Selective deprotection of an acetal group in monosaccharide derivatives and related compounds using Me_3SiCH_2MgCl

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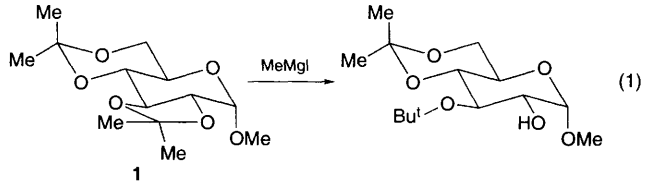
Treatment of an acetal of a contiguous diol with Me_3SiCH_2MgCl liberates the corresponding diol regioselectively; chelation is used to rationalize the selectivity.

Selective deprotection of an acetal group in carbohydrate derivatives and related compounds liberating the corresponding contiguous diols is important in organic synthesis but difficult to achieve.[1] We recently found an effective regioselective C–O bond cleavage of acetals of various polyols (*e.g.* **1**) with a Grignard reagent to give the corresponding alkoxy alcohols [(eqn. (1)].[2] It is believed that chelation plays a key role in



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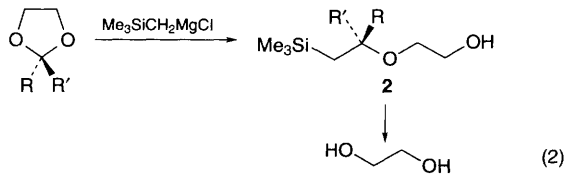
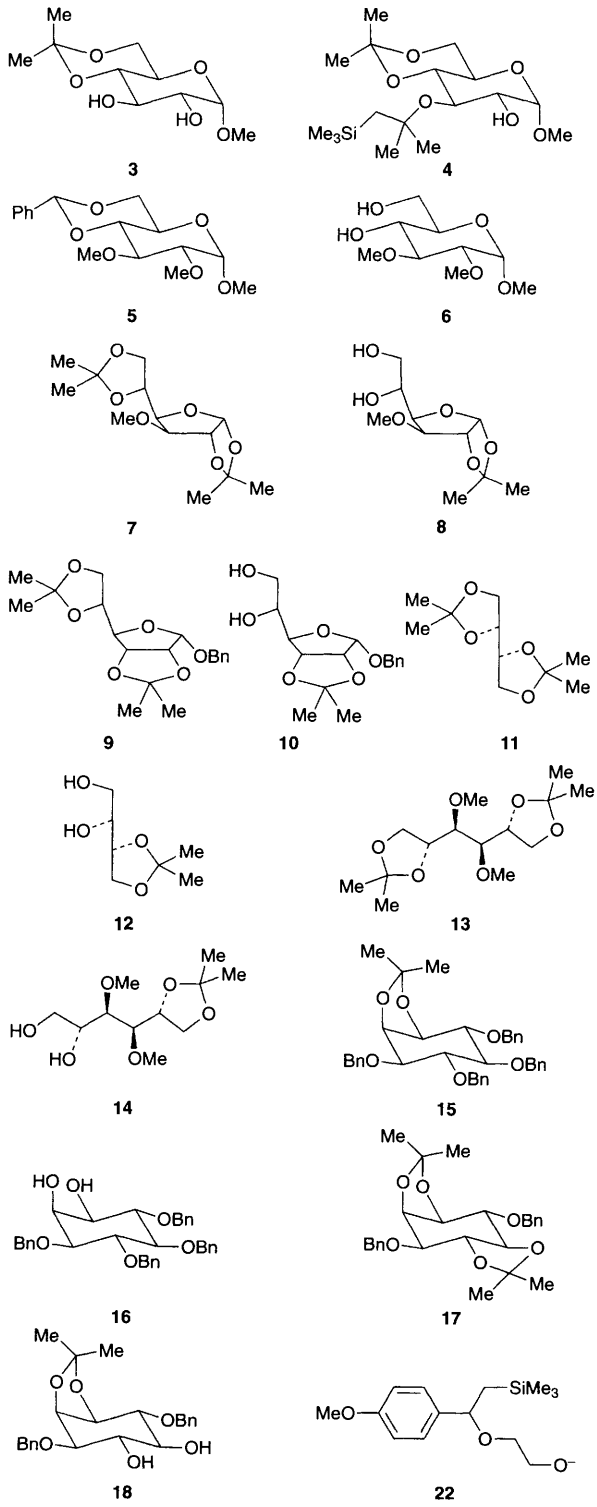
directing the selectivity of this ring opening reaction.[2] This methodology has been shown to be particularly useful in the synthesis of different kinds of monosaccharide derivatives having only one free hydroxy group. The Grignard reagent can be a primary, secondary or aryl magnesium halide. It is known that a β-silylethyl group can be used to protect alcohols and can readily be removed by treatment with BF_3.[3] We felt that treatment of an acetal of a contiguous diol with R_3SiCH_2MgCl would lead to the corresponding β-silyl-substituted *tert*-alkoxy alcohol **2** which could be readily converted to the diol [eqn. (2)].



