Total Synthesis of Calditol: Structural Clarification of this Typical Component of Archaea Order *Sulfolobales***

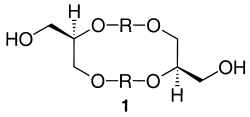
Yves Blériot, Edouard Untersteller, Benoît Fritz, and Pierre Sinaÿ*[a]

Abstract: The original structure of calditol—that is, an open-chain branched nonitol—has recently been questioned by various research groups and cyclopentane-based structures have been proposed. To unambiguously clear up this confusion, four isomeric cyclopentane candidates **26–29** have been synthesized. Of these, compound **27** was found to be fully identical to the natural product present in *Sulfolobus solfataricus* (A.T.C.C. 49155). The synthesis of **27** uses a samarium-diiodide-induced pinacolization reaction of the ketoaldehyde **15** as the critical step.

Keywords: archaea · calditol · structure elucidation · sulfolobales · total synthesis

Introduction

In addition to prokaryotes and eukaryotes, archae have been introduced, on the basis of 16S ribosomal RNA sequence analyses,[1] as the third group of living organisms. *Sulfolobus* is a genus of sulfur-oxidizing archae characterized by aerobic growth at high temperatures and low pH in the presence of elemental sulfur.[2] Organisms of this genus are usually found in sulfur-containing habitats such as acidic hot springs and mud holes. The known species of *Sulfolobus* include *Sulfolobus acidocaldarius*, originally discovered in Yellowstone National Park (USA) and *Sulfolobus solfataricus*, originally discovered in Pisciarelli (Italy), and these have been widely used in research. Brock et al. suggested that *Sulfolobus* may be important geochemical agents in the production of sulfuric acid from elemental sulfur in high-temperature hydrothermal systems.[2a] The membranes of extreme thermoacidophiles are based on two major types of complex macrocyclic tetraethers in which two polyols are linked together through two isoprenoid chains.[3] In one type, the hydrophilic portions are two glycerol units in which the ether bonds are located at the *sn*-2 and *sn*-3 positions of glycerol.[4] The diglycerol tetraether structure **1** has been termed diglycerocaldarchaeol[5] or GDGT (glycerodialkylglycerol tetraether).[6]



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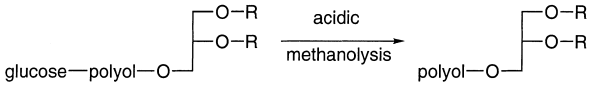
The second type is based on glycerol on one hand and on a polyol on the other, for which the trivial name calditol has been coined.[7] It may thus be termed calditoglycerocaldarchaeol according to Nishihara et al.,[5] or glycerodialkyl calditol tetraether (GDCT). The history of this polyol is very interesting.

The early history of calditol—Langworthy and De Rosa: In 1974, Langworthy et al.[8] studied the structure of various lipids extracted from *Sulfolobus acidocaldarius* (Strain 98-3), an archae originally isolated by Brock et al.[2] from Locomotive Spring in Yellowstone National Park. One component, identified as a glycolipid B, after acidic methanolysis to remove the glucose unit gave a product which was identified as the polyol dialkyl glycerol triether **2** (Scheme 1). Although



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Scheme 1. Isolation of a polyol dialkyl glycerol triether **2** by Langworthy.

the structure of this new polyol was not determined at that time, they suggested that it might be cyclic, and demonstrated that it was connected through an ether linkage to glycerol.

At about the same time, the Italian group of De Rosa studied the structure of the second lipid type from *Caldariella acidophila* (Strain MT-4), isolated from an acid hot spring in

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Supporting information for this article is available on the WWW under http://wiley-vch.de/home/chemistry/ or from the author: ^{1}H and ^{13}C NMR spectra of the synthetic peracetates **26–29** and the natural product.

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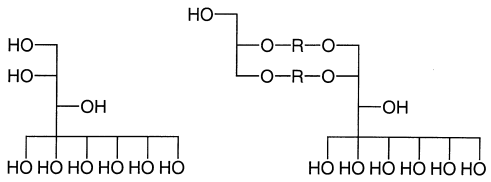
Agnano, Naples.[9] This archaeon should now be renamed[2c] *Sulfolobus solfataricus* (A.T.C.C. 49155). In complete contrast to Langworthy, they proposed that calditol was a unique acyclic branched-chain nonitol **3** containing no ether bond, and the structure of the corresponding calditol glycerol tetraether **4** was proposed by the Italian group. The stereochemistry of the calditol was not determined.



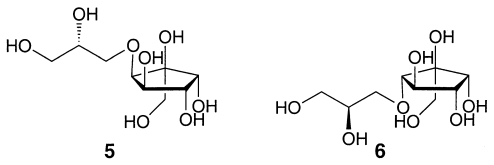
3 **4** R = $C_{40}H_{72\text{-}76}$

An improved purification of this so-called glycerol dialkyl nonitol tetraether (GDNT) has subsequently been reported.[10]

Structural and chemical investigations—doubts about the correctness of the original structure of calditol: In 1990, Jeganathan and Vogel reported the first synthesis of two defined stereoisomers of De Rosa's nonitol.[11] The ^{1}H NMR spectra of the corresponding peracetates were both different from the one reported by De Rosa et al. for the natural calditol peracetate. They concluded at this stage that the natural product was another stereoisomer. In 1995, we reported the chemical synthesis of another defined peracetylated isomer.[12] Comparison of the ^{13}C NMR skeletal chemical shifts of this synthetic compound with those given by De Rosa for the nonacetate of calditol revealed odd discrepancies. From a critical analysis of De Rosa's structural work, we detected various significant anomalies, so that we seriously questioned the correctness of the original structure assigned to this natural product by the Italian group.[12]

In addition to these synthetic efforts, two independent structural investigations of calditol also invalidated the original open-chain structure. Sugaï et al.,[13] in accordance with Langworthy's prediction and on the basis of NMR analysis, proposed the new structure **5** for calditol, which could be isolated in pure form from type two lipids of *Sulfolobus acidocaldarius* (A.T.C.C. 33909). Arigoni's group independently reinvestigated the structure of the calditol

Abstract in French: *La structure d'origine du calditol—à savoir un nonitol branché en chain droite—a été sérieusement remise en question récemment par plusieurs groupes de recherche, et des structures cyclopentaniques ont été proposées. Afin de totalement clarifier cette situation plutôt confuse, quatre candidats isomères structuraux cyclopentaniques* ***26–29*** *ont été synthétisés. Seul l'un d'eux, le composé* ***27****, est totalement identique au produit naturel présent chez Sulfolobus solfataricus (A.T.C.C. 49155). La synthèse de* ***27*** *met en jeu dans l'étape critique une réaction de pinacolisation du cétoaldéhyde* ***15****, initiée par le diiodure de samarium.*



5 **6**

tetraether lipids from *Sulfolobus solfataricus* and also detected several significant differences in comparison with the spectral data reported by De Rosa et al.[14] The interpretation of NMR data of their own lipid sample led to the proposed new structure **6** for calditol. In both structures **5** and **6**, a cyclic polyol is connected to *sn*-1 glycerol by an ether linkage. These structures only differ in the configuration at a single stereocenter.

