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Supporting Information

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Synthesis of the Carbocyclic Core of Zoanthenol: Implementation of an Unusual Acid-Catalyzed Cyclization

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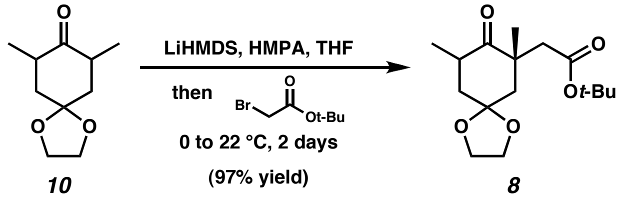
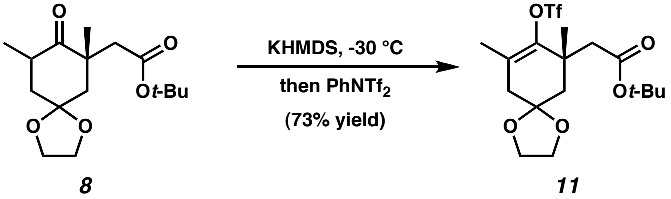
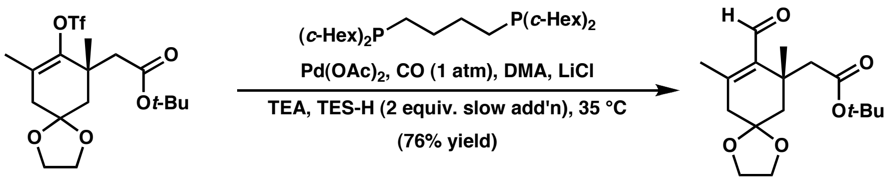
Materials and Methods. Unless otherwise stated, reactions were performed at ambient temperature (typically 19-24 °C) in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. TMEDA, HMPA, TEA, DIPA and pyridine were freshly distilled from CaH. KHMDS (95%) was purchased from Aldrich and stored in a glovebox until use. Trifluoroacetic acid (99%) was purchased from Aldrich. Tf_2O was freshly distilled from P_2O_5. Magnesium chloride (~325 mesh, <1.5% H_2O) was purchased from Aldrich. All other commercially obtained reagents were used as received. Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, anisaldehyde, $KMnO_4$, or CAM staining. ICN silica gel (particle size 0.032-0.063 mm) was used for flash chromatography. Optical rotations were measured with a Jasco P-1010 polarimeter at 589 nm. ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 (at 300 MHz and 75 MHz respectively), or a Varian Inova 500 (at 500 MHz and 125 MHz respectively) and are reported relative to Me_4Si (δ 0.0). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, sept. = septet, m = multiplet, comp. m = complex multiplet, app. = apparent, bs = broad singlet. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra were obtained from the California Institute of Technology Mass Spectral Facility. Crystallographic analyses were performed at the California Institute of Technology Beckman Institute X-Ray Crystallography Laboratory. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, from the CCDC by quoting the publication citation and the deposition number (see Appendix 3 for deposition numbers).



Ketoester 8. To a cooled (0 °C) 1.00 M LiHMDS (52.2 mL, 52.2 mmol, 1.20 equiv) solution in THF was added ketone **10** (8.00 g, 43.5 mmol, 1.00 equiv) in THF (50 mL) in a dropwise manner over 30 min. After an additional 30 min at 0 °C, HMPA (8.31 mL, 47.8 mmol, 1.10 equiv) was added and maintained at 0 °C for 1 h. *t*-butyl bromoacetate (10.6 mL, 69.5 mmol, 1.60 equiv) was added in portions over 1 h and after a further 2 h at 0 °C, allowed to warm to ambient temperature. After 48 h, the reaction mixture was poured into H_2O (300 mL), extracted with Et_2O (6 x 150 mL), dried ($MgSO_4$), and concentrated to an oil, which was purified by flash chromatography on silica gel (7 to 10% EtOAc in hexanes) to provide ketoester **8** (12.5 g, 97% yield) as a pale yellow oil (as a ~3:1 mixture of diastereomers). See below for full characterization of both methyl diastereomers, synthesized in enantioenriched form via asymmetric allylation.

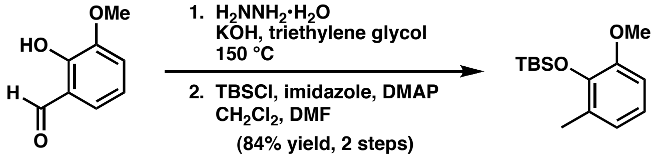


Triflate 11. To a cooled (-30 °C) solution of KHMDS (4.41 g, 22.1 mmol, 1.20 equiv) in THF (35 mL) was added ketoester **8** (5.50 g, 18.5 mmol, 1.00 equiv) in THF (30 mL) in a dropwise manner over 10 min. After 5 h at -30 °C, $PhNTf_2$ (7.20 g, 20.2 mmol, 1.09 equiv) in THF (30 mL) was added, maintained for an additional 30 min at -30 °C, and warmed to 0 °C for 2 h. The reaction mixture was diluted with Et_2O (200 mL), poured into a mixture of brine (150 mL), H_2O (150 mL), and 1 M NaOH (50 mL), and extracted with Et_2O (3 x 50 mL). The organic layers were washed with 1 M NaOH (6 x 50 mL), H_2O (50 mL), and brine (3 x 50 mL), dried (Na_2SO_4), and concentrated to an oil, which was purified by flash chromatography on silica gel (7 to 10% EtOAc in hexanes and 0.5 % TEA) to provide triflate **11** (5.74 g, 73% yield) as a pale yellow oil: R_f 0.63 (35% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02-3.92 (comp. m, 4H), 2.71 (d, J = 14.5 Hz, 1H), 2.45 (s, 2H), 2.42 (d, J = 13.5 Hz, 1H), 2.30 (d, J = 14.7 Hz, 1H), 1.78 (s, 3H), 1.70 (d, J = 13.8 Hz, 1H), 1.42 (s, 9H), 1.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 70.2, 146.9, 124.5, 118.7 (q, $J_{C\text{-}F}$ = 319 Hz), 106.2, 80.5, 64.4, 64.3, 43.1, 42.0, 41.9, 39.2, 28.0, 25.0, 17.8; IR (Neat film NaCl) 2980, 2935, 2888, 1726, 1403, 1212, 1142, 1007, 862 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{17}H_{25}SF_3O_7+H]^+$: *m/z* 431.1351, found 431.1365.



11 ***7***

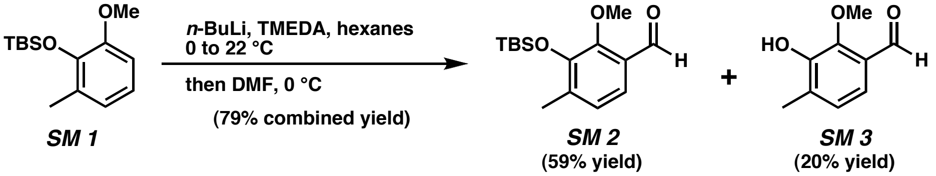
Enal 7. A solution of flame-dried LiCl (600 mg, 14.2 mmol, 2.69 equiv), $Pd(OAc)_2$ (156 mg, 0.695 mmol, 0.132 equiv), and 1,4-bis-(dicyclohexylphosphino)butane (314 mg, 0.695 mmol, 0.132 equiv) in DMA (16 mL) was sparged with CO and warmed to 90 °C until a color change from red/orange to pale yellow was observed, at which point, the reaction mixture was cooled to 35 °C. To the homogenous reaction mixture was added TEA (2.60 mL, 18.6 mmol, 3.53 equiv) and enol triflate **135** (2.27 g, 5.27 mmol, 1.00 equiv) in DMA (16 mL). A solution of Et_3SiH (1.47 mL, 9.28 mmol, 1.76 equiv) in DMA (8.5 mL) was added by syringe pump to the reaction over 10 h. After an additional 14 h at 35 °C, the reaction mixture was cooled to ambient temperature, $KF•2H_2O$ (2.00 g) was added, the mixture was stirred for 45 min, and then poured into ice water (200 mL). This mixture was extracted with 1:1 Et_2O:hexanes (5 x 100 mL). The combined organic layers were washed with brine (2 x 100 mL), dried (Na_2SO_4), and concentrated to give an oil, which was purified by gradient flash chromatography on silica gel (10 to 20% EtOAc in hexanes) to give enal **7** (1.24 g, 76% yield) as a pale yellow oil: R_f 0.42, 0.41 (35% EtOAc in hexanes, 20% EtOAc in hexanes developed twice); ^1H NMR (300 MHz, $CDCl_3$) δ 10.13 (s, 1H), 4.00-3.90 (comp. m, 4H), 3.04 (d, J = 14.4 Hz, 1H), 2.54 (app. dt, J = 1.0, 19.2 Hz, 1H), 2.37 (dd, J = 1.8, 18.9 Hz, 1H), 2.34 (d, J = 14.7 Hz, 1H), 2.15 (d, J = 13.6 Hz, 1H), 2.12 (s, 3H), 1.53 (dd, J = 2, 13.6 Hz, 1H), 1.35 (s, 9H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 91.0, 171.3, 152.8, 137.4, 106.5, 79.8, 64.3, 64.0, 44.7 (2C), 42.4, 38.3, 28.0, 26.5, 19.3; IR (Neat film NaCl) 2977, 2932, 2884, 1721, 1673, 1368, 1161, 1141, 1079 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{17}H_{26}O_5+H]^+$: m/z 311.1858, found 311.1849.



o*-Vanillin** ***SM 1

Arene SM 1. To a warmed solution (110 °C for 45 min) of *o*-vanillin (60.0 g, 0.394 mol, 1.00 equiv) and $NH_2NH_2•H_2O$ (53.6 mL, 1.10 mol, 2.79 equiv) in triethylene glycol (320 mL) in a 1 L round bottom flask was added KOH (132 g, 2.37 mol, 6.02 equiv) [*Caution: gas evolution and exotherm*] in portions over 20 min. The reaction mixture was maintained at 150 °C under a reflux condenser for 5 h, cooled to ambient temperature, and poured into H_2O (750 mL), ice (200 g), and 6 M HCl (500 mL). The mixture was further acidified to pH 2 with 6 M HCl, then extracted with $CHCl_3$ (7 x 200 mL), dried ($MgSO_4$), and evaporated to give a green solid (~60 g) that was immediately used in the next step without further purification.

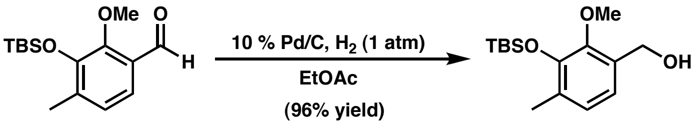
To a solution of this crude solid in DMF (300 mL) and CH_2Cl_2 (300 mL) were added imidazole (53.6 g, 0.788 mol, 2.00 equiv), DMAP (62.5 g, 0.512 mol, 1.30 equiv), and TBSCl (62.1 g, 0.414 mol, 1.05 equiv). After 4 h at ambient temperature, the reaction mixture was poured into H_2O (1.3 L), extracted with CH_2Cl_2 (3 x 150 mL), and the combined organic layers were washed with cold 0.25 M HCl (2 x 250 mL), 1 M NaOH (250 mL), and brine (2 x 200 mL). Evaporation of the organics gave an oil, which was purified by distillation at reduced pressure (~2 mmHg) to give arene **SM 1** (83.6 g, bp 120-127 °C at 2 mmHg, 84% yield over 2 steps) as a colorless oil: R_f 0.74 (10% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83-6.69 (comp. m, 3H), 3.78 (s, 3H), 2.24 (s, 3H), 1.01 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 143.1, 129.6, 122.8, 120.5, 109.1, 54.8, 26.1, 18.9, 17.1, -3.9; IR (Neat film NaCl) 2955, 2930, 1488, 1280, 1251, 1233, 1086, 920, 781 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{14}H_{24}SiO_2+H]^+$: *m/z* 253.1624, found 253.1633.



Benzaldehyde SM 2 from arene SM 1. To a cooled (0 °C) solution of arene **SM 1** (30.0 g, 119 mmol, 1.00 equiv), and TMEDA (25.1 mL, 166 mmol, 1.40 equiv) in hexanes (200 mL) was added *n*-BuLi (2.25 M in hexanes, 63.4 mL, 142 mmol, 1.20 equiv) in a dropwise manner over 15 min. After 1 h at 0 °C, the reaction mixture was allowed to warm to ambient temperature for 6 h. The reaction mixture was cooled (0 °C) again and DMF (15.6 mL, 202 mmol, 1.70 equiv) was added dropwise over 10 min. After an additional 1 h at 0 °C, saturated aqueous NH_4Cl (100 mL) was added, and the mixture was allowed to warm to ambient temperature overnight. The mixture was poured into H_2O (200 mL) and Et_2O (200 mL), then extracted with Et_2O (2 x 100 mL). The aqueous layers were then acidified with 2 M HCl to pH 1, and further extracted with Et_2O (5 x 150 mL). The combined organic layers were washed with brine (50 mL), dried (Na_2SO_4), and evaporated to give an oil that was purified by gradient flash chromatography on silica gel (2 to 20% EtOAc in hexanes) to give benzaldehyde **SM 2** (19.7 g, 59% yield) as a colorless oil: R_f 0.67 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.28 (s, 1H), 7.36 (d, J = 7.5 Hz, 1H), 6.98 (d, J = 8.1 Hz, 1H), 3.81 (s, 3H), 2.28 (s, 3H), 1.03 (s, 9H), 0.20 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.7, 154.2, 147.2, 138.4, 128.1, 126.4, 120.7, 62.5, 26.0, 18.6, 17.9, -4.1; IR (Neat film NaCl) 2957, 2932, 2859, 1691, 1464, 1273, 1255, 838 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{15}H_{24}SiO_3+H]^+$: *m/z* 281.1573, found 281.1572 and phenol **SM 3** (3.9 g, 20% yield) as a white solid: mp 90.0-91.0 °C; R_f 0.25 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.18 (s, 1H), 7.27 (d, J = 8.1 Hz, 1H), 7.01 (d, J = 8.1 Hz, 1H), 6.02 (bs, 1H), 3.95 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.4, 148.4, 147.5, 132.8, 126.7, 126.5, 121.3, 63.8, 16.3; IR (Neat film NaCl) 3410, 2938, 2857, 1686, 1466, 1261, 1061, 782 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_9H_{10}O_3+H]^+$: *m/z* 167.0708, found 167.0708.

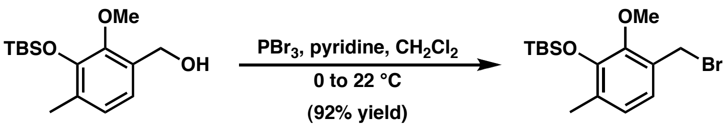
SM 3 *SM 2*

Benzaldehyde SM 2 from phenol SM 3. To a solution of phenol **SM 3** (10.0 g, 60.2 mmol, 1.00 equiv) in DMF (60 mL) and CH_2Cl_2 (60 mL) were added imidazole (8.20 g, 120 mmol, 2.00 equiv), DMAP (9.55 g, 78.3 mmol, 1.30 equiv), and TBSCl (11.7 g, 78.3 mmol, 1.30 equiv). After 36 h, the reaction mixture was quenched with H_2O (200 mL) and CH_2Cl_2 (200 mL), and extracted with CH_2Cl_2 (3 x 50 mL) The combined organics were washed with H_2O (200 mL) and then brine (100 mL), dried ($MgSO_4$), and concentrated to an oil, which was purified by flash chromatography on silica gel (2% EtOAc in hexanes) to provide benzaldehyde **SM 2** (15.5 g, 92% yield).



