Highly sulphated cellulose: A versatile, reusable and selective desilylating agent for deprotection of alcoholic TBDMS ethers

Journal:	*Organic & Biomolecular Chemistry*
Manuscript ID	OB-ART-06-2018-001438.R1
Article Type:	Paper
Date Submitted by the Author:	26-Jul-2018

Complete List of Authors:	Dachavaram, Soma Shekar; University of Arkansas for Medical Sciences College of Medicine, College of Pharmacy, Pharmaceutical Sciences Penthala, Narsimha; University of Arkansas for Medical Sciences, Pharmaceutical Sciences Calahan, Julie; The University of Kentucky, Pharmaceutical Sciences Munson, Eric; The University of Kentucky, Pharmaceutical Sciences Crooks, Peter; University of Arkansas for Medical Sciences, Pharmaceutical Sciences

Journal Name

ARTICLE

Highly sulphated cellulose: A versatile, reusable and selective desilylating agent for deprotection of alcoholic TBDMS ethers

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Soma Shekar Dachavaram,[a] Narsimha R. Penthala,[a] Julie L. Calahan,[b] Eric J. Munson,[b] Peter A. Crooks[a]*

A mild, efficient and rapid protocol was developed for the deprotection of alcoholic TBDMS ethers using a recyclable, eco-friendly highly sulphated cellulose sulphate acid catalyst in methanol. This acid catalyst selectively cleaves alcoholic TBDMS ethers in *bis*-TBDMS ethers containing both alcoholic and phenolic TBDMS ether moieties.

Introduction

Protection and deprotection sequences are commonly utilized[1-5] in the total synthesis of natural products, in multi-step synthesis of complex organic molecules, and in the synthesis of small molecules in medicinal chemistry. As the complexity of synthetic targets are increasing, the ability to protect multiple hydroxy groups in the same molecule, and the sequential deprotection of selective moieties has become essential.

Protection of hydroxyl groups by formation of silyl ethers has been extensively utilized in organic synthesis to achieve the target molecule,[6-12] due to facile synthetic procedures for preparing silyl ethers. Silyl ethers are resistant to oxidation and have good thermal stability and low viscosity; they are also easily deprotectable to afford the desired parent compound.

Although numerous silylating protection methods are currently being utilized in organic synthesis[13, 14], the *tert*-butyldimethylsilyl (TBDMS) moiety has earned a place of prominence. Commercially available *tert-n*-butyldimethylsilyl chloride (TBDMS-Cl) was initially used as a silylating agent by Corey for the mild conversion of various alcohols to TBDMS ethers.[15] In multi-step organic syntheses, functional group protection, as well as subsequent deprotection, with TBDMS groups without affecting other functional groups in the same molecule is often challenging.[16] Corey was able to achieve the rapid cleavage of TBDMS ethers to alcohols by treatment with 2-3 eq. of tetra-*n*-butylammonium fluoride (TBAF) in THF at 25°C.[15] Subsequently, several literature methods for the deprotection of TBDMS ethers were reported.[4] A variety of acid-catalyzed desilylation methods were also reported for the cleavage of the Si-O bond of TBDMS ethers to their respective alcohols utilizing reagents such as CCl_3COOH,[17] HF,[18] AcOH,[19] TsOH,[20] HCl,[21] and TFA.[22]

The cleavage of TBDMS ethers proceeds mainly by reaction with fluoride anion or under mild acid conditions. It is well-known that fluoride-mediated deprotection of TBDMS ethers proceeds through a pentavalent-silicon intermediate pathway,[23, 24] permitted by hybridization with silicon's vacant 3d orbital. Among the many desilylating agents, TBAF is most often used as the source of fluoride anion for desilylation.[15] Patel et al. has described the mechanism for the desilylation of TBDMS ethers utilizing tetrabutylammonium tribromide (TBATB) in MeOH as being due to the released HBr[25]; however, TBATB is not a selective reagent for deprotection of alcoholic TBDMS ethers, since it also deprotects phenolic TBDMS ethers.

