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Tetrahedron
Tetrahedron 60 (2004) 3625–3636

Full and partial differentiation of tris-1,1,1-(hydroxymethyl)ethane via direct and indirect methodology

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Received 12 December 2003; revised 2 February 2004; accepted 25 February 2004

Abstract—Tris-1,1,1-(hydroxymethyl)ethane **1** was converted to a series of mono- and disubstituted derivatives. An indirect protocol for the differentiation of the alcohol groups was employed for the synthesis of partially and fully differentiated **1** containing a protected aldehyde unit. Complete differentiation of the alcohol groups was also achieved using a direct strategy (two steps from **1**). The first synthesis of 1,3-dialdehydes derived from **1** is reported in two steps.

1. Introduction

Tris-1,1,1-(hydroxymethyl)ethane $CH_3C(CH_2OH)_3$ **1** and pentaerythritol $C(CH_2OH)_4$ are very cheap bulk chemicals. They are obtained on industrial scale via a mixed aldol reaction of formaldehyde with, propanal and ethanal, respectively, followed by a Cannizzarro reaction.[1] Due to the polyfunctional, symmetrical nature of these small molecules, they are interesting and useful starting materials/precursors for a range of applications, for example, as low-molecular weight scaffolds for combinatorial chemistry purposes,[2] as building blocks for dendrimer synthesis,[3] as initiators for polymerisation reactions,[4] or for a range of other purposes.[5] In most cases, a chemical differentiation of the alcohol groups needs to be achieved prior to use in the aforementioned applications.

Three typical differentiation levels, labelled A–C, that are commonly found in the literature for **1** are shown in Figure 1. In type A, two hydroxyl groups are protected as an acetal group, leaving one hydroxyl group available for reaction. In type B, only one hydroxyl group is functionalised, leaving two hydroxyl groups available for further conversion. Type C differs from type A in that different substituents were introduced on two alcohol groups, resulting in the presence of a chiral quaternary carbon atom.

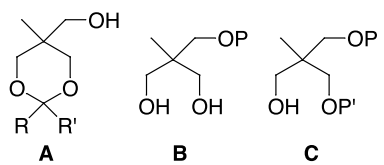

Figure 1. Differentiation levels of tris-1,1,1-(hydroxymethyl)ethane.

The traditional synthetic approach to obtain these three differentiated forms of **1** is shown in Scheme 1. Acetal formation of **1** leads directly to type A differentiated molecules. Functionalisation of the remaining hydroxyl group is now possible, leading to **2**. Removal of the acetal group then gives rise to type B differentiation. Following this three-step method, monosilylated product **3** has been obtained.[4] This differentiation method also has been applied for the construction of dendrimers with **1** as a building block (where, in this context, P represents the attachment to the dendrimer core in **2**).[3]Alternatively, type B monobenzylated product **4** was directly obtained from type A benzylidene acetal **5** by a reductive acetal-opening reaction with $LiAlH_4$–BF_3.[5f]

When **2** is subjected to reductive acetal cleavage, then the fully differentiated type C can be obtained in a three-step sequence. Following this process, Gardiner reported the synthesis of type C products **6** and **7** via cleavage of the corresponding benzylidene or *para*-methoxy benzylidene acetals.[6]

In an alternative indirect differentiation strategy, **1** was converted to the oxetane-containing product **8** via a two-step procedure.[5e,7] Acid-catalysed opening of the oxetane ring with an alcohol leads to type B differentiated substrates in

Keywords: Scaffold; Building block; Alcohol differentiation; Chemoselective acetal cleavage.
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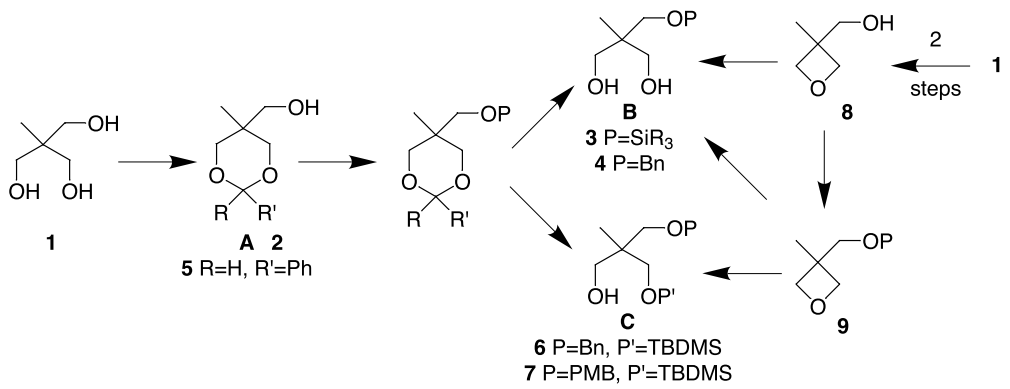
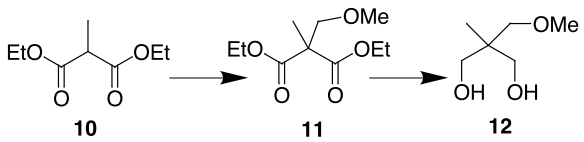
0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.02.056



Scheme 1. Indirect differentiation methods for tris-1,1,1-(hydroxymethyl)ethane.

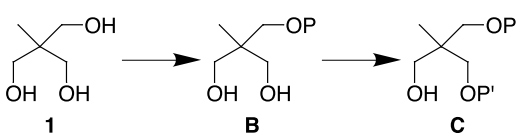
three steps. Alternatively, the free alcohol group in **8** can be functionalised to give **9**. Acid-catalysed alcoholysis at this stage gives rise to type C functionalisation in four steps. A disadvantage of this method is that the alcohol is used as a solvent in the oxetane opening reaction, which has obvious implications to its scope. Hydrolysis of **9** leads to the type B differentiated products.

Another method for the synthesis of (alkylated) type B differentiation products was achieved starting from diethyl methyl malonate **10** (Scheme 2). Alkylation with chloromethyl methyl ether gives rise to **11**, which subsequently is reduced to give **12**.[5a]



Scheme 2. Formation of type B molecule from diethyl methyl malonate.

A shorter, more efficient synthesis of type B and type C differentiated tris-1,1,1-(hydroxymethyl)ethane could be achieved via direct monofunctionalisation which, surprisingly, has been only scarcely explored (Scheme 3). This approach relies twice on a monofunctionalisation reaction, of the triol and a diol, respectively. Type B structures were obtained via monotritylation using 5.5 equiv. of **1**, in 68% yield.[8] Monoalkylation of **1** via a Williamson alkylation was reported in good yield as well (80%).[9] With a weak base (K_2CO_3) and a reactive alkylating agent (allyl bromide), a 6:1 ratio of mono- to diallylation product was achieved in 85% combined yield.[10] Surprisingly, to the best of our knowledge, no direct monosilylation of **1** has yet been reported.



Scheme 3. Direct differentiation of tris-1,1,1-(hydroxymethyl)ethane.

Following this methodology, type C differentiation can be obtained in two steps from **1**. Type B structures have been monoalkylated (allyl, benzyl) in moderate to good yields (56 and 76%, respectively).[4a,10] Monoesterification (Ac, $C(O)CMe_2Br$) was achieved in good yields (77–78%).[4b,10]

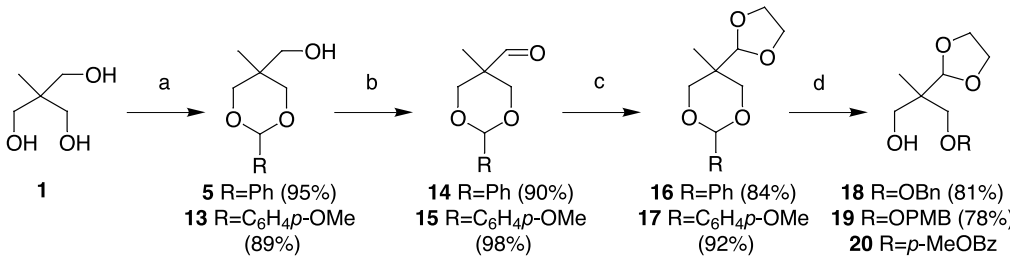
The direct differentiation strategy is more appealing than the indirect strategy in terms of number of steps. In addition, the acetal formation of **1** is often reported to proceed in rather moderate yield. Though the yield of this transformation is of less importance due to the low cost of the starting materials, it could complicate purification and isolation of the desired acetals. In addition, lower yields generate additional waste, which could be important on large scale. Nevertheless, the indirect differentiation method remains important for applications where initial monofunctionalisation is not possible.

In this paper, we wish to describe an improved procedure for the initial acetal protection in the synthesis of type A compounds, leading to an efficient indirect differentiation protocol to type B and type C products of tris-1,1,1-(hydroxymethyl)ethane **1** that contain a protected aldehyde group. This synthesis includes investigations concerning selective reactions between two different acetal groups. We report the first direct silyl monoprotection of **1** (TBDMS, TBDPS, TIPS), leading to an efficient direct differentiation protocol for type B and type C compounds containing orthogonal protecting groups. The first type B 1,3-dialdehyde structures derived from **1** in two steps are described as well. Their straightforward synthesis of all these derivatives should make these compounds readily available as interesting building blocks for a range of applications.

2. Results and discussion

2.1. Indirect differentiation of tris-1,1,1-(hydroxymethyl)ethane

Our indirect differentiation protocol conventionally started with reaction of tris-1,1,1-(hydroxymethyl)ethane **1** with benzaldehyde (Scheme 4). Several conditions have been described in the literature for this reaction (Table 1). However, for large scale purposes, the use of large quantities of $ZnCl_2$ (entry 4) in conjunction with a workup which was described as difficult,[5f] was deemed impractical. Benzaldehyde dimethyl acetal (entry 3), though still cheap, is five times as expensive as benzaldehyde itself. When the reaction was performed in aqueous medium (entry 1), the acetal product was reported to precipitate from the reaction mixture, albeit with a yield of only 60%.



