Synthesis of (±)-Symbioimine

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Supporting Material

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General procedures. NMR spectra were recorded at 400 MHz in CDCl₃, CD₃OD or DMSO-*d*₆ with TMS as internal standard at ambient temperature unless otherwise indicated. Chemical shifts are reported in δ and coupling constants in Hz. Spectra in CD₃OD are referenced to the residual solvent peaks at δ 3.31 (¹H) and δ 49.15 (¹³C). Spectra in DMSO-*d*₆ are referenced to the residual solvent peaks at δ 2.50 (¹H) and δ 39.51 (¹³C). IR spectra are reported in cm⁻¹. Powdered zinc was activated by washing sequentially with 3 M HCl, water, EtOH, and ether and drying under reduced pressure.^{S1}

Ethyl 7,7-dimethoxy-3-oxoheptanoate (S1) was prepared by the literature procedure.^{S2} To an ice-cooled solution of diisopropylamine (2.33 g, 3.22 mL, 23 mmol) in 40 mL of THF under N₂ at 0 °C was added *n*-BuLi (1.6 M in hexanes, 13.8 mL, 22 mmol) dropwise. The resulting mixture was stirred for an additional 30 min, and ethyl acetoacetate (1.30 g, 1.27 mL, 10 mmol) was added dropwise over a period of 5 min. The solution was stirred for 1 h and treated with 3-bromo-1,1-dimethoxypropane (1.83 g, 1.35 mL, 10 mmol). The mixture was allowed to warm slowly to 25 °C and stirring was continued for an additional 1.5 h. The reaction was quenched with saturated NH₄Cl (20 mL) and the product was extracted with Et₂O (3 × 50 mL). The combined ether extracts were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography on silica gel (5:1 hexanes/EtOAc) gave 1.72 g (75%) of **S1**^{S2b} as colorless oil: ¹H NMR (CDCl₃) 4.25 (t, 1, *J* = 5.3), 4.09 (q, 2, *J* = 7.3), 3.34 (s, 2), 3.21 (s, 6), 2.49 (t, 2, *J* = 6.7), 1.58-1.49 (m, 4), 1.18 (t, 3, *J* = 7.0); ¹³C NMR (CDCl₃) 202.2, 166.9, 104.0, 61.0, 52.5 (2 C), 49.0, 42.2, 31.4, 18.2, 13.8; IR (neat) 1744, 1716, 1448, 1412, 1315, 1127, 1070.

Ethyl 3-Amino-2-methyl-propionate (S2) was prepared by the literature procedure.^{S3}

To a solution of benzylamine (107 g, 1 mol) in 200 mL of EtOH was added ethyl methacrylate (137 g, 1.2 mol) at 25 °C. The resulting solution was heated to reflux for 24 h. The solvent was removed under reduced pressure. The residual solvent, ethyl methacrylate and benzylamine was distilled out under reduced pressure (95-120 °C oil bath, 160 Torr) to give 149.9 g (68%) of ethyl 3-benzylamino-2-methylpropanoate as a clear liquid that was >90% pure and was used for the next step: ¹H NMR (CDCl₃) 7.35-7.22 (m, 5), 4.14 (q, 2, *J* = 7.0), 3.79 (m, 2), 2.92-2.85 (m, 1), 2.71-2.62 (m, 2), 1.25 (t, 3, *J* = 7.0), 1.16 (d, 3, *J* = 7.0); ¹³C NMR (CDCl₃) 175.8, 140.3, 128.3 (2 C), 127.9 (2 C), 126.8, 60.3, 53.7, 52.1, 40.1, 15.3, 14.2; IR (neat) 1730, 1182. The spectral data are identical to those reported previously.^{S3}

To a solution of ethyl 3-benzylamino-2-methylpropanoate (22.1 g, 100 mmol) in 75 mL of EtOH at 25 °C was added 10% palladium on charcoal (2.0 g). The resulting mixture was hydrogenated at 25 °C and under 1 atm H₂ for 24 h at which time TLC (silica gel, 10:1 hexanes/EtOAc) showed that no starting material was left. The reaction mixture was filtered and the filter cake was washed with EtOH (2 × 10 mL). The combined organic phases were concentrated under reduced pressure and the oily residue was distilled in vacuum (70 °C/12 Torr) to give 9.16 g (97%) of **S2** as a colorless liquid: ¹H NMR (CDCl₃) 4.16 (q, 2, *J* = 7.0), 2.92 (dd, 1, *J* = 13.6, 8.0), 2.79 (dd, 1, *J* = 13.6, 4.8), 2.52 (ddq, 1, *J* = 8.0, 4.8, 7.0), 1.27 (t, 3, *J* = 7.0), 1.16 (d, 3, *J* = 7.0); ¹³C NMR (CDCl₃) 175.6, 60.3, 45.1, 42.8, 14.7, 14.1; IR (neat) 2979, 1731, 1465, 1182. The spectral data are identical to those reported previously.^{S3}

Ethyl 7,7-dimethoxy-2-yl-3-(2-ethoxycarbonyl-propylamino)-2-heptenoate (3). To a solution of amine **S2**^{S3} (655 mg, 5 mmol) in 5 mL of MeOH was added 1 mL of HOAc. The solution was stirred at 25 °C for 5 minutes, and the solvent was evaporated. The residue was dissolved in 25 mL of dry toluene and the resulting solution was treated with HOAc (0.1 mL) and ketoester **S1**^{S2b} (1.16 g, 5 mmol). A Dean-Stark trap was attached to the flask and the solution was heated to reflux. After the reaction was completed (~2 h), the solution was cooled to 25 °C and treated with 10 mL of 20% K₂CO₃ solution. The mixture was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography on MeOH-deactivated silica gel (9:1 hexanes/EtOAc) gave 1.66 g (97%) of **S3** as a colorless oil: ¹H NMR (CDCl₃) 8.64 (br t, 1, NH), 4.40 (s, 1), 4.31 (t, 1, *J* = 5.2), 4.10 (q, 2, *J* = 7.0), 4.01 (q, 2, *J* = 7.0), 3.42 (ddd, 1, *J* = 13.5, 6.9, 6.9), 3.26 (s, 6), 3.20 (ddd, 1, *J* = 13.5, 6.9, 6.9), 2.58 (ddq, 1, *J* = 6.9, 6.9, 6.9), 2.20-2.10 (m, 2), 1.63-1.49 (m, 4), 1.22-1.13 (m, 9); ¹³C NMR (CDCl₃) 174.3, 170.4, 164.5, 104.0, 82.2, 60.6, 58.2, 52.7 (2 C), 45.2, 40.7, 31.79, 31.73, 22.8, 14.7, 14.4, 14.0; IR (neat) 1731, 1651, 1607, 1233, 1173, 1127; HRMS (TOF MS ES⁺) calcd for C₁₇H₃₂NO₆ (MH⁺) 346.2230, found 346.2230.

Ethyl 2-(4,4-dimethoxybutyl)-5-methyl-4-oxo-1,4,5,6-tetrahydropyridine-3-

carboxylate (S4). To a solution of **S3** (1.66 g, 4.82 mmol) in 20 mL of dry THF at 25 °C was added NaH (60% in mineral oil, 0.6 g, 15 mmol) in one portion. The resulting mixture was heated to reflux for 1 h and cooled to 25 °C. Saturated NH₄Cl solution (10 mL) was carefully added and the layers were separated. The aqueous phase was extracted with CH₂Cl₂ (3 × 20 mL), and the combined organic layers were washed with saturated NaHCO₃ and brine, dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography on silica gel (20:1 CH₂Cl₂/MeOH) gave 1.37 g (95%) of **S4** as a tan oil: ¹H NMR (CDCl₃) 6.18 (br s, 1, NH), 4.36 (t, 1, *J* = 4.9), 4.24 (q, 2, *J* = 7.3), 3.57 (ddd, 1, *J* = 13.4, 6.1, 3.7), 3.34 (s, 6), 3.22 (ddd, 1, *J* = 13.4, 11.0, 2.4), 2.66-2.58 (m, 2), 2.48-2.42 (m, 1), 1.75-1.64 (m, 4), 1.32 (t, 3, *J* = 7.3), 1.13 (d, 3, *J* = 6.7); ¹³C NMR (CDCl₃) 191.9, 169.5, 166.9, 104.2, 101.4, 59.7, 52.83, 52.81, 46.4, 37.9, 33.6, 31.8, 23.6, 14.2, 13.1; IR (neat) 3263, 2956, 1694, 1566, 1289; HRMS (TOF MS ES+) calcd for C₁₅H₂₆NO₅ (MH⁺) 300.1811, found 300.1183.

