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A Short Synthesis of (+)-Cyclophellitol

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A new synthesis of (+)-cyclophellitol, a potent β-glucosidase inhibitor, has been completed in nine steps from D-xylose. The key transformations involve a zinc-mediated fragmentation of benzyl-protected methyl 5-deoxy-5-iodo-xylofuranoside followed by a highly diastereoselective indium-mediated coupling with ethyl 4-bromocrotonate. Subsequent ring-closing olefin metathesis, ester reduction, olefin epoxidation, and deprotection then afford the natural product. This constitutes the shortest synthesis of (+)-cyclophellitol reported to date.

(+)-Cyclophellitol was isolated in 1990 from the culture filtrates of a mushroom *Phellinus sp.* and shown to be a strong and specific inhibitor of almond β-glucosidase.[1,2] It is a carbocyclic analogue of D-glucopyranose with an epoxide ring on the β-face of the molecule. The inhibition of β-glucosidase is irreversible, which is presumably due to protonation and ring opening of the epoxide by a carboxylate in the active site of the enzyme.[3,4] (+)-Cyclophellitol has been the target for a number of total syntheses starting from either a carbohydrate,[5] a naturally occurring cyclitol,[6] or a synthetic cyclohexene derivative.[7] In the former case, the carbohydrate carbocyclization reaction is either a Ferrier reaction, a cycloaddition, a radical cyclization, or a ring-closing olefin metathesis reaction.

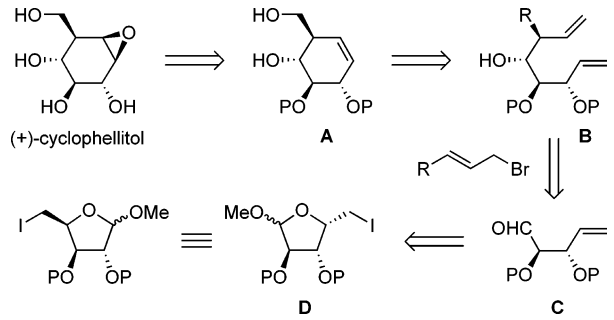

FIGURE 1. Retrosynthesis for (+)-cyclophellitol.

Olefin metathesis has now become one of the most popular tools for forming carbo- and heterocyclic ring systems in organic chemistry.[8] We have recently described several strategies for converting carbohydrates into functionalized carbocycles by the use of ring-closing metathesis.[9,10] During this work, a metal-mediated tandem reaction has been a key transformation to generate dienes from carbohydrates. In this procedure, methyl iodoglycosides are subjected to a reductive fragmentation to produce unsaturated aldehydes, which are then alkylated by unsaturated organometallics (e.g., allylic reagents).[11] This tandem reaction combined with olefin metathesis has been applied in the synthesis of several natural products, including the inositols[12] and the calystegines.[13]

Herein, we describe a nine-step synthesis of (+)-cyclophellitol from D-xylose by the use of these organometallic transformations. To date, this represents the shortest method for the preparation of enantiopure cyclophellitol.

The epoxide can be introduced at a late stage in the synthesis from the corresponding olefin. This strategy has been used in several previous syntheses of cyclophellitol, but the epoxidation only occurs with good stereocontrol when it is directed by the primary hydroxy group.[3] Thus, we embarked on a strategy where the epoxide is generated from cyclohexene **A**, which will be prepared by ring-closing metathesis from diene **B** (Figure 1). This diene can arise from unsaturated aldehyde **C** by a metal-

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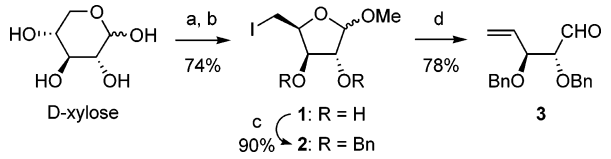
SCHEME 1[a]



[a] Reagents and conditions: (a) MeOH, HCl, 5 °C. (b) I_2, PPh_3, imidazole, THF, 65 °C. (c) $BnOC(NH)CCl_3$, TfOH, dioxane, rt. (d) Zn, THF/H_2O, ultrasound, 40 °C.

