Total Syntheses of (+)- and (-)-Cacospongionolide B. New Insight into Structural Requirements for Phospholipase A₂ Inhibition

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Supporting Information

General: Starting materials and reagents were purchased from commercial suppliers and used without further purification except the following: diisopropylethylamine, triethylamine, dimethylsulfoxide, and pentane were distilled from CaH₂ under anhydrous nitrogen atmosphere; diisopropylcarbodiimide was distilled prior to use; *tert*-butyl alcohol was distilled from CaH₂ and stored over 4 Å MS; methyltriphenylphosphonium bromide was dried *in vacuo* over P₂O₅ for 2 d prior to use; tetrahydrofuran, diethyl ether, and dichloromethane were dried on alumina columns using a solvent dispensing system;¹ pentane, hexanes, and ether used in chromatography were distilled prior to use. All reactions were conducted in oven (135 °C) or flame-dried glassware under an inert atmosphere of dry nitrogen.

Infrared (**FTIR**) spectra were recorded on a Nicolet 210 FT-Infrared spectrophotometer or a Nicolet Avatar 360 spectrophotometer, ν_{max} cm⁻¹. Bands are characterized as broad (br), strong (s), medium (m), and weak (w). Proton nuclear magnetic resonance spectra (**¹H NMR**) were recorded on either a Varian Gemini-400 instrument (400 MHz), or a Varian Gemini-500 instrument (500 MHz). Chemical shifts are reported in ppm downfield from tetramethylsilane with the solvent reference as the internal standard (CHCl₃: δ 7.26 ppm). Data is reported as

¹ Pangborn, A.B.; Giardello, M.A.; Grubbs, R.H.; Rosen, R.K.; Timmers, F.J. *Organometallics* **1996**, *15*, 1518-1520.

follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on either a Varian Gemini-400 instrument (100 MHz), or a Varian Gemini-500 instrument (125 MHz) with complete proton decoupling. Chemical shifts are reported in ppm downfield from tetramethylsilane with the solvent as the internal reference (CDCl_3 ; δ 77.23 ppm). Enantiomeric ratio for compound **13** was determined by chiral HPLC on a Varian Dynamax HPLC instrument utilizing a Chiralcel OB-H column (4.6 x 250 mm) from Chiral Technologies (HPLC conditions: 97.5 : 2.5 hexanes/*i*-PrOH, 0.75 mL/min, λ =250 nm). Enantiomeric ratios for compounds **6** and **7** were determined by chiral GC on a Hewlett Packard HP 6890 Series II Gas Chromatograph utilizing either a Beta Dex 120 (30 m x 0.25 mm x 0.25 μm film thickness) or Gamma Dex 120 (30 m x 0.25 mm x 0.25 μm film thickness) columns from Supelco. Optical rotations were performed on a Rudolph Research Analytical Autopol IV Automatic Polorimeter. Elemental analyses (**Anal**) were performed by Robertson Microlit Laboratories, Inc. Madison, NJ and are reported in percent abundance. High resolution mass spectral analyses (**HRMS**) were performed by Mass Spectrometry Facility, Boston College.

X-ray data were collected using a Bruker SMART APEX CCD diffractometer with Mo (λ =0.71073 Å) radiation equipped with an LT-3 low-temperature apparatus operating at 183 K. A stable crystal was chosen and mounted on a glass fiber using grease. Data were measured using omega scans of 0.3 ° per frame for 30 seconds, such that a hemisphere was collected. A total of 1305 frames were collected with a maximum resolution of 0.75 Å. Cell parameters were retrieved using SMART² software and refined using SAINT on all observed reflections. The

² SMART V 5.050 (NT) *Software for the CCD Detector System*; Bruker Analytical X-ray Systems, Madison, WI (1998).

structures are solved by the direct method using the SHELXS-97³ program and refined by least squares method on F², SHELXTL-97,⁴ incorporated in SHELXTL-PC V 5.10.⁵ The crystal used for the diffraction study showed no decomposition during data collection. The drawing was displayed at 35% ellipsoids. The structure was solved by Jarred T. Blank at Boston College.

Experimental Procedures:

(+)-(1-Furan-3-yl-but-3-enyloxy)-acetic acid ethyl ester (8). To a suspension of sodium hydride (washed previously with dry pentane, 208 mg, 8.68 mmol) in THF (25 mL) at 0 °C was added alcohol **6** (800 mg, 5.79 mmol, 94% ee) in THF (5 mL). The reaction was heated to reflux for 30 min until hydrogen evolution ceased, cooled to -10 °C, and ethyl bromoacetate (0.963 mL, 8.68 mmol) in THF (9 mL) was added dropwise. After stirring at -10 °C for 3 h, the reaction mixture was poured into a solution of sat. NH₄Cl (50 mL) and extracted with Et₂O (4 x 50 mL). The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification of the residue by chromatography on silica gel (10:1 hexanes/ether) recovered 195 mg of **6** (24%), and afforded 829 mg of compound **8** (64%) as a colorless oil: **FTIR** (NaCl, thin film) 3131 (w), 3075 (w), 2987 (m), 2911 (m), 1759 (s), 1734 (s), 1508 (m), 1206 (s), 1124 (s), 1023 (m) cm⁻¹. **¹H NMR** (400 MHz,

³ Sheldrick, G.M. SHELXS-90, *Program for the Solution of Crystal Structure*, Univeristy of Gottingen, Germany, 1990.

⁴ Sheldrick, G.M. SHELXS-97, *Program for the Refinement of Crystal Structure*, Univeristy of Gottingen, Germany, 1997.

⁵ SHELXTL 5.10 (PC-Version), *Program Library for Structure Solution and Molecular Graphics*; Bruker Analytical X-ray Systems, Madison, WI (1998).

CDCl₃): δ 1.26 (t, J = 7.0 Hz, 3H), 2.48 (dt, J = 14.0, 7.0 Hz, 1H), 2.68 (dt, J = 14.0, 7.0 Hz, 1H), 3.92 (d, J = 16.4 Hz, 1H), 4.02 (d, J = 16.4 Hz, 1H), 4.17 (dq, J = 10.8, 3.6 Hz, 1H), 4.20 (dq, J = 10.8, 3.6 Hz, 1H), 4.47 (t, J = 6.8 Hz, 1H), 5.04 (ddd, J = 10.4, 2.4, 1.2 Hz, 1H), 5.10 (ddd, J = 17.2, 3.2, 1.6 Hz, 1H), 5.80 (ddd, J = 16.8, 14.0, 10.0 Hz, 1H), 6.41 (s with fine splitting, 1H, Ar), 7.37 (s, 1H, Ar), 7.40 (t, J = 1.6 Hz, 1H, Ar). ¹³C NMR (100 MHz, CDCl₃) δ 170.5, 143.7, 140.7, 134.2, 124.7, 117.3, 108.8, 74.2, 65.5, 60.9, 40.9, 14.5. $[\alpha]_D^{20}$ + 70.6 (c 1.00, EtOH). **Anal** Calcd for C₁₂H₁₆O₄: C, 64.27; H, 7.19. Found: C, 64.50; H, 7.21.