6-(4,4-Dimethoxybutyl)-3-methyl-2,3-dihydropyridin-4(1H)-one (S5). To a solution of **S4** (0.90 g, 3 mmol) in 10 mL of MeOH was added 10 mL of 25% aqueous NaOH. The mixture was heated to reflux for 16 h. After the mixture was cooled to 25 °C, 10 mL of saturated NH₄Cl solution was added. The solution was extracted with CH₂Cl₂ (5 × 20 mL), and the combined organic layers were dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (20:1 CH₂Cl₂/MeOH) afforded 626 mg (92%) of **S5** as a tan oil: ¹H NMR (CDCl₃) 5.15 (br s, 1, NH), 4.95 (s, 1), 4.35 (br t, 1, *J* = 4.2), 3.54 (ddd, 1, *J* = 12.8, 6.1, 3.0), 3.33 (s, 6), 3.20 (ddd, 1, *J* = 12.8, 11.0, 1.9), 2.41-2.36 (m, 1), 2.23-2.18 (m, 2), 1.84-1.63 (m, 4), 1.12 (d, 3, *J* = 6.7); ¹³C NMR (CDCl₃) 195.7, 165.3, 104.2, 97.2,

53.0 (2 C), 48.1, 38.2, 34.3, 31.6, 22.7, 13.5; IR (neat) 3253, 2956, 1609, 1538, 1127; HRMS (TOF MS ES⁺) calcd for C₁₂H₂₂NO₃ (MH⁺) 228.1600, found 228.1605.

2,2,2-Trichloroethyl 3,4-Dihydro-6-(4,4-dimethoxybutyl)-3- methyl-4- oxopyridine - 1(2H)-carboxylate (S6). To a solution of **S5** (454 mg, 2 mmol) in 20.0 mL of THF at -78 °C was added *n*-BuLi (1.6 M in hexanes, 1.38 mL, 2.2 mmol), and the solution was stirred for 30 min. A solution of Troc chloride (289 μ L, 445 mg, 2.1 mmol) in 2 mL of THF was added dropwise via cannula over 5 min. After stirring for 30 min at the same temperature, the reaction was treated with 10 mL of saturated NaHCO₃ and the mixture was stirred at 25 °C for 20 min. The reaction mixture was extracted with EtOAc (3 $\times$ 20 mL), and the combined organic layers were washed with water, dried over MgSO₄, and concentrated under reduced pressure. Flash chromatography on silica gel (4:1 hexanes/EtOAc) afforded 767 mg (96%) of **S6** as a colorless oil: ¹H NMR (CDCl₃) 5.50 (s, 1), 4.87 (s, 2), 4.86 (t, 1, *J* = 4.4), 4.28 (dd, 1, *J* = 4.4, 12.8), 4.00-3.80 (m, 4), 3.72 (dd, 1, *J* = 12.8, 10.0), 2.95-2.72 (m, 2), 2.58-2.49 (m, 1), 1.72-1.62 (m, 4), 1.15 (d, 3, *J* = 6.8); ¹³C NMR (CDCl₃) 197.2, 159.3, 151.4, 113.6, 103.9, 94.6, 75.6, 64.8 (2 C), 52.8, 40.6, 34.7, 33.0, 22.1, 12.5; IR (neat) 1734, 1673, 1602, 1396, 1193; HRMS (DCI/NH₃) calcd for C₁₅H₂₁Cl₃NO₅ (MH⁺) 400.0485, found 400.0485.

2,2,2-Trichloroethyl 6-(4-oxobutyl)-3,4-dihydro-3-methyl-4-oxopyridine -1(2H)-carboxylate (4). A solution of **S6** (180 mg, 0.45 mmol) in 10 mL of wet acetone was treated with PPTS (35 mg, 0.14 mmol). The reaction mixture was stirred at 60 °C for 3 h, cooled to 25 °C and concentrated. The residue was dissolved in 25 mL of Et₂O. The solution was washed with 10 mL of saturated NaHCO₃, and the aqueous phase was extracted with Et₂O (2 × 10 mL). The combined organic phases were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. Flash chromatography on silica gel (4:1 hexanes/EtOAc) afforded 140 mg (87%) of aldehyde **4** as a colorless oil: ¹H NMR (CDCl₃) 9.78 (s, 1), 5.48 (s, 1), 4.86 (s, 2), 4.29 (dd, 1, *J* = 13.2, 4.4), 3.73 (dd, 1, *J* = 13.2, 9.8), 2.89 (dt, 1, *J* = 14.0, 7.0), 2.74 (dt, 1, *J* = 14.0, 7.0), 2.60-2.50 (m, 1), 2.52 (t, 2, *J* = 7.0), 1.88 (tt, 2, *J* = 7.0, 7.0), 1.15 (d, 3, *J* = 6.8); ¹³C NMR (CDCl₃) 201.2, 197.0, 158.4, 151.4, 113.6, 94.6, 75.6, 52.7, 42.9, 40.6, 34.2, 20.2, 12.5; IR (neat) 2965., 2937, 2882, 1735, 1673, 1599; HRMS (DCI/NH₃) calcd for C₁₃H₁₇Cl₃NO₄ (MH⁺) 358.0194, found 358.0198. This step requires great care to avoid condensation of the aldehyde with the enamide.

(E)-methyl 3-(3,5-bis(tert-butyldimethylsilyloxy)phenyl)acrylate (S8). To a solution of methyl (triphenylphosphoranylidene)acetate (4.35 g, 13.03 mmol) in 100 mL of CH₂Cl₂ at room temperature was added 3,5-bis(tert-butyldimethylsilyloxy)benzaldehyde (**S7**)⁹ (3.98 g, 10.86 mmol) dropwise over 5 min. Upon completion of the addition the mixture was stirred for an additional 8 h and then the solvent was removed by concentration. The resulting pasty oil was diluted with 40 mL of hexanes and the Ph₃PO that precipitated was removed by filtration and the filter cake was washed with 40 mL of hexanes. The combined organic layers were concentrated under reduced pressure. Flash chromatography on silica gel (11:1 hexanes/EtOAc) afforded 4.17 g (91%) of **S8** as a colorless oil: ¹H NMR (CDCl₃) 7.64 (d, 1, *J* = 15.9), 6.72 (d, 2, *J* = 2.1), 6.46

(t, 1, $J = 2.1$), 6.44 (d, 1, $J = 15.9$), 3.88 (s, 3), 0.99 (s, 18), 0.19 (s, 12); ^{13}C NMR (CDCl_3) 167.4, 156.8 (2 C), 144.8, 136.0, 117.9, 114.2, 113.1 (2 C), 51.7, 25.6 (6 C), 18.1 (2 C), -4.4 (4 C); IR (neat) 2955, 2927, 1725, 1583, 1283, 1169; HRMS (TOF MS ES+) Calcd for $\text{C}_{22}\text{H}_{39}\text{O}_4\text{Si}_2$ (MH^+) 423.2387, found 423.2381.

(E)-3-(3,5-bis(*tert*-butyldimethylsilyloxy)phenyl)-2-propen-1-ol (S9). To a solution of **S8** (3.97 g, 9.4 mmol) in 100 mL of dry toluene at $-78\text{ }^\circ\text{C}$ under N_2 was added dropwise a solution of DIBAL-H (1.5 M solution in toluene, 15.7 mL, 23.5 mmol). Upon completion of the addition, the reaction mixture was allowed to warm to room temperature over 2 h and then carefully added dropwise to a stirred mixture of 2 M HCl (100 mL) and ice. After stirring for 30 min, the aqueous layer was extracted with CH_2Cl_2 ($3 \times 50\text{ mL}$). The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure to afford 3.52 g (95%) of **S9** as colorless oil: ^1H NMR (CDCl_3) 6.50 (d, 2, $J = 1.8$), 6.48 (d, 1, $J = 15.4$), 6.28 (dt, 1, $J = 15.4, 5.5$), 6.25 (t, 1, $J = 1.8$), 4.30 (d, 2, $J = 5.5$), 0.98 (s, 18), 0.19 (s, 12); ^{13}C NMR (CDCl_3) 156.6 (2 C), 138.4, 131.0, 128.5, 111.70 (2 C), 111.67, 63.7, 25.7 (6 C), 18.2 (2 C), -4.4 (4 C); IR (neat) 3332, 2951, 2930, 1583, 1438, 1253, 1165; HRMS (TOF MS ES+) Calcd for $\text{C}_{21}\text{H}_{39}\text{O}_3\text{Si}_2$ (MH^+) 395.2438, found 395.2426.

