A New Stereoselective Total Synthesis of Phomonol

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A stereoselective total synthesis of phomonol, following organocatalytic enantioselective epoxidation and intramolecular oxa-*Michael* reaction as key steps, is described. The use of readily available D-tartaric acid as a chiral source renders this approach quite simple and attractive.

Introduction. – The 2,6-disubstituted-tetrahydropyran-containing natural products such as phorboxazoles [1], aspergillides [2], (–)-diospongin B [3], decytospolide A [4], and neopeltolide [5] were found to exhibit promising biological properties, which make them attractive synthetic targets. In particular, phomonol (**1**) [6] (*Fig.*) was isolated from the leaves of mangrove species collected in the Fugong Mangrove Conservation Area, Fujian, P. R. China. The structure of **1** was established by 1D- and 2D-NMR spectroscopy and HR-Q-TOF mass spectrometry.

Due to the scarcity of phomonol in Nature, we attempted its total synthesis to produce enough quantity for further biological evaluations [7]. In continuation of our interest in the total synthesis of biologically active molecules [8], we herein report the stereoselective total synthesis of phomonol (**1**) employing dimethyl D-tartrate as a cost-effective and readily available precursor.

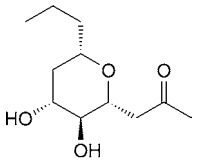

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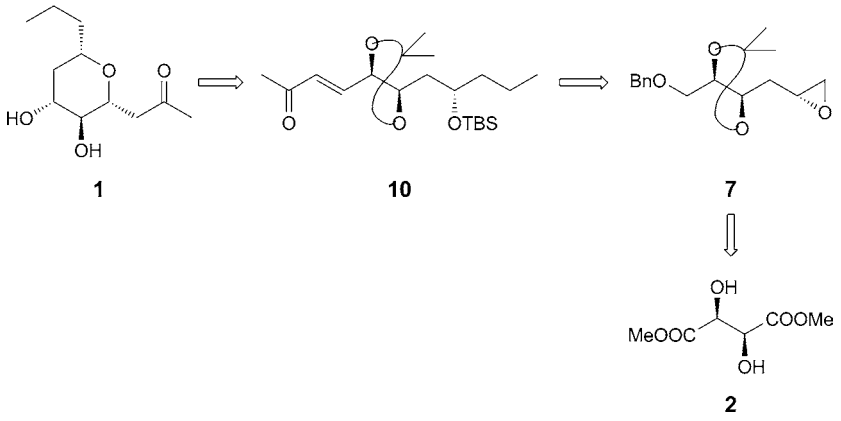
Figure. *The structure of phomonol*

Results and Discussion. – As per our retrosynthetic analysis, we assumed that the phomonol (**1**) could be prepared by intramolecular oxa-*Michael* addition of a secondary alcohol to the α,β-unsaturated ketone **11**, which in turn could easily be prepared from the readily available dimethyl D-tartrate **2** (*Scheme 1*).

Accordingly, tetrapropylammonium perruthenate (TPAP) oxidation and *Wittig* olefination of compound **3** [9] gave the (*E*)-ester **4** in 80% overall yield (*Scheme 2*). Reduction of **4** with diisobutylaluminium hydride (DIBAL-H) afforded the allylic alcohol **5** in 85% yield. Isomerization of the unsaturated alcohol **5** using 7 mol-% of

Scheme 1. *Retrosynthetic Analysis of Phomonol* (**1**)



activated $Pd(OH)_2/C$ in benzene at room temperature furnished the corresponding aldehyde **6** in 90% yield [10]. The crude aldehyde **6** was subjected to organocatalyzed asymmetric epoxidation with catalyst A (see [11]) to give the terminal epoxide **7** (93% de; by HPLC analysis) in 86% yield [11]. Regioselective ring opening of **7** with EtMgBr in the presence of a catalytic amount of CuCN gave the corresponding alcohol **8** in 90% yield. Protection of the secondary OH group of **8** using TBSOTf and 2,6-lutidine at 0° gave the TBS ether **9** in 91% yield. Debenzylation of the latter with Li/naphthalene in THF afforded the primary alcohol in 91% yield, and subsequent oxidation with DMP in CH_2Cl_2 led to the corresponding aldehyde, which was homologated with 1-(triphenylphosphoranylidene)propan-2-one in THF to furnish the α,β-unsaturated ketone **10** in 87% yield over two steps [12]. Removal of the TBS group with HF/pyridine in THF gave the secondary alcohol **11** in 90% yield.