Results and Discussion

To clarify this rather confusing situation, we launched a programme of chemical synthesis of various stereoisomers. A key derivative in this piece of work was the protected D-glucopyranose derived diol **14**. In this compound, the hexitol derivative is connected through an ether linkage to the *sn*-1 position of di-*O*-benzylated glycerol. The strategy was then to convert the diol into a substituted cyclopentane ring by pinacolization. The synthesis of the key diol **14** is given in Scheme 2. To alkylate the *sn*-1 position of glycerol, we first transformed the *sn*-3-*O*-benzyl glycerol (**7**)[15] into the cyclic sulfate **9**, via the cyclic sulfite **8**. Sharpless demonstrated that cyclic sulfates are easily opened by nucleophilic attack at the less hindered position.[16] Indeed, phenyl 2,3,6-tri-*O*-benzyl-1-thio-β-D-glucopyranose (**10**)[17] was efficiently alkylated[18] with cyclic sulfate **9** to give, after acidic hydrolytic removal of the transient sulfate, the secondary alcohol **11**. Benzylation of this product gave compound **12**, which was converted into the hemiacetal **13** using *N*-bromosuccinimide in moist acetone, and then into the target intermediate **14** (in 84% yield from **12**) after reduction with lithium aluminum hydride. This synthetic pathway is of general interest for the efficient anchoring of a glyceryl appendage onto a secondary alcohol. As shown in Scheme 3, the glucitol derivative **14** was submitted to Swern oxidation[19] to afford the unstable ketoaldehyde **15** which was not isolated. Immediate samarium-diiodide-promoted pinacolization gave an inseparable mixture of two *cis* diols, **16** and **17**, in a 3:1 ratio (78% yield). A similar pinacolization reaction has recently been reported.[20]

We then moved on to the problem of the inversion of configuration at C-1 of **16** and **17**. Our first approach consisted of the transformation of the *cis* diols into the corresponding separable cyclic sulfates and their subsequent opening with a nucleophile by an S_N2 mechanism. Several nucleophiles such as lithium acetate, cesium acetate, ammonium benzoate, and sodium azide were tried in various solvents (DMF, HMPT, acetonitrile), but only elimination products and/or starting material were detected and no opening of the sulfate was observed.

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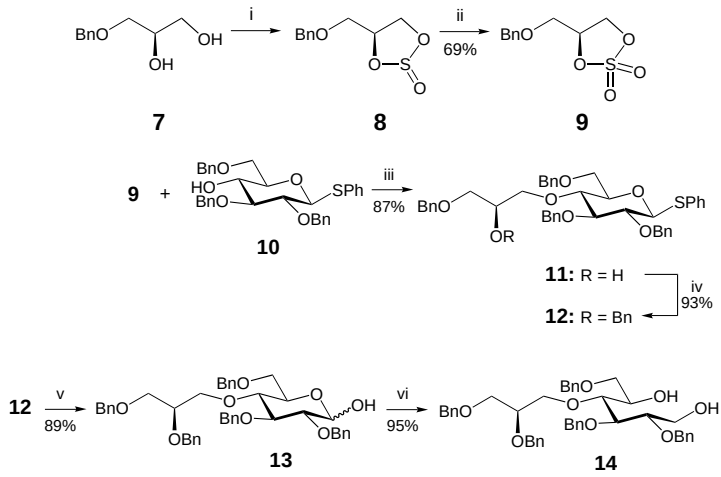
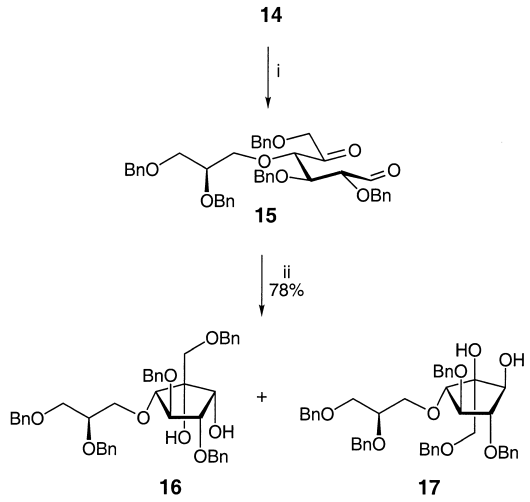


Scheme 2. Synthesis of glucitol derivative **14.** i) $SOCl_2$, Et_3N, CH_2Cl_2; ii) $NaIO_4$, $RuCl_3$, 0 °C, CH_2Cl_2; iii) a) *n*BuLi, THF, HMPA; b) 2 M H_2SO_4; iv) BnBr, NaH, THF; v) NBS, dark, acetone/H_2O; vi) $LiAlH_4$, THF.



Scheme 3. Synthesis of *cis* diols **16** and **17** by pinacol coupling. i) oxalyl chloride, DMSO, Et_3N, CH_2Cl_2, – 65 °C; ii) SmI_2, *t*BuOH, THF, – 40 °C.

A strategy consisting of the oxidation of the alcohol at C-1, followed by the reduction of the resulting ketone to the inverted alcohol was then examined. For this purpose, the mixture of *cis* diols **16** and **17** were conveniently separated as their carbonates **18** and **19** (Scheme 4), which were then deprotected with potassium carbonate in 87 – 92 % yield to afford the pure *cis* diols **16** and **17**, respectively. The structures of the two cyclopentane rings were unambiguously established at this stage by recording NOESY spectra of the corresponding acetonides **20** and **21** (Figure 1, Table 1). The discriminating nuclear Overhauser effects observed were as follows: 1) irradiation of H-6 of acetonide **20** gave an NOE with H-1 and H-4 indicating that H-1 and H-4 are on the same (top) face of the cyclopentane ring, and 2) irradiation of one of the methyl groups of the acetonide **21** gave an NOE with H-4 and H-2 indicating that H-4, H-2 and the hydroxyl groups of the corresponding diol **17** are all on the same (top) face of the cyclopentane ring. Thus compound **16** has the diol moiety located under the cyclopentane ring, whereas compound **17** has the diol unit pointing above the cyclopentane ring.

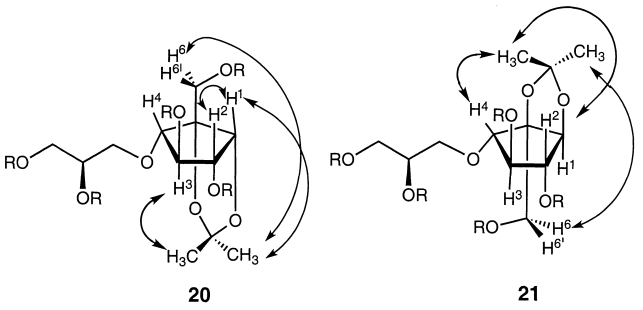
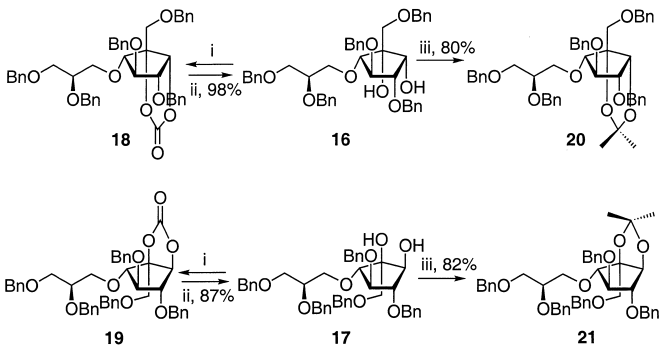


Figure 1. Nuclear Overhauser effects observed for acetonides **20** and **21**. Benzyl groups (R) are not shown for clarity.

Table 1. Nuclear Overhauser effects observed for acetonides **20** and **21**.

Irradiated proton[a]	NOE observed	
	Acetonide **20**	Acetonide **21**
CH_3 (isopropylidene)	H-1, H-6	H-4 (weak), H-6, benzyl
CH_3 (isopropylidene)	H-3	**H-2 (weak), H-4**
H-1	H-2	H-4, H-6
H-2	H-1, benzyl	benzyl
H-3	H-2, H-4, CH_3	H-4, H-6
H-4	**H-1, H-3 (weak)**	–
H-6, H-6′	**H-1, H-4, benzyl**	H-4, CH_3

[a] Key NOEs are indicated in bold.



Scheme 4. Protection of the cis diols **16** and **17** as carbonates **18** and **19** and acetonides **20** and **21**. i) 1,1′-carbonyl diimidazole, CH_2Cl_2; ii) K_2CO_3, CH_3OH; iii) 2,2 dimethoxypropane, acetone, CSA.