(+)-(1-Furan-3-yl-but-3-enyloxy)-acetic acid (8a). To ester **8** (980 mg, 4.37 mmol) in a solution of 3:1 MeOH/H₂O (40 mL) was added LiOH (520 mg, 21.9 mmol) neat at 0 °C. The reaction was warmed to room temperature (rt) and stirred at this temperature for 12 h. The reaction mixture was then acidified to pH 2 with 20 % HCl, and diluted with H₂O (20 mL). The aqueous layer was extracted with ethyl acetate (4 x 60 mL). The combined organic layers were washed with H₂O, and brine. The aqueous wash was back-extracted with ethyl acetate, and this organic layer was washed with brine. The organic layers were dried over MgSO₄, filtered, and concentrated *in vacuo* to give 860 mg of compound **8a** (100%) as a colorless oil. The crude material was taken on to the next reaction without further purification: **FTIR** (NaCl, thin film) 3128 (br), 3072 (m), 2978 (m), 2915 (br), 1736 (s), 1510 (m), 1435 (m), 1128 (s) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 2.50 (dt, J = 14.0, 7.0 Hz, 1H), 2.68 (dt, J = 14.0, 7.0 Hz, 1H), 3.97 (d, J = 16.8 Hz, 1H), 4.07 (d, J = 17.2 Hz, 1H), 4.46 (t, J = 6.8 Hz, 1H), 5.07 (d with fine splitting, J = 11.6 Hz, 1H), 5.11 (ddd, J = 16.4, 3.2, 1.6 Hz, 1H), 5.77 (ddd, J = 17.2, 14.0, 10.0 Hz, 1H), 6.40

(s with fine splitting, 1H, Ar), 7.39 (s, 1H, Ar), 7.42 (t, $J = 1.6$ Hz, 1H, Ar), 9.58 (br s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 175.4, 144.1, 141.0, 134.1, 124.4, 118.0, 108.8, 74.6, 65.1, 40.8. $[\alpha]_D^{20} + 65.0$ (c 1.00, EtOH). **Anal** Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_4$: C, 61.22; H, 6.16. Found: C, 61.36; H, 6.14.

(+)-2-(1-Furan-3-yl-but-3-enyloxy)-N-methoxy-N-methyl-acetamide (8b). To a stirring solution of acid **8a** (1.10 g, 5.61 mmol) in CH_2Cl_2 (15 mL) was added methoxymethyl amine hydrochloride (0.656 g, 6.73 mmol) and dimethylaminopyridine (DMAP) (0.343 g, 2.81 mmol). The mixture was cooled to 0 °C, and triethylamine (TEA) (1.10 mL, 7.85 mmol) followed by diisopropylcarbodiimide (DIC) (1.23 mL, 7.85 mmol), were added via syringe. After warming to rt, the reaction was stirred for 4 h, and determined complete by TLC (1:1 hexanes/ethyl acetate). After diluting with brine (25 mL), the aqueous layer was extracted with ether/ CH_2Cl_2 (1:1, 5 x 25 mL), and the combined organic layers were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (1:1 hexanes/ethyl acetate) to provide 1.15 g of compound **8b** (86%) as a colorless oil: **FTIR** (NaCl, thin film) 3122 (w), 3076 (w), 2975 (m), 2939 (m), 1680 (s), 1429 (m), 1085 (m), 995 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 2.50 (dt, $J = 14.0, 7.0$ Hz, 1H), 2.70 (dt, $J = 14.0, 7.0$ Hz, 1H), 3.16 (s, 3H), 3.60 (s, 3H), 4.09 (d, $J = 15.6$ Hz, 1H), 4.23 (d, $J = 16.0$ Hz, 1H), 4.54 (t, $J = 6.4$ Hz, 1H), 5.03 (d with fine splitting, $J = 10.0$ Hz, 1H), 5.08 (d with fine splitting, $J = 17.2$ Hz, 1H), 5.81 (ddd, $J = 17.2, 13.6, 10.4$ Hz, 1H), 6.42 (s with fine splitting, 1H, Ar), 7.38 (s, 1H, Ar), 7.41 (s with fine splitting, 1H, Ar). ^{13}C NMR (100 MHz, CDCl_3): δ 170.9, 143.4, 140.5,

134.2, 124.8, 117.1, 108.8, 73.7, 65.0, 61.4, 40.9, 32.3. $[\alpha]_D^{20} + 61.6$ (*c* 1.00, EtOH). **Anal**
 Calcd for C₁₂H₁₇NO₄: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.47; H, 7.25; N, 5.88.

(+)-1-(1-Furan-3-yl-but-3-enyloxy)-but-3-en-2-one (7). To a Schlenk flask (50 mL) charged with a solution of amide **8b** (873 mg, 3.65 mmol) in THF (6 mL) at -78 °C, vinyl magnesium bromide (9.12 mmol) in THF (10.1 mL, 0.9 M) was added dropwise. After stirring for 0.5 h, reaction was warmed to 0 °C, and stirred for an additional 1 h at which time the reaction was determined complete by TLC (1:1 ether/hexanes). The cold reaction mixture was added slowly to a cold, stirring solution of 5 % NaHSO₄ (50 mL). The aqueous layer was extracted with ether (4 x 50 mL), and the combined organic extracts were washed with brine, dried over MgSO₄, and filtered. The mixture was concentrated *in vacuo*, and the residue was purified by silica gel chromatography (5 : 1 pentane/ether). The reaction afforded 625 mg of compound **7** (83%, 94% ee) as a colorless oil: **FTIR** (NaCl, thin film) 3131 (m), 3081 (m), 2974 (m), 2905 (br), 2357 (w), 1697 (s), 1621 (s), 1401 (s) cm⁻¹. **¹H NMR** (400 MHz, CDCl₃): δ 2.49 (dt, *J* = 14.0, 7.0 Hz, 1H), 2.69 (dt, *J* = 14.0, 7.0 Hz, 1H), 4.09 (d, *J* = 17.2 Hz, 1H), 4.20 (d, *J* = 16.8 Hz, 1H), 4.40 (t, *J* = 6.4 Hz, 1H), 5.06 (d with fine splitting, *J* = 10.8 Hz, 1H), 5.10 (d with fine splitting, *J* = 15.6 Hz, 1H), 5.79 (m, 2H), 6.30 (dd, *J* = 17.6, 1.6 Hz, 1H), 6.40 (s with fine splitting, 1H, Ar), 6.53 (dd, *J* = 17.6, 10.4 Hz, 1H), 7.36 (s, 1H, Ar), 7.41 (s with fine splitting, 1H, Ar). **¹³C NMR** (100 MHz, CDCl₃): δ 197.2, 143.7, 140.6, 134.1, 132.5, 129.1, 124.8, 117.5,

108.8, 74.4, 72.3, 41.0. $[\alpha]_D^{20} + 67.58$ (c 1.00, CHCl_3). **Anal** Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$: C, 69.88; H, 6.84. Found: C, 69.50; H, 6.67.