SM 2 *SM 4*

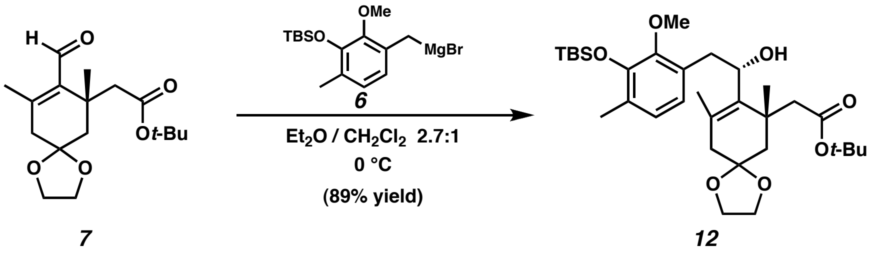
Benzyl alcohol SM 4. A flame-dried 100 mL round bottom flask was charged with 10% Pd/C (270 mg), EtOAc (55 mL), and benzaldehyde **SM 2** (2.0 g, 7.13 mmol, 1.00 equiv) under an N_2 atmosphere. The reaction mixture and head space were sparged with H_2 (5 min) and stirred vigorously under an atmosphere of H_2 (balloon) for 3 h. Immediately following the completion of the reaction, as indicated by TLC, the reaction mixture was sparged with N_2 for 15 min then concentrated to an oil, which was purified by flash chromatography on silica gel (10 to 15% EtOAc in hexanes) to provide benzyl alcohol **SM 4** (1.93 g, 96% yield) as a colorless oil: R_f 0.33 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 (d, J = 7.5 Hz, 1H), 6.83 (d, J = 8.1 Hz, 1H), 4.65 (d, J = 6.3 Hz, 2H), 3.75 (s, 3H), 2.25 (t, J = 6.3 Hz, 1H), 2.21 (s, 3H), 1.03 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.4, 147.0, 132.4, 130.6, 126.1, 121.1, 61.7, 60.5, 26.0, 18.6, 17.2, -4.2; IR (Neat film NaCl) 3340, 2956, 2931, 2859, 1464, 1420, 1285, 839, 782 cm^{-1}; HRMS (FAB) $[M+H-H_2]^+$ calc'd for $[C_{15}H_{25}SiO_3]^+$: m/z 281.1573, found 281.1564.



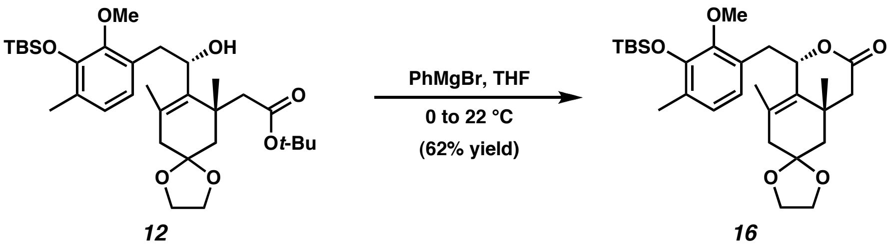
SM 4 *SM 5*

Benzyl bromide SM 5. To a cooled (0 °C) solution of benzyl alcohol **SM 4** (16.0 g, 56.7 mmol, 1.00 equiv) and pyridine (4.36 mL, 53.9 mmol, 0.95 equiv) in CH_2Cl_2 (200 mL) was added PBr_3 (4.84 mL, 51.0 mmol, 0.90 equiv) in CH_2Cl_2 (50 mL) over 30 min. After stirring an additional

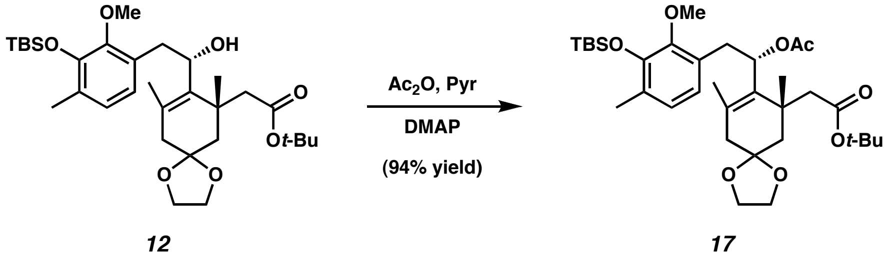
30 min at 0 °C, the reaction mixture was allowed to come to ambient temperature and stirred for a further 2.5 h. The reaction mixture was diluted with CH_2Cl_2 (300 mL), brine (500 mL), and H_2O (250 mL), then extracted with Et_2O (2 x 150 mL), dried over Na_2SO_4, and concentrated. The resulting oil was passed through a plug of silica gel (10 cm h x 5.5 cm d) (1:1 hexanes:CH_2Cl_2), concentrated, and the resultant oil was purified by distillation at reduced pressure (~2 mmHg) to provide benzyl bromide **SM 5** (27.4 g, bp 146-147 °C at ~2 mmHg, 92% yield) as a colorless oil: R_f 0.50 (2.5% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (d, J = 8 Hz, 1H), 6.87 (d, J = 8 Hz, 1H), 4.56 (s, 2H), 3.83 (s, 3H), 2.23 (s, 3H), 1.04 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 49.7, 147.2, 131.9, 129.6, 126.2, 123.2, 60.4, 28.8, 26.0, 18.6, 17.3, -4.2; IR (Neat film NaCl) 2957, 2931, 2859, 1464, 1421, 1289, 1259, 1239, 1072, 840, 782 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{15}H_{25}SiBrO_2+H]^+$: m/z 345.0885, found 345.0885.



Allylic alcohol 12. A flame-dried two-neck round bottom flask equipped with a reflux condenser and septum was charged with magnesium turnings (9.00 g, 370 mmol, 34.6 equiv) and Et_2O (120 mL) under an N_2 atmosphere and heated to reflux. To this mixture was added 1,2-dibromoethane (1.53 mL, 17.8 mmol, 1.66 equiv) in a dropwise manner [*Caution: gas evolution!*]. When gas evolution ceased, a solution of benzyl bromide **SM 5** (5.91 g, 17.1 mmol, 1.60 equiv) in Et_2O (50 mL) was added in a dropwise manner over 30 min and heating was continued for an additional 30 min. The Grignard reagent was then cooled (0 °C), and added to a cooled (0 °C) solution of enal **7** (3.32 g, 10.7 mmol, 1.00 equiv) in Et_2O (100 mL) and CH_2Cl_2 (100 mL). After 1 h, the reaction mixture was quenched with H_2O (200 mL) and saturated aqueous NH_4Cl (100 mL), extracted with Et_2O (3 x 200 mL), dried ($MgSO_4$), and concentrated to an oil, which was purified by gradient flash chromatography on silica gel (7.5 to 20% EtOAc in hexanes) to give allylic alcohol **12** (5.51 g, 89% yield) as a thick syrup: R_f 0.59 (20% EtOAc in hexanes developed twice); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83 (s, 2H), 4.43 (dd, J = 2.1, 9.9 Hz, 1H), 4.04-3.90 (comp. m, 4H), 3.68 (s, 3H), 3.22 (bs, 1H), 3.17 (dd, J = 9.9, 13.8 Hz, 1H), 2.84 (dd, J = 3.3, 13.8 Hz, 1H), 2.64 (d, J = 13.5 Hz, 1H), 2.31 (d, J = 17.4 Hz, 1H), 2.24-2.04 (comp. m, 3H), 2.19 (s, 3H), 2.07 (s, 3H), 1.57 (dd, J = 2.3, 13.8 Hz, 1H), 1.40 (s, 9H), 1.12 (s, 3H), 1.02 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.1, 149.6, 147.0, 136.7, 131.3, 130.5, 128.7, 125.7, 123.5, 107.6, 80.9, 70.6, 64.2, 63.9, 59.9, 46.4, 43.3, 42.0, 41.3, 36.6, 28.0, 26.8, 26.0, 21.1, 18.6, 17.0, -4.1 (2C); IR (Neat film NaCl) 3499, 2957, 2931, 2896, 2859, 1706, 1462, 1419, 1368, 1286, 1075, 840 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{32}H_{52}SiO_7+H]^+$: m/z 577.3561, found 577.3543.

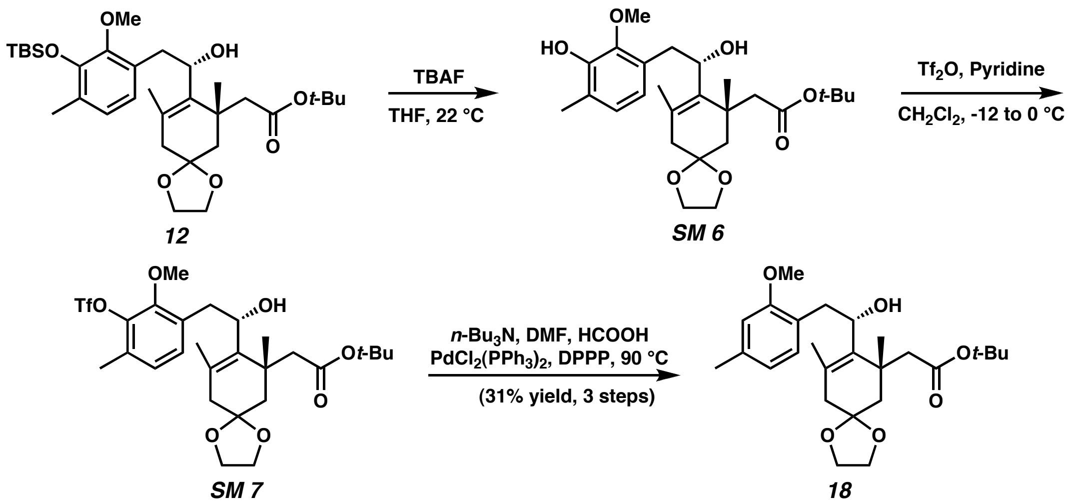


Lactone 16. To a cooled (0 °C) solution of allylic alcohol **12** (108 mg, 0.187 mmol, 1.00 equiv) in THF (12 mL) was added 3.0 M PhMgBr in Et_2O (68.6 μL, 0.206 mmol, 1.10 equiv). Additional 3.0 M PhMgBr in Et_2O (85.0 μL, 0.255 mmol, 1.36 equiv) was added in portions over 4 h. The reaction mixture was quenched into H_2O (30 mL) and EtOAc (30 mL), acidified to pH 2 with 0.1 M HCl, extracted with EtOAc (3 x 20 mL), dried over Na_2SO_4, and concentrated to an oil, which was purified by gradient flash chromatography on silica gel (10 to 20% EtOAc in hexanes) to give lactone **16** (58.5 mg, 62% yield) as white solid. Crystals suitable for X-ray analysis were obtained by crystallization from hexanes at ambient temperature: mp 139-140 °C (hexanes); R_f 0.40 (35% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83 (d, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 1H), 5.40 (d, *J* = 9.0 Hz, 1H), 4.08-3.95 (m, 2H), 3.95-3.86 (m, 2H), 3.67 (s, 3H), 3.07 (dd, *J* = 3.5, 14.3 Hz, 1H), 2.75 (dd, *J* = 10.2, 14.4 Hz, 1H), 2.48 (s, 2H), 2.43 (s, 2H), 2.19 (s, 3H), 1.82 (d, *J* = 13.2 Hz, 1H), 1.71 (d, *J* = 13.2 Hz, 1H), 1.71 (s, 3H), 1.22 (s, 3H), 1.03 (s, 9H), 0.18 (s, 3H), 0.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 71.4, 149.7, 147.0, 131.2, 129.8, 128.1, 126.0, 125.5, 123.5, 107.8, 80.0, 64.4, 63.6, 60.0, 45.7, 44.1, 43.4, 38.2, 35.9, 26.0, 25.9, 19.0, 18.5, 17.1, -4.2 (2C); IR (Neat film NaCl) 2957, 2931, 2886, 2859, 1751, 1463, 1419, 1251, 1237, 1078, 841 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{28}H_{42}SiO_6+H]^+$: *m/z* 503.2829, found 503.2809.



Allylic acetate 17. To a solution of allylic alcohol **12** (88.0 mg, 0.153 mmol, 1.00 eq) in pyridine (250 μL) and acetic anhydride (3.00 mL) was added DMAP (28.0 mg, 0.229 mmol, 1.50 equiv). After 2 h, the reaction mixture was concentrated to an oil, which was purified by gradient flash chromatography on silica gel (5 to 10% EtOAc in hexanes) to give allylic acetate **17** (89.3 mg, 94% yield) as a colorless oil: R_f 0.68 (20% EtOAc in hexanes developed twice); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (d, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 7.5 Hz, 1H), 5.73 (dd, *J* = 2.8, 10.8 Hz, 1H), 4.12-4.04 (m, 1H), 4.00-3.90 (comp. m, 3H), 3.70 (s, 3H), 3.07 (app. t, *J* = 12.5 Hz, 1H), 2.97 (dd, *J* = 3.3, 13.8 Hz, 1H), 2.66 (d, *J* = 15.0 Hz, 1H), 2.57 (d, *J* = 14.5 Hz, 1H), 2.38 (d, *J* = 17.5 Hz, 1H), 2.26 (d, *J* = 13.0 Hz, 1H), 2.24 (d, *J* = 17.5 Hz, 1H), 2.18 (s, 3H), 1.97 (s, 3H), 1.80 (s, 3H), 1.48 (d, *J* = 14.5 Hz, 1H), 1.42 (s, 9H), 1.28 (s, 3H), 1.03 (s, 9H), 0.19

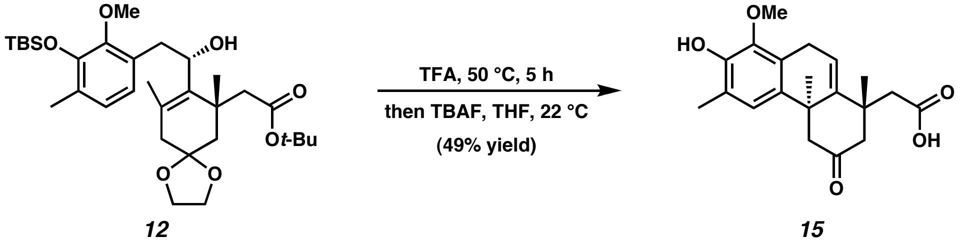
(s, 3H), 0.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 169.3, 150.0, 146.9, 135.0, 131.1, 129.3, 129.2, 125.3, 123.4, 107.3, 79.7, 71.5, 64.3, 63.9, 59.9, 43.5, 40.7, 39.9, 35.9, 28.2, 26.2, 26.1, 21.3, 21.0, 18.5, 17.1, -4.2, -4.4; IR (Neat film NaCl) 2958, 2931, 2896, 2860, 1740, 1463, 1419, 1368, 1287, 1235, 1147, 1079, 1014, 854, 841, 783, 734 cm^{-1}; HRMS (FAB) $[M+H-H_2]^+$ calc'd for $[C_{34}H_{53}O_8Si]^+$: *m/z* 617.3510, found 617.3487.