In addition to the above reported literature methods, a variety of Lewis acids and other reagents have also been developed for the desilylation of various TBDMS ethers, which include BF_3,[26] BCl_3,[27] $BiBr_3$,[28] $CuBr_2$,[29] $ZnBr_2$,[30] NIS,[31] $FeCl_3$,[32] $Bi(OTf)_3$,[33] camphor sulfonic acid (CSA),[34] $NaAuCl_4.2H_2O$,[35] $KF.2H_2O$,[36] $LiOAc.2H_2O$,[37] and $Fe(OTs)_3.6H_2O$.[38] All these reagents are noble desilylating agents, however, some have limitations, which include being non-ecofriendly reagents, having poor selectivity and non-recyclability, and involving tedious workup procedures.[39]

Previously, our research group reported the applications of cellulose sulphuric acid (CSA) as a catalyst in various organic reactions the Bignelli reaction,[40] the Pechman condensation reaction,[41] the synthesis of xanthenes[42], thiadiazolo benzimidazoles,[43] 1-oxo-hexahydroxanthenes,[44] and in the synthesis of quinoxalines.[45] Cellulose sulphuric acid (CSA) is partially sulphated cellulose prepared by the reaction of cellulose (**1**) with chlorosulphonic acid in hexanes (analytical data for CSA is given in the supporting information).[40, 46, 47]

To address the above issues of other acid catalysts in the selective deprotection of alcoholic TBDMS ethers we attempted the deprotection of alcoholic TBDMS ethers using chlorosulphonic acid-derived CSA as a mild acid catalyst in methanol. Unfortunately, this CSA did not deprotect alcoholic TBDMS ethers.

[a]Department of Pharmaceutical Sciences College of Pharmacy, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA.
Email: PACrooks@uams.edu
[b]Department of Pharmaceuticals Sciences, University of Kentucky, Lexington, KY, 40536, USA.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x.

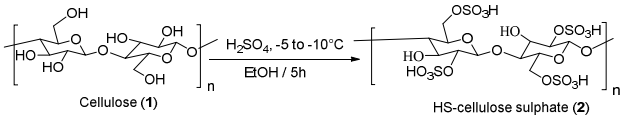
In the present study we investigate the use of a highly sulphated cellulose sulphate (HS-cellulose sulphate; **2**) as a potential catalyst for deprotection of alcoholic TBDMS ethers in molecules which contain both phenolic and alcoholic *bis*-TBDMS ether moieties. To the best of our knowledge, HS-cellulose sulphate has not been reported previously as a catalyst for the selective deprotection of alcoholic TBDMS ethers.

HS-Cellulose sulphate is an inexpensive, non-toxic, eco-friendly catalyst which can be prepared easily from the most abundant, naturally occurring biopolymer, α-cellulose (**1**).[48] We found that HS-cellulose sulphate-mediated heterogeneous catalysis can cleave the Si-O bond in TBDMS ethers very efficiently to afford the desired desilylated product. When compared to currently used homogeneous catalysts, this mild catalytic methodology offers major advantages, such as facile separation of catalyst from the reaction mixture, reusability, and minimal environmental pollution on disposal.

Results and discussion

Catalyst preparation and structure determination

To a cooled solution of EtOH (58 mL) at -10°C was added H_2SO_4 (45 mL) drop-wise over a period of 5 minutes, and the reaction mixture was stirred vigorously for a further 15 min, followed by addition of α-cellulose (4g). The reaction mixture was then stirred at -5°C to -10°C for 5h, the heterogeneous reaction mixture was filtered, and the resulting solid was washed with ethanol (3x100 mL) and dried, to afford HS-cellulose sulphate as a white solid (Scheme 1).[49]



Scheme 1 Synthesis of HS-cellulose sulphate (**2**) from α-cellulose (**1**).

Solution-state NMR analysis of HS-cellulose sulphate **2** was not possible, due to its insolubility in all available deuterated solvents. To solve this insolubility problem, the HS-cellulose sulphate was suspended in deionized water under vigorous stirring over a period of 30 min, and the pH of the mixture adjusted to 9 with 2M sodium hydroxide solution (100 mL) at room temperature. The above reaction mass was filtered to remove insoluble material, and the sodium salt of HS-cellulose sulphate was precipitated from the filtrate by adding EtOH (200 mL). The filtered solid was then dried to afford HS-cellulose sulphate sodium, which is readily soluble in H_2O and is amenable to characterization by solution-state NMR in D_2O.

