A Highly Efficient Synthetic Protocol for Tetrahydropyranylation/ Depyranylation of Alcohols and Phenols

Abu T. Khan,*[a] Subrata Ghosh,[a] and Lokman H. Choudhury[a]

Dedicated to Professor K. Dey on the occasion of his 65th birthday

Keywords: Tetrahydropyranylations / Alcohols / Phenols / Bismuth(III) nitrate pentahydrate / Synthetic methods

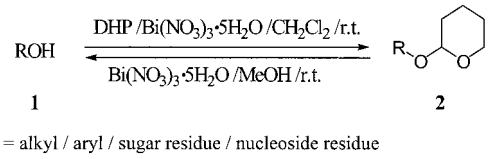
Bismuth(III) nitrate pentahydrate [$Bi(NO_3)_3 \cdot 5H_2O$] is found to be an effective catalyst for both tetrahydropyranylation and depyranylation of alcohols and phenols. Some of the major advantages of this protocol are: non-aqueous workup, good yields, the involvement of a less-expensive and nontoxic catalyst, and compatibility in the presence of a large number of other protecting groups. Notably, isopropylidene, benzylidene, and thioacetal groups are also unaffected under the experimental conditions. Remarkably, a selective mono-protection of diols and primary alcohols can be achieved chemoselectively by employing the same catalyst.

Introduction

The protection/deprotection strategy is a very common practice for manipulation of other functional groups during multistep organic synthesis. Among various functional groups, the protection of the hydroxy group as tetrahydropyranyl (THP) ether is usually preferred because of its low cost, ease of preparation, and stability of THP ethers towards metal hydrides, and acylating, alkylating, Grignard, and organometallic reagents.[1] Sometimes THP ethers also serve as a stable protecting groups in peptide, nucleoside and nucleotide, carbohydrate, and steroid chemistry. Tetrahydropyranylation of alcohols or phenols is usually achieved by using *p*TsA,[2] $BF_3 \cdot OEt_2$,[3] or PPTS.[4] Many other reagents, such as $ZrCl_4$,[5] I_2,[6] LiBr,[7] acetonyltriphenylphosphonium bromide (ATPB),[8] TBATB,[9] aluminium chloride hexahydrate,[10] LiOTf,[11] $In(OTf)_3$,[12] dialkylimidazolium tetrachloroaluminates,[13] $InCl_3$ immobilized in ionic liquids,[14] $Bi(OTf)_3$,[15] bromodimethylsulfonium bromide,[16] cupric sulfate pentahydrate,[17] and $NbCl_5$,[18] have also been employed for both tetrahydropyranylation/depyranylation in recent years. Though metal triflates have been found to be effective catalysts for the above transformations, they still have some drawbacks, such as they are relatively expensive, difficult to handle, and not readily available. They also require harsh[11] and inert reaction conditions.[15] Very recently, one more method has been reported that involves a heterogeneous catalyst such as a solid silica-based sulfonic acid.[19] Further, more methods have recently been reviewed that employ various heterogeneous catalysts.[20] Unfortunately, many of these procedures have a disadvantage such as harsh reaction conditions, long reaction times, incompatibility with other acid-sensitive functional groups,[3,9,10,13] the involvement of more expensive and moisture sensitive reagents, and some also have to be freshly prepared prior to use.[4,8,9,15,16] As part of our ongoing research to develop new synthetic methodologies by using various new reagents,[21–23] we realized that there is further scope for a cleaner and greener methodology for tetrahydropyranylation/depyranylation, one that might work under mild catalytic conditions and that is economically cheaper. In recent years, bismuth compounds have been gaining interest in various organic transformations.[24,25] We thought that bismuth(III) nitrate pentahydrate, which is commercially available at a very low cost and is relatively nontoxic, might be a useful catalyst for tetrahydropyranylation/depyranylation. So far, bismuth(III) nitrate pentahydrate has been utilized in various organic transformations: i) acetylation and benzoylation of alcohols and phenols,[26a] ii) guanidylation of *N*-benzoylthiourea,[26b] iii) conversion of thiocarbonyl compounds to the corresponding carbonyl compounds,[26c] iv) Michael reaction,[26d] v) oxidation of thiols to disulfides,[26e] and vi) for the synthesis of acylals[26f] and dihydropyrimidinone.[26g] In this paper, we report the tetrahydropyranylation of alcohols and phenols and depyranylation in the presence of catalytic amounts of bismuth(III) nitrate pentahydrate, as shown in Scheme 1.

[a] Department of Chemistry, Indian Institute of Technology Guwahati,
Guwahati-781 039, India

 DOI: 10.1002/ejoc.200500400



Scheme 1.

