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Selective cleavage of acetals with $ZnBr_2$ in dichloromethane

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Abstract—A selective cleavage of acetals of 1,2- and 1,3-diols has been achieved under mild conditions using $ZnBr_2$ in dichloromethane at room temperature. Acetal types cleavable by this procedure include benzylidene, isopropylidene and cyclohexylidene acetals. This method is compatible with several other types of hydroxyl protecting groups such as Bn, Bz, TBDPS, TIPS and TBDMS.

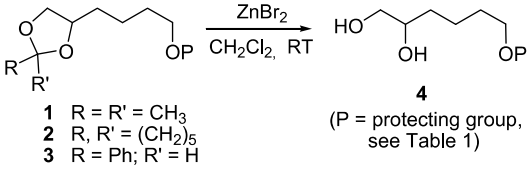
1. Introduction

The selective protection and deprotection of hydroxyl groups has played a crucial role in the synthesis of complex organic molecules. Among the many reported hydroxyl protecting groups, acetals are used with high frequency.[1] Although protic acids are commonly used to cleave acetal moieties, a number of Lewis acids have also been shown to be effective for this purpose. Examples taken from the literature are $FeCl_3 \cdot 6H_2O$,[2] $FeCl_3/SiO_2$,[3] $CuCl_2 \cdot 2H_2O$,[4] $Zn(NO_3)_2 \cdot 6H_2O$[5] and $(NH_4)_2Ce(NO_3)_6$.[6] However, some of these reagents show a limited compatibility with other commonly used hydroxyl protecting groups such as silyl or benzyl fragments.[7]

In the course of a research project aimed at the synthesis of polyfunctionalized, natural compounds, we observed that $ZnBr_2$ provides extremely mild aprotic conditions for acetal cleavage. While $ZnBr_2$ has been extensively used for deprotection of MEM,[8] *N*-Boc,[9] *t*-butyl ester[10] and even silyl groups,[11] it has not been systematically used for the cleavage of acetals.[12]

2. Results and discussion

We here report a very mild and efficient method to cleave acetals in the presence of several other types of hydroxyl protecting groups. Scheme 1 shows the case of acetals of 1,2-diols. Thus, the vicinal diol moiety of the commercially available 1,2,6-hexanetriol was protected as an acetal, and the distal primary alcohol was protected with other various groups. In the event, 4–6 equiv of $ZnBr_2$ in dichloromethane at room temperature were found necessary to perform a complete acetal cleavage in a reasonable time (Table 1).



Scheme 1.

Table 1. Selective cleavage of acetals of 1,2-diols using $ZnBr_2$

Entry	Acetal	P	$ZnBr_2$ (equiv)	Time (h)	Yield (%)
1	**1**	TPS	4	2	94
2	**1**	TIPS	4	2	95
3	**1**	TBS	4	3	65
4	**1**	Bn	4	3	86
5	**1**	Bz	4	3	78
6	**1**	THP	4	6	18[a]
7	**1**	MOM	4	6	—[a]
8	**1**	MEM	4	6	—[a]
9	**2**	TPS	4	5	92
10	**2**	TIPS	6	6	78
11	**2**	TBS	6	7	61
12	**2**	Bn	6	5	73
13	**2**	Bz	6	5	72
14	**2**	THP	6	6	43[a]
15	**2**	MOM	6	6	—[a]
16	**2**	MEM	6	6	—[a]
17	**3**	TPS	4	5	62
18	**3**	TIPS	4	3	75
19	**3**	TBS	5	5	50
20	**3**	Bn	5	5	60
21	**3**	Bz	5	5	68
22	**3**	THP	5	7	11[a]

[a] Formation of unprotected 1,2,6-hexanetriol was observed.

Keywords: Acetals; Protecting groups; Selective cleavage; Mild conditions; Lewis acid.
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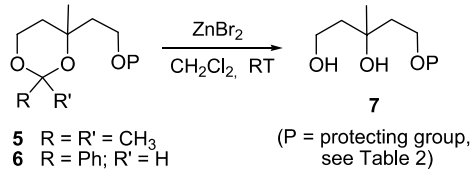
As shown in Table 1, the method is applicable to substrates containing a range of protecting groups such as *t*-butyldiphenyl silyl (TPS, entries 1, 9 and 17), triisopropyl-silyl (TIPS, entries 2, 10 and 18), *t*-butyldimethylsilyl (TBS, entries 3, 11 and 19), benzyl (Bn, entries 4, 12 and 20) and benzoyl (Bz, entries 5, 13 and 21). However, $ZnBr_2$ proved less selective towards other kind of acetals such as tetrahydropyranyl (THP) ethers, which are extensively removed under these conditions (entries 6, 14 and 22) and methoxymethyl (MOM) or methoxyethoxymethyl (MEM) ethers, which are eliminated simultaneously with the acetonide function (entries 7, 8, 15 and 16).[8]

The procedure also allows the cleavage of acetals of 1,3-diols under the same conditions. Here, 3-methyl-1,3,5-pentanetriol was used as the precursor alcohol (see Scheme 2 and Table 2).