Scheme 4. Reagents and conditions: (a) ArCHO, PPTS, toluene, reflux (Dean and Stark), 1 h. (b) SO_3·py, DMSO, Et_3N, CH_2Cl_2, 0 °C, 3–6 h. (c) $TMSOCH_2CH_2OTMS$, TMSOTf, CH_2Cl_2, 0 °C, 1 h. (d) BH_3·SMe_2, TMSOTf, CH_2Cl_2, −78 °C, 3 h.

Table 1. Reaction of tris-1,1,1-(hydroxymethyl)ethane with benzaldehyde

Entry	PhCHO (equiv.)	Conditions	Yield (%)	*c*/*t* ratio	Reference
1	1.0	HCl (cat), H_2O, 70–80 °C, 3 h	60	[a]	11
2	2.2	Toluene, *p*TSA (cat), Dean and Stark, 6 h	66	[a]	12
3	1.05[b]	THF, *p*TSA (cat), room temperature, 3 h	74	[a]	4
4	5.9	$ZnCl_2$ (0.9 equiv.), room temperature, 12 h	81	7:1	5f
5	0.83	Toluene, PPTS (cat), Dean and Stark, 1 h	95	3.8:1	This work

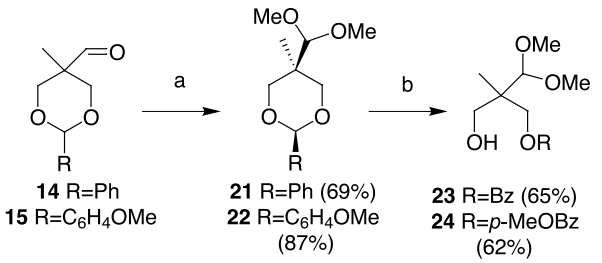
[a] Not determined.
[b] Benzaldehyde dimethyl acetal was used.

Hence, it was decided to optimise the acetal formation reaction. Refluxing **1** and benzaldehyde (1.5 equiv.) in toluene with PPTS as catalyst and $MgSO_4$ to bind the liberated water[13] only returned 43% of **5**. When these conditions were used in conjunction with a Dean and Stark trap, a mixture of *cis* and *trans* **5** was formed. However, the remaining primary alcohol subsequently reacted with excess benzaldehyde to form the corresponding acyclic acetal 'dimer' as a mixture of isomers, which could be separated by preparative HPLC (see Section 4). Hence, when a limiting amount of benzaldehyde was used, subsequent acetal formation involving the free alcohol in **5** did not take place, and a 95% yield of **5** was obtained, with a 3.8:1 ratio of *cis*/*trans* isomers. Structural assignment of the isomers was easily achieved based on the characteristic downfield shift of the equatorial methyl group of the major isomer compared to the upfield shift of the axial methyl group of the minor isomer.[14]

Reaction of **1** with anisaldehyde under identical conditions gave **13** as a mixture of *cis*/*trans* isomers in good yield as well. The acetals **5** and **13** were subsequently oxidised under Parikh–Doering[15] conditions, leading to the corresponding aldehydes **14** and **15** in excellent yield. The subsequent protection of the aldehyde as 1,3-dioxolane proved difficult. Reaction of **14** with 1,2-ethanediol in toluene or cyclohexane with a range of acid-catalysts under Dean and Stark conditions did not provide the desired product **16**. However, reaction of **14** with 1,2-ethanediol in toluene with *p*TSA at room temperature gave **16** in 69% yield. In the event, the very mild Noyori-conditions[16] using 1,2-bis-(trimethylsilyloxy)ethane and trimethylsilyltriflate as catalyst were found to give the highest yield for the protection reaction (84%). The protection of **15**, which contains a more acid-sensitive *para*-methoxybenzylidene acetal group, was also successfully achieved under Noyori conditions, leading to **17** in 92% yield.

With the acetals **16** and **17** in hand, the final transformation to type C differentiated products was attempted, which would rely on selective acetal cleavage reactions. Treatment of **16** with trimethylsilyl trifluoromethane sulfonate and borane dimethyl sulfide complex[17] resulted in selective reduction of the benzylidene acetal to give the corresponding benzyl ether **18** in 81% yield. Similarly, selective reductive cleavage of the *para*-methoxybenzylidene acetal **17** under the same conditions gave **19** in 78% yield. It has been reported, based on competition experiments, that 1,3-dioxane based acetals are more reactive towards reductive ringopening than 1,3-dioxolane based acetals. However, there are very few synthetic examples in the literature that exploit this selectivity. While the selective reductive cleavage of a *para*-methoxybenzylidene acetal in the presence of a dimethyl acetal has been reported, to the best of our knowledge no such selective reaction has been reported involving the less reactive benzylidene acetal.[18]

Unfortunately, in our hands, an attempted selective oxidation of the *para*-methoxybenzylidene acetal **17** with DDQ did not give a significant yield of the type C **20**. As it is known that cyclic acetals oxidise faster than acyclic acetals,[19a] it was decided to change the 1,3-dioxolane protecting group to an acyclic dimethyl acetal (Scheme 5). Aldehyde **14** was subjected to Noyori conditions at −78 °C with triflic acid as the catalyst. Surprisingly, this provided the dimethyl acetal **21** as a single isomer, even though the



Scheme 5. Reagents and conditions: (a) $TMSOCH_3$, CF_3SO_3H (cat), CH_2Cl_2, −78 °C, 3 h. (b) O_3, EtOAc, −78 °C, 1 h.

starting material was a mixture of *cis*/*trans* isomers. A similar result was achieved with **15** as starting material. The structure of both **21** and **22** were elucidated by X-ray crystallography,[20] and determined to be the *cis*-isomer in both cases.

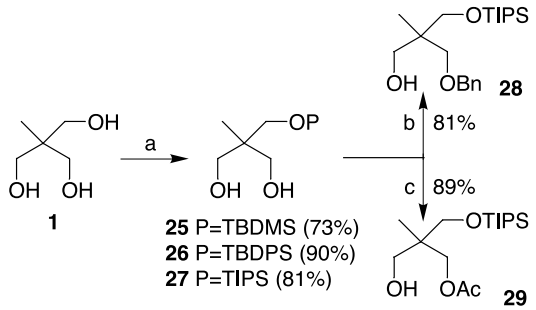
Finally, ozone treatment[19] of the diacetals **21** and **22** was chemoselective, with the acyclic acetal left untouched. The corresponding benzoate and *para*-methoxybenzoate esters **23** and **24** were obtained in 65 and 62% yield, respectively. To the best of our knowledge, this is the first example of such a selective oxidative cleavage between these two types of acetals.

It can be noted that the selective acetal cleavage of the benzylidene acetal occurs in similar yield compared to the *para*-methoxybenzylidene acetal, which adds to the versatility of the described indirect differentiation process, as a range of protecting groups are made accessible.

Hence, the fully differentiated compounds **18**, **19**, **23**, and **24** are accessible from **1** in four steps.

2.2. Synthesis of type C structures by direct differentiation of tris-1,1,1-(hydroxymethyl)ethane

The first direct preparation of monosilylated tris-1,1,1-(hydroxymethyl)ethane was successfully accomplished, based on a similar protocol as reported for pentaerythritol.[21] An excess of **1** was used (Scheme 6), not only to reduce polysilylation, but also for economic reasons, as **1** is vastly cheaper than any silylating agent. By using a 5-fold excess of **1**, yields of the corresponding silyl ethers **25**–**27** ranged from 73 to 90%.[22] Any residual starting material was easily removed during aqueous workup, and the small amounts of disilylated compounds were separated in a straightforward manner by column chromatography.



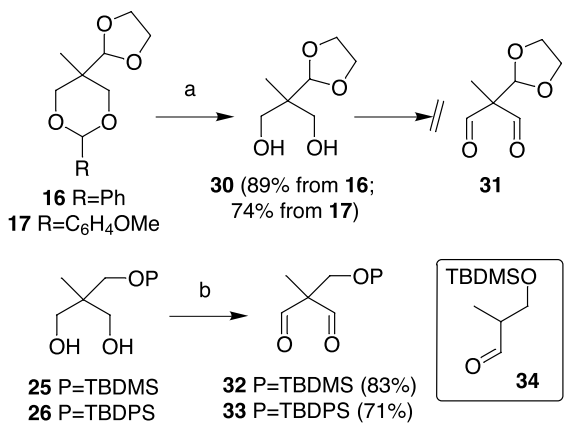
Scheme 6. Reagents and conditions: (a) R_3SiCl, imidazole, DMF, room temperature, 24 h. (b) NaH, BnBr, THF, reflux, 22 h. (c) Ac_2O, $CeCl_3$, room temperature, 5 h.

With the monosilyl ethers in hand, further direct differentiation was investigated. The selective monofunctionalisation of *meso* and C_2-symmetric 1,3-diols, including 2-substituted propanediols, has been the subject of extensive research,[23] yet is scarcely exploited for the synthesis of type-B differentiated tris-1,1,1-(hydroxymethyl)ethane.[4,10] As shown in Scheme 6, deprotonation with 1 equiv. of NaH in THF,[23d] followed by benzyl bromide addition at reflux temperature led to the formation of type C product **28** in 81% yield, together with 8% of recovered starting material. Attempted monobenzylation using silver oxide[23c] was not successful. Monoacetylation was successfully achieved with Clarke's $CeCl_3$-catalysed process[23a] using 10 equiv. of acetic anhydride. Though stirring the reaction mixture for 24 h as described mainly returned diacetylated product (69%, with 29% of **29**), close monitoring of the reaction by TLC revealed an optimum reaction time of 5 h, after which 89% of **29** was obtained. Hence, the synthesis of fully differentiated tris-1,1,1-(hydroxymethyl)ethane possessing orthogonal protecting groups is easily obtained in a high-yielding two-step operation.