(E)-1-(3-Bromo-1-propenyl)-(3,5-bis(*tert*-butyldimethylsilyloxy))benzene (S10). To a solution of **S9** (3.2 g, 7.85 mmol) in 40 mL of CCl_4 at $-20\text{ }^\circ\text{C}$ was added dropwise PBr_3 (0.45 mL, 1.28 g, 4.73 mmol) over 5 min. Upon completion of the addition, the solution was warmed

to room temperature over 2.5 h. The reaction mixture was then poured into 20 mL of ice water, and the separated aqueous layer was extracted with CH₂Cl₂ (3 × 10 mL). The combined organic layers were washed with 5% NaHCO₃ and brine, dried over MgSO₄, and concentrated under reduced pressure. Flash chromatography on silica gel (20:1 hexanes/EtOAc) afforded 2.87 g (80%) of **S10** as a yellow oil: ¹H NMR (CDCl₃) 6.54 (d, 1, *J* = 15.0), 6.53 (d, 2, *J* = 1.8), 6.35 (dt, 1, *J* = 15.0, 7.9), 6.30 (t, 1, *J* = 1.8), 4.15 (d, 2, *J* = 7.9), 1.02 (s, 18), 0.23 (s, 12); ¹³C NMR (CDCl₃) 156.6 (2 C), 137.5, 134.4, 125.2, 112.2, 111.9 (2 C), 33.2, 25.6 (6 C), 18.2 (2 C), -4.4 (4 C); IR (neat) 2956, 2930, 1583, 1433, 1347, 1255, 1167; HRMS (TOF MS ES⁺) Calcd for C₂₁H₃₈BrO₂Si₂ (MH⁺) 457.1594, found 457.1583.

3,5-Bis(*tert*-butyldimethylsilyloxy)cinnamyl triphenylphosphonium bromide (**S11**).

To a solution of **S10** (2.7 g, 5.9 mmol) in 20 mL of dry toluene was added PPh₃ (1.62 g, 6.2 mmol). The resulting solution was heated at reflux for 16 h. Upon cooling to room temperature, the solution was concentrated to 5 mL. The precipitate was filtered, and washed with hexanes to give 3.4 g (80%) of phosphonium bromide **S11** as a white solid: mp (decomp) 172-173 °C; ¹H NMR (CDCl₃) 7.90-7.66 (m, 15), 6.62 (dd, 1, *J* = 15.9, 5.5), 6.28 (d, 2, *J* = 1.8), 6.23 (d, 1, *J* = 1.8), 5.81 (ddt, 1, *J* = 15.9, 7.3, 5.5), 5.01 (dd, 2, *J* = 15.2, 7.3), 0.95 (s, 18), 0.15 (s, 12); ¹³C NMR (CDCl₃) 156.5 (2 C), 139.9 (d, *J* = 13.8), 137.5 (d, *J* = 3.8), 134.9 (d, 3 C, *J* = 2.3), 133.9 (d, 6 C, *J* = 9.2), 130.3 (d, 6 C, *J* = 12.2), 114.4 (d, 3 C, *J* = 83.3), 113.7 (d, *J* = 11.5), 112.2, 111.6 (2 C), 28.2 (d, *J* = 48.9), 25.5 (6 C), 18.1 (2 C), -4.5 (4 C); IR (KBr) 2956, 2930, 1584, 1438, 1166, 1031; HRMS (TOF MS ES⁺) Calcd for C₃₉H₅₂O₂PSi₂ (M-Br)⁺ 639.3244, found 639.3235.

2,2,2-Trichloroethyl (4*E*,6*E*)-[7-(3,5-bis(*tert*-butyldimethylsilyloxy)phenyl)-hepta-4,6-dienyl]-3-methyl-4-oxo-3,4-dihydro-2*H*-pyridine-1-carboxylate (12b**).** To a solution of

S11 (360 mg, 0.5 mmol) in 10 mL of THF at -78 °C was added *n*-BuLi (1.6 M in hexanes, 313 μ L, 0.5 mmol) dropwise over 5 min under N₂. After stirring at -78 °C for 0.5 h, the orange ylide solution of **11b** was treated with a solution of aldehyde **4** (360 mg, 1.0 mmol) in 2 mL of THF via cannula over 5 min. The reaction was stirred at -78 °C for 30 min and at 25 °C for 3 h. The reaction was quenched with saturated NH₄Cl and extracted with Et₂O (3 $\times$ 20 mL). The combined ether extracts were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 296 mg (83%) of an inseparable 2:1 mixture of diene **12b** and its 4*Z*,6*E* isomer.

The 2:1 mixture of diene **12b** and its 4*Z*,6*E* isomer was dissolved in 15 mL of dry CH₂Cl₂. The solution was treated with 5 mg of I₂ and stirred at 25 °C for 1 h. The solution was treated with 5 mL of saturated Na₂S₂O₃ to reduce the I₂. The layers were separated and the aqueous phase was extracted with CH₂Cl₂ (2 $\times$ 10 mL). The combined organic layers were washed with brine, dried over MgSO₄ and concentrated to afford 263 mg (98%) of an inseparable 6:1 mixture of **12b** and its 4*Z*,6*E* isomer

Data for **12b**: ¹H NMR (CDCl₃) 6.64 (dd, 1, *J* = 15.3, 10.4), 6.49 (d, 2, *J* = 2.2), 6.33 (d, 1, *J* = 15.3), 6.21 (t, 1, *J* = 2.2), 6.18 (dd, 1, *J* = 15.3, 10.4), 5.77 (dt, 1, *J* = 15.3, 7.1), 5.50 (s, 1), 4.88 (s, 2), 4.29 (dd, 1, *J* = 13.1, 4.4), 3.73 (dd, 1, *J* = 13.1, 9.8), 2.87 (dt, 1, *J* = 15.3, 7.4), 2.74 (dt, 1, *J* = 15.3, 7.4), 2.54 (ddq, 1, *J* = 9.8, 4.4, 7.0), 2.18 (dt, 2, *J* = 7.1, 7.4), 1.66 (tt, 2, *J* = 7.4, 7.4), 1.15 (d, 3, *J* = 7.0), 0.98 (s, 18), 0.20 (s, 12); ¹³C NMR (CDCl₃) 197.1, 159.4, 156.5 (2 C), 151.4, 139.1, 134.0, 131.4, 130.6, 129.0, 113.6, 111.4 (2 C), 111.3, 94.6, 75.6, 52.8, 40.6, 34.4, 32.1, 27.4, 25.7 (6 C), 18.2 (2 C), 12.5, -4.4 (4 C); IR (neat) 2956, 2931, 1733, 1674, 1590, 1580, 1188, 1167; HRMS (TOF MS ES⁺) calcd for C₃₄H₅₂NO₅Cl₃Si₂ (M⁺) 715.2450, found 715.2459.

Partial data for the *Z* isomer were determined from the mixture: ¹H NMR (CDCl₃) 6.90 (dd, 1, *J* = 15.3, 11.0), 6.53 (d, 2, *J* = 2.2), 6.41 (d, 1, *J* = 15.3), 6.23 (t, 1, *J* = 2.2), 6.17 (dd, 1, *J* = 11.0, 11.0), 5.50 (s, 1), 5.49 (dt, 1, *J* = 11.0, 7.3), 4.86 (s, 2), 4.19 (dd, 1, *J* = 13.1, 4.4), 3.58 (dd, 1, *J* = 13.1, 10.0), 2.87 (dt, 1, *J* = 15.2, 7.3), 2.73 (dt, 1, *J* = 15.2, 7.3), 2.54 (ddq, 1, *J* = 10.0, 4.4, 7.3), 2.33 (dt, 2, *J* = 7.4, 7.4), 1.66 (tt, 2, *J* = 7.4, 7.4), 1.14 (d, 3, *J* = 7.3), 0.96 (s, 18), 0.21

(s, 12).

Luche Reduction of 12b to give 13b. To a stirred solution of a 6:1 mixture of **12b** and its *Z* isomer (143 mg, 0.2 mmol) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (74.5 mg, 0.2 mmol) in 5 mL of MeOH was added NaBH_4 (7.5 mg, 0.2 mmol) in one portion over 5 min at -78°C . The reaction mixture was warmed to 0°C and stirred at the same temperature for 30 min, the reaction was quenched with saturated NaHCO_3 , and MeOH was removed under reduced pressure. The mixture was extracted with EtOAc (4×5 mL). The combined organic layers were washed with brine, dried over MgSO_4 , and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (6:1 hexanes/EtOAc) afforded 137 mg (96%) of an inseparable 3:1 mixture of *cis*- and *trans*-**13b**, each as a 6:1 mixture of *E/Z* isomers.