Scheme 2.

Table 2. Selective cleavage of acetals of 1,3-diols using $ZnBr_2$

Entry	Acetal	P	$ZnBr_2$ (equiv)	Time (h)	Yield (%)
1	**5**	TPS	4	1	86
2	**6**	TPS	5	3	85
3	**6**	Bn	5	3	81

$ZnBr_2$ does not dissolve in dichloromethane, where it forms a cloudy suspension. We thus, explored more polar solvents such as THF, ethyl acetate or acetonitrile, where a total or more pronounced solubilization of the reagent might be achieved. However, no improvements were obtained with these solvents. Although $ZnBr_2$ is soluble in THF, no reaction took place in this solvent, probably because coordination of $ZnBr_2$ with the Lewis-basic THF may compete with the acetal coordination, thereby preventing cleavage of the protecting group. Acetonitrile, which partially solubilizes $ZnBr_2$, was also useless as no reaction was observed, either. Ethyl acetate solubilizes $ZnBr_2$ but its use gave rise to very long reaction times (3–5 days) and low yields. The very weakly Lewis-basic dichlorometane is thus the solvent of choice.

In addition to $ZnBr_2$, we have also investigated the use of $ZnCl_2$ for acetal cleavage. However, longer reaction times were needed than with $ZnBr_2$ and yields were lower.

Although we initially ran the reaction under anhydrous conditions, we later observed that the addition of few drops of water to the reaction medium did not cause noticeable changes in either reaction times or yields. In consequence, simple distilled CH_2Cl_2 may be used and no special caution as regards solvent dryness is needed.[13]

3. Conclusions

We have described a very mild, simple and selective method for deprotection of acetals using $ZnBr_2$ in dichloromethane at room temperature. Furthermore, this deprotection procedure is selective in the presence of some other types of hydroxyl protecting groups.

4. Experimental

4.1. General

NMR spectra were measured at 300 or 500 MHz in $CDCl_3$ solution at 25 °C. The signals of the deuterated solvent ($CDCl_3$) were taken as the reference (the singlet at δ 7.25 for ^1H NMR and the triplet centered at 77.00 ppm for ^{13}C NMR data). Carbon atom types (C, CH, CH_2, CH_3) were determined with the DEPT pulse sequence. THF was freshly distilled from sodium/benzophenone. Dichloromethane was freshly distilled from CaH_2. Tertiary amines were freshly distilled from KOH. Commercially available reagents were used as received. Unless detailed otherwise, 'work-up' means pouring the reaction mixture into brine, followed by extraction with the solvent indicated in parenthesis. If the reaction medium was acidic (basic), an additional washing with 5% aq $NaHCO_3$ (aq NH_4Cl) was performed. Drying over anhydrous Na_2SO_4 and elimination of the solvent under reduced pressure were followed by chromatography of the residue on a silica gel column (60–200 μm) with the indicated eluent. Where solutions were filtered through a Celite pad, the pad was additionally washed with the same solvent used, and the washings incorporated to the main organic layer.

4.2. Synthesis of the substrates in Tables 1 and 2

Compounds **1** (P=H, TPS, TBS, Bn, THP, MOM, MEM),[14] **2** (P=H),[15] **3** (P=H),[16] **4** (P=TPS, TBS, Bn, THP),[17] and **7** (P=TPS, Bn)[18] have been previously reported. Analytical data are given hereafter only for new compounds.

4.2.1. General procedure for the preparation of silyl ethers from the corresponding alcohols. A solution of the alcohol (1 mmol) in dry CH_2Cl_2 (5 mL) was treated under N_2 with triethyl amine (1.5 mmol), DMAP (0.03 mmol) and the corresponding silyl chloride (1.1 mmol). The reaction mixture was stirred for 12 h at room temperature and worked up (extraction with CH_2Cl_2).