Results and Discussion

When a mixture of 1-decanol (entry **1a**) and 3,4-dihydro-2*H*-pyran (DHP) in dichloromethane was treated with 5 mol-% of bismuth(III) nitrate pentahydrate, it was smoothly converted into the corresponding THP ether **2a** within 15 min in 92% yield. Similarly, 2-phenylethanol (entry **1b**) was converted into the corresponding THP ether **2b** in fairly good yield under identical reaction conditions. Various benzylic alcohols (entries **1c**–**g**), allyl alcohols (entry **1h**), secondary alcohols (entries **1i**–**l**), and tertiary alcohols (entries **1m** and **1n**) were smoothly converted into the corresponding THP ethers **2c**–**n**, respectively, in very good yields, as shown in Table 1. Here, it is worth mentioning that our procedure is more highly efficient in terms of reaction times and yields than some of the recently reported procedures.[15,18] For example, tetrahydropyranylation of 4-nitrobenzylalcohol (entry **1d**), geraniol (entry **1h**), and (–)menthol (entry **1k**) to form the corresponding THP ethers was completed much more quickly and also provided better yields than the bismuth triflate method.[15] We were then interested in whether the same catalyst could be employed for tetrahydropyranylation of phenolic compounds. By following identical reaction procedures, various phenols (entries **1o**–**q**) were smoothly converted into the corresponding THP ethers **2o**–**q** in good yields. It had been observed previously that the formation of the THP ether **2q** from β naphthol (entry **1q**) by employing $Bi(OTf)_3$ as catalyst was a failure,[15] whereas we have shown that it can be easily accessible by our method; this offers an additional advantage. We then turned our attention on whether the same catalyst could be useful for tetrahydropyranylation of substrates containing other protecting groups. We observed that various protected alcohols (entries **1r**–**x**) containing protecting groups such as acetyl, benzyl, benzoyl, trityl, tosyl, TBS and TBDPS ethers were smoothly converted into the corresponding THP ethers **2r**–**x** without affecting the other protecting groups. Furthermore, substrates with thioacetal groups (entries **1y** and **1z**), and isopropylidene protected alcohols (entries **1a′** and **1b′**) and benzylidene protected diol (entry **1c′**) can be easily transformed into the desired THP ethers in good yields as shown in the Table 1. Interestingly, it should be noted that the formation of THP ethers **2y** and **2z** from the compounds **1y** and **1z**, respectively, was difficult by our recently reported procedure, where we used cupric sulfate pentahydrate as catalyst.[17] Remarkably, by employing our current protocol, various carbohydrates (entries **1d′** and **1e′**), as well as a nucleoside compound (entry **1f′**), were smoothly converted into the corresponding THP ethers in good yields, as shown in Table 1. The formation of the products was confirmed by IR, ^{1}H- and ^{13}C NMR spectroscopy and by elemental analysis. In addition, we have also compared some of the spectroscopic data with that obtained by a method reported earlier.[28]

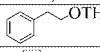
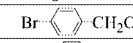
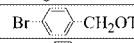
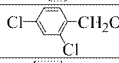
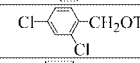
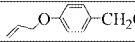
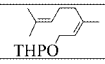
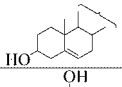
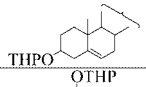
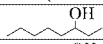
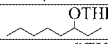
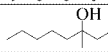
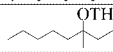
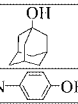
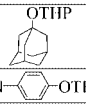
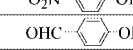
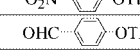
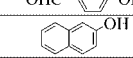
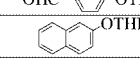
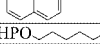
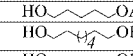
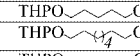
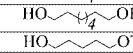
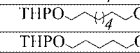
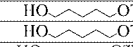
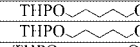
The most significant advantage of this protocol is that various symmetric diols can be chemoselectively protected when transformed into the mono THP ethers **(2g′**–**k′)** [with 5–10% di-THP ethers] by using 5 mol-% catalyst under identical conditions; this is sometimes difficult to achieve with other methods, see Table 2. It should also be noted that primary alcohols can be protected chemoselectively in the presence of a secondary alcohol (entry **1l′**). An additional feature of our protocol is that tetrahydropyranylation can be carried out even on a large scale (for example, on 10–100 mmol) without any difficulty.

The formation of the product can be explained as follows. We believe that the actual catalyst is nitric acid, which is generated from bismuth(III) nitrate pentahydrate in the reaction medium. This fact is verified in two ways: i) the tetrahydropyranylation of 4-nitrobenzyl alcohol (entry **1d**) in the presence of bismuth(III) nitrate pentahydrate (0.05 mmol) and potassium carbonate (1 mmol) did not show the formation of any product; ii) the formation of THP ether **2d** from 4-nitrobenzyl alcohol is possible in 72% yield in the presence of a catalytic amount of concentrated HNO_3. However, Banik et al. reported[26d] while studying Michael reactions that bismuth(III) nitrate pentahydrate acts only as a Lewis acid because they did not observe any Michael addition product in the presence of other metal nitrates that can readily generate nitric acid in the medium.

Notably, the same catalyst can be used for depyranylation reactions. For example, the THP ether **2b** undergoes cleavage in methanol within 45 min in 82% yield with 5 mol-% of catalyst. Likewise, various THP ethers **2c**, **2f**, **2n**, **2r**, and **2z** were converted into the parent hydroxyl compounds **1c**, **1f**, **1n**, **1r**, and **1z**, respectively, within 35–50 min in 80–90% yields under similar reaction conditions, which are given in the Experimental Section.

The efficiency and generality of the present method can be realized at a glance by comparing our results with those of some recently reported procedures (shown in Table 3). The results have been compared with respect to the reaction times, mol-% of the catalyst used, and yields. Here we have chosen some of the substrates as model substrates. In case of entry **1**, the yields are comparable, but the reaction time proves the efficiency of our protocol. For entry **2**, the desired THP ether **2q** was difficult to obtain when $Bi(OTf)_3 \cdot 4H_2O$ was used, but it can be prepared in good yield and without any difficulty by employing our protocol. For entries **3**, **4** and **5**, the yields are better and reaction times are lower when our protocol is used. The protocol with $Bi(OTf)_3 \cdot 4H_2O$ requires not only an inert atmosphere, but also $Bi(OTf)_3 \cdot 4H_2O$ has to be prepared prior to use. Therefore, considering all these facts we believe that bismuth(III) nitrate pentahydrate is a relatively better catalyst for tetrahydropyranylation of hydroxyl compounds.