The oxidation of the *cis* diols **16** and **17** was problematic. Swern oxidation[19] gave a mixture of elimination products, whereas the Dess – Martin periodinane[21] cleaved the C–C bond formed during the pinacol coupling to afford the glucitol derivative **14** after sodium borohydride reduction. Bromine oxidation of the diol-derived stannylenes, followed by sodium borohydride reduction, also gave poor results. Finally, and as

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observed by Adinolfi et al. in a similar case,[22] oxidation was achieved in a satisfying yield using sodium hypochlorite/2,2,6,6-tetramethylpiperidine-*N*-oxide (TEMPO) methodology.[23] Subsequent sodium borohydride reduction of the resulting ketones **22** and **23**, probably directed by the tertiary alcohol, selectively afforded the expected *trans* diols **24** (Scheme 5) and **25** (Scheme 6). Traces of *cis* diols were easily separated after conversion into their corresponding acetonides **20** and **21**, respectively. Catalytic hydrogenolysis of the *trans* diols **24** and **25** afforded the corresponding heptitols, which were directly peracetylated to give compounds **26** and **27**, respectively. The same sequence was applied to the *cis* diols **16** and **17** to afford the peracetylated compounds **28** and **29**, respectively (Scheme 5 and 6). Comparison of the ^{1}H and ^{13}C NMR spectra of the peracetates **26–29** with an authentic sample of peracetylated calditol, kindly provided to us by A. Sugaï, showed that the peracetylated natural product and compound **27** were identical. Furthermore, the optical rotations of both synthetic **27** and natural calditol heptacetate were very close (natural sample: $[\alpha]_D = -14.6$ ($c = 1.56$ in $CHCl_3$), synthetic compound **27**: $[\alpha]_D = -14$ ($c = 0.27$ in $CHCl_3$)).

Conclusion

This synthetic work unambiguously demonstrates for the first time that the structure of calditol (including its absolute configuration) isolated from the archaeon *Sulfolobus acidocaldarius* (A.T.C.C. 33909) by Sugaï et al.[13] is that shown in Figure 2.

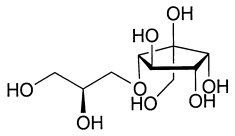
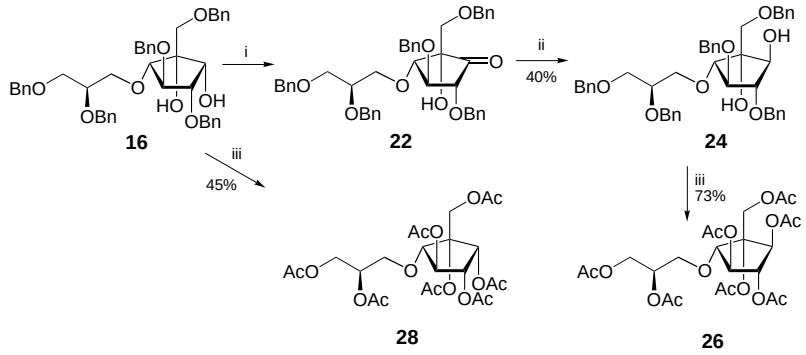
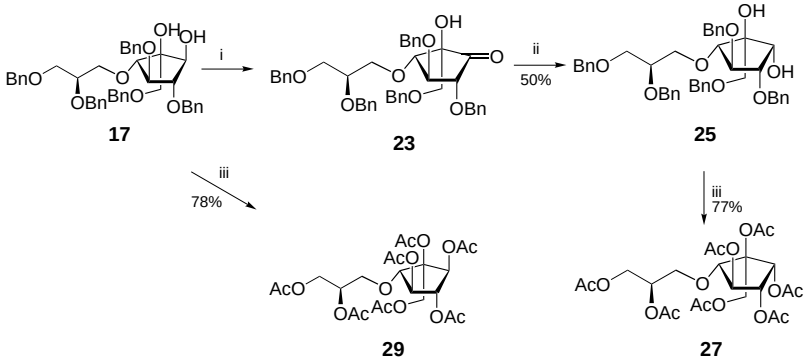


Figure 2. Structure of calditol.

The depicted relative stereostructure is indeed that previously proposed by Gräther and Arigoni, working on a sample isolated from *Sulfolobus solfataricus* (A.T.C.C. 49155), the same archaeon that had been extensively studied by De Rosa et al. and initially named *Caldariella acidophila*. Although no sample of peracetylated calditol has been available to us from De Rosa or Arigoni for direct comparison, we consider it highly probable that the calditol present in various archaea has the same structure. This work also firmly establishes that the cyclic part of calditol is connected through an ether linkage to the *sn*-1 carbon atom of glycerol. It is worth noting that kerufarrides[24] and crasserides,[25] which are natural products of marine origin, contain a cyclopentane-pentol moiety that is also connected through an ether linkage, probably to *sn*-1 position of glycerol.



Scheme 5. Synthesis of peracetylated compounds **26** and **28**. i) TEMPO, NaOCl, CH_2Cl_2, H_2O; ii) $NaBH_4$, CH_3OH; iii) H_2, 10% Pd/C, EtOAc, CH_3OH then Ac_2O, pyridine, DMAP.



Scheme 6. Synthesis of peracetylated compounds **27** and **29.** i) TEMPO, NaOCl, CH_2Cl_2, H_2O; ii) $NaBH_4$, CH_3OH; iii) H_2, 10% Pd/C, EtOAc, CH_3OH then Ac_2O, pyridine, DMAP.

Experimental Section

Cyclic sulfite 8: Diol **7** (9.0 g, 49.4 mmol) and Et_3N (27.7 mL, 198 mmol) were dissolved in anhydrous CH_2Cl_2 (100 mL), and the solution was cooled to 0 °C. A solution of freshly distilled $SOCl_2$ (5.4 mL, 74.1 mmol) in anhydrous CH_2Cl_2 (50 mL) was added dropwise under argon. The reaction mixture was then stirred at RT for 1 h, diluted with cold Et_2O (100 mL), and washed with cold water (2×100 mL) and brine (100 mL). The organic phase was dried over $MgSO_4$ and filtered, and the solvent was removed in vacuo. Purification by column chromatography (EtOAc/cyclohexane 1:6 then 1:4) afforded cyclic sulphite **8** (8.0 g, 78%). This compound was immediately used in the next step.

Cyclic sulfate 9: H_2O (120 mL), $RuCl_3 \cdot 3H_2O$ (1 mg), and then $NaIO_4$ (15 g, 70 mmol) were added to a solution of **8** (8.0 g, 38.5 mmol) in CH_3CN (80 mL) and CH_2Cl_2 (80 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 45 min, diluted with diethyl ether (150 mL), and the aqueous phase was extracted with Et_2O (2×100 mL). Organic extracts were combined, washed with 5% aq $Na_2S_2O_3$ solution (2×100 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure to afford **9** (8.42 g, 89%) as a brown oil. MS (CI, NH_3): *m*/*z* (%): 245 (15) $[M+H]^+$, 262 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{10}H_{12}O_5S$ (244.3): C 49.17, H: 4.95; found: C 49.54, H 4.82.

Alcohol 11: Compound **10** (15 g, 27.7 mmol) and 2,2′-bisquinoline (20 mg) were dissolved in anhydrous THF (150 mL). The solution was cooled to −40 °C, and *n*BuLi (17.4 mL, 10.9 mmol, 1.6 M in hexane) was added dropwise until the solution became orange. Hexamethyl phosphoramide (HMPA; 30 mL) was

