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CARO'S ACID SUPPORTED ON SILICA GEL. PART V: A MILD AND SELECTIVE REAGENT FOR CONVERSION OF TRIMETHYL SILYL ETHERS TO THE CORRESPONDING HYDROXY COMPOUNDS

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Mild and efficient method for deprotection of silyl ethers to alcohols is described using Caro's acid supported on silica gel. Reactions are carried out in dichloromethane at room temperature and their parent hydroxy compounds obtained in good to excellent yields. Using this procedure, tetrahydropyranyl ethers (THP) remain intact during desilylation reaction.

Keywords: Caro's acid; desilylation; tetrahydropyranyl ethers; trimethyl silyl ethers

Hydroxyl groups are present in a number of compounds of biological and synthetic interest including nucleosides, carbohydrates, steroids, and the side chain of some amino acids. During oxidation, acylation and halogenation with phosphorus- or hydrogen halides, or dehydration reaction of these compounds a hydroxyl group must be protected.¹ The protective group must be selectively removed in good yield by readily available preferably nontoxic reagents that do not attack the regenerated functional group.

The trimethyl silyl group has been used widely as a protective group for alcohols. Their popularity is due in part to their ease of formation and removal and their stability to a wide range of reagents and reaction conditions.²

There are several known methods for the deprotection of silyl ethers.³ These include catalytic transfer hydrogenation using Pd,⁴ reductive cleavage by DIBAL-H,⁵ ultrasonic cleavage in MeOH/CCl₄,⁶ DDQ,⁷ CAN,⁸ CAN-SiO₂,⁹ I₂,¹⁰ K₂CO₃/EtOH,¹¹ LiCl/DMF/H₂O/90°C,¹²

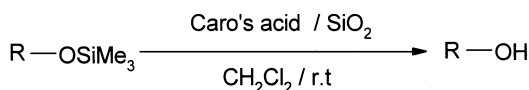
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DMSO/H₂O/90°C,¹³ CBr₄/MeOH/65°C,¹⁴ TASF/DMF,¹⁵ I₂/MeOH,¹⁶ TMSCl/MeCN/H₂O,¹⁷ SC(OTf)₃,¹⁸ bismuth bromide in wet acetonitrile,¹⁹ potassium fluoride,²⁰ hydrogen fluoride,²¹ acetic anhydride and iron(III),²² aqueous acetic acid,²³ aqueous mineral acids,²⁴ boron trifluoride etherate,²⁵ fluoroborate salts,²⁶ NBS in DMSO,²⁷ sodium azide in DMF,²⁸ sodium hydride in HMPA,²⁹ P(MeNCH₂CH₂)₃N,³⁰ and TBAF/THF,³¹ and have been described well in the literatures.

Protic as well as aqueous conditions are not safe for sensitive compounds and suffer from aqueous work-up which makes difficult the isolation of water soluble compounds. Some procedures that do not need water for work-up suffer very seriously from long reaction time. Using oxidizing agents for deprotection, the corresponding carbonyl groups may be obtained due to oxidation of the parent alcohols.³² Although Caro's acid is a strong oxidizing agent, its utility in organic synthesis has been limited by its insolubility in common organic solvents, and its rapid deactivation on storage. This reagent is prepared in situ from potassium persulfate and sulfuric acid.³³ Caro's acid has been used recently for oxidation of organic compounds.³⁴ We herein have examined Caro's acid supported on silica gel for selective deprotection of silyl ethers.

We found that Caro's acid supported on silica gel can be used to deprotect aliphatic as well as aromatic silyl ethers to the corresponding hydroxy compounds in good to excellent yields under mild conditions (Scheme 1).



SCHEME 1



The typical reaction consists of stirring the trimethyl silyl ethers with equimolar quantity of the reagent in dichloromethane.