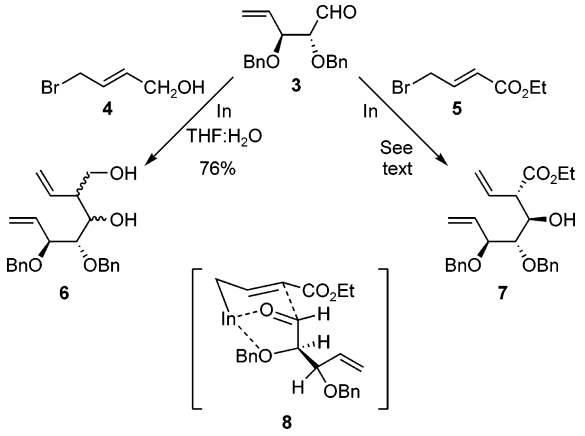
promoted reaction with a substituted allylic halide. Aldehyde **C** is available from a protected derivative of methyl 5-iodoxylofuranoside **D** by a zinc-mediated reductive fragmentation. The alkylation introduces two new stereogenic centers, and controlling the stereochemistry in this reaction is crucial.

The required starting material for the reductive fragmentation was prepared in three steps from D-xylose. First, this cheap pentose was converted into the furanose form by a Fischer glycosylation with methanol under kinetic conditions (Scheme 1). The crude product consisting of a 1:1 mixture of the α- and the *β*-furanoside was treated with iodine and triphenylphosphine. The obtained methyl 5-iodofuranoside **1** was separated from triphenylphosphine oxide on a reverse-phase column and isolated in 74% overall yield from D-xylose.[14] The 2- and 3-hydroxy groups were then protected as benzyl ethers by reaction with benzyl trichloroacetimidate under acidic conditions. The resulting dibenzyl ether **2** was sonicated with zinc to afford unsaturated aldehyde **3**.[9c] With this compound in hand, the pivotal alkylation was then examined under Barbier conditions.

Two allylic bromides were selected for these studies: 4-bromobut-2-en-1-ol (**4**) and ethyl 4-bromocrotonate (**5**). Alcohol **4** is available from ester **5** by reduction with DIBAL-H.[15] Treatment of **3** and **4** with indium metal in a 10:1 THF/water mixture at room temperature gave the desired allylation product **6**, but unfortunately the reaction was not stereoselective and yielded a mixture of three stereoisomers in the ratio 3:2:2 (Scheme 2). The allylic bromide was then changed to ester **5**. The indium-mediated addition reaction with this reagent gave diene **7** in 55% yield as a 1:1 mixture of two diastereomers. The reaction was slow and required 2 days at room temperature. We attempted to carry out the reaction as a tandem sequence where the same metal performs the reductive fragmentation of iodide **2** and the alkylation of intermediate **3** in the same pot. Unfortunately, these experiments were not successful. When a mixture of **2** and **5** was reacted with zinc metal, the major product obtained was aldehyde **3**, while no reaction occurred with indium metal. Apparently, zinc would not promote the coupling between aldehyde **3** and ester **5**, while indium would not mediate the fragmentation of iodide **2**.