(+)-Furanyl diketone (10). To a deep blue solution of lithium (12.0 mg, 1.76 mmol) in anhydrous liquid ammonia (10 mL) maintained at $-33\text{ }^\circ\text{C}$ with a dry ice/acetone condenser was added dropwise a solution of enone **9** (167 mg, 0.705 mmol, 99% ee) and *tert*-butyl alcohol (61.0 μL , 0.635 mmol) in diethyl ether (1.5 mL). After refluxing for 1 h, the reaction was quenched by the addition of several drops of freshly distilled isoprene (Na°). The ammonia was evaporated at rt over 0.5 h, and the remaining solvent was removed on high vacuum at $40\text{ }^\circ\text{C}$ for 10 min. The residue was then taken up in diethyl ether (10 mL), and cooled to $-78\text{ }^\circ\text{C}$. The reaction was protected from light. A solution of vinyl ketone **7** (160 mg, 0.776 mmol) in diethyl ether (3 mL) was then added over 20 min via syringe pump to the stirring reaction. After stirring an additional 10 min at $-78\text{ }^\circ\text{C}$, the reaction was quenched by adding rapidly to a solution of sat. NH_4Cl (15 mL). The aqueous layer was extracted with diethyl ether (4 x 20 mL), and the combined organic extracts were washed with brine, dried over MgSO_4 , and filtered. The mixture was concentrated *in vacuo*, and the residue purified on silica gel prewashed with pyridine (3:1 hexanes/ether). The reaction afforded 198 mg of compound **10** (70%) as a colorless oil: **FTIR** (NaCl , thin film) 2941 (br), 2882 (br), 1700 (s), 1443 (m), 1131 (m), 1099 (m) cm^{-1} . **^1H NMR** (400 MHz, CDCl_3): δ 1.04 (s, 3H), 1.21 (s, 3H), 1.43 (m, 3H), 1.53-1.72 (m, 5H), 1.92 (m, 3H),

2.30 (m, 3H), 2.47 (dt, $J = 13.6, 6.8$ Hz, 1H), 2.53 (ddd, $J = 16.0, 13.2, 6.8$ Hz, 1H), 2.66 (dt, $J = 13.6, 6.8$ Hz, 1H), 3.91 (m, 5H), 4.00 (d, $J = 17.2$ Hz, 1H), 4.36 (t, $J = 6.8$ Hz, 1H), 5.05 (d, $J = 12.4$ Hz, 1H), 5.09 (dd, $J = 17.2, 1.2$ Hz, 1H), 5.80 (ddd, $J = 17.2, 14.0, 10.4$ Hz, 1H), 6.40 (s with fine splitting, 1H, Ar), 7.37 (s, 1H, Ar), 7.40 (s with fine splitting, 1H, Ar). ^{13}C NMR (100 MHz, CDCl_3): δ 216.2, 209.0, 143.9, 140.8, 134.5, 125.1, 117.7, 113.0, 109.0, 74.5, 73.4, 65.4, 65.1, 50.5, 45.2, 42.7, 41.0, 35.1, 35.0, 31.0, 30.4, 29.4, 23.0, 21.8, 21.7, 16.7. $[\alpha]_D^{20} + 40.0$ (c 0.50, CHCl_3). **Anal** Calcd for $\text{C}_{26}\text{H}_{36}\text{O}_6$: C, 70.24; H, 8.16. Found: C, 69.90; H, 8.07.

(+)-Triene (11). In a 100 mL, two-neck flask fitted with a reflux condenser, dry sodium hydride (0.30 g, 12.3 mmol) was stirred in DMSO (12 mL) at 75 °C for 1 h with a color change from colorless to blue-green signifying the formation of the dimsyl ylide. The solution was cooled to 5 °C, and a solution of methyltriphenylphosphonium bromide (4.4 g, 12.3 mmol) in warm DMSO (24 mL) was added dropwise over 30 min. The resulting yellow solution was stirred at rt for 1 h. The Wittig reagent was titrated to 0.17 M with acetophenone.

The Wittig reagent (4.5 mL, 0.675 mmol) and the diketone **10** (50 mg, 0.112 mmol) were combined, and stirred at 75 °C for 2 h. The mixture was then cooled to rt and quenched by adding rapidly to a solution of sat. $\text{NH}_4\text{Cl}/\text{H}_2\text{O}$ (20 mL). The aqueous layer was extracted with diethyl ether (5 x 20 mL), and the combined organic layers were washed with brine, dried over MgSO_4 , and filtered. The mixture was concentrated *in vacuo*, and the residue purified on basic

alumina (gradient 9:1, 5:1, 2.5:1, 1:1 hexanes/ether). The reaction afforded 29.5 mg of compound **11** (60%) as a colorless oil: **FTIR** (NaCl, thin film) 3077 (w), 2982 (m), 2936 (br), 2869 (br), 1632 (m), 1442 (m), 1066 (s) cm^{-1} . **^1H NMR** (400 MHz, CDCl_3): δ 0.96 (s, 3H), 1.15 (s, 3H), 1.30-1.71 (m, 10H), 1.72 (dd, $J = 12.0, 2.4$ Hz, 1H), 1.87 (m, 1H), 2.10 (m, 2H), 2.38 (m, 1H), 2.43 (dt, $J = 13.5, 6.8$ Hz, 1H), 2.59 (dt, $J = 14.0, 7.0$ Hz, 1H), 3.73 (d, $J = 12.4$ Hz, 1H), 3.81-3.95 (m, 5H), 4.29 (t, $J = 6.8$ Hz, 1H), 4.59 (s, 1H), 4.74 (s, 1H), 4.89 (s, 1H), 4.94 (s, 1H), 5.03 (d with fine splitting, $J = 10.0$ Hz, 1H), 5.06 (d with fine splitting, $J = 17.2$ Hz, 1H), 5.78 (ddd, $J = 17.2, 14.0, 10.0$ Hz, 1H), 6.39 (s with fine splitting, 1H, Ar), 7.34 (s, 1H, Ar), 7.40 (s with fine splitting, 1H, Ar). **^{13}C NMR** (100 MHz, CDCl_3): δ 154.1, 147.4, 143.6, 140.5, 134.9, 126.0, 117.3, 113.6, 111.1, 109.1, 106.5, 72.7, 71.3, 65.5, 65.0, 44.2, 43.5, 42.5, 41.3, 37.2, 31.6, 30.6, 29.8, 27.6, 24.6, 23.2, 21.3, 17.7. $[\alpha]_D^{20} + 5.86$ (c 0.27, CHCl_3). **Anal** Calcd for $\text{C}_{28}\text{H}_{40}\text{O}_6$: C, 76.33; H, 9.15. Found: C, 76.06; H, 9.34.