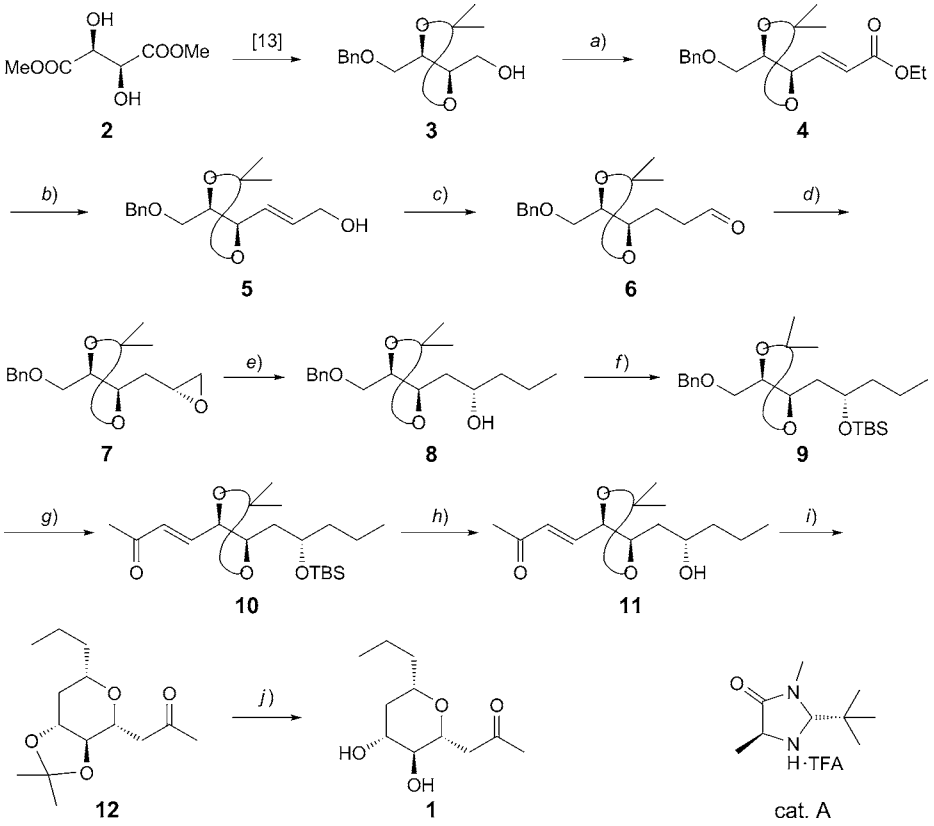
Next, we investigated the *cis*-annular oxa-*Michael* reaction of **11**. Surprisingly, no intramolecular oxa-*Michael* addition of **11** (*Table*, *Entries 1* and *2*) was observed either with catalytic CSA (camphorsulfonic acid) or with TsOH. Though NaH has been used for the same cyclization in a previous synthesis [7], the desired tetrahydropyran **12** was obtained in low yield (*Table*, *Entry 3*). ^{t}BuOK also gave **12** in poor yield (*Table*, *Entry 4*).

Therefore, we next attempted the cyclization with DBU (1,8-diazabicycloundec-7-ene) in the presence of LiCl in MeCN at room temperature. Interestingly, the oxa-*Michael* reaction of **11** proceeded well under the above conditions [13] to give the tetrahydropyran derivative **12** exclusively in 90% yield (*Table*, *Entry 5*). Finally, the

Table. cis-*Annular Oxa*-Michael *Reaction of Compound* **11**

Entry	Reagent	Solvent	Temp. [°]	Yield [%]
1	CSA	CH_2Cl_2	0	0
2	TsOH	CH_2Cl_2	0	0
3	NaH	THF	0	45 [7]
4	^{t}BuOK	THF	0	15
5	DBU/LiCl	MeCN	r.t.	90