Increased rates and selectivities have previously been observed in indium-mediated allyl addition reactions when lanthanide triflates are added.[16] Accordingly, the reaction between **3** and **5** was repeated in the presence

SCHEME 2



of 2 equiv of $La(OTf)_3$. Notably, only one diastereomer was formed in this case, although the reaction was still slow and only afforded a 36% yield after 24 h. This isomer was shown to be the desired diastereomer after completing the synthesis (vide infra). Incomplete conversion and decomposition of aldehyde **3** seemed to be the main reason for the low yield, and several experiments with added $La(OTf)_3$ were performed to improve the yield. Changing the solvent to pure water gave essentially the same yield, while the addition proceeded poorly in saturated ammonium chloride solution. We also attempted to use a more reactive reagent, ethyl 4-iodocrotonate, which was prepared from **5** by a Finkelstein reaction. However, in aqueous solution no indium-mediated coupling occurred between this iodide and aldehyde **3**. It was then decided to change the indium source to a more finely dispersed indium powder. All the experiments so far had been conducted with indium powder containing 1% magnesium as anticaking agent. Hence, the coupling between **3** and **5** was repeated in the presence of a 60 mesh indium powder (99.999% pure). Gratifyingly, this now provided the desired product **7** in 85% yield as a single diastereomer. The reaction was performed in water with 2 equiv of $La(OTf)_3$ and required about 48 h for complete conversion of aldehyde **3**. A slower conversion was observed in the absence of $La(OTf)_3$, but the reaction still furnished only one diastereomer. The stereochemical outcome can be explained by invoking a chelated intermediate such as **8** (Scheme 2). Chelation to flanking heteroatoms has previously been observed in indium-mediated allylations in water.[17]

Diene **7** was converted into the corresponding cyclohexene **9** by ring-closing metathesis with Grubbs second generation catalyst[18] (Scheme 3). The highly colored ruthenium catalyst was removed in the workup by treating the reaction mixture with tris(hydroxymethyl)-phosphine.[19] The ester functionality was then reduced with DIBAL-H to afford diol **10**. This reduction was quite sluggish and afforded minor amounts of the intermediate

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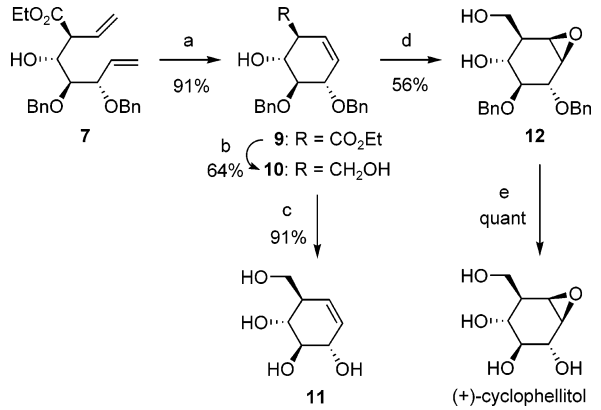
SCHEME 3[a]



[a] Reagents and conditions: (a) $(PCy_3)(C_3H_4N_2Mes_2)Cl_2Ru{=}CHPh$, CH_2Cl_2, 40 °C. (b) DIBAL-H, THF, 0 °C → rt, then $NaBH_4$, H_2O, rt. (c) $FeCl_3$, CH_2Cl_2, rt. (d) *m*-CPBA, CH_2Cl_2, 40 °C. (e) H_2, $Pd(OH)_2$/C, MeOH, rt.

aldehyde as a byproduct. Using a larger excess of DIBAL-H or a higher reaction temperature did not solve the problem. Instead, water and sodium borohydride were added in the workup to drive the reaction to completion. Deprotection of diol **10** with ferric chloride in dichloromethane[20] gave tetrol **11**, which is an olefin analogue of cyclophellitol. Several carbasugars have previously shown good inhibition of glycosidases,[21] and we speculated if **11** would be a reversible inhibitor. Thus, compound **11** was tested against yeast α-glucosidase, almond *β*-glucosidase, green coffee bean α-galactosidase, *Escherichia coli β*-galactosidase, and Jack bean α-mannosidase.[22] However, it showed no inhibition of these enzymes, which underlines the importance of the epoxide ring for the inhibition by cyclophellitol.