4.2.2. General procedure for the preparation of benzoates from the corresponding alcohols. A solution of the alcohol (1 mmol) in dry CH_2Cl_2 (5 mL) was treated under N_2 with triethyl amine (1.5 mmol), DMAP (0.03 mmol) and benzoyl chloride (1.5 mmol). The reaction mixture was stirred for 12 h at room temperature and worked up (extraction with CH_2Cl_2).

4.2.3. General procedure for the preparation of benzyl ethers from the corresponding alcohols. A solution of the alcohol (1 mmol) in dry THF (8 mL) was added dropwise at 0 °C under N_2 to a suspension of defatted NaH (1.5 mmol) in dry THF (5 mL). After stirring the mixture for 1 h at room

temperature, tetra-*n*-butylammonium iodide (0.03 mmol) and benzyl chloride (1.5 mmol) were added. The reaction mixture was then stirred for 12 h at 60 °C and worked up (extraction with AcOEt).

4.2.4. General procedure for the preparation of THP ethers from the corresponding alcohols. A solution of the alcohol (1 mmol) in dry CH_2Cl_2 (5 mL) was treated under N_2 with 3,4-dihydro-2*H*-pyran (1.5 mmol) and PPTS (0.03 mmol). The reaction mixture was stirred for 12 h at room temperature and worked up (extraction with CH_2Cl_2).

4.2.5. General procedure for the preparation of MEM/MOM ethers from the corresponding alcohols. A solution of the alcohol (1 mmol) in dry CH_2Cl_2 (5 mL) was treated under N_2 with diisopropylethyl amine (3 mmol), DMAP (0.03 mmol) and the corresponding alkoxymethyl chloride (2 mmol). The reaction mixture was stirred for 3 h at room temperature and worked up (extraction with CH_2Cl_2).

4.2.5.1. 1,2-*O*,*O*-Isopropylidene-6-*O*-triisopropylsilyl-hexane-1,2,6-triol (1, P=TIPS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **1** (P=TIPS) (88% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 4.08 (1H, q, J=6.4 Hz), 4.25 (1H, dd, J=7.5, 6.0 Hz), 3.69 (2H, t, J=3.1 Hz), 3.51 (1H, t, J=7.5 Hz), 1.68 (2H, m), 1.60–1.45 (3H, m), 1.41 (3H, s), 1.35 (3H, s), 1.07–1.05 (18H, m); ^{13}C NMR (125 MHz) δ 108.7 (C), 76.0, 12.0 (CH), 69.3, 63.4, 33.3, 32.9, 22.0 (CH_2), 26.9, 25.7, 18.0 (×4) (CH_3). Anal. Calcd for $C_{18}H_{38}O_3Si$: C, 65.40; H, 11.59. Found: C, 65.58; H, 11.60.

4.2.5.2. 1,2-*O*,*O*-Isopropylidene-6-*O*-benzoylhexane-1,2,6-triol (1, P=Bz). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **1** (P=Bz) (80% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 8.03 (2H, dd, J=7.9, 1.1 Hz), 7.55 (1H, td, J=7.9, 1.1 Hz), 7.43 (2H, t, J=7.9 Hz), 4.33 (2H, t, J=6.4 Hz), 4.10 (1H, m), 4.04 (1H, dd, J=7.5, 6.4 Hz), 3.52 (1H, t, J=7.5 Hz), 1.82–1.48 (6H, m), 1.41 (3H, s), 1.35 (3H, s); ^{13}C NMR (125 MHz) δ 166.6, 130.4, 108.7 (C), 132.8, 129.5, 128.3, 75.8 (CH), 69.3, 64.7, 33.2, 28.9, 22.3 (CH_2), 26.9, 25.6 (CH_3). Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.98; H, 7.87.

4.2.5.3. 1,2-*O*,*O*-Cyclohexylidene-6-*O*-*t*-butyldiphenylsilyl-hexane-1,2,6-triol (2, P=TPS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **2** (P=TPS) (85% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.71–7.67 (4H, m), 7.43–7.40 (6H, m), 4.05 (2H, m), 3.70 (2H, t, J=6.00 Hz), 3.51 (1H, t, J=6.0 Hz), 1.65–1.58 (10H, m), 1.54–1.39 (6H, m), 1.08 (9H, s); ^{13}C NMR (125 MHz) δ 134.1, 109.1, 19.2 (C), 135.6, 129.5, 127.6, 75.6 (CH), 69.1, 63.6, 36.6, 35.3, 33.4, 32.5, 25.2, 24.0, 23.9, 22.0 (CH_2), 26.9 (CH_3). Anal. Calcd for $C_{28}H_{40}O_3Si$: C, 74.29; H, 8.91. Found: C, 74.42; H, 8.96.