2.3. Synthesis of type B 1,3-dialdehydes derived from tris-1,1,1-(hydroxymethyl)ethane

Finally the synthesis towards type B 1,3-dialdehydes was undertaken. To our surprise, there were only a handful reported examples for the synthesis of 1,3-dialdehydes from the corresponding 2,2-disubstituted 1,3-propanediol starting materials, mostly from 2,2-dimethyl-1,3-propanediol. PCC was used as oxidant, though without mention of yields.[24] Under Swern conditions, very divergent results were reported, ranging from very low to good yields.[25] However, Frigerio obtained a high yield for the oxidation of a 1,1-bis(hydroxymethyl)cyclohexene derivative to the corresponding 1,3-dialdehyde using *o*-iodoxybenzoic acid (IBX) as oxidant.[26]

The 1,3-diol precursor, type B diol **30**, was obtained in good yields from the acetals **16** and **17** via hydrogenolysis (Scheme 7). It is clear that **30** would be difficult to synthesise in a direct differentiation protocol from **1**. Unfortunately, though a range of oxidants was explored, we were not able to obtain **31** in good yields. IBX, Dess–Martin periodinane (DMP) and TPAP/NMO, all returned complex reaction mixtures, while with silver(I)carbonate only starting material was recovered. Oxidation with PCC and PDC gave complex reaction mixtures, though the use of 1 equiv. of PDC cleanly led to the corresponding monoaldehyde.[27] Under Swern conditions, the monoaldehyde was also isolated after a reaction time of 1 h, but when longer reaction times were applied, again a complex mixture was obtained.



Scheme 7. Reagents and conditions: (a) $Pd(OH)_2/C$, MeOH, room temperature, 18 h. (b) IBX, EtOAc, room temperature, 3.5 h.

In the event, the oxidation was more successful starting from the type B monosilyl ethers **25** and **26**. Though most of the oxidation methods mentioned before gave complex reaction mixtures as well, encouraging results were obtained with PDC/AcOH(cat) and Dess–Martin periodinane as oxidants, where, starting from **25**, a mixture of **32** and **34** was obtained in 52 and 20% yield, respectively. The side-product **34** is likely to arise from a retro-aldol reaction at the intermediate mono-aldehyde stage. When IBX was used, **32** was obtained in 58% yield after chromatography. However, the procedure that was used could not be scaled up. The reaction is conducted in DMSO as solvent under dilute conditions in order to dissolve the oxidant, and the workup procedure simply consists of evaporating the solvent under vacuum, followed by chromatography of the residue. Since **32** is quite volatile, loss of material during evaporation of large quantities of DMSO reduced the yield to 39% on 4 mmol scale. A solution was found by using the higher-boiling sulpholane as solvent. As IBX is not very soluble in sulpholane, the reagent was used as a suspension. Distillation of the 1,3-dialdehyde product from the reaction mixture was now possible, leading to an isolated yield of 69%. The yield could be raised to 76% when DMSO was used as a co-solvent to obtain a homogeneous reaction mixture. Finally, the best procedure was found to use excess IBX reagent under heterogeneous conditions using ethyl acetate as solvent.[28] This method allowed simple filtration of excess IBX and its byproducts, followed by evaporation of the solvent and isolation after column chromatography. Hence, reaction of **25** or **26** in EtOAc at 80 °C for 3.5 h, followed by the aforementioned workup protocol gave the corresponding dialdehydes **32** and **33** in 83 and 71% isolated yields, respectively.

3. Conclusion

We have established a short, high-yielding, direct differentiation strategy for the synthesis of fully differentiated derivatives of tris-1,1,1-(hydroxymethyl)ethane **1**, possessing orthogonal functional groups. An indirect differentiation strategy, based on the initial protection of **1** as a benzylidene acetal, was used to prepare fully differentiated derivatives of **1** where one hydroxyl group was converted to an acetal-protected aldehyde. A key aspect in this synthesis was the selective oxidative or reductive ring-opening of the benzylidene and *para*-methoxybenzylidene acetal groups in the presence of, respectively, a cyclic 1,3-dioxolane type acetal and an acyclic dimethylacetal. These investigations resulted in an extension of the scope of selective transformations between different acetal groups which should be of use in general synthetic organic chemistry. In addition, an improved preparation of the benzylidene acetal of **1** is reported. Finally, the first synthesis of a 1,3-dialdehyde building block from **1** is reported in two high yielding steps. The reactions involved are very straightforward and this work should further extend the usefulness of the very cheap building block **1** for a range of applications in organic, combinatorial and polymer chemistry.

4. Experimental

4.1. General

1,1,1-Tris(hydroxymethyl)ethane **1** was obtained from commercial sources and used without further purification. Reaction solvents were dried immediately prior to use as follows: Et_3N and CH_2Cl_2 were distilled from CaH_2. EtOAc was distilled from $CaCl_2$. MeOH was dried with Mg/I_2, followed by distillation. THF was distilled from Na/benzophenone. Toluene was distilled from Na. DMSO was distilled from CaH_2 under reduced pressure and stored over molecular sieves. Anhydrous DMF was purchased from commercial sources and stored in a Schlenk flask. All non-aqueous reactions were carried out under an atmosphere of nitrogen. Chromatography refers to column chromatography and was performed on 230–400 mesh silica gel. Reactions were monitored by TLC (Merck) with detection by UV illumination or through alkaline $KMnO_4$ oxidation. The melting points are reported uncorrected. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a Bruker DPX400 spectrometer at 300K in either d^6-acetone or $CDCl_3$ referenced to residual solvent peaks; chemical shifts are quoted in ppm. IR spectra were recorded on a Nicolet Impact 400 spectrometer. The MS were run on a Thermoquest 2000 spectrometer.

4.1.1. (1-Methyl-4-phenyl-3,5-dioxanyl) methanol (5). To a stirred solution of 1,1,1-tris(hydroxymethyl)ethane **1** (4.32 g, 36.0 mmol) in toluene (125 mL) was added PPTS (86 mg). Benzaldehyde (3.1 mL, 30.0 mmol) was added dropwise and the mixture was refluxed for 1 h using a Dean and Stark apparatus. A 5% $NaHCO_3$ (100 mL) solution was added and the reaction was allowed to cool to room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×100 mL). The organic phases were combined, dried (Na_2SO_4), and after filtration the solvents were removed in vacuo. The crude product was purified by chromatography (hexanes/acetone 8:2) to yield **5** as a white solid (5.95 g, 95%, 3.8:1 *cis*/*trans*). The isomers were separated for identification purposes by preparative HPLC (hexane/acetone 8:2).

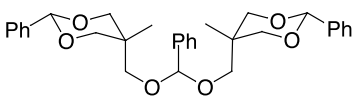
Compound cis-**5**. Mp 100–102 °C; IR (CH_2Cl_2-solution ca. 10 mg mL^{-1}): 3054 (m), 2978 (w), 2959 (w), 2850 (w), 1460 (m), 1420 (m), 1379 (m), 1195 (s), 1043 (s), 888 (m) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.51–7.49 (2H, m, Ar*H*); 7.38–7.36 (3H, m, Ar*H*); 5.46 (1H, s, ArC*H*); 4.02 (2H, br d, J=11.5 Hz, 2×C*H*HOCHAr); 3.93 (1H, t, J=5.3 Hz, OH); 3.84 (2H, d, J=4.8 Hz, CH_2OH); 3.62 (2H, dd, J=10.3, 1.3 Hz, 2×C*H*HOCHAr); 0.79 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 140.8 (C), 129.4 (CH), 129.3 (2×CH), 127.8 (2×CH), 102.8 (CH) 74.2 (2×CH_2), 65.6 (CH_2), 36.2 (C), 18.0 (CH_3); CIMS: *m*/*z* (%): 209 ($(M+H)^+$, 100).

Compound trans-**5**. Mp 60–62 °C; IR (solution CH_2Cl_2 ca. 10 mg mL^{-1}): 339 (m), 2950 (w), 2860 (w), 1451 (m), 1100 (s), 1039 (s), 741 (m) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.52–7.49 (2H, m, Ar*H*); 7.37–7.34 (3H, m, Ar*H*); 5.42 (1H, s, ArC*H*); 3.94 (2H, m, 2×C*H*HOCHAr); 3.87 (1H, m, O*H*); 3.78 (2H, m, 2×CH*H*OCHAr); 3.35 (2H, m, CH_2OH); 1.25 (3H, m, CH_3); ^{13}C NMR+DEPT

(100 MHz, d^6-acetone): δ 141.0 (C), 130.0 (CH), 129.5 (2×CH), 127.9 (2×CH), 103.0 (CH) 75.4 (2×CH_2), 67.5 (CH_2), 36.7 (C), 19.9 (CH_3); CIMS: *m/z* (%): 209 ($(M+H)^+$, 100), 105 (10).

Anal. (mixture of isomers) for $C_{12}H_{16}O_3$ calcd C=69.21; H=7.74. Found C=69.26; H=7.80.

4.1.2. Synthesis of the 'dimeric' acetal isomers. To a stirred solution of 1,1,1-tris(hydroxymethyl)ethane **1** (8.93 g, 74.5 mmol) in toluene (250 mL) was added PPTS (86 mg) and $MgSO_4$ (13.4 g). Benzaldehyde (11.3 mL, 111.7 mmol) was added dropwise and the mixture was refluxed overnight using a Dean and Stark trap. 5% $NaHCO_3$ (100 mL) solution was added and the reaction was allowed to cool to room temperature. The layers were separated and the aqueous layer extracted with CH_2Cl_2 (2×100 mL). The organic phases were combined and dried (Na_2SO_4). After filtration the solvents were removed in vacuo. The crude product was purified by column chromatography (95:5 hexanes/ethyl acetate) to yield the acyclic acetals as a mixture of three ring isomers as a white solid (7.30 g, 14.5 mmol, 39%, ratio **35/36/37** 4.6:2.3:1). The isomers were separated by HPLC (hexanes/ethyl acetate 95:5).



