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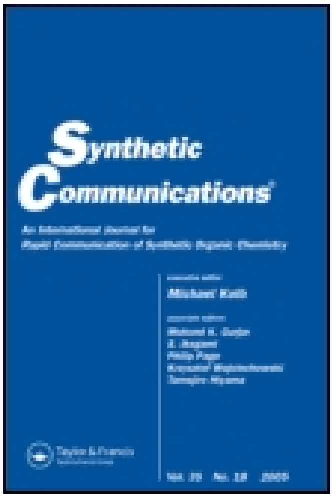

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Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers and of Ethylene Acetals with Tetramethylammonium Chlorochromate

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Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers and of Ethylene Acetals with Tetramethylammonium Chlorochromate

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ABSTRACT

This paper describes the preparation of tetramethylammonium chlorochromate (**TMACC**) as a new and efficient reagent for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers or ethylene acetals and ketals to the corresponding carbonyl

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compounds in refluxing acetonitrile in the presence of catalytic amounts of aluminum chloride.

The protection and deprotection of the hydroxy and carbonyl groups play an essential role in synthetic strategy.[1–7] Chromium (VI) oxide is an inexpensive, water-soluble and stable oxidizing reagent, that is commercially available, but this reagent is insoluble in organic solvents. Very recently, we have introduced new reagents to oxidize different substrates.[8] We now report **TMACC 1** as a new and efficient reagent for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers or ethylene acetals and ketals to the corresponding carbonyl compounds in refluxing acetonitrile in the presence of catalytic amounts of aluminum chloride.

This reagent is an orange powder, which is prepared by the dropwise addition of CrO_3 in 6 N HCl solution to an aqueous solution of tetramethylammonium chloride at room temperature. Filtration and drying of the precipitates produced an orange powder, which could be stored for months without losing its oxidation ability. This reagent is quite soluble in methylene chloride, chloroform, acetone, and acetonitrile and insoluble in non-polar solvents such as carbon tetrachloride, *n*-hexane, and diethyl ether (Sch. 1).

Since deprotection of benzyltrimethylsilyl ether in refluxing acetonitrile with this reagent failed in the absence of catalyst, the effect of several Lewis acids such as $ZnCl_2$, $FeCl_3$, $FeBr_3$, $SnCl_2$, $SnCl_4$, $CuCl_2$, $BiCl_3$, $AlBr_3$, and $AlCl_3$ were also examined. Surprisingly, only $AlCl_3$ was shown to be effective catalyst for this purpose (Table 1). The reaction in the presence of $ZnCl_2$, $FeCl_3$, $FeBr_3$, $SnCl_2$, $SnCl_4$, $CuCl_2$, $BiCl_3$, and $AlBr_3$ (0.5 mmol) proceeds with lower efficiency even with a higher molar ratio of the oxidant (1.5 mmol) in comparison with the amount of oxidant used in the presence of $AlCl_3$ (0.3 mmol). This could be the effect of hardness of $AlCl_3$ in comparison with the other Lewis acids, which have been used in these experiments.

Under these conditions primary and secondary trimethylsilyl ethers were converted to the corresponding carbonyl compounds in high yields and short reaction times (Table 2). The reaction of primary and

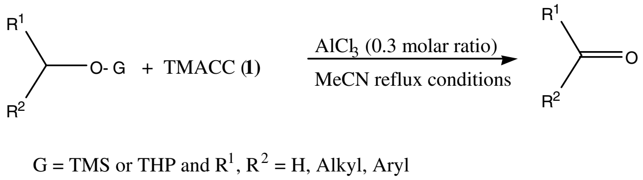
$$Me_4N^+Cl^- + CrO_3\ (HCl\ 6\ N) \xrightarrow[96\ \%]{H_2O/10\ min} \underset{\mathbf{1}}{Me_4N.CrO_3HCl}$$

Scheme 1.

Table 1. Deprotection of benzyltrimethylsilyl ether with reagent **1** with different Lewis acids in acetonitrile under reflux conditions.[a,b]

Entry	Lewis acid	Time (min.)	Yield (%)
1	$ZnCl_2^c$	80	25
2	$CuCl_2$	80	30
3	$FeCl_3^c$	120	30
4	$BiCl_3^c$	70	65
5	$FeBr_3^c$	90	40
6	$SnCl_2^c$	90	30
7	$SnCl_4^c$	90	40
8	$AlBr_3$	80	70
9	$AlCl_3$	60	96

[a] Monitored by TLC analysis.
[b] Oxidant/Alcohol/Lewis acid (1:1:0.3).
[c] Oxidant/Alcohol/Lewis acid (1.5:1:0.5).



Scheme 2.

secondary tetrahydropyranyl ethers with **TMACC** was carried out in acetonitrile under reflux to the corresponding carbonyl compounds in good to excellent yields (Table 2, Sch. 2).

