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Short Report

Mono and Dibromo-5,5-diethylbarbituric Acids for Cleavage of Trimethylsilyl Ethers

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Os ácidos 1-bromo-5,5-dietilbarbitúrico e 1,3-dibromo-5,5-dietilbarbitúrico foram preparados e usados na conversão de diferentes tipos de éteres de trimetilsilila aos correspondentes compostos carbonílicos em bons rendimentos, em diclorometano, à temperatura ambiente.

1-Bromo and 1,3-dibromo-5,5-diethylbarbituric acid were prepared and used for the conversion of different kinds of trimethylsilyl ethers to the corresponding carbonyl compounds in good yields in dichloromethane at room temperature.

Keywords: mono bromo-5,5-diethylbarbituric acid, dibromo-5,5-diethylbarbituric acid, deprotection, trimethylsilyl ethers, *N*-bromo agent

Introduction

N-Bromo reagents such as *N*-bromosuccinimide (NBS), *N*-bromophthalimide, *N*,*N*-dibromosulphonimide and 1,3-dibromo-5,5-dimethylhydantoinhave found widespread application in organic transformations. *N*-Bromo compounds are widely applicable in industrial processes for the synthesis of drugs, pharmaceuticals and agrochemicals.[1] These materials have also been used as brominating and oxidative agents and can catalyze many organic reactions via in-situ generation of Br^+.[2]

Effective methods for protection and deprotection of functional groups play a major role in the total synthesis of natural products. Trimethylsilyl ethers have attained a position of prominence in the area of hydroxyl group protection due to their ease of formation, removal, and stability to a wide range of reagents and reaction conditions.[4,5] Although there are many new reports on the protection and deprotection of silyl ether groups,[6-19] only a few procedures for the oxidative deprotection are known.[20-28] Some of these procedures utilize expensive and hazardous reagents, Lewis acid catalysts, need long reaction times, afford low yields, and need tedious work up. Thus, there is still a need for developing mild and eco-friendly procedures for the oxidative deprotection of trimethylsilyl ethers. In continuation of our earlier work on the application of a series of *N*-bromo reagents,[3] here we report the preparation of some bromo compounds that are stable and applicable for different purposes.

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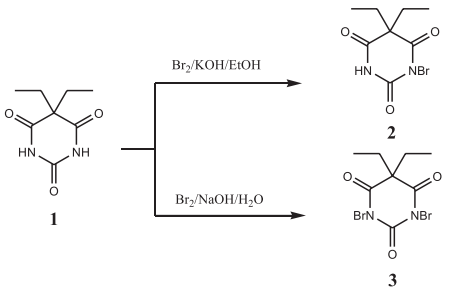
Results and Discussion

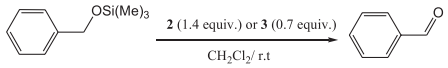
At first, mono (**2**) and dibromo-1,5-diethylbarbituric acid (**3**)[29] were produced and used for the cleavage of trimethylsilyl ethers. It was found that after treatment of **1** with KOH and molecular bromine after 2 hours, compound **2** was produced in 65% yields. The addition of molecular bromine to a mixture of NaOH and **1** in water gave compound **3** in 80% yield (see experimental section) (Scheme 1). Compounds **2** and **3** are stable and can be stored for several months without losing their activity.



Scheme 1.

At this point we decided to check the applicability of these new reagents for organic transformations. Therefore, reaction of benzyl trimethylsilyl ether was performed in the presence of **2** (1.4 equiv.) in dichloromethane and reaction was completed after 3 hours at room temperature, leading to benzaldehyde. The same reaction was

investigated using 0.7 equivalents of compound **3**, and the reaction was completed after 0.5 hours (Scheme 2).



Scheme 2.

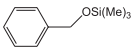
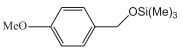
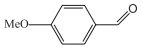
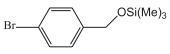
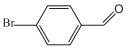
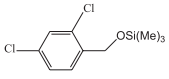
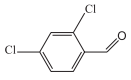
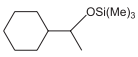
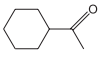
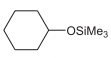
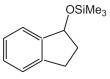
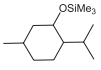
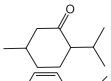
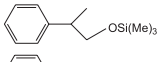
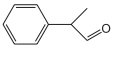
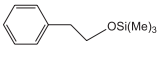
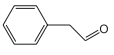
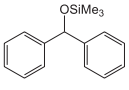
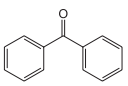
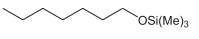
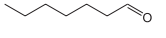
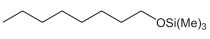
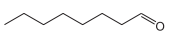
The conversion of benzyl trimethylsilyl ether to benzaldehyde in the presence of both **2** and **3** was also conducted in different solvents. The results show that the efficiency and the yield of the reaction in dichloromethane were better than in other solvents (Table 1).