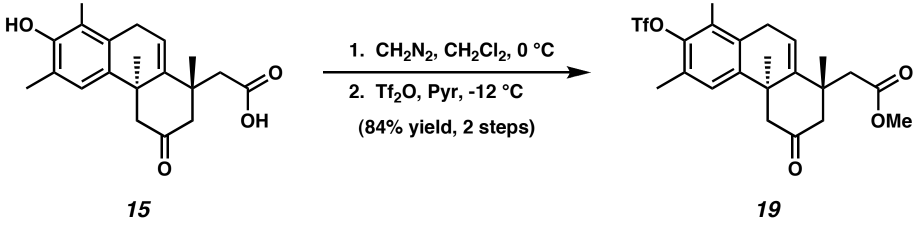
Arene 18. To a solution of allylic alcohol **12** (554 mg, 0.962 mmol, 1.0 equiv) in THF (10 mL) was added 1.00 M TBAF in THF (1.50 mL, 1.50 mmol, 1.56 equiv). After 5 min, the reaction mixture was concentrated to ~5 mL and was purified by gradient flash chromatography on silica gel (20 to 40% EtOAc in hexanes) to give phenol **SM 6** (223 mg, 52% yield).

To a cooled (-12 °C) solution of phenol **SM 6** (202 mg, 0.438 mmol, 1.00 equiv) and pyridine (142 μL, 1.75 mmol, 4.0 equiv) in CH_2Cl_2 (5 mL) was added Tf_2O (74.3 μL, 0.526 mmol, 1.2 equiv). After 2 h, additional Tf_2O (10.0 μL, 0.071 mmol, 0.16 equiv) was added. After a further 2 h, the reaction mixture was quenched into a mixture of H_2O (10 mL), brine (10 mL), and CH_2Cl_2 (10 mL), then extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried (Na_2SO_4), and concentrated to an oil, which was purified by gradient flash chromatography on silica gel (15 to 25% EtOAc in hexanes + 1% TEA) to give triflate **SM 7** (193 mg, 75% yield).

A flame-dried 25 mL Schlenk flask was charged with triflate **SM 7** (193 mg, 0.325 mmol, 1.00 equiv), $PdCl_2(PPh_3)_2$ (27.3 mg, 0.0389 mmol, 0.12 equiv), 1,4-bis-(diphenylphosphino)butane (40.2 mg, 0.0974 mmol, 0.30 equiv), DMF (4 mL), *n*-Bu_3N (650 μL, 2.73 mmol, 8.40 equiv), and HCOOH (61.3 μL, 1.62 mmol, 5.00 equiv) under an Ar atmosphere and heated to 90 °C. After 22 h, the reaction mixture was quenched with H_2O (40 mL), extracted with Et_2O (5 x 15 mL), dried ($MgSO_4$), and concentrated to a residue, which was purified by gradient flash chromatography on silica gel (10 to 15% acetone in hexanes) to give arene **18** (117 mg, 80% yield) as a white solid: mp 135-136 °C; R_f 0.50 (35% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, J = 7.5 Hz, 1H), 6.73 (d, J = 7.5 Hz, 1H), 6.68 (s, 1H), 4.46 (dd, J = 2.3, 10.1 Hz, 1H), 4.02-3.90 (comp. m, 4H), 3.80 (s, 3H), 3.08 (dd, J = 10.2, 13.8 Hz, 1H), 3.07 (s, 1H), 2.94 (dd, J = 3.0, 13.8 Hz, 1H), 2.65 (d, J = 13.5 Hz, 1H), 2.33 (s, 3H), 2.30-2.10 (comp. m, 3H), 2.07 (s, 3H), 1.58 (dd, J = 2.1, 13.8 Hz, 1H), 1.40 (s, 9H), 1.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.1, 157.3, 137.3, 136.8, 131.4, 130.3, 125.1, 121.0, 111.2, 107.6, 80.8, 69.5, 64.2, 63.9, 55.0, 46.4, 43.3, 42.0, 41.3, 36.7, 28.0, 26.7, 21.5, 21.1; IR (Neat film NaCl) 3501, 2974, 2934, 1705, 1368, 1259, 1155, 1126, 1080, 1042 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{26}H_{38}O_6+H]^+$: *m/z* 447.2747, found 447.2749.

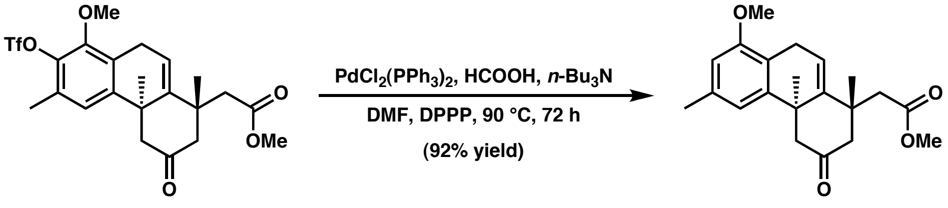


Acid 15. A solution of allylic alcohol **12** (5.50 g, 9.53 mmol, 1.00 equiv) in TFA (240 mL) was warmed to 50 °C for 5 h. The reaction mixture was concentrated and the resulting residue was dissolved in THF (100 mL) and 1.0 M TBAF (12.0 mL, 12.0 mmol, 1.26 equiv) in THF was added. After 1 h, the reaction mixture was concentrated to ~25 mL, quenched with H_2O (100 mL), brine (100 mL), and 3 M HCl (100 mL), and extracted with EtOAc (6 x 100 mL). The organic layers were concentrated to an oil, which was purified by flash chromatography on silica gel (1:1 CH_2Cl_2:$CHCl_3$ + 1% AcOH) to give acid **15** (1.62 g, 49% yield) as a white foam. Crystals suitable for X-ray analysis were obtained by crystallization from $CDCl_3$ at ambient temperature: mp 112-113 °C ($CDCl_3$); R_f 0.32 (1:1 CH_2Cl_2 : $CHCl_3$ + 3% MeOH developed twice); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.76 (s, 1H), 6.05 (dd, *J* = 1.8, 6.3 Hz, 1H), 5.63 (bs, 1H), 3.78 (s, 3H), 3.58 (dd, *J* = 6.6, 20.7 Hz, 1H), 3.47 (d, *J* = 17.7 Hz, 1H), 3.17 (d, *J* = 18.3 Hz, 1H), 3.11 (d, *J* = 17.4 Hz, 1H), 2.93 (d, *J* = 15.9 Hz, 1H), 2.76 (d, *J* = 17.4 Hz, 1H), 2.50 (d, *J* = 15.6 Hz, 1H), 2.34 (d, *J* = 17.1 Hz, 1H), 2.24 (s, 3H), 1.24 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (75 MHz, CD_2Cl_2) δ 210.8, 176.8, 146.0, 145.4, 143.9, 137.6, 125.3, 123.1, 121.6, 120.6, 61.2, 50.1, 49.2, 46.2, 39.5, 39.0, 33.3, 30.7, 24.9, 16.0; IR (Neat film NaCl) 3500-2500, 2963, 2926, 1707, 1489, 1461, 1422, 1360, 1295, 1228, 1071, 955, 711 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{20}H_{24}O_5+H]^+$: *m/z* 345.1702, found 345.1709. Due to the presence of an inseparable contaminant, an isolated yield of the diastereomeric product could not be determined. Based on the ^{1}H NMR-determined dr (5:1), the combined yield of cyclized products is 59%.



Triflate 19. To a cooled (0 °C) solution of acid **15** (994 mg, 2.88 mmol, 1.00 equiv) in CH_2Cl_2 (30 mL) was added a cooled (0 °C) solution of CH_2N_2 in Et_2O (~0.2 M, 18.7 mL, 1.30 equiv) in a dropwise manner over 10 min. After 20 min, TLC analysis indicated complete consumption of

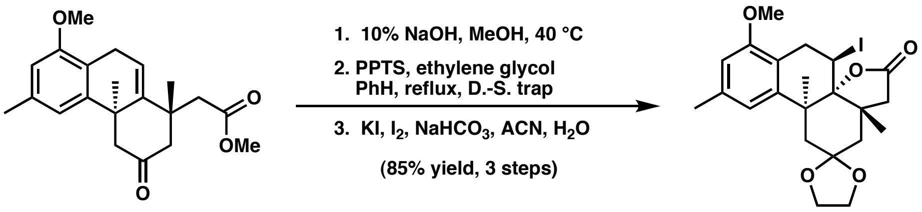
the starting material and the reaction mixture was concentrated *in vacuo*. To a cooled (-12 °C) solution of the crude reaction mixture and pyridine (2.45 mL, 28.8 mmol, 10.0 equiv) in CH_2Cl_2 (50 mL) was added Tf_2O (1.01 mL, 7.20 mmol, 2.50 equiv) in a dropwise manner over 5 min. After 30 min, additional Tf_2O (1.01 mL, 7.20 mmol, 2.50 equiv) was added. After a further 1 h at -12 °C, the reaction mixture was allowed to warm to 0 °C, stirred for 1 h, and quenched with saturated aqueous $NaHCO_3$ (30 mL). The reaction mixture was poured into half saturated aqueous $NaHCO_3$ (60 mL), extracted with CH_2Cl_2 (5 x 30 mL), dried over K_2CO_3, and concentrated to an oil, which was purified by gradient flash chromatography on silica gel (10 to 25% EtOAc in hexanes) to give triflate **19** (1.18 g, 84% yield) as an off-white solid: mp 123-125 °C (decomp.) (benzene); R_f 0.45 (35% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (s, 1H), 6.03 (dd, *J* = 2.0, 6.5 Hz, 1H), 3.82 (s, 3H), 3.67 (s, 3H), 3.66 (dd, *J* = 6.3, 21.0 Hz, 1H), 3.50 (d, *J* = 17.7 Hz, 1H), 3.17 (app. d, *J* = 21.9 Hz, 1H), 3.09 (d, *J* = 17.4 Hz, 1H), 2.91 (d, *J* = 15.3 Hz, 1H), 2.76 (d, *J* = 17.4 Hz, 1H), 2.46 (d, *J* = 15.6 Hz, 1H), 2.34 (s, 3H), 2.33 (d, *J* = 17.4 Hz, 1H), 1.29 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.1, 171.5, 148.5, 146.0, 144.7, 140.0, 129.4, 127.6, 121.9, 119.7, 118.6 (q, $J_{C\text{-}F}$ = 318 Hz), 61.0, 51.5, 49.3, 48.8, 45.9, 39.4, 38.5, 33.1, 30.3, 24.3, 16.5; IR (Neat film NaCl) 2960, 1735, 1715, 1417, 1210, 1138, 1072, 903, 856 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{22}H_{25}SO_7F_3+H]^+$: *m/z* 491.1351, found 491.1363.



19

20

Ketoester 20.[1] A flame-dried 250 mL Schlenk flask was charged with triflate **19** (azeotroped from PhH solution, 1.150 g, 2.34 mmol, 1.00 equiv), $PdCl_2(PPh_3)_2$ (198 mg, 0.282 mmol, 0.12 equiv), 1,4-bis-(diphenylphosphino)pentane (290 mg, 0.704 mmol, 0.30 equiv), DMF (20 mL), *n*-Bu_3N (4.70 mL, 19.7 mmol, 8.40 equiv), and HCOOH (443 μL, 11.7 mmol, 5.00 equiv) under an N_2 atmosphere and heated to 90 °C. After 72 h, the reaction mixture was quenched with H_2O (150 mL) and Et_2O (40 mL), extracted with Et_2O (6 x 50 mL), dried ($MgSO_4$), and concentrated to a residue, which was purified by gradient flash chromatography on silica gel (5 to 10% acetone in hexanes) to give ketoester **20** (735 mg, 92% yield) as a colorless oil: R_f 0.53 (35% acetone in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.68 (s, 1H), 6.57 (s, 1H), 6.04 (dd, *J* = 1.8, 6.3 Hz, 1H), 3.83 (s, 3H), 3.66 (s, 3H), 3.64 (dd, *J* = 6.3, 21.8 Hz, 1H), 3.47 (d, *J* = 17.4 Hz, 1H), 3.14 (d, *J* = 17.7 Hz, 1H), 3.02 (app. d, *J* = 21.6 Hz, 1H), 2.89 (d, *J* = 15.6 Hz, 1H), 2.77 (d, *J* = 17.4 Hz, 1H), 2.46 (d, *J* = 15.6 Hz, 1H), 2.35 (s, 3H), 2.32 (d, *J* = 17.4 Hz, 1H), 1.28 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.2, 171.6, 156.1, 146.0, 144.0, 136.9, 120.8, 119.7, 116.3, 108.4, 55.3, 51.4, 49.6, 49.1, 46.2, 39.2, 38.5, 33.2, 30.9, 24.1, 21.9; IR (Neat film NaCl) 2956, 1735, 1711, 1584, 1462, 1314, 1198, 1134, 1064 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{21}H_{26}O_4+H]^+$: *m/z* 343.1909, found 343.1894.

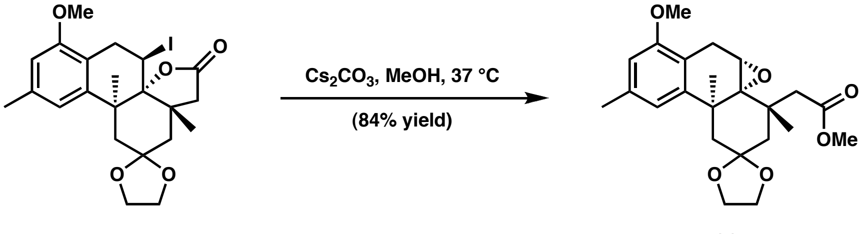


20 ***21***

Iodolactone 21. A solution of ketoester **20** (200 mg, 0.581 mmol, 1.00 equiv) in MeOH (13 mL), and 10% w/v aqueous NaOH (13 mL) was heated at 40 °C for 10 h. The reaction mixture was cooled to ambient temperature, poured into brine (50 mL) and H_2O (10 mL), acidified with 3 M HCl to pH 0, extracted with EtOAc (6 x 20 mL), dried (Na_2SO_4), concentrated, and used in the next step without further purification.

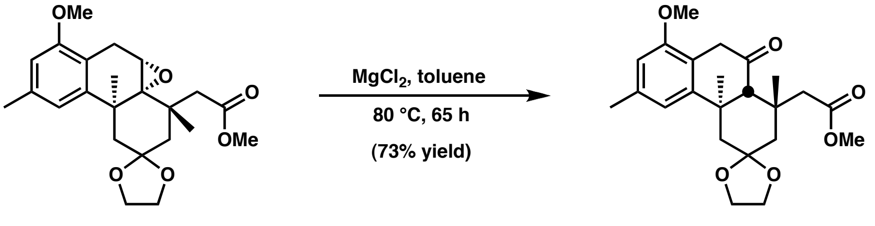
A solution of the above crude carboxylic acid, ethylene glycol (500 μL, 8.97 mmol, 15.4 equiv), and pyridinium *p*-toluenesulfonate (500 mg, 1.99 mmol, 3.42 equiv) in benzene (50 mL) was fitted with a Dean-Stark apparatus and refluxed at 100 °C for 2 h. The cooled (0 °C) reaction mixture was diluted with H_2O (25 mL), brine (25 mL), and CH_2Cl_2 (50 mL), and extracted with CH_2Cl_2 (6 x 30 mL). The combined organics were dried (Na_2SO_4), concentrated, and used immediately in the next step without further purification.