The ^{1}H NMR spectral data of cellulose sulphate **2** is consistent with the ^{1}H NMR spectrum of a cellulose sulphate reported by Zeng et al[50] and Kamide et al.[51] While the NMR spectrum of the Zeng cellulose sulphate shows a proton resonance (4.39 ppm) attributable to a C_6-sulphated hydroxyl moiety, no proton resonance at 4.97 ppm (indicative of the absence of a C_3-sulphated hydroxyl moiety) was observed. However, these investigators concluded from their studies that the structure of their product could not be determined, since the NMR spectrum was run in D_2O, which affords a broad signal that would mask the expected proton resonance at 4.83 ppm attributable to a cellulose product that was sulphated at the C_2-hydroxyl group. These data are consistent with our own NMR data, since we also utilized D_2O as the NMR solvent, and indicate that ^{1}H-NMR data alone when run in D_2O does not present enough information to determine whether the C_2-hydroxyl is sulphated or not. When elemental sulphur combustion analysis was carried out on the sodium salt of **2** a value of 15.42% was obtained, i.e. 88.06% of theoretical for 2,6-disubstituted cellulose sulphate sodium ($C_6H_8S_2O_{11}Na_2$), indicating that the product is predominantly the disulphated cellulose rather than the monosulphated cellulose (see Supporting Information for more data).

Elemental sulphur content of chlorosulphonic acid-derived CSA afforded only 0.42% (equivalent to 2.04% sulphation of α-cellulose), indicating a comparatively much higher sulphate content in the sulphuric acid-derived HS-cellulose **2**.

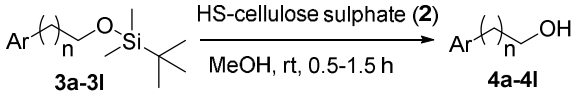
HS-cellulose sulphate sodium was also characterized by ^{13}C-NMR, and solid-state ^{13}C-NMR. In addition, HS-cellulose sulphate and HS-cellulose sulphate sodium were analyzed by FT-IR spectrophotometry (see Supporting Information).

Deprotection of TBDMS ethers with HS-cellulose sulphate catalyst

TBDMS ethers **3a-3j** and **5a-5d** were prepared from alcohols/phenols (**4a-4j** and **6a-6d**) using a known standard procedure.[8] Alcohols/phenols (**4a-4j** and **6a-6d**) were reacted with TBDMS chloride in the presence of imidazole in DCM to afford their respective TBDMS ethers.[8] The TBDMS ethers of **3k**, **5e**, **5f** were synthesized by the Barbier allylation procedure.[52] Compound **3l** was prepared by the reduction of methyl 8-(4-chlorophenyl)-1,4-dioxaspiro[4.5]dec-7-ene-7-carboxylate using lithium aluminum hydride (LAH) as reducing agent to afford **4l**. Compound **4l** was converted to its TBDMS ether (**3l**) by reaction with TBDMS chloride and imidazole in DCM.[8] ^{1}H-NMR, ^{13}C-NMR and mass spectral data for all new TBDMS ethers and for new alcohols are provided in the Supporting Information.

Method

Initially, we carried out the deprotection of TBDMS ether groups attached to both primary and secondary hydroxyl moieties of various organic molecules utilizing cellulose sulphate as catalyst. Treatment of simple alcoholic TBDMS ethers (**3a-3l**) with a catalytic amount of HS-cellulose sulphate in methanol at room temperature for 0.5 to 1.5 h (Tables 1 and 2) afforded the corresponding desilylated products (**4a-4l**) in generally good yields (Scheme 2).