Table 1. Tetrahydropyranylation of alcohols and phenols in the presence of a catalytic amount of bismuth(III) nitrate pentahydrate [$Bi(NO_3)_3{\cdot}5H_2O$].

Entry	Substrate (**1**)	Time [min]	Product[a] (**2**)	Yield[b,c] [%]
a		15		92[18a]
b		15		84
c		15		91
d		20		90
e		25		77[18a]
f		12		85[27]
g		22		84[18a]
h		18		88[27]
i		45		82[8]
j		18		90[18a]
k		22		90[8]
l		18		90
m		22		65
n		25		76
o		30		83[28]
p		25		87
q		45		74
r		16		83
s		18		86[28]
t		15		87
u		15		81
v		12		86
w		15		87
x		12		85
y		27		83
z	Ar = 4-Methoxyphenyl	18		81
a′		20		84[18b]
b′		35		79
c′		55		60
d′		32		79
e′		25		84
f′		40		83

[a] All starting materials and final products were characterized by IR, ^1H NMR, and ^{13}C NMR spectroscopy and by elemental analysis. [b] Isolated yield. [c] The reference refers to the spectroscopic data for the particular compound.

Table 2. Selective tetrahydropyranylation of diols using a catalytic amount of $Bi(NO_3)_3{\cdot}5H_2O$.

Entry	Substrate (**1**)	Time [min]	Product[a] (**2**)	Yield[b] [%]
g′		12		73
h′		15		70[18a]
i′		12		83[18a]
j′		20		75
k′		15		62
l′		18		76

[a] All starting materials and final products were characterized by IR, ^1H NMR, and ^{13}C NMR spectroscopy and by elemental analysis. [b] Isolated yield.

Table 3. Comparison of results of tetrahydropyranylation of alcohols and phenols with other catalysts.

Entry	Alcohol/Phenol	Catalyst	Mol-%	Time	Yield [%]
1		LiOTf	60–70	3 h	92[11]
		$Bi(OTf)_3{\cdot}4H_2O$	0.1	4 h	85[15]
		$Bi(NO_3)_3{\cdot}5H_2O$	5	20 min	90
2		LiOTf	60–70	6 h	92[11]
		$Bi(OTf)_3{\cdot}4H_2O$	0.1	–	0[15]
		$Bi(NO_3)_3{\cdot}5H_2O$	5	45 min	74
3		H_2O	–	9 h	55[18a]
		$Bi(OTf)_3{\cdot}4H_2O$	0.1	3.25 h	78[15]
		$Bi(NO_3)_3{\cdot}5H_2O$	5	20 min	84
4		$NbCl_5$	10	3 h	89[18b]
		H_2O	–	10 h	76[18a]
		$Bi(OTf)_3{\cdot}4H_2O$	0.1	2 h	74[15]
		$Bi(NO_3)_3{\cdot}5H_2O$	5	22 min	90
		TBATB	0.1	1 h	74[9]
		TBATB	2.5	45 min	88[9]
5		LiOTf	60–70	2.5 h	94[11]
		$Bi(OTf)_3{\cdot}4H_2O$	0.1	1h	82[15]
		$Bi(NO_3)_3{\cdot}5H_2O$	15	22 min	90

Conclusions

In conclusion, the present methodology demonstrates $Bi(NO_3)_3{\cdot}5H_2O$ as an effective catalyst for tetrahydropyranylation/depyranylation of alcohols and phenols. The main advantages of this method are: mild, clean and simple reaction conditions, good yields, nonaqueous workup, and environmentally benign reagents. In addition, our methodology might be useful for substrates containing a wide variety of other protecting groups. Furthermore, this method is also expected to have much better application in organic synthesis because of the very low cost and nontoxic nature of the reagent. We believe this methodology will be a valuable addition to modern synthetic methodologies.

Experimental Section

Melting points were recorded on a Büchi B-545 melting point apparatus and are uncorrected. IR spectra were recorded in KBr or neat on a Nicolet Impact 410 spectrophotometer. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 200 MHz, Bruker 300 MHz, and Jeol 400 MHz spectrometer in $CDCl_3$ by using TMS as internal reference. Elemental analyses were carried out with a Perkin–Elmer 2400 automatic carbon, hydrogen, nitrogen, and sulfur analyzer. Column chromatographic separations were done on SRL silica gel (60–120 mesh).

Typical Procedure for Tetrahydropyranylation: Bismuth(III) nitrate pentahydrate (0.024 g, 0.05 mmol) was added to a mixture of alcohol or phenol (1 mmol) and 3,4-dihydro-2*H*-pyran (109 μL, 1.2 mmol) in dichloromethane (2 mL). The mixture was stirred at room temperature. After completion of the reaction as confirmed by TLC, the reaction mixture was reduced to approximately 1 mL, and then it was passed through a short basic alumina column to afford the desired THP ether.