Scheme 2. *Synthesis of Phomonol from Dimethyl* D-*Tartrate*



a) Tetrapropylammonium perruthenate (TPAP), *N*-methylmorpholine *N*-oxide (NMO), CH_2Cl_2; Ph_3P=CHCOOEt; 80%. *b*) Diisobutylaluminium hydride (DIBAL-H), CH_2Cl_2, 0°, 15 min; 85%. *c*) $Pd(OH)_2$/C, Et_3N, benzene. *d*) 50 mol-% $Cu(TFA)_2 \cdot H_2O$ (TFA, CF_3COOH), 20 mol-% cat. A (see [11]), LiCl, $Na_2S_2O_8$, MeCN, $NaBH_4$, 0°, 15 min, KOH, r.t., 30 min. *e*) EtMgBr, CuCN, THF, 0°, 1 h; 90%. *f*) (*tert*-Butyl)dimethylsilyl trifluoromethanesulfonate (TBSOTf), 2,6-lutidine, CH_2Cl_2, 91%. *g*) 1. Li, naphthalene, −20°, 91%; 2. 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, r.t., 3 h; 3. 1-(triphenylphosphoranylidene)propan-2-one, dry THF, reflux, 8 h; 87%. *h*) HF/pyridine, THF, 90%. *i*) DBU, LiCl, THF; 90%. *j*) $CeCl_3 \cdot 7\ H_2O$, MeOH/MeCN 1:1, reflux, 4 h; 66%.

removal of acetonide from compound **12** using $CeCl_3 \cdot 7\ H_2O$ afforded phomonol (**1**) in 66% yield (*Scheme 2*). The spectroscopic and analytical data of synthetic **1** are in accordance with those reported in [6].

Conclusions. – In summary, we have developed a concise total synthesis of phomonol (**1**) in a highly stereoselective manner. Our approach involves mainly the organocatalytic *MacMillan* asymmetric epoxidation and intramolecular oxa-*Michael* reaction as key steps. This approach provides an easy access to produce **1** in large scale for further biological screening.

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Experimental Part

General. All reagents were of reagent grade and used without further purification unless specified otherwise. Solvents were distilled prior to use: THF, toluene, and Et_2O were distilled from Na and benzophenone ketyl; MeOH from Mg and I_2; and CH_2Cl_2 from CaH_2. All air- or moisture-sensitive reactions were conducted under N_2 or Ar in flame- or oven-dried glassware. Column chromatography (CC): silica gel (60–120 mesh or 100–200 mesh) packed in glass columns; technical-grade AcOEt and petroleum ether (PE) used were distilled prior to use. Optical rotations: *Perkin-Elmer P241* polarimeter and *Jasco-DIP-360* digital polarimeter using a 1-ml cell with a 1-dm path length. FT-IR Spectra: *Perkin-Elmer* FT-IR spectrometer, KBr pellets $CHCl_3$, neat (as mentioned); in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Varian-Gemini-200*, *Bruker-Avance-300*, *Varian-Unity-400*, or *Varian-Inova-500* spectrometer, in $CDCl_3$ or benzene 200, 300, or 500 MHz spectrometers at r.t.; the coupling constant J in Hz; the chemical shifts, δ, in ppm downfield from TMS (Me_4Si) as internal standard. ESI-MS: *Micro-Mass-VG-7070H* and *VG-Autospec-M* spectrometer; in m/z.