Data for *cis*-**13b** *E* isomer were determined from the mixture: ^1H NMR (CDCl_3) 6.64 (dd, 1, $J = 15.4, 10.4$), 6.49 (d, 2, $J = 1.8$), 6.32 (d, 1, $J = 15.4$), 6.21 (t, 1, $J = 1.8$), 6.19 (dd, 1, $J = 15.3, 10.4$), 5.80 (dt, 1, $J = 15.3, 6.7$), 5.21 (d, 1, $J = 4.3$), 4.91 (d, 1, $J = 12.2$), 4.72 (d, 1, $J = 12.2$), 4.02-3.98 (m, 2), 2.99 (dd, 2, $J = 11.9, 11.9$), 2.90 (dt, 1, $J = 14.6, 7.3$), 2.41 (dt, 1, $J = 14.6, 7.3$), 2.13 (dt, 2, $J = 7.3, 7.3$), 1.95-1.89 (m, 1), 1.58 (tt, 2, $J = 7.3, 7.3$), 1.06 (d, 3, $J = 6.7$), 0.98 (s, 18), 0.20 (s, 12); ^{13}C NMR (CDCl_3) 156.5 (2 C), 152.0, 141.3, 139.3, 135.1, 130.9, 130.2, 129.3, 114.6, 111.4 (2 C), 111.2, 95.2, 75.2, 65.1, 47.1, 34.9, 34.1, 32.2, 27.5, 25.7 (6 C), 18.2 (2 C), 12.6, -4.1 (4 C); IR (neat) 2956, 2931, 1728, 1580, 1436, 1254, 1166; HRMS (TOF MS ES⁺) calcd for $\text{C}_{34}\text{H}_{54}\text{O}_5\text{Cl}_3\text{Si}_2$ (M^+) 717.2607, found 715.2596.

Partial data for *trans*-**13b** *E* isomer were determined from the mixture: ^1H NMR (CDCl_3) 6.93 (dd, 1, $J = 15.4, 11.0$), 6.53 (d, 2, $J = 1.8$), 6.40 (d, 1, $J = 15.3$), 6.21 (t, 1, $J = 1.8$), 6.18 (dd, 1, $J = 15.4, 11.0$), 5.49 (dt, 1, $J = 15.3, 7.3$), 5.11 (d, 1, $J = 3.7$), 4.86 (d, 1, $J = 12.2$), 4.77 (d, 1, $J = 12.2$), 3.80-3.74 (m, 1), 3.54 (dd, 1, $J = 12.4, 3.0$), 2.79 (dt, 1, $J = 14.6, 7.7$), 2.54 (dt, 1, $J = 14.6, 7.7$), 2.29 (dt, 2, $J = 7.3, 7.3$).

Diels-Alder Reaction of 13a and Reduction of the Crude Product to Give 19a. To a solution of the **13a** (3:1 mixture of *cis/trans* isomers, *E/Z* = 6:1, 27 mg, 0.052 mmol) in 2 mL of Et_2O at -78°C was added $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (7 μL , 0.052 mmol) dropwise under N_2 . The resulting

mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 10 min, and warmed slowly to $25\text{ }^{\circ}\text{C}$ over 10 min. The reaction was stirred at $25\text{ }^{\circ}\text{C}$ for 10 min and quenched with 1 mL of saturated NaHCO_3 . The reaction mixture was extracted with CH_2Cl_2 ($3 \times 5\text{ mL}$), the combined extracts were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (96:4 hexanes/EtOAc) gave 12 mg (46%) of a 10:35:1 mixture of **16a**, **18a**, and **20a** as a white foam.

To the white foam in 1 mL of MeOH was added activated zinc (200 mg). The mixture was stirred at $25\text{ }^{\circ}\text{C}$ for 5 min, and glacial HOAc (1 mL) was added. The mixture was heated at $60\text{ }^{\circ}\text{C}$ for 30 min, cooled and concentrated under reduced pressure. The residue was treated with 5 mL of 5% aqueous NaOH, and the solution was extracted with EtOAc ($5 \times 5\text{ mL}$). The combined extracts were washed with brine, dried over anhydrous K_2CO_3 , and concentrated under reduced pressure. Flash chromatography on silica gel (100:1 $\text{CH}_2\text{Cl}_2/\text{MeOH}$) gave 5.9 mg (35%) of **19a** as a viscous oil: ^1H NMR (CDCl_3) 6.82 (dd, 1, $J = 15.2, 11.0$), 6.54 (d, 2, $J = 1.8$), 6.42 (d, 1, $J = 15.2$), 6.35 (t, 1, $J = 1.8$), 6.08 (d, 1, $J = 11.0$), 5.77 (br d, 1, $J = 11.6, 2.2$), 5.46 (dd, 1, $J = 11.6, 1.9$), 3.81 (s, 6), 3.04 (dd, 1, $J = 14.6, 5.5$), 2.74 (dd, 1, $J = 18.4, 9.2$), 2.52-2.44 (m, 2), 2.19-2.15 (m, 1), 1.93-1.88 (m, 1), 1.87-1.76 (m, 2), 1.65-1.50 (m, 1), 0.97 (d, 3, $J = 7.3$); ^{13}C NMR (CDCl_3) 160.8 (2 C), 132.8, 132.3, 131.3, 127.1, 122.5, 112.9, 104.3 (2 C), 99.4, 64.0, 55.3 (2 C), 47.3, 40.0, 39.9, 29.9, 22.5, 19.1 (one sp^2 carbon was not observed); IR (neat) 2929, 1577, 1404, 1260, 1115; HRMS (TOF MS ES+) calcd for $\text{C}_{21}\text{H}_{28}\text{NO}_2$ (MH^+) 326.2120, found 326.2111.

Diels-Alder Reaction of 13a to give 23a. To a solution of **13a** (3:1 mixture of *cis/trans* isomers, *E/Z* = 6:1, 20 mg, 0.038 mmol) in 2 mL of toluene at -78 °C was added $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (5.2 μL , 0.038 mmol) dropwise under N_2 . The resulting mixture was stirred at -78 °C for 10 min, and warmed slowly to 25 °C over 10 min. The reaction was stirred at 25 °C for 10 min and quenched with 1 mL of saturated NaHCO_3 . The reaction mixture was extracted with CH_2Cl_2 (3 $\times$ 5 mL), the combined extracts were washed with brine, dried over MgSO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (6:1 hexanes/ EtOAc) gave 5.9 mg (31%) of **23a** as a viscous oil: ^1H NMR (CDCl_3) 6.83-6.79 (m, 1), 6.38 (d, 1, $J = 2.2$), 6.34 (d, 1, $J = 2.2$), 5.55 (ddd, 1, $J = 9.8, 6.4, 2.6$), 5.38 (d, 1, $J = 9.8$), 4.75 (br s, 1, NH), 4.74 (d, 1, $J = 12.2$), 4.67 (d, 1, $J = 12.2$), 3.83 (s, 3), 3.81 (s, 3), 3.27-3.18 (m, 3), 2.71-2.66 (m, 1), 2.61-2.58 (m, 1), 2.29-2.16 (m, 3), 1.65 (dd, 1, $J = 10.9, 2.2$), 1.15-1.08 (m, 1), 1.03-0.96 (m, 1), 0.82 (d, 3, $J = 6.7$); ^{13}C NMR (CDCl_3) 158.7, 157.5, 154.8, 139.1, 134.4, 133.7, 129.1, 126.2, 117.3, 104.6, 104.2, 97.0, 74.4, 55.4, 55.3, 44.6, 41.3, 41.1, 38.2, 35.4, 34.2, 29.1, 23.5, 15.3; IR (neat) 2948, 1722, 1586, 1423, 1285, 1117; HRMS (TOF MS ES^+) calcd for $\text{C}_{24}\text{H}_{29}\text{Cl}_3\text{NO}_4$ (MH^+) 550.1162,

found 500.1153. COSY and 1D NOESY correlations are shown on the structure above.