2b: Yield: 0.173 g, 84%. IR (Neat): 2942, 2869, 1600, 1465, 1357, 1127, 1038 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.47–1.82 (m, 6 H), 2.91 (t, J = 7.2 Hz, 2 H), 3.41–3.47 (m, 1 H), 3.61 (dt, J = 7.2, J = 4.0, 10.0 Hz, 1 H), 3.72–3.77 (m, 1 H), 3.94 (dt, J = 7.6, 5.2, 9.6 Hz, 1 H), 4.58 (t, J = 3.5 Hz, 1 H), 7.16–7.28 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.6, 25.6, 30.8, 36.5, 62.2, 68.3, 98.7, 126.0, 128.1 (2 C), 128.9 (2 C), 140.0 ppm. $C_{13}H_{18}O_2$ (206.28): calcd. C 75.69, H 8.79; found C 75.43, H 8.73%.

2c: Yield: 0.247 g, 91%. IR (Neat): 2942, 2865, 1595, 1465, 1357, 1130, 1075, 1038 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.53–1.87 (m, 6 H), 3.50–3.56 (m, 1 H), 3.85–3.91 (m, 1 H), 4.44 (d, J = 12.4 Hz, 1 H), 4.66–4.68 (m, 1 H), 4.71 (d, J = 12.0 Hz, 1 H), 7.23 (d, J = 8.8 Hz, 2 H), 7.46 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 25.5, 30.6, 62.2, 68.0, 97.7, 121.2, 129.2 (2 C), 131.3 (2 C), 137.2 ppm. $C_{12}H_{15}O_2Br$ (271.15): calcd. C 53.16, H 5.58; found C 53.24, H 5.49%.

2d: Yield: 0.213 g, 90%. IR (Neat): 2943, 2869, 1605, 1522, 1346, 1202, 1127, 1036 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.52–1.92 (m, 6 H), 3.51–3.59 (m, 1 H), 3.86–3.92 (m, 1 H), 4.61 (d, J = 13.6 Hz, 1 H), 4.73–4.74 (m, 1 H), 4.89 (d, J = 13.2 Hz, 1 H), 7.53 (d, J = 9.2 Hz, 2 H), 8.20 (d, J = 8.8 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 25.4, 30.5, 62.3, 67.6, 98.2, 123.4 (2 C), 127.6 (2 C), 145.9, 147.3 ppm. $C_{12}H_{15}NO_4$ (237.25): calcd. C 60.75, H 6.37, N 5.90; found C 60.54, H 6.29, N 5.78%.

2l: Yield: 0.193 g, 90%. IR (neat): 2935, 2873, 1460, 1347, 1204, 1132, 1030 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, J = 7.3 Hz, 3 H), 0.90 (t, J = 7.3 Hz, 3 H), 1.25–1.31 (m, 6 H), 1.39–1.83 (m, 10 H), 3.42–3.56 (m, 2 H), 3.85–3.91 (m, 1 H), 4.61–4.63 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.1, 14.0, 19.7, 22.6, 24.7, 25.8, 31.1, 32.1, 32.9, 34.3, 62.6, 78.0, 97.2 ppm. $C_{13}H_{26}O_2$ (214.35): calcd. C 72.85, H 12.23; found C 72.78, H 12.19%.

2m: Yield: 0.148 g, 65%. IR (neat): 2945, 2863, 1460, 1378, 1281, 1204, 1132, 1086, 1030, 994 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, J = 6.8 Hz, 3 H), 0.89 (t, J = 7.2 Hz, 3 H), 1.15 (s, 3 H), 1.26–1.39 (m, 6 H), 1.41–1.84 (m, 10 H), 3.42–3.45 (m, 1 H), 3.93–3.97 (m, 1 H), 4.70 (br. s, 1 H) ppm. $C_{14}H_{28}O_2$ (228.37): calcd. C 73.63, H 12.36; found C 73.84, H 12.27%.

2n: Yield: 0.180 g, 76%. IR (neat): 2935, 2858, 1440, 1245, 1204, 1158, 1132, 1068, 1046, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.47–1.54 (m, 4 H), 1.56–1.66 (m, 8 H), 1.76–1.85 (m, 6 H), 2.12 (s, 3 H), 3.40–3.48 (m, 1 H), 3.91–3.99 (m, 1 H), 4.82–4.85 (m, 1 H) ppm. $C_{15}H_{24}O_2$ (236.35): calcd. C 76.23, H 10.23; found C 76.03, H 10.29%.

2p: Yield: 0.179 g, 87%. IR (neat): 2945, 2858, 1696, 1609, 1511, 1358, 1306, 1250, 1209, 1163, 1112, 1040 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.49–1.78 (m, 4 H), 1.81–1.99 (m, 2 H), 3.57–3.62 (m, 1 H), 3.80–3.86 (m, 1 H), 5.47–5.51 (m, 1 H), 7.12 (d, J = 8.8 Hz, 2 H), 7.79 (d, J = 8.8 Hz, 2 H), 9.84 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4, 24.9, 30.6, 62.0, 96.0, 116.4 (2 C), 131.8 (2 C), 132.3, 162.1, 191.1 ppm. $C_{12}H_{14}O_3$ (206.24): calcd. C 69.89, H 6.84; found C 69.78, H 6.78%.