*Ethyl (2*E*)-6-*O*-Benzyl-2,3-dideoxy-4,5-O-(1-methylethylidene)*-D-threo-*hex-2-enonate* (**4**). To a soln. of **3** [9] (2 g, 7.9 mmol) and molecular sieves (4 Å, 500 mg) in CH_2Cl_2 (80 ml) at 0° were added TPAP (0.28 mg, 0.79 mmol) and NMO (1.39 g, 11.9 mmol), and the mixture was stirred for 30 min at r.t. The mixture was filtered through a short SiO_2 column (AcOEt/hexane 1:4) to give the crude aldehyde, which was used for the next reaction directly. A mixture of aldehyde and $Ph_3P{=}CHCOOEt$ (4.0 g, 12 mmol) in benzene (60 ml) was heated under reflux for 4 h. Removal of the solvent, followed by purification over SiO_2, gave **4** (2.0 g, 80% for the two steps). Pale-yellow oil. R_f (AcOEt/hexane, 1:4) 0.80. $[\alpha]_D^{27} = -11.31$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3454, 2998, 2936, 1724, 1375, 1043, 763. ^1H-NMR ($CDCl_3$, 300 MHz): 1.24 (*t*, $J = 6.2$, 3 H); 1.36 (*s*, 3 H); 1.39 (*s*, 3 H); 3.33–3.51 (*m*, 1 H); 3.58–3.67 (*m*, 2 H); 4.13–4.18 (*m*, 2 H); 4.39–4.47 (*m*, 1 H); 4.56 (*s*, 2 H); 5.64–6.01 (*m*, 1 H); 6.62–6.77 (*m*, 1 H); 7.24–7.36 (*m*, 5 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 14.1; 26.6; 27.1; 61.4; 62.3; 76.8; 78.6; 81.0; 109.2; 127.5; 127.7; 128.3; 137.6; 139.2; 166.9. ESI-MS: 343 ($[M+Na]^+$).

*(2*E*)-6-*O*-Benzyl-2,3-dideoxy-4,5-*O*-(1-methylethylidene)*-D-threo-*hex-2-enitol* (**5**). To a stirred soln. of **4** (2 g, 6.25 mmol) in CH_2Cl_2 (20 ml) at −78° was added DIBAL-H (1.0M in CH_2Cl_2; 12.50 ml, 12.5 mmol), the mixture was warmed to 25° and then stirred at the same temp. for 15 min. The resulting mixture was then diluted with CH_2Cl_2 (50 ml), and a soln. of sat. aq. *Rochelle*'s salt (60 ml) was added. The biphasic soln. was stirred vigorously at 25° for 3 h and then extracted with CH_2Cl_2 (3 × 25 ml). The combined org. layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by CC (SiO_2) to provide **5** (1.7 g, 85%). Colorless oil. R_f (AcOEt/hexane, 1:4) 0.50. $[\alpha]_D^{27} = -42.2$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3448, 2988, 2939, 1378, 1042, 727. ^1H-NMR ($CDCl_3$, 300 MHz): 1.36 (*s*, 3 H); 1.39 (*s*, 3 H); 3.49–3.60 (*m*, 2 H); 3.64–3.70 (*m*, 2 H); 3.72–3.81 (*m*, 1 H); 4.56 (*s*, 2 H); 4.62–4.70 (*m*, 1 H); 5.32–5.42 (*m*, 1 H); 5.66–5.74 (*m*, 1 H); 7.28–7.37 (*m*, 5 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 26.6; 27.2; 62.3; 71.1; 76.8; 78.6; 81.0; 109.3; 127.4; 128.2; 130.5; 137.5; 138.1. ESI-MS: 301 ($[M+Na]^+$).

*1,2-Anhydro-6-*O*-benzyl-3-deoxy-4,5-*O*-(1-methylethylidene)*-D-xylo-*hexitol* (**7**). A 100-ml two neck round-bottomed flask was charged with 7 mol-% of $Pd(OH)_2/C$ in benzene (10 ml) and purged it with H_2 *via* the balloon for 30 min (for the activation of the catalyst). Then, H_2 supply was stopped, and the stirring was continued for 10 min, and a soln. of **5** (1.0 g, 3.50 mmol) in benzene (5 ml) was added. The resulting mixture was stirred for another 10 min, After completion of the reaction, as indicated by TLC, the mixture was filtered through a *Celite* pad and washed with AcOEt (20 ml). The filtrate was concentrated *in vacuo* to afford the crude aldehyde **6**. To a stirred soln. of catalyst A [11] (20 mol-%, 190 mg, 0.72 mmol), LiCl (226 mg, 5.3 mmol), $Cu(TFA)_2 \cdot H_2O$ (520 mg, 1.7 mmol), $Na_2S_2O_8$ (856 mg, 3.5 mmol) in MeCN (40 ml) and H_2O (0.14 ml, 7.9 mmol) was added **6** (1 g, 3.5 mmol) at 10°, and the mixture was stirred vigorously for 2 h at the same temp. The mixture was then cooled to 0° before $NaBH_4$ (340 mg, 8.9 mmol) was added. After 10 min, the mixture was warmed to r.t, and then a freshly prepared aq. soln. of KOH (20 ml) in EtOH (8 ml; 6 g of KOH dissolved in 15 ml of dist. H_2O) was added. The resulting mixture was stirred vigorously for 30 min. After completion, the reaction was quenched with

