# A Simple and Facile Chemo- and Regioselective Deprotection of Acetonides Using Silica Supported Sodium Hydrogen Sulfate as a Heterogeneous Catalyst

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Silica supported sodium hydrogen sulfate ($NaHSO_4{\cdot}SiO_2$) has been found to be an efficient heterogeneous catalyst for chemo- and regioselective deprotection of acetonides at room temperature to produce the corresponding diols in excellent yields.

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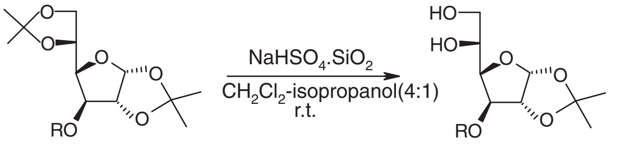
Protection of functional groups and subsequent deprotection is highly useful in multistep transformations and synthesis of complex organic molecules. Acetonides have frequently been used for protection of 1,2-diols in carbohydrates and nucleosides.[2] The acetonides are subsequently cleaved to generate the diols at an appropriate stage of a synthetic sequence. Several protic acids (such as aq. HCl,[3a] aq. HBr,[3b] aq. HOAc,[3c] 0.8% $H_2SO_4$ in MeOH,[3d] TFA,[3e] CSA[3f] and *p*-TsOH[3g]) are commonly used for this purpose. However, strong acids may affect other functional groups and lower the selectivity of hydrolysis of acetonides. The control of pH, temperature and reaction time is thus necessary. A few Lewis acid based reagents (like $FeCl_3{\cdot}6H_2O/SiO_2$,[4a] $CuCl_2{\cdot}2H_2O$,[4b] $Zn(NO_3)_2{\cdot}6H_2O$,[4c] $CeCl_3{\cdot}7H_2O/(COOH)_2$[4d] and $BICl_3$[4e]) have also been applied for deprotection of acetonides. However, most of the methods utilizing these reagents are associated with certain drawbacks such as strong oxidizing and acidic conditions, long reaction time, necessity of higher temperature and large amount of reagent, unsatisfactory yields and low selectivity. Additionally, the majority of the protic and Lewis acids works under homogenous conditions and so it is some times difficult to handle them as well as to remove from the reaction mixture.

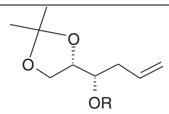
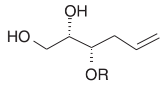
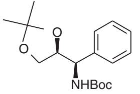
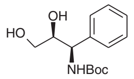
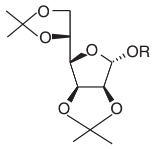
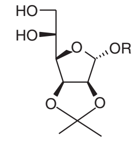
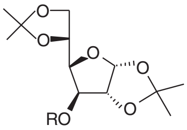
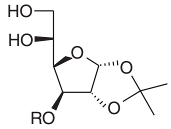
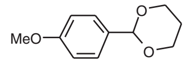
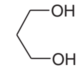
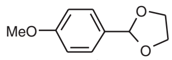
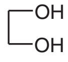
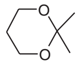
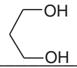
Recently, we have observed that silica supported sodium hydrogen sulfate ($NaHSO_4{\cdot}SiO_2$) is an efficient heterogeneous catalyst for deprotection of acetonides. Several acetonides were cleaved to the corresponding diols (Table 1) using this catalyst at room temperature.



92-100%

The method worked well with different acetonides of polyhydroxylated compounds. The conversion occurred with high regioselectivity. The less hindered terminal acetonides of sugars could only be cleaved. The partially protected sugars are applicable as synthons for the preparation of various useful molecules. The present method was also found to be associated with high chemoselectivity. Several functional groups such as Me, Bn, MOM, MEM, PMB ethers and Ac, Bz, and Ts esters remained intact under the reaction conditions. N-Boc group was also unaffected. The isomerisation of double bond and epimerization of a chiral centre were not observed. However with the diols with -OTBS, -OTHP and –OTrityl the yields of the deprotected products were somewhat low (44-55%) and the order of yields with these groups was observed as follows; -OTHP< -OTBS< -OTrityl. The structures of the products were settled from their spectral ($^1$H NMR and MS) data.

**Table 1.** Deprotection of acetonides using $NaHSO_4{\cdot}SiO_2$[a]

| Entry | Substrate (1) | Product (2) | Time (h) | Isolated yield / % |
|---|---|---|---|---|
| |  |  | | |
| a | R=H | R=H | 2 | 90 |
| b | R=MOM | R=MOM | 4 | 86 |
| c | R=MEM | R=MEM | 4 | 82 |
| d |  |  | 6 | 88 |
| |  |  | | |
| e | R=H | R=H | 2 | 95 |
| f | R=Ac | R=Ac | 4 | 92 |
| g | R=Bn | R=Bn | 4 | 88 |
| |  |  | | |
| h | R=H | R=H | 1 | 100 |
| i | R=Ac | R=Ac | 2 | 99 |
| j | R=Bn | R=Bn | 4 | 95 |
| k | R=MOM | R=MOM | 4 | 95 |
| l | R=MEM | R=MEM | 6 | 92 |
| m | R=Bz | R=Bz | 3 | 99 |
| n | R=Ts | R=Ts | 4 | 96 |
| o | R=PMB | R=PMB | 4 | 95 |
| p |  |  | 3 | 92 |
| q |  |  | 2 | 95 |
| s |  |  | 5 | 95 |

[a]The structure of all the products were settled from their spectral ($^1$H-NMR and MS data).