To a solution of the crude ketal and $NaHCO_3$ (68.4 mg, 0.814 mmol, 1.4 equiv) in H_2O (5 mL) and acetonitrile (5 mL) was added KI (125 mg, 0.756 mmol, 1.3 equiv) and I_2 (192 mg, 0.756 mmol, 1.3 equiv). The reaction mixture was stirred in the dark for 30 h and quenched with saturated aqueous $Na_2S_2O_3$ (10 mL), H_2O (20 mL), and brine (20 mL). The reaction mixture was extracted with EtOAc (8 x 20 mL), dried (Na_2SO_4), concentrated, and recrystallized (15% acetone in hexanes, ~25 mL, from 80 to –20 °C) to give iodolactone **21** (247 mg, 85% yield) as a white solid: mp 155-160 °C (decomp.) (acetone/hexanes); R_f 0.37 (35% EtOAc in hexanes); ^1H NMR (500 MHz, C_6D_6) δ 6.92 (s, 1H), 6.22 (s, 1H), 5.29 (app. t, *J* = 10.0 Hz, 1H), 3.75 (dd, *J* = 10.0, 19.3 Hz, 1H), 3.52-3.34 (comp. m, 3H), 3.34-3.26 (comp. m, 2H), 3.24 (s, 3H), 3.01 (d, *J* = 18.0 Hz, 1H), 2.76 (d, *J* = 16.0 Hz, 1H), 2.49 (d, *J* = 16.0 Hz, 1H), 2.45 (d, *J* = 18.0 Hz, 1H), 2.12 (s, 3H), 1.54 (d, *J* = 14.5 Hz, 1H), 1.13 (s, 3H), 0.98 (d, *J* = 14.5 Hz, 1H), 0.95 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 173.5, 156.9, 143.6, 138.1, 121.2, 117.6, 109.4, 107.2, 87.2, 64.5, 64.2, 55.1, 46.1, 45.8, 45.4, 43.2, 42.6, 36.5, 30.9, 30.8, 25.2, 22.2; IR (Neat film NaCl) 2964, 2881, 1790, 1461, 1229, 1203, 1071, 1023 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{22}H_{27}IO_5+H]^+$: *m/z* 499.0982, found 499.0986.



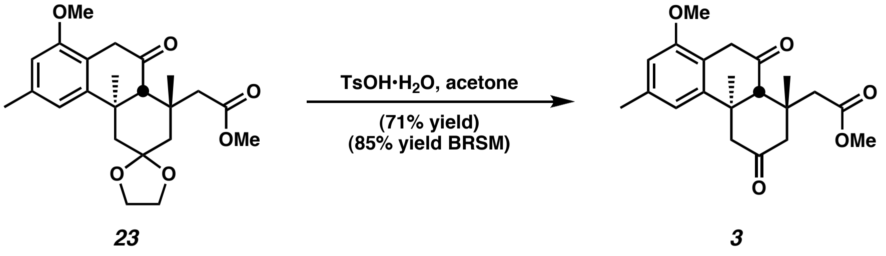
21 22

Epoxide 22. To a solution of iodolactone **21** (75.0 mg, 0.151 mmol, 1.00 equiv) in MeOH (15 mL) was added Cs_2CO_3 (981 mg, 3.01 mmol, 20.0 equiv). The reaction mixture was warmed to 37 °C and vigorously stirred for 19 h. The reaction mixture was cooled to ambient temperature, diluted with H_2O (20 mL), brine (20 mL), and CH_2Cl_2 (20 mL), extracted with CH_2Cl_2 (5 x 20 mL) and EtOAc (5 x 25 mL), dried (Na_2SO_4), and concentrated. The resulting residue was purified by flash chromatography on silica gel (15% EtOAc in hexanes + 1% TEA) to give epoxide **22** (51.0 mg, 84% yield) as a colorless oil: R_f 0.54, 0.28 (35% EtOAc in hexanes, 10% EtOAc in hexanes developed 3 times); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.72 (s, 1H), 6.45 (s, 1H), 4.12-4.08 (m, 1H), 4.06-4.01 (m, 1H), 3.94-3.86 (comp. m, 2H), 3.78 (s, 3H), 3.66 (s, 3H), 3.58 (d, J = 2.5 Hz, 1H), 3.24 (d, J = 19.5 Hz, 1H), 2.90 (dd, J = 3.5, 20.0 Hz, 1H), 2.80 (dd, J = 1.0, 14.5 Hz, 1H), 2.79 (d, J = 14.5 Hz, 1H), 2.37 (d, J = 14.0 Hz, 1H), 2.31 (dd, J = 1.0, ~15 Hz, 1H), 2.30 (s, 3H), 2.03 (d, J = 15.0 Hz, 1H), 1.72 (d, J = 15.0 Hz, 1H), 1.63 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 172.8, 157.5, 144.9, 136.6, 120.4, 116.1, 108.9, 108.2, 65.7, 64.8, 63.7, 57.1, 55.2, 51.1, 48.8, 43.4, 41.7, 39.7, 38.3, 27.5, 26.7, 24.4, 22.2; IR (Neat film NaCl) 2950, 1734, 1590, 1462, 1360, 1196, 1135, 1075, 1017 cm^{-1}; HRMS (FAB) $[M+H]^+$ calc'd for $[C_{23}H_{30}O_6+H]^+$: m/z 403.2121, found 403.2113.

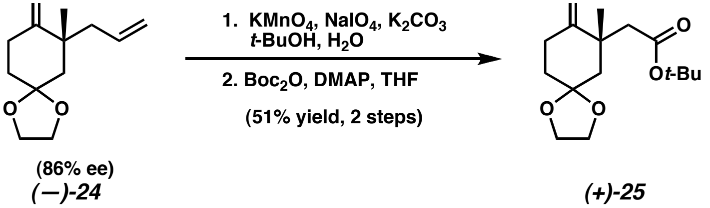


22 23

Ketone 23. A solution of epoxide **22** (49.0 mg, 0.122 mmol, 1.00 equiv) in toluene (30 mL) in a flame-dried Schlenk flask under an N_2 atmosphere was treated with magnesium chloride (2.00 g, 21.0 mmol, 172 equiv) and heated to 80 °C for 65 h. After cooling to ambient temperature, the reaction mixture was filtered and the filter cake was washed with toluene (2 x 25 mL). The filter cake was partitioned between EtOAc (20 mL) and ice cold water (20 mL), and further extracted with EtOAc (3 x 20 mL). The combined organics were dried (Na_2SO_4), and concentrated to an oil, which was purified by gradient flash chromatography on silica gel (10 to 20% EtOAc in hexanes) to give ketone **23** (36.0 mg, 73% yield) as a colorless oil: R_f 0.55, 0.33 (35% EtOAc in hexanes, 10% EtOAc in hexanes developed 3 times); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.73 (s, 1H), 6.57 (s, 1H), 4.15-4.05 (m, 2H), 4.00-3.88 (m, 2H), 3.80 (s, 3H), 3.67 (s, 3H), 3.64 (d, J = 22.5 Hz, 1H), 3.47 (dd, J = 1.5, 14.5 Hz, 1H), 3.34 (d, J = 22.0 Hz, 1H), 3.23 (d, J = 14.5 Hz, 1H), 2.58 (dd, J = 2.5, 14.5 Hz, 1H), 2.56 (s, 1H), 2.45 (dd, J = 2.5, 13.5 Hz, 1H), 2.35 (s, 3H), 2.13 (d, J = 13.0 Hz, 1H), 1.30 (s, 3H), 1.21 (s, 3H), 1.14 (dd, J = 1.5, 14.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.0, 173.9, 156.4, 149.4, 137.6, 117.3, 116.1, 108.7, 108.3, 65.2, 63.0, 62.8, 55.3, 50.9, 46.4, 42.5, 42.3, 40.0, 36.0, 35.6, 28.9, 25.6, 21.9; IR (Neat film NaCl) 2953, 2885, 1731, 1713, 1586, 1462, 1360, 1193, 1065 cm^{-1}; HRMS (EI) $[M]^+$ calc'd for $[C_{23}H_{30}O_6]^+$: m/z 402.2042, found 402.2027.

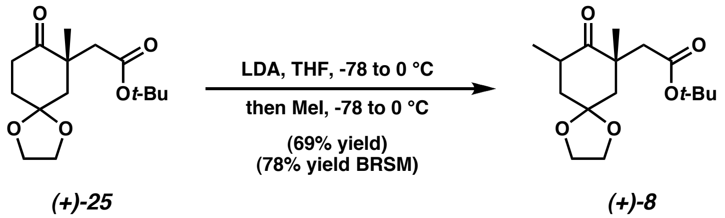


Diketone 3. A solution of ketone **23** (29.3 mg, 0.728 mmol, 1.00 equiv) in acetone (10 mL) was treated with TsOH•H_2O (100 mg, 0.526 mmol, 7.22 equiv) and stirred at ambient temperature for 4 h. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (25 mL), extracted with CH_2Cl_2 (6 x 15 mL), dried (Na_2SO_4), and concentrated to an oil, which was purified by gradient flash chromatography on silica gel (7.5 to 12.5% EtOAc in hexanes) to give starting ketone **23** (4.6 mg, 16% yield) and diketone **3** (18.6 mg, 71% yield) as a white solid. Crystals suitable for X-ray analysis were obtained by crystallization from acetone/heptanes at ambient temperature: mp 184-186 °C (acetone/heptanes); R_f 0.40 (35% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.61 (s, 1H), 6.59 (s, 1H), 3.82 (s, 3H), 3.71 (d, J = 22.0 Hz, 1H), 3.69 (s, 3H), 3.46 (dd, J = 1.5, 14.5 Hz, 1H), 3.39 (d, J = 22.5 Hz, 1H), 3.08 (s, 1H), 2.99 (dd, J = 2.3, 12.8 Hz, 1H), 2.93 (dd, J = 2.3, 12.8 Hz, 1H), 2.89 (d, J = 12.5 Hz, 1H), 2.36 (s, 3H), 2.33 (d, J = 14.5 Hz, 1H), 2.21 (d, J = 12.5 Hz, 1H), 1.36 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.7, 207.8, 171.9, 156.6, 147.6, 138.2, 117.1, 115.5, 109.3, 62.7, 55.4, 53.6, 52.2, 51.4, 45.7, 40.1, 39.5, 37.6, 28.0, 26.6, 21.9; IR (Neat film NaCl) 2953, 1732, 1713, 1586, 1462, 1331, 1194, 1063, 731 cm^{-1}; HRMS (EI) $[M]^+$ calc'd for $[C_{21}H_{26}O_5]^+$: m/z 358.1780, found 358.1774.



***(+)-t*-Butyl Ester 25**.[2] A solution of ketone *(–)*-**24** (1.00 g, 4.76 mmol, 1.00 equiv) and K_2CO_3 (987 mg, 7.14 mmol, 1.5 equiv) in *t*-BuOH (60 mL) was treated (slight exotherm) with a premixed (30 min) solution of $NaIO_4$ (8.14 g, 38.1 mmol, 8.00 equiv) and $KMnO_4$ (113 mg, 0.714 mmol, 0.15 equiv) in H_2O (100 mL) and stirred in a room temperature bath for 3 h. The reaction mixture was diluted with CH_2Cl_2 (100 mL) and H_2O (100 mL), extracted with CH_2Cl_2 (6 x 50 mL), dried ($MgSO_4$), and concentrated to an oil, which was used immediately in the next step.

A solution of the above crude carboxylic acid in THF (40 mL) was treated with Boc_2O (3.40 g, 15.6 mmol, 3.27 equiv) and DMAP (200 mg, 1.64 mmol, 0.344 equiv). After 12 h, additional Boc_2O (2.00 g, 9.16 mmol, 1.93 equiv) and DMAP (175 mg, 1.43 mmol, 0.30 equiv) were added, and the reaction was stirred for a further 3 h. The reaction mixture was concentrated and purified by gradient flash chromatography on silica gel (5 to 25% Et_2O in hexanes) to give *(+)-t*-butyl ester **25** (688 mg, 51% yield) as a colorless oil: R_f 0.27 (10% EtOAc in hexanes developed 2 times); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.03-3.94 (comp. m, 4H), 2.70 (d, *J* = 15.9 Hz, 1H), 2.63 (d, *J* = 6.6 Hz, 1H), 2.60 (d, *J* = 6.0 Hz, 1H), 2.49 (d, *J* = 15.9 Hz, 1H), 2.22 (dd, *J* = 1.4, 14.0 Hz, 1H), 2.20-2.08 (m, 1H), 2.04-1.92 (m, 1H), 1.78 (dd, *J* = 2.4, 14.1 Hz, 1H), 1.40 (s, 9H), 1.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.7, 170.7, 107.6, 80.7, 64.4, 64.2, 46.0, 44.7, 44.5, 35.6, 33.9, 28.0, 25.1; IR (Neat film NaCl) 2976, 2935, 2885, 1725, 1714, 1368, 1157, 1120, 1074 cm^{-1}; HRMS (EI) $[M]^+$ calc'd for $[C_{15}H_{24}O_5]^+$: *m/z* 284.1624, found 284.1633; $[\alpha]_D^{26}$ +45.63 (c 1.89, CH_2Cl_2, 86% ee).



Methyl ketones 8a and 8b. A solution of LDA in THF was prepared by dropwise addition of 2.45 M *n*-BuLi solution in hexanes (787 µL, 1.93 mmol, 1.4 equiv) to diisopropylamine (290 µL, 2.07 mmol, 1.5 equiv) in THF (20.7 mL) at 0 °C, followed by stirring for 1 h. Upon cooling the solution to -78 °C, a solution of *(+)-t*-butyl ester **25** (392 mg, 1.38 mmol, 1.00 equiv) in THF (2.00 mL) was added in a dropwise manner, and the reaction mixture was stirred at -78 °C for 1 h, then 0 °C for 1 h. After cooling again to –78 °C, the reaction mixture was treated with MeI (258 µL, 4.13 mmol, 3.00 equiv), allowed to warm to ambient temperature slowly over 5 h, and stirred for an additional 12 h at ambient temperature. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (6 x 30 mL), dried ($MgSO_4$), and concentrated to an oil, which was purified by gradient flash chromatography on silica gel (3 to 10% EtOAc in hexanes) to give diastereomeric methyl ketones **8a** and **8b** (284 mg, 69% combined yield) as colorless oils and recovered *t*-butyl ester **25** (43.2 mg, 11% yield). High R_f diastereomer **8a**: R_f 0.43 (10% EtOAc in hexanes developed 2 times); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.10-3.90 (comp. m, 4H), 2.89 (app. d of sept., *J* = 1.2, 6.6 Hz, 1H), 2.73 (d, *J* = 16.5 Hz, 1H), 2.36 (d, *J* = 13.8 Hz, 1H), 2.16 (d, *J* = 16.2 Hz, 1H), 2.06-1.96 (comp. m, 1H), 1.93 (d, *J* = 13.5 Hz, 1H), 1.85 (dd, *J* = 3.3, 13.8 Hz, 1H), 1.42 (s, 9H), 1.29 (s, 3H), 1.07 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.0, 170.9, 107.5, 80.4, 64.6, 64.0, 46.0, 44.5, 44.3, 41.9, 38.0, 28.1, 26.4, 14.7; IR (Neat film NaCl) 2976, 2932, 2880, 1726, 1710, 1367, 1146, 1080 cm^{-1}; HRMS (EI) $[M]^+$ calc'd for $[C_{16}H_{26}O_5]^+$: *m/z* 298.1780, found 298.1791; $[\alpha]_D^{26}$ +45.13 (c 1.06, CH_2Cl_2, 86% ee). Low R_f diastereomer **8b**: R_f 0.32 (10% EtOAc in hexanes developed 2 times);

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.10-3.85 (comp. m, 4H), 3.21 (d, *J* = 14.7 Hz, 1H), 3.09 (app. d of sept., *J* = 1.5, 6.6 Hz, 1H), 2.32 (d, *J* = 14.4 Hz, 1H), 2.14-2.00 (comp. m, 2H), 1.76 (d, *J* = 14.7 Hz, 1H), 1.68 (app. t, *J* = 14.0 Hz, 1H), 1.36 (s, 9H), 1.08 (s, 3H), 1.03 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.8, 170.4, 107.2, 80.8, 64.6, 64.0, 46.8, 46.1, 45.2, 43.9, 37.7, 27.9, 23.0, 14.4; IR (Neat film NaCl) 2976, 2933, 2884, 1726, 1717, 1457, 1367, 1232, 1160, 1141, 1084, 979 cm^{-1}; HRMS (EI) $[M]^+$ calc'd for $[C_{16}H_{26}O_5]^+$: *m/z* 298.1780, found 298.1775; $[\alpha]_D^{26}$ –25.44 (c 1.17, CH_2Cl_2, 86% ee).