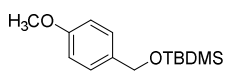
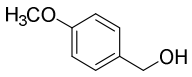
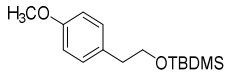
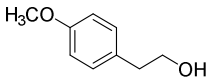
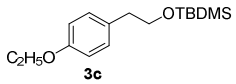
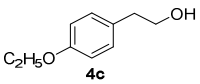
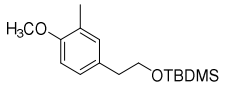
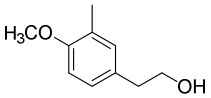
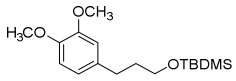
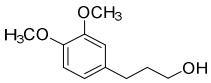
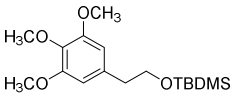
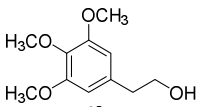
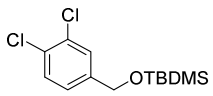
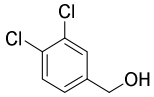
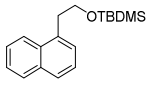
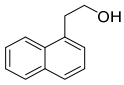
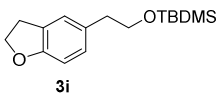
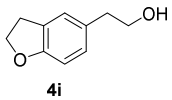
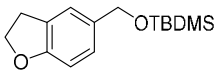
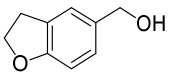
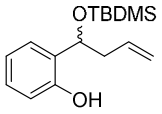
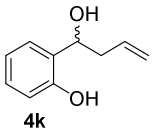
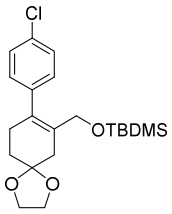
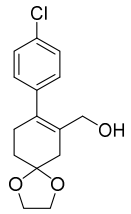


Ar = simple and substitued aromatic groups: n = 0 to 2

Scheme 2 Desilylation of alcoholic TBDMS ethers (**3a**-**3l**) utilizing HS-cellulose sulphate catalyst.

We also attempted the deprotection of alcoholic TBDMS ethers that incorporated the acid-sensitive ethylene glycol (**3l**) protecting group within the same molecule utilizing HS-cellulose sulphate as catalyst and found that ethylene glycol protection was not affected during the TBDMS ether deprotection process (Table 1).

Table **1.** Desilylation of different alcoholic TBDMS ethers (**3a-3l**) to their corresponding alcohols (**4a-4l**) using HS-cellulose sulphate[a] acid catalyst.

Substrate[b]	Product	Time[c] (min)	Yield (%)[d]
 **3a**	 **4a**	**30**	**97**
 **3b**	 **4b**	**20**	**90**
 **3c**	 **4c**	**20**	**90**
 **3d**	 **4d**	**20**	**90**
 **3e**	 **4e**	**30**	**82**
 **3f**	 **4f**	**30**	**85**
 **3g**	 **4g**	**25**	**85**
 **3h**	 **4h**	**30**	**88**
 **3i**	 **4i**	**20**	**92**
 **3j**	 **4j**	**30**	**75**
 **3k**	 **4k**	**45**	**82**
 **3l**	 **4l**	**45**	**91**

[a]5 % w/w of HS-cellulose sulphate acid catalyst was used; [b]100 mg of TBDMS ether in 1 ml methanol, [c]TLC monitoring time (ethyl acetate/n-hexane 1:10), [d]isolated yields.

In order to evaluate the effect of various solvents on the desilylation of alcoholic TBDMS ethers utilizing HS-cellulose sulphate, the desilylation reaction was carried out for the synthesis of compound **4a** in the following solvents: dichloromethane, tetrahydrofuran (THF), dioxane, dimethyl formamide (DMF), methanol, ethanol and isopropyl alcohol. The relative rates of deprotection of the TBDMS ether moiety under these conditions was methanol > ethanol > isopropyl alcohol, and is likely due to the more polar nature of methanol compared to either ethanol and isopropyl alcohol. It is well documented in the literature that a more protic medium such as methanol favors the desilylation of OH groups.[25] Among the solvents utilized, methanol was found to be the optimal solvent for efficient desilylation.