This reagent was also used to convert ethylene acetals to aldehydes and ketones in acetonitrile under reflux conditions in good to excellent yields (Table 3, Sch. 3). It was also found that C=C bonds, methoxy groups, and hydroxy groups remained intact during deprotection (Table 2 and 3).

The tetramethylammonium cation could be recovered in quantitative yield. When the reaction was completed, the reaction mixture was cooled to room temperature and passed through a short pad of silica gel, and then washed with acetonitrile. The silica gel layer was washed with HCl 10% and then this aqueous layer was treated with a fresh bath of a solution of chromium (VI) oxide in HCL 6 N to produce the reagent **1** in quantitave yield.

Table 2. Oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers with **TMACC**/$AlCl_3$ in refluxing MeCN.[a]

Entry	Substrate	Product	Time (min.)	Yield (%)[b]
1	$PhCH_2OTMS$	PCHO	65	96
2	$2\text{-}MeOC_6H_4CH_2OTMS$	$2\text{-}MeOC_6H_4CHO$	90	86
3	$3\text{-}MeOC_6H_4CH_2OTMS$	$2\text{-}MeOC_6H_4CHO$	65	98
4	$3\text{-}O_2NC_6H_4CH_2OTMS$	$3\text{-}O_2NC_6H_4CHO$	100	92
5	$2,5\text{-}(MeO)_2C_6H_3CH_2OTMS$	$2,5\text{-}(MeO)_2C_6H_3CHO$	65	95
6	PhCH(Me)OTMS	PhCOMe	45	98
7	$4\text{-}ClC_6H_4CH(Me)OTMS$	$4\text{-}ClC_6H_4COMe$	80	92
8	$Ph_2CHOTMS$	Ph_2CO	40	98
9	$4\text{-}PhC_6H_4CH(Me)OTMS$	$4\text{-}PhC_6H_4COMe$	55	96
10	$CH_3(CH_2)_5OTMS$	$CH_3(CH_2)_4CHO$	80	90
11	$C_6H_5CH{=}CHCH_2OTMS$	$C_6H_5CH{=}CHCHO$	45	88
12	MentolTMS	Menthone	60	88
13	4-COOH– $C_6H_4CH_2OTMS$	4-COOH– C_6H_4CHO	55	90
14	TetralolTMS	Tetralone	55	98
15	2-Methylcyclohexyl-TMS	2-Methylcyclohexanone	60	85
16	Benzoin-TMS	Benzil	60	95
17	$PhCH_2OTHP$	PhCHO	45	98
18	$2\text{-}MeOC_6H_4CH_2OTHP$	$2\text{-}MeOC_6H_4CHO$	80	85
19	$3\text{-}MeOC_6H_4CH_2OTHP$	$3\text{-}MeOC_6H_4CHO$	60	85
20	$4\text{-}MeOC_6H_4CH_2OTHP$	$4\text{-}MeOC_6H_4CHO$	70	80
21	$3,4\text{-}(MeO)_2C_6H_3CH_2OTHP$	$3,4\text{-}(MeO)_2C_6H_3CHO$	60	80
22	$2,5\text{-}(MeO)_2C_6H_3CH_2OTHP$	$2,5\text{-}(MeO)_2C_6H_3CHO$	60	88
23	PhCH(Me)OTHP	PhCOMe	35	98
24	$4\text{-}ClC_6H_4CH(Me)OTHP$	$4\text{-}ClC_6H_4COMe$	60	85
25	$Ph_2CHOTHP$	Ph_2CO	35	90
26	$CH_3(CH_2)_5OTHP$	$CH_3(CH_2)_4CHO$	60	94
27	$C_6H_5CH{=}CHCH_2OTHP$	$C_6H_5CH{=}CHCHO$	55	92
28	MentolTHP	Menthone	50	90
29	4-COOH– $C_6H_4CH_2OTHP$	4-COOH– C_6H_4CHO	50	90
30	TetralolTHP	Tetralone	50	88
31	2-Methylcyclohexyl-TMS	2-Methylcyclohexanone	50	88
32	Benzoin-THP	Benzil	55	92

[a] Substrate/Oxidant/$AlCl_3$ (1:1:0.3).

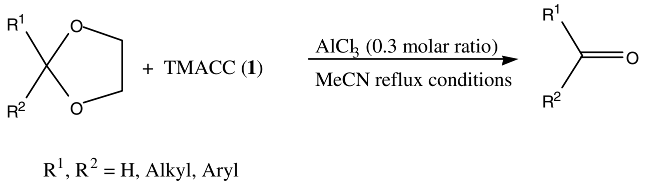
[b] Yields based on the products after column chromatography.