CALIFORNIA INSTITUTE OF TECHNOLOGY

BECKMAN INSTITUTE
X-RAY CRYSTALLOGRAPHY LABORATORY

Crystal Structure Analysis of:

Lactone 16 (DCB06)

(CCDC 175859)

Contents:

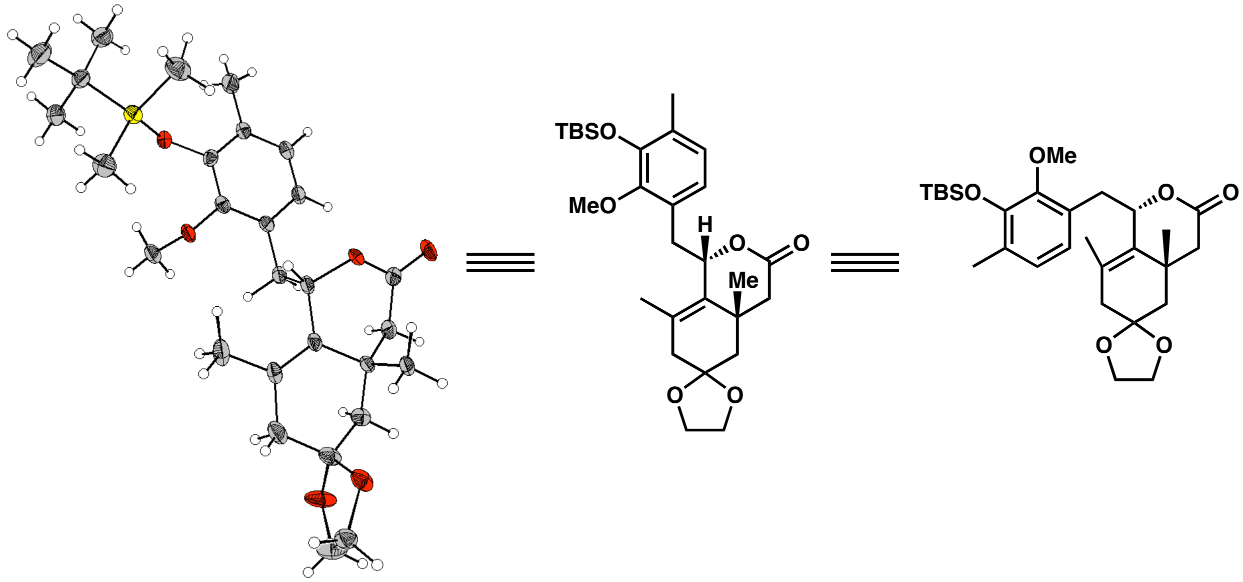


Table 1. Crystal data and structure refinement for DCB06_(CCDC_175859).

Empirical formula	$C_{28}H_{42}O_6Si$
Formula weight	502.71
Crystallization Solvent	Hexanes
Crystal Habit	Block
Crystal size	0.33 x 0.17 x 0.14 mm^3
Crystal color	Colorless

Data Collection

Type of diffractometer	Bruker P4	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	96(2) K	
θ range for 8201 reflections used in lattice determination	2.79 to 26.49°	
Unit cell dimensions	a = 29.220(3) Å	
	b = 6.7215(8) Å	β= 90.035(2)°
	c = 14.4249(17) Å	
Volume	2833.0(6) Å^3	
Z	4	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Density (calculated)	1.179 Mg/m^3	
F(000)	1088	
Data collection program	Bruker SMART v5.054	
θ range for data collection	1.39 to 28.38°	
Completeness to θ = 28.38°	93.9 %	
Index ranges	$-37 \leq h \leq 38, -8 \leq k \leq 8, -19 \leq l \leq 19$	
Data collection scan type	ω scans at 5 ϕ settings	
Data reduction program	Bruker SAINT v6.22	
Reflections collected	38935	
Independent reflections	6656 [R_{int}= 0.0985]	
Absorption coefficient	0.120 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.9829 and 0.9610	

Table 1 (cont.)

Structure solution and Refinement

Structure solution program	Bruker SHELXTL
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	Bruker SHELXTL
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	6656 / 0 / 484
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.403
Final R indices [$I>2\sigma(I)$, 3988 reflections]	R1 = 0.0584, *w*R2 = 0.0804
R indices (all data)	R1 = 0.1062, *w*R2 = 0.0844
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.001
Average shift/error	0.000
Largest diff. peak and hole	0.333 and -0.349 e.Å^{-3}

Special Refinement Details

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for DCB06_(CCDC_175859). U(eq) the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Si(1)	6142(1)	3545(1)	4087(1)	25(1)
O(1)	6571(1)	5169(2)	4135(1)	23(1)
O(2)	7293(1)	2606(2)	3725(1)	23(1)
O(3)	8211(1)	1108(2)	6169(1)	28(1)
O(4)	8640(1)	2202(2)	7317(1)	44(1)
O(5)	9414(1)	-4435(2)	4438(1)	30(1)
O(6)	9725(1)	-2363(2)	3364(1)	45(1)
C(1)	5665(1)	5006(3)	3527(1)	27(1)
C(2)	5841(1)	5905(4)	2608(2)	35(1)
C(3)	5260(1)	3633(5)	3329(2)	43(1)
C(4)	5503(1)	6694(4)	4154(2)	36(1)
C(5)	6282(1)	1358(4)	3362(2)	34(1)
C(6)	5995(1)	2734(5)	5291(2)	39(1)
C(7)	6962(1)	5171(3)	4672(1)	21(1)
C(8)	6990(1)	6481(3)	5429(1)	24(1)
C(9)	6595(1)	7823(4)	5660(2)	37(1)
C(10)	7397(1)	6526(4)	5928(1)	27(1)
C(11)	7762(1)	5352(3)	5700(1)	26(1)
C(12)	7740(1)	4049(3)	4942(1)	22(1)
C(13)	7334(1)	3973(3)	4446(1)	20(1)
C(14)	7349(1)	3475(4)	2815(1)	32(1)
C(15)	8145(1)	2785(3)	4670(1)	22(1)
C(16)	8169(1)	761(3)	5164(1)	22(1)
C(17)	8623(1)	1598(3)	6522(1)	28(1)
C(18)	9030(1)	1238(4)	5922(2)	26(1)
C(19)	8979(1)	-684(3)	5354(1)	19(1)
C(20)	8948(1)	-2437(4)	6036(1)	24(1)
C(21)	9394(1)	-899(3)	4715(1)	24(1)
C(22)	9349(1)	-2544(3)	4006(1)	28(1)
C(23)	9638(1)	-5668(3)	3767(2)	29(1)
C(24)	9927(1)	-4215(4)	3241(2)	39(1)
C(25)	8901(1)	-2427(4)	3480(2)	33(1)
C(26)	8502(1)	-1441(3)	3960(1)	24(1)
C(27)	8074(1)	-1401(5)	3388(2)	35(1)
C(28)	8545(1)	-548(3)	4787(1)	19(1)

Table 3. Bond lengths [Å] and angles [°] for DCB06_(CCDC_175859).

Si(1)-O(1)	1.6629(15)	C(16)-C(28)	1.510(3)
Si(1)-C(5)	1.849(3)	C(16)-H(16)	0.995(16)
Si(1)-C(6)	1.872(2)	C(17)-C(18)	1.490(3)
Si(1)-C(1)	1.887(2)	C(18)-C(19)	1.538(3)
O(1)-C(7)	1.379(2)	C(18)-H(18A)	0.96(2)
O(2)-C(13)	1.392(2)	C(18)-H(18B)	0.96(2)
O(2)-C(14)	1.446(2)	C(19)-C(28)	1.512(3)
O(3)-C(17)	1.350(2)	C(19)-C(21)	1.531(3)
O(3)-C(16)	1.473(2)	C(19)-C(20)	1.538(3)
O(4)-C(17)	1.218(2)	C(20)-H(20A)	0.987(19)
O(5)-C(22)	1.428(2)	C(20)-H(20B)	1.016(18)
O(5)-C(23)	1.433(2)	C(20)-H(20C)	1.003(19)
O(6)-C(24)	1.389(3)	C(21)-C(22)	1.512(3)
O(6)-C(22)	1.443(2)	C(21)-H(21A)	0.99(2)
C(1)-C(4)	1.527(3)	C(21)-H(21B)	0.99(2)
C(1)-C(3)	1.528(3)	C(22)-C(25)	1.516(3)
C(1)-C(2)	1.545(3)	C(23)-C(24)	1.498(3)
C(2)-H(2A)	1.05(2)	C(23)-H(23A)	0.98(2)
C(2)-H(2B)	0.99(2)	C(23)-H(23B)	0.940(19)
C(2)-H(2C)	1.00(2)	C(24)-H(24A)	0.86(3)
C(3)-H(3A)	0.98(2)	C(24)-H(24B)	0.97(3)
C(3)-H(3B)	0.95(2)	C(25)-C(26)	1.509(3)
C(3)-H(3C)	1.04(2)	C(25)-H(25A)	0.99(2)
C(4)-H(4A)	0.99(2)	C(25)-H(25B)	0.98(2)
C(4)-H(4B)	0.99(2)	C(26)-C(28)	1.340(2)
C(4)-H(4C)	0.99(2)	C(26)-C(27)	1.498(3)
C(5)-H(5A)	0.97(2)	C(27)-H(27A)	0.95(2)
C(5)-H(5B)	1.01(2)	C(27)-H(27B)	0.97(2)
C(5)-H(5C)	0.98(2)	C(27)-H(27C)	1.06(2)
C(6)-H(6A)	1.03(3)		
C(6)-H(6B)	0.98(3)	O(1)-Si(1)-C(5)	112.26(10)
C(6)-H(6C)	0.98(2)	O(1)-Si(1)-C(6)	109.05(11)
C(7)-C(13)	1.392(3)	C(5)-Si(1)-C(6)	110.16(13)
C(7)-C(8)	1.405(3)	O(1)-Si(1)-C(1)	103.44(9)
C(8)-C(10)	1.389(3)	C(5)-Si(1)-C(1)	109.60(11)
C(8)-C(9)	1.503(3)	C(6)-Si(1)-C(1)	112.21(11)
C(9)-H(9A)	1.02(2)	C(7)-O(1)-Si(1)	130.34(12)
C(9)-H(9B)	0.92(2)	C(13)-O(2)-C(14)	113.73(17)
C(9)-H(9C)	0.95(2)	C(17)-O(3)-C(16)	118.89(15)
C(10)-C(11)	1.369(3)	C(22)-O(5)-C(23)	106.28(14)
C(10)-H(10)	0.98(2)	C(24)-O(6)-C(22)	109.25(17)
C(11)-C(12)	1.403(3)	C(4)-C(1)-C(3)	108.6(2)
C(11)-H(11)	0.965(19)	C(4)-C(1)-C(2)	108.7(2)
C(12)-C(13)	1.388(3)	C(3)-C(1)-C(2)	109.5(2)
C(12)-C(15)	1.508(3)	C(4)-C(1)-Si(1)	111.25(15)
C(14)-H(14A)	0.99(2)	C(3)-C(1)-Si(1)	109.77(18)
C(14)-H(14B)	1.00(2)	C(2)-C(1)-Si(1)	108.96(15)
C(14)-H(14C)	1.05(2)	C(1)-C(2)-H(2A)	113.2(11)
C(15)-C(16)	1.538(3)	C(1)-C(2)-H(2B)	109.5(13)
C(15)-H(15A)	1.047(18)	H(2A)-C(2)-H(2B)	106.4(17)
C(15)-H(15B)	0.950(18)	C(1)-C(2)-H(2C)	108.6(12)

H(2A)-C(2)-H(2C)	108.2(18)
H(2B)-C(2)-H(2C)	110.9(18)
C(1)-C(3)-H(3A)	110.1(14)
C(1)-C(3)-H(3B)	110.8(14)
H(3A)-C(3)-H(3B)	108.4(19)
C(1)-C(3)-H(3C)	113.7(12)
H(3A)-C(3)-H(3C)	108.5(18)
H(3B)-C(3)-H(3C)	105.0(19)
C(1)-C(4)-H(4A)	109.9(14)
C(1)-C(4)-H(4B)	112.8(12)
H(4A)-C(4)-H(4B)	110.7(17)
C(1)-C(4)-H(4C)	115.2(12)
H(4A)-C(4)-H(4C)	104.1(17)
H(4B)-C(4)-H(4C)	103.8(18)
Si(1)-C(5)-H(5A)	113.1(14)
Si(1)-C(5)-H(5B)	112.4(13)
H(5A)-C(5)-H(5B)	108(2)
Si(1)-C(5)-H(5C)	110.5(14)
H(5A)-C(5)-H(5C)	106.6(19)
H(5B)-C(5)-H(5C)	106.0(18)
Si(1)-C(6)-H(6A)	110.3(13)
Si(1)-C(6)-H(6B)	114.0(13)
H(6A)-C(6)-H(6B)	107(2)
Si(1)-C(6)-H(6C)	107.1(13)
H(6A)-C(6)-H(6C)	111.0(19)
H(6B)-C(6)-H(6C)	108(2)
O(1)-C(7)-C(13)	120.97(17)
O(1)-C(7)-C(8)	119.01(17)
C(13)-C(7)-C(8)	119.93(18)
C(10)-C(8)-C(7)	117.79(19)
C(10)-C(8)-C(9)	121.9(2)
C(7)-C(8)-C(9)	120.24(19)
C(8)-C(9)-H(9A)	109.2(13)
C(8)-C(9)-H(9B)	112.5(13)
H(9A)-C(9)-H(9B)	111.6(18)
C(8)-C(9)-H(9C)	112.0(13)
H(9A)-C(9)-H(9C)	106.5(18)
H(9B)-C(9)-H(9C)	104.8(19)
C(11)-C(10)-C(8)	122.0(2)
C(11)-C(10)-H(10)	120.2(12)
C(8)-C(10)-H(10)	117.8(12)
C(10)-C(11)-C(12)	120.8(2)
C(10)-C(11)-H(11)	120.4(11)
C(12)-C(11)-H(11)	118.8(11)
C(13)-C(12)-C(11)	117.63(19)
C(13)-C(12)-C(15)	121.07(18)
C(11)-C(12)-C(15)	121.30(19)
C(12)-C(13)-C(7)	121.79(18)
C(12)-C(13)-O(2)	118.78(17)
C(7)-C(13)-O(2)	119.39(17)
O(2)-C(14)-H(14A)	107.7(11)
O(2)-C(14)-H(14B)	103.7(13)
H(14A)-C(14)-H(14B)	111.7(17)
O(2)-C(14)-H(14C)	109.9(11)
H(14A)-C(14)-H(14C)	108.8(17)
H(14B)-C(14)-H(14C)	114.6(17)
C(12)-C(15)-C(16)	114.35(16)
C(12)-C(15)-H(15A)	112.3(10)
C(16)-C(15)-H(15A)	104.7(10)
C(12)-C(15)-H(15B)	109.6(11)
C(16)-C(15)-H(15B)	108.4(11)
H(15A)-C(15)-H(15B)	107.1(14)
O(3)-C(16)-C(28)	112.77(15)
O(3)-C(16)-C(15)	108.69(16)
C(28)-C(16)-C(15)	112.34(16)
O(3)-C(16)-H(16)	101.4(9)
C(28)-C(16)-H(16)	113.5(10)
C(15)-C(16)-H(16)	107.4(10)
O(4)-C(17)-O(3)	118.11(19)
O(4)-C(17)-C(18)	124.7(2)
O(3)-C(17)-C(18)	117.06(17)
C(17)-C(18)-C(19)	111.65(18)
C(17)-C(18)-H(18A)	109.4(12)
C(19)-C(18)-H(18A)	112.2(12)
C(17)-C(18)-H(18B)	111.5(11)
C(19)-C(18)-H(18B)	111.1(12)
H(18A)-C(18)-H(18B)	100.5(16)
C(28)-C(19)-C(21)	110.20(15)
C(28)-C(19)-C(18)	108.56(17)
C(21)-C(19)-C(18)	108.89(16)
C(28)-C(19)-C(20)	110.06(16)
C(21)-C(19)-C(20)	111.11(17)
C(18)-C(19)-C(20)	107.94(16)
C(19)-C(20)-H(20A)	111.0(10)
C(19)-C(20)-H(20B)	108.3(10)
H(20A)-C(20)-H(20B)	107.8(14)
C(19)-C(20)-H(20C)	110.5(11)
H(20A)-C(20)-H(20C)	104.4(15)
H(20B)-C(20)-H(20C)	114.8(14)
C(22)-C(21)-C(19)	113.99(17)
C(22)-C(21)-H(21A)	107.4(12)
C(19)-C(21)-H(21A)	112.5(11)
C(22)-C(21)-H(21B)	107.6(10)
C(19)-C(21)-H(21B)	110.2(10)
H(21A)-C(21)-H(21B)	104.7(16)
O(5)-C(22)-O(6)	104.75(15)
O(5)-C(22)-C(21)	110.15(16)
O(6)-C(22)-C(21)	107.79(17)
O(5)-C(22)-C(25)	112.29(19)
O(6)-C(22)-C(25)	109.41(17)
C(21)-C(22)-C(25)	112.09(19)
O(5)-C(23)-C(24)	102.91(18)
O(5)-C(23)-H(23A)	110.8(11)
C(24)-C(23)-H(23A)	113.5(12)
O(5)-C(23)-H(23B)	109.3(12)
C(24)-C(23)-H(23B)	112.7(12)
H(23A)-C(23)-H(23B)	107.6(17)
O(6)-C(24)-C(23)	106.3(2)