Here we report an unprecedented procedure for a one-pot selective deprotection of an acetal group in carbohydrate derivatives and related compounds.

In a typical procedure, glucopyranoside bisacetonide **1** was treated with 2 equiv. of Me_3SiCH_2MgCl in benzene under reflux for 48 h followed by the usual workup and chromatographic separation to give the corresponding 2,3-diol **3**[1d] in 68% yield. Attempts to isolate the possible β-silyl-substituted *tert*-butoxy alcohol **4** were unsuccessful. Presumably, this ether moiety is labile under these conditions and is cleaved accordingly to give compound **3**. In a similar manner, the 4,6-diol of glucopyranoside **6**[1e] was obtained in 76% yield from the reaction of **5** under similar conditions.

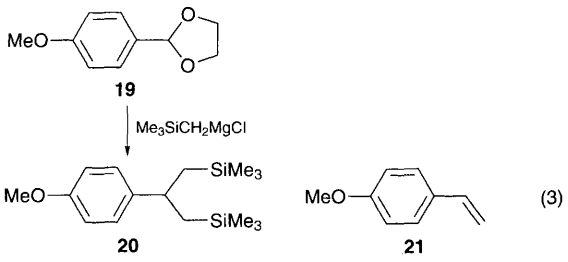
Treatments of acetals of furanosides **7** and **9** with Me_3SiCH_2MgCl in refluxing benzene yielded 5,6-diols **8**[1f] (57%) and **10**[1g] (72%), respectively. It appears that the oxygen atom of the furanoside heterocycle in **7** and **9** direct the regioselective deprotection of the acetonide moiety.



3 **4** **5** **6** **7** **8** **9** **10** **11** **12** **13** **14** **15** **16** **17** **18** **22**

The extension of this reaction to the selective deprotection of one acetal moiety of a symmetrical bisacetonide has been executed. Thus, the bisacetal of threitol **11** was treated with Me_3SiCH_2MgCl under similar conditions to give the diol **12**† in 67% yield. Diol **14** was also obtained similarly in 61% yield from the reaction of **13**. *myo*-Inositol derivatives **16**[1h] and **18**[1i] were obtained in 67 and 79% yield from the acetals **15** and **17**, respectively.

The fate of the carbonyl equivalent of these acetals has been investigated. Interestingly, the isolation of bis-silylmethylated product **20** (72%) in addition to styrene **21** (21%) from the reaction of **19** with Me_3SiCH_2MgCl illustrates two interesting features [eqn. (3)]. First, this reaction demonstrates an unusual



(3)

displacement of two C–O bonds of an acetal by the Grignard reagent. Secondly, the isolation of **21** demonstrates the first example of Peterson alkenation[4] of an acetal group. Although the actual mode for this reaction remains unclear, an intermediate **22** is speculated. Further displacement of the remaining C–O bond in **22** by the Grignard reagent may give **20** and an elimination process may lead to **21**. The reaction can be considered as using an acetal as a geminal dication synthon.[5]

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Footnote

† *Selected Physical Data*: For **12**: $[\alpha]_D^{20}$: +2.1 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz) δ 1.35 (s, 3 H), 1.41 (s, 3 H), 2.26 (bs, 1 H), 2.60 (bs, 1 H), 3.62–3.67 (m, 3 H), 3.84 (dd, *J* 6.4, 8.2 Hz, 1 H), 4.03 (dd, *J* 6.4, 8.2 Hz, 1 H) and 4.15 (q, *J* 6.4 Hz, 1 H); ^{13}C NMR (100 MHz) δ 25.3, 26.4, 64.3, 65.9, 71.4, 76.6 and 109.6. For **14**: $[\alpha]_D^{20}$: +2.8 (*c* 3.3, $CHCl_3$); ^1H NMR (300 MHz) δ 1.31 (s, 3 H), 1.38 (s, 3 H), 2.37 (br s, 1 H), 2.93 (bs, 1 H), 3.31 (dd, *J* 2.5, 7.9 Hz, 1 H), 3.42 (s, 3 H), 3.49 (s, 3 H), 3.59 (dd, *J* 2.5, 6.4 Hz, 1 H), 3.65–3.67 (m, 1 H), 3.74–3.80 (m, 2 H), 3.91 (dd, *J* 6.4, 8.0 Hz, 1 H), 4.06 (dd, *J* 6.4, 8.0 Hz, 1 H) and 4.15 (dd, *J* 6.4, 12.6 Hz, 1 H); ^{13}C NMR (100 MHz) δ 25.3, 26.5, 60.0, 60.7, 63.7, 66.5, 70.8, 75.7, 80.6, 81.1 and 108.6. For **20**: ^1H NMR (200 MHz) δ −0.22 (s, 18 H), 0.85–1.06 (m, 4 H), 2.80 (tt, *J* 6.6, 8.4 Hz, 1 H), 3.77 (s, 3 H), 6.77 (d, *J* 8.8 Hz, 2 H) and 7.07 (d, *J* 8.8 Hz, 2 H); ^{13}C NMR (50 MHz) δ −1.0, 30.4, 37.6, 55.3, 113.6, 128.0, 141.6 and 157.8.

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