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Supporting Information

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Synthesis of (±)-Deoxysymbioimine Using an Intramolecular Diels-Alder Reaction with an *N*-Alkoxycarbonyl 2,3-Dihydropyrdinium Cation as the Dienophile

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General procedures. NMR spectra were recorded at 400 MHz in $CDCl_3$ with TMS as internal standard at ambient temperature unless otherwise indicated. Chemical shifts are reported in δ and coupling constants in Hz. IR spectra are reported in cm^{-1}.

2-(3-(1,3-Dioxolan-2-yl)propyl)-4-methoxy-5-methylpyridine. To a solution of 4-methoxy-2,5-dimethylpyridine (**10b**)[10] (685 mg, 5.0 mmol) in 10 mL of THF was added *n*-BuLi (1.6 M in hexanes, 3.2 mL, 5.1 mmol) at –20 ºC over 10 min. After stirring at –20 ºC for 1 h, the solution was cooled to –78 ºC and 2-(2-bromomethyl)-1,3-dioxolane (905 mg, 585 µL, 5.0 mmol) in 10 mL of THF was added dropwise via a cannula. The reaction mixture was stirred at –78 ºC for 1 h and at 25 °C for 3 h. The reaction was quenched with 10 mL of H_2O and extracted with CH_2Cl_2 (3 × 50 mL). The combined ether extracts were washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (2.5:1 hexanes/EtOAc) gave 1.04 g (86%) of the dioxolane as a colorless liquid: R_f = 0.60 (1:1 hexanes/EtOAc); ^{1}H NMR 8.13 (s, 1), 6.61 (s, 1), 4.88 (t, 1, J = 4.6), 3.98-3.82 (m, 4), 3.86 (s, 3), 2.78 (t, 2, J = 7.6), 2.12 (s, 3), 1.90-1.70 (m, 4); ^{13}C NMR 164.2, 161.4, 149.7, 119.5, 104.35, 104.32, 64.8 (2 C), 54.9, 38.0, 33.3, 24.3, 12.7; IR (neat) 1603, 1500, 1136, 1037; HRMS (DCI/NH_3) Calcd for $C_{13}H_{20}NO_3$ (MH^+) 238.1443, found 238.1440.

4-Methoxy-5-methyl-2-pyridinebutanal (11b). The above dioxolane (2.37 g, 10 mmol) was dissolved in 50 mL of 1 M HCl at 25 °C and the solution was stirred at 25 °C for 1 h. The solution was cooled to 0 °C and carefully neutralized with solid Na_2CO_3 until no CO_2 evolved. The solution was extracted with $CHCl_3$ (3 × 50 mL) and the combined extracts were washed with brine and dried over Na_2SO_4. Concentration of the solution under reduced pressure gave 1.88 g (98%) of aldehyde **11b** as a colorless liquid: R_f = 0.30 (1:1 hexanes/EtOAc); ^{1}H NMR 9.75 (br s, 1), 8.16 (s, 1), 6.60 (s, 1), 3.86 (s, 3), 2.77 (t, 2, *J* = 7.7), 2.50 (dt, 2, *J* = 1.2, 7.7), 2.13 (s, 3), 2.07 (tt, 2, *J* = 7.7, 7.7); ^{13}C NMR 202.1, 164.0, 160.4, 149.7, 119.6, 104.3, 54.8, 43.0, 37.1, 22.0, 12.5; IR (neat) 2926, 1721, 1602, 1571, 1501, 1459, 1310, 1037; HRMS (DCI/NH_3) Calcd for $C_{11}H_{16}NO_2$ (MH^+) 194.1181, found 194.1173. Crude **11b** was pure enough for the next step; further purification can be achieved by flash chromatography on silica gel (20:1 CH_2Cl_2/MeOH).