added dropwise under stirring followed by a solution of cyclic sulfate **9** (6.7 g, 27.7 mmol) in anhydrous THF (10 mL). The reaction mixture was allowed to warm to RT and acidified to pH 1 with H_2SO_4 (2 M). The reaction mixture was then heated at reflux for 3 h, cooled to RT, neutralized with solid $NaHCO_3$, filtered, diluted with Et_2O (200 mL), and washed with water (200 mL). The aqueous layer was extracted with Et_2O (2 × 200 mL). Organic extracts were combined and dried over $MgSO_4$, and the solvent removed under reduced pressure. Purification by column chromatography (EtOAc/cyclohexane 1:4 then 1:2) afforded alcohol **11** (17 g, 87 %) as a white solid. M.p. 60–61 °C; $[\alpha]_D^{22} = +3.8$ ($c = 0.51$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.64-7.30$ (m, 25H; 5Ph), 4.97 (d, $J = 10.7$ Hz, 2H; 2CHPh), 4.91 (d, $J = 10.7$ Hz, 1H; CHPh), 4.78 (d, $J = 10.2$ Hz, 1H; CHPh), 4.72 (d, $J = 9.7$ Hz, 1H; H-1), 4.69 (d, $J = 12.0$ Hz, 1H; CHPh), 4.63 (d, $J = 12.0$ Hz, 1H; CHPh), 4.57 (s, 2H; CH_2Ph), 3.94 (m, 1H; H-8), 3.90–3.82 (m, 3H; H-6, H-6′, H-7), 3.78 (dd, $J = 3.8$ Hz, 10.2 Hz, 1H; H-7′), 3.72 (app t, $J = 8.9$ Hz, 1H; H-3), 4.02 (app t, $J = 9.3$ Hz, 1H; H-4), 3.57 (app t, $J = 9.5$ Hz, 1H; H-2), 3.51 (m, 1H; H-5), 3.49 (app d, $J = 5.3$ Hz, 2H; H-9, H-9′), 3.05 (d, $J = 4.3$ Hz, 1H; OH); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta =$ 137.99, 137.89, 137.84, 137.83, 133.58 (5C_{ipso}), 131.86–127.41 (5Ph), 87.32 (CH-1), 86.14 (CH-3), 80.69 (CH-2), 78.92 (CH-5), 78.37 (CH-4), 75.67 (CH_2Ph), 75.26 (CH_2Ph), 74.21 (CH_2Ph), 73.36 (CH_2Ph), 73.29 (CH_2Ph), 70.92 (CH_2-9), 69.93 (CH-8), 68.84 (CH_2-6); MS (CI, NH_3): m/z (%): 724 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{43}H_{46}O_7S$ (706): C 73.06, H 6.56; found: C 73.05, H 6.65.

Thiophenyl derivative 12: A solution of alcohol **11** (9 g, 12.7 mmol) in anhydrous THF (80 mL) was added dropwise to a cooled suspension of BnBr (1.8 mL, 15.1 mmol) and NaH (624 mg, 15.6 mmol, 60 % dispersion in mineral oil) in anhydrous THF (30 mL). The solution was stirred at RT for 3 h, cooled to 0 °C, and quenched with CH_3OH (100 mL). The solvent was removed under reduced pressure, and the residue dissolved in Et_2O (200 mL), and washed with water (3 × 200 mL). The organic layer was dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by column chromatography (EtOAc/cyclohexane 1:8 then 1:7) afforded **12** (9.43 g, 93 %) as a yellow oil. $[\alpha]_D^{22} = -2.1$ ($c = 0.93$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.82-7.30$ (m, 30H; 6Ph), 5.03 (d, $J =$ 10.7 Hz, 1H; CHPh), 4.99 (s, 2H; CH_2Ph), 4.81 (d, $J = 10.7$ Hz, 1H; CHPh), 4.73 (d, $J = 9.1$ Hz, 1H; H-1), 4.63 (s, 2H; CH_2Ph), 4.56 (d, $J =$ 12.0 Hz, 1H; CHPh), 4.51 (d, $J = 12.0$ Hz, 1H; CHPh), 4.43 (s, 2H; CH_2Ph), 4.16 (dd, $J = 5.2$, 9.8 Hz, 1H; H-7), 3.91 (dd, $J = 4.6$, 9.8 Hz, 1H; H-7′), 3.82–3.76 (m, 3H; H-6, H-6′, H-8), 3.70–3.60 (m, 5H; H-2, H-3, H-4, H-9, H-9′), 3.31 (m, 1H; H-5); ^{13}C NMR (C_6D_6, 100 MHz): $\delta =$ 139.95, 139.93, 139.66, 139.55, 139.45, 135.49 (6C_{ipso}), 132.65, 129.61, 129.04–127.90 (6Ph), 88.32 (CH-1), 87.40 (CH-2), 81.69 (CH-4), 79.93 (CH-5), 79.08 (CH-3), 78.57 (CH-8), 75.93 (CH_2Ph), 75.90 (CH_2Ph), 73.93 (CH_2Ph), 73.91 (CH_2Ph), 73.37 (CH_2-7), 72.69 (CH_2Ph), 71.08 (CH_2-9), 69.74 (CH_2-6); MS (CI, NH_3): m/z (%): 724 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{50}H_{52}O_7S$ (797.03): C 75.34, H 6.57; found: C 75.31, H 6.60.

Alcohol 13: Compound **12** (5.9 g, 7.4 mmol) was dissolved in acetone/water (290 mL, 95 % v/v). The reaction mixture was cooled to 0 °C and NBS (6.6 g, 36.9 mmol, recrystallized from water) was added in one portion in the dark. After 3 min of vigorous stirring, sat. aq Na_2CO_3 solution (200 mL) was added, and a white precipitate formed. The acetone was evaporated, and the remaining aqueous white suspension was extracted with CH_2Cl_2/cyclohexane (2 × 200 mL, 50 % v/v). Organic extracts were combined and dried over $MgSO_4$, and the solvent removed under reduced pressure. The resulting solid was recrystallized from cyclohexane to afford **13** (4.6 g, 89 %) as a white solid. Data for the major α anomer: ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.37-7.30$ (m, 25H; 5Ph), 5.23 (app t, $J = 3.0$ Hz, 1H; H-1), 4.92 (d, $J = 10.8$ Hz, 1H; CHPh), 4.84 (d, $J = 10.8$ Hz, 1H; CHPh), 4.79 (d, $J = 11.8$ Hz, 1H; CHPh), 4.69 (d, $J = 11.8$ Hz, 1H; CHPh), 4.63 (d, $J =$ 12.1 Hz, 1H; CHPh), 4.59 (d, $J = 12.1$ Hz, 1H; CHPh), 4.55 (d, $J = 12.2$ Hz, 1H; CHPh), 4.51 (s, 2H; CH_2Ph), 4.49 (d, $J = 12.2$ Hz, 1H; CHPh), 4.01 (m, 2H; H-5, H-7), 3.90 (t, $J = 9.2$ Hz, 1H; H-3), 3.72–3.65 (m, 4H; H-6, H-6′, H-7′, H-8), 3.56 (dd, $J = 3.0$ Hz, $J = 9.2$ Hz, 1H; H-2), 3.54 (m, 2H; H-9, H-9′), 3.48 (t, $J = 9.2$ Hz, 1H; H-4), 2.87 (d, $J = 2.2$ Hz, 1H; OH); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 138.63$, 138.60, 137.94, 137.90, 137.81 (5C_{ipso}), 128.46–127.51 (5Ph), 91.26 (CH-1), 81.46 (CH-3), 79.77 (CH-2), 78.16 (CH-4), 77.45 (CH-8), 75.47 (CH_2Ph), 73.35 (CH_2Ph), 73.31 (CH_2Ph), 73.21 (CH_2Ph), 72.53 (CH_2-7), 72.04 (CH_2Ph), 70.26 (CH-5), 70.31 (CH_2-9), 68.64 (CH_2-6); MS (CI, NH_3): m/z (%): 722 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{44}H_{48}O_8$ (704.86): C 74.97, H 6.86; found: C 74.89, H 6.80.

