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Chemoselective deprotection of trityl ethers using silica-supported sodium hydrogen sulfate☆

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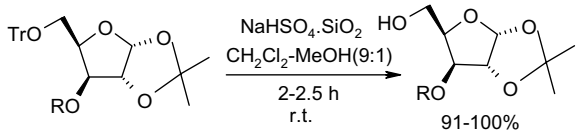
Abstract—A highly selective method for the cleavage of trityl ethers over a wide range of functional groups has been developed using silica-supported sodium hydrogen sulfate ($NaHSO_4$–SiO_2) as a heterogeneous catalyst. The conversion occurred at room temperature and the yields of the alcohols were found to be excellent.

Protection and deprotection of functional groups is very important in organic transformations and syntheses. Trityl (triphenylmethyl) ethers are widely used as protecting groups of primary alcohols, especially in carbohydrate chemistry.[1] Formation and removal of these ethers are easy and they are stable under a variety of reaction conditions. The trityl group also has a high steric demand. However, the methods for selective cleavage of trityl ethers are limited. The reported methods use different protic and Lewis acids such as mineral acids,[2a] formic acid,[2b] acetic acid,[2c] trifluoroacetic acid,[2d] $ZnBr_2$,[2e] I_2,[2f] BCl_3,[2g] $CeCl_3$,[2h] CBr_4,[2i] and CAN[2j] for this purpose. Many of these methods are associated with several drawbacks including strongly acidic conditions, corrosive reagents, necessity for reflux or cold temperatures, incompatibility with other functional groups, longer reaction times, and unsatisfactory yields. Several methods also cleave glycosidic bonds. Additionally, various catalysts work under homogeneous conditions and so the removal of these catalysts is a problem. Thus there is still a need for mild and selective methods for cleavage of trityl ethers using suitable catalysts.

In recent years, heterogeneous catalysts have gained much importance due to enviro-economic factors. In continuation of our work[3] on the applications of heterogeneous catalysts for development of new synthetic methodologies we have recently observed that silica-supported sodium hydrogen sulfate ($NaHSO_4$–SiO_2) is an efficient catalyst for deprotection of trityl ethers.



R= H, Me, Bn, MOM, MEM, Allyl, Bz, Ts

Several trityl ethers were cleaved to produce the parent alcohols in excellent yields (Table 1). The conversion occurred at room temperature. In other reported methods for cleavage of trityl ethers reflux or low temperature was required.[2] The present reaction took place smoothly without requiring strongly acidic or basic conditions. The glycoside moiety was completely intact and thus the method is highly suitable for carbohydrate chemistry. Different types of sugars with various functionalities were examined in order to determine the scope of the reaction. Several other hydroxyl protecting groups such as alkyl, Bn, MOM, MEM, Allyl, Ac, Bz, and Ts remained unaffected. Trityl ethers derived from long-chain alcohols were also easily cleaved. The method was also found to be suitable for deprotection of trityl-protected amines. The yields of the generated amines were excellent.

The catalyst $NaHSO_4$–SiO_2 can easily be prepared[4] from the readily available $NaHSO_4$ and silica gel (finer than 200 mesh). It works under heterogeneous conditions and can easily be handled and removed from the

Keywords: Trityl ether; Alcohol; $NaHSO_4$–SiO_2; Chemoselectivity.
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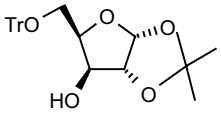
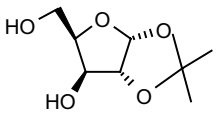
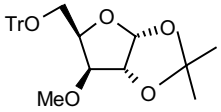
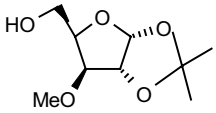
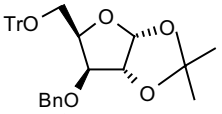
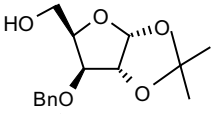
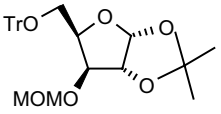
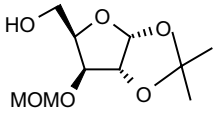
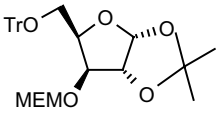
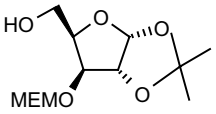
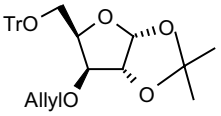
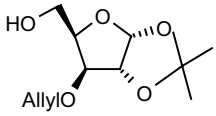
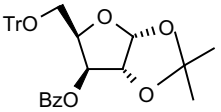
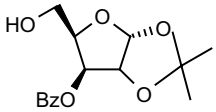
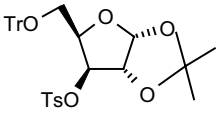
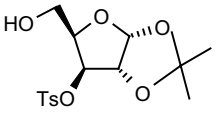
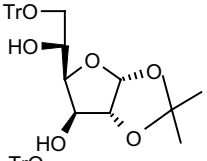
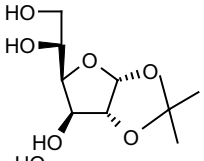
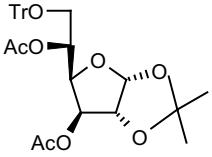
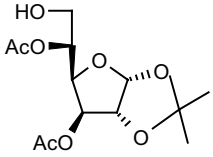
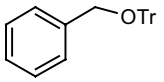
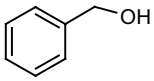
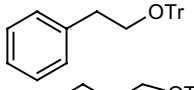
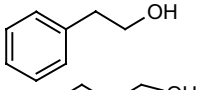
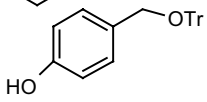
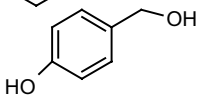
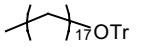
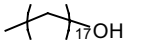
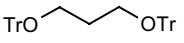
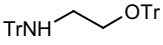
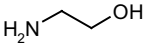
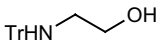
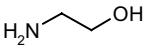
Table 1. Selective cleavage of trityl ethers using $NaHSO_4$–SiO_2[a]