This epoxide was then installed by treating diol **10** with *m*-CPBA to give the desired product **12**. The epoxidation was completely stereoselective, and none of the other isomer was observed. Finally, epoxide **12** was deprotected by hydrogenolysis to afford (+)-cyclophellitol, mp 150−151 °C, $[\alpha]_D$ +100.0 (*c* 1.0, H_2O), with spectral and physical data in excellent agreement with those reported for the natural product.[1,5]

In conclusion, we have developed a concise synthesis of enantiopure cyclophellitol. The strategy requires nine steps from D-xylose and gives rise to the natural product in 14% overall yield. The key steps are three consecutive organometallic reactions: zinc-mediated fragmentation of **2**, indium-mediated coupling between **3** and **5**, and ruthenium-catalyzed ring-closing metathesis of **7**. The synthesis highlights the usefulness of these organometallic reactions in the development of more efficient synthetic routes from carbohydrates.

Experimental Section

Methyl 2,3-Di-*O*-benzyl-5-deoxy-5-iodo-D-xylofuranoside (2). To a solution of iodide **1**[14] (1.97 g, 7.22 mmol) and benzyl trichloroacetimidate (4.1 mL, 22.0 mmol) in dioxane (20 mL, dried over 4 Å molecular sieves) was added triflic acid (0.45 mL, 5.12 mmol). The mixture was cooled in an ice bath for 1 min, followed by stirring at room temperature for 5 min. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc. The organic phase was concentrated, and the residue was purified by dry column chromatography (EtOAc/heptane = 1:9 → 2:8) to give **2** (2.94 g, 90%) as a 1:1 mixture of anomers. Clear oil. R_f 0.19 and 0.29 (heptane/EtOAc = 5:1). ^{1}H NMR ($CDCl_3$, 300 MHz): *δ* 7.40−7.30 (m, 20H), 5.00 (d, *J* = 1.1 Hz, 1H), 4.90 (d, *J* = 4.0 Hz, 1H), 4.70−4.40 (m, 10H), 4.20 (m, 2H), 4.10−4.00 (m, 2H), 3.44 (s, 3H), 3.42 (s, 3H), 3.40−3.30 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 137.6, 137.6, 137.4, 129.2, 128.7, 128.6, 128.6, 128.6, 128.5, 128.3, 128.3, 128.2, 128.1, 128.1, 128.0, 127.9, 127.9, 127.9, 108.4, 101.0, 86.8, 83.9, 82.1, 82.0, 81.8, 77.7, 72.9, 72.8, 72.7, 72.2, 56.0, 55.4, 4.4, 2.9. HRMS calcd for $C_{20}H_{23}IO_4Na$ $[M + Na]^+$ *m/z* 477.0533, found *m/z* 477.0532.

(2*R*,3*S*)-2,3-Bis(benzyloxy)pent-4-enal (3). To a solution of iodide **2** (1.04 g, 2.29 mmol) in THF/H_2O (30 mL, 9:1) was added activated zinc dust[9c] (1.52 g, 23.2 mmol). The reaction was sonicated at 40 °C for 2.5 h, whereupon the mixture was filtered through Celite, which was rinsed with Et_2O. The filtrate was concentrated and purified by flash chromatography (EtOAc/heptane = 3:17) to give **3** (530.6 mg, 78%) as a clear oil. R_f 0.29 (EtOAc/heptane = 1:3). $[\alpha]_D$ +68.7 (*c* 1.0, $CHCl_3$). IR (KBr): 3029, 1733, 1072, 737, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): *δ* 9.70 (d, *J* = 1.5 Hz, 1H), 7.41−7.26 (m, 10H), 5.96 (ddd, *J* = 7.7, 10.5, 17.2 Hz, 1H), 5.42−5.32 (m, 2H), 4.78 (d, *J* = 12.2 Hz, 1H), 4.69−4.61 (m, 2H), 4.37 (d, *J* = 12.1 Hz, 1H), 4.19 (dd, *J* = 4.1, 7.6 Hz, 1H), 3.85 (dd, *J* = 1.4, 4.1 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 202.7, 137.6, 137.1, 133.9, 128.6, 128.5, 128.3, 128.3, 128.1, 127.9, 120.1, 85.2, 80.0, 73.6, 70.7. HRMS calcd for $C_{19}H_{20}O_3Na$ $[M + Na]^+$ *m/z* 319.1305, found *m/z* 319.1305.