Diels-Alder Reaction of 13b to Give 16b and 18b. To a solution of **13b** (3:1 mixture of *cis/trans* isomers, *E/Z* = 6:1, 108 mg, 0.15 mmol,) in 6 mL of 1:1 toluene and benzene at -42 °C was added BF₃•Et₂O (19 µL, 0.15 mmol) dropwise under N₂. The resulting mixture was stirred at -42 °C for 20 min, and warmed slowly to 25 °C over 20 min. The reaction was stirred at 25 °C for 20 min and quenched with 3 mL of saturated NaHCO₃. The reaction mixture was extracted with CH₂Cl₂ (3 × 5 mL), the combined extracts were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. Flash chromatography on silica gel (100:1 hexanes/EtOAc) gave 44 mg (42%, 49% based on *E* isomer) of **16b** as a colorless oil followed by 12 mg (11%) of **18b** as a colorless oil.

Data for **16b**: ¹H NMR (CDCl₃) 6.19 (d, 2, *J* = 1.8), 6.15 (t, 1, *J* = 1.8), 5.70-5.64 (m, 2), 4.50-4.35 (br, 2), 3.50-3.42 (br, 1), 2.93-2.85 (m, 3), 2.27-2.21 (m, 1), 2.03-1.92 (m, 3), 1.70-1.35 (m, 4), 0.97 (d, 3, *J* = 7.3), 0.95 (s, 18), 0.15 (s, 12); ¹³C NMR (CDCl₃) 156.0 (2 C), 142.8, 132.4, 130.3, 128.2, 126.9, 122.0 (br), 114.9 (2 C), 110.7, 95.7, 74.5, 50.2 (br), 45.9, 45.6 (br), 37.6, 31.9, 30.4, 29.7, 25.7 (6 C), 22.9, 18.2 (2 C), 17.5, -4.3 (2 C), -4.4 (2 C), (NMR spectra were broad due to slow rotation about the carbamate CO-N bond); IR (neat) 2956, 2931, 1725, 1590, 1449, 1398, 1162; HRMS (TOF MS ES+) calcd for C₃₄H₅₂NO₄Cl₃Si₂ (M⁺) 699.2501, found 699.2502.

Data for 2,2,2-trichloroethyl (1*S*,8*R*)-2-[(*E,E*)-3-(3,5-bis(*tert*-butyldimethylsilyloxyphenyl)-2-propenylidene]-8-methyl-6-azaspiro[4.5]dec-9-ene-6-carboxylate (**18b**): ¹H NMR (CDCl₃) 6.79-6.70 (br, 1), 6.45 (d, 2, *J* = 1.8), 6.24 (d, 1, *J* = 15.9), 6.19 (t, 1, *J* = 1.8), 5.96 (d, 1, *J* = 11.6), 5.55 (br d, 1, *J* = 9.8), 5.48 (dd, 1, *J* = 9.8, 1.9), 4.86-4.76 (br, 1), 4.69-4.59 (br, 1), 4.36-4.26 (br, 1), 2.92-2.83 (m, 1), 2.73-2.65 (m, 2), 2.59-2.53 (m, 1), 2.32-2.25 (m, 1), 2.05-1.94 (m, 2), 1.72-1.63 (m, 1), 1.02 (d, 3, *J* = 7.3), 0.97 (s, 18), 0.19 (s, 12); ¹³C NMR (CDCl₃) 156.5 (2 C), 151.1, 139.6, 131.5, 130.6, 127.0, 126.7, 120.9, 111.4 (2 C), 111.1, 75.7, 74.6, 67.0, 48.7, 36.8, 31.9, 29.7, 25.7 (6 C), 22.7, 18.2 (2 C), 18.1, -4.4 (4 C), (NMR spectra were broad and the carbamate carbon was not observed due to slow rotation about

the carbamate CO-N bond); IR (neat) 2958, 2923, 1722, 1590, 1401, 1153, 1114.

The stereochemistry of **18b** was established by an NOESY 1D experiment. Irradiation of H₁₁ at δ 5.96 in a 1D NOESY experiment showed NOEs to the H₈ multiplet at δ 2.59-2.53 and H₁₃ doublet at δ 6.24. Irradiation of H₈ multiplet at δ 2.59-2.53 in a 1D NOESY experiment showed NOEs to the H₁₁ doublet at δ 5.96 and Me doublet at δ 1.02. Irradiation of Me doublet at δ 1.02 in a 1D NOESY experiment showed NOEs to the H₈ multiplet at δ 2.59-2.53 and H₉ double doublet at δ 5.48.

Preparation of (1*S*,8*R*)-2-[(*E,E*)-3-(3,5-Bis(*tert*-butyldimethylsilyloxyphenyl)-2-propenylidene]-8-methyl-6-azaspiro[4.5]dec-9-ene (19b**).** To a solution of **18b** (4 mg, 5.7 μmol) in 1 mL of MeOH was added activated zinc (90 mg). The mixture was stirred at 25 °C for 5 min, and glacial HOAc (1 mL) was added. The mixture was heated at 60 °C for 30 min, cooled and concentrated under reduced pressure. The residue was treated with 5 mL of 5% aqueous NaOH, and the solution was extracted with EtOAc (5 × 5 mL). The combined extracts were washed with brine, dried over anhydrous K₂CO₃, and concentrated under reduced pressure. Flash chromatography on silica gel (100:1 CH₂Cl₂/MeOH) gave 2.7 mg (90%) of **19b** as a viscous oil: ¹H NMR (CDCl₃) 6.50 (dd, 1, *J* = 15.8, 11.0), 6.49 (d, 2, *J* = 1.8), 6.37 (d, 1, *J* = 15.8), 6.21 (t, 1, *J* = 1.8), 6.07 (d, 1, *J* = 11.0), 5.78 (br d, 1, *J* = 9.8, 2.2), 5.45 (d, 1, *J* = 9.8), 3.06 (dd, 1, *J* = 12.8, 4.8), 2.75 (dd, 1, *J* = 16.5, 8.5), 2.54-2.45 (m, 2), 2.30-2.22 (m, 2), 1.94-1.81 (m, 2), 1.65-1.57 (m, 1), 0.98 (d, 3, *J* = 7.3), 0.98 (s, 18), 0.19 (s, 12); ¹³C NMR (CDCl₃) 156.5 (2 C), 139.5, 132.6, 132.2, 131.4, 126.6, 122.9, 111.5 (2 C), 111.3, 64.1, 47.0, 39.8, 29.7, 28.8, 25.7 (6 C), 22.5, 19.1, 18.2 (2 C), -4.4 (4 C) (one sp² carbon was not observed); IR (neat) 2949, 2930, 1581, 1436, 1165; HRMS (EI⁺) calcd for C₃₁H₅₁NO₂Si₂ (M⁺) 525.3458, found

525.3456.

Preparation of 24b. To a solution of Diels-Alder adduct **16b** (40 mg, 57 μ mol) in 4 mL of MeOH was added activated zinc (400 mg). The mixture was stirred at 25 °C for 5 min, and glacial HOAc (4 mL) was added. The mixture was heated at 60 °C for 30 min, cooled and concentrated under reduced pressure. The residue was treated with 5 mL of 5% aqueous NaOH, and the solution was extracted with EtOAc (5 $\times$ 5 mL). The combined extracts were washed with brine, dried over anhydrous K₂CO₃, and concentrated under reduced pressure. Flash chromatography on silica gel (100:1 CH₂Cl₂/MeOH) gave 25 mg (86%) of **24b** as a viscous oil: ¹H NMR (CDCl₃) 6.41 (d, 2, *J* = 1.8), 6.24 (t, 1, *J* = 1.8), 5.76 (br d, 1, *J* = 10.4), 5.65 (dd, 1, *J* = 10.4, 4.3), 3.62-3.57 (m, 2), 2.99 (dd, 1, *J* = 17.0, 9.8), 2.39 (br d, 1, *J* = 12.8), 2.15-1.93 (m, 4), 1.64-1.56 (m, 2), 1.41-1.35 (m, 1), 1.12-1.00 (m, 1), 1.01 (d, 3, *J* = 7.3), 0.96 (s, 18), 0.18 (s, 12); ¹³C NMR (CDCl₃) 171.8, 156.0 (2 C), 141.7, 131.8, 129.8, 115.6 (2 C), 110.8, 57.1, 44.7, 43.2, 42.8, 40.1, 37.5, 31.9, 27.5, 25.9, 25.7 (6 C), 18.3 (2 C), 17.0, -4.3 (4 C); IR (neat) 2951, 2929, 1669, 1590, 1444, 1398, 1162; HRMS (EI⁺) calcd for C₃₁H₅₁NO₂Si₂ (M⁺) 525.3458, found 525.3462.