D-Glucitol derivative 14: Alcohol **13** (5.1 g, 7.3 mmol) was dissolved in anhydrous THF (80 mL) under argon, the solution was cooled to 0 °C, and $LiAlH_4$ (0.55 g, 14.6 mmol) was added portionwise. The reaction mixture was allowed to warm to RT over 2 h. Ethyl acetate (80 mL) was added, and the solution acidified to pH 1 with 1 M HCl. The aqueous phase was extracted with EtOAc (3 × 80 mL), the organic extracts were combined, dried over $MgSO_4$, and concentrated. Purification by column chromatography (EtOAc/cyclohexane 1:5 then 1:2) afforded diol **14** (4.9 g, 95 %) as a colorless oil. $[\alpha]_D^{22} = +12.5$ ($c = 0.56$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.37-7.34$ (m, 25H; 5Ph), 4.64–4.53 (m, 10H; 5CH_2Ph), 4.02 (m, 1H; H-5), 3.96 (dd, $J = 4.4$, 5.9 Hz, 1H; H-3), 3.82 (m, 2H; H-1, H-2), 3.77 (m, 5H; H-1′, H-4, H-7, H-7′, H-8), 3.69 (dd, $J = 4.0$, 9.7 Hz, 1H; H-6), 3.62 (dd, $J = 5.3$, 9.7 Hz, 1H; H-6′), 3.61 (m, 2H; H-9, H-9′), 3.35 (d, $J = 6.1$ Hz, 1H; OH-5), 2.37 (app t, 1H; OH-1); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 138.18$, 138.14, 138.02, 138.00, 137.91 (5C_{ipso}), 128.35–127.55 (5Ph), 79.61 (CH-4), 79.38 (CH-2), 79.30 (CH-3), 77.27 (CH-8), 74.50 (CH_2Ph), 73.31 (CH_2Ph), 73.26 (CH_2Ph), 72.69 (CH_2Ph), 72.06 (CH_2Ph), 71.63 (CH_2-7), 71.04 (CH_2-6), 70.32 (CH-5), 69.61 (CH_2-9), 61.62 (CH_2-1); MS (CI, NH_3): m/z (%): 724 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{44}H_{50}O_8$ (706): C 74.87, H 6.99; found: C 74.77, H 7.05.

***Cis* diols 16 and 17**: Oxalyl chloride (2.3 mL, 26.7 mmol) was dissolved in anhydrous THF (180 mL) under argon. The solution was cooled to −78 °C, anhydrous DMSO (2.3 mL, 32.0 mmol) was added dropwise, and the solution stirred for 10 min at −60 °C. A solution of compound **14** (3.8 g, 5.3 mmol) in anhydrous THF (60 mL) was then added slowly, and the resulting solution stirred for 10 min at −60 °C. The reaction mixture was allowed to warm to −45 °C and stirred for 45 min. Anhydrous Et_3N (7.5 mL, 53.4 mmol) was then added, the solution was stirred for 10 min and allowed to warm up to RT for 1 h. The resulting white suspension was then transferred by cannula under argon to a 1 M solution of SmI_2 in THF (60 mL) containing degassed *tert*-butanol (1 mL) at −78 °C. The reaction mixture was stirred for 4 h at −40 °C and then allowed to warm up to RT. A semi-saturated aq. NH_4Cl solution (80 mL) was added to the reaction mixture, and the aqueous phase was extracted with EtOAc (3 × 80 mL). Organic extracts were combined and dried over $MgSO_4$, and the solvent removed under reduced pressure. Purification by column chromatography (EtOAc/cyclohexane 1:4 then 1:1) afforded an inseparable 3:1 mixture of the *cis* diols **16** and **17** (2.9 g, 78 %) as a yellow oil.

Carbonates 18 and 19: Diols **16** and **17** (2.4 g, 3.4 mmol) and 1,1′-carbonyl diimidazole (2.2 g, 13.75 mmol) were dissolved in anhydrous CH_2Cl_2 (150 mL) under argon. The solution was heated at reflux for 16 h, cooled to RT, and washed with water (2 × 100 mL). The organic phase was dried over $MgSO_4$, and the solvent removed under reduced pressure. Purification by column chromatography (EtOAc/cyclohexane 1:7 then 1:5) afforded carbonate **19** (490 mg, 19 %) as a colourless oil. $[\alpha]_D^{22} = -10.0$ ($c = 0.55$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.41-7.20$ (m, 25H; 5Ph), 4.82 (dd, $J = 1.8$, 3.5 Hz, 1H; H-1), 4.76 (d, $J = 12.0$ Hz, 1H; CHPh), 4.72 (d, $J =$ 12.0 Hz, 1H; CHPh), 4.59 (m, 3H; 3CHPh), 4.41 (m, 3H; 3CHPh), 4.26 (app d, $J = 12.1$ Hz, 2H; CH_2Ph), 3.89 (m, 2H; H-2, H-3), 3.82 (dd, $J = 4.4$, 5.7 Hz, 1H; H-4), 3.75 (m, 2H; H-7, H-7′), 3.72 (d, $J = 11.2$ Hz, 1H; H-6), 3.71 (m, 1H; H-8), 3.58 (m, 2H; H-9, H-9′), 3.51 (d, $J = 11.2$ Hz, 1H; H-6′); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 153.87$ (C=O), 138.25, 137.99, 137.67, 137.18, 136.82 (5C_{ipso}), 128.65–127.51 (5Ph), 87.57 (C-5), 86.82 (CH-4), 83.85 (CH-3), 82.56 (CH-2), 82.18 (CH-1), 76.82 (CH-8), 73.64, 73.41, 73.03, 72.26, 72.11 (5CH_2Ph), 71.84 (CH_2-7), 69.37 (CH_2-9), 68.11 (CH_2-6); MS (CI, NH_3): m/z (%): 748 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{45}H_{46}O_9$ (730.8): C 73.95, H 6.34; found: C 73.78, H 6.52.

Further elution afforded carbonate **18** (1.7 g, 67 %) as a colourless oil. $[\alpha]_D^{22} = +30.1$ ($c = 1.02$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.44-7.19$ (m, 25H; 5Ph), 4.76 (d, $J = 11.7$ Hz, 1H; CHPh), 4.68 (d, $J = 12.0$ Hz, 1H; CHPh), 4.64 (d, $J = 12.0$ Hz, 1H; CHPh), 4.63 (d, $J = 11.7$ Hz, 1H; CHPh), 4.59 (d, $J = 11.7$ Hz, 1H; CHPh), 4.51 (d, $J = 5.4$ Hz, 1H; H-1), 4.45 (s, 2H; CH_2Ph), 4.35 (app t, $J = 8.7$ Hz, 1H; H-3), 4.30 (d, $J = 11.7$ Hz, 1H; CHPh), 4.26 (d, $J = 12.0$ Hz, 1H; CHPh), 4.15 (d, $J = 12.0$ Hz, 1H; CHPh), 3.94 (m, 2H; H-7, H-7′), 3.83 (m, 1H; H-8), 3.73 (d, $J = 8.6$ Hz, 1H; H-4), 3.67 (app d, $J = 4.6$ Hz, 2H; H-9, H-9′), 3.61 (dd, $J = 5.4$, 8.7 Hz, 1H; H-2), 3.36 (d, $J = 10.1$ Hz, 1H; H-6), 3.38 (d, $J = 10.1$ Hz, 1H; H-6′); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 154.52$ (C=O), 139.88, 139.51, 139.43, 138.41, 138.07 (5C_{ipso}), 129.27–128.12 (5Ph), 85.96 (C-5), 85.39 (C-3), 81.55 (CH-4), 79.91 (CH-2), 78.36 (CH-8), 77.52 (CH-1), 74.12 (CH_2Ph), 74.01 (CH_2Ph), 73.93 (CH_2Ph), 72.76 (CH_2Ph), 72.64 (CH_2-7), 72.59 (CH_2Ph), 70.58 (CH_2-9),

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70.34 (CH_2-6); MS (CI, NH_3): *m*/*z* (%): 748 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{45}H_{46}O_9$ (730.8): C 73.95, H 6.34; found: C 73.83, H 6.50.

