An Efficient Method for Selective Deprotection of Trimethylsilyl Ethers and Tetrahydropyranyl Ethers under Solvent-free Conditions

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1-Butyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (BAABOD) **3** is a useful reagent for the selective cleavage of trimethylsilyl ethers and tetrahydropyranyl ethers to their corresponding aldehydes and ketones in the presence of $AlCl_3$ under solvent-free conditions. This method is very simple and efficient and the reaction has been carried out under solvent-free conditions in the presence of a catalytically amount of aluminum chloride.

Key Words : Deprotection, Trimethylsilyl ether, Tetrahydropyranyl ethers, Solvent-free

Introduction

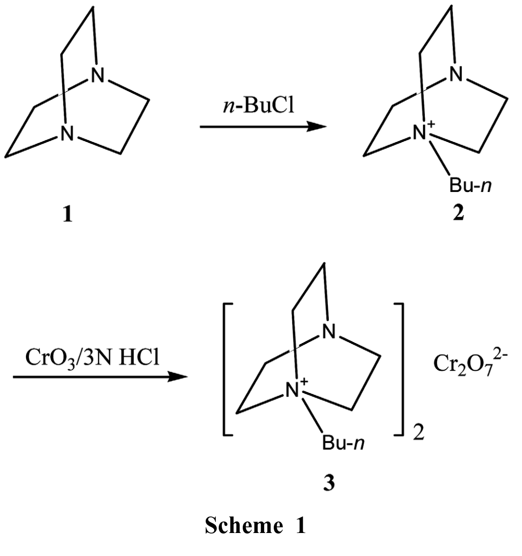
Development of a mild and selective method for the protection of functional groups and then deprotection of the protected derivatives continues to be a significant aspect in the synthetic organic chemistry of polyfunctional molecules including the total synthesis of natural products. Thus a large variety of protective groups has been developed along with numerous methods for their removal.

Trimethylsilyl ether and tetrahydropyranyl ether are widely used as protective groups during the modern synthesis of natural compounds.[1-3]

A wide variety of methods are available for the conversion of alcohols to their trimethylsilyl ether and tetrahydropyranyl ether and several attention has been paid for deprotection of these derivatives to the parent alcohol or to their corresponding carbonyl compounds via oxidative cleavage of the protected groups.[4-19]

Heterogeneous reactions that are facilitated by supported reagents on various inorganic surfaces have recently attracted attention.[20] The most advantage of these methods over conventional classical method is that they show cleaner reactions, decreased reaction time and straightforward work-up.

In continuation of our ongoing program to develop environmentally benign methods using solid supports,[20] we wish herein to introduce 1-butyl-4-aza-1-azoniabicyclo-[2.2.2] octane dichromate **3** for deprotection oxidation of trimethylsilyl ether and tetrahydropyranyl ether to the corresponding carbonyl compounds in the presence of $AlCl_3$ under solvent-free conditions. This new reagent has been readily prepared by reaction of an aqueous solution of 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride **2** with CrO_3 in 3N solution of HCl at room temperature as shown in Scheme 1. The resulting orange powder which can be stored for months without losing its activity is soluble in acetonitrile, acetone and *N,N*-dimethylformamide and slightly soluble in chloroform, ethylacetate and dichloromethane, but is not soluble in carbon tetrachloride, *n*-hexane and diethyl ether.



Scheme 1

Table 1. Deprotection of Benyltrimethylsilyl Ether with Reagent **1** in the Presence of Different Lewis Acids under solvent-free.conditions[a,b]

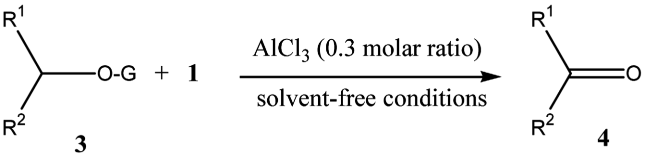
Entry	Lewis acid	Time (sec)	Yield (%)
1	$ZnCl_2$[c]	80	25
2	$CuCl_2$	80	30
3	$FeCl_3$[c]	120	30
4	$BiCl_3$[c]	70	65
5	$FeBr_3$[c]	90	40
6	$SnCl_2$[c]	90	30
7	$SnCl_4$[c]	90	40
8	$AlBr_3$	80	70
9	$AlCl_3$	65	100

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

This reagent is able to deprotected TMS- and THP-protected molecules to their corresponding carbonyl compounds. Since deprotection of butyltrimethylsilyl ether under solvent-free conditions 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 under solvent-free conditions. 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.