Preparation of 25. To a solution of **24b** (20 mg, 38 μ mol) in 5 mL of THF was added TBAF/AcOH (38 μ L, 1:1, 1 M in THF). The mixture was stirred at 25 °C for 15 min. The mixture was concentrated under reduced pressure. The residue was treated with 2 mL of brine and 5-7 drops of saturated NaHCO₃ to adjust the pH to 7, and the solution was extracted with Et₂O (7 $\times$ 10 mL). The combined extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure to give 9.7 mg (86%) of **25** as a white solid: mp (decomp) 286-288 °C; ¹H NMR (CD₃OD) 6.29 (d, 2, *J* = 1.8), 6.15 (t, 1, *J* = 1.8), 5.75 (br d, 1, *J* = 9.6), 5.65 (ddd, 1, *J* = 9.6, 4.3, 2.4), 3.57 (br t, 1, *J* = 4.3), 3.49 (dd, 1, *J* = 16.5, 3.7), 2.96 (ddd, 1, *J* = 16.5, 11.0, 2.2), 2.91-2.81 (TBAF residue), 2.39-2.34 (m, 1), 2.24-2.19 (m, 2, partially exchanged with deuterium), 2.11-2.05 (m, 1), 2.02-1.90 (m, 2), 1.69-1.56 (m, 2), 1.47 (dddd, 1, *J* = 12.2, 12.2, 12.2, 3.7), 1.14-1.06 (m, 1), 1.04 (d, 3, *J* = 6.2); ¹³C NMR (CD₃OD) 176.1, 159.2 (2 C), 143.6, 132.6, 131.4, 110.3 (2 C), 102.2, 57.4, 45.9, 44.7, 44.6, 42.2, 32.9, 31.0, 29.0, 27.0,

17.2; ^1H NMR ($\text{DMSO}-d_6$) 9.12 (s, 2), 6.16 (d, 2, $J = 1.8$), 6.06 (t, 1, $J = 1.8$), 5.71 (br d, 1, $J = 9.6$), 5.58 (ddd, 1, $J = 9.6, 4.3, 2.4$), 3.51-3.34 (m, 2), 2.95-2.83 (m, 1), 2.28 (br d, 1, $J = 14$), 2.19-2.12 (m, 1), 2.05-1.99 (m, 2), 1.93-1.87 (m, 1), 1.58-1.46 (m, 2), 1.40-1.30 (m, 1), 0.99-0.94 (m, 4); ^{13}C NMR ($\text{DMSO}-d_6$) 157.7 (2 C), 141.9, 131.4, 129.9, 108.5 (2 C), 100.8, 56.3, 44.0, 42.6, 42.5, 36.9, 34.0, 31.4, 27.5, 25.4, 16.6 (the carbamate carbon was not observed and the carbon at δ 34.0 was observed as a very low broad peak as previously reported.⁵); IR (film) 3286, 2918, 2851, 1664, 1595, 1447, 1336, 1154; HRMS (TOF MS ES+) calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_2$ (MH^+) 298.1807, found 298.1812.

Preparation of (±)-Symbioimine (1) and Bis sulfate 26. To a solution of **25** (10 mg, 33.7 μmol) and Na_2SO_4 (10 mg) in dry pyridine (2 mL) was added $\text{SO}_3\cdot\text{DMF}$ (2 M in DMF, 160 μL , 0.32 mmol) at 25 °C. The mixture was stirred under N_2 at 25 °C for 15 h. The residue was treated with phosphate buffer (0.2 M, pH = 6.9, 2.0 mL) and concentrated under reduced pressure. The residue was purified on a Zorbax Eclipse XDB-C18 reversed-phase HPLC column (4.6 $\times$ 250 mm, Agilent) eluting with 4:1 H_2O /acetonitrile at a flow rate of 1 mL/min with monitoring at 215 nm to give bis sulfate **26** (3.2 mg, ~25%, $t_R = 7.3$ min), which hydrolyzed to give a mixture of **26**, symbioimine (**1**) and **25** during concentration, followed by symbioimine (**1**) (7.3 mg, 58%, $t_R = 12.9$ min) as a white power: mp (decomp) 218-219 °C; ^1H NMR ($\text{DMSO}-d_6$) 12.84 (br s, 1, NH), 9.36 (s, 1, OH), 6.64 (t, 1, $J = 1.8$), 6.54 (t, 1, $J = 1.8$), 6.41 (t, 1, $J = 1.8$), 5.80 (d, 1, $J = 9.8$), 5.67 (ddd, 1, $J = 9.8, 4.3, 2.4$), 3.65 (br t, 1, $J = 4.3$), 3.58 (dd, 1, $J = 14.3, 4.7$), 3.13 (dd, 1, $J = 14.3, 12.0$), 2.68-2.62 (m, 2), 2.52 (dd, 1, $J = 12.0, 11.1$), 2.38 (br ddd, 1, $J = 12.9, 12.0, 2.4$), 2.08-2.01 (m, 1), 1.94 (br dd, 1, $J = 12.9, 2.3$), 1.77 (dt, 1, $J = 4.3, 11.1$), 1.69-1.63 (m, 1), 1.50 (dq, 1, $J = 12.9, 4.2$), 1.24 (dddq, 1, $J = 4.7, 11.1, 12.0, 6.1$), 1.05 (d, 3, $J = 6.1$); ^{13}C NMR ($\text{DMSO}-d_6$) 188.0, 157.3, 154.2, 139.9, 130.4, 129.6, 112.8, 111.8, 106.0, 49.8, 41.7, 41.5, 41.0, 40.3, 33.4, 29.7, 26.2, 24.4, 15.6; IR (film) 3340, 2914, 1695, 1610, 1510, 1450, 1260, 1230, 1140, 1050; HRMS (TOF MS ES+) calcd for $\text{C}_{19}\text{H}_{24}\text{NO}_5\text{S}$ (MH^+) 378.1375, found 378.1387. The spectral data are identical to those previously reported.^{1,5}

In acidic CD_3OD , the aromatic protons of **25** absorb at δ 6.28 (d, 2, $J \approx 2$) and 6.18 (t, 1, J

≈ 2), whereas those of **1** absorb at δ 6.83 (t, 1, $J \approx 2$), 6.64 (t, 1, $J \approx 2$), and 6.61 (t, 1, $J \approx 2$), and those of **26** absorb at δ 7.26 (d, 2, $J \approx 2$), and 7.00 (t, 1, $J \approx 2$).

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INDEX	FREQUENCY	PPM	HEIGHT
1	20327.578	202.228	31.3
2	16780.564	166.941	49.6
3	10452.551	103.987	103.3
4	7771.500	77.314	20.0
5	7739.455	76.996	20.3
6	7707.411	76.677	19.4
7	6132.656	61.010	68.0
8	5275.085	52.479	151.4
9	4924.886	48.995	119.9
10	4238.982	42.171	126.2
11	3151.760	31.355	108.3
12	1831.835	18.224	102.8
13	1388.553	13.814	77.8

INDEX	FREQUENCY	PPM	HEIGHT
1	17517.256	174.270	46.8
2	17130.436	170.421	56.0
3	16535.324	164.501	63.9
4	10449.933	103.961	110.5
5	8264.045	82.215	99.7
6	7771.934	77.319	28.5
7	7739.889	77.000	29.2
8	7707.845	76.681	29.2
9	6094.179	60.628	86.9
10	5846.216	58.161	83.9
11	5292.305	52.650	107.9
12	4546.890	45.235	113.3
13	4087.587	40.665	123.3
14	3194.920	31.785	128.1
15	3189.580	31.731	134.2
16	2293.861	22.820	114.2
17	1472.913	14.653	116.2
18	1450.024	14.426	102.3
19	1402.721	13.955	90.6

200 180 160 140 120 100 80 60 40 20 0 ppm

INDEX	FREQUENCY	PPM	HEIGHT
1	19294.197	191.948	50.5
2	17035.064	169.473	43.3
3	16777.184	166.907	57.6
4	10478.926	104.249	100.9
5	10189.763	101.372	26.1
6	7771.934	77.319	48.0
7	7739.890	77.000	50.6
8	7707.845	76.681	48.0
9	5996.520	59.656	81.3
10	5310.616	52.832	92.9
11	5308.327	52.810	91.1
12	4663.624	46.396	59.3
13	3806.817	37.872	90.3
14	3378.031	33.606	69.9
15	3201.024	31.845	93.9
16	2367.869	23.557	73.2
17	1430.188	14.228	92.6
18	1317.269	13.105	104.3