Acetonide 20: Camphorsulphonic acid (3 mg) and 2,2-dimethoxypropane (2 mL, 16 mmol) were added to a solution of diol **16** (207 mg, 0.29 mmol) in acetone (18 mL) under argon. The solution was stirred at RT for 17 h, and the reaction mixture then neutralized with Et_3N. The solvent was removed in vacuo and purification by column chromatography (EtOAc/cyclohexane 1:5) afforded acetonide **20** (175 mg, 80%) as a colorless oil. $[\alpha]_D^{20} = -10.8$ ($c = 1.0$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.50-7.19$ (m, 25H; 5Ph), 5.03 (d, $J = 12.0$ Hz, 2H; CH_2Ph), 4.81 (m, 3H; 3CHPh), 4.71 (dd, $J = 7.5$, 8.9 Hz, 1H; H-3), 4.63 (d, $J = 4.1$ Hz, 1H; H-1), 4.62 (d, $J = 11.9$ Hz, 1H; CHPh), 4.48 (s, 2H; CH_2Ph), 4.33 (app q, 2H; CH_2Ph), 4.15 (dd, $J =$ 4.8, 9.7 Hz, 1H; H-7), 4.04 (app q, $J = 4.8$ Hz, 1H; H-8), 3.97 (dd, $J = 4.1$, 8.9 Hz, 1H; H-2), 3.94 (d, $J = 7.3$ Hz, 1H; H-4), 3.84 (dd, $J = 4.8$, 9.7 Hz, 1H; H-7′), 3.81 (dd, $J = 4.5$, 10.1 Hz, 1H; H-9),3.73 (dd, $J = 4.5$, 10.1 Hz, 1H; H-9′), 3.53 (d, $J = 9.5$ Hz, 1H; H-6), 3.49 (d, $J = 9.5$ Hz, 1H; H-6′), 1.69, 1.44 (2s, 6H; $2CH_3$); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 138.80$, 139.59, 139.67, 140.21, 140.22, (5C_{ipso}), 129.17–127.90 (5Ph), 112.74 ($C(CH_3)_2$), 87.20 (CH-3), 85.24 (C-5), 83.39 (CH-4), 80.76 (CH-1), 80.21 (CH-2), 78.65 (CH-8), 74.22 (CH_2-6), 74.10 (CH_2Ph), 73.88 (CH_2Ph), 73.59 (CH_2Ph), 72.79 (CH_2Ph), 72.32 (CH_2Ph), 71.79 (CH_2-7), 71.67 (CH_2-9), 27.55, 27.59 ($2CH_3$); MS (CI, NH_3): *m*/*z* (%): 762 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{47}H_{52}O_8$ (744.9): C 75.78, H 7.03; found: C 75.71, H 7.16.

Acetonide 21: This compound was synthesized from **17** by the procedure described for **20** and was obtained as a colorless oil. $[\alpha]_D^{22} = +6.2$ ($c = 0.7$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.45-7.19$ (m, 25H; 5Ph), 4.96 (d, $J = 12.0$ Hz, 1H; CHPh), 4.94 (d, $J = 2.5$ Hz, 1H; H-1), 4.92 (d, $J = 12.0$ Hz, 1H; CHPh), 4.83 (d, $J = 12.0$ Hz, 1H; CHPh), 4.73 (d, $J = 12.0$ Hz, 1H; CHPh), 4.68 (d, $J = 12.0$ Hz, 1H; CHPh), 4.62 (d, $J = 12.0$ Hz, 1H; CHPh), 4.49 (dd, $J = 7.1$, 9.5 Hz, 1H; H-3), 4.50–4.41 (m, 4H; $2CH_2$Ph), 4.35 (dd, $J = 2.5$, 7.1 Hz, 1H; H-2), 4.32 (d, $J = 9.5$ Hz, 1H; H-4), 4.19 (dd, $J = 4.3$, 10.3 Hz, 1H; H-7), 4.00 (dd, $J = 5.1$, 10.3 Hz, 1H; H-7′), 3.97 (d, $J = 10.3$ Hz, 1H; H-6), 3.91 (m, 1H; H-8), 3.90 (d, $J = 10.3$ Hz, 1H; H-6′), 3.71 (m, $J =$ 5.3 Hz, 2H; H-9, H-9′), 1.57, 1.52 (2s, 6H; $2CH_3$); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 140.01$, 139.84, 139.55, 139.35, 139.11 (5C_{ipso}), 129.02–127.84 (5Ph), 113.68 ($C(CH_3)_2$), 90.87 (CH-4), 88.39 (C-5), 87.46 (CH-4), 86.15 (CH-2), 84.57 (CH-1), 78.46 (CH-8), 74.15 (CH_2Ph), 73.90 (CH_2Ph), 73.37 (CH_2Ph), 72.71 (CH_2Ph), 72.26 (CH_2Ph), 72.00 (CH_2-7), 71.03 (CH_2-9), 70.72 (CH_2-6), 29.16, 27.43 ($2CH_3$); MS (CI, NH_3): *m*/*z* (%): 762 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{47}H_{52}O_8$ (744.9): C 75.78, H 7.03; found: C 75.67, H 7.15.

***Cis* diol 16**: Carbonate **18** (545 mg, 0.75 mmol) was dissolved in CH_3OH (50 mL). Potassium carbonate (309 mg, 2.24 mmol) was added under argon, and the reaction mixture stirred at RT. After 20 h, the reaction mixture was stirred with ion exchange resin IR-120 (2 g) for 30 min and then filtered. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (EtOAc/cyclohexane 1:2) to afford the *cis* diol **16** (505 mg, 98% yield) as a colorless oil. $[\alpha]_D^{22} = +7.4$ ($c = 0.51$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.43-7.19$ (m, 25H; 5Ph), 4.69 (d, $J = 11.8$ Hz, 1H; CHPh), 4.67 (s, 2H; CH_2Ph), 4.66 (d, $J =$ 11.0 Hz, 1H; CHPh), 4.62 (d, $J = 11.0$ Hz, 1H; CHPh), 4.52 (d, $J = 11.8$ Hz, 1H; CHPh), 4.44 (s, 2H; CH_2Ph), 4.43 (m, 1H; H-3), 4.42 (d, $J = 12.0$ Hz, 1H; CHPh), 4.35 (d, $J = 12.0$ Hz, 1H; CHPh), 4.32 (dd, $J = 6.1$, 8.1 Hz, 1H; H-1), 4.11 (d, $J = 6.0$ Hz, 1H; H-4), 4.02 (dd, $J = 4.5$, 10.2 Hz, 1H; H-7), 3.94 (m, 2H; H-2, H-7′), 3.81 (m, 1H; H-8), 3.66 (app d, $J = 5.2$ Hz, 2H; H-9, H-9′), 3.58 (d, $J = 9.4$ Hz, 1H; H-6), 3.53 (d, $J = 9.4$ Hz, 1H; H-6′), 3.52 (s, 1H; OH-5), 3.19 (d, $J = 8.1$ Hz, 1H; OH-1); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 139.80$, 139.54, 139.41, 139.24, 139.13, (5C_{ipso}), 129.08–128.14 (5Ph), 88.47 (CH-3), 83.76 (CH-4), 82.22 (CH-2), 78.12 (C-5), 78.11 (CH-8), 74.01 (CH_2Ph), 73.93 (CH_2Ph), 73.02 (CH_2Ph), 72.81 (CH_2Ph), 72.66 (CH_2Ph), 72.60 (CH_2-6), 71.76 (CH_2-7), 71.53 (CH-1), 70.88 (CH_2-9); MS (CI, NH_3): *m*/*z* (%): 722 (100) $[M+NH_4]^+$; elemental analysis calcd (%) for $C_{44}H_{48}O_8$ (704.8): C 74.97, H 6.86; found: C 74.85, H 7.00.

***Cis* diol 17**: This compound was synthesized from carbonate **19** by the procedure described for diol **16** and was obtained as a colorless oil. $[\alpha]_D^{22} = +9.0$ ($c = 0.1$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.48-7.17$ (m, 25H; 5Ph), 4.91 (d, $J = 11.9$ Hz, 1H; CHPh), 4.76 (s, 2H; CH_2Ph), 4.69 (d, $J = 11.9$ Hz, 1H; CHPh), 4.64 (d, $J = 2.1$ Hz, 2H; CH_2Ph), 4.44 (s, 2H; CH_2Ph), 4.30 (d, $J = 11.9$ Hz, 2H; CH_2Ph), 4.27 (m, 1H; H-2), 4.26 (app t, $J = 4.5$ Hz, 1H; H-1), 4.15 (d, $J = 5.4$ Hz, 1H; H-4), 4.11 (app t, $J = 5.4$ Hz, 1H; H-3), 3.93 (dd, $J = 4.4$, 10.4 Hz, 1H; H-7), 3.89 (dd, $J = 5.0$, 10.4 Hz, 1H; H-7′), 3.88 (d, $J = 9.5$ Hz, 1H; H-6), 3.80 (m, 1H; H-8), 3.71 (d, $J =$ 9.5 Hz, 1H; H-6′), 3.65 (app d, $J = 5.4$ Hz, 2H; H-9, H-9′), 3.40 (s, 1H; OH-5), 2.90 (d, $J = 4.4$ Hz, 1H; OH-1); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 139.87$, 139.61, 139.58, 139.47, 138.84, (5C_{ipso}), 129.15–128.10, (5Ph), 88.28 (CH-4), 87.94 (CH-2), 84.40 (CH-3), 79.11 (C-5), 78.36 (CH-8), 77.58 (CH-1), 74.18 (CH_2Ph), 73.92 (CH_2Ph), 72.70 (CH_2-6, CH_2Ph), 72.60 (CH_2Ph), 72.53 (CH_2Ph), 71.56 (CH_2-7), 70.97 (CH_2-9); MS (CI, NH_3): *m*/*z* (%): 722 (100) $[M+NH_4]^+$, 290 (15); elemental analysis calcd (%) for $C_{44}H_{48}O_8$ (704.8): C 74.97, H 6.86; found: C 74.91, H 6.98.