4-Methoxy-5-methyl-2-((4*E*,6*E*)-7-phenylhepta-4,6-dienyl)pyridine (12b*E*) and 4-methoxy-5-methyl-2-((4*Z*,6*E*)-7-phenylhepta-4,6-dienyl)pyridine (12b*Z*). Lithium diisopropylamide (LDA) was prepared from *n*-BuLi (1.60 M in hexanes, 1.25 mL, 2.0 mmol) and diisopropylamine (280 μL, 202 mg, 2.0 mmol) in 5 mL of THF at 0 °C under N_2. To a solution of freshly prepared LDA at 0 °C was added dropwise a solution of (*E*)-diethyl cinnamylphosphonate (488 mg, 2.0 mmol) in 5 mL of THF via a cannula over 5 min. The solution was stirred at 30 min at 0 °C and cooled to –78 °C. A solution of aldehyde **11b** (386 mg, 2 mmol) in 5 mL of THF was then added dropwise via a cannula under N_2. The mixture was stirred at –78 °C for 1 h and slowly warmed to 25 °C overnight. The reaction was quenched with 10 mL of brine and extracted with Et_2O (4 × 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated under reduced pressure. Flash chromatography on silica gel (3:1 hexanes/EtOAc) gave 479 mg (82%) of diene **12b** as a 20:1 inseparable mixture of 4*E*/4*Z* isomers: R_f = 0.25 (3:1 hexanes/EtOAc); ^{1}H NMR (4*E* isomer) 8.15 (s, 1), 7.37 (d, 2, *J* = 7.3), 7.29 (t, 2, *J* = 7.3), 7.19 (t, 1, *J* = 7.3), 6.75 (dd, 1, *J* = 15.6, 10.4), 6.59 (s, 1), 6.44 (d, 1, *J* = 15.6), 6.22 (dd, 1, *J* = 15.6, 10.4), 5.85 (dt, 1, *J* = 15.6, 7.3), 3.86 (s, 3), 2.75 (t, 2, *J* = 7.3), 2.22 (dt, 2, *J* = 7.3, 7.3), 2.13 (s, 3), 1.86 (tt, 2, *J* = 7.3, 7.3);

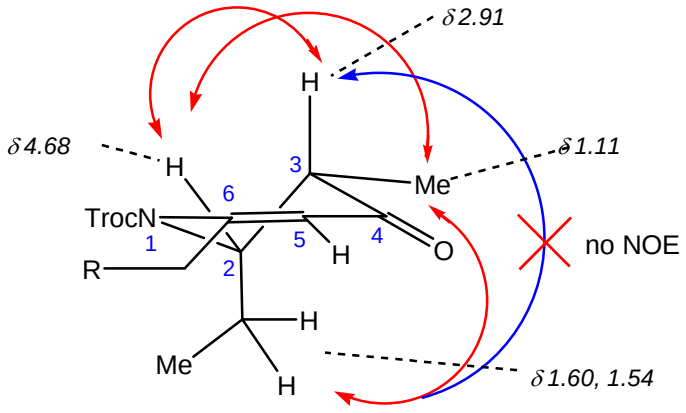
^{1}H NMR (4*Z* isomer) 8.15 (s, 1), 7.37 (d, 2, *J* = 7.3), 7.29 (t, 2, *J* = 7.3), 7.19 (t, 1, *J* = 7.3), 6.99 (dd,1, *J* = 15.0, 11.6), 6.58 (s, 1), 6.55 (d, 1, *J* = *1*5.0), 6.19 (dd, 1, *J* = *1*1.6, 11.6), 5.55 (dt, 1, *J* = 11.6, 7.3), 3.79 (s, 3), 2.75 (t, 2, *J* = 7.3), 2.35 (dt, 2, *J* = 7.3, 7.3), 2.22 (s, 3), 1.86 (tt, 2, *J* = 7.3, 7.3); ^{13}C NMR (4*E* isomer) 164.0, 161.6, 149.9, 137.5, 135.1, 130.9, 130.1, 129.2, 128.4 (2 C), 127.0, 126.0 (2 C), 119.4, 104.3, 54.9, 37.9, 32.4, 29.5, 12.7; IR (neat) 2928, 1678, 1602, 1571, 1498, 1038; HRMS (DCI/NH_3) Calcd for $C_{20}H_{24}NO$ (MH^+) 294.1858, found 294.1872.