4.2.5.4. 1,2-*O*,*O*-Cyclohexylidene-6-*O*-triisopropylsilyl-hexane-1,2,6-triol (2, P=TIPS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **2** (P=TIPS) (95% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 4.05 (1H, m), 4.00 (1H, dd, J=7.51, 5.51 Hz), 3.67 (2H, t, J=6.50 Hz), 3.48 (1H, t, J=7.51 Hz), 1.55–1.30 (9H, m), 1.20–0.80 (18H, m); ^{13}C NMR (125 MHz) δ 109.1 (C), 75.6, 12.3, 12.0 (CH), 69.0, 63.1, 36.6, 35.2, 33.5, 32.9, 25.2, 24.0, 23.8, 22.0 (CH_2), 18.0, 17.6 (CH_3). Anal. Calcd for $C_{21}H_{42}O_3Si$: C, 68.05; H, 11.42. Found: C, 67.97; H, 11.41.

4.2.5.5. 1,2-*O*,*O*-Cyclohexylidene-6-*O*-*t*-butyldimethylsilyl-hexane-1,2,6-triol (2, P=TBS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **2** (P=TBS) (80% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 4.06 (1H, m), 4.00 (1H, dd, J=7.51, 6.05 Hz), 3.60 (2H, t, J=6.41 Hz), 3.48 (1H, t, J=7.51 Hz), 1.65–1.30 (16H, m), 0.88 (9H, s), 0.04 (6H, s); ^{13}C NMR (125 MHz) δ 109.1, 18.3 (C), 75.6 (CH), 69.1, 62.9, 36.6, 35.3, 33.5, 32.7, 24.0, 23.8, 22.0 (CH_2), 25.9, −5.3 (CH_3). Anal. Calcd for $C_{18}H_{36}O_3Si$: C, 65.80; H, 11.04. Found: C, 65.88; H, 10.99.

4.2.5.6. 1,2-*O*,*O*-Cyclohexylidene-6-*O*-benzoylhexane-1,2,6-triol (2, P=Bz). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **2** (P=Bz) (86% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 8.00 (2H, m), 7.50 (1H, m), 7.38 (2H, m), 4.30 (2H, m), 4.05 (1H, m), 4.00 (1H, m), 3.46 (1H, m), 1.70 (2H, m), 1.80–1.30 (14H, m); ^{13}C NMR (125 MHz) δ 166.3, 130.2, 109.5 (C), 132.6, 129.3, 128.1, 75.2 (CH), 68.8, 64.5, 36.5, 35.1, 33.1, 28.5, 25.0, 23.8, 23.7, 22.2 (CH_2). Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.79; H, 8.22.

4.2.5.7. 4.2.5.7. 1,2-Di-*O*,*O*-cyclohexylidene-6-*O*-benzylhexane-1,2,6-triol (2, P=Bn). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **2** (P=Bn) (80% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.34–7.30 (5H, m), 4.50 (2H, s), 4.10–3.98 (2H, m), 3.50–3.46 (3H, m), 1.65–1.42 (16H, m); ^{13}C NMR (125 MHz) δ 138.6, 109.1 (C), 128.3, 127.6, 127.5, 75.6 (CH), 72.9, 70.1, 69.1, 36.6, 35.3, 33.5, 29.7, 25.2, 24.0, 23.8, 22.5 (CH_2). Anal. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.08; H, 9.27.

4.2.5.8. 1,2-*O*,*O*-Cyclohexylidene-6-*O*-(tetrahydropyran-2-yl)hexane-1,2,6-triol (2, P=THP). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **2** (P=THP) (84% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 4.52 (1H, dd, J=4.0, 2.7 Hz), 4.01 (1H, dd, J=6.50, 6.01 Hz), 3.97 (1H, dd, J=7.69, 5.89 Hz), 3.80 (1H, m), 3.69 (dt, J=9.7, 6.8 Hz), 3.45 (2H, m), 3.34 (dt, J=9.7, 6.8 Hz), 1.85–1.31 (22H, m); ^{13}C NMR (125 MHz) δ 109.0 (C), 98.8, 98.7, 75.5 (CH), 69.0, 67.2, 62.2, 36.5, 35.2, 33.5, 30.6, 29.6, 25.4, 25.1, 23.9, 23.8, 22.4, 19.5 (CH_2). Anal. Calcd for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.60; H, 10.23.