RESULTS AND DISCUSSION

As seen in Table I, a variety of TMS ethers were treated with this oxidizing agent at ambient temperature. Aryl silyl ethers as well as alkyl silyl ethers were easily converted to the corresponding parent hydroxy compounds.

An advantage must be mentioned in that although Caro's acid is a powerful oxidant it never oxidizes the parent alcohol. At the above conditions this reagent does not affect the THP ethers even after 24 h.

TABLE I Deprotection of Silyl Ethers Using Caro's Acid Supported on Silica Gel

Entry	Substrate	Product ^a	Time (min) ^b	Yield (%) ^c
1	C ₆ H ₅ CH ₂ OSiMe ₃	C ₆ H ₅ CH ₂ OH	20	93
2	o-ClC ₆ H ₄ CH ₂ OSiMe ₃	o-ClC ₆ H ₄ CH ₂ OH	1.5	96
3	p-ClC ₆ H ₄ CH ₂ OSiMe ₃	p-ClC ₆ H ₄ CH ₂ OH	3	94
4	C ₆ H ₅ OSiMe ₃	C ₆ H ₅ OH	5	93
5	2,4-(Me) ₂ C ₆ H ₃ OSiMe ₃	2,4-(Me) ₂ C ₆ H ₃ OH	20	90
6	PhCH=CHCH ₂ OSiMe ₃	PhCH=CHCH ₂ OH	12	94
7	o-MeC ₆ H ₄ CH ₂ OSiMe ₃	o-MeC ₆ H ₄ CH ₂ OH	3	96
8	(C ₆ H ₅) ₂ CHOSiMe ₃	(C ₆ H ₅) ₂ CHOH	10	90
9	2,4-(Cl) ₂ C ₆ H ₃ OSiMe ₃	2,4-(Cl) ₂ C ₆ H ₃ OH	40	90
10	C ₆ H ₁₁ OSiMe ₃	C ₆ H ₁₁ OH	10	95
11	C ₆ H ₅ COCH(OSiMe ₃)C ₆ H ₅	C ₆ H ₅ COCHOHC ₆ H ₅	25	90
12	C ₆ H ₅ (CH ₂) ₂ OSiMe ₃	C ₆ H ₅ (CH ₂) ₂ OH	2.5	96
13	ClCH ₂ CH ₂ OSiMe ₃	ClCH ₂ CH ₂ OH	10	93
14	CH ₃ (CH ₂) ₆ CH ₂ OSiMe ₃	CH ₃ (CH ₂) ₆ CH ₂ OH	7	94
15	 -SiMe ₃	 -OH	8	95

^aAll products were fully characterized by spectroscopic methods.^bThe reaction was carried out in dichloromethane at room temperature.^cIsolated yields.

In order to show the ability of this reagent in selective deprotection of silyl ethers, equimolar amounts of trimethyl silyl ether and tetrahydropyranyl ether were dissolved in CH₂Cl₂ and treated with Caro's acid on silica gel. As shown in Table II, after a short time trimethyl silyl ethers were deprotected in excellent yields, while THP ethers were unchanged.

TABLE II Competitive Deprotection of Trimethyl Silyl Ethers to the Corresponding Alcohols in the Presence of THP Ethers

Substrate	Time (min)	Yield (%) ^a
o-ClC ₆ H ₄ CH ₂ OTMS	1.5	96
o-ClC ₆ H ₄ CH ₂ OTHP		0
o-MeC ₆ H ₄ CH ₂ OTMS	3	95
o-MeC ₆ H ₄ CH ₂ OTHP		0
C ₆ H ₅ CH ₂ OTMS	20	93
C ₆ H ₅ CH ₂ OTHP		0
C ₆ H ₅ CH ₂ CH ₂ OTMS	2.5	96
C ₆ H ₅ CH ₂ CH ₂ OTHP		0

^aIsolated yields.