Table 2. Effect of different solvents on the desilylation of alcoholic TBDMS ether **3a.**

Solvents	Reaction time (h)	Yield (%)
Water	12.0	nil
Methanol	0.5	97.0
Ethanol	12.0	11.0
Ethanol	24.0	77.0
Isopropanol	12.0	4.0
Isopropanol	24.0	30
Dichloromethane	12.0	nil
Tetrahydrofuran	12.0	nil
Dioxane	12.0	nil
Dimethylformamide	12.0	nil

A plausible mechanism for the deprotection of TBDMS ethers by HS-cellulose sulphate initially involves silyl ether protonation by abstraction of hydronium ion from the HS-cellulose sulfate catalyst, followed by cleavage of the silyl oxygen bond by methanol, to afford the deprotected alcohol, as illustrated in Figure 1.

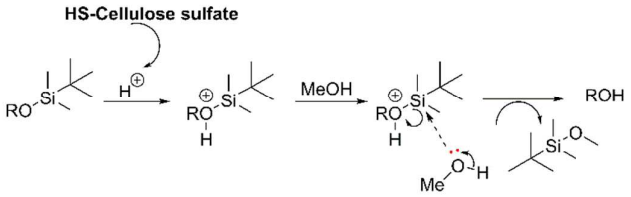
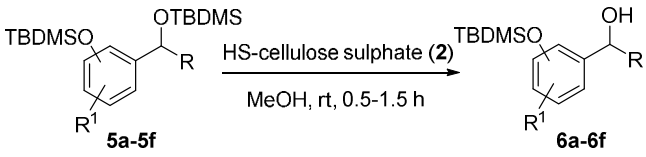


Fig 1. Plausible mechanism for the deprotection of TBDMS ethers by HS-cellulose sulphate

As part of this study, we investigated the selectivity of HS-cellulose sulphate as a suitable reagent for the selective deprotection of alcoholic TBDMS ethers in the presence of phenolic TBDMS ethers (**5a-5f**) (Scheme 3). Interestingly, HS-cellulose sulphate efficiently deprotected alcoholic TBDMS ethers without effecting phenolic TBDMS ethers, in a subset of compounds that incorporated both alcoholic and phenolic TBDMS ether moieties, demonstrating the chemoselective nature of this catalyst.

The above chemoselective TBDMS ether deprotection mechanism likely results from the alkyl TBDMS ether moiety being more favorable than the aryl TBDMS ether moiety to protonation by the HS-cellulose sulfate catalyst, facilitating selective deprotection of alkyl TBDMS ethers over aryl TBDMS ethers. Considering that both alcoholic and phenolic hydroxyl groups exist in the structures of many complex natural products, the differential deprotection of alcoholic and phenolic silyl ethers is of considerable interest.

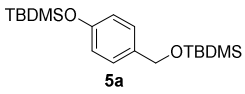
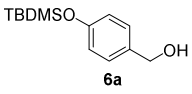
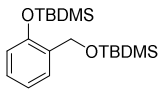
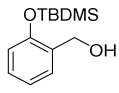
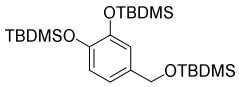
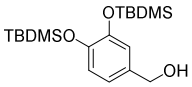
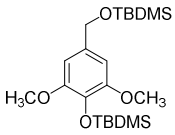
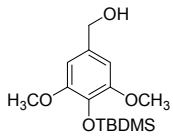
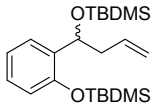
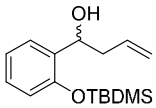
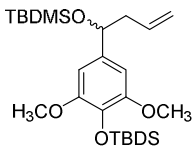
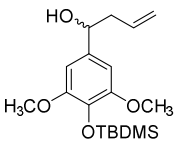
Several literature methods and reagents are also available for the selective deprotection of alcoholic silyl ethers in the presence of phenolic silyl ether moieties, i.e. Selectfluor,[53] TMSCl,[54] HF[18] and TMSBr[55], dicationic ionic liquid.[56] However, most of these reagents are hazardous, toxic and require special care in their use. We believe that the use of HS-cellulose sulphate in place of the above reagents constitutes a superior, simple, rapid, inexpensive and more environmentally friendly method for the chemoselective desilylation of alcoholic TBDMS ethers in the presence of phenolic TBDMS ethers.



Scheme 3 Chemoselective desilylation of alcoholic TBDMS ethers in the presence of phenolic TBDMS ethers (**5a-5f**) utilizing HS-cellulose sulphate catalyst.