4.2.5.9. 1,2-*O*,*O*-Cyclohexylidene-6-*O*-(methoxymethyl)hexane-1,2,6-triol (2, P=MOM). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **2** (P=MOM) (86% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 4.57 (2H, s), 4.04–3.94 (2H, m), 3.50–3.40 (3H, m), 3.31 (3H, s), 1.65–1.30 (16H, m); ^{13}C NMR (125 MHz) δ 109.1 (C), 75.5 (CH), 96.3, 69.0, 67.5, 36.5, 35.2, 33.5, 29.6, 25.1, 23.9, 23.8, 22.4 (CH_2), 55.0 (CH_3). Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14. Found: C, 65.17; H, 10.12.

4.2.5.10. 1,2-*O*,*O*-Cyclohexylidene-6-*O*-(methoxyethoxymethyl)hexane-1,2,6-triol (2, P=MEM). Column

chromatography on silica gel (hexanes/EtOAc 9:1) afforded **2** (P=MEM) (80% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 4.54 (2H, s), 3.90 (1H, m), 3.86 (1H, dd, J= 7.53, 6.0 Hz), 3.52 (1H, dd, J=7.53, 6.0 Hz), 3.40 (4H, m), 3.34 (2H, t, J=7.50 Hz), 3.23 (3H, s), 1.50–1.20 (16H, m); ^{13}C NMR (125 MHz) δ 109.1 (C), 75.5 (CH), 96.4, 69.0, 67.5, 36.6, 35.2, 33.5, 29.7, 25.2, 24.0, 23.8, 22.5 (CH_2), 55.0 (CH_3). Anal. Calcd for $C_{16}H_{30}O_5$: C, 63.55; H, 10.00. Found: C, 63.64; H, 9.99.

4.2.5.11. 1,2-*O*,*O*-Benzylidene-6-*O*-*t*-butyldiphenylsilyl-hexane-1,2,6-triol (3, P=TPS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **3** (P= TPS) (87% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.91–7.38 (30H, m), 5.94 (1H, s), 5.83 (1H, s), 4.42 (4H, m), 4.21 (2H, m), 3.73–3.61 (4H, m), 2.80–1.20 (12H, m), 1.09 (18H, s); ^{13}C NMR (125 MHz) δ 138.2, 137.8, 136.1, 22.0, 19.2 (C), 134.4, 134.0, 129.7, 129.51, 128.9, 128.2, 126.6, 126.3, 103.9, 103.0, 77.3, 76.4 (CH), 70.6, 70.0, 63.6, 33.0, 32.9, 32.3 (CH_2), 26.8 (CH_3). Anal. Calcd for $C_{29}H_{36}O_3Si$: C, 75.61; H, 7.88. Found: C, 75.71; H, 7.90.

4.2.5.12. 1,2-*O*,*O*-Benzylidene-6-*O*-triisopropylsilyl-hexane-1,2,6-triol (3, P=TIPS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **3** (P=TIPS) (92% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.52–7.36 (10H, m), 5.95 (1H, s), 5.82 (1H, s), 4.25 (4H, m), 4.12 (2H, t, J=7.0 Hz), 3.75–3.68 (4H, m), 3.64 (2H, t, J= 7.0 Hz), 1.65–1.10 (12H, m), 1.09 (18H, s), 1.08 (6H, s), 1.07 (12H, s); ^{13}C NMR (125 MHz) δ 139.0, 138.6, 136.1 (C), 129.1, 128.9, 128.3, 126.6, 126.3, 103.9, 103.1, 77.4, 76.5, 13.0, 12.0 (CH), 70.7, 70.0, 63.1, 33.2, 33.0, 32.8, 22.1, 22.0 (CH_2), 18.0, 17.7 (CH_3). Anal. Calcd for $C_{22}H_{38}O_3Si$: C, 69.79; H, 10.12. Found: C, 69.63; H, 10.25.