O(6)-C(24)-H(24A)	111(2)
C(23)-C(24)-H(24A)	121(2)
O(6)-C(24)-H(24B)	107.4(15)
C(23)-C(24)-H(24B)	109.6(15)
H(24A)-C(24)-H(24B)	101(2)
C(26)-C(25)-C(22)	117.35(18)
C(26)-C(25)-H(25A)	105.2(13)
C(22)-C(25)-H(25A)	103.6(13)
C(26)-C(25)-H(25B)	109.0(12)
C(22)-C(25)-H(25B)	108.3(12)
H(25A)-C(25)-H(25B)	113.4(18)
C(28)-C(26)-C(27)	124.0(2)
C(28)-C(26)-C(25)	122.27(19)
C(27)-C(26)-C(25)	113.50(18)
C(26)-C(27)-H(27A)	111.8(14)
C(26)-C(27)-H(27B)	110.0(13)
H(27A)-C(27)-H(27B)	108.2(19)
C(26)-C(27)-H(27C)	118.2(11)
H(27A)-C(27)-H(27C)	102.5(18)
H(27B)-C(27)-H(27C)	105.5(18)
C(26)-C(28)-C(16)	120.96(18)
C(26)-C(28)-C(19)	122.09(18)
C(16)-C(28)-C(19)	116.83(16)

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Table 4. Anisotropic displacement parameters ($Å^2 x 10^4$) for DCB06_(CCDC_175859). The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [$h^2 a^{*2}U^{11}$ + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	252(3)	279(4)	224(3)	4(3)	10(3)	-5(3)
O(1)	223(8)	280(9)	195(7)	-17(6)	-35(6)	7(6)
O(2)	277(8)	286(9)	134(7)	-31(6)	-19(6)	-16(7)
O(3)	292(9)	444(10)	110(7)	15(7)	31(6)	67(7)
O(4)	623(12)	535(12)	148(8)	-121(7)	-86(7)	211(9)
O(5)	483(10)	221(9)	186(7)	34(7)	67(7)	24(7)
O(6)	607(11)	324(10)	426(9)	130(8)	373(8)	165(8)
C(1)	206(12)	327(14)	273(12)	19(10)	-8(10)	-14(10)
C(2)	339(16)	452(18)	257(13)	51(12)	-44(12)	55(14)
C(3)	243(15)	500(19)	547(18)	-31(17)	-58(13)	-29(14)
C(4)	287(15)	436(17)	370(15)	43(13)	11(12)	69(14)
C(5)	344(16)	311(15)	366(15)	-48(12)	17(12)	-74(14)
C(6)	465(18)	396(17)	313(14)	73(13)	77(13)	51(15)
C(7)	190(12)	250(13)	199(11)	50(9)	-14(9)	-7(10)
C(8)	254(12)	283(13)	190(10)	6(10)	-4(9)	29(10)
C(9)	400(17)	389(17)	309(15)	-133(14)	-63(12)	122(14)
C(10)	315(14)	336(14)	170(11)	-59(11)	-37(10)	-4(11)
C(11)	274(14)	329(14)	165(11)	3(10)	-41(10)	-10(11)
C(12)	225(12)	279(13)	143(10)	36(9)	23(9)	1(9)
C(13)	237(12)	217(13)	151(10)	13(9)	9(9)	-59(10)
C(14)	336(16)	453(16)	160(11)	-4(12)	-1(10)	-19(14)
C(15)	208(13)	273(13)	170(11)	13(10)	-15(9)	-33(10)
C(16)	202(12)	323(14)	128(10)	10(9)	-18(9)	-19(10)
C(17)	328(14)	308(14)	207(11)	3(10)	-45(10)	114(11)
C(18)	266(14)	297(15)	202(11)	-55(11)	-68(10)	5(11)
C(19)	191(11)	245(12)	126(10)	-11(9)	3(8)	-18(9)
C(20)	228(14)	356(15)	125(11)	21(11)	-11(10)	15(11)
C(21)	253(13)	218(14)	240(12)	33(10)	54(10)	-15(10)
C(22)	378(14)	250(13)	209(11)	52(10)	128(10)	45(11)
C(23)	364(15)	201(13)	292(13)	-18(11)	14(12)	51(12)
C(24)	351(17)	247(15)	576(18)	-68(13)	127(15)	-24(12)
C(25)	501(16)	330(16)	164(12)	6(12)	1(11)	53(13)
C(26)	318(13)	239(12)	150(10)	21(10)	-44(9)	-16(10)
C(27)	458(17)	310(16)	269(13)	-22(13)	-157(12)	-2(13)
C(28)	208(12)	244(13)	125(10)	42(9)	2(9)	-23(9)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10 ^{3}) for DCB06_(CCDC_175859).

	x	y	z	U_{iso}
H(2A)	6133(7)	6800(30)	2693(13)	38(6)
H(2B)	5928(7)	4820(40)	2180(15)	49(7)
H(2C)	5594(8)	6750(40)	2334(15)	49(7)
H(3A)	5005(8)	4400(40)	3059(15)	54(8)
H(3B)	5343(7)	2620(40)	2906(15)	47(8)
H(3C)	5141(7)	2890(30)	3909(15)	48(7)
H(4A)	5371(7)	6140(40)	4734(15)	53(7)
H(4B)	5749(7)	7660(30)	4298(13)	29(6)
H(4C)	5256(7)	7520(30)	3897(14)	38(6)
H(5A)	6544(8)	620(40)	3588(15)	55(8)
H(5B)	6018(8)	410(40)	3306(15)	53(7)
H(5C)	6356(8)	1770(40)	2728(16)	53(7)
H(6A)	5864(8)	3910(40)	5662(16)	68(8)
H(6B)	5767(8)	1660(40)	5317(15)	60(8)
H(6C)	6278(8)	2230(30)	5577(15)	50(7)
H(9A)	6319(8)	6970(30)	5851(14)	47(7)
H(9B)	6667(7)	8740(30)	6106(14)	36(7)
H(9C)	6499(7)	8590(30)	5140(16)	48(7)
H(10)	7416(7)	7440(30)	6454(14)	36(6)
H(11)	8045(6)	5450(30)	6044(12)	27(6)
H(14A)	7663(7)	4000(30)	2774(12)	28(6)
H(14B)	7302(7)	2330(40)	2385(15)	49(7)
H(14C)	7118(7)	4650(30)	2727(13)	39(6)
H(15A)	8144(6)	2430(30)	3962(13)	27(5)
H(15B)	8421(6)	3490(30)	4792(11)	16(5)
H(16)	7859(6)	150(20)	5125(10)	8(4)
H(18A)	9081(6)	2380(30)	5535(13)	31(6)
H(18B)	9308(7)	1230(30)	6276(13)	31(6)
H(20A)	8897(6)	-3700(30)	5704(12)	18(5)
H(20B)	9252(6)	-2550(30)	6377(12)	21(5)
H(20C)	8673(7)	-2290(30)	6446(12)	26(5)
H(21A)	9683(7)	-1130(30)	5063(13)	34(6)
H(21B)	9448(6)	360(30)	4373(12)	24(5)
H(23A)	9815(7)	-6710(30)	4072(13)	34(6)
H(23B)	9417(6)	-6290(30)	3393(13)	24(6)
H(24A)	9995(11)	-4420(50)	2670(20)	112(14)
H(24B)	10229(9)	-4160(40)	3514(16)	64(9)
H(25A)	8972(7)	-1560(30)	2948(15)	51(7)
H(25B)	8812(7)	-3770(30)	3298(14)	39(7)
H(27A)	8088(8)	-420(40)	2917(16)	56(8)
H(27B)	8027(7)	-2690(40)	3096(15)	48(7)
H(27C)	7762(7)	-1060(30)	3722(13)	43(7)

CALIFORNIA INSTITUTE OF TECHNOLOGY

BECKMAN INSTITUTE
X-RAY CRYSTALLOGRAPHY LABORATORY

Crystal Structure Analysis of:

Acid 15•CHCl$_3$ (DCB05)

(CCDC 175588)

Contents:

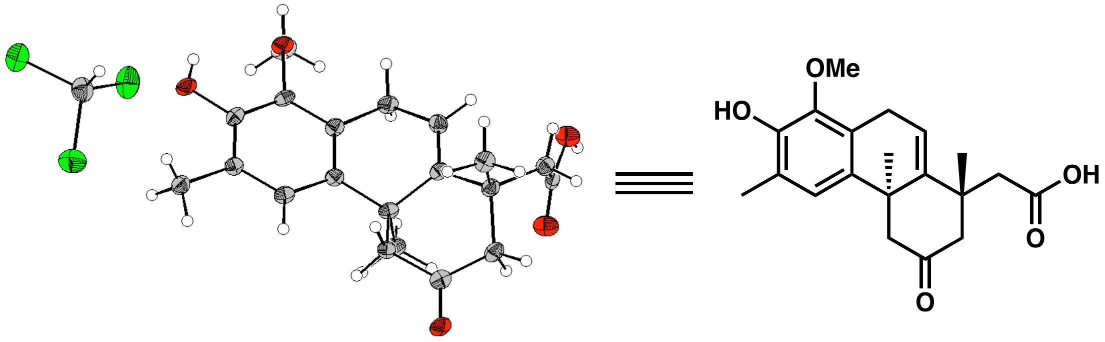

Table 1. Crystal data and structure refinement for DCB05 (CCDC 175588).

Empirical formula	$C_{20}H_{24}O_5 \cdot CHCl_3$
Formula weight	463.76
Crystallization Solvent	Chloroform
Crystal Habit	Fragment
Crystal size	0.22 x 0.15 x 0.15 mm^3
Crystal color	Colorless

Data Collection

Preliminary Photos	Rotation	
Type of diffractometer	Bruker SMART 1000	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	98(2) K	
θ range for 4336 reflections used in lattice determination	2.47 to 25.80°	
Unit cell dimensions	a = 11.137(3) Å b = 13.282(3) Å c = 15.008(4) Å	 β= 98.762(4)°
Volume	2194.3(10) Å^3	
Z	4	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Density (calculated)	1.404 Mg/m^3	
F(000)	968	
Data collection program	Bruker SMART v5.054	
θ range for data collection	2.06 to 28.36°	
Completeness to θ = 28.36°	93.7 %	
Index ranges	$-14 \le h \le 14$, $-17 \le k \le 17$, $-19 \le l \le 19$	
Data collection scan type	ω scans at 5 ϕ settings	
Data reduction program	Bruker SAINT v6.22	
Reflections collected	32070	
Independent reflections	5144 [R_{int}= 0.1503]	
Absorption coefficient	0.447 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.9368 and 0.9072	

Table 1 (cont.)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	5144 / 0 / 362
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	1.064
Final R indices [$I>2\sigma(I)$, 2718 reflections]	R1 = 0.0468, *w*R2 = 0.0744
R indices (all data)	R1 = 0.1218, *w*R2 = 0.0862
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.000
Average shift/error	0.000
Largest diff. peak and hole	0.402 and -0.348 e.Å^{-3}

Special Refinement Details

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for DCB05 (CCDC 175588). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
O(1)	2996(2)	1246(2)	424(1)	23(1)
O(2)	3667(2)	289(1)	2011(1)	23(1)
O(3)	10816(2)	767(1)	809(1)	24(1)
O(4)	10340(2)	21(1)	3988(1)	28(1)
O(5)	9289(2)	-1153(1)	4583(1)	27(1)
C(1)	4196(2)	1102(2)	735(2)	20(1)
C(2)	4579(2)	649(2)	1547(2)	19(1)
C(3)	5789(2)	489(2)	1874(2)	19(1)
C(4)	6178(2)	-65(2)	2727(2)	22(1)
C(5)	7352(2)	-608(2)	2734(2)	20(1)
C(6)	8184(2)	-314(2)	2243(2)	18(1)
C(7)	9343(2)	-929(2)	2231(2)	20(1)
C(8)	9093(3)	-1750(2)	1504(2)	25(1)
C(9)	9748(3)	-1452(2)	3131(2)	22(1)
C(10)	9824(2)	-789(2)	3926(2)	21(1)
C(11)	10377(2)	-254(2)	2003(2)	23(1)
C(12)	10036(2)	410(2)	1214(2)	21(1)
C(13)	8738(2)	652(2)	926(2)	19(1)
C(14)	7993(2)	658(2)	1710(2)	18(1)
C(15)	8424(3)	1530(2)	2337(2)	22(1)
C(16)	6654(2)	805(2)	1345(2)	18(1)
C(17)	6244(2)	1260(2)	531(2)	19(1)
C(18)	5037(2)	1421(2)	199(2)	19(1)
C(19)	4615(3)	1892(3)	-688(2)	24(1)
C(20)	3502(3)	888(3)	2774(2)	28(1)
C(21)	1118(3)	3109(2)	603(2)	31(1)
Cl(1)	1475(1)	3147(1)	1778(1)	41(1)
Cl(2)	2089(1)	3910(1)	117(1)	45(1)
Cl(3)	-397(1)	3458(1)	263(1)	39(1)

Table 3. Bond lengths [Å] and angles [°] for DCB05 (CCDC 175588).

