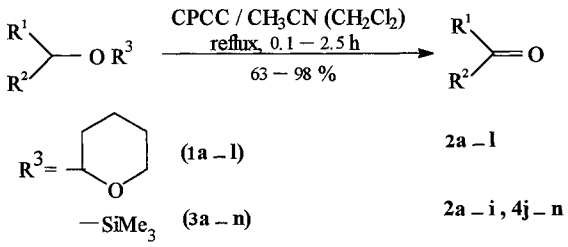
Recently, we have introduced 3-carboxypyridinium chlorochromate as an efficient reagent for cleavage of the carbon–nitrogen double bonds under non-aqueous conditions.[1] We now report a new and convenient method for the oxidative deprotection of tetrahydropyranyl ethers to their carbonyl compounds in high yields using 3-carboxypyridinium chlorochromate.[1] In refluxing acetonitrile this reagent is able to convert primary and secondary tetrahydropyranyl ethers **1a–l** to their corresponding aldehydes and ketones **2a–l** (Scheme 1, Table).

Table. Oxidative Deprotection of Tetrahydropyranyl (THP) and Trimethylsilyl Ethers with 3-Carboxypyridinium Chlorochromate

Substrate	Reaction Time (h)	Product	Yield (%)	mp (°C) or bp (°C)/Torr	
				found	reported[30]
$PhCH_2OTHP$ (**1a**)	0.1	PhCHO (**2a**)	94[a]	176–178/760	178–179/760
2-$MeOC_6H_4CH_2OTHP$ (**1b**)	0.1	2-$MeOC_6H_4CHO$ (**2b**)	96	236–238/760	238/760
3-$MeOC_6H_4CH_2OTHP$ (**1c**)	0.1	3-$MeOC_6H_4CHO$ (**2c**)	93	141–142/50	143/50
	0.75		62[b]		
4-$MeOC_6H_4CH_2OTHP$ (**1d**)	0.1	4-$MeOC_6H_4CHO$ (**2d**)	93	247–248/760	248/760
	0.75		65[b]		
2-$NO_2C_6H_4CH_2OTHP$ (**1e**)	0.5	2-$NO_2C_6H_4CHO$ (**2e**)	80	151–153/23	153/23
3-$NO_2C_6H_4CH_2OTHP$ (**1f**)	0.5	3-$NO_2C_6H_4CHO$ (**2f**)	85	57–58	57–59
α-tetralol tetrahydropyranyl ether (**1g**)	0.15	α-tetralone (**2g**)	98	126–127/23	127/23
	0.75		67[b]		
c-$C_6H_{11}OTHP$ (**1h**)	0.15	cyclohexanone (**2h**)	95[a]	153–155/760	155/760
$C_6H_{13}CH_2OTHP$ (**1i**)	0.1	$C_6H_{13}CHO$ (**2i**)	78[a]	152–153/760	153/760
2,5-$(MeO)_2C_6H_3CH_2OTHP$ (**1j**)	0.15	2,5-$(MeO)_2C_6H_3CHO$ (**2j**)	97	50–52	49–52
(*E*)-PhCH=$CHCH_2OTHP$ (**1k**)	0.15	(*E*)-PhCH=CHCHO (**2k**)	63	246–247/760	248/760
		PhCHO (**2a**)	30	176–178/760	178–179/760
(−)-menthol tetrahydropyranyl ether (**1l**)	0.5	(−)-menthone (**2l**)	90	208–210/760	207–210/760
$PhCH_2OSiMe_3$ (**3a**)	0.75	**2a**	97[a]	176–178/760	178–179/760
2-$MeOC_6H_4CH_2OSiMe$ (**3b**)	0.75	**2b**	93	236–238/760	238/760
3-$MeOC_6H_4CH_2OSiMe_3$ (**3c**)	0.75	**2c**	90	141–142/50	143/50
4-$MeOC_6H_4CH_2OSiMe_3$ (**3d**)	0.75	**2d**	90	247–248/760	248/760
2-$NO_2C_6H_4CH_2OSiMe_3$ (**3e**)	2.5	**2e**	92	151–153/23	153/23
3-$NO_2C_6H_4CH_2OSiMe_3$ (**3f**)	2	**2f**	94	58–59	57–59
α-tetralol trimethylsilyl ether (**3g**)	0.75	**2g**	97	126–127/23	127/23
c-$C_6H_{11}OSiMe_3$ (**3h**)	0.75	**2h**	89[a]	153–155/760	155/760
$C_6H_{13}CH_2OSiMe_3$ (**3i**)	0.75	**2i**	88[a]	152–153/760	153/760
$Ph_2CHOSiMe_3$ (**3j**)	2	benzophenone (**4j**)	80	50–51	49–51
4-$PhC_6H_4CH(Me)OSiMe_3$ (**3k**)	2	4-PhC_6H_4COMe (**4k**)	98	117–118	116–118
$PhCH_2CH(Ph)OSiMe_3$ (**3l**)	1.15	$PhCH_2COPh$ (**4l**)	98	55–57	55–56.5
$PhCH_2CH_2CH(Me)OSiMe_3$ (**3m**)	1.15	$PhCH_2CH_2COMe$ (**4m**)	96	234–235/760	235/760
$PhCH(Me)OSiMe_3$ (**3n**)	1.15	acetophenone (**4n**)	93[a]	200–202/760	202/760

[a] Yield based on the isolation of 2,4-dinitrophenylhydrazine derivative.
[b] Oxidation was carried out in refluxing CH_2Cl_2.