(+)-Dienyl furan (12). In a 50 mL Schlenk flask, triene **11** (225 mg, 0.51 mmol) was dissolved in CH_2Cl_2 (20 mL), and the ruthenium catalyst (22 mg, 0.026 mmol) in CH_2Cl_2 (1 mL) was added. The reaction was stirred at rt for 14 h, concentrated to an oil, and purified through silica gel chromatography (15 : 1 hexanes/ether). The reaction afforded 192 mg of compound **12** (91%) as a colorless oil: **FTIR** (NaCl, thin film) 3079 (w), 2936 (br), 2869 (br), 1632 (w), 1063 (s), 876 (m) cm^{-1} . **^1H NMR** (400 MHz, CDCl_3): δ 0.97 (s, 3H), 1.14 (s, 3H), 1.32-1.80 (m, 12H),

1.95 (t, $J = 12.8$ Hz, 1H), 2.13 (dt, $J = 14.0, 4.8$ Hz, 1H), 2.22 (m, 1H), 2.35 (m, 2H), 3.87 (m, 4H), 4.10 (d, $J = 15.6$ Hz, 1H), 4.22 (d with fine splitting, $J = 15.6$ Hz, 1H), 4.49 (dd, $J = 10.0, 3.6$ Hz, 1H), 4.57 (s, 1H), 4.74 (s, 1H), 5.57 (br s with fine splitting, 1H), 6.42 (s with fine splitting, 1H, Ar), 7.38 (s with fine splitting, 1H, Ar), 7.40 (s with fine splitting, 1H, Ar). ^{13}C NMR (100 MHz, CDCl_3): δ 153.9, 143.3, 139.5, 138.0, 127.0, 117.0, 113.6, 109.2, 106.5, 68.9, 68.7, 65.5, 65.0, 44.1, 43.5, 42.4, 37.0, 31.6, 31.5, 30.6, 29.7, 27.2, 24.6, 23.2, 21.3, 17.6. $[\alpha]_{\text{D}}^{20} + 31.42$ (c 0.42, CHCl_3). **Anal** Calcd for $\text{C}_{26}\text{H}_{36}\text{O}_4$: C, 75.60; H, 8.80. Found: C, 75.95; H, 9.05.

(+)-Furanyl ketal (12a). In a sealed tube with sidearm joint and teflon screwcap, diene **12** (15 mg, 0.036 mmol) in CH_2Cl_2 (0.20 mL) was added and mixture degassed twice utilizing a freeze/vacuum/thaw protocol (1. Freeze solution in liquid N_2 . 2. Place under high vacuum for several seconds, then seal the reaction tube. 3. Thaw the solution, then repeat.) and refilled with nitrogen. In a glovebox, a solution of (R)-BINAP (5.4 mg, 0.0086 mmol) and $[(\text{COD})\text{RhCl}]_2$ (1.8 mg, 0.0036 mmol) in CH_2Cl_2 (0.30 mL) was added to the sealed tube. The reaction was degassed three times utilizing the freeze/vacuum/thaw protocol and refilled with hydrogen at -196°C (in liquid N_2) and sealed. The reaction was stirred at 30°C for 6.5 d, opened to air, and concentrated *in vacuo*. The resulting residue was purified through silica gel chromatography (15 : 1 hexanes/ether) to give the desired β -diastereomer **12a** (8.0 mg) and an inseparable mixture of the α -diastereomer and the starting material **12** (6.0 mg, 1.5:1 sm/ α -diast.). Based on these ratios, the reaction afforded a combined yield of 10.4 mg of compound **12a** and its

α -diastereomer (91% based on 76% conversion) as a white solid. The product was recrystallized from acetonitrile to obtain crystals suitable for X-ray crystallography. **mp** 124-126 °C. **FTIR** (NaCl, thin film) 3140 (w), 3112 (w), 2955 (s), 2880 (s), 2836 (s), 1453 (m), 1381 (m), 1061 (s) cm^{-1} . **^1H NMR** (400 MHz, CDCl_3): δ 0.89 (s, 3H), 0.95 (d, J = 6.8 Hz, 3H), 1.09 (m, 1H), 1.10 (s, 3H), 1.16-1.30 (m, 3H), 1.38-1.93 (m, 12H), 2.18-2.38 (m, 2H), 3.80-4.00 (m, 4H), 4.10 (br d, J = 16.0 Hz, 1H), 4.23 (br d with fine splitting, J = 16.0 Hz, 1H), 4.50 (dd, J = 10.0, 3.6 Hz, 1H), 5.55 (br s with fine splitting, 1H), 6.42 (s with fine splitting, 1H, Ar), 7.38 (s with fine splitting, 1H, Ar), 7.41 (s with fine splitting, 1H, Ar). **^{13}C NMR** (100 MHz, CDCl_3): δ 143.1, 139.3, 138.2, 126.9, 117.1, 113.8, 109.1, 68.9, 68.7, 65.5, 65.1, 44.1, 43.1, 38.4, 37.7, 35.4, 31.7, 30.7, 26.5, 25.2, 24.0, 23.5, 20.7, 20.3, 18.0, 15.0. $[\alpha]_D^{20}$ + 53.99 (c 1.00, CHCl_3). **Anal** Calcd for $\text{C}_{26}\text{H}_{38}\text{O}_4$: C, 75.32; H, 9.24. Found: C, 75.15; H, 8.96.

ORTEP of Compound **12a**.

Table 1. Crystal data and structure refinement for compound **12a**.