Examples of the chemoselective desilylation of alcoholic TBDMS ethers in the presence of phenolic TBDMS ethers (**5a-5f**) utilizing HS-cellulose sulphate as the acid catalyst are presented in Table 3.

Table 3. Chemoselective deprotection of alcoholic TBDMS ethers over phenolic TBDMS ethers with HS-cellulose sulphate as acid[a] catalyst.

Substrate[b]	Product	Time[c] (min)	Yield (%)[d]
 **5a**	 **6a**	60	93
 **5b**	 **6b**	30	92
 **5c**	 **6c**	90	80
 **5d**	 **6d**	90	82
 **5e**	 **6e**	50	90
 **5f**	 **6f**	30	88

[a]5 % w/w of HS-cellulose sulphate acid catalyst was used; [b]100 mg of TBDMS ether in 1 ml methanol, [c]TLC monitoring time (ethyl acetate/n-hexane 1:10), [d]isolated yields.

To assess the selective deprotection of TBDMS ethers utilizing standard H^+ sources such as TFA, HCl or H_2SO_4 (0.1 eq), deprotection of compound **5a** in methanol (10 vol) at room temperature for 20 minutes was also carried out. In every case, desilylation resulted in deprotection of both the phenolic and alcoholic TBDMS groups in **5a**.

To evaluate the reusable efficiency of HS-cellulose sulphate as a desilylating agent we recovered the catalyst from the reaction mass after the synthesis of compound **6a**. The synthesis of compound **6a** from **5a** was repeated thrice by recovering HS-cellulose sulphate each time, and we observed that the catalyst could be quantitatively recovered and reused in these three successive TBDMS deprotection reactions without considerable loss of catalytic activity, and with minimal change in the yield of product (99.0%, 97.5% and 96.5%). We also determined that the chemical structure of the catalyst was retained after recovery from the reaction mass by running ^{1}H and ^{13}C-NMR spectra on the recovered HS-cellulose sulphate and comparing the spectra with that of the fresh catalyst.

Conclusions

In conclusion, HS-cellulose sulphate prepared from commercially available α-cellulose, is an efficient, thermally stable and recoverable acid catalyst that can be used for the deprotection of alcoholic TBDMS ethers in methanol at 25°C. Selective desilylation of TBDMS ethers of alcohols in the presence of TBDMS phenolic ethers can also be achieved. This protocol is the first report of the deprotection of an alcoholic TBDMS ether in which the catalyst can be quantitatively recovered and reused over three times without considerable loss of catalytic activity and without any significant change in the yields of the products. Considering the utility of the above features, we believe that this catalyst could be an excellent choice for selective alcohol group deprotection in both lab-scale and manufacturing scale chemistries.

Experimental

General procedure for the deprotection of alcoholic TBDMS ethers

To a solution of TBDMS ether (1 mmol) in methanol (5 mL) was added HS-cellulose sulphate (**2**; 5% w/w). The heterogenous reaction mixture was stirred at 25°C for 0.5 to 1.5 hrs. Progress of the deprotection reaction was monitored by TLC. After completion of the reaction the catalyst was separated by filtration and the filtrate was concentrated under reduced pressure to remove methanol to afford the corresponding deprotected crude alcohol. The crude product was purified by silica gel column chromatography by elution with ethyl acetate and n-hexane (1:10) to afford the parent alcohol (Tables 1 and 3).

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This research work was supported by EPSCoR grant no. 216 EPSCoR G1-51050-03-03.