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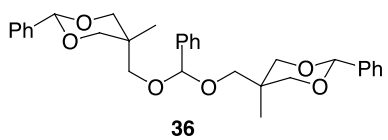
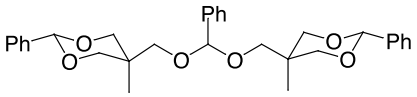
Compound **35**. Mp 110–111 °C; IR 2950 (w), 2868 (w), 1454 (w), 1393 (m), 1205 (m), 1095 (s), 1045 (s), 1025 (s), 967 (m) 756 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.57–7.55 (2H, m, Ar*H*); 7.45–7.39 (4H, m, Ar*H*); 7.38–7.37 (2H, m, Ar*H*); 7.35–7.32 (7H, m, Ar*H*); 5.72 (1H, s, C*H*Ph); 5.46 (2H, s, 2×ring C*H*Ph); 4.07–4.02 (4H, m, 4×ring C*H*HOCHPh); 3.89 (2H, d, *J*=9.0 Hz, 2×C*H*HOCHPh); 3.80 (2H, d, *J*=8.9 Hz, 2×CH*H*OCHPh); 3.65 (4H, d, *J*=12.5 Hz, 4×ring CH*H*OCHPh); 0.95 (6H, s, 2×CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 140.8 (2×C), 140.5 (C), 130.1 (2×CH), 129.7 (2×CH), 129.67 (2×CH), 129.4 (2×CH), 128.3 (2×CH), 127.9 (5×CH), 103.3 (CH), 103.0 (CH), 74.8 (2×CH_2), 74.4 (2×CH_2), 69.0 (2×CH_2), 35.6 (2×C), 18.6 (2×CH_3); ESMS: *m/z* (%) 543 ($(M+K)^+$, 30), 527 ($(M+Na)^+$, 35), 225 (100); HRMS (ES^+) calcd for $C_{31}H_{36}O_6Na$ $(M+Na)^+$ 527.2404, found 527.2399.



36

Compound **36**. Mp 96–98 °C; IR 2950 (w), 2868 (w), 1454 (w), 1393 (m), 1205 (m), 1095 (s), 1045 (s), 1025 (s), 968 (m), 756 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.47–7.31 (15H, m, Ar*H*); 5.66 (1H, s, C*H*Ph); 5.49 (1H, s, C*H*Ph); 5.30 (1H, s, C*H*Ph); 4.09 (1H, dd, *J*=6.0, 2.5 Hz, ring C*H*HOCHPh); 4.07 (1H, dd, *J*=6.0, 2.5 Hz, ring C*H*HOCHPh); 3.92 (1H, d, *J*=10.8 Hz, ring CH*H*OCHPh); 3.89 (1H, d, *J*=10.5 Hz, ring CH*H*OCHPh); 3.86 (1H, d, *J*=9.0 Hz, CH*H*OCHPh); 3.80 (1H, dd, *J*=7.3, 2.5 Hz, ring C*H*HOCHPh); 3.78 (1H, dd, *J*=7.0, 2.3 Hz, ring C*H*HOCHPh); 3.76 (1H, d, *J*=9.0 Hz, C*H*HOCHPh); 3.69 (2H, d, *J*=11.3 Hz, 2×ring CH*H*OCHPh); 3.34 (1H, d, *J*=9.5 Hz, CH*H*OCHPh); 3.28 (1H, d, *J*=9.5 Hz, C*H*HOCHPh); 1.29 (3H, s, CH_3); 0.89 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 140.9 (C), 140.7 (C), 140.3 (C), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.8 (2×CH), 129.5 (3×CH), 128.5 (2×CH), 127.9 (2×CH), 127.8 (3×CH), 103.02 (CH), 130.00 (CH), 102.9 (CH), 75.48 (CH_2), 75.45 (CH_2), 74.56 (CH_2), 74.54 (CH_2), 70.1 (CH_2), 68.8 (CH_2), 35.8 (C), 35.7 (C), 20.3 (CH_3), 18.6 (CH_3); ESMS: *m/z* (%) 543 ($(M+K)^+$, 8), 527 ($(M+Na)^+$, 5), 225 (100); HRMS (ES^+) calcd for $C_{31}H_{36}O_6Na$ $(M+Na)^+$ 527.2404, found 527.2409.



37

Compound **37**. Mp 104–106 °C; IR 2992 (w), 2972 (w), 2907 (w), 2869 (w), 1453 (m), 1382 (m), 1100 (s), 1038 (s), 1025 (s), 994 (s), 980 (s), 745 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.52–7.48 (6H, m, Ar*H*); 7.46–7.42 (2H, m, Ar*H*); 7.39–7.34 (7H, m, Ar*H*); 5.58 (1H, s, C*H*Ph); 5.46 (2H, s, 2×ring C*H*Ph); 4.00 (2H, d, *J*=10.8 Hz, 2×ring C*H*HOCHPh); 3.97 (2H, d, *J*=9.5 Hz, 2×ring C*H*HOCHPh); 3.86 (2H, dd, *J*=7.0, 2.5 Hz, 2×ring CH*H*OCHPh); 3.84 (2H, dd, *J*=7.0, 2.3 Hz, 2×ring CH*H*OCHPh); 3.36 (2H, d, *J*=9.5 Hz, 2×C*H*HOCHPh); 3.29 (2H, d, *J*=9.5 Hz, 2×CH*H*OCHPh); 1.34 (6H, s, 2×CH_3); ^{13}C NMR+DEPT (100M Hz, d^6-acetone): δ 140.95 (2×C), 140.0 (C), 130.1 (2×CH), 129.9 (2×CH), 129.5 (5×CH), 128.3 (2×CH), 127.9 (4×CH), 103.3 (2×CH), 103.2 (CH), 75.5 (2×CH_2), 75.4 (2×CH_2), 70.6 (2×CH_2), 35.9 (2×C), 20.4 (2×CH_3); ESMS: *m/z* (%) 527 ($(M+Na)^+$, 100), 522 ($(M+NH_4)^+$, 40); HRMS (ES^+) calcd for $C_{31}H_{36}O_6Na$ $(M+Na)^+$ 527.2404, found 527.2399.

4.1.3. [2-(4-Methoxyphenyl)-5-methyl-1,3-dioxan-5yl]methanol (13). An identical procedure was followed as for the preparation of **5** (same scale). The crude product was recrystallised (hexane/ethyl acetate 9:2) and the residue purified by chromatography (hexanes/acetone 8:2) to yield **13** as a white solid (6.36 g, 89%, 2.9:1 *cis*/*trans*). The isomers were separated for identification purposes by preparative HPLC (hexanes/acetone 8:2).

Compound cis-**13**. Mp 82–84 °C; IR (solution CH_2Cl_2 ca. 10 mg mL^{-1}): 3290 (m), 2968 (m), 2935 (m), 2864 (m), 1620 (w), 1502 (w), 1379 (m), 1247 (s), 1006 (s), 816 (m) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.39 (2H, d, *J*=8.5 Hz, ArH); 6.90 (2H, d, *J*=8.7 Hz, ArH); 5.39 (1H, s, ArC*H*); 3.89 (2H, m, 2×CH*H*OCHAr); 3.87 (1H, br s, O*H*); 3.81 (2H, s, CH_2OH); 3.77 (3H, s, OCH_3); 3.59 (2H, m, 2×C*H*HOCHAr); 0.77 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 161.4 (C), 133.2 (C), 129.0 (2×CH), 114.7 (2×CH) 102.8 (CH), 74.2 (2×CH_2), 65.6 (CH_2), 56.2 (CH_3), 36.1 (C), 18.0 (CH_3); CIMS: *m/z* (%): 239 ($(M+H)^+$, 100), 137 (27), 121, (82).

Compound trans-**13**. Mp 122–123° C; IR (solution CH_2Cl_2 ca. 10 mg mL^{-1}): 3465 (m), 2968 (w), 2907 (w), 2850 (w),

1611 (m), 1516 (m), 1266 (s), 1062 (s), 987 (m), 835 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.41 (2H, d, J=8.8 Hz, ArH); 6.91 (2H, d, J=8.8 Hz, ArH); 5.35 (1H, s, ArC*H*); 3.91 (2H, br d, J=10.8 Hz, 2×CH*H*OCHAr); 3.83 (1H, t, J=5.3 Hz, O*H*); 3.78 (3H, s, ArOCH_3); 3.75 (2H, dd, J=10.0, 1.0 Hz, 2×C*H*HOCHAr); 3.34 (2H, d, J=5.3 Hz, CH_2OH); 1.24 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 161.5 (C), 133.5 (C), 129.2 (2×CH), 114.8 (2×CH) 103.0 (CH), 75.4 (2×CH_2), 67.5 (CH_2), 56.3 (CH_3), 36.6 (C), 19.9 (CH_3); CIMS: *m*/*z* (%): 239 ((M+H)$^+$, 20), 137 (52), 121, (100).

Anal. (mixture of isomers) for $C_{13}H_{18}O_4$ calcd. C=65.53; H=7.61. Found C=65.69; H=7.79.