2q: Yield: 0.169 g, 74%. M.p. 44–46 °C. IR (KBr): 3056, 2941, 1617, 1599, 1510, 1466, 1390, 1253, 1217, 1173, 1037 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.60–1.73 (m, 3 H), 1.89–1.92 (m, 2 H), 1.99–2.08 (m, 1 H), 3.62–3.66 (m, 1 H), 3.91–3.97 (m, 1 H), 5.56 (t, J = 3.3 Hz, 1 H), 7.21–7.25 (m, 1 H), 7.32 (d, J = 8.0 Hz, 1 H), 7.39–7.43 (m, 2 H), 7.72–7.76 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.7, 25.2, 30.4, 61.9, 96.4, 110.4, 119.1, 123.8, 126.2, 127.0, 127.5, 129.2, 129.4, 134.5, 154.8 ppm. $C_{15}H_{16}O_2$ (228.29): calcd. C 78.92, H 7.06; found C 78.71, H 6.98%.

2r: Yield: 0.191 g, 83%. IR (neat): 2945, 2873, 1471, 1460, 1439, 1372, 1250, 1034 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 1.39–1.84 (m, 12 H), 2.04 (s, 3 H), 3.36–3.41 (m, 1 H), 3.48–3.51 (m, 1 H), 3.71–3.76 (m, 1 H), 3.82–3.88 (m, 1 H), 4.06 (t, J = 6.8 Hz, 2 H), 4.56–4.58 (m, 1 H) ppm. $C_{12}H_{22}O_4$ (230.30): calcd. C 62.58, H 9.63; found C 62.72, H 9.57%.

2t: Yield: 0.291 g, 87%. IR (neat): 2930, 2857, 1719, 1453, 1276, 1217, 1114, 1038 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ = 1.36–1.86 (m, 18 H), 3.35–3.41 (m, 1 H), 3.50–3.56 (m, 1 H), 3.70–3.78 (m, 1 H), 3.86–3.89 (m, 1 H), 4.31 (t, J = 6.8 Hz, 2 H), 4.56–4.60 (m, 0.5 H), 4.94–4.98 (m, 0.5 H), 7.43 (t, J = 7.2 Hz, 2 H), 7.55 (t, J = 7.2 Hz, 1 H), 8.04 (d, J = 8.4 Hz, 2 H) ppm. $C_{20}H_{30}O_4$ (334.45): calcd. C 71.83, H 9.04; found C 71.56, H 9.10%.

2u: Yield: 0.291 g, 81%. IR (neat): 2950, 2868, 1598, 1496, 1450, 1332, 1163, 1071, 1030 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ = 1.38–1.83 (m, 12 H), 3.02 (t, J = 6.6 Hz, 2 H), 3.31–3.36 (m, 1 H), 3.45–3.50 (m, 1 H), 3.66–3.69 (m, 1 H), 3.80–3.86 (m, 1 H), 4.50–4.52 (m, 0.3 H), 4.90–4.92 (m, 0.7 H), 7.15–7.28 (m, 12 H), 7.39–7.41 (m, 3 H) ppm. $C_{29}H_{34}O_3$ (430.58): calcd. C 80.90, H 7.96; found C 80.66, H 7.89%.

2v: Yield: 0.295 g, 86%. IR (neat): 2945, 2868, 1603, 1465, 1362, 1183, 1132, 1081, 1050, 968, 963 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.40–1.70 (m, 12 H), 2.45 (s, 3 H), 3.32–3.35 (m, 1 H), 3.49–3.50 (m, 1 H), 3.68–3.70 (m, 1 H), 3.80–3.89 (m, 1 H), 4.03 (t, J = 6.8 Hz, 2 H), 4.53–4.54 (m, 1 H), 7.34 (d, J = 8.0 Hz, 2 H), 7.78 (d, J = 8.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 21.7, 22.3, 25.5, 28.8, 29.1, 30.8, 62.4, 67.1, 70.5, 98.8, 127.7 (2 C), 129.6 (2 C), 133.0, 144.5 ppm. $C_{17}H_{26}O_5S$ (342.45): calcd. C 59.63, H 7.65, S 9.36; found C 59.40, H 7.71, S 9.15%.

2w: Yield: 0.300 g, 87%. IR (neat): 2937, 2860, 1465, 1358, 1254, 1106, 1031 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.04 (s, 6 H), 0.89 (s, 9 H), 1.25–1.30 (m, 6 H), 1.48–1.87 (m, 12 H), 3.34–3.40 (m, 1 H), 3.47–3.50 (m, 1 H), 3.59 (t, J = 6.4 Hz, 2 H), 3.69–3.73 (m, 1 H), 3.84–3.89 (m, 1 H), 4.56–4.57 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.3 (2 C), 18.3, 19.6, 25.5, 25.7, 25.9 (3 C), 26.1, 29.3, 29.4, 29.7, 30.7, 32.8, 62.2, 63.2, 67.6, 98.8 ppm. $C_{19}H_{40}O_3Si$ (344.61): calcd. C 66.22, H 11.70; found C 66.46, H 11.62%.

2x: Yield: 0.399 g, 85%. IR (neat): 2935, 2858, 1475, 1440, 1388, 1363, 1204, 1112, 1030, 979 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): (mixture of diastereomers): δ = 1.04 (s, 9 H), 1.10–1.35 (m, 8 H), 1.52–1.85 (m, 10 H), 3.35–3.54 (m, 2 H), 3.64 (t, J = 6.4 Hz, 2 H), 3.70–3.92 (m, 2 H), 4.52–4.62 (m, 0.4 H), 4.90–5.00 (m, 0.6 H), 7.30–7.46 (m, 6 H), 7.61–7.71 (m, 4 H) ppm. $C_{29}H_{44}O_3Si$ (468.75): calcd. C 74.31, H 9.46; found C 74.09, H 9.40%.