Table 1. Solvent effects on conversion of benzyl trimethylsilyl ether to benzaldehyde in the presence of **2** or **3**

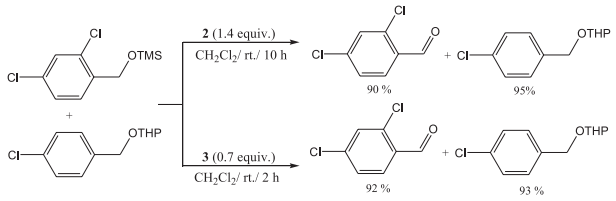
Entry	Solvent	**2**		**3**	
		time/h	Yield/(%)	time/h	Yield/(%)
1	CH_2Cl_2	3	91	0.5	90
2	CCl_4	48	0	48	0
3	$CHCl_3$	24	50	24	70
4	CH_3CN	24	90	12	90

Cleavage of different types of trimethylsilyl ethers was next investigated. The results showed that a variety of primary and secondary trimethylsilyl ethers were converted to the corresponding carbonyl compounds selectively in good to excellent yields, without any over oxidation. Benzylic trimethylsilyl ethers were converted to the corresponding carbonyl groups more easily than other silyl ethers. We predicted that the oxidative reaction has been performed via in-situ generation of Br^+.[3] The results are tabulated in Table 2. In order to check the chemoselectivity of the described systems some competitive reactions were conducted. A 1:1 mixture of 2,4-dichlorobenzyl trimethylsilyl ether and 4-chlorobenzyl tetrahydropyranyl ether was subjected to oxidation by **2** or **3** in CH_2Cl_2 at room temperature. We have observed that either **2** or **3** promoted the deprotection of 2,4-dichlorobenzyl trimethylsilyl ether with concomitant oxidation leading to 2,4-dichlorobenzaldehyde in good yield. We have also observed that all of the THP-ether was remained intact under the reaction conditions (Scheme 3).

Table 2. Conversion of different trimethylsilyl ethers to the corresponding carbonyl groups in the presence of **2** or **3** in CH_2Cl_2 at room temperature

Entry	Substrate	*N*-bromo (equiv).	Product	time/h	Isolated yields/(%)
1		**2** (1.4) **3** (0.7)		3 0.5	91 90
2		**2** (1.4) **3** (0.7)		5 1.5	90 92
3		**2** (1.4) **3** (0.7)		6 1.33	91 95
4		**2** (1.4) **3** (0.7)		6 1.5	93 95
5		**2** (2) **3** (1)		15 8.5	84 88
6		**2** (2) **3** (1)		10 5.5	85 90
7		**2** (2) **3** (1)		13 9	86 89
8		**2** (2) **3** (1)		12 8.5	87 88
9		**2** (2) **3** (1)		14 7.30	84 89
10		**2** (2) **3** (1)		12 7	82 81
11		**2** (1.4) **3** (0.7)		8.30 4.55	80 86
12		**2** (2) **3** (1)		13 7.5	82 95
13		**2** (2) **3** (1)		15 9	83 92

2: 1-bromo-5,5-diethylbarbituric acid. **3:** 1,3-dibromo-5,5-diethylbarbituric acid.



Scheme 3.

Experimental

All products were characterized by comparison of their spectra (^{1}H NMR and IR) and physical data with those reported for authentic samples. The trimethylsilyl ethers were prepared by previously reported procedure.[30]

Preparation of 1-bromo-5,5-diethylbarbituric acid

In a 250 mL flask placed **1** (0.026 mol, 5g), KOH (0.03 mol, 3.4 g) in absolute ethanol (100 mL). The mixture was stirred until a clear solution was produced, and then molecular bromine (0.028 mol, 1.45 mL) was added. After 2 hours the results were filtered off and filtrate was washed with 10% solution of $NaHCO_3$. 1-Bromo-5,5-diethylbarbituric acid was produced in 65% yield. mp 240 ºC, ^{1}H NMR, ($CDCl_3$, 90 MHz): δ (ppm) 4.278 (s, 1H, NH), 1.615 (t, 6H, $2CH_3$), 0.808 (q, 4H, $2CH_2$), 172.2, 146, 143, 57.1, 31, 10. IR (KBr) ν_{max}/cm^{-1}: 3205, 2922, 2853, 1699, 1661, 1461 cm^{-1}. MS *m/z*: 264.

Preparation of 1,3-dibromo-5,5-diethylbarbituric acid

To a solution of **1** (11.62 g, 0.0625 mol) and NaOH (5g, 0.125 mol) in water (100 mL), molecular bromine (7 mL) was added at room temperature. After 3 hours precipitate was filtered off and washed with aqueous solution of 10% Na_2CO_3. 1,3-dibromo-5,5-diethylbarbituric acid as yellow solid obtained in 70% yield. mp 150 ºC, ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.615 (t, 6H, $2CH_3$), 0.808 (q, 4H, $2CH_2$), 173, 148, 57, 31, 10. IR (KBr) ν_{max}/ cm^{-1}: 2924, 2854, 1688, 1682, 1462. MS *m/z*: 343.

General Procedure for the conversion of the trimethylsilyl ethers to the corresponding carbonyl compounds

A solution of trimethylsilyl ethers (1 mmol) and **2** (1.4-2 mmol) or **3** (0.7-1 mmol) in dichloromethane (5 mL) was stirred at room temperature for appropriate time. After the completion of reaction, dichloromethane was removed under reduced pressure. Then *n*-hexane was added to the residue and was stirred for 10 minutes. The resulting mixture was filtered and the residue was washed thoroughly with *n*-hexane (20 mL). Evaporation of the solvent gave the almost pure carbonyl compound. Column chromatography of crude products on silica gel, using *n*-hexane–EtOAc as eluents, gives highly pure carbonyl compounds.

Conclusions

Preparation of compounds **2** and **3** as two *N*-bromo reagents were described which are stable and easily producible. These reagents are very efficient for the conversion of trimethylsilyl ethers to the corresponding carbonyl compounds. They are also selective reagents for the cleavage of trimethylsilyl ethers in the presence of *THP*-ethers.

Acknowledgment

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