Identification code	akc01a	
Empirical formula	C ₂₆ H ₃₈ O ₄	
Formula weight	414.56	
Temperature	183(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 7.6082(11) Å b = 11.3828(16) Å c = 13.3218(19) Å	$\alpha = 90^\circ$. $\beta = 106.309(3)^\circ$. $\gamma = 90^\circ$.
Volume	1107.3(3) Å ³	
Z	2	
Density (calculated)	1.243 Mg/m ³	
Absorption coefficient	0.082 mm ⁻¹	
F(000)	452	
Crystal size	0.3 x 0.25 x 0.2 mm ³	
Theta range for data collection	2.40 to 28.32°	
Index ranges	-9 ≤ h ≤ 10, -13 ≤ k ≤ 15, -17 ≤ l ≤ 16	
Reflections collected	8246	
Independent reflections	4311 [R(int) = 0.0442]	
Completeness to theta = 28.32°	99.2 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	4311 / 1 / 271	
Goodness-of-fit on F ²	1.033	
Final R indices [I > 2σ(I)]	R1 = 0.0508, wR2 = 0.1167	
R indices (all data)	R1 = 0.0578, wR2 = 0.1200	
Absolute structure parameter	0.4(11)	
Largest diff. peak and hole	0.560 and -0.178 e.Å ³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **12a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(3)	2275(2)	7375(2)	3712(1)	37(1)
O(2)	7276(2)	8419(2)	-2641(1)	39(1)
O(1)	6106(2)	7055(1)	-1741(1)	34(1)
C(16)	5682(3)	8434(2)	1742(2)	25(1)
C(6)	6043(2)	8631(2)	-78(2)	23(1)
C(20)	4698(3)	5980(2)	4421(2)	32(1)
O(4)	-175(2)	5392(2)	5815(1)	40(1)
C(7)	6954(3)	8909(2)	1107(2)	25(1)
C(1)	7247(3)	8855(2)	-829(2)	29(1)
C(18)	5318(3)	7721(2)	3468(2)	26(1)
C(8)	8833(3)	8266(2)	1460(2)	34(1)
C(17)	6451(3)	8455(2)	2944(2)	28(1)
C(23)	1737(3)	6007(2)	4921(2)	32(1)
C(2)	6246(3)	8286(2)	-1892(2)	30(1)
C(3)	4358(3)	8805(2)	-2361(2)	36(1)
C(5)	4138(3)	9184(2)	-524(2)	32(1)
C(10)	9118(3)	8259(3)	-397(2)	42(1)
C(19)	5853(3)	6698(2)	3914(2)	31(1)
C(21)	3165(3)	6727(2)	4622(2)	31(1)
C(25)	-257(3)	4618(2)	5028(2)	41(1)

Table 2 (cont). Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **12a**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(22)	3470(3)	8208(2)	3453(2)	33(1)
C(4)	3179(3)	8691(2)	-1612(2)	36(1)
C(12)	7221(4)	10223(2)	1339(2)	38(1)
C(9)	10030(3)	8565(3)	747(2)	49(1)
C(13)	8711(3)	6941(2)	1557(2)	45(1)
C(14)	6559(4)	6458(2)	-2567(2)	44(1)
C(26)	860(3)	4953(2)	4456(2)	42(1)
C(15)	7827(4)	7289(3)	-2889(2)	48(1)
C(11)	7551(4)	10156(2)	-1042(2)	49(1)
C(24)	1055(3)	6225(2)	5726(2)	38(1)

Table 3. Bond lengths [$\text{\AA}$] and angles [$^\circ$] for **12a**.

O(3)-C(21)	1.417(3)
O(3)-C(22)	1.422(3)
O(2)-C(15)	1.420(3)
O(2)-C(2)	1.439(3)
O(1)-C(14)	1.416(3)
O(1)-C(2)	1.424(3)
C(16)-C(17)	1.542(3)
C(16)-C(7)	1.551(3)
C(6)-C(5)	1.538(3)
C(6)-C(1)	1.556(3)
C(6)-C(7)	1.567(3)
C(20)-C(19)	1.494(3)
C(20)-C(21)	1.526(3)
O(4)-C(25)	1.356(3)
O(4)-C(24)	1.360(3)
C(7)-C(12)	1.530(3)
C(7)-C(8)	1.556(3)
C(1)-C(10)	1.536(3)
C(1)-C(11)	1.537(3)
C(1)-C(2)	1.549(3)
C(18)-C(19)	1.318(3)
C(18)-C(22)	1.506(3)
C(18)-C(17)	1.507(3)
C(8)-C(13)	1.520(4)
C(8)-C(9)	1.527(3)
C(23)-C(24)	1.339(3)
C(23)-C(26)	1.427(4)
C(23)-C(21)	1.501(3)
C(2)-C(3)	1.516(3)
C(3)-C(4)	1.522(3)
C(5)-C(4)	1.535(3)
C(10)-C(9)	1.527(3)
C(25)-C(26)	1.345(4)
C(14)-C(15)	1.497(4)
C(21)-O(3)-C(22)	111.72(17)
C(15)-O(2)-C(2)	108.67(18)

Table 3 (cont). Bond lengths [Å] and angles [°] for **12a**.