50 ml of dist. H_2O, and the mixture was extracted with AcOEt (3×30 ml), washed with brine (1×50 ml), dried (Na_2SO_4), filtered, and concentrated *in vacuo* maintaining the bath temp. at 30°. The resulting oil was purified by CC (SiO_2) to afford **7** (900 mg, 86%). Colorless oil. R_f (AcOEt/hexane 1:4) 0.65. $[\alpha]_D^{27} = +44.6$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2928, 2848, 1495, 1452, 1363, 1259, 1026, 925, 769. ^{1}H-NMR ($CDCl_3$, 300 MHz): 1.42 (*s*, 6 H); 1.82–1.90 (*m*, 2 H); 2.48–2.54 (*m*, 1 H); 2.72–2.83 (*m*, 1 H); 3.03–3.13 (*m*, 1 H); 3.54–3.66 (*m*, 2 H); 3.84–4.00 (*m*, 2 H); 4.58 (*s*, 2 H); 7.26–7.39 (*m*, 5 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 26.9; 27.3; 36.7; 47.7; 49.4; 73.5; 75.7; 76.0; 79.9; 109.1; 127.7; 127.8; 128.4; 137.9. HR-ESI-MS: 301.1410 ($[M+Na]^+$, $C_{16}H_{22}NaO_4^+$; calc. 301.1402).

*(2*S*)-1-{(4*R*,5*R*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}pentan-2-ol* (**8**). To a stirred soln. of **7** (0.9 g, 3.3 mmol) and CuCN (120 mg, 0.6 mmol) in THF (50 ml) at $-40°$ was added EtMgBr (6.6 ml of a 1.0M soln. in Et_2O, 6.6 mmol). The resulting mixture was stirred at this temp. for 30 min before warming to r.t over a period of 1 h. The reaction was quenched with sat. aq. NH_4Cl (15 ml). The org. phase was separated, and the aq. layer was extracted with Et_2O (3×20 ml). The combined org. phases were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Purification by CC (SiO_2) provided **8** (810 mg, 90%). Colorless oil. R_f (AcOEt/hexane 1:4) 0.40. $[\alpha]_D^{27} = +42.1$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3456, 2986, 2926, 2856, 1462, 1376, 1218, 1169, 1056, 925. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.94 (*t*, $J = 7.0$, 3 H); 1.39–1.48 (*m*, 10 H); 1.71–1.79 (*m*, 2 H); 3.38–3.45 (*m*, 1 H); 3.53–3.64 (*m*, 2 H); 3.83–3.93 (*m*, 1 H); 4.00–4.10 (*m*, 1 H); 4.58 (*s*, 3 H); 7.27–7.39 (*m*, 5 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 14.1; 18.7; 26.9; 38.0; 39.8; 68.7; 70.5; 76.3; 78.8; 80.2; 109.0; 127.7; 127.8; 128.4; 137.9. HR-ESI-MS: 331.1879 ($[M+Na]^+$, $C_{18}H_{28}NaO_4^+$; calc. 331.1872).