4.1.4. 2-Phenyl-5-methyl-1,3-dioxane-5-carbaldehyde (14). A suspension of SO_3·pyridine (10.06 g, 63.3 mmol) in CH_2Cl_2 (50 mL) was dissolved in a mixture of DMSO (50 mL) and Et_3N (10.6 mL, 76.5 mmol). This solution was immediately added dropwise to a stirred solution of **5** (6.01 g, 28.8 mmol) in CH_2Cl_2 (62 mL) at 0 °C, and the reaction mixture was stirred at 0 °C for 3 h. The reaction mixture was poured into a mixture of saturated aqueous NH_4Cl/water/Et_2O/pentane (1:1:1:1, 300 mL), and the aqueous phase extracted with an Et_2O/pentane mixture (1:1, 3×100 mL). The combined organic phases were dried over anhydrous Na_2SO_4. After removing the solvent in vacuo, the pale yellow oil was purified by chromatography (hexane/ethyl acetate 9:1) to yield a white solid (5.34 g, 90%). The isomers were separated for identification purposes by preparative HPLC (hexane/ethyl acetate 9:1).

Major isomer. Mp 58–60 °C; IR (solution CH_2Cl_2 ca. 10 mg mL^{-1}): 2968 (w), 2860 (w),1725 (s), 1460 (m), 1375 (m), 1095 (s), 1015 (w) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 9.89 (1H, s, C*H*O); 7.44–7.41 (2H, m, Ar*H*); 7.37–7.32 (3H, m, Ar*H*); 5.55 (1H, s, ArC*H*); 4.50 (2H, d, J=12.0 Hz, 2×C*H*HOCHAr); 3.86 (2H, d, J=11.3 Hz, 2×CH*H*OCHAr); 0.84 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 205.8 (CH), 140.2 (C), 130.2 (CH), 129.5 (2×CH); 127.8 (2×CH), 102.7 (CH), 73.3 (2×CH_2), 46.7 (C), 15.1 (CH_3); CIMS: *m*/*z* (%): 205 (M−H$^+$, 15), 123 (25), 105 (100), 77 (53).

Minor isomer. Mp 56–58 °C; IR (solution CH_2Cl_2 ca. 10 mg mL^{-1}): 2954 (w), 2850 (w), 2727 (w), 1715 (s), 1455 (m), 1379 (m), 1105 (w), 987 (m) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 9.56 (1H, s, C*H*O); 7.51–7.48 (2H, m, Ar*H*); 7.39–7.36 (3H, m, Ar*H*); 5.52 (1H, s, ArC*H*); 4.19 (2H, m, 2×C*H*HOCHAr); 3.97 (2H, m, 2×CH*H*OCHAr); 1.48 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 204.5 (CH), 140.0 (C), 130.4 (CH), 129.6 (2×CH); 127.9 (2×CH), 103.0 (CH), 72.2 (2×CH_2), 47.6 (C), 17.4 (CH_3); EIMS: *m*/*z* (%): 206 (M$^+$, 34), 205 (70), 123 (51), 105 (100), 77 (78).

Anal. (mixture of isomers) for $C_{12}H_{14}O_3$ calcd C=69.89; H=6.84. Found C=69.77; H=6.89.

4.1.5. 2-(4-Methoxyphenyl)-5-methyl-1,3dioxane-5-carbaldehyde (15). An identical procedure was followed as for the preparation of **14** (2.50 mmol scale). The crude product (pale yellow oil) was purified by chromatography (8:2 hexane/acetone) to yield a white solid (0.58 g, 98%). The isomers were separated for identification purposes by preparative HPLC (hexane/ethyl acetate 9:1).

Major isomer. Mp 102–104 °C; IR (solution CH_2Cl_2 ca. 10 mg mL^{-1}): 2973 (m), 2940 (m), 2874 (m), 2836 (m), 1715 (s), 1611 (s), 1524 (s), 1393 (s), 1242 (s), 1001 (s), 821 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 9.89 (1H, s, C*H*O); 7.33 (2H, d, J=8.3 Hz, Ar*H*); 6.89 (2H, d, J=9.0 Hz, Ar*H*); 5.48 (1H, s, ArC*H*); 4.47 (2H, d, J=11.8 Hz, 2×C*H*HOCHAr); 3.83 (2H, dd, J=11.8, 1.0 Hz, 2×CH*H*OCHAr); 3.77 (3H, s, OCH_3); 0.83 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 205.9 (CH), 161.6 (C), 132.6 (C), 129.1 (2×CH), 114.8 (2×CH), 102.6 (CH), 73.3 (2×CH_2), 56.2 (CH_3), 46.6 (C), 15.1 (CH_3); EIMS: *m*/*z* (%): 236 (M$^+$, 7), 235 (M−H$^+$, 12), 135 (100).

Minor isomer. Mp 108–110 °C; IR (solution CH_2Cl_2 ca. 10 mg mL^{-1}): 3049 (w), 2959 (w), 2831 (w), 1720 (m), 1621 (m), 1516 (m), 1270 (w), 1171 (m), 736 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 9.59 (1H, s, C*H*O); 7.41 (2H, d, J=8.8 Hz, Ar*H*); 6.92 (2H, d, J=8.8 Hz, Ar*H*); 5.46 (1H, s, ArC*H*); 4.15 (2H, m, 2×C*H*HOCHAr); 3.94 (2H, m, 2×CH*H*OCHAr); 3.80 (3H, s, OCH_3); 1.47 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 204.5 (CH), 161.8 (C), 132.7 (C), 129.2 (2×CH), 114.9 (2×CH), 102.9 (CH), 72.1 (2×CH_2), 56.3 (CH_3), 47.5 (C), 17.4 (CH_3); EIMS: *m*/*z* (%): 235 (M−H$^+$, 13), 152 (20), 135 (100).

Anal. (mixture of isomers) for $C_{13}H_{16}O_4$ calcd C=66.09; H=6.83. Found C=66.17; H=6.89.

4.1.6. 5-(1,3-Dioxalan-2-yl)-2-phenyl-5-methyl-1,3-dioxane (16). A solution of aldehyde **14** (0.78 g, 3.78 mmol) in CH_2Cl_2 (10 mL) was cooled to 0 °C. 1,2-Bis-(trimethylsilyloxy) ethane (1.4 mL, 5.7 mmol) was added and trimethylsilyl trifluoromethane sulphonate (0.3 mL, 1.9 mmol) was added dropwise. The solution was stirred at 0 °C for 1 h. Pyridine (3 mL) was added and the mixture was poured into saturated aqueous $NaHCO_3$ solution (75 mL). The aqueous layer was extracted with CH_2Cl_2 (2×90 mL) and the combined organic phases dried (Na_2SO_4). After filtration the CH_2Cl_2 was removed in vacuo. The crude product was subjected to chromatography (hexane/acetone 85:15) to yield the product as a mixture of ring isomers (0.79 g, 3.18 mmol, 84%). The isomers were separated for identification purposes by preparative HPLC, both were isolated as white solids (hexanes/acetone 9.5:0.5).

Major isomer. Mp 104–106 °C; IR (CH_2Cl_2 soln ca. 10 mg mL^{-1}) 3054 (w), 2988 (w), 2889 (w) 2865 (w), 1451 (w), 1385 (w), 1266 (s), 1214 (m), 1105 (m), 1015 (w), 722 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.47–7.44 (2H, m, Ar*H*); 7.35–7.34 (3H, m, Ar*H*); 5.50 (1H, s, ArC*H*); 5.47 (1H, s, C*H*(OCH$_2$)$_2$); 4.20 (2H, m, 2×CH*H*OCHAr); 3.93 (4H, m, CH(OCH_2)$_2$); 3.72 (2H, m, 2×CH*H*OCHAr); 0.67 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 138.9 (C), 130.7 (CH), 129.5 (2×CH) 127.9 (2×CH), 104.8 (CH), 103.0 (CH), 74.9 (2×CH_2), 66.9 (2×CH_2), 38.1 (C), 13.1 (CH_3); CIMS: *m*/*z* (%): 251 ((M+H)$^+$, 38), 105 (30), 73 (100).

Minor isomer. Mp 68–70 °C; IR (CH_2Cl_2 soln ca.

10 mg mL^{-1}) 2964 (w), 2893 (w), 2845 (w), 1445 (m), 1384 (s), 1328 (m), 1162 (w), 1082 (s), 1034 (m), 935 (m), 750 (m) cm^{-1}; ^{1}H NMR (400 MHz, d^6-acetone): δ 7.53–7.51 (2H, m, Ar*H*); 7.40–7.37 (3H, m, Ar*H*); 5.54 (1H, s, ArC*H*); 4.58 (1H, s, C*H*(OCH$_2$)$_2$); 4.03–3.96 (4H, m, 2× C*H*HOCHAr, CH(OC*H*H)$_2$); 3.89–3.83 (4H, m, 2× CH*H*OCHAr, CH(OCH*H*)$_2$); 1.31 (3H, s, C*H*$_3$); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 140.9 (C), 130.1 (CH), 129.5 (2×CH), 127.9 (2×CH), 107.1 (CH), 103.2 (CH), 73.7 (2×CH$_2$), 66.6 (2×CH$_2$), 38.6 (C), 17.3 (CH$_3$); CIMS: *m*/*z* (%): 251 ((M+H)$^+$, 100), 105 (20), 73 (80).

Anal. (mixture of isomers) for $C_{14}H_{18}O_4$ calcd C=67.18; H=7.25. Found C=67.38; H=7.36.

4.1.7. 5-(1,3-Dioxalan-2-yl)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane (17). An identical procedure was followed as for the preparation of **16** (8.47 mmol scale). The crude product was subjected to chromatography (hexane/acetone 85:15) to yield the product as a mixture of ring isomers (2.18 g, 92%). The isomers were separated for identification purposes by preparative HPLC, both were isolated as white solids (hexane/acetone 95:5).