4.2.5.13. 1,2-*O*,*O*-Benzylidene-6-*O*-*t*-butyldimethylsilyl-hexane-1,2,6-triol (3, P=TBS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **3** (P= TBS) (83% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.55–7.38 (10H, m), 5.98 (1H, s), 5.82 (1H, s), 4.26 (4H, m), 4.15 (2H, t, J=7.0 Hz), 3.68 (4H, m), 1.82–1.15 (12H, m), 0.97 (18H, s), 0.12 (6H, s), 0.11 (6H, s); ^{13}C NMR (125 MHz) δ 139.2, 138.8, 22.0 (C), 129.0, 128.8, 128.1, 126.5, 126.2, 103.8, 103.0, 77.2, 76.3 (CH), 70.5, 70.0, 62.7, 33.1, 33.0, 32.6 (CH_2), 25.8, −5.4 (CH_3). Anal. Calcd for $C_{19}H_{32}O_3Si$: C, 67.81; H, 9.58. Found: C, 67.92; H, 9.62.

4.2.5.14. 1,2-*O*,*O*-Benzylidene-6-*O*-benzoylhexane-1,2,6-triol (3, P=Bz). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **3** (P=Bz) (80% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 8.10–8.00 (4H, m), 7.59–7.36 (16H, m), 5.95 (1H, s), 5.83 (1H, s), 4.36 (4H, dt, J=6.41, 3.47 Hz), 4.25 (4H, m), 4.13 (2H, t, J=7.0 Hz), 4.13 (2H, t, J=7.0 Hz), 3.72 (2H, t, J=7.0 Hz), 3.64 (2H, m), 1.90–1.55 (12H, m); ^{13}C NMR (125 MHz) δ 166.5, 138.4, 137.8 (C), 132.8, 129.5, 129.2, 128.3, 126.6, 126.3, 104.0, 103.1, 77.0, 76.2 (CH), 70.6, 70.0, 64.6, 33.0, 32.9, 28.6, 22.4, 22.3 (CH_2). Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.50; H, 6.93.

4.2.5.15. 1,2-*O*,*O*-Benzylidene-6-*O*-benzylhexane-1,2,6-triol (3, P=Bn). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **3** (P=Bn) (76% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.56–7.24 (20H, m), 5.91 (1H, s), 5.79 (1H, s), 4.50 (2H, s), 4.49 (2H, s), 4.24–4.18 (5H, m), 4.09 (1H, t, J=7.0 Hz), 3.70 (1H, t, J= 7.0 Hz), 3.60 (1H, t, J=7.0 Hz), 3.48 (4H, dt, J=6.0, 2.5 Hz), 1.77–1.45 (12H, m); ^{13}C NMR (125 MHz) δ 138.5, 138.4, 137.9 (C), 129.2, 129.0, 128.3, 127.7, 127.6, 127.5, 126.6, 126.3, 103.9, 103.0, 77.3, 76.4 (CH), 72.9, 70.7, 70.0, 33.2, 33.0, 29.7, 22.5 (CH_2). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 77.00; H, 7.77.

4.2.5.16. 1,2-*O*,*O*-Benzylidene-6-*O*-(tetrahydropyran-2-yl)hexane-1,2,6-triol (3, P=THP). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **3** (P= THP) (65% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.49–7.35 (10H, m), 5.93 (1H, s), 5.81 (1H, s), 4.58 (2H, s ancho), 4.49 (2H, s), 4.27–4.19 (3H, m), 4.10 (1H, dd, J= 7.8, 6.9 Hz), 3.90–3.82 (2H, m), 3.80–3.72 (2H, m), 3.68 (1H, t, J=7.2 Hz), 3.62 (1H, stma AB), 3.52–3.48 (2H, m), 3.43–3.38 (2H, m), 1.86–1.50 (12H, m); ^{13}C NMR (125 MHz) δ 138.5, 137.8 (C), 129.2, 129.0, 128.3, 126.6, 126.3, 103.9, 103.0, 98.9, 98.8, 77.2, 76.3 (CH), 70.6, 70.0, 67.2, 62.2, 33.1, 33.0, 29.6, 25.4, 22.5, 19.6 (CH_2). Anal. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.68; H, 8.61.

4.2.5.17. 1,3-*O*,*O*-Isopropylidene-3-methylpentane-1,3,5-triol (5, P=H). A solution of 3-methylpentane-1,3,5-triol (610 mg, 5 mmol) in dry acetone (25 mL) was treated under N_2 with 2,2-dimethoxypropane (5 mL) and camphorsulfonic acid (7 mg, 0.03 mmol). The reaction mixture was stirred for 24 h at room temperature, then filtered through Celite and evaporated under reduced pressure. Column chromatography on silica gel (hexanes/ EtOAc 9:1) afforded **5** (P=H) (574 mg, 66% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 3.92–3.88 (4H, m), 1.91–183 (2H, m), 1.91 (3H, s), 1.38 (3H, s), 1.28–1.20 (2H, m), 1.21 (3H, s); ^{13}C NMR (125 MHz) δ 97.7, 70.7 (C), 60.6, 44.0, 20.8 (CH_2), 27.8, 26.7 (CH_3). Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.15; H, 10.45.