In addition, we also report oxidative deprotection of trimethylsilyl ethers with this reagent under mild conditions and in high yields. Primary and secondary trimethylsilyl ethers **3a–n** are converted to their corresponding carbonyl compounds **2a–i,4j–n** by 3-carboxypyridinium chlorochromate in refluxing dichloromethane (Scheme 1, Table). Overoxidation of the products was not observed by this method.



Scheme 1

We have also competitively oxidized tetrahydropyranyl and trimethylsilyl ethers and found that trimethylsilyl ethers are oxidized selectively in the presence of tetrahydropyranyl ethers with this reagent in refluxing dichloromethane (Scheme 2).

In conclusion 3-carboxypyridinium chlorochromate represents a convenient reagent for one-pot oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers to their corresponding carbonyl compounds. This reagent also shows high selectivity for the oxidation of trimethylsilyl ethers in the presence of tetrahydropyranyl ethers. Oxidation of tetrahydropyranyl ethers with other chlorochromates is under investigation.

Trimethylsilyl and tetrahydropyranyl ethers were prepared according to described procedures.[26,29] All oxidation products are known compounds; they are identified by comparison of their physical data, IR and NMR spectra with those of authentic samples. Yields refer to isolated products or their 2,4-dinitrophenylhydrazones. IR spectra were recorded on a Philips PU9716 spectrophotometer. Melting points were determined using a Mettler FP 5 apparatus and are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ solvent on a Bruker AM 80 MHz spectrometer using TMS as an internal standard. GC analysis was performed with a Shimadzu 16 A Gas Chromatograph with a flame ionization detector using a column of 15% Carbowax 20M Chromosorb-W 60–80 mesh.

3-Carboxypyridinium chlorochromate (CPCC) was prepared as described previously.[1]

Oxidative Deprotection of Tetrahydropyranyl Ethers 1a–l; General Procedure:

To a solution of tetrahydropyranyl ether **1** (1 mmol) in MeCN (15 mL) in a 50 mL round-bottomed flask equipped with a condenser and a magnetic stirrer, was added 3-carboxypyridinium chlorochromate (0.519 g, 2 mmol). The reaction mixture was refluxed for 0.1–0.5 h. The progress of the reaction was monitored by GC or TLC (eluent: hexane/EtOAc, 40:1). The mixture was filtered and the solid material was washed with MeCN (20 mL). The filtrate was evaporated and the resulting crude material was purified on a silica gel plate or silica gel column with appropriate eluent. Pure carbonyl compounds **2a–l** were obtained in 63–98% yields (Table).

Oxidative Deprotection of Trimethylsilyl Ethers 3a –n; General Procedure:

In a round-bottomed flask (50 mL) equipped with a magnetic stirrer and a condenser, a solution of trimethylsilyl ether **3** (1 mmol) in CH_2Cl_2 (20 mL) was prepared. 3-Carboxypyridinium chlorochromate (0.519 g, 2 mmol) was added to the solution and refluxed for 0.75–2.5 h. The progress of the reaction was monitored by GC or TLC (eluent: CCl_4/Et_2O, 3:1). The mixture was filtered and the solid material was washed with CH_2Cl_2 (20 mL). The filtrate was evaporated on a rotary evaporator and the resulting crude material was purified on a silica gel plate or silica gel column with appropriate eluent. Pure carbonyl compounds **2a–i,4j–n** were obtained in 80–98% yields (Table).

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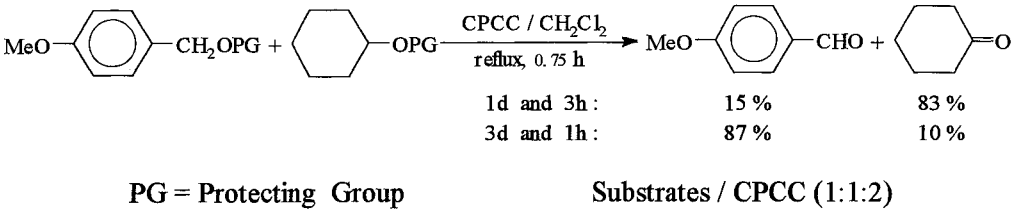

Scheme 2

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