Notes and references

1. P. G. M. Wuts, *Greene's Protective Groups in Organic Synthesis*, 5th edn., 2014.
2. P. J. Kocienski, *Protecting Groups*, Thieme, 2005.
3. K. Jarowicki and P. Kocienski, *J. Chem. Soc., Perkin Trans. 1*, 2001, DOI: 10.1039/B103282H, 2109-2135.
4. R. D. Crouch, *Tetrahedron*, 2013, **69**, 2383-2417.
5. M. Smith, Elsevier Science & Technology, 3rd edn., 2011, ch. 7, pp. 587-622.
6. K. C. Nicolaou, H. Ding, J.-A. Richard and D. Y. K. Chen, *J. Am. Chem. Soc.*, 2010, **132**, 3815-3818.
7. E. J. Martinez and E. J. Corey, *Org. Lett.*, 2000, **2**, 993-996.
8. S. S. Dachavaram, K. B. Kalyankar and S. Das, *Tetrahedron Lett.*, 2014, **55**, 5629-5631.
9. Y. Xing, S. M. Hande and Y. Kishi, *J. Am. Chem. Soc.*, 2012, **134**, 19234-19239.
10. J. S. Yadav and P. Dutta, *J. Org. Chem.*, 2016, **81**, 1786-1797.
11. J. S. Yadav and C. S. Reddy, *Org. Lett.*, 2009, **11**, 1705-1708.
12. J. S. Yadav and L. Chetia, *Org. Lett.*, 2007, **9**, 4587-4589.
13. P. Patschinski, C. Zhang and H. Zipse, *J. Org. Chem.*, 2014, **79**, 8348-8357.
14. B. A. D'Sa, D. McLeod and J. G. Verkade, *J. Org. Chem.*, 1997, **62**, 5057-5061.
15. E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, 1972, **94**, 6190-6191.
16. M. Schelhaas and H. Waldmann, *Angew. Chem. Int.Ed.*, 1996, **35**, 2056-2083.
17. A. Larivée, J. B. Unger, M. Thomas, C. Wirtz, C. Dubost, S. Handa and A. Fürstner, *Angew. Chem. Int. Ed.*, 2011, **50**, 304-309.
18. E. W. Collington, H. Finch and I. J. Smith, *Tetrahedron Lett.*, 1985, **26**, 681-684.
19. K. Watanabe, K. Iwasaki, T. Abe, M. Inoue, K. Ohkubo, T. Suzuki and T. Katoh, *Org. Lett.*, 2005, **7**, 3745-3748.
20. C. R. Reddy, G. Dharmapuri and N. N. Rao, *Org. Lett.*, 2009, **11**, 5730-5733.
21. A. B. Smith, 3rd, M. Xian and F. Liu, *Org. Lett.*, 2005, **7**, 4613-4616.
22. O. Loiseleur, G. Koch, J. Cercus and F. Schürch, *Org.Process Res. Dev.*, 2005, **9**, 259-271.
23. J. M. Buriak, *Chem. Rev.*, 2002, **102**, 1271-1308.
24. X. Liu, C. Xu, M. Wang and Q. Liu, *Chem. Rev.*, 2015, **115**, 683-730.
25. R. Gopinath and B. K. Patel, *Org. Lett.*, 2000, **2**, 4177-4180.
26. K. Toshima, S. Takai, Y. Maeda, R. Takano and S. Matsumura, *Angew. Chem. Int. Ed.*, 2000, **39**, 3656-3658.
27. Y.-Y. Yang, W.-B. Yang, C.-F. Teo and C.-H. Lin, *Synlett*, 2000, **2000**, 1634-1636.
28. J. S. Bajwa, J. Vivelo, J. Slade, O. Repič and T. Blacklock, *Tetrahedron Lett.*, 2000, **41**, 6021-6024.
29. S. Bhatt and S. K. Nayak, *Tetrahedron Lett.*, 2006, **47**, 8395-8399.
30. J. McGarvey Glenn, *ed. L. A. Paquette, John Wiley, New York, 1995*, **8**, 5539.
31. B. Karimi, A. Zamani and D. Zareyee, *Tetrahedron Lett.*, 2004, **45**, 9139-9141.
32. Y.-Q. Yang, J.-R. Cui, L.-G. Zhu, Y.-P. Sun and Y. Wu, *Synlett*, 2006, **2006**, 1260-1262.
33. R. F. Lambert, R. J. Hinkle, S. E. Ammann, Y. Lian, J. Liu, S. E. Lewis and R. D. Pike, *J.Org. Chem.*, 2011, **76**, 9269-9277.