2y: Yield: 0.235 g, 83%. IR (neat): 2930, 1614, 1511, 1255, 1240, 1122, 1040 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.46–2.00 (m, 6 H), 3.31–3.41 (m, 2 H), 3.48–3.63 (m, 3 H), 3.89–3.93 (m, 1 H), 5.41 (t, J = 3.0 Hz, 1 H), 5.64 (s, 1 H), 7.00 (d, J = 8.8 Hz, 2 H), 7.44 (d, J = 8.7 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =

19.1, 25.6, 30.7, 40.6 (2 C), 56.5, 62.4, 96.7, 116.8 (2 C), 129.8 (2 C), 133.1, 157.3 ppm. $C_{14}H_{18}O_2S_2$ (282.41): calcd. C 59.54, H 6.42, S 22.70; found C 60.05, H 6.39, S 22.54%.

2z: Yield: 0.359 g, 81%. IR (neat): 2966, 2925, 2843, 1619, 1516, 1450, 1327, 1260, 1178, 1086, 1030 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.53–1.87 (m, 12 H), 2.70–2.80 (m, 2 H), 2.92–2.98 (m, 2 H), 3.45–3.60 (m, 4 H), 3.85–3.88 (m, 4 H), 3.88 (s, 3 H), 4.85–4.95 (m, 2 H), 6.22 (s, 1 H), 7.00 (d, J = 8.8 Hz, 2 H), 7.84 (d, J = 8.0 Hz, 2 H) ppm. $C_{22}H_{34}O_5S_2$ (442.63): calcd. C 59.70, H 7.74, S 14.49; found C 59.56, H 7.67, S 14.32%.

2b′: Yield: 0.272 g, 79%. IR (neat): 2945, 1470, 1388, 1271, 1230, 1076, 1009 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ = 1.28 (s, 3 H), 1.29 (s, 3 H), 1.39 (s, 3 H), 1.49 (s, 3 H), 1.50–1.82 (m, 6 H), 3.43–3.49 (m, 1 H), 3.56–3.85 (m, 2 H), 3.93–3.98 (m, 1 H), 4.20 (dd, J = 1.7, 7.8 Hz, 1 H), 4.23–4.29 (m, 1 H), 4.52–4.61 (m, 2 H), 4.88 (d, J = 4.9 Hz, 1 H), 5.48 (dd, J = 5.2, 9.0 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 19.5, 19.7 (2 C), 24.4, 24.5, 24.9, 25.4 (2 C), 25.9, 26.0, 30.5, 30.7 (2 C), 62.2, 62.4, 62.9, 65.9, 66.1, 66.5, 67.4, 70.5, 70.6, 70.7, 71.0, 71.4, 94.6, 96.3, 96.4, 99.0, 99.1, 108.5, 109.1, 109.2 ppm. $C_{17}H_{28}O_7$ (344.40): calcd. C 59.29, H 8.19; found C 59.52, H 8.23%.

2c′: Yield: 0.288 g, 60%. IR (neat): 2935, 2858, 1634, 1470, 1383, 1265, 1086, 1030, 974 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ = 1.33 (t, J = 7.6 Hz, 3 H), 1.42–1.76 (m, 12 H), 2.63–2.67 (m, 2 H), 3.23–3.67 (m, 7 H), 3.90–4.00 (m, 1 H), 4.22–4.27 (m, 1 H), 4.38–4.48 (m, 3 H), 4.64–4.70 (m, 1 H), 5.44 (s, 1 H), 7.21–7.27 (m, 3 H), 7.34–7.38 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.04, 15.16, 19.03, 19.63, 20.03, 21.13, 24.44, 24.87, 25.22, 25.44, 29.03, 30.69, 31.00, 65.40, 65.63, 66.96, 68.65, 70.09, 70.83, 72.15, 73.29, 79.34, 80.57, 83.97, 84.20, 84.87, 86.23, 101.24, 101.72, 102.35, 102.79, 125.98, 126.33, 128.21, 137.28 ppm. $C_{25}H_{36}SO_7$ (480.62): calcd. C 62.48, H 7.55, S 6.67; found C 62.71, H 7.59, S 6.62

2d′: Yield: 0.493 g, 79%. IR (neat): 2935, 2858, 1634, 1470, 1383, 1265, 1086, 1030, 974 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.41–1.94 (m, 6 H), 3.49–4.15 (m, 10 H), 4.51–4.96 (m, 7 H), 5.20–5.30 (m, 1 H), 7.15–7.40 (m, 20 H) ppm. $C_{39}H_{44}O_7$ (624.77): calcd. C 74.98, H 7.10; found C 74.73, H 7.01

2e′: Yield: 0.473 g, 84%. IR (neat): 2941, 2873, 1453, 1354, 1202, 1074, 1033 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.43–1.95 (m, 6 H), 2.47 (t, J = 6.0 Hz, 1 H, 4-H), 3.39 (s, 3 H), 3.40–4.02 (m, 11 H), 4.47–4.77 (m, 5 H), 4.95–5.02 (m, 1 H), 7.24–7.37 (m, 15 H) ppm. $C_{34}H_{42}O_7$ (562.70): calcd. C 72.57, H 7.52; found C 72.63, H 7.48.