O(1)-C(1)	1.361(3)	C(21)-Cl(3)	1.749(3)
O(1)-H(1)	0.72(3)	C(21)-Cl(1)	1.749(3)
O(2)-C(2)	1.401(3)	C(21)-Cl(2)	1.753(3)
O(2)-C(20)	1.428(3)	C(21)-H(21)	0.91(3)
O(3)-C(12)	1.230(3)		
O(4)-C(10)	1.216(3)	C(1)-O(1)-H(1)	107(3)
O(5)-C(10)	1.319(3)	C(2)-O(2)-C(20)	113.6(2)
O(5)-H(5A)	0.97(4)	C(10)-O(5)-H(5A)	111.0(18)
C(1)-C(2)	1.368(4)	O(1)-C(1)-C(2)	121.6(2)
C(1)-C(18)	1.390(3)	O(1)-C(1)-C(18)	118.2(2)
C(2)-C(3)	1.378(3)	C(2)-C(1)-C(18)	120.3(2)
C(3)-C(16)	1.403(3)	C(1)-C(2)-C(3)	122.7(2)
C(3)-C(4)	1.483(4)	C(1)-C(2)-O(2)	116.2(2)
C(4)-C(5)	1.492(4)	C(3)-C(2)-O(2)	120.9(2)
C(4)-H(4A)	0.94(3)	C(2)-C(3)-C(16)	118.1(2)
C(4)-H(4B)	0.96(3)	C(2)-C(3)-C(4)	121.7(2)
C(5)-C(6)	1.328(3)	C(16)-C(3)-C(4)	120.1(2)
C(5)-H(5)	0.97(3)	C(3)-C(4)-C(5)	112.8(2)
C(6)-C(14)	1.516(4)	C(3)-C(4)-H(4A)	108.3(16)
C(6)-C(7)	1.529(3)	C(5)-C(4)-H(4A)	109.2(15)
C(7)-C(9)	1.525(4)	C(3)-C(4)-H(4B)	108.8(16)
C(7)-C(8)	1.538(4)	C(5)-C(4)-H(4B)	107.1(16)
C(7)-C(11)	1.539(3)	H(4A)-C(4)-H(4B)	111(2)
C(8)-H(8A)	0.95(3)	C(6)-C(5)-C(4)	122.6(3)
C(8)-H(8B)	1.02(3)	C(6)-C(5)-H(5)	119.0(14)
C(8)-H(8C)	1.03(3)	C(4)-C(5)-H(5)	118.4(14)
C(9)-C(10)	1.475(4)	C(5)-C(6)-C(14)	119.3(2)
C(9)-H(9A)	0.92(3)	C(5)-C(6)-C(7)	120.7(2)
C(9)-H(9B)	0.93(2)	C(14)-C(6)-C(7)	119.97(19)
C(11)-C(12)	1.478(4)	C(9)-C(7)-C(6)	111.69(19)
C(11)-H(11A)	0.99(3)	C(9)-C(7)-C(8)	107.6(2)
C(11)-H(11B)	1.00(3)	C(6)-C(7)-C(8)	109.0(2)
C(12)-C(13)	1.480(4)	C(9)-C(7)-C(11)	109.4(2)
C(13)-C(14)	1.541(3)	C(6)-C(7)-C(11)	110.7(2)
C(13)-H(13A)	0.94(2)	C(8)-C(7)-C(11)	108.4(2)
C(13)-H(13B)	1.00(2)	C(7)-C(8)-H(8A)	108.3(15)
C(14)-C(16)	1.520(4)	C(7)-C(8)-H(8B)	107.9(16)
C(14)-C(15)	1.523(4)	H(8A)-C(8)-H(8B)	109(2)
C(15)-H(15A)	1.00(2)	C(7)-C(8)-H(8C)	113.1(14)
C(15)-H(15B)	1.00(2)	H(8A)-C(8)-H(8C)	106(2)
C(15)-H(15C)	1.01(3)	H(8B)-C(8)-H(8C)	113(2)
C(16)-C(17)	1.378(4)	C(10)-C(9)-C(7)	114.7(2)
C(17)-C(18)	1.377(4)	C(10)-C(9)-H(9A)	111.5(15)
C(17)-H(17)	0.97(2)	C(7)-C(9)-H(9A)	114.9(16)
C(18)-C(19)	1.481(4)	C(10)-C(9)-H(9B)	105.6(15)
C(19)-H(19A)	0.94(3)	C(7)-C(9)-H(9B)	111.0(15)
C(19)-H(19B)	0.92(3)	H(9A)-C(9)-H(9B)	97(2)
C(19)-H(19C)	1.03(2)	O(4)-C(10)-O(5)	122.0(2)
C(20)-H(20A)	1.00(3)	O(4)-C(10)-C(9)	123.9(2)
C(20)-H(20B)	0.95(2)	O(5)-C(10)-C(9)	114.2(2)
C(20)-H(20C)	0.99(3)	C(12)-C(11)-C(7)	114.6(2)

C(12)-C(11)-H(11A)	106.0(16)
C(7)-C(11)-H(11A)	112.5(15)
C(12)-C(11)-H(11B)	113.7(14)
C(7)-C(11)-H(11B)	108.6(15)
H(11A)-C(11)-H(11B)	101(2)
O(3)-C(12)-C(11)	120.7(2)
O(3)-C(12)-C(13)	120.3(2)
C(11)-C(12)-C(13)	119.0(2)
C(12)-C(13)-C(14)	113.2(2)
C(12)-C(13)-H(13A)	109.8(13)
C(14)-C(13)-H(13A)	108.8(12)
C(12)-C(13)-H(13B)	110.1(13)
C(14)-C(13)-H(13B)	109.3(12)
H(13A)-C(13)-H(13B)	105.3(19)
C(6)-C(14)-C(16)	110.5(2)
C(6)-C(14)-C(15)	108.5(2)
C(16)-C(14)-C(15)	108.9(2)
C(6)-C(14)-C(13)	110.5(2)
C(16)-C(14)-C(13)	109.8(2)
C(15)-C(14)-C(13)	108.6(2)
C(14)-C(15)-H(15A)	109.5(14)
C(14)-C(15)-H(15B)	111.6(14)
H(15A)-C(15)-H(15B)	107.9(18)
C(14)-C(15)-H(15C)	116.1(16)
H(15A)-C(15)-H(15C)	111(2)
H(15B)-C(15)-H(15C)	100(2)
C(17)-C(16)-C(3)	118.0(2)
C(17)-C(16)-C(14)	123.4(2)
C(3)-C(16)-C(14)	118.6(2)
C(18)-C(17)-C(16)	124.3(2)
C(18)-C(17)-H(17)	117.2(15)
C(16)-C(17)-H(17)	118.6(15)
C(17)-C(18)-C(1)	116.7(2)
C(17)-C(18)-C(19)	123.3(2)
C(1)-C(18)-C(19)	120.0(2)
C(18)-C(19)-H(19A)	114.1(17)
C(18)-C(19)-H(19B)	111.4(17)
H(19A)-C(19)-H(19B)	109(2)
C(18)-C(19)-H(19C)	109.9(15)
H(19A)-C(19)-H(19C)	104(2)
H(19B)-C(19)-H(19C)	107(2)
O(2)-C(20)-H(20A)	111.9(14)
O(2)-C(20)-H(20B)	104.7(14)
H(20A)-C(20)-H(20B)	108(2)
O(2)-C(20)-H(20C)	112.1(16)
H(20A)-C(20)-H(20C)	108(2)
H(20B)-C(20)-H(20C)	111(2)
Cl(3)-C(21)-Cl(1)	110.32(16)
Cl(3)-C(21)-Cl(2)	110.32(17)
Cl(1)-C(21)-Cl(2)	109.98(17)
Cl(3)-C(21)-H(21)	109.2(19)
Cl(1)-C(21)-H(21)	105.5(19)
Cl(2)-C(21)-H(21)	111.4(16)

Table 4. Anisotropic displacement parameters ($Å^2$x 10^4) for DCB05 (CCDC 175588). The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	149(10)	334(13)	235(11)	33(9)	80(9)	-25(9)
O(2)	182(10)	311(11)	210(10)	7(9)	113(8)	-10(8)
O(3)	154(10)	348(11)	253(11)	24(9)	102(8)	-2(8)
O(4)	324(11)	318(12)	214(10)	-30(9)	98(9)	-60(9)
O(5)	325(11)	325(12)	182(11)	-13(10)	95(9)	-42(9)
C(1)	142(14)	230(15)	221(15)	-30(12)	23(11)	8(12)
C(2)	142(14)	248(15)	205(15)	-29(12)	82(11)	-27(11)
C(3)	174(15)	228(15)	167(14)	-8(12)	58(11)	4(11)
C(4)	183(15)	279(17)	222(16)	16(14)	92(12)	-9(13)
C(5)	223(15)	228(16)	165(15)	17(13)	41(12)	4(12)
C(6)	155(14)	222(15)	159(14)	-23(11)	31(11)	-4(11)
C(7)	164(14)	230(15)	198(15)	8(12)	36(11)	1(11)
C(8)	240(17)	298(18)	208(16)	-20(14)	47(13)	18(14)
C(9)	190(16)	242(16)	242(16)	20(13)	49(12)	24(14)
C(10)	148(14)	267(17)	208(15)	27(13)	-21(12)	41(12)
C(11)	150(15)	294(17)	243(16)	-13(14)	53(12)	15(13)
C(12)	216(15)	196(15)	230(16)	-72(12)	56(12)	-7(12)
C(13)	175(15)	235(16)	172(15)	24(13)	71(12)	9(12)
C(14)	158(14)	222(15)	186(14)	-19(12)	92(11)	-10(11)
C(15)	192(15)	254(16)	217(16)	-18(13)	85(12)	-7(13)
C(16)	169(14)	203(14)	180(14)	-3(11)	79(11)	13(11)
C(17)	176(14)	229(15)	194(15)	-22(12)	92(12)	-2(12)
C(18)	184(14)	216(15)	191(14)	-5(12)	67(11)	22(11)
C(19)	181(16)	298(18)	228(16)	44(15)	29(13)	-2(14)
C(20)	237(18)	400(20)	250(17)	-48(15)	140(15)	-19(15)
C(21)	345(18)	274(18)	296(17)	-15(15)	10(14)	23(15)
Cl(1)	443(5)	519(5)	245(4)	-55(4)	17(3)	122(4)
Cl(2)	415(5)	447(5)	491(5)	63(4)	117(4)	-38(4)
Cl(3)	331(4)	475(5)	339(4)	-10(4)	21(3)	69(4)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for DCB05 (CCDC 175588).

	x	y	z	U_{iso}
H(1)	2670(30)	960(20)	710(20)	37(11)
H(4A)	6260(20)	400(20)	3203(17)	23(7)
H(4B)	5570(20)	-560(20)	2799(17)	29(7)
H(5)	7500(20)	-1210(20)	3098(17)	29(8)
H(5A)	9470(30)	-750(30)	5120(20)	60(10)
H(8A)	8480(20)	-2180(20)	1656(18)	30(8)
H(8B)	9870(30)	-2160(20)	1514(18)	40(8)
H(8C)	8770(20)	-1467(19)	875(19)	30(7)
H(9A)	9340(20)	-2040(20)	3214(16)	19(7)
H(9B)	10520(20)	-1729(19)	3152(16)	22(7)
H(11A)	10710(20)	190(20)	2508(19)	39(8)
H(11B)	11100(20)	-680(20)	1959(16)	29(7)
H(13A)	8666(18)	1287(17)	642(14)	3(6)
H(13B)	8370(20)	165(18)	456(16)	16(7)
H(15A)	8294(19)	2176(18)	1999(15)	11(6)
H(15B)	7970(20)	1565(18)	2856(17)	22(7)
H(15C)	9280(30)	1480(20)	2670(19)	39(8)
H(17)	6830(20)	1466(18)	154(16)	23(7)
H(19A)	4240(20)	2520(20)	-652(18)	31(8)
H(19B)	4110(20)	1470(20)	-1056(19)	33(8)
H(19C)	5350(20)	2042(19)	-1011(17)	32(7)
H(20A)	4260(30)	910(20)	3234(18)	29(8)
H(20B)	2880(20)	553(17)	3031(15)	14(6)
H(20C)	3270(20)	1590(20)	2602(19)	38(9)
H(21)	1220(20)	2450(20)	447(19)	39(9)

Table 6. Hydrogen bonds for DCB05 (CCDC 175588) [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(3)#1	0.72(3)	2.10(3)	2.656(2)	135(3)
O(1)-H(1)...O(2)	0.72(3)	2.28(3)	2.703(3)	119(3)
O(5)-H(5A)...O(4)#2	0.97(4)	1.64(4)	2.600(3)	175(3)

Symmetry transformations used to generate equivalent atoms:
#1 x-1,y,z #2 -x+2,-y,-z+1

CALIFORNIA INSTITUTE OF TECHNOLOGY

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X-RAY CRYSTALLOGRAPHY LABORATORY

Crystal Structure Analysis of:

Diketone 3 (DCB11)

(CCDC 201187)

Contents:

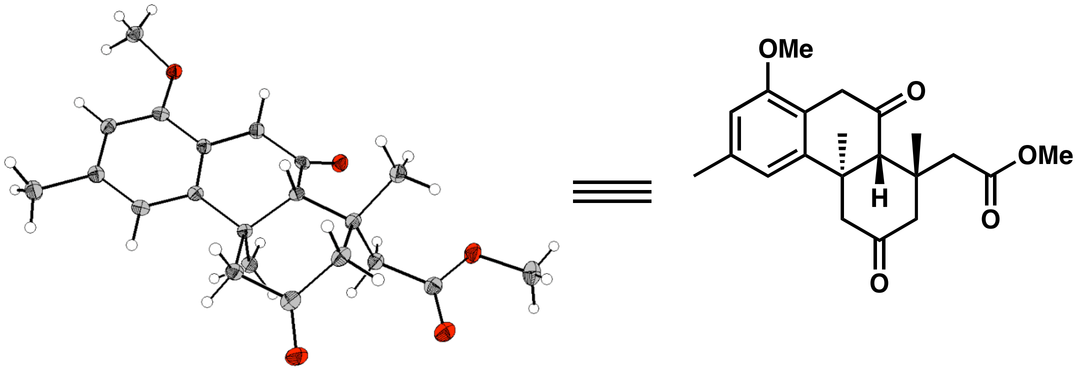

Table 1. Crystal data and structure refinement for DCB11 (CCDC 201187).

Empirical formula	$C_{21}H_{26}O_5$
Formula weight	358.42
Crystallization Solvent	Acetone/heptane
Crystal Habit	Fragment
Crystal size	0.26 x 0.22 x 0.17 mm^3
Crystal color	Colorless

Data Collection

Preliminary Photos	Rotation	
Type of diffractometer	Bruker SMART 1000	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	98(2) K	
θ range for 11980 reflections used in lattice determination	2.28 to 28.32°	
Unit cell dimensions	a = 9.0211(6) Å b = 11.3617(7) Å c = 17.9596(12) Å	 β= 97.5510(10)°
Volume	1824.8(2) $Å^3$	
Z	4	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Density (calculated)	1.305 Mg/m^3	
F(000)	768	
Data collection program	Bruker SMART v5.054	
θ range for data collection	2.13 to 28.32°	
Completeness to θ = 28.32°	93.0 %	
Index ranges	$-11 \le h \le 11, -14 \le k \le 14, -23 \le l \le 23$	
Data collection scan type	ω scans at 5 ϕ settings	
Data reduction program	Bruker SAINT v6.022	
Reflections collected	25862	
Independent reflections	4226 [R_{int}= 0.0517]	
Absorption coefficient	0.092 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	0.9845 and 0.9764	

Table 1 (cont.)