4.2.5.18. 1,3-*O*,*O*-Isopropylidene-5-*O*-*t*-butyldiphenylsilyl-3-methylpentane-1,3,5-triol (5, P=TPS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **5** (P=TPS) (85% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.71–7.68 (4H, m), 7.42–7.38 (6H, m), 3.94–3.80 (4H, m), 1.94–1.74 (2H, m), 1.54–1.46 (2H, m), 1.40 (3H, s), 1.32 (3H, s), 1.27 1.40 (3H, s), 1.07 (9H, s); ^{13}C NMR (125 MHz) δ 134.0, 97.8, 71.7, 19.1 (C), 135.6, 129.5, 127.6 (CH), 60.1, 56.6, 45.6, 34.2 (CH_2), 28.8, 27.8, 27.4, 26.9 (CH_3). Anal. Calcd for $C_{25}H_{36}O_3Si$: C, 72.77; H, 8.79. Found: C, 72.89; H, 8.80.

4.2.5.19. 1,3-*O*,*O*-Benzylidene-3-methylpentane-1,3,5-triol (6, P=H). A solution of 3-methyl-1,3,5-pentanetriol (610 mg, 5 mmol) in dry toluene (25 mL) was treated under N_2 with benzaldehyde (1.5 mL, 15 mmol) and *p*-toluenesulfonic acid monohydrate (6 mg, 0.03 mmol). The reaction mixture was stirred for 24 h at 60 °C, then filtered through Celite and evaporated under reduced pressure. Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **6** (P=H) (695 mg, 63% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.50–7.35 (10H, m), 5.80 (1H, s), 5.75 (1H, s), 4.16–4.10 (4H, m), 3.91–3.70 (4H, m), 2.65 (2H, m), 2.41

(2H, m), 2.05 (2H, dt, J=6.0, 12 Hz), 1.88 (2H, t, J=6.0 Hz), 1.12 (2H, td, J=5.5, 12 Hz), 1.52 (3H, s), 1.37 (3H, s); ^{13}C NMR (125 MHz) δ 138.8, 138.7, 75.6, 74.1, 70.7 (C), 128.8, 128.7, 128.2, 126.1, 125.9, 95.3, 95.2 (CH), 63.2, 63.1, 45.3, 35.8, 35.1, 33.8 (CH_2), 28.5, 20.5 (CH_3). Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.35; H, 8.19.

4.2.5.20. 1,3-*O*,*O*-Benzylidene-5-*O*-*t*-butyldiphenylsilyl-3-methylpentane-1,3,5-triol (6, P=TPS). Column chromatography on silica gel (hexanes/EtOAc 9:1) afforded **6** (P=TPS) (90% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.79–7.72 (8H, m), 7.47–7.39 (22H, m), 5.77 (1H, s), 5.52 (1H, s), 4.35–4.15 (4H, m), 3.90–3.68 (4H, m), 2.40–1.90 (4H, m), 2.0 (4H, t, J=4.1 Hz), 1.47 (3H, s), 1.30 (3H, s), 1.13 (9H, s), 1.12 (9H, s); ^{13}C NMR (125 MHz) δ 139.3, 139.0, 134.2, 73.3, 20.2, 19.1 (C), 135.6, 129.5, 128.1, 127.7, 127.6, 126.1, 126.0, 94.9, 94.7 (CH), 63.2, 59.8, 59.4, 46.7, 35.9, 35.5, 34.4 (CH_2), 28.9, 26.9, 26.8 (CH_3). Anal. Calcd for $C_{29}H_{36}O_3Si$: C, 75.61; H, 7.88. Found: C, 75.71; H, 7.89.