2f′: Yield: 0.306 g, 83%. IR (neat): 3235, 3109, 2966, 2935, 2817, 1788, 1690, 1481, 1409, 1271, 1209, 1107, 1055, 989 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ = 1.33 (s, 3 H), 1.34 (s, 3 H), 1.49 (s, 3 H), 1.51 (s, 3 H), 1.47–1.90 (m, 12 H), 3.49–3.57 (m, 4 H), 3.65 (dd, J = 2.4, 11.2 Hz, 1 H), 3.78–3.83 (m, 2 H), 3.94 (dd, J = 3.2, 11.2 Hz, 1 H), 4.01–4.05 (m, 2 H), 4.37–4.42 (m, 1 H), 4.57–4.59 (m, 1 H), 4.73–4.74 (m, 1 H), 4.81–4.82 (m, 1 H), 4.87–4.88 (m, 1 H), 4.89–4.95 (m, 1 H), 5.64 (d, J = 8.0 Hz, 1 H), 5.66 (d, J = 8.0 Hz, 1 H), 5.88 (d, J = 2.4 Hz, 1 H), 5.90 (d, J = 2.4 Hz, 1 H), 7.61 (d, J = 8.0 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 8.58 (br. s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.01, 20.84, 25.56, 25.58, 25.62, 25.78, 25.84, 27.64, 30.81, 32.42, 63.05, 63.11, 64.22, 67.52, 67.78, 80.99, 81.20, 85.45, 85.68, 85.91, 92.89, 94.85, 99.22, 99.84, 102.05, 102.33, 114.24, 114.44, 140.88, 141.48, 150.46 (2 C), 163.86 (2 C) ppm. $C_{17}H_{24}N_2O_7$ (368.38): calcd. C 55.43, H 6.57, N 7.60; found C 55.61, H 6.59, N 7.53.

2g′: Yield: 0.117 g, 73%. IR (neat): 3416, 2950, 2879, 1455, 1352, 1209, 1127, 1081, 1035 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.51–1.63 (m, 3 H), 1.67–1.89 (m, 3 H), 2.25 (br. s, 1 H, D_2O exchangeable), 3.48–3.61 (m, 2 H), 3.78 (t, J = 5.2 Hz, 2 H), 3.83–3.95 (m, 2 H), 4.57–4.59 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.8, 25.4, 30.7, 32.1, 61.5, 62.6, 66.3, 99.1 ppm. $C_8H_{16}O_3$ (160.21): calcd. C 59.98, H 10.07; found C 60.05, H 10.12.

2j′: Yield: 0.173 g, 75%. IR (neat): 3422, 2931, 2858, 1454, 1354, 1276, 1127, 1030 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.30–1.40 (br. s, 8 H), 1.50–1.61 (m, 6 H), 1.69–174 (m, 2 H), 1.80–1.90 (m, 2 H), 2.05 (br. s, 1 H, D_2O exchangeable), 3.35–3.41 (m, 1 H), 3.48–3.51 (m, 1 H), 3.64 (t, J = 6.8 Hz, 2 H), 3.70–3.74 (m, 1 H), 3.84–3.89 (m, 1 H), 4.56–4.58 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 25.5, 25.7, 26.2, 29.3, 29.4, 29.7, 30.7, 32.7, 62.2, 62.7, 67.6, 98.7 ppm. $C_{13}H_{26}O_3$ (230.35): calcd. C 67.79, H 11.38; found C 67.65, H 11.29.

2k′: Yield: 0.106 g, 62%. IR (neat): 3411, 2945, 2863, 1450, 1393, 1358, 1271, 1127, 1020 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): 1.52–1.85 (m, 7 H), 3.53–3.56 (m, 1 H), 3.81–3.86 (m, 1 H), 4.23–4.37 (m, 4 H), 4.81 (t, J = 3.2 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.4, 25.7, 30.6, 51.5, 54.7, 62.3, 82.1, 84.6, 97.2 ppm. $C_9H_{14}O_3$ (170.21): calcd. C 63.51, H 8.29; found C 63.64, H 8.24.

2l′: Yield: 0.148 g, 76%. IR (neat): 3416, 2940, 2873, 1445, 1393, 1265, 1204, 1132, 1081, 1035, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): (mixture of diastereomers): δ = 1.52–1.83 (m, 6 H), 3.27–3.37 (br. s, 1 H, D_2O exchangeable), 3.51–3.99 (m, 7 H), 4.51–4.53 (m, 0.5 H), 4.57–4.59 (m, 0.5 H) ppm.^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.3, 20.6, 25.5, 25.6, 31.0, 31.1, 45.8, 46.2, 63.5, 64.0, 70.1, 70.5, 70.8 (2 C), 100.4, 100.9 ppm. $C_8H_{15}O_3Cl$ (194.66): calcd. C 49.36, H 7.77; found C 49.52, H 7.84.

Typical Procedure for Depyranylation: Bismuth(III) nitrate pentahydrate (0.024 g, 0.05 mmol) was added into a stirred solution of the THP ether of 4-bromobenzyl alcohol **2c** (0.271 g, 1 mmol) in methanol (2 mL) at room temperature. The reaction was complete within 40 min, and the mixture was concentrated in rotavapor. The crude residue was purified through a short silica gel column. The desired 4-bromobenzyl alcohol (**1c**) was obtained (0.170 g) in 91% yield.

Acknowledgments

A. T. K. thanks the DST, New Delhi for a financial grant (Grant No. SP/S1/G-35/98), S. G. is grateful to IITG and L. H. C. is thankful to CSIR for their research fellowships. We are thankful to the Director, IIT Guwahati for the general facilities to carry out the research work. We are thankful to Prof. G. Sundararajan, Department of Chemistry, IIT Madras and Dr. N. G. Ramesh, Department of Chemistry, IIT Delhi for recording some of the ^1H NMR and ^{13}C NMR spectra. We are very grateful to referees for their valuable comments and suggestions.