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INDEX	FREQUENCY	PPM	HEIGHT
1	19671.100	195.697	26.7
2	16620.012	165.344	31.4
3	10478.925	104.249	71.9
4	9771.659	97.213	73.9
5	7771.934	77.319	58.2
6	7739.889	77.000	60.3
7	7707.845	76.681	57.5
8	5325.875	52.984	60.7
9	4839.868	48.149	71.5
10	3841.149	38.214	81.5
11	3452.038	34.342	88.2
12	3174.320	31.580	84.9
13	2281.654	22.699	70.3
14	1359.995	13.530	67.6

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INDEX	FREQUENCY	PPM	HEIGHT
1	19822.167	197.200	16.9
2	16016.508	159.340	19.5
3	15220.738	151.423	13.3
4	11414.317	113.555	37.8
5	10455.273	104.014	38.2
6	9513.014	94.640	10.7
7	7771.933	77.319	109.6
8	7739.889	77.000	110.2
9	7707.844	76.681	110.7
10	7595.689	75.565	46.4
11	5313.667	52.863	37.6
12	5308.326	52.810	48.6
13	4085.297	40.642	44.3
14	3490.186	34.722	31.0
15	3206.364	31.898	37.0
16	2299.201	22.874	31.6
17	1255.468	12.490	32.1

Synthesis of Symbioimine

Zou, Che, and Snider

INDEX	FREQUENCY	PPM	HEIGHT
1	20220.815	201.166	25.9
2	19800.436	196.984	13.4
3	15924.703	158.426	15.9
4	15214.407	151.360	10.0
5	11421.834	113.630	40.7
6	9510.671	94.617	5.4
7	7771.932	77.319	132.5
8	7739.889	77.000	133.2
9	7708.608	76.689	127.5
10	7596.456	75.573	44.3
11	5299.245	52.719	28.5
12	4318.105	42.959	40.9
13	4077.779	40.568	38.0
14	3436.910	34.192	31.5
15	2033.102	20.226	31.9
16	1254.903	12.484	26.2

INDEX	FREQUENCY	PPM	HEIGHT
1	16823.289	167.366	29.3
2	15765.059	156.838	58.6
3	14553.474	144.785	46.8
4	13669.963	135.995	30.9
5	11849.534	117.885	40.9
6	11481.786	114.226	58.8
7	11369.631	113.110	106.2
8	7770.735	77.307	40.1
9	7739.454	76.996	41.1
10	7707.409	76.677	42.0
11	5194.210	51.674	45.3
12	2574.196	25.609	347.3
13	1827.256	18.178	49.8
14	-445.610	-4.433	133.0

Zou, Che, and Snider

Synthesis of Symbioimine

200 180 160 140 120 100 80 60 40 20 0 ppm

INDEX	FREQUENCY	PPM	HEIGHT
1	15741.407	156.603	27.2
2	13910.297	138.386	18.1
3	13167.934	131.001	37.7
4	12919.208	128.526	32.7
5	11227.720	111.699	79.9
6	11224.668	111.668	49.7
7	7771.498	77.314	59.8
8	7739.454	76.996	61.5
9	7707.409	76.677	60.5
10	6398.166	63.652	31.9
11	2578.774	25.655	261.0
12	1828.019	18.186	21.2
13	-443.322	-4.410	84.0

INDEX	FREQUENCY	PPM	HEIGHT
1	15743.696	156.626	20.3
2	13823.319	137.521	11.1
3	13508.216	134.386	20.7
4	12588.846	125.240	19.1
5	11278.838	112.207	20.8
6	11252.135	111.941	38.0
7	3341.737	33.245	22.3
8	2578.774	25.655	147.1
9	2571.908	25.587	10.8
10	1825.730	18.163	19.1
11	-442.558	-4.403	48.0

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INDEX	FREQUENCY	PPM	HEIGHT
1	15731.161	156.501	16.9
2	14065.613	139.931	7.2
3	14051.880	139.795	6.5
4	13821.465	137.502	6.7
5	13817.650	137.464	6.2
6	13563.584	134.937	29.4
7	13560.532	134.906	27.3
8	13468.977	133.996	57.8
9	13459.821	133.905	62.3
10	13097.413	130.299	60.5
11	13084.443	130.170	64.9
12	11898.799	118.375	15.2
13	11813.348	117.525	13.8
14	11434.154	113.752	6.9
15	11422.710	113.638	6.5
16	11278.511	112.204	11.1
17	11219.763	111.619	20.7
18	7771.934	77.319	47.0
19	7739.889	77.000	48.2
20	7707.845	76.681	45.6
21	2858.454	28.437	6.5
22	2809.624	27.951	7.1
23	2567.765	25.545	139.8
24	1816.246	18.069	28.6
25	-452.042	-4.497	61.9

200 180 160 140 120 100 80 60 40 20 0 ppm

INDEX	FREQUENCY	PPM	HEIGHT
1	19815.301	197.132	12.8
2	16024.901	159.423	13.1
3	15735.738	156.546	5.4
4	15732.687	156.516	31.6
5	15221.501	151.431	8.4
6	13987.027	139.149	13.9
7	13465.161	133.958	20.7
8	13208.043	131.400	19.2
9	13201.176	131.331	3.7
10	13131.746	130.641	21.1
11	12966.184	128.994	18.7
12	11416.606	113.578	20.9
13	11215.185	111.574	6.2
14	11197.636	111.399	45.1
15	11185.429	111.278	17.5
16	9513.015	94.640	6.8
17	7771.933	77.319	28.4
18	7739.889	77.000	29.6
19	7707.844	76.681	29.5
20	7595.689	75.565	25.2
21	7591.874	75.527	5.0
22	5308.327	52.810	19.4
23	4084.534	40.635	25.8
24	3460.431	34.426	18.9
25	3228.490	32.119	21.8
26	2756.216	27.420	19.7
27	2578.446	25.652	200.0
28	1826.165	18.168	30.1
29	1256.995	12.505	24.3
30	-440.598	-4.383	11.2
31	-443.649	-4.414	69.2

200 180 160 140 120 100 80 60 40 20 0 PPM

INDEX	FREQUENCY	PPM	HEIGHT
1	1573.449	156.524	44.2
2	14205.998	141.328	8.4
3	14001.523	139.294	23.9
4	13575.791	135.058	29.7
5	13155.398	130.876	31.8
6	13088.258	130.208	31.6
7	12997.465	129.305	29.6
8	11519.606	114.602	15.2
9	11216.710	111.589	6.3
10	11196.873	111.392	83.6
11	11178.562	111.210	30.9
12	7771.933	77.319	44.1
13	7739.889	77.000	45.4
14	7707.844	76.681	45.0
15	7556.778	75.178	20.2
16	6541.274	65.076	26.5
17	4731.526	47.071	22.8
18	3663.379	36.445	6.8
19	3511.549	34.935	29.2
20	3423.045	34.054	20.0
21	3237.646	32.210	33.4
22	2766.897	27.526	25.9
23	2580.735	25.674	314.0
24	1828.453	18.190	56.7
25	1477.490	14.699	8.8
26	1270.728	12.642	31.5
27	-442.124	-4.398	92.8

200 180 160 140 120 100 80 60 40 20 0 ppm

INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	21825.707	217.132	-27.740	1	2904.231	28.893	58.0
2	21226.781	211.174	-28.741	2	2461.712	24.490	-25.0
3	20558.426	204.525	-23.842	3	2262.579	22.509	51.0
4	20288.336	201.838	-23.243	4	1921.535	19.116	37.5
5	20030.455	199.272	-25.344	5	830.498	8.262	21.7
6	19356.760	192.570	-25.345	6	102.631	1.021	32.1
7	18042.174	179.492	-39.646	7	-1.131	-0.011	28.6
8	17646.959	175.560	-27.047	8	-1044.865	-10.395	24.6
9	16461.316	163.765	-26.548	9	-2051.212	-20.406	-22.2
10	16167.575	160.843	41.849	10	-2248.820	-22.372	21.4
11	15435.894	153.563	-31.1				
12	14967.435	148.903	20.9				
13	14650.805	145.753	-23.9				
14	14027.465	139.552	-21.6				
15	13348.428	132.796	46.9				
16	13296.546	132.280	40.5				
17	13195.835	131.278	44.6				
18	13121.064	130.534	24.6				
19	12772.391	127.066	35.0				
20	12318.428	122.549	41.2				
21	12267.310	122.041	-31.9				
22	11592.851	115.331	-40.5				
23	11344.124	112.857	59.0				
24	10488.843	104.348	77.9				
25	9991.392	99.399	44.2				
26	7771.933	77.319	2351.9				
27	7760.488	77.205	235.7				
28	7739.889	77.000	2417.2				
29	7707.844	76.681	2362.2				
30	7134.096	70.973	26.2				
31	6438.274	64.051	28.5				
32	6192.600	61.607	21.7				
33	6014.830	59.838	-20.3				
34	5561.630	55.330	79.4				
35	4753.652	47.292	45.6				
36	4025.023	40.043	74.8				
37	4007.475	39.868	54.8				
38	3349.801	33.325	-31.4				
39	3009.520	29.940	47.6