34. K. Tanaka, M. Watanabe, K. Ishibashi, H. Matsuyama, Y. Saikawa and M. Nakata, *Org. Lett.*, 2010, **12**, 1700-1703.
35. Q. Zhang, X. Kang, L. Long, L. Zhu and Y. Chai, *Synthesis*, 2015, **47**, 55-64.
36. Y. Peng and W.-D. Z. Li, *Synlett*, 2006, **2006**, 1165-1168.
37. B. Wang, H.-X. Sun and Z.-H. Sun, *J. Org. Chem.*, 2009, **74**, 1781-1784.
38. J. M. Bothwell, V. V. Angeles, J. P. Carolan, M. E. Olson and R. S. Mohan, *Tetrahedron Lett.*, 2010, **51**, 1056-1058.
39. Y. Kaburagi and Y. Kishi, *Org. Lett.*, 2007, **9**, 723-726.
40. P. N. Reddy, Y. T. Reddy, M. N. Reddy, B. Rajitha and P. A. Crooks, *Synth. Commun.*, 2009, **39**, 1257-1263.
41. B. S. Kuarm, J. V. Madhav, S. V. Laxmi, B. Rajitha, Y. T. Reddy, P. N. Reddy and P. A. Crooks, *Synth. Commun.*, 2010, **40**, 3358-3364.
42. J. Venu Madhav, Y. Thirupathi Reddy, P. Narsimha Reddy, M. Nikhil Reddy, S. Kuarm, P. A. Crooks and B. Rajitha, *J. Mol. Catal. A: Chem.*, 2009, **304**, 85-87.
43. B. S. Kuarm, J. V. Madhav, B. Rajitha, Y. T. Reddy, P. N. Reddy and P. A. Crooks, *Synth. Commun.*, 2011, **41**, 662-669.
44. B. S. Kuarm, J. V. Madhav, S. V. Laxmi, B. Rajitha, Y. T. Reddy, P. N. Reddy and P. A. Crooks, *Synth. Commun.*, 2011, **41**, 1719-1724.
45. B. S. Kuarm, P. A. Crooks and B. Rajitha, *Green Chem. Lett. Rev*, 2013, **6**, 228-232.
46. A. Shaabani and A. Maleki, *Appl. Cata. A: General*, 2007, **331**, 149-151.
47. J. Safari, S. H. Banitaba and S. D. Khalili, *J. Mol. Catal. A: Chem.*, 2011, **335**, 46-50.
48. J. Coombs Obrien, L. Torrente-Murciano, D. Mattia and J. L. Scott, *ACS Sustainable Chem. Eng*, 2017, **5**, 5931-5939.
49. G. Chen, B. Zhang, J. Zhao and H. Chen, *Carbohydr. Polym.*, 2013, **95**, 332-337.
50. Z. Xianhai, D. M. K., P. Ravichandra, C. Jia, C. X. Dong and L. Yinghua, *J. Chem. Technol. Biotechnol*, 2013, **88**, 599-605.
51. K. Kamide and K. Okajima, *Polym. J.*, 1981, **13**, 163.
52. C. Petrier and J. L. Luche, *J. Org. Chem.*, 1985, **50**, 910-912.
53. S. T. A. Shah, S. Singh and P. J. Guiry, *J. Org. Chem.*, 2009, **74**, 2179-2182.
54. P. A. Grieco and C. J. Markworth, *Tetrahedron Lett.*, 1999, **40**, 665-666.
55. S. T. A. Shah and P. J. Guiry, *Org. Biomol. Chem.*, 2008, **6**, 2168-2172.
56. A. H. Jadhav and H. Kim, *Tetrahedron Lett.*, 2012, **53**, 5338-5342.

Table of Contents

Graphical Abstract

Highly sulphated cellulose: A versatile, reusable and selective desilylating agent for deprotection of alcoholic TBDMS ethers

Soma Shekar Dachavaram, Narsimha R. Penthala, Julie L. Calahan, Eric J. Munson, Peter A. Crooks

A mild, efficient and rapid protocol was developed for the deprotection of alcoholic TBDMS ethers using a recyclable, eco-friendly highly sulphated HS-cellulose sulphate acid catalyst in methanol. This acid catalyst selectively cleaves alcoholic TBDMS ethers in *bis*-TBDMS ethers containing both alcoholic and phenolic TBDMS ether moieties.