***Trans* diol 24**: Diol **16** (36 mg, 0.05 mmol) was dissolved in CH_2Cl_2 (1 mL) and potassium bromide (4 mg, 0.034 mmol), TEMPO (40 mg, 0.25 mmol), and water (50 μL) were added. The solution was cooled to 0 °C and a large excess of NaOCl (0.2 mL, technical solution diluted with water and adjusted to pH 9 just before use) was added dropwise. Some more NaOCl and TEMPO were added to complete the reaction. After 50 min, the reaction mixture was diluted with CH_2Cl_2 (5 mL) and washed with saturated aq. $Na_2S_2O_3$ solution (5 mL) and water (5 mL). The organic phase was dried over $MgSO_4$, and the solvent removed under reduced pressure to afford the crude ketone **22** as an orange oil. The ketone **22** was then dissolved in CH_3OH (5 mL), the solution was cooled to 0 °C and $NaBH_4$ (6 mg, 0.15 mmol) was added. After 1 h, the solvent was removed under reduced pressure. Purification by column chromatography (EtOAc/cyclohexane 1:2) afforded the *trans* diol **24** (15 mg, 40%) as a colorless oil.

*Data for cyclopentanone **22***: ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.43-7.17$ (m, 25H; 5Ph), 5.18 (d, $J = 11.8$ Hz, 1H; CHPh), 4.83 (d, $J = 11.8$ Hz, 1H; CHPh), 4.75 (app d, $J = 11.9$ Hz, 2H; CH_2Ph), 4.51 (app d, $J = 3.8$ Hz, 2H; CH_2Ph), 4.42 (m, 1H; H-4), 4.41 (m, 3H; 3CHPh), 4.38 (d, $J = 6.5$ Hz, 1H; H-2), 4.36 (d, $J = 11.9$ Hz, 1H; CHPh), 4.32 (dd, $J = 0.8$, 6.5 Hz, 1H; H-3), 3.88 (dd, $J = 4.5$, 10.0 Hz, 1H; H-7), 3.83 (d, $J = 8.9$ Hz, 1H; H-6), 3.82 (dd, $J = 4.5$, 5.6 Hz, 1H; H-7′), 3.72 (s, 1H; OH), 3.65 (m, 1H; H-8), 3.61–3.55 (m, 3H; H-9, H-9′, H-6′); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 209.77$ (C=O), 139.42, 139.31, 139.16, 138.74, 138.50, (5C_{ipso}), 129.13–128.25 (5Ph), 85.06, 83.82, 80.78, 77.76 (CH-2, CH-3, CH-4, CH-8), 77.64 (C-5), 74.10, 73.98, 73.44, 73.40, 72.65, 72.42, 71.98, 70.25 (5CH_2Ph, CH_2-6, CH_2-7, CH_2-9); MS (CI, NH_3): *m*/*z* (%): 720 (8) $[M+NH_4^+]$, 290 (100); HRMS (CI+, NH_3): *m*/*z* (%): calcd for $C_{44}H_{49}O_8$ $[M+NH_4]^+$: 720.3536; found: 720.3542.

*Data for trans diol **24***: $[\alpha]_D^{20} = +5.2$ ($c = 0.3$ in $CHCl_3$); ^{1}H NMR (C_6D_6, 400 MHz): $\delta = 7.49-7.18$ (m, 25H; 5Ph), 4.96 (d, $J = 12.0$ Hz, 1H; CHPh), 4.87 (d, $J = 11.9$ Hz, 1H; CHPh), 4.79 (d, $J = 11.9$ Hz, 1H; CHPh), 4.88 (d, $J = 12.0$ Hz, 1H; CHPh), 4.57 (s, 2H; CH_2Ph), 4.46 (app t, $J = 5.8$ Hz, 1H; H-1), 4.43 (s, 2H; CH_2Ph), 4.39 (d, $J = 12.0$ Hz, 1H; CHPh), 4.32 (app t, $J =$ 7.0 Hz, 1H; H-3), 4.29 (d, $J = 12.0$ Hz, 1H; CHPh), 4.07 (m, 2H; H-2, H-4), 3.93 (dd, $J = 4.5$, 10.2 Hz, 1H; H-7), 3.85 (dd, $J = 4.3$, 10.2 Hz, 1H; H-7′), 3.72 (s, 2H; H-6, H-6′), 3.70 (m, 1H; H-8), 3.63 (m, 2H; H-9, H-9′), 3.57 (s, 1H; OH-5), 2.98 (d, $J = 5.6$ Hz, 1H; OH-1); ^{13}C NMR (C_6D_6, 100 MHz): $\delta = 139.74$, 139.72, 139.61, 139.32, 138.73 (5C_{ipso}), 129.15–128.07 (5Ph), 87.18 (CH-2), 86.01 (CH-3), 83.43 (CH-4), 83.09 (CH-1), 78.10 (C-5), 77.94 (CH-8), 74.25 (CH_2Ph), 73.96 (CH_2Ph), 73.67 (CH_2-6), 73.07 (CH_2Ph), 72.62 (CH_2Ph), 72.60 (CH_2Ph), 71.57 (CH_2-7), 70.57 (CH_2-9); MS (CI, NH_3): *m*/*z* (%): 722 (100) $[M+NH_4]^+$, 290 (80); HRMS (CI+, NH_3): *m*/*z* calcd for $C_{44}H_{49}O_8$ $[M+H]^+$: 705.3427; found: 705.3434.

***Trans* diol 25**: This compound was obtained from diol **14** by the procedure described for diol **24** and was obtained as a colorless oil. $[\alpha]_D^{22} = +10.2$ ($c =$ 0.56 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 7.40-7.30$ (m, 25H; 5Ph), 4.72–4.53 (m, 10H; 5CH_2Ph), 4.17 (t, $J = 5.1$ Hz, 1H; H-2), 4.04 (m, 2H; H-1, H-3), 3.93 (d, $J = 9.7$ Hz, 1H; H-6), 3.78–3.71 (m, 5H; H-4, H-6′, H-7, H-7′, H-8), 3.59 (m, 2H; H-9, H-9′), 3.03 (s, 1H; OH-5), 2.87 (d, $J = 5.5$ Hz, 1H; OH-1); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 138.50$, 138.17, 138.03, 137.75, 137.73 (5C_{ipso}), 128.45–127.49 (5Ph), 88.80 (C-4), 87.74 (C-3), 80.21 (C-5), 76.97 (C-8), 75.73 (CH-1), 73.67 (CH_2Ph), 73.32 (CH_2Ph), 72.23 (CH_2Ph), 72.09 (CH_2Ph), 71.97 (CH_2Ph), 70.83 (CH_2-7), 70.33 (CH_2-6), 70.05 (CH_2-9); MS (CI, NH_3): *m*/*z* (%): 722 (100) $[M+NH_4]^+$; HRMS (CI+, NH_3): *m*/*z* calcd for $C_{44}H_{52}NO_8$ $[M+NH_4]^+$: 722.3693; found: 722.3681.