The catalyst, $NaHSO_4 \cdot SiO_2$ can easily be prepared[5] from the readily available $NaHSO_4$ and $SiO_2$ (finer than 200 mesh) and can properly be activated. Both the ingredients are inexpensive and nonhazardous. The experimental procedure is simple and the catalyst can easily be removed by filtration. From the economic and ecological considerations the catalyst is highly suitable to apply for cleavage of acetonides.

In conclusion, a novel, mild, and efficient method has been developed for chemo- and regioselective deprotection of acetonides using $NaHSO_4 \cdot SiO_2$ as a heterogeneous catalyst. The operational simplicity, excellent yields, availability of the inexpensive catalyst and high selectivity are the advantages of the present protocol. We feel the method will find important applications in the selective cleavage of acetonides of polyhydroxylated molecules.

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### References and Notes

1 Part 28 in the series, "Studies on Novel Synthetic Methodologies," for Part 27 see K. V. N. S. Srinivas, I. Mahender, and B. Das, *Adv. Synth. Catal.*, (2003), submitted.

2 a) T. W. Green, P. G. M. Wuts, "Protecting Groups in Organic Synthesis," 2nd ed., Wiley, New York (1991). b) P. J. Kocienski, "Protecting Groups," Thieme, Stuttgart, New York (1994).

3 a) G. W. J. Fleet and P. W. Smith, *Tetrahedron Lett.*, **26**, 1465 (1985). b) M. Gerspacher and H. Rapaport, *J. Org. Chem.*, **56**, 3700 (1991). c) J. S. Yadav, M. C. Chander, and K. K. Reddy, *Tetrahedron Lett.*, **33**, 135 (1992). d) S. Manna, V. Jacques, Y. Pendri, and J. R. Falck, *Tetrahedron Lett.*, **27**, 2679 (1986). e) Y. Lablanc, B. J. Fitzsimmons, J. Adams, E. Perez, and J. Rokach, *J. Org. Chem.*, **51**, 789 (1986). f) S. Baurle, S. Hoppen, and U. Koert, *Angew. Chem., Int. Ed.*, **38**, 1263 (1999). g) A. Ichihara, M. Ubukata, and S. Sakamura, *Tetrahedron Lett.*, **18**, 3473 (1977).

4 a) K. S. Kim, Y. H. Song, B. H. Lee, and C. S. Hahn, *J. Org. Chem.*, **51**, 404 (1986). b) M. Iwata and H. Ohrui, *Bull. Chem. Soc. Jpn.*, **54**, 2837 (1981). c) S. Vijayasaradhi, J. Singh, and I. S. Aidhen, *Synlett*, **2000**, 110. d) X. Xiao and D. Bai, *Synlett*, **2001**, 535.

5 G. W. Breton, *J. Org. Chem.*, **62**, 8952 (1997).

6 Typical Experimental Procedure: To a solution of acetonide (1 mmol) in $CH_2Cl_2$–isopropanol (4:1, 5 mL) $NaHSO_4 \cdot SiO_2$ (100 mg) was added. The mixture was stirred at room temperature and the reaction was monitored by TLC. After completion, the mixture was filtered and the filtrate was concentrated. The residue was subjected to column chromatography over silica gel to obtain pure diol. The spectral data of some representative compounds are given below: **2c**: $^1$H-NMR (200 MHz, $CDCl_3$): $\delta$ 5.80 (1H, m), 5.18-5.01 (2H, m), 4.97 (1H, m), 4.64 (2H, s), 4.04 (1H, m), 3.78 (1H, m), 3.66-3.42 (5H, m), 3.38 (3H, s), 4.42-2.15 (2H, m); FABMS: $m/z$ 221 $[M+1]^+$. **2f**: $^1$H-NMR (200 MHz, $CDCl_3$): $\delta$ 6.15 (1H, s), 4.87 (1H, dd, $J = 7.5$, 6.0 Hz), 4.65 (1H, d, $J = 6.0$ Hz), 4.04 (1H, m), 3.90 (1H, m), 3.78 (1H, d, $J = 11.5$, 6.0 Hz), 3.62 (1H, m), 2.01 (3H, s), 1.34 (3H, s), 1.23 (3H, s); FABMS: $m/z$ 263 $[M+1]^+$. **2j**: $^1$H-NMR (200 MHz, $CDCl_3$): $\delta$ 7.38 (5H, m), 5.89 (1H, s), 4.78 (1H, d, $J = 7.5$ Hz), 4.56-4.43 (2H, m), 4.05-3.97 (2H, m), 3.92 (1H, m), 3.78 (1H, dd, $J = 11.0$, 5.5 Hz), 3.55 (1H, dd, $J = 11.0$, 6.5 Hz); FABMS: $m/z$ 311 $[M+1]^+$. **2k**: $^1$H-NMR (200 MHz, $CDCl_3$): $\delta$ 5.86 (1H, d, $J = 2.0$ Hz), 4.73-4.64 (2H, m), 4.52 (1H, d, $J = 2.0$ Hz), 4.10 (1H, m), 4.03 (1H, dd, $J = 9.0$, 2.0 Hz), 3.86-3.75 (2H, m), 3.72 (1H, m), 3.38 (3H, s), 1.42 (3H, s), 1.21 (3H, s); FABMS: $m/z$ 265 $[M+1]^+$ **2n**: $^1$H-NMR (200 MHz, $CDCl_3$): $\delta$ 7.80 (2H, d, $J = 8$ Hz), 7.32 (2H, d, $J = 8.0$ Hz), 5.81 (1H, d, $J = 2.0$ Hz), 4.86 (1H, d, $J = 2.0$ Hz), 4.42 (1H, m), 4.02 (1H, dd, $J = 9.5$, 2.0 Hz), 3.78-3.64 (2H, m), 3.58 (1H, m); FABMS: $m/z$ 359 $[M+1]^+$.

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