TABLE III Comparison of Caro's Acid Supported on Silica Gel with Some of the Other Reagents in Regeneration of the Hydroxyl Group

Substrate	Condition	Time (min)/Yield (%)	Reagent	Ref.
C ₆ H ₅ CH ₂ OSiMe ₃	CH ₂ Cl ₂ /r.t	3/97	Caro's acid/SiO ₂	—
C ₆ H ₅ CH ₂ OSiMe ₃	n-Hexane/reflux	540/90	O ₂ /CO&Mn salts/SiO ₂	36
C ₆ H ₅ OSiMe ₃	EtOH/H ₂ O/75°C	600/100	K ₂ CO ₃	11
C ₆ H ₅ OSiMe ₃	CH ₂ Cl ₂ /r.t	5/93	Caro's acid/SiO ₂	—
n-C ₈ H ₁₇ OSiMe ₃	THF/H ₂ O/r.t.	1020/96	Distannoxane/ Catalyst	37
CH ₃ CH(CH ₂) ₅ OSiMe ₃				
OSiMe ₃	CH ₂ Cl ₂ /25°C	180/20	Ph ₃ CBF ₄	38
PhCH ₂ OSiMe ₃	Benzene/80°C	5/87	[(NO ₃) ₃ Ce] ₃ H ₂ O ₆	39
PhOSiMe ₃	CH ₃ OH/r.t.	6/98	Mont.K-10	40
C ₅ H ₉ OSiMe ₃	CH ₃ CN/H ₂ O, 80°C/N ₂	720/75	CAN/BrO ₃	41
PhCH=CHCH ₂ OSiMe ₃	n-Hexane/reflux	660/95	O ₂ /CO&Mn salts/SiO ₂	36
C ₆ H ₅ CH ₂ OSiMe ₃	MW	20/96	Zeofen	42

To examine the effect of the silica gel on the deprotection of silyl ethers, we carried out the desilylation reaction only in the presence of silica gel. It has been found that the reaction does not occur and the reaction mixture remained intact under this condition. In comparison with some other reported methods, this method is remarkably convenient, inexpensive, and works at ambient temperature. The advantage of this reagent over other compounds is illustrated in Table III. This method exhibits several preferred qualities for regeneration of parent hydroxy compounds, for example: (1) easier work-up involving only filtering, drying, and concentration. (2) higher selectivity and yields, and (3) simpler experimental manipulations and pure products. Summing up, the Caro's acid supported on silica gel is shown to be a mild, efficient, selective, and practical reagent for the deprotection of various trimethyl silyl ethers to the corresponding alcohols in high to excellent yields.

EXPERIMENTAL

All yields refer to the pure isolated products which were characterized by IR, ¹H-NMR, and comparison with authentic samples. ¹H-NMR spectra were recorded with a EM 360 A (60 MHz) spectrometer. IR spectra

were determined on a SP-1100, P-UV-Com instrument, and trimethyl silyl ethers were prepared according to the reported method.³⁵

PREPARATION OF CARO'S ACID

To ice cooled 98% sulfuric acid (4.7 g) is added in small portions potassium persulfate (4.5 g) with stirring; to this is added crushed ice (13 g) and water (4 g) while the temperature is kept below 15°C. Silica gel (5 g, TLC grade, kieselgel 60 G, particle size 15 μm) is added in portions to the mixture and stirred for 4 h in an ice-water bath. The mixture is then filtered under suction and dried in a desiccator to give a white free flowing powder.

GENERAL DEPROTECTION PROCEDURE

A suspension of trimethyl silyl ether (1 mmol) and Caro's acid/silica gel (0.6 g, 1 mmol) in CH_2Cl_2 (4 ml) is prepared. The mixture is stirred magnetically at room temperature for 1.5–40 min. Progress of the reaction is monitored by TLC (hexane/ethyl acetate 3:1). After completion of the reaction, the reaction mixture was filtered in a sinter glass funnel. Evaporation of solvent on a rotary evaporator gave the desired hydroxy compounds in high yields.

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