2,2,2-Trichloroethyl 2-Ethyl-2,3-dihydro-3-methyl-4-oxo-6-((4*E*,6*E*)-7-phenylhepta-4,6-dienyl)pyridine-1(2*H*)-carboxylate (13) and 2,2,2-Trichloroethyl 2-Ethyl-2,3-dihydro-5-methyl-4-oxo-2-((4*E*,6*E*)-7-phenylhepta-4,6-dienyl)pyridine-1(2*H*)-carboxylate (14). To a solution of pyridine **12b** (293 mg, 1 mmol) in 10 mL of THF at –78 ºC was added dropwise Troc chloride (275 µL, 2 mmol) under N_2. The solution was stirred at –78 ºC for 1 h and EtMgCl (1.0 M in hexanes, 2 mL, 2 mmol) was added dropwise via a cannula over 5 min. The mixture was stirred at –78 °C for 30 min and at 25 °C for 1 h. The reaction was cooled to 0 °C and treated with 10 mL of 1 N HCl. The resulting mixture was stirred at 25 °C for 30 min at what time TLC (10:1 Hexanes/EtOAc, silica gel) showed that all the enol ether had hydrolyzed. The reaction was extracted with Et_2O (3 × 30 mL), and the combined ether extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (15:1-10:1 hexanes/EtOAc) gave 86 mg (18%) of dihydropyridinone **14** as a 15:1 inseparable mixture of 4*E*/4*Z* isomers, followed by 321 mg (67%) of dihydropyridinone **13** as a 20:1 inseparable mixture of 4*E*/4*Z* isomers.

Data for Dihydropyridinone **13**: R_f = 0.25 (10:1 hexanes/EtOAc); ^{1}H NMR (4*E* isomer) 7.37 (d, 2, *J* = 7.3), 7.30 (t, 2, *J* = 7.3), 7.20 (t, 1, *J* = 7.3), 7.74 (dd, 1, *J* = 15.3, 10.4), 6.45 (d, 1, *J* = 15.3), 6.21 (dd, 1, *J* = 15.3, 10.4), 5.76 (dt, 1, *J* = 15.3, 7.3), 5.53 (s, 1), 4.86 (s, 2), 4.68 (ddd, 1, *J* = 11.2, 4.9, 3.6), 3.12 (ddd, 1, *J* = *1*5.2, 9.1, 5.5), 2.91 (dq, 1, *J* = 4.9, 7.3), 2.47 (ddd, 1, *J* = 15.2, 9.1, 6.7), 2.19 (dt, 2, *J* = 7.3, 7.3), 1.70-1.59 (m, 3), 1.54 (ddq, 1, *J* = 14.6, 3.6, 7.3), 1.11 (d, 3, *J* = 7.3), 0.98 (t, 3, *J* = 7.3); ^{13}C NMR (4*E* isomer) 196.3, 156.3, 151.9, 137.4, 133.8,

131.5, 130.7, 128.9, 128.5 (2 C), 127.2, 126.1 (2 C), 114.4, 94.7, 75.6, 63.7, 44.9, 34.7, 32.2, 27.6, 17.6, 11.1, 10.8; IR (neat, mixture) 2970, 1731, 1673, 1312, 1263, 1120, 990.

The stereochemistry of dihydropyridinone **13** was assigned based on NOE studies and ^{1}H NMR coupling constants analysis. PC model calculations indicates that the coupling constant between H-2 at 4.68 and H-3 at δ 2.91 should be 4.05-2.96 Hz for the *cis* enone, and 1.66-0.95 Hz for the *trans* enone. In both cases, the ethyl group adapts the *pseudo*-axial position. The observed coupling constant between H-1 and H-2 is 4.9 Hz, which matches better with the *cis* isomer. In the NOE studies, Irradiation of H-3 at δ 2.91 showed NOE to H-2 at δ 4.68 but no NOE to the ethyl protons at δ 1.70-1.54. Irradiation of H-2 at δ 4.68 showed NOEs to both H-3 at δ 2.91 and the methyl group at δ 1.11. Irradiation of the methyl group at δ 1.11 showed NOEs to both H-2 at δ 4.68 and the ethyl protons at δ 1.70-1.54. Selected NOE correlations are shown below.