4.2.5.21. 1,3-*O*,*O*-Benzylidene-5-*O*-benzyl-3-methylpentane-1,3,5-triol (6, P=Bn). Column chromatography on silica gel (hexanes/EtOAc 4:1) afforded **6** (P=Bn) (73% yield) as a colourless oil. ^{1}H NMR (500 MHz) δ 7.60–7.39 (20H, m), 5.83 (1H, s), 5.79 (1H, s), 4.60 (4H, s), 4.19–4.14 (4H, m), 3.81 (3H, m), 3.74 (1H, t, J=7.0 Hz), 2.6 (2H, m), 2.40–1.98 (6H, m), 1.54 (3H, s), 1.41 (3H, s); ^{13}C NMR (125 MHz) δ 139.2, 139.0, 138.4, 138.2, 73.2, 73.1 (C), 128.4, 128.2, 128.0, 127.5, 127.4, 127.3, 126.0, 94.9, 94.7 (CH), 73.0, 72.8, 65.8, 65.6, 43.6, 35.5, 34.1, 33.1, 28.1 (CH_2), 20.2 (CH_3). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 77.01; H, 7.75.

4.3. General procedure for acetal cleavage with $ZnBr_2$

Anhydrous $ZnBr_2$ (4–6 mmol, see Tables 1 and 2) was added to a solution of the appropriate acetal (1 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for the time indicated in the tables. The reaction progress was monitored by TLC. After disappearance of the starting material, $EDTANa_2$ (2 mmol/mmol of $ZnBr_2$) dissolved in 10 mL of water was added to the reaction mixture. The stirring was then continued for 2 min. Finally, the reaction mixture was poured into brine and extracted twice with CH_2Cl_2. The organic layers were dried over anhydrous Na_2SO_4 and filtered. Solvent removal in vacuo and flash chromatography on silica gel provided the reaction products.

4.3.1. 6-*O*-(Triisopropylsilyl)hexane-1,2,6-triol (4, P=TIPS). Colourless oil; ^{1}H NMR (500 MHz) δ 3.74 (1H, m), 3.71 (2H, t, J=6.0 Hz), 3.67 (1H, dd, J=11, 3.0 Hz), 3.45 (1H, dd, J=11, 7.5 Hz), 1.62–1.43 (3H, m), 1.10–1.05 (24H, m); ^{13}C NMR (125 MHz) δ 72.3, 12.0 (CH), 66.8, 63.2, 32.9, 32.8, 21.9 (CH_2), 18.0 (CH_3). Anal. Calcd for $C_{15}H_{34}O_3Si$: C, 62.01; H, 11.80. Found: C, 62.20; H, 11.71.

4.3.2. 6-*O*-Benzoylhexane-1,2,6-triol (4, P=Bz). Colourless oil; ^{1}H NMR (500 MHz) δ 8.02 (2H, d, J=7.32 Hz), 7.54 (1H, t, J=7.50 Hz), 7.43 (2H, t, J=7.7 Hz), 4.32 (2H, t, J=6.6 Hz), 3.71 (1H, m), 3.64 (1H, dd, J=11.0, 2.74 Hz), 3.44 (1H, dd, J=11, 7.7 Hz), 2.89 (1H, d ancho, J=8.4 Hz), 1.79 (2H, m), 1.62 (2H, m), 1.51 (2H, m); ^{13}C NMR (125 MHz) δ 166.7, 130.3 (C), 132.9, 129.5, 128.3, 72.0 (CH), 66.7, 64.8, 32.6, 28.7, 22.1 (CH_2). Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.62; H, 7.66.

Note added in proof

For a very recent example of cyclohexilidene acetal deprotection using $ZnBr_2$ in a multifunctionalized substrate see: Diaz-Oltra, S.; Murga, J.; Falomir, E.; Carda, M.; Peris, G.; Marco, J. A. *J. Org. Chem.* **2005**, *70*, 8130–8139.

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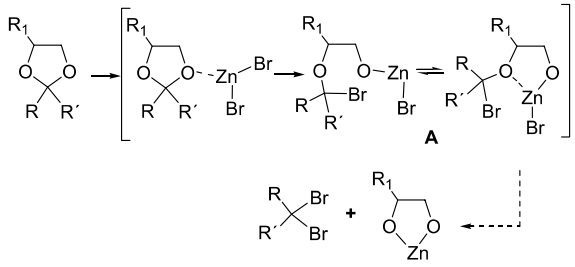

In control experiments with cyclohexanone acetals, we were not able to detect the formation of 1,1-dibromocyclohexane. In fact, we did isolate cyclohexanone, but it seems unlikely that it was formed through hydrolysis of the *gem*-dibromo derivative during the work-up. However, the formation of **A** does seem likely. Its hydrolysis to diol and ketone should occur easily during the work-up.
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