[1] a) T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 3rd ed., John Wiley & Sons Inc., New York, **1999**, pp. 49–54; b) P. J.Kocieński, *Protecting Groups*, 1st ed., Georg Thieme Verlag, Stuttgart, **1994**, pp. 83–85.
[2] a) E. J. Corey, H. Niwa, J. Knolle, *J. Am. Chem. Soc.* **1978**, *100*, 1942–1943; b) K. F. Bernady, M. B. Floyd, J. F. Poletto, M. J. Weiss, *J. Org. Chem.* **1979**, *44*, 1438–1447.
[3] H. Alper, L. Dinkes, *Synthesis* **1972**, 81.
[4] M. Miyashita, A. Yoshikoshi, P. A. Grieco, *J. Org. Chem.* **1977**, *42*, 3772–3774.
[5] N. Rezai, F. A. Meybodi, P. Salehi, *Synth. Commun.* **2000**, *30*, 1799–1805.
[6] N. Deka, J. C. Sarma, *Synth. Commun.* **2000**, *30*, 4435–4441.

[7] M. A. Reddy, L. R. Reddy, N. Bhanumathi, K. R. Rao, *Synth. Commun.* **2000**, *30*, 4323–4328.
[8] Y.-S. Hon, C.-F. Lee, R.-J. Chen, P.-H. Szu, *Tetrahedron* **2001**, *57*, 5991–6001.
[9] S. Naik, R. Gopinath, B. K. Patel, *Tetrahedron Lett.* **2001**, *42*, 7679–7681.
[10] V. V. Namboodiri, R. S. Varma, *Tetrahedron Lett.* **2002**, *43*, 1143–1146.
[11] B. Karimi, J. Maleki, *Tetrahedron Lett.* **2002**, *43*, 5353–5355.
[12] T. Mineno, *Tetrahedron Lett.* **2002**, *43*, 7975–7978.
[13] V. V. Namboodiri, R. S. Verma, *Chem. Commun.* **2002**, 342–343.
[14] J. S. Yadav, B. V. Subba Reddy, D. Gnaneshwar, *New J. Chem.* **2003**, *27*, 202–204.
[15] J. R. Stephens, P. L. Butler, C. H. Clow, M. C. Oswald, R. C. Smith, R. S. Mohan, *Eur. J. Org. Chem.* **2003**, 3827–3831.
[16] A. T. Khan, E. Mondal, B. M. Borah, S. Ghosh, *Eur. J. Org. Chem.* **2003**, 4113–4117.
[17] A. T. Khan, L. H. Choudhury, S. Ghosh, *Tetrahedron Lett.* **2004**, *45*, 7891–7894.
[18] a) V. Kavala, A. K. Samal, B. K. Patel, K. Nagaiah, *ARKIVOC* **2005**, *i*, 22–29; b) K. Nagaiah, B. V. S. Reddy, D. Sreenu, A. V. Narsaiah, *ARKIVOC* **2005**, *iii*, 192–199.
[19] B. Karimi, M. Khalkhali, *J. Mol. Catal. A: Chem.* **2005**, *232*, 113–117.
[20] G. Sartori, R. Ballini, F. Bigi, G. Bosica, R. Maggi, P. Righi, *Chem. Rev.* **2004**, *104*, 199–250.
[21] A. T. Khan, E. Mondal, S. Ghosh, S. Islam, *Eur. J. Org. Chem.* **2004**, 2002–2009.
[22] A. T. Khan, S. Ghosh, L. H. Choudhury, *Eur. J. Org. Chem.* **2004**, 2198–2204.
[23] A. T. Khan, S. Islam, L. H. Choudhury, S. Ghosh, *Tetrahedron Lett.* **2004**, *45*, 9617–9621.
[24] H. Gaspard-Iloughmane, C. L. Roux, *Eur. J. Org. Chem.* **2004**, 2517–2532.
[25] N. M. Leonard, L. C. Wieland, R. S. Mohan, *Tetrahedron* **2002**, *58*, 8373–8397.
[26] a) I. M. Baltork, H. Aliyan, A. R. Khosropour, *Tetrahedron* **2001**, *57*, 5851–5854; b) S. Cunha, B. R. de Lima, A. R. De Souza, *Tetrahedron Lett.* **2002**, *43*, 49–52; c) I. M. Baltork, M. M. Khodaei, K. Nikoofar, *Tetrahedron Lett.* **2003**, *44*, 591–594; d) N. Srivastava, B. K. Banik, *J. Org. Chem.* **2003**, *68*, 2109–2114; e) M. M. Khodaei, I. M. Baltork, K. Nikoofar, *Bull. Korean Chem. Soc.* **2003**, *24*, 885–886; f) D. H. Aggen, J. N. Arnold, P. D. Hayes, N. J. Smoter, R. S. Mohan, *Tetrahedron* **2004**, *60*, 3675–3679; g) M. M. Khodaei, A. R. Khosropour, M. Jowkar, *Synthesis* **2005**, 1301–1304.
[27] S. Hoyer, P. Laszlo, *Synthesis* **1986**, 655–657.
[28] A. Semwal, S. K. Nayak, *Synthesis* **2005**, 71–74.

Received: June 6, 2005
Published Online: October 4, 2005