Ethyl (2*S*,3*R*,4*S*,5*S*)-4,5-Bis(benzyloxy)-3-hydroxy-2-vinylhept-6-enoate (7). To a solution of aldehyde **3** (134.4 mg, 0.45 mmol) in H_2O (2 mL) were added ethyl 4-bromocrotonate (282 mg, 1.46 mmol), $La(OTf)_3$ (548 mg, 0.94 mmol), and indium (60 mesh, 120.5 mg, 1.05 mmol). After being stirred for 47 h at room temperature, the mixture was filtered through Celite, which was rinsed with Et_2O. The filtrate was concentrated and purified by flash chromatography (EtOAc/heptane = 3:17) to afford **7** (157.7 mg, 85%) as a clear oil. R_f 0.23 (EtOAc/heptane = 1:3). $[\alpha]_D$ −12.1 (*c* 1.0, $CHCl_3$). IR (KBr): 1734, 1064, 928, 734, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): *δ* 7.40−7.17 (m, 10H), 5.82 (ddd, *J* = 7.9, 10.3, 17.5 Hz, 1H), 5.71 (ddd, *J* = 9.4, 10.1, 17.1 Hz, 1H), 5.38−5.28 (m, 2H), 5.19−5.08 (m, 2H), 5.01 (d, *J* = 11.5 Hz, 1H), 4.62 (d, *J* = 11.8 Hz, 1H), 4.58 (d, *J* = 11.5 Hz, 1H), 4.33 (d, *J* = 11.5 Hz, 1H), 4.11 (t, *J* = 7.5 Hz, 1H), 4.03 (q, *J* = 7.1 Hz, 2H), 3.90 (t, *J* = 9.5 Hz, 1H), 3.47 (d, *J* = 7.6 Hz, 1H), 3.21 (t, *J* = 9.3 Hz, 1H), 2.64 (d, *J* = 10.0 Hz, 1H), 1.15 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 172.6, 138.5, 138.4, 135.0, 133.0, 128.5, 128.5, 128.1, 127.9, 127.9, 127.7, 120.2, 120.1, 83.0, 79.4, 74.7, 72.2, 70.9, 61.0, 55.3, 14.2. HRMS calcd for $C_{25}H_{30}O_5Na$ $[M + Na]^+$ *m/z* 433.1985, found *m/z* 433.1975.

Ethyl (1*S*,4*S*,5*S*,6*R*)-4,5-Bis(benzyloxy)-6-hydroxycyclohex-2-enecarboxylate (9). To a solution of diene **7** (105.1 mg, 0.26 mmol) in CH_2Cl_2 (10 mL) was added Grubbs second generation catalyst (23.9 mg, 0.028 mmol), and the mixture was stirred at 40 °C in the dark for 50 h. A 1.5 M solution of $P(CH_2OH)_3$ in 2-propanol (0.6 mL) was added, and the solution was refluxed for another 25 h. The mixture was then washed with H_2O, evaporated to dryness, and purified by flash chromatography (EtOAc/heptane = 3:17) to give **9** (89.3 mg, 91%) as a yellow oil. R_f 0.21 (EtOAc/heptane = 1:3). $[\alpha]_D$ +127.5 (*c* 1.1, $CHCl_3$). IR (KBr): 3492, 1733, 1180, 1055, 737, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): *δ* 7.37−7.28 (m, 10H), 5.81 (dt, *J* = 2.1, 10.3 Hz, 1H), 5.67 (dt, *J* = 2.1, 10.3 Hz, 1H), 4.97 (d, *J* = 11.3 Hz, 1H), 4.79 (d, *J* = 11.3 Hz, 1H), 4.71 (d, *J* = 11.4 Hz, 1H), 4.66 (d, *J* = 11.4 Hz, 1H) 4.23−4.11 (m, 4H), 3.66 (dd, *J* = 7.7, 10.0 Hz, 1H), 3.29−3.23 (m, 1H), 2.96 (d, *J* = 2.0 Hz, 1H), 1.28 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): *δ* 172.1,