Calditol isomer heptacetate 26: The diol **24** (7 mg, 0.01 mmol) was dissolved in CH_3OH (5 mL). Hydrogenolysis with 10% Pd/C was performed for 17 h by which time TLC (EtOAc/CH_3OH/H_2O 3:3:1) showed one non-UV active spot. The solution was filtered through Celite

and eluted with CH_3OH, and the solvent removed under reduced pressure. The residue was then dissolved in anhydrous pyridine (1 mL) under argon, and the solution cooled to 0 °C. Ac_2O (0.5 mL) and DMAP (1 mg) were added. The reaction mixture was allowed to warm to RT and was stirred for 4 h. The solvent was then removed under reduced pressure and co-evaporated with toluene (3 × 5 mL). Purification by flash chromatography (EtOAc/cyclohexane 1:1 then EtOAc) afforded the heptacetate **26** (4 mg, 73 %) as a colorless oil. $[\alpha]_D^{20} = +15.2$ ($c = 0.3$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 5.80$ (m, 1H; H-1), 5.26 (m, 2H; H-2, H-3), 5.17 (m, 1H; H-8), 4.60 (d, $J = 12.0$ Hz, 1H; H-6), 4.49 (d, $J = 12.0$ Hz, 1H; H-6′), 4.33 (dd, $J = 4.1$, 11.9 Hz, 1H; H-7), 4.15 (dd, $J = 6.4$, 11.9 Hz, 1H; H-7′), 4.09 (dd, $J = 1.7$, 2.7 Hz, 1H; H-4) 3.90 (dd, $J = 5.0$, 10.3 Hz, 1H; H-9), 3.64 (dd, $J = 4.7$, 10.7 Hz, 1H; H-9′), 2.15 (s, 3H; OAc), 2.14 (s, 3H; OAc), 2.13 (s, 3H; OAc), 2.12 (s, 3H; OAc), 2.11 (2s, 6H; 2OAc), 2.10 (s, 3H; OAc); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 170.61$, 170.42, 170.19, 169.96, 169.74, 169.59, 169.47 (7C=O), 83.02 (C-5), 81.72 (CH-4), 77.79 (CH-3), 76.54 (CH-1), 69.91 (CH-2), 69.05 (CH_2-9), 62.37 (CH_2-7), 61.81 (CH_2-6), 21.24, 20.95, 20.84, 20.83, 20.77, 20.73, 20.71 (7CH_3); MS (CI, NH_3): m/z (%): 722 (100) $[M+NH_4]^+$; HRMS (CI+, CH_4): m/z calcd for $C_{23}H_{33}O_{15}$ $[M+H]^+$: 549.1819; found: 549.1815.

Calditol heptacetate 27: This compound was obtained from diol **17** by the procedure described for compound **26** and was obtained as a colorless oil. $[\alpha]_D^{20} = -14.4$ ($c = 0.27$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 5.48$ (dd, $J = 1.8$, 4.6 Hz, 1H; H-1), 5.45 (dd, $J = 4.6$, 8.4 Hz, 1H; H-3), 5.37 (dd, $J = 4.6$, 8.4 Hz, 1H; H-2), 5.16 (m, 1H; H-8), 4.93 (d, $J = 12.8$ Hz, 1H; H-6), 4.53 (d, $J = 12.8$ Hz, 1H; H-6′), 4.36 (dd, $J = 4.0$, 11.8 Hz, 1H; H-7), 4.22–4.18 (m, 2H; H-4, H-7′), 3.81 (m, 2H; H-9, H-9′), 2.17 (s, 3H; OAc), 2.14 (s, 3H; OAc), 2.13 (s, 3H; OAc), 2.12 (s, 3H; OAc), 2.11 (s, 3H; OAc), 2.06 (s, 3H; OAc), 2.05 (s, 3H; OAc); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 170.66$, 170.35, 170.32, 170.00, 169.88, 169.75, 169.13 (7C=O), 86.98 (C-5), 85.42 (CH-4), 80.21 (CH-3), 73.03 (CH-1), 72.78 (CH-2), 69.96 (CH-8), 69.94 (CH_2-7), 62.43 (CH_2-9), 58.73 (CH_2-6), 21.89, 20.94, 20.87, 20.73, 20.63, 20.59, 20.55 (7CH_3); HRMS (CI+, CH_4): calcd for $C_{23}H_{33}O_{15}$ $[M+H]^+$: 549.1819; found: 549.1823.

Calditol isomer heptacetate 28: This compound was synthesized from diol **16** by the procedure described for compound **26** and was obtained as a colorless oil. $[\alpha]_D^{20} = +17.9$ ($c = 0.7$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 5.66$ (dd, $J = 0.8$, 5.4 Hz, 1H; H-1), 5.37 (dd, $J = 2.7$, 6.2 Hz, 1H; H-3), 5.25 (dd, $J = 5.4$, 5.9 Hz, 1H; H-2), 5.19 (m, 1H; H-8), 4.92 (d, $J = 12.8$ Hz, 1H; H-6), 4.33 (dd, $J = 3.9$, 11.8 Hz, 1H; H-7), 4.20 (d, $J = 12.8$ Hz, 1H; H-6′), 4.17 (dd, $J = 6.9$, 11.8 Hz, 1H; H-7′), 3.89 (dd, $J = 4.7$, 10.1 Hz, 1H; H-9), 3.81 (dd, $J = 0.6$, 2.4 Hz, 1H; H-4), 3.56 (dd, $J = 4.3$, 10.1 Hz, 1H; H-9′), 2.17 (s, 3H; OAc), 2.15 (s, 3H; OAc), 2.14 (s, 3H; OAc), 2.12 (s, 3H; OAc), 2.11 (s, 3H; OAc), 2.09 (s, 3H; OAc), 2.08 (s, 3H; OAc); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 170.66$, 170.22, 170.17, 169.74, 169.69, 169.61, 169.57 (7C=O), 83.09 (CH-4), 82.55 (C-5), 82.32 (CH-3), 73.18 (CH-2), 71.59 (CH-1), 69.98 (CH-8), 69.08 (CH_2-9), 62.51 (CH_2-7), 61.77 (CH_2-6), 21.22, 20.95, 20.87, 20.71, 20.68, 20.49, 20.47 (7CH_3C=O); elemental analysis calcd (%) for $C_{23}H_{32}O_{15}$ (548.5): C 50.36, H 5.88; found: C 50.26, H 6.02.

Calditol isomer heptacetate 29: This compound was synthesized from diol **17** by the procedure described for compound **26** and was obtained as a colorless oil. $[\alpha]_D^{20} = -6.3$ ($c = 0.35$ in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 5.59$ (d, $J = 7.7$ Hz, 1H; H-1), 5.48 (ddd, $J = 0.9$, 4.5, 7.7 Hz, 1H; H-2), 5.17 (m, 1H; H-8), 5.12 (dd, $J = 2.9$, 4.5 Hz, 1H; H-3), 4.66 (d, $J = 12.1$ Hz, 1H; H-6′), 4.62 (d, $J = 12.1$ Hz, 2H; H-6, H-6′), 4.33 (m, 2H; H-4, H-7), 4.17 (dd, $J = 5.9$, 11.9 Hz, 1H; H-7′), 3.90 (dd, $J = 5.0$, 10.7 Hz, 1H; H-9), 3.78 (dd, $J = 4.5$, 10.7 Hz, 1H; H-9′), 2.14 (s, 3H; OAc), 2.13 (s, 3H; OAc), 2.11 (4s, 12H; 4OAc), 2.07 (s, 3H; OAc); ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta =$ 170.55, 170.28, 170.26, 169.94, 169.85, 169.69, 169.67 (7C=O), 84.85 (C-5), 82.81 (CH-4), 78.25 (CH-2), 77.81 (CH-3), 75.52 (CH-1), 69.72 (CH-8), 69.21 (CH_2-9), 62.19 (CH_2-7), 61.85 (CH_2-6), 21.53, 20.86, 20.78, 20.72, 20.70, 20.66, 20.64 (7CH_3C=O); elemental analysis calcd (%) for $C_{23}H_{32}O_{15}$ (548.5): C 50.36, H 5.88; found: C 50.20, H 5.96.

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