The optimum molar ratio of aluminum chloride for this purpose was 0.3 molar ratio. One equimolar of TMS- or THP-protected alcohols **4** were mixed with **3** in the presence of 0.3 molar ratio of aluminum chloride in a mortar and ground with a pestle until TLC showed complete disappearance of starting TMS or THP derivatives (Scheme 2). Following the reaction by TLC shows that by disappearing the starting materials spots, the corresponding carbonyl compounds appeared as the only product and no by-product was observed. The reactions were completed within 50-100 Sec and the pure carbonyl compounds were obtained by a straightforward work-up. The results illustrated in Table 2 indicate that the reaction can be used for a variety of TMS- and THP- protected alcohols.

In conclusion, we have developed a mild, fast and efficient



G = TMS or THP and R^1, R^2 = H, Alkyl, aryl

Scheme 2

Table 2. Deprotection of Tetrahydropyranyl (THP) and Trimethylsilyl (TMS) ethers **4** with reagent 3 in the presence of $AlCl_3$[a]

Entry	Substrate	Product	Time (Sec)	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	50	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	$4\text{-}COOH\text{-}C_6H_4CH_2OTMS$	$4\text{-}COOH\text{-}C_6H_4CHO$	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	90
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	60	98
24	$4\text{-}ClC_6H_4CH(Me)OTHP$	$4\text{-}ClC_6H_4COMe$	60	85
25	$Ph_2CHOTHP$	Ph_2CO	65	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	$4\text{-}COOH\text{-}C_6H_4CH_2OTHP$	$4\text{-}COOH\text{-}C_6H_4CHO$	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.

method for the cleavage of TMS- and THP-ether under solvent-free conditions, which is superior to previously reported methods in terms of selectivity, high yield, purity of the products, simple and rapid work-up. This method does not require a large excess of reagent and long reaction time. Notably ether, nitro, halogen and double bond functional groups present in the molecules were found to be resistant under the employed conditions.

Experimental Section

General. Trimethylsilyl ethers and tetrahydropyranyl ethers were prepared according to described procedures.[16-18] All of the products were characterized by comparison of their spectral (IR, ^{1}H-NMR and TLC) and physical data (melting and boiling point) with those of authentic samples.[16-18] All 1H-NMR spectra were recorded at 300 MHz in $CDCl_3$ and CCl_4 relative to TMS (0.00 ppm). All of the reactions were carried out in a hood with strong ventilation. Spectra of solids were carried out using KBr pellets.

Preparation of 1-butyl-4-aza-1-azoniabicyclo[2.2.2]-octane chlorochromate: A solution of 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane chloride (12.45 g, 50 mmol) in 50 mL of water was prepared, and then CrO_3 (10.0 g, 100 mmol) in HCl 3 N (100 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 (25.76, 46.1 mmol, 93% yield), which decomposed at 117-118 °C to a dark-brown material. ^{1}H-NMR (d_6-DMSO, 500 MHz): δ= 3.84-3.53 (m, 24 H), 1.65-0.91 (m, 18 H). ^{13}C-NMR (d_6-DMSO, 125 MHz) δ= 64.74, 51.86, 44.93, 41.45, 41.29, 41.12, 40.95, 40.79, 40.62, 40.46, 24.69, 20.42, 14.83;. Anal. Calcd. For $C_{20}H_{42}N_4Cr_2O_7$: C, 43.32; H, 7.58; N, 10.11. Found: C, 43.15; H, 7.68; N, 10.30.

General procedure.

Deprotection of TMS-, THP- ether: The deprotection of 2-nitrobenzyl alcohol TMS ether is representative of the general procedure employed. In a mortar a mixture of the 2-nitrobenzyl alcohol TMS ether (0.39 g, 1.6 mmole), 1-butyl-4-aza-1-azoniabicyclo[2.2.2]octane dichromate (0.89 g, 1.6 mmole) and aluminum chloride (65.1 mg, 0.16 mmole) was added in one portion. The mixture was ground with a pestle for the specified time (Table 2). After completion of the reaction (following by TLC), CCl_4 (15 mL) was added to the reaction mixture and after vigorous stirring the mixture was filtered off and the solvent was evaporated by rotary evaporator. The residue was purified by column chromatography using silica gel (EtOAc/cyclohexane, 1 : 9) to afford pure 2-nitrobenzaldehyde.

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