C(14)-O(1)-C(2)	108.55(17)
C(17)-C(16)-C(7)	116.62(16)
C(5)-C(6)-C(1)	110.23(17)
C(5)-C(6)-C(7)	114.11(16)
C(1)-C(6)-C(7)	116.15(15)
C(19)-C(20)-C(21)	110.51(19)
C(25)-O(4)-C(24)	105.59(19)
C(12)-C(7)-C(16)	107.34(17)
C(12)-C(7)-C(8)	109.89(18)
C(16)-C(7)-C(8)	109.38(18)
C(12)-C(7)-C(6)	113.40(18)
C(16)-C(7)-C(6)	108.17(15)
C(8)-C(7)-C(6)	108.58(16)
C(10)-C(1)-C(11)	108.9(2)
C(10)-C(1)-C(2)	108.90(19)
C(11)-C(1)-C(2)	107.19(19)
C(10)-C(1)-C(6)	109.69(18)
C(11)-C(1)-C(6)	115.03(19)
C(2)-C(1)-C(6)	106.96(16)
C(19)-C(18)-C(22)	120.07(19)
C(19)-C(18)-C(17)	123.65(19)
C(22)-C(18)-C(17)	116.27(18)
C(13)-C(8)-C(9)	109.6(2)
C(13)-C(8)-C(7)	114.80(18)
C(9)-C(8)-C(7)	111.4(2)
C(18)-C(17)-C(16)	111.91(16)
C(24)-C(23)-C(26)	105.3(2)
C(24)-C(23)-C(21)	125.7(2)
C(26)-C(23)-C(21)	129.0(2)
O(1)-C(2)-O(2)	106.17(17)
O(1)-C(2)-C(3)	109.99(18)
O(2)-C(2)-C(3)	108.12(18)
O(1)-C(2)-C(1)	108.68(17)
O(2)-C(2)-C(1)	111.42(17)
C(3)-C(2)-C(1)	112.28(19)
C(2)-C(3)-C(4)	111.18(18)
C(4)-C(5)-C(6)	111.19(18)
C(9)-C(10)-C(1)	112.8(2)
C(18)-C(19)-C(20)	122.7(2)
O(3)-C(21)-C(23)	107.64(18)
O(3)-C(21)-C(20)	110.20(18)
C(23)-C(21)-C(20)	112.8(2)
C(26)-C(25)-O(4)	110.8(2)
O(3)-C(22)-C(18)	114.14(19)
C(3)-C(4)-C(5)	112.12(19)
C(8)-C(9)-C(10)	112.76(18)
O(1)-C(14)-C(15)	103.7(2)
C(25)-C(26)-C(23)	106.6(2)
O(2)-C(15)-C(14)	104.4(2)
C(23)-C(24)-O(4)	111.8(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for **12a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(3)	33(1)	39(1)	40(1)	11(1)	12(1)	3(1)
O(2)	47(1)	44(1)	34(1)	-4(1)	25(1)	-5(1)
O(1)	46(1)	28(1)	32(1)	-5(1)	16(1)	-4(1)
C(16)	22(1)	31(1)	25(1)	-2(1)	9(1)	-1(1)
C(6)	23(1)	23(1)	25(1)	-2(1)	11(1)	-2(1)
C(20)	35(1)	34(1)	28(1)	7(1)	12(1)	8(1)
O(4)	43(1)	38(1)	44(1)	5(1)	22(1)	-1(1)
C(7)	24(1)	26(1)	26(1)	-4(1)	11(1)	-5(1)
C(1)	28(1)	34(1)	29(1)	-5(1)	15(1)	-10(1)
C(18)	25(1)	31(1)	21(1)	-2(1)	6(1)	-2(1)
C(8)	20(1)	51(2)	29(1)	-12(1)	7(1)	0(1)
C(17)	26(1)	33(1)	25(1)	-2(1)	8(1)	-3(1)
C(23)	35(1)	29(1)	34(1)	7(1)	12(1)	7(1)
C(2)	34(1)	31(1)	28(1)	-1(1)	15(1)	-8(1)
C(3)	40(1)	42(1)	26(1)	6(1)	10(1)	2(1)
C(5)	29(1)	39(1)	30(1)	6(1)	14(1)	7(1)
C(10)	25(1)	70(2)	34(1)	-14(1)	15(1)	-6(1)
C(19)	27(1)	38(1)	28(1)	2(1)	10(1)	7(1)
C(21)	34(1)	34(1)	27(1)	1(1)	10(1)	1(1)
C(25)	37(1)	36(1)	51(2)	-1(1)	14(1)	-4(1)
C(22)	33(1)	30(1)	39(1)	8(1)	16(1)	4(1)
C(4)	27(1)	49(2)	30(1)	7(1)	7(1)	6(1)
C(12)	54(1)	29(1)	37(1)	-10(1)	22(1)	-12(1)
C(9)	21(1)	89(2)	37(1)	-17(1)	10(1)	-10(1)
C(13)	40(1)	52(2)	39(1)	-8(1)	3(1)	20(1)
C(14)	57(2)	41(2)	34(1)	-7(1)	14(1)	3(1)
C(26)	44(1)	46(2)	38(1)	-4(1)	13(1)	-1(1)
C(15)	51(2)	56(2)	43(2)	-16(1)	23(1)	-4(1)
C(11)	70(2)	44(2)	42(1)	-6(1)	29(1)	-28(1)
C(24)	42(1)	33(1)	44(1)	-1(1)	20(1)	-3(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for **12a**.

	x	y	z	U(eq)
H(16A)	4559	8888	1553	30
H(16B)	5364	7629	1528	30
H(6A)	5828	7781	-106	27
H(20A)	5453	5667	5078	38
H(20B)	4173	5324	3972	38
H(8A)	9469	8566	2157	40
H(17A)	7698	8162	3138	33
H(17B)	6478	9260	3188	33
H(3A)	3766	8403	-3010	43
H(3B)	4474	9628	-2519	43
H(5A)	3394	9025	-55	38
H(5B)	4262	10029	-569	38
H(10A)	8959	7414	-462	50
H(10B)	9917	8495	-814	50
H(19A)	6998	6412	3912	37
H(21A)	3700	7280	5189	38
H(25A)	-985	3948	4902	49
H(22A)	3644	8858	3942	39
H(22B)	2889	8517	2760	39
H(4A)	2892	7869	-1548	43
H(4B)	2036	9108	-1899	43
H(12A)	7788	10336	2073	57
H(12B)	6053	10610	1143	57
H(12C)	7989	10548	948	57
H(9A)	11177	8140	984	58
H(9B)	10307	9398	802	58
H(13A)	9923	6615	1779	68
H(13B)	8064	6614	892	68
H(13C)	8069	6755	2063	68
H(14A)	5475	6309	-3142	52
H(14B)	7163	5718	-2329	52
H(26A)	1027	4572	3872	50
H(15A)	9090	7134	-2505	58
H(15B)	7700	7224	-3632	58
H(11A)	8317	10214	-1504	74
H(11B)	8134	10545	-395	74
H(11C)	6392	10523	-1362	74
H(24A)	1382	6867	6171	46

Table 6. Torsion angles [°] for **12a**.