Table 3. Deprotection of ethylene acetals with **TMACC**/$AlCl_3$ in refluxing MeCN.[a]

Entry	Substrate	Product	Time (min.)	Yield (%)[b]
1	Acetophenone ethylene acetal	Acetophenone	30	94
2	2-Methoxybenzaldehyde ethylene acetal	2-Methoxybenzaldehyde	40	92
3	3-Nitrobenzaldehyde ethylene acetal	3-Nitrobenzaldehyde	60	90
4	4-Chloroactophenone ethylene acetal	4-Chloroactophenone	50	92
5	Tetralone ethylene acetal	Tetralone	45	98
6	4-Phenylacetophenone ethylene acetal	4-Phenylacetophenone	50	94
7	Menthone ethylene acetal	Menthone	45	91
8	Cyclohexanone ethylene acetal	Cyclohexanone	60	88
9	2-Methylcyclohexanone ethylene acetal	2-Methylcyclohexanone	60	90
10	4-*t*-butylcyclohexanone ethylene acetal	4-*t*-butylcyclohexanone	70	88
11	Cinnamaldehyde ethylene acetal	Cinnamaldehyde	30	92
12	6-Hydroxyhexanal ethylene acetal	6-Hydroxyhexanal	60	85

[a] Substrate/Oxidant/$AlCl_3$ (1:1:0.3).

[b] Yields based on the products after purification with column chromatography.



Scheme 3.

In order to evaluate the synergy between **TMACC** and aluminum chloride, several experiments were performed. The reaction of $2\text{-MeOC}_6H_4CH_2OTMS$ (1 mmol) with **TMACC** (1 mmol) without aluminum chloride failed after 2 h refluxing in acetonitrile. When equimolar amount of aluminum chloride and $2\text{-MeOC}_6H_4CH_2OTMS$

was refluxed in acetonitrile without **TMACC** for 2 h, the corresponding alcohol was obtained in only 20% yield. Only when **TMACC** was used in the presence of a catalytic amount of aluminum chloride (0.3 mmol) the corresponding aldehyde obtained in excellent yield (Table 1).

EXPERIMENTAL

Trimethylsilyl ethers, tetrahydropyranyl ethers, ethylene acetals were prepared according to described procedures.[4–7] All yields refer to isolated products. The products were characterized by comparison with authentic samples (IR, ^{1}H-NMR spectra, melting and boiling points and TLC). All ^{1}H-NMR spectra were recorded at 300 MHz in $CDCl_3$ and CCl_4 relative to TMS (0.00 ppm).

Preparation of Tetramethylammonium Chlorochromate 1 (TMACC)

A solution of tetramethylammonium chloride (10.95 g, 100 mmol) in 100 ml of water was prepared, and then CrO_3 (10.0 g, 100 mmol) in HCl 6 N (50 ml) was added dropwise to the above solution and stirred for 10 min. at room temperature. The resulting orange precipitate was filtered and washed with cooled distilled water (2 × 50 ml), and dried in a desiccator under vacuum over calcium chloride to afford an orange powder (20.2 g, 96% yield), which decomposed at 210–212°C to a dark-brown material. ^{1}H-NMR: d 3.58 (s). Anal. Calcd. for $C_4H_{13}ClCrNO_3$: C, 22.80; H, 6.18%. Found: C, 22.96; H, 6.28%.

General Procedures. Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers with TMACC/$AlCl_3$

In a round-bottomed flask (25 mL) equipped with a reflux condenser and a magnetic stirrer, a solution of trimethylsilyl ether or tetrahydropyranyl ether (1 mmol) and $AlCl_3$ (0.04 g, 0.3 mmol) in acetonitrile (10 mL) was prepared. **TMACC** (0.21 g, 1 mmol) was added to the solution and refluxed for time specified in Table 2. The reaction progress was followed by TLC (eluent: cyclohexane/EtOAc: 8:2). To remove the tetramethylammonium cation, the reaction mixture was cooled to room temperature and the mixture was passed through a short pad of silica gel and washed with acetonitrile (15 mL). The filtrate was evaporated and the resulting crude material was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (10:90).

Conversion of Ethylene Acetals and Ketals to the Corresponding Carbonyl Compounds with TMACC/$AlCl_3$

In a round-bottomed flask (25 mL) equipped with a reflux condenser and a magnetic stirrer, a solution of ethylene acetal or ketal (1 mmol) and $AlCl_3$ (0.04 g, 0.3 mmol) in acetonitrile (10 mL) was prepared. Tetramethylammonium chlorochromate (0.21 g, 1 mmol) was added to the solution and refluxed for the time being specified in Table 3. The reaction progress was followed by TLC (eluent: cyclohexane/EtOAc: 8:2). The reaction mixture was then cooled to room temperature and passed through a short pad of silica gel and washed with acetonitrile (15 mL). The filtrate was evaporated and the resulting crude material was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (10:90).

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