*{[(2*S*)-1-{(4*R*,5*R*)-5-[(Benzyloxy)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}pentan-2-yl]oxy}(*tert*-butyl)dimethylsilane* (**9**). To a stirred soln. of **8** (0.8 g, 2.7 mmol) and 2,6-lutidine (0.58 g, 5.4 mmol) in CH_2Cl_2 (20 ml) was added TBSOTf (0.60 g, 2.7 mmol) portionwise. The resulting mixture was stirred for 1 h at r.t., diluted with sat. $NaHCO_3$, and then extracted with CH_2Cl_2. The org. layer was washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The crude residue was purified by CC (SiO_2) to give the **9** (1.01 g, 91.0%). Colorless oil. R_f (AcOEt/hexane 1:4) 0.8 $[\alpha]_D^{27} = +14.31$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3307, 3067, 2956, 2856, 1466, 1361, 1253, 1097, 835, 775. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.09 (*s*, 6 H); 0.90 (*t*, $J = 3.3$, 3 H); 0.93 (*s*, 9 H); 1.39–1.48 (*m*, 8 H); 1.59–1.73 (*m*, 2 H); 1.76–1.82 (*m*, 2 H); 3.55–3.62 (*m*, 1 H); 3.82–3.89 (*m*, 2 H); 3.98–4.04 (*m*, 1 H); 4.10–4.16 (*m*, 1 H); 4.60 (*s*, 3 H); 7.27–7.40 (*m*, 5 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): −3.6; −2.9; 14.2; 17.7; 18.5; 25.7; 25.8; 25.9; 26.9; 27.3; 38.7; 41.2; 68.9; 70.4; 73.4; 75.1; 80.1; 108.7; 127.4; 127.6; 128.3; 137.8. HR-ESI-MS: 423.2912 ($[M+H]^+$, $C_{24}H_{43}O_4Si^+$; calc. 423.2925).

*(3*E*)-4-{(4*R*,5*R*)-5-[(2*S*)-2-{[(*tert*-Butyl)(dimethyl)silyl]oxy}pentyl]-2,2-dimethyl-1,3-dioxolan-4-yl}but-3-en-2-one* (**10**). To a soln. of naphthalene (1.56 g, 12.2 mmol) in THF (12 ml) was added small pieces of Li metal (0.08 g, 12.2 mmol). The mixture was stirred at r.t. under an Ar until Li metal was completely dissolved. The resulting dark green soln. of lithium naphthalenide was cooled to −25°, and then a soln. of **9** (1.0 g, 2.4 mmol) in THF (4 ml) was added dropwise over 5 min. The resulting mixture was stirred at −25° for 70 min. Upon completion, the reaction was quenched with a sat. aq. NH_4Cl soln. (3 ml) and H_2O (3 ml), and then the mixture was extracted with Et_2O (3×15 ml). The combined extracts were washed with H_2O and brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The crude product was then purified by CC (SiO_2) to give the primary alcohol (700 mg, 91% yield) as a colorless oil. R_f (AcOEt/hexane 3:7) 0.4. To a stirred soln of the primary alcohol (0.7 g, 2. 2 mmol) in dry CH_2Cl_2 at 0°, DMP (1.12 g, 2.64 mmol) was added, and then the mixture was stirred it at r.t. for 1 h. The mixture was diluted with CH_2Cl_2 (10 ml) and filtered through a small pad of *Celite*, evaporated *in vacuo*, and the residue was directly used in the next reaction. Thus obtained aldehyde was then treated with 1-(triphenylphosphoranylidene)propan-2-one (1.41 g, 4.4 mmol) under reflux for 8 h. The solvent was evaporated *in vacuo* and the residue was purified by CC (SiO_2) to afford **10** (0.65 g, 87% over two steps). Pale-yellow liquid. R_f (AcOEt/hexane 1:9) 0.8. $[\alpha]_D^{27} = +50.31$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3032, 1684, 1454, 1374, 1248, 1096, 964, 884, 764. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.06 (*s*, 6 H); 0.85–0.94 (*m*, 12 H); 1.39–1.48 (*m*, 8 H); 1.58–1.63 (*m*, 2 H); 2.29 (*s*, 3 H); 3.80–3.95 (*m*, 2 H); 4.07–4.16 (*m*, 1 H); 6.32 (*dd*, $J = 15.1$, 8.3, 1 H); 6.60–6.78 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): −4.8; −4.2; 14.3; 17.8; 19.1; 25.8; 26.7; 27.3; 27.4; 29.7; 38.7; 40.5; 68.8; 69.5; 80.8; 109.3; 131.7; 142.8; 197.8. HR-ESI-MS: 393.2429 ($[M+Na]^+$, $C_{20}H_{38}NaO_4Si^+$; calc. 393.2435.