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INDEX	FREQUENCY	PPM	HEIGHT
1	15950.894	158.687	33.0
2	15833.397	157.518	30.6
3	15561.020	154.808	17.5
4	13983.213	139.111	25.7
5	13504.835	134.352	71.1
6	13439.983	133.707	32.9
7	12979.917	129.130	67.5
8	12684.650	126.193	67.1
9	11795.035	117.342	28.8
10	10518.599	104.644	69.0
11	9749.532	96.993	90.1
12	7771.170	77.311	1207.8
13	7759.726	77.197	85.5
14	7739.889	77.000	1253.5
15	7707.844	76.681	1276.8
16	7477.429	74.389	80.5
17	5563.156	55.345	95.3
18	5554.763	55.261	77.0
19	4480.512	44.574	62.2
20	4153.201	41.318	90.6
21	4134.126	41.128	81.4
22	3836.571	38.168	78.3
23	3558.853	35.405	75.8
24	3438.305	34.206	78.3
25	2984.342	29.690	30.1
26	2926.357	29.113	66.1
27	2365.579	23.534	72.7
28	1534.713	15.268	70.9
29	-1.894	-0.019	71.2

INDEX	FREQUENCY	PPM	HEIGHT
1	15676.227	155.954	19.7
2	14349.435	142.755	20.5
3	13313.331	132.447	7.8
4	13101.990	130.345	77.7
5	12883.021	128.166	44.8
6	11551.650	114.921	25.2
7	11128.969	110.716	35.6
8	9622.117	95.725	23.5
9	7771.933	77.319	424.8
10	7760.489	77.205	23.2
11	7739.889	77.000	442.4
12	7707.844	76.681	439.7
13	7487.348	74.488	39.8
14	4609.453	45.857	19.1
15	3774.771	37.553	28.1
16	3207.127	31.906	83.0
17	3058.349	30.426	71.6
18	2984.342	29.690	61.5
19	2582.260	25.690	526.4
20	2305.305	22.934	31.8
21	1829.979	18.205	43.3
22	1757.498	17.484	53.3
23	1419.505	14.122	4.8
24	101.869	1.013	8.8
25	-1.894	-0.019	10.2
26	-434.494	-4.323	85.7
27	-443.650	-4.414	105.6

INDEX	FREQUENCY	PPM	HEIGHT
1	21449.895	213.393	-8.1
2	21335.449	212.255	-7.1
3	19702.709	196.012	-7.1
4	15728.437	156.474	47.1
5	15186.733	151.085	32.4
6	14033.134	139.608	27.6
7	13219.052	131.509	10.3
8	13130.549	130.629	37.3
9	12766.615	127.008	43.1
10	12727.704	126.621	12.4
11	12152.431	120.898	35.5
12	11201.016	111.433	88.7
13	11172.023	111.144	53.2
14	7771.498	77.314	797.0
15	7739.454	76.996	824.1
16	7707.409	76.677	824.2
17	6731.580	66.969	40.1
18	4898.181	48.729	8.8
19	3703.381	36.843	15.6
20	3207.455	31.909	9.5
21	2983.907	29.685	136.7
22	2581.826	25.685	426.0
23	2279.692	22.679	9.7
24	1831.070	18.216	54.5
25	1821.152	18.118	45.1
26	101.434	1.009	16.0
27	-2.329	-0.023	13.7
28	-441.033	-4.388	135.4

INDEX	FREQUENCY	PPM	HEIGHT
1	15767.780	156.865	33.4
2	14052.640	139.802	19.4
3	13358.344	132.895	15.6
4	13319.433	132.508	31.5
5	13245.425	131.772	19.5
6	12756.366	126.906	22.0
7	12384.040	123.202	12.6
8	11236.544	111.786	65.5
9	11215.182	111.574	28.7
10	7803.975	77.638	551.1
11	7791.768	77.516	33.5
12	7771.931	77.319	578.5
13	7739.886	77.000	580.5
14	6475.657	64.423	14.7
15	4758.228	47.337	22.9
16	4029.598	40.088	25.9
17	3239.932	32.232	8.3
18	3024.776	30.092	27.1
19	3016.384	30.008	78.9
20	2982.813	29.674	10.9
21	2930.932	29.158	31.2
22	2614.302	26.008	225.8
23	2312.169	23.003	8.0
24	2290.806	22.790	30.2
25	1949.762	19.397	30.9
26	1863.547	18.539	33.7
27	133.911	1.332	21.8
28	30.148	0.300	12.5
29	-408.556	-4.065	70.2

INDEX	FREQUENCY	PPM	HEIGHT
1	15677.753	155.970	28.2
2	14248.724	141.753	15.5
3	13253.058	131.848	30.3
4	13043.242	129.760	29.8
5	11623.369	115.635	68.6
6	11137.361	110.800	30.9
7	7771.933	77.319	128.3
8	7760.489	77.205	8.8
9	7739.889	77.000	130.8
10	7707.844	76.681	126.8
11	5738.637	57.091	16.8
12	4489.667	44.665	28.1
13	4345.467	43.231	35.5
14	4306.556	42.844	31.8
15	4028.838	40.081	34.4
16	3774.771	37.553	23.6
17	3211.705	31.952	27.1
18	2763.845	27.496	33.2
19	2599.809	25.864	28.7
20	2582.260	25.690	219.8
21	1835.320	18.259	33.9
22	1705.616	16.968	32.8
23	-434.494	-4.323	63.9

200 180 160 140 120 100 80 60 40 20 0 PPM

in CD₃OD

INDEX	FREQUENCY	PPM	HEIGHT
1	21782.113	216.698	-21.5
2	19338.342	192.386	-21.9
3	16661.869	165.760	-23.2
4	16007.247	159.247	111.2
5	14429.440	143.550	43.7
6	13324.671	132.560	62.2
7	13204.886	131.368	72.4
8	11082.323	110.252	160.7
9	10783.241	107.276	-29.9
10	10268.242	102.153	81.2
11	6023.880	59.928	-21.8
12	6014.725	59.837	-22.6
13	5768.288	57.385	46.6
14	5004.562	49.788	1072.8
15	4990.829	49.651	46.4
16	4983.199	49.575	3258.9
17	4968.703	49.431	167.4
18	4961.836	49.363	7897.7
19	4940.473	49.150	8164.1
20	4931.317	49.059	-44.1
21	4919.110	48.937	5784.2
22	4903.088	48.778	-21.9
23	4897.747	48.725	3194.1
24	4876.384	48.512	1158.8
25	4613.925	45.901	61.8
26	4494.903	44.717	73.4
27	4484.984	44.619	82.2
28	4239.310	42.175	48.9
29	3306.207	32.892	31.2
30	3120.044	31.040	32.6
31	2913.281	28.983	74.5
32	2711.096	26.971	35.5
33	1727.637	17.187	73.5

200 180 160 140 120 100 80 60 40 20 0 PPM

in DMSO-d₆

INDEX	FREQUENCY	PPM	HEIGHT
1	16498.574	164.135	-31.7
2	15856.922	157.751	33.6
3	14932.211	148.552	-23.7
4	14265.381	141.918	20.5
5	13238.434	131.701	-20.5
6	13207.152	131.390	32.3
7	13057.611	129.902	38.8
8	12914.174	128.476	-18.6
9	10901.479	108.452	76.3
10	10128.598	100.763	40.1
11	9435.827	93.871	-19.6
12	8442.450	83.989	15.3
13	5863.636	58.334	-23.1
14	5664.502	56.353	22.9
15	5234.191	52.072	-21.0
16	4420.873	43.981	25.2
17	4271.333	42.493	41.5
18	4034.051	40.132	1041.8
19	4013.451	39.927	2989.4
20	3992.088	39.715	5805.0
21	3971.488	39.510	6668.8
22	3950.125	39.297	5706.2
23	3929.525	39.093	2828.4
24	3908.162	38.880	952.9
25	3154.355	31.381	34.6
26	2803.392	27.889	-17.3
27	2769.059	27.548	40.6
28	2598.918	25.855	-16.4
29	2553.140	25.400	30.4
30	2516.518	25.035	-17.1
31	1670.392	16.618	39.6
32	1634.533	16.261	-21.9