C(17)-C(16)-C(7)-C(12)	-65.8(2)
C(17)-C(16)-C(7)-C(8)	53.3(2)
C(17)-C(16)-C(7)-C(6)	171.45(18)
C(5)-C(6)-C(7)-C(12)	-59.3(2)
C(1)-C(6)-C(7)-C(12)	70.6(2)
C(5)-C(6)-C(7)-C(16)	59.6(2)
C(1)-C(6)-C(7)-C(16)	-170.47(18)
C(5)-C(6)-C(7)-C(8)	178.21(18)
C(1)-C(6)-C(7)-C(8)	-51.9(2)
C(5)-C(6)-C(1)-C(10)	-177.80(18)
C(7)-C(6)-C(1)-C(10)	50.4(2)
C(5)-C(6)-C(1)-C(11)	59.1(2)
C(7)-C(6)-C(1)-C(11)	-72.7(3)
C(5)-C(6)-C(1)-C(2)	-59.8(2)
C(7)-C(6)-C(1)-C(2)	168.40(18)
C(12)-C(7)-C(8)-C(13)	163.6(2)
C(16)-C(7)-C(8)-C(13)	46.0(2)
C(6)-C(7)-C(8)-C(13)	-71.8(2)
C(12)-C(7)-C(8)-C(9)	-71.1(2)
C(16)-C(7)-C(8)-C(9)	171.32(19)
C(6)-C(7)-C(8)-C(9)	53.5(2)
C(19)-C(18)-C(17)-C(16)	107.0(2)
C(22)-C(18)-C(17)-C(16)	-72.2(2)
C(7)-C(16)-C(17)-C(18)	-166.25(18)
C(14)-O(1)-C(2)-O(2)	-15.9(2)
C(14)-O(1)-C(2)-C(3)	100.8(2)
C(14)-O(1)-C(2)-C(1)	-135.87(19)
C(15)-O(2)-C(2)-O(1)	-3.1(2)
C(15)-O(2)-C(2)-C(3)	-121.1(2)
C(15)-O(2)-C(2)-C(1)	115.1(2)
C(10)-C(1)-C(2)-O(1)	56.6(2)
C(11)-C(1)-C(2)-O(1)	174.21(19)
C(6)-C(1)-C(2)-O(1)	-61.9(2)
C(10)-C(1)-C(2)-O(2)	-60.1(2)
C(11)-C(1)-C(2)-O(2)	57.6(2)
C(6)-C(1)-C(2)-O(2)	-178.56(18)
C(10)-C(1)-C(2)-C(3)	178.5(2)
C(11)-C(1)-C(2)-C(3)	-63.9(2)
C(6)-C(1)-C(2)-C(3)	60.0(2)
O(1)-C(2)-C(3)-C(4)	64.2(2)
O(2)-C(2)-C(3)-C(4)	179.74(19)
C(1)-C(2)-C(3)-C(4)	-56.9(3)
C(1)-C(6)-C(5)-C(4)	58.0(2)
C(7)-C(6)-C(5)-C(4)	-169.17(18)
C(11)-C(1)-C(10)-C(9)	76.0(3)
C(2)-C(1)-C(10)-C(9)	-167.4(2)
C(6)-C(1)-C(10)-C(9)	-50.7(3)
C(22)-C(18)-C(19)-C(20)	-0.2(3)
C(17)-C(18)-C(19)-C(20)	-179.4(2)
C(21)-C(20)-C(19)-C(18)	-16.2(3)
C(22)-O(3)-C(21)-C(23)	171.75(19)
C(22)-O(3)-C(21)-C(20)	-64.8(2)
C(24)-C(23)-C(21)-O(3)	-105.9(3)
C(26)-C(23)-C(21)-O(3)	76.2(3)
C(24)-C(23)-C(21)-C(20)	132.3(2)

Table 6 (cont). Torsion angles [$^{\circ}$] for **12a**.

C(26)-C(23)-C(21)-C(20)	-45.6(3)
C(19)-C(20)-C(21)-O(3)	47.7(3)
C(19)-C(20)-C(21)-C(23)	168.07(18)
C(24)-O(4)-C(25)-C(26)	-0.7(3)
C(21)-O(3)-C(22)-C(18)	47.3(3)
C(19)-C(18)-C(22)-O(3)	-14.3(3)
C(17)-C(18)-C(22)-O(3)	164.95(18)
C(2)-C(3)-C(4)-C(5)	52.5(3)
C(6)-C(5)-C(4)-C(3)	-53.6(3)
C(13)-C(8)-C(9)-C(10)	70.3(3)
C(7)-C(8)-C(9)-C(10)	-57.8(3)
C(1)-C(10)-C(9)-C(8)	56.5(3)
C(2)-O(1)-C(14)-C(15)	27.5(3)
O(4)-C(25)-C(26)-C(23)	0.9(3)
C(24)-C(23)-C(26)-C(25)	-0.8(3)
C(21)-C(23)-C(26)-C(25)	177.5(2)
C(2)-O(2)-C(15)-C(14)	19.5(2)
O(1)-C(14)-C(15)-O(2)	-28.5(3)
C(26)-C(23)-C(24)-O(4)	0.4(3)
C(21)-C(23)-C(24)-O(4)	-178.0(2)
C(25)-O(4)-C(24)-C(23)	0.2(3)

Symmetry transformations used to generate equivalent atoms:

(+)-Furanyl ketone (12b). The ketal **12a** (13 mg, 0.029 mmol) was stirred in 1 N HCl/THF (1:2, 0.50 mL) at rt for 16 h. The mixture was diluted with ether, and washed consecutively with water, sat. NaHCO₃, and brine. The organic layer was dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting residue was purified through silica gel chromatography (10:1 hexanes/ether) to afford 10.5 mg of compound **12b** (90%) as a white solid: **mp** 79-82 °C. **FTIR** (NaCl, thin film) 2936 (s), 2873 (m), 1704 (s), 1502 (w), 1455 (m), 1383 (m), 1159 (m), 1069 (m), 1025 (m), 882 (m) cm⁻¹. **¹H NMR** (400 MHz, CDCl₃): δ 0.90 (d, J = 7.2 Hz, 3H), 1.00 (s, 3H), 1.15 (m, 1H), 1.19 (s, 3H), 1.28 (m, 2H), 1.36 (dd, J = 11.2, 3.0

Hz, 2H), 1.46-1.92 (m, 8H), 2.07 (m, 1H), 2.17-2.39 (m, 3H), 2.58 (td, $J = 13.6, 7.2$ Hz, 1H), 4.11 (br d, $J = 16.0$ Hz, 1H), 4.23 (br d with fine splitting, $J = 16.8$ Hz, 1H), 4.50 (dd, $J = 9.6, 3.6$ Hz, 1H), 5.57 (br s with fine splitting, 1H), 6.42 (s with fine splitting, 1H, Ar), 7.39 (s with fine splitting, 1H, Ar), 7.41 (s with fine splitting, 1H, Ar). ^{13}C NMR (125 MHz, CDCl_3): δ 216.0, 143.4, 139.5, 138.0, 127.0, 118.0, 109.1, 68.9, 68.5, 49.5, 47.5, 38.7, 38.2, 37.7, 35.0, 31.5, 26.4, 26.3, 26.1, 24.8, 21.0, 20.3, 19.8, 14.6. $[\alpha]_{\text{D}}^{20} + 61.32$ (c 0.60, CHCl_3). HRMS (ESI+) m/z calcd for $\text{C}_{24}\text{H}_{34}\text{O}_3\text{Na}$: 393.2406. Found: 393.2410.