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Difference Fourier map
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	4226 / 0 / 339
Treatment of hydrogen atoms	Unrestrained
Goodness-of-fit on F^2	2.153
Final R indices [$I>2\sigma(I)$, 3426 reflections]	R1 = 0.0404, *w*R2 = 0.0704
R indices (all data)	R1 = 0.0511, *w*R2 = 0.0715
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.001
Average shift/error	0.000
Largest diff. peak and hole	0.326 and -0.254 e.Å^{-3}

Special Refinement Details

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for DCB11 (CCDC 201187). U(eq) is defined as the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
O(1)	7731(1)	4507(1)	529(1)	19(1)
O(2)	4749(1)	8200(1)	472(1)	21(1)
O(3)	9216(1)	11345(1)	2166(1)	25(1)
O(4)	3377(1)	11397(1)	1288(1)	24(1)
O(5)	5418(1)	12446(1)	1710(1)	29(1)
C(1)	10631(1)	7158(1)	1330(1)	16(1)
C(2)	11220(1)	6047(1)	1256(1)	16(1)
C(3)	12869(2)	5814(1)	1455(1)	23(1)
C(4)	10262(1)	5133(1)	986(1)	16(1)
C(5)	8757(1)	5346(1)	789(1)	15(1)
C(6)	8217(2)	3305(1)	562(1)	20(1)
C(7)	8162(1)	6478(1)	851(1)	14(1)
C(8)	6510(1)	6650(1)	623(1)	18(1)
C(9)	5914(1)	7834(1)	811(1)	15(1)
C(10)	6851(1)	8484(1)	1442(1)	14(1)
C(11)	6098(1)	9579(1)	1751(1)	15(1)
C(12)	4682(1)	9175(1)	2071(1)	19(1)
C(13)	5708(1)	10548(1)	1148(1)	17(1)
C(14)	4865(1)	11569(1)	1417(1)	18(1)
C(15)	2478(2)	12330(1)	1540(1)	31(1)
C(16)	7204(1)	10084(1)	2400(1)	18(1)
C(17)	8678(1)	10359(1)	2139(1)	18(1)
C(18)	9450(1)	9319(1)	1844(1)	18(1)
C(19)	8466(1)	8626(1)	1220(1)	14(1)
C(20)	8500(2)	9259(1)	463(1)	19(1)
C(21)	9104(1)	7387(1)	1138(1)	14(1)

Table 3. Bond lengths [Å] and angles [°] for DCB11 (CCDC 201187).

O(1)-C(5)	1.3673(13)	C(20)-H(20A)	0.996(14)
O(1)-C(6)	1.4332(14)	C(20)-H(20B)	0.987(13)
O(2)-C(9)	1.2162(13)	C(20)-H(20C)	0.985(13)
O(3)-C(17)	1.2186(13)		
O(4)-C(14)	1.3457(14)	C(5)-O(1)-C(6)	117.41(9)
O(4)-C(15)	1.4438(16)	C(14)-O(4)-C(15)	115.32(10)
O(5)-C(14)	1.2036(14)	C(2)-C(1)-C(21)	121.54(11)
C(1)-C(2)	1.3828(16)	C(2)-C(1)-H(1)	118.7(7)
C(1)-C(21)	1.3997(16)	C(21)-C(1)-H(1)	119.8(7)
C(1)-H(1)	1.006(12)	C(1)-C(2)-C(4)	118.97(11)
C(2)-C(4)	1.3963(16)	C(1)-C(2)-C(3)	121.17(11)
C(2)-C(3)	1.5069(17)	C(4)-C(2)-C(3)	119.86(11)
C(3)-H(3A)	0.967(14)	C(2)-C(3)-H(3A)	109.9(8)
C(3)-H(3B)	0.963(16)	C(2)-C(3)-H(3B)	111.4(9)
C(3)-H(3C)	0.980(15)	H(3A)-C(3)-H(3B)	109.7(12)
C(4)-C(5)	1.3783(16)	C(2)-C(3)-H(3C)	111.9(9)
C(4)-H(4)	0.958(11)	H(3A)-C(3)-H(3C)	108.7(12)
C(5)-C(7)	1.4037(15)	H(3B)-C(3)-H(3C)	105.1(12)
C(6)-H(6A)	0.978(12)	C(5)-C(4)-C(2)	120.19(11)
C(6)-H(6B)	0.973(12)	C(5)-C(4)-H(4)	119.0(7)
C(6)-H(6C)	0.999(13)	C(2)-C(4)-H(4)	120.8(7)
C(7)-C(21)	1.3926(16)	O(1)-C(5)-C(4)	124.44(10)
C(7)-C(8)	1.5051(16)	O(1)-C(5)-C(7)	114.64(10)
C(8)-C(9)	1.5034(16)	C(4)-C(5)-C(7)	120.92(11)
C(8)-H(8A)	0.993(13)	O(1)-C(6)-H(6A)	105.1(7)
C(8)-H(8B)	0.996(13)	O(1)-C(6)-H(6B)	110.4(7)
C(9)-C(10)	1.5144(16)	H(6A)-C(6)-H(6B)	110.7(10)
C(10)-C(11)	1.5546(16)	O(1)-C(6)-H(6C)	111.8(7)
C(10)-C(19)	1.5679(16)	H(6A)-C(6)-H(6C)	110.0(10)
C(10)-H(10)	0.982(11)	H(6B)-C(6)-H(6C)	108.8(10)
C(11)-C(12)	1.5377(16)	C(5)-C(7)-C(21)	119.20(11)
C(11)-C(13)	1.5525(16)	C(5)-C(7)-C(8)	118.20(10)
C(11)-C(16)	1.5420(16)	C(21)-C(7)-C(8)	122.58(10)
C(12)-H(12A)	0.986(12)	C(7)-C(8)-C(9)	115.21(10)
C(12)-H(12B)	1.025(12)	C(7)-C(8)-H(8A)	112.9(8)
C(12)-H(12C)	0.993(12)	C(9)-C(8)-H(8A)	106.4(7)
C(13)-C(14)	1.5018(16)	C(7)-C(8)-H(8B)	109.6(8)
C(13)-H(13A)	0.986(12)	C(9)-C(8)-H(8B)	105.9(8)
C(13)-H(13B)	0.957(11)	H(8A)-C(8)-H(8B)	106.3(11)
C(15)-H(15A)	0.969(14)	O(2)-C(9)-C(10)	124.61(11)
C(15)-H(15B)	0.980(15)	O(2)-C(9)-C(8)	120.35(11)
C(15)-H(15C)	0.989(15)	C(10)-C(9)-C(8)	115.03(10)
C(16)-C(17)	1.4999(17)	C(9)-C(10)-C(11)	115.52(10)
C(16)-H(16A)	0.980(12)	C(9)-C(10)-C(19)	107.82(9)
C(16)-H(16B)	0.982(12)	C(11)-C(10)-C(19)	118.21(9)
C(17)-C(18)	1.5039(17)	C(9)-C(10)-H(10)	104.1(6)
C(18)-C(19)	1.5492(16)	C(11)-C(10)-H(10)	105.7(6)
C(18)-H(18A)	0.966(12)	C(19)-C(10)-H(10)	103.8(6)
C(18)-H(18B)	0.996(12)	C(12)-C(11)-C(10)	108.53(9)
C(19)-C(21)	1.5357(15)	C(12)-C(11)-C(13)	110.46(10)
C(19)-C(20)	1.5424(16)	C(10)-C(11)-C(13)	112.81(9)

C(12)-C(11)-C(16)	108.40(10)
C(10)-C(11)-C(16)	107.36(9)
C(13)-C(11)-C(16)	109.15(10)
C(11)-C(12)-H(12A)	109.5(7)
C(11)-C(12)-H(12B)	110.2(7)
H(12A)-C(12)-H(12B)	109.2(9)
C(11)-C(12)-H(12C)	109.5(7)
H(12A)-C(12)-H(12C)	108.7(10)
H(12B)-C(12)-H(12C)	109.7(9)
C(14)-C(13)-C(11)	113.64(10)
C(14)-C(13)-H(13A)	104.7(7)
C(11)-C(13)-H(13A)	110.9(7)
C(14)-C(13)-H(13B)	108.1(7)
C(11)-C(13)-H(13B)	109.4(7)
H(13A)-C(13)-H(13B)	110.0(10)
O(5)-C(14)-O(4)	122.87(11)
O(5)-C(14)-C(13)	125.55(12)
O(4)-C(14)-C(13)	111.58(10)
O(4)-C(15)-H(15A)	107.3(8)
O(4)-C(15)-H(15B)	109.3(9)
H(15A)-C(15)-H(15B)	110.0(12)
O(4)-C(15)-H(15C)	110.6(8)
H(15A)-C(15)-H(15C)	111.5(12)
H(15B)-C(15)-H(15C)	108.1(12)
C(17)-C(16)-C(11)	110.67(10)
C(17)-C(16)-H(16A)	108.5(7)
C(11)-C(16)-H(16A)	111.5(7)
C(17)-C(16)-H(16B)	108.4(7)
C(11)-C(16)-H(16B)	107.5(7)
H(16A)-C(16)-H(16B)	110.2(9)
O(3)-C(17)-C(18)	122.40(11)
O(3)-C(17)-C(16)	122.92(11)
C(18)-C(17)-C(16)	114.67(11)
C(17)-C(18)-C(19)	113.93(10)
C(17)-C(18)-H(18A)	109.0(7)
C(19)-C(18)-H(18A)	110.2(7)
C(17)-C(18)-H(18B)	105.8(7)
C(19)-C(18)-H(18B)	109.9(7)
H(18A)-C(18)-H(18B)	107.8(9)
C(21)-C(19)-C(20)	106.90(9)
C(21)-C(19)-C(18)	110.43(9)
C(20)-C(19)-C(18)	108.92(10)
C(21)-C(19)-C(10)	107.65(9)
C(20)-C(19)-C(10)	113.48(10)
C(18)-C(19)-C(10)	109.42(9)
C(19)-C(20)-H(20A)	108.7(7)
C(19)-C(20)-H(20B)	111.1(7)
H(20A)-C(20)-H(20B)	107.8(10)
C(19)-C(20)-H(20C)	112.4(7)
H(20A)-C(20)-H(20C)	107.0(10)
H(20B)-C(20)-H(20C)	109.7(10)
C(1)-C(21)-C(7)	119.14(11)
C(1)-C(21)-C(19)	121.02(10)
C(7)-C(21)-C(19)	119.82(10)

Table 4. Anisotropic displacement parameters (Å²x 10⁴) for DCB11 (CCDC 201187). The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	179(5)	129(4)	246(5)	-34(4)	5(4)	-8(3)
O(2)	175(5)	198(5)	252(5)	-10(4)	-23(4)	19(4)
O(3)	239(5)	164(5)	340(5)	-50(4)	-12(4)	-28(4)
O(4)	181(5)	202(5)	316(5)	-22(4)	1(4)	57(4)
O(5)	270(5)	197(5)	396(6)	-85(4)	44(4)	-6(4)
C(1)	170(6)	162(6)	152(6)	-5(5)	26(5)	-28(5)
C(2)	160(6)	188(7)	140(6)	12(5)	29(5)	5(5)
C(3)	165(7)	220(8)	302(8)	-28(7)	7(6)	13(6)
C(4)	189(7)	140(6)	158(6)	10(5)	43(5)	31(5)
C(5)	176(6)	159(6)	118(6)	-7(5)	29(5)	-31(5)
C(6)	223(8)	142(7)	237(7)	-9(6)	13(6)	-2(6)
C(7)	145(6)	157(6)	123(6)	7(5)	31(5)	4(5)
C(8)	162(7)	168(7)	209(7)	-33(6)	8(5)	0(5)
C(9)	142(6)	161(6)	161(6)	30(5)	48(5)	-18(5)
C(10)	151(6)	128(6)	143(6)	26(5)	21(5)	7(5)
C(11)	173(6)	128(6)	153(6)	1(5)	32(5)	14(5)
C(12)	202(7)	167(7)	216(7)	13(6)	73(6)	27(6)
C(13)	185(7)	159(7)	171(7)	4(5)	29(5)	13(5)
C(14)	209(7)	164(7)	163(6)	30(5)	19(5)	19(5)
C(15)	218(8)	287(9)	419(10)	-13(7)	64(7)	94(7)
C(16)	241(7)	145(7)	153(7)	-7(5)	26(5)	29(5)
C(17)	203(7)	172(7)	130(6)	-11(5)	-53(5)	9(5)
C(18)	158(7)	159(7)	206(7)	-1(5)	4(5)	-17(5)
C(19)	139(6)	125(6)	166(6)	0(5)	15(5)	-6(5)
C(20)	196(7)	182(7)	201(7)	18(5)	58(6)	0(6)
C(21)	162(6)	150(6)	114(6)	8(5)	37(5)	3(5)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for DCB11 (CCDC 201187).

	x	y	z	U_{iso}
H(1)	11324(13)	7813(10)	1530(6)	16(3)
H(3A)	13385(15)	6538(12)	1604(7)	35(4)
H(3B)	13289(17)	5469(13)	1039(9)	50(5)
H(3C)	13068(16)	5243(13)	1865(9)	48(5)
H(4)	10635(12)	4351(10)	941(6)	13(3)
H(6A)	7338(14)	2849(10)	357(7)	21(3)
H(6B)	8556(13)	3077(10)	1078(7)	18(3)
H(6C)	9048(14)	3171(10)	254(7)	19(3)
H(8A)	6202(14)	6529(11)	77(8)	29(4)
H(8B)	5944(15)	6062(11)	886(7)	33(4)
H(10)	6980(11)	7914(9)	1856(6)	9(3)
H(12A)	4310(12)	9821(10)	2363(6)	17(3)
H(12B)	3867(14)	8942(10)	1643(7)	22(3)
H(12C)	4927(13)	8491(11)	2410(7)	20(3)
H(13A)	6623(14)	10898(10)	997(6)	18(3)
H(13B)	5112(12)	10214(10)	719(6)	12(3)
H(15A)	1440(17)	12099(12)	1419(8)	38(4)
H(15B)	2664(16)	13060(13)	1277(8)	43(4)
H(15C)	2744(16)	12466(12)	2086(9)	44(4)
H(16A)	6816(13)	10804(10)	2604(6)	16(3)
H(16B)	7366(13)	9478(10)	2792(7)	18(3)
H(18A)	10357(14)	9583(10)	1663(6)	16(3)
H(18B)	9741(13)	8799(10)	2285(7)	22(3)
H(20A)	9509(15)	9153(10)	304(7)	26(3)
H(20B)	7759(14)	8917(10)	69(7)	22(3)
H(20C)	8331(13)	10112(11)	498(6)	21(3)

References

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[1] J. M. Saa, M. Dopico, G. Martorell, A. Garcia-Raso, *J. Org. Chem.* **1990**, *55*, 991-995.

[2] For the asymmetric synthesis of ketone (–)-**24**, see: (a) D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2004**, *126*, 15044-15045; (b) J. T. Mohr, D. C. Behenna, A. M. Harned, B. M. Stoltz, *Angew. Chem., Int. Ed.* **2005**, *44*, 6924-6927.