Entry	Substrate	Product	Time (h)	Yield
a			2	100
b			2	94
c			2	96
d			2.5	92
e			2.5	91
f			2.5	96
g			2	97
h			2	95
i			2	100
j			2	95
k			2	97
l			1.5	95
m			2	93
n			3.5	94
o			2.5	87
p			3.5	95
q			3.5	90

[a] The structures of the products were established by direct comparison their spectral (^{1}H NMR) data with those of the parent alcohols.

reaction mixture. Moreover, the conversions occurred at room temperature and therefore the experimental procedure is simple.[5] The structures of the generated alcohols were established by direct comparison of their spectral (^{1}H NMR) data with that of the authentic alcohols.

In conclusion, we have developed a novel, simple, inexpensive, and efficient protocol for deprotection of trityl ethers using $NaHSO_4$–SiO_2 at room temperature. The mild reaction conditions, experimental simplicity, utilization of a cheap heterogeneous catalyst, high chemoselectivity and excellent yields are the main advantages of the present procedure. We believe that the method will find applications for selective cleavage of trityl ethers in organic synthesis.

Acknowledgements

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5. General procedure for detritylation: The trityl ether (100 mg) was dissolved in CH_2Cl_2–MeOH (9:1) (3 mL). The solution was stirred at room temperature for 5 min. A catalytic amount of $NaHSO_4$–SiO_2 was added. The mixture was stirred and the reaction was monitored by TLC until completion, when the mixture was filtered. The filtrate was concentrated and the residue washed with *n*-hexane (3×10 mL). The residue was purified by column chromatography using hexane–EtOAc (4:1) over silica gel to generate the parent alcohol.
Spectral data of some representative trityl ethers are given below. The deprotected products were characterized by direct comparison (TLC, ^{1}H NMR) with the parent alcohols.
1a: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.44–7.12 (15H, m), 5.92 (1H, d, J = 4.0 Hz), 4.45 (1H, d, J = 4.0 Hz), 4.18 (2H, br s), 3.52 (1H, dd, J = 8.0, 6.0 Hz), 3.41 (1H, dd, J = 8.0, 4.0 Hz), 3.02 (1H, br s), 1.46 (3H, s), 1.27 (3H, s).
1c: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.45–7.02 (20H, m), 5.82 (1H, d, J = 4.0 Hz), 4.58–4.24 (4H, m), 3.92 (1H, d, J = 4.0 Hz), 3.48 (1H, dd, J = 8.0, 6.0 Hz), 3.22 (1H, dd, J = 8.0, 6.0 Hz), 1.48 (3H, s), 1.25 (3H, s).
1h: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.60 (2H, d, J = 8.0 Hz), 7.34–7.18 (15H, m), 7.14 (2H, d, J = 8.0 Hz), 5.83 (1H, d, J = 4.0 Hz), 4.65 (2H, m), 4.12 (1H, m), 3.40 (1H, dd, J = 8.0, 6.0 Hz), 3.00 (1H, dd, J = 8.0 Hz), 2.40 (3H, s), 1.42 (3H, s), 1.24 (3H, s).
1j: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.58–7.12 (15H, m), 5.88 (1H, d, J = 4.0 Hz), 5.38 (1H, m), 5.18 (1H, m), 4.64 (1H, dd, J = 10 Hz, 4.0 Hz), 4.42 (1H, d, J = 4.0 Hz), 3.22–3.13 (2H, m), 2.02 (3H, s), 2.01 (3H, s), 1.48 (3H, s), 1.21 (3H, s).
1l: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.46–7.18 (20H, m), 3.38 (2H, t, J = 7.0 Hz), 2.92 (2H, t, J = 7.0 Hz).
1q: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.54–7.08 (30H, m), 3.08 (4H, dd, J = 7.0, 2.0 Hz), 2.35 (4H, dd, J = 7.0, 2.0 Hz).