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138.5, 138.1, 128.6, 128.6, 128.3, 128.0, 128.0, 128.0, 128.0 124.2, 82.6, 79.3, 75.0, 72.0, 70.5, 61.4, 50.1, 14.3. Anal. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 71.98; H, 6.61.

(1*R*,2*R*,5*S*,6*S*)-5,6-Bis(benzyloxy)-2-(hydroxymethyl)cyclohex-3-enol (10). DIBAL-H (0.78 mL, 4.38 mmol) was added slowly to a solution of ester **9** (186.6 mg, 0.49 mmol) in THF (15 mL) at 0 °C. After being stirred for 35 min at 0 °C, the reaction was warmed to room temperature and stirred for 2 h. The mixture was cooled to 0 °C again, and EtOAc (1 mL) was added slowly. Then, H_2O (2 mL) and $NaBH_4$ (120 mg, 3.17 mmol) were added, and the mixture was allowed to warm to room temperature and was stirred for 19 h. The organic layer was separated, and the aqueous phase was extracted with EtOAc. The combined organic phases were concentrated, and the residue was purified by flash chromatography (EtOAc/heptane = 3:7 → 1:1) to give **10** (106.6 mg, 64%) as a clear oil. R_f 0.39 (EtOAc). $[\alpha]_D$ +104.7 (*c* 1.0, $CHCl_3$). IR (neat): 3407, 1454, 1097, 1055, 735, 698 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.30−7.20 (m, 10H), 5.70 (dt, J = 2.9, 10.2 Hz, 1H), 5.40 (dt, J = 1.7, 10.3 Hz, 1H), 5.02 (d, J = 11.3 Hz, 1H), 4.71 (d, J = 11.3 Hz, 1H), 4.71 (d, J = 11.4 Hz, 1H), 4.63 (d, J = 11.4 Hz, 1H), 4.20−4.10 (m, 1H), 3.70−3.50 (m, 4H), 2.55−2.46 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.6, 138.3, 128.8, 128.7, 128.2, 128.2, 128.1, 128.1, 127.7, 127.5, 83.5, 80.4, 75.1, 73.0, 71.7, 65.7, 45.4. Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.93; H, 7.27.

(1*R*,2*R*,3*S*,6*R*)-6-(Hydroxymethyl)cyclohex-4-ene-1,2,3-triol (11). To an ice-cold solution of dibenzyl ether **10** (96.8 mg, 0.28 mmol) in CH_2Cl_2 (2 mL) was added anhydrous $FeCl_3$ (459 mg, 2.83 mmol). After being stirred for 1.5 h at room temperature, the reaction was stopped by addition of H_2O, and the mixture was evaporated to dryness. The residue was dissolved in MeOH and poured through a mixture of two ion-exchange resins (Amberlite IR-120 (H^+) (20 mL) and Amberlite IRA-420 (OH^-) (10 mL)) eluting with MeOH. The eluent was treated with activated charcoal, filtered through Celite, and concentrated to give compound **11** as a clear oil (41.3 mg, 91%). R_f 0.23 (EtOAc). $[\alpha]_D$ −13.4 (*c* 1.1, MeOH). IR (KBr): 3333, 1652, 1083, 725 cm^{-1}. ^1H NMR (CD_3OD, 300 MHz): δ 5.60−5.51 (m, 2H), 4.02−3.94 (m, 1H), 3.74 (dd, J = 10.6, 3.9 Hz, 1H), 3.55 (dd, J = 10.5, 6.0 Hz, 1H), 3.41−3.34 (m, 2H), 2.25−2.17 (br s, 1H). ^{13}C NMR (CD_3OD, 75 MHz): δ 131.0, 128.6, 78.8, 73.6, 71.9, 63.4, 47.7. HRMS calcd for $C_7H_{12}O_4Na$ $[M + Na]^+$ *m/z* 183.0628, found *m/z* 183.0626.