Major isomer. Mp 126–128 °C; IR (CH_2Cl_2 soln ca. 10 mg mL^{-1}) 3054 (w), 2974 (m), 2889 (m), 2846 (m), 1621 (m), 1512 (s), 1470 (m), 1389 (s), 1262 (s), 1186 (s), 1087 (s), 826 (m), 727 (s) cm^{-1}; ^{1}H NMR (400 MHz, d^6-acetone): δ 7.37 (2H, d, *J*=7.8 Hz, Ar*H*); 6.89 (2H, d, *J*=8.7 Hz, Ar*H*); 5.47 (1H, s, ArC*H*); 5.44 (1H, s, C*H*(CH$_2$)$_2$); 4.17 (2H, m, 2×C*H*HOCHAr); 3.87 (4H, m, CH(C*H*$_2$)$_2$); 3.71 (3H, s, OC*H*$_3$); 3.69 (2H, m, 2× CH*H*OCHAr); 0.66 (3H, s, CH$_3$); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 161.6 (C), 133.1 (C), 129.1 (2×CH), 114.8 (2×CH), 104.9 (CH), 102.9 (CH), 74.9 (2×CH$_2$), 66.9 (2×CH$_2$), 56.3 (CH$_3$), 38.0 (C), 13.1 (CH$_3$); CIMS: *m*/*z* (%): 281 (M+H)$^+$, 29), 151 (10), 133 (100).

Minor isomer. Mp 116–118 °C; IR (CH_2Cl_2 soln ca. 10 mg mL^{-1}) 3045 (m), 2978 (m), 2931 (m), 2832 (m), 1620 (m), 1522 (s), 1465 (m), 1389 (s), 1270 (s), 1176 (s), 1086 (s), 1034 (m), 822 (m), 736 (s) cm^{-1}; ^{1}H NMR (400 MHz, d^6-acetone): δ 7.39 (2H, m, Ar*H*); 6.91 (2H, m, Ar*H*); 5.36 (1H, s, ArC*H*); 4.53 (1H, s, C*H*(CH$_2$)$_2$); 3.96–3.91 (4H, m, CH(C*H*$_2$)$_2$); 3.83–3.77 (7H, m, OC*H*$_3$+2× C*H*HOCHAr); 1.27 (3H, s, C*H*$_3$); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 161.8 (C), 133.5 (C), 129.4 (2×CH), 115.0 (2×CH), 107.3 (CH), 103.3 (CH), 73.8 (2×CH$_2$), 66.7 (2×CH$_2$), 56.5 (CH$_3$), 38.7 (C), 17.5 (CH$_3$); CIMS: *m*/*z* (%): 281 (M+H)$^+$, 64), 136 (78), 73 (100).

Anal. (mixture of isomers) for $C_{15}H_{20}O_5$ calcd C=64.27; H=7.19. Found C=64.43; H=7.31.

4.1.8. 3-Benzyloxy-2-[1,3]dioxolan-2-yl-2-methyl-propan-1-ol (18). A solution of diacetal **16** (0.25 g, 1 mmol) in CH_2Cl_2 (5 mL) was cooled to −78 °C. Borane dimethyl sulfide complex (0.19 mL, 2 mmol) was added followed by dropwise addition of trimethylsilyl trifluoromethane sulfonate (0.36 mL, 2 mmol). The reaction mixture was stirred at −78 °C for 3 h. After this time NaOMe (0.5 M solution in MeOH, 16 mL) was added, followed by saturated aqueous $NaHCO_3$ solution (5 mL). When the reaction mixture had warmed to room temperature it was poured into a saturated aqueous $NaHCO_3$ solution (15 mL) and water (15 mL) and was extracted with CH_2Cl_2 (3×30 mL). The organic phases were combined and dried ($MgSO_4$). After filtration the CH_2Cl_2 was removed in vacuo. The crude product was subjected to chromatography (hexane/ethyl acetate 6:4) to yield the product as a colourless oil (0.202 g, 81%).

IR (film) 3494 (m), 2983 (m), 2936 (m), 2874 (s), 1503 (w), 1451 (s), 1366 (m), 1101 (s), 1034 (s), 945 (s), 741 (s), 703 (s) cm^{-1}; ^{1}H NMR (400 MHz, d^6-acetone): δ 7.39–7.35 (4H, m, Ar*H*); 7.32 (1H, m, Ar*H*); 4.88 (1H, s, C*H*(OCH$_2$)$_2$); 4.55 (2H, s, CHHOC*H*$_2$Ar); 3.95–3.81 (4H, m, CH(OC*H*$_2$)$_2$); 3.68 (1H, dd, *J*=10.8, 4.5 Hz, C*H*HOH); 3.64 (1H, m, CH*H*OH); 3.60 (1H, d, *J*=8.7 Hz, C*H*HOCH$_2$-Ar); 3.52 (1H, d, *J*=8.8 Hz, C*H*HOCH$_2$Ar); 3.35 (1H, br s, CHHO*H*); 0.95 (3H, s, C*H*$_3$); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 140.7 (C), 129.8 (CH), 128.8 (4×CH), 107.1 (CH), 74.7 (CH$_2$), 74.0 (CH$_2$), 66.42 (CH$_2$), 66.36 (CH$_2$), 65.8 (CH$_2$), 44.9 (C), 15.1 (CH$_3$); CIMS: *m*/*z* (%): 253 ((M+H)$^+$, 28), 205 (12), 115 (40), 73 (100): HRMS (EI) calcd for $C_{14}H_{19}O_4$ (M−H)$^+$ 251.1283, found 251.1279.

4.1.9. 2-[1,3]Dioxolan-2-yl-3-(4-methoxy-benzyloxy)-2-methyl-propan-1-ol (19). Starting from **17**, an identical procedure was followed as for the preparation of **18** (same scale). The crude product was subjected to chromatography (hexane/ethyl acetate 6:4) to give the product as a colourless oil (0.221 g, 78%).

IR (film) 3489 (m), 2936 (s), 2988 (s), 2841 (s), 1621 (s), 1516 (s), 1465 (s), 1304 (s), 1034 (m), 1252 (s), 1105 (s), 1025 (s) cm^{-1}; ^{1}H NMR (400 MHz, d^6-acetone): δ 7.31 (2H, m, Ar*H*); 6.93 (2H, m, Ar*H*); 4.86 (1H, s, C*H*(OCH$_2$)$_2$); 4.47 (2H, s, CHHOC*H*$_2$Ar); 3.94–3.81 (4H, m, CH(OC*H*$_2$)$_2$); 3.82 (3H, s, ArOC*H*$_3$); 3.64 (1H, dd, *J*=10.8, 5.5 Hz, C*H*HOH); 3.58 (1H, m, CH*H*OH); 3.55 (1H, d, *J*=8.8 Hz, C*H*HOCH$_2$Ar); 3.47 (1H, d, *J*=9.0 Hz, CH*H*OCH$_2$Ar); 3.29 (1H, t, *J*=5.5 Hz, CHHO*H*); 0.93 (3H, s, C*H*$_3$); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 160.8 (C), 132.6 (C), 130.5 (2×CH), 115.2 (2×CH), 107.2 (CH), 74.4 (CH$_2$), 73.8 (CH$_2$), 66.43 (CH$_2$), 66.37 (CH$_2$), 65.9 (CH$_2$), 56.2 (CH$_3$), 44.8 (C), 15.1 (CH$_3$); EIMS: *m*/*z* (%): 281 ((M−H)$^+$, 4), 220 (12), 189 (27), 121 (100): HRMS (EI) calcd for $C_{15}H_{22}O_5$ (M)$^+$ 282.1467, found 282.1460.

4.1.10. *cis*-5-Dimethoxymethyl-5-methyl-2-phenyl-[1,3]-dioxane (21). A solution of aldehyde **14** (2.99 g, 14.5 mmol) in CH_2Cl_2 (58 mL) was cooled to −78 °C. Methoxytrimethylsilane (6.0 mL, 43.5 mmol) was added followed by dropwise addition of triflic acid (0.76 mL, 4.2 mmol). The solution was stirred at −78 °C for 3 h. Pyridine (7 mL) was added and the mixture poured on to satd $NaHCO_3$ solution (50 mL). The aqueous layer was extracted with CH_2Cl_2 (3×100 mL) and the organic phases were combined and dried (Na_2SO_4). After filtration, the CH_2Cl_2 was removed in vacuo. The crude product was subjected to chromatography (hexane/acetone 9:1) to yield a single isomer as a white solid (2.53 g, 69%).

Mp 108–112 °C; IR (CH_2Cl_2 soln ca. 10 mg mL^{-1}) 3054 (m), 2978 (m), 1393 (w), 1209 (w), 1167 (w), 1101 (m),

1072 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.51–7.49 (2H, m, Ar*H*); 7.42–7.37 (3H, m, Ar*H*); 5.47 (1H, s, ArC*H*); 4.89 (1H, s, C*H*$(OCH_3)_2$); 4.24 (2H, m, 2×C*H*HOCHAr); 3.62 (6H, s, CH$(OCH_3)_2$); 3.59 (2H, m, 2×CH*H*OCHAr); 0.74 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, $CDCl_3$): δ 138.4 (C), 128.9 (CH), 128.3 (2×CH), 126.1 (2×CH), 107.1 (CH), 102.0 (CH), 74.1 (2×CH_2), 58.8 (2×CH_3), 39.0 (C), 12.2 (CH_3); CIMS: *m/z* (%): 221 ($(M-OMe)^+$, 30), 105 (35), 75 (100). Anal. for $C_{14}H_{20}O_4$ calcd C=66.65; H=7.99. Found C=66.64; H=8.03.

4.1.11. *cis*-5-Dimethoxymethyl-2-(4-methoxy-phenyl)-5-methyl-[1,3]dioxane (22). Starting from **15**, an identical procedure was followed as for the preparation of **21** (2.45 mmol scale). The crude product was subjected to chromatography (hexane/acetone 9:1) to give a single isomer as a white solid (0.601 g, 87%).