(1S,5R)-1,5-Anhydro-2-deoxy-3,4-O-(1-methylethylidene)-5-(2-oxopropyl)-1-propyl-D-threo-*pentitol* (**12**). To a soln. of **10** (0.65 g, 1.8 mmol) in THF (4 ml) was added HF/pyridine (1.8 ml, 1.8 mmol) at 0°. After stirring the mixture for 3 h at r.t., the reaction was quenched with sat. aq. $NaHCO_3$ soln. (10 ml). The aq. layer was extracted with AcOEt (2 × 5 ml). The combined org. phases were dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by CC (SiO_2) to afford alcohol **11** (0.4 g, 90%) as a pale-yellow liquid. To a stirred soln. of alcohol **11** (0.100 g, 0.41 mmol) in MeCN (10 ml) were added LiCl (0.173 g, 4.1 mmol) and DBU (0.62 g, 4.1 mmol) at r.t. After stirring at the same temp. for 1.5 h, the reaction was quenched with sat. aq. NH_4Cl soln., and the mixture was extracted with Et_2O. The combined extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by CC to afford pure **12** (0.09 g, 90%). Colorless liquid. R_f (AcOEt/hexane 3 : 7) 0.5. R_f (AcOEt/hexane 1 : 9) 0.8. $[\alpha]_D^{27} = +9.58$ ($c = 1.0$, $CHCl_3$). IR (KBr): 2956, 2928, 1684, 1364, 1179, 1035, 833, 773. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.90 (*t*, *J* = 7.3, 3 H); 1.20–1.62 (*m*, 11 H); 2.11 (*td*, *J* = 6.5, 4.1, 1 H); 2.21 (*s*, 3 H); 2.76–2.61 (*m*, 2 H); 3.04 (*t*, *J* = 8.8, 1 H); 3.38–3.49 (*m*, 1 H); 3.54–3.62 (*m*, 1 H); 3.91 (*dt*, *J* = 8.5, 4.1, 1 H). ^{13}C-NMR ($CDCl_3$, 75 MHz):13.7; 18.6; 26.8; 30.7; 37.4; 38.9; 46.5; 73.2; 75.4; 76.4; 78.1; 79.8; 109.6; 208.2. HR-ESI-MS: 279.1571 ($[M + Na]^+$, $C_{14}H_{24}NaO_4^+$; calc. 279.1566).

Phomonol (=*(1S,5R)-1,5-Anhydro-2-deoxy-5-(2-oxopropyl)-1-propyl*-D-threo-*pentitol*; **1**). A mixture of **12** (0.09 g, 0.35 mmol) and $CeCl_3 \cdot 7\ H_2O$ (0.39 g, 1.05 mmol) in MeCN (5 ml) was stirred at reflux temp. for a specified time as required to complete the reaction. After completion of the reaction (TLC), the mixture was extracted with AcOEt, and the combined org. layers were washed with H_2O and brine, dried (Na_2SO_4), and concentrated under reduced pressure to remove the solvent. The crude product was purified by CC to afford pure **1** (0.05 g, 66%). Colorless liquid. R_f (AcOEt/hexane 3 : 7) 0.5. $[\alpha]_D^{27} = +10.2$ ($c = 1.0$, $CHCl_3$). IR (KBr): 3368, 2966, 2924, 1686, 1365, 1248, 1036, 843, 778. ^{1}H-NMR ($CDCl_3$, 300 MHz): 0.91 (*t*, *J* = 7.4, 3 H); 1.29–1.42 (*m*, 4 H); 1.44–1.54 (*m*, 1 H); 2.00 (*ddd*, *J* = 12.4, 5.5, 2.1, 1 H); 2.22 (*s*, 3 H); 2.69 (*dd*, *J* = 15.4, 7.5, 1 H); 2.88 (*dd*, *J* = 15.6, 4.5, 1 H); 3.10 (*t*, *J* = 8.4, 1 H); 3.38–3.48 (*m*, 1 H); 3.58–3.69 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$, 75 MHz): 14.0; 18.8; 31.1; 37.6; 39.0; 46.6; 73.2; 75.6; 75.4; 76.3; 208.4. HR-ESI-MS: 239.1258 ($[M + Na]^+$, $C_{11}H_{20}NaO_4^+$; calc. 239.1253).

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