(1*R*,2*R*,3*R*,4*S*,5*R*,6*S*)-4,5-Bis(benzyloxy)-2-(hydroxymethyl)-7-oxa-bicyclo[4.1.0]heptan-3-ol (12). To a solution of diol **10** (103 mg, 0.30 mmol) in CH_2Cl_2 (5 mL) was added *m*-CPBA (85 mg, 0.45 mmol). The mixture was heated at reflux for 60 h and then concentrated and purified by flash chromatography (EtOAc/heptane = 2:3) to give **12** (60.1 mg, 56%) as a clear oil. R_f 0.33 (EtOAc). $[\alpha]_D$ +45.9 (*c* 0.23, MeOH). IR (KBr): 3467, 1100, 1049, 734, 696 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.46−7.25 (m, 10H), 4.96 (d, J = 11.3 Hz, 1H), 4.82 (d, J = 11.3 Hz, 1H), 4.68 (d, J = 11.4 Hz, 1H), 4.66 (d, J = 11.4 Hz, 1H), 4.05−3.88 (m, 2H), 3.82 (d, J = 8.1 Hz, 1H), 3.49 (t, J = 9.9 Hz, 1H), 3.42−3.36 (t, J = 9.9 Hz, 1H), 3.29−3.26 (m, 1H), 3.17 (dd, J = 0.9, 3.6 Hz, 1H), 2.79 (br s, 2H), 2.21−2.13 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.2, 137.4, 128.8, 128.7, 128.3, 128.1, 128.1, 128.0, 83.5, 79.5, 75.0, 72.7, 68.8, 64.3, 55.0, 53.0, 43.4. Anal. Calcd for $C_{21}H_{24}O_5$: C, 70.77; H, 6.79. Found: C, 70.48; H, 6.80.

(1*S*,2*R*,3*S*,4*R*,5*R*,6*R*)-5-(Hydroxymethyl)-7-oxa-bicyclo-[4.1.0]heptane-2,3,4-triol ((+)-Cyclophellitol). To a solution of dibenzyl ether **12** (59.4 mg, 0.17 mmol) in MeOH (2 mL) was added 20% $Pd(OH)_2/C$ (10.0 mg). The mixture was stirred vigorously at room temperature under an atmosphere of H_2 for 22 h and was then filtered through cotton and rinsed with MeOH. The filtrate was concentrated, and the product was isolated as white crystals without further purification (29.5 mg, quant). R_f 0.38 ($MeOH/CH_2Cl_2$ = 1:3). $[\alpha]_D$ +100.0 (*c* 1.0, H_2O) (lit.[1] $[\alpha]^{27}_D$ +103.0 (*c* 0.5, H_2O)). mp 150−151 °C (EtOAc/MeOH) (lit.[1] mp 149−151 °C). ^1H NMR (D_2O, 300 MHz): δ 4.00 (dd, J = 4.0, 11.3 Hz, 1H), 3.82 (dd, J = 7.5, 11.0 Hz, 1H), 3.78 (d, J = 8.5 Hz, 1H), 3.55 (m, 1H), 3.41−3.36 (m, 1H), 3.26 (d, J = 3.8 Hz, 1H), 3.25 (t, J = 10.2 Hz, 1H), 2.12 (m, 1H). ^{13}C NMR (D_2O, 75 MHz): δ 78.5, 72.8, 68.8, 62.5, 57.4, 56.0, 45.9. NMR data are in accordance with literature values.[1,5]

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Supporting Information Available: General experimental methods and copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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