(+)-Furan (13). The Wittig solution was prepared as described in the preparation of compound **11**. Ketone **12b** (13.4 mg, 0.036 mmol) was stirred with the Wittig solution (1.2 mL) at 75 °C for 1h. The reaction was quenched by adding rapidly to sat. $\text{NH}_4\text{Cl}/\text{H}_2\text{O}$ (5 mL), and extracted with ether (4 x 5 mL). The combined organic layers were washed with brine, dried over MgSO_4 , and filtered. The mixture was concentrated *in vacuo*, and purified through silica gel chromatography (20 : 1 hexanes/ether) to afford 11.1 mg of compound **13** (84%) as a white solid: mp 36-39 °C. FTIR (NaCl, thin film) 3083 (w), 2936 (s), 2868 (m), 1628 (w), 1450 (m), 1377 (m), 1152 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 0.92 (d, $J = 7.2$ Hz, 3H), 0.93 (s, 3H), 1.08 (m, 1H), 1.10 (s, 3H), 1.17 (dd, $J = 12.0, 2.4$ Hz, 1H), 1.20-1.53 (m, 5H), 1.60 (m, 2H), 1.76-1.91 (m, 4H), 1.99 (tt, $J = 13.8, 3.6$ Hz, 1H), 2.09 (d with fine splitting, $J = 13.6$ Hz, 1H), 2.17-2.39 (m, 3H), 4.11 (br d, $J = 16.0$ Hz, 1H), 4.23 (br d with fine splitting, $J = 16.0$ Hz, 1H), 4.48 (s, 1H), 4.50 (m, 1H), 4.52 (s, 1H), 5.56 (br s with fine splitting, 1H), 6.42 (s with fine

splitting, 1H, Ar), 7.38 (s with fine splitting, 1H, Ar), 7.40 (s with fine splitting, 1H, Ar). ^{13}C NMR (125 MHz, CDCl_3): δ 160.8, 143.3, 139.5, 138.3, 127.0, 117.3, 109.1, 102.2, 68.9, 68.6, 48.1, 40.6, 38.2, 38.1, 35.7, 33.1, 31.6, 30.4, 28.9, 26.3, 25.8, 21.51, 21.50, 20.7, 15.0. $[\alpha]_{\text{D}}^{20} + 92.61$ (c 0.76, CHCl_3). **Anal** Calcd for $\text{C}_{25}\text{H}_{36}\text{O}_2$: C, 81.47; H, 9.85. Found: C, 81.42; H, 9.98.

(+)-Cacospongionolide B (1). To a flask charged with rose bengal (0.8 mg, 0.0008 mmol) was added furan **13** (6.0 mg, 0.016 mmol) in a solution of CH_2Cl_2 (3.2 mL), followed by $i\text{-Pr}_2\text{NEt}$ (14 μL , 0.08 mmol). The bright red reaction was cooled to $-78\text{ }^\circ\text{C}$, and irradiated with a 150 W tungsten lamp while anhydrous O_2 was bubbled through the solution for 8 min. The irradiation continued for a total of 1 h under a blanket of anhydrous O_2 . The reaction was then protected from light, and warmed to rt under N_2 . Sat. aqueous oxalic acid (3 mL) was added, and the mixture stirred until colorless (15 min). The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), and the combined organic layers were dried over MgSO_4 , and filtered. The mixture was concentrated *in vacuo*, and the resulting residue was purified through silica gel chromatography (1:1 hexanes/ether) to provide cacospongionolide B (**1**) (4.4 mg, 69%, white solid) as a mixture of diastereomers that was identical to an authentic sample provided by Dr. S. De Rosa: **mp** 135-140 $^\circ\text{C}$. **FTIR** (NaCl, thin film) 3340 (br), 3082 (w), 2930 (s), 2867 (m), 2850 (m), 1756 (s), 1742 (s), 1637 (w), 1452 (m), 1380 (m), 1130 (m), 942 (m) cm^{-1} . ^1H NMR (400 MHz, CDCl_3): δ 0.91 (d, $J = 7.2$ Hz, 3H), 0.93 (s, 3H), 1.06 (m, 1H), 1.10 (s, 3H), 1.16 (dd, $J = 12.4, 2.0$ Hz, 1H), 1.23-1.51 (m, 5H), 1.55-1.63 (m, 2H), 1.76-1.91 (m, 4H), 1.99 (tt, $J = 14.0, 3.2$ Hz, 1H),

2.10 (dd, $J = 13.6, 4.0$ Hz, 1H), 2.18-2.38 (m, 3H), 3.70 (br s, 1H), 4.17 (m, 2H), 4.40 (ddd, $J = 9.6, 4.4, 1.2$ Hz, 0.5H), 4.42 (ddd, $J = 10.0, 4.4, 1.6$ Hz, 0.5H), 4.49 (s, 1H), 4.52 (s, 1H), 5.55 (br s, 1H), 6.02 (s with fine splitting, 0.5H), 6.09 (s with fine splitting, 1H), 6.23 (s, 0.5H). ^{13}C NMR (125 MHz, CDCl_3): δ 170.3, 167.7, 167.0, 138.6, 138.3, 118.7, 117.7, 116.2, 116.0, 102.3, 97.6, 97.1, 70.1, 69.3, 68.7, 68.6, 48.1, 40.6, 38.2, 38.1, 35.7, 33.1, 30.4, 29.9, 29.6, 29.1, 28.9, 26.3, 25.8, 21.5, 20.7, 15.0. $[\alpha]_{\text{D}}^{20} +124.0$ (c 0.25, CHCl_3). HRMS (ESI+) m/z calcd for $\text{C}_{25}\text{H}_{36}\text{O}_4\text{Na}$: 423.2511. Found: 423.2522.

Assay of the Inhibition of Bee Venom sPLA₂. The IC_{50} values for compounds (+)-**1**, (-)-**1**, **2**, (+)-**13**, and (-)-**13** were determined using sPLA₂ Assay Kit obtained from Cayman Chemical, Ann Arbor, MI (Cat. No. 765001), and UV data recorded on a Molecular Devices Thermomax microplate reader. Manoalide was obtained from BIOMOL Research Laboratories Inc., Plymouth Meeting, PA. Following the assay procedure, the initial rates of hydrolysis for a series of substrates with final concentrations from 400-0.5 μM (400, 200, 100, 50, 25, 12.5, 5, 2.5, 1, 0.5 μM) were obtained, and percent inhibition was calculated compared to a control. The percent inhibition was plotted versus the log[inhibitor], and the IC_{50} was extrapolated from the resulting curves. The values reported are the average of 3-4 measurements with error bars representing plus and minus one standard deviation unit.

Bee Venom sPLA₂ Inhibition:

Inhibitor	IC_{50}
manoalide (2)	38 ($\pm$ 3) μM
(+)-cacospongionolide B (1)	49 ($\pm$ 9) μM
(-)-cacospongionolide B (1)	114 ($\pm$ 7) μM
(+)-furan (13)	71 ($\pm$ 4) μM
(-)-furan (13)	167 ($\pm$ 32) μM