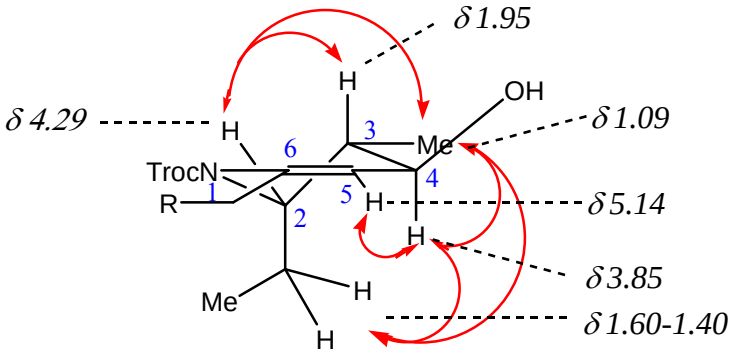


Data for dihydropyridinone **14**: R_f = 0.30 (10:1 hexanes/EtOAc); ^{1}H NMR (4*E* isomer) 7.76 (q, 1, *J* = 1.2), 7.37 (d, 2, *J* = 7.3), 7.30 (t, 2, *J* = 7.3), 7.20 (t, 1, *J* = 7.3), 6.73 (dd, 1, *J* = 15.3, 10.4), 6.44 (d, 1, *J* = 15.3), 6.17 (dd, 1, *J* = 15.3, 10.4), 5.74 (dt, *J* = 15.3, 7.3), 4.87 (s, 2), 2.67 (d, 1, *J* = 16.5), 2.58 (d, 1, *J* = 16.5), 2.34 (dq, 1, *J* = 14.0, 7.3), 2.26 (ddd, 1, *J* = 14.0, 12.2, 4.9), 2.12 (dt, 2, *J* = 7.3, 7.3), 1.77 (d, 3, *J* = 1.2), 1.66-1.54 (m, 2), 1.46-1.35 (m, 2), 0.89 (t, 3, *J* = 7.3); ^{13}C NMR (4*E* isomer) 193.9, 151.3, 140.3, 137.4, 134.4, 131.2, 130.5, 129.0, 128.5 (2 C), 127.2, 126.1 (2 C), 114.5, 94.7, 75.6, 65.9, 44.7, 37.2, 32.9, 30.6, 23.7, 12.9, 8.4; IR (neat) 2934, 1736, 1635, 1384, 1266, 1113, 989.

2,2,2-Trichloroethyl 2-Ethyl-3,4-dihydro-4-hydroxy-3-methyl-6-((4*E*,6*E*)-7-phenylhepta-4,6-dienyl)pyridine-1(2*H*)-carboxylate (16). To a stirred solution of dihydropyridinone **13** (96.6 mg, 0.2 mmol) and $CeCl_3 \bullet 7H_2O$ (93.2 mg, 0.25 mmol) in 4 mL of anhydrous MeOH was added $NaBH_4$ (7.6 mg, 0.2 mmol) in one portion at –78 °C. After stirring at –78 °C for 30 min, the reaction was warmed to 0 °C and quenched with saturated $NaHCO_3$. The mixture was concentrated to remove MeOH, and the remaining aqueous solution was extracted with Et_2O (4 × 10 mL). The combined ether extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (6:1 hexanes/EtOAc) afforded 88.2 mg (91%) of tetrahydropyridinol **16** as a 15:1 mixture of 4*E*/4*Z* isomers: R_f = 0.20 (6:1 hexanes/EtOAc); ^{1}H NMR (4*E* isomer) 7.37 (d, 2, *J* = 7.3), 7.30 (t, 2, *J* = 7.3), 7.19 (t, 1, *J* = 7.3), 6.74 (dd, 1, *J* = 15.3, 10.4), 6.44 (d, 1, *J* = 15.3), 6.19 (dd, 1, *J* = 15.3, 10.4), 5.78 (dt, 1, *J* = 15.3, 7.3), 5.14 (d, 1, *J* = 3.0), 4.84 (d, 1, *J* = 11.6), 4.76 (d, 1, *J* = 11.6), 4.29 (ddd, 1, *J* = 11.6, 3.7, 3.1), 3.85 (br dd, 1, *J* = 8.5, 8.0; br d, 1, *J* = 8.5 after adding D_2O), 3.05 (ddd, 1, *J* = 14.6, 9.7, 4.9), 2.22 (ddd,1, *J* = *1*4.6, 8.5, 6.1) , 2.15 (dt, 2, *J* = 7.3, 7.3), 1.99-1.91 (m, 1), 1.60-1.40 (m, 4), 1.31 (d, 1, *J* = 8.0, OH, disappeared after adding D_2O), 1.09 (d, 3, *J* = 6.7), 0.98 (t, 3, *J* = 6.7); ^{1}H NMR (4*Z* isomer, partial) 7.40 (d, 2, *J* = 7.3), 7.03 (dd, 1, *J* = 15.3, 10.4), 6.53 (d, 1, *J* = 15.3); ^{13}C NMR (4*E* isomer) 152.4, 138.4, 137.5, 134.8, 131.0, 130.3, 129.2, 128.5 (2 C), 127.1, 126.1 (2 C), 115.7, 95.3, 75.2, 70.1, 63.0, 41.0, 34.1, 32.3, 27.7, 17.5, 15.7, 11.4; IR (neat) 2966, 1721, 1399, 1308, 1115, 987, 714; HRMS (DCI/NH_3) calcd for $C_{24}H_{29}Cl_3NO_2$ (MH^+-H_2O) 468.1264 found 468.1215.