Mp 118–119 °C; IR (CH_2Cl_2 soln ca. 10 mg mL^{-1}) 2964 (m), 2860 (m), 2827 (m), 1616, (m), 1497 (s), 1384 (s), 1261 (s), 1152 (s), 1053 (s), 816 (m) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 7.43 (2H, d, *J*=8.6 Hz, Ar*H*); 6.94 (2H, d, *J*=8.8 Hz, Ar*H*); 5.48 (1H, s, ArC*H*); 4.90 (1H, s, C*H*$(OCH_3)_2$); 4.13 (2H, m, 2×C*H*HOCHAr); 3.82 (3H, s, ArOCH_3); 3.61 (2H, m, 2×CH*H*OCHAr); 3.59 (6H, s, CH$(OCH_3)_2$); 0.68 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 161.7 (C), 133.3 (C), 129.1 (2×CH), 114.9 (2×CH), 108.5 (CH), 103.2 (CH), 75.1 (2×CH_2), 59.4 (2×CH_3), 56.3 (CH_3), 40.3 (C), 13.3 (CH_3); CIMS: *m/z* (%): 283 ($(M+H)^+$, 4), 251 (6), 133 (100). Anal. for $C_{15}H_{22}O_5$ calcd C=63.81; H=7.85. Found C=64.06; H=8.11.

4.1.12. Benzoic acid 2-hydroxymethyl-3,3-dimethoxy-2-methyl-propyl ester (23). A solution of diacetal **21** (0.126 g, 0.5 mmol) in ethyl acetate (40 mL) was cooled to −78 °C. Ozone was passed through the solution for 1 h. After this time nitrogen was passed through the solution until the blue colouration disappeared. The ethyl acetate was removed in vacuo and the residue subjected to chromatography (hexane/acetone 8:2). The product **23** was obtained as a colourless oil (0.087 g, 65%).

IR (film) 3503 (br s), 2936 (s), 2837 (s), 1725 (s), 1592 (s), 1469 (w), 1445 (s), 1271 (s), 1176 (s), 1105 (s), 1067 (s), 703 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 8.09 (2H, m, Ar*H*); 7.66 (1H, m, Ar*H*); 7.55 (2H, m, Ar*H*); 4.47 (1H, s, C*H*$(OCH_3)_2$); 4.33 (2H, s, CH_2OCOAr); 3.66 (3H, m, CH_2O*H*); 3.57 (3H, s, 1×CHOCH_3); 3.55 (3H, s, 1×CHOCH_3); 1.03 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): 167.5 (C), 134.6 (CH), 132.3 (C), 130.9 (2×CH), 130.2 (2×CH), 110.7 (CH), 67.8 (CH_2), 65.2 (CH_2), 59.5 (CH_3), 59.2 (CH_3), 46.6 (C), 15.4 (CH_3); CIMS: *m/z* (%): 237 ($(M-OCH_3)^+$, 54), 105 (62), 85 (72), 75 (100); HRMS (ES^+) calcd for $C_{14}H_{20}O_5Na$ $(M+Na)^+$ 291.1203, found 291.1204.

4.1.13. 4-Methoxy-benzoic acid 2-hydroxymethyl-3,3-dimethoxy-2-methyl-propyl ester (24). Starting from **22**, an identical procedure was followed as for the preparation of **23** (0.47 mmol scale). The crude product was subjected to chromatography (hexane/acetone 8:2) to give the product as a colourless oil (0.092 g, 62%).

IR (film) 3522 (br m), 2936 (m), 2841 (m), 1706 (s), 1606 (s), 1507 (s), 1469 (s), 1261 (s), 1167 (s), 1072 (s), 845 (m), 765 (m), 689 (m) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 8.03 (2H, d, *J*=9.0 Hz, Ar*H*); 7.06 (2H, d, *J*=8.8 Hz, Ar*H*); 4.45 (1H, s, C*H*$(OCH_3)_2$); 4.29 (2H, s, CH_2OCOAr); 3.92 (3H, s, ArOCH_3); 3.67–3.63 (3H, m, CH_2O*H*); 3.56 (3H, s, CHOCH_3); 3.54 (3H, s, CHOCH_3); 1.01 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 167.3 (C), 165.2 (C), 133.0 (2×CH), 124.5 (C), 115.4 (2×CH), 110.7 (CH), 67.5 (CH_2), 65.2 (CH_2), 59.6 (CH_3), 59.3 (CH_3), 56.7 (CH_3), 46.7 (C), 15.4 (CH_3); CIMS: *m/z* (%): 268 (M^+, 6), 267 (28), 135 (40), 85 (100); HRMS (ES^+) calcd for $C_{15}H_{22}O_6Na$ $(M+Na)^+$ 321.1308, found 321.1311.

4.1.14. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-2-methyl-propane-1,3-diol (25). To 1,1,1-tris(hydroxymethyl)ethane **1** (2.39 g, 19.9 mmol) and imidazole (0.903 g, 13.26 mmol) was added DMF (20 mL) and the reaction was stirred until complete dissolution occurred. TBDMSCl (1.00 g, 6.63 mmol) was added dropwise and the reaction mixture stirred at room temperature for 24 h. The reaction was poured into water (10 mL) and the resultant solution extracted with EtOAc (3×100 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated in vacuo. Chromatography (hexane/acetone 4:1) gave **25** as a colourless oil (1.13 g, 73%).

IR 3354 (w), 2952 (m), 2927 (m), 2881 (m), 2855 (m), 1470 (m), 1252 (m), 1092 (s), 1035 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.70 (2H, dd, *J*=11.0, 4.8 Hz, 2×CH*H*OH); 3.59 (2H, s, CH_2OSi); 3.56 (2H, dd, *J*=11.0, 6.6 Hz, 2×C*H*HOH); 2.83 (2H, dd, *J*=7.0, 4.8 Hz, 2×CH_2O*H*); 0.89 (9H, s, C$(CH_3)_3$); 0.79 (3H, s, CH_3); 0.07 (6H, s, Si$(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 68.8 (CH_2), 67.7 (2×CH_2), 41.0 (C), 25.8 (3×CH_3), 18.1 (C), 16.8 (CH_3), −5.7 (2×CH_3); CIMS *m/z* (%) 235 ($(M+H)^+$, 100), 217 (6), 159 (57), 129 (9), 92 (26); HRMS (EI) calcd for $C_7H_{17}O_2Si$ $(M-{}^tBu)^+$ 177.0947, found 177.0943.

4.1.15. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-methyl-propane-1,3-diol (26). To a stirred solution of 1,1,1-tris(hydroxymethyl)ethane **1** (1.31 g, 10.91 mmol) and imidazole (0.49 g, 7.2 mmol) in dry DMF (20 mL), TBDPSCl (1.0 g, 3.64 mmol) was added dropwise over 90 min. The reaction was then stirred at ambient temperature for 24 h. The reaction was poured into water (60 mL) and the aqueous solution extracted with Et_2O (2×50 mL). The organic phases were combined, washed with H_2O (50 mL), brine (50 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The resultant colourless oil was purified by chromatography (hexane/acetone 75:25) to yield **26** as a colourless oil (1.18 g, 90%).

IR 3394 (s), 3069 (m), 3049 (m), 2958 (s), 2929 (s), 2857 (s), 1589 (m), 1470 (s), 1427 (s),1049 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71–7.69 (4H, m, Ar*H*); 7.49–7.40 (6H, m, Ar*H*); 3.75 (2H, d, *J*=10.5 Hz, 2×C*H*HOH); 3.65 (2H, s, CH_2OSi); 3.60 (2H, d, *J*=11.0 Hz, 2×CH*H*OH); 2.84 (2H, br s, 2×CH_2O*H*); 1.11 (9H, s, C$(CH_3)_3$); 0.84 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.6 (4×CH), 132.9 (2×C), 129.8 (2×CH), 127.8 (4×CH), 68.4 (CH_2), 67.6 (2×CH_2), 41.5 (C), 26.8 (3×CH_3), 19.2 (C), 16.7 (CH_3); ES *m/z* (%) 739 ($(2M+Na)^+$, 100), 717 (53), 696 (12), 619 (21),

460 (58), 381 (33), 127 (50); HRMS (ES^+) calcd for $C_{21}H_{30}O_2SiNa$ $(M+Na)^+$ 381.1856, found 381.1857.

4.1.16. 2-Methyl-2-triisopropylsilanyloxymethyl-propane-1,3-diol (27). To a stirred solution of 1,1,1-tris(hydroxymethyl)ethane **1** (5.61 g, 46.7 mmol) and imidazole (1.27 g, 18.7 mmol) in dry DMF (25 mL), TIPSCl (2.0 mL, 9.34 mmol) was added dropwise. The reaction was stirred overnight at room temperature before pouring into water (50 mL). The resultant solution was extracted with EtOAc (3×20 mL), the organic phases were combined, washed with water (20 mL), brine (20 mL), dried over Na_2SO_4 and then concentrated in vacuo. Chromatography of the crude product (hexane/acetone 4:1) yielded **27** as a colourless oil (1.44 g, 81%).

IR 3385 (s), 2943 (s), 2893 (s), 2867 (s), 1464 (m), 1384 (m), 1104 (s), 1105 (s), 882 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.74 (2H, br d, J=10.8 Hz, 2×C*H*HOH); 3.71 (2H, s, CH_2OSi); 3.60 (2H, dd, J=10.8, 5.0 Hz, 2×CH*H*OH); 2.68 (2H, br s, 2×CH_2O*H*); 1.15–1.06 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); 0.82 (3H, s, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.5 (CH_2), 67.8 (2×CH_2), 41.3 (C), 17.9 (6×CH_3), 16.9 (CH_3), 11.8 (3×CH); CIMS *m*/*z* (%) 277 ($(M+H)^+$, 76), 259 (12), 233 (16), 215 (30), 173 (98), 119 (34), 75 (100); HRMS (EI) calcd for $C_{11}H_{25}O_3Si$ $(M-C_3H_7)^+$ 233.1573, found 233.1575.

4.1.17. 3-Benzyloxy-2-methyl-2-triisopropylsilanyloxy-methyl-propan-1-ol (28). To a suspension of sodium hydride (0.22 g, 5.58 mmol, 60% dispersion in mineral oil) in THF (8 mL) was added dropwise a solution of **27** (1.50 g, 5.42 mmol) in THF (5 mL) over a period of 10 min. The reaction mixture was then heated under reflux for 1 h and then allowed to cool to room temperature. Benzyl bromide (0.70 mL, 5.91 mmol) was then added dropwise over a period of 10 min. The reaction mixture was then heated under reflux for 22 h and then allowed to cool to room temperature. Water (20 mL) was then added and the layers separated. The aqueous layer was then extracted with Et_2O (3×25 mL). The organic phases were then combined, dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. The residue was subjected to chromatography (hexane/acetone 6:1) to give **28** as a colourless oil (1.599 g, 81%).

IR 3447 (br m), 3089 (vw), 3065 (w), 3031 (w), 2943 (s), 2891 (m), 2866 (s), 1714 (w), 1497 (w), 1463 (s), 1455 (s), 1384 (m), 1363 (m), 1248 (w), 1207 (w), 1098 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.28 (5H, m, Ar*H*); 4.52 (2H, s, ArCH_2O); 3.76 (1H, d, J=9.5 Hz, C*H*HOCH_2Ar); 3.72 (1H, d, J=9.0 Hz, CH*H*OCH_2Ar); 3.63 (2H, s, CH_2OSi); 3.53 (1H, d, J=8.5 Hz, C*H*HOH); 3.48 (1H, d, J=8.5 Hz, CH*H*OH); 2.99 (1H, br s, CH_2O*H*); 1.15–1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); 0.89 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, $CDCl_3$): δ 138.3 (C), 128.3 (CH), 127.52 (2×CH), 127.48 (2×CH), 74.4 (CH_2), 73.5 (CH_2), 69.6 (CH_2), 68.1 (CH_2), 41.3 (C), 18.0 (6×CH_3), 17.3 (CH_3), 11.8 (3×CH); ES^+MS: *m*/*z* (%) 389 ($(M+Na)^+$, 100); HRMS (ES^+) calcd for $C_{21}H_{38}O_3SiNa$ $(M+Na)^+$ 389.2482, found 389.2485.

4.1.18. 3-Acetyl-2-methyl-2-triisopropylsilanyloxy-methyl-propan-1-ol (29). To $CeCl_3$ (88 mg, 0.36 mmol) was added a solution of **27** (1.00 g, 3.62 mmol) in THF (15 mL) and the mixture was stirred for 5 min. Acetic anhydride (3.4 mL, 36.2 mmol) was added and the reaction mixture was stirred at ambient temperature for 5 h. The mixture was diluted with Et_2O (25 mL) and was then washed with satd aq. $NaHCO_3$ solution (2×20 mL), and brine (20 mL). The organic layer was dried (Na_2SO_4), filtered and the solvent removed in vacuo. The residue was subjected to chromatography (ethyl acetate/hexane 80:20) to give **29** as a colourless oil (1.032 g, 89%).

IR 3469 (br w), 2943 (s), 2892 (m), 2867 (s), 1743 (s), 1725 (s), 1464 (m), 1382 (m), 1242 (s), 1103 (s), 1039 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.12 (2H, s, CH_2OAc); 3.69 (1H, d, J=9.5 Hz, C*H*HOSi); 3.65 (1H, d, J=9.5 Hz, CH*H*OSi); 3.56 (1H, dd, J=11.0, 5.5 Hz, C*H*HOH); 3.52 (1H, dd, J=11.0, 7.0 Hz, CH*H*OH); 2.73 (1H, dd, J=6.5, 5.5 Hz, CH_2O*H*); 2.07 (3H, s, OCOCH_3); 1.11–1.05 (21H, m, Si(C*H*(CH_3)$_2$)$_3$); 0.87 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, $CDCl_3$): δ 171.3 (C), 68.2 (CH_2), 67.6 (CH_2), 66.3 (CH_2), 40.8 (C), 20.8 (CH_3), 17.9 (6×CH_3), 16.8 (CH_3), 11.8 (3×CH); CIMS: *m*/*z* (%) 319 ($(M+H)^+$, 79), 301 ($(M-H_2O)^+$, 100), 275 ($(M-{}^iPr)^+$, 34), 173 (87), 145 ($(M-OTIPS)^+$, 47); HRMS (ES^+) calcd for $C_{32}H_{68}O_8Si_2$-Na $(2M+Na)^+$ 659.4344, found 659.4348.

4.1.19. 2-(1,3-Dioxolan-2yl)-2methyl-1,3-propanediol (30). To a stirred solution of **16** (0.76 g, 3.04 mmol) in methanol (20 mL) was added 20% palladium hydroxide on carbon (201 mg). The flask was evacuated and filled with hydrogen gas three times and was then left under an atmosphere of hydrogen (balloon) at room temperature for 18 h. The reaction mixture was then filtered through a plug of Celite and was washed with methanol (2×25 mL). The solvent was removed in vacuo and the residue chromatographed on silica (hexane/acetone 6:4) to give the product **30** as a white solid (0.437 g, 89%).

Starting from **17**, using an identical procedure (3.57 mmol scale) **30** was obtained (0.427 g, 74%) after a reaction time of 48 h.

Mp 48–52 °C; IR (CH_2Cl_2 10 mg mL^{-1}) 3380 (br s), 2959 (m), 2889 (s), 1696 (m), 1649 (m), 1394 (m), 1091 (s), 1044 (s), 727 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 4.83 (1H, s, $(CH_2O)_2$C*H*); 3.96–3.82 (4H, m, (CH_2O)$_2$CH); 3.66 (2H, d, J=10.0 Hz, 2×C*H*HOH); 3.57 (2H, d, J=11.0 Hz, 2×CH*H*OH); 3.54 (2H, br s, CHHO*H*); 0.89 (3H, s, CH_3); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 107.7 (CH), 66.4 (2×CH_2), 66.3 (2×CH_2), 44.8 (C), 14.9 (CH_3); CIMS: *m*/*z* (%) 163 ($(M+H)^+$, 12), 115 (18), 73 (100). Anal. for $C_7H_{14}O_4$ calcd C=51.84; H=8.70. Found C=51.40; H=8.63.

4.1.20. 2-(*tert*-Butyl-dimethyl-silanyloxymethyl)-2-methyl-malonaldehyde (32). To a solution of diol **25** (0.23 g, 1 mmol) in ethyl acetate (7 mL) was added iodoxybenzoic acid (1.66 g, 6 mmol). The suspension was then warmed in an oil bath at 80 °C for 3.5 h. After this time, the reaction was cooled to room temperature and the IBX removed by filtration. The filtrate was concentrated and subjected to chromatography (hexane/ethyl acetate 95:5) to give the product as a colourless oil (0.189 g, 83%).

IR (film) 2954 (s), 2931 (s), 2860 (s), 2728 (w), 1706 (s), 1474 (m), 1379 (w), 1256 (m), 1096 (s), 1011 (w), 831 (s), 779 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 9.82 (2H, s, 2×C*H*O); 4.16 (2H, s, CH_2); 1.27 (3H, s, CH_3); 0.92 (9H, s, SiC(CH_3)$_3$); 0.13 (6H, s, Si(CH_3)$_2$); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 202.2 (2×CH), 66.0 (CH_2), 65.5 (C), 26.8 (CH_3), 19.5 (C),13.4 (3×CH_3), −4.8 (2×CH_3); EIMS: *m/z* (%) 201 ((M−CHO)$^+$, 4), 143 (M−^{t}Bu−2CH_3)$^+$, 100), 57 (19). HRMS (ES$^+$) calcd for $C_{12}H_{26}O_4$-SiNa (M+Na+MeOH)$^+$ 285.1493, found 285.1496.

4.1.21. 2-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-methyl-malonaldehyde (33). Starting from **26**, an identical procedure was followed as for the preparation of **32** (same scale). The crude product was subjected to chromatography (hexane/ethyl acetate 95:5) to give the product as a colourless oil (0.248 g, 71%).

IR (film) 3078 (w), 2955 (s), 2931 (s), 2869 (s), 2718 (w), 1715 (s), 1474 (m), 1422 (s), 1384 (w), 1110 (s), 816 (s), 689 (s) cm^{-1}; ^1H NMR (400 MHz, d^6-acetone): δ 9.90 (2H, s, 2×C*H*O); 7.75–7.73 (4H, m, Ar*H*); 7.50–7.47 (6H, m, Ar*H*); 4.21 (2H, s, CH_2); 1.33 (3H, s, CH_3); 1.09 (9H, s, C(CH_3)$_3$); ^{13}C NMR+DEPT (100 MHz, d^6-acetone): δ 201.9 (2×CH), 137.1 (4×CH), 134.1 (2×C), 131.6 (2×CH), 129.5 (4×CH), 66.6 (CH_2), 66.0 (C), 27.8 (3×CH_3), 20.5 (C), 13.6 (CH_3); EIMS: *m/z* (%) 297 ((M−^{t}Bu)$^+$, 40), 267 ((M−^{t}Bu−CHO)$^+$, 67), 199 (100). HRMS (ES$^+$) calcd for $C_{22}H_{30}O_4SiNa$ (M+Na+MeOH)$^+$ 409.1806, found 409.1809.

Acknowledgements

We thank the University of Southampton, the EPSRC, Pfizer, and the Royal Society for support. We are indebted to Joan Street and Dr. Neil Wells for NMR support, and to Dr. John Langley and Julie Herniman for MS support. We wish to acknowledge the use of the EPSRC's Chemical database service at Daresbury.[29]

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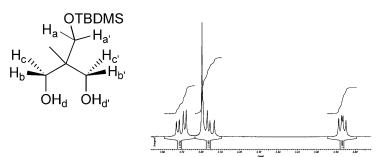

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