PC model calculations indicate that the ethyl group is *pseudo*-axial in both the *trans*- and *cis*-tetrahydropyridinol. The calculated coupling constant between H-4 at δ 3.85 and H-3 at δ 1.95 is 9.08 Hz for *trans* tetrahydropyridinol **16**, and 3.66 Hz for the *cis* tetrahydropyridinol. The observed value of this coupling constant is 8.5 Hz. The calculated coupling constant between H-5 at δ 5.14 and H-4 at δ 3.85 is 3.23 Hz for *trans* tetrahydropyridinol **16**, and 4.22 Hz for the *cis* tetrahydropyridinol. The observed value of this coupling constant is 3.0 Hz. Both observed values match better with those calculated for *trans* tetrahydropyridinol **16**. Further

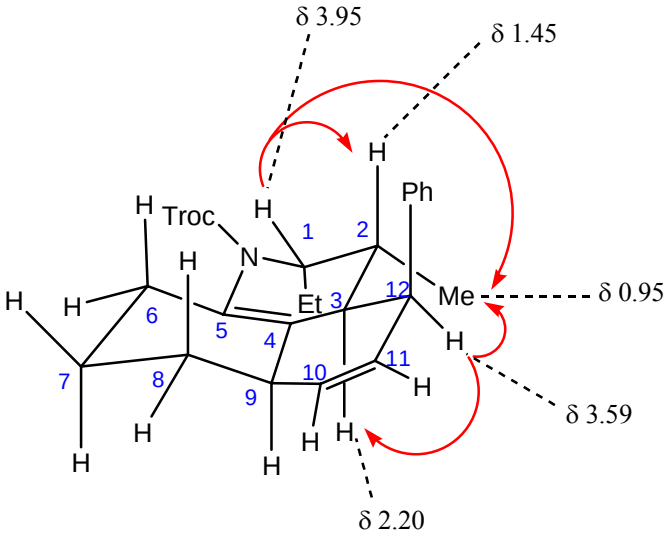
support of the *trans* stereochemistry was obtained by 2D NOE studies. NOEs were observed between H-2 at δ 4.29 and both H-3 at δ 1.95, and H-Me at δ 1.95, between H-4 at δ 3.85 and the methyl proton at δ 1.09, H-5 at δ 5.14, and the ethyl proton at δ 1.60-1.40, between the methyl proton at δ 1.09 and the ethyl proton at δ 1.60-1.40. Selected NOE correlations are drawn below.



Tricyclic Adduct 19. To a solution of diene **16** (mixture of 15:1 4*E*/4*Z* isomers, 24.3 mg, 0.05 mmol,) in 5 mL of CH_2Cl_2 at –78 °C was added BF_3•OEt_2 (60 μL, 1.0 M in CH_2Cl_2, 0.06 mmol) dropwise under N_2. The resulting mixture was stirred at -78 °C for 10 min and warmed to 25 °C over 20 min. The reaction was stirred at 25 °C for 20 min and quenched with 2 mL of saturated $NaHCO_3$. The reaction was extracted with CH_2Cl_2 (3 × 5 mL). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Flash chromatography on silica gel (100:1 hexanes/EtOAc) gave 19.2 mg (87% based on 4*E* diene) of **19** as a colorless oil: R_f = 0.9 (20:1 hexanes/EtOAc); ^{1}H NMR 7.21 (t, 2, *J* = 7.3), 7.13 (t, 1, *J* = 7.3), 7.07 (d, 2, *J* = 7.3), 5.73 (ddd, 1, *J* = 2.7, 4.8, 9.6), 5.65 (br d, 1, *J* = 9.6), 4.79 (d, 1, *J* = 12.0), 4.43 (br d, 1, *J* = 12.0), 3.95 (ddd, 1, *J* = 11.6, 4.7, 3.8), 3.59 (dd, 1, *J* = 4.8, 4.8), 3.17-2.86 (m, 2), 2.20 (br d, 1, *J* = 12.0), 2.07-1.92 (m, 3), 1.60 (dddd, 1, *J* = 12.9, 12.9, 12.9, 3.6), 1.50-1.20 (m, 4), 0.95 (d, 3, *J* = 6.7), 0.85 (br t, 3, *J* = 7.3); ^{13}C NMR 141.0, 129.9, 129.2 (2 C), 128.7 (br), 128.0 (2 C), 126.5, 126.1, 123.1 (br), 95.4 (br), (75.3, 74.1, 1 C), 59.6, 45.5, (43.0, 42.3, 1 C), (37.6, 37.2, 1 C), 34.9 (br), 30.3, 23.0 (br), 18.3, 16.4, 11.1 (br) (The Troc carbonyl carbon and one other carbon were not observed due to slow rotation about the carbamate CO-N bond. Three other carbons appear to absorb separately for the two rotamers.); IR (neat) 2933,

1712, 1401, 1309, 1100;. HRMS (DCI/NH_3) Calcd for $C_{24}H_{29}NO_2Cl_3(MH^+)$ 468.1264, found 468.1243.

The numbering corresponds to that previously used for symbioimine.[1a] Irradiation of H-1 at δ 3.95 showed NOEs to both H-2 at δ 1.45 and the methyl proton at δ 0.95. Irradiation of H-12 at δ 3.59 showed NOEs to H-3 at δ 2.20, H-11 at δ 5.65 and the methyl protons at δ 0.95. Selected NOE correlations are shown below.



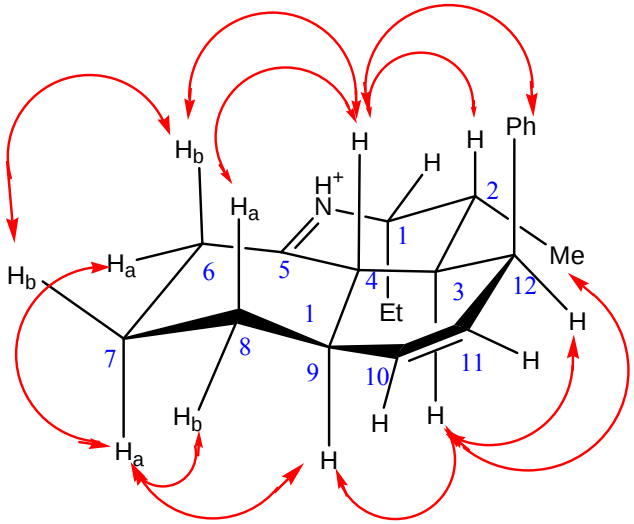
Preparation of Symbioimine Analogue 21. Powdered zinc was activated by washing sequentially with 3 M HCl, water, EtOH, and ether and drying under reduced pressure.[14] To a solution of tricyclic adduct **19** (9.3 mg, 20 μmol) in 1 mL of MeOH was added activated zinc dust (200 mg). The mixture was stirred 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 reduced pressure. The residue was treated with 2 mL of 5% aqueous NaOH, and the solution was extracted with Et_2O (5 × 5 mL). The combined ether extracts were washed with brine, dried over anhydrous K_2CO_3, and concentrated under reduced pressure. Flash chromatography on silica gel (1:1 hexanes/Et_2O to pure Et_2O) gave 4.8 mg (83%) of the free imine **20** as a viscous oil: R_f = 0.20 (EtOAc); ^{1}H NMR 7.31-7.20 (m, 5), 5.77 (ddd, 1, J = 9.8, 1.8, 1.2), 5.68 (ddd, 1, J = 9.8, 4.9, 2.4), 3.61 (dddd, 1, J = 4.8, 4.8), 3.37-3.31 (m, 1), 2.41 (br d, 1, J = 14.0), 2.17 (dddd, 1, J = 14.0, 14.0, 5.5, 1.8), 2.07 (br d, 1, J = 9.8), 2.04-1.92 (m, 2), 1.88 (ddd, 1, J = 12.4, 10.0, 4.8), 1.78-1.68 (m,

1), 1.61 (ddddd, 1, *J* = 14.0, 12.4, 12.4, 4.4, 3.8), 1.42 (ddd, 1, *J* = 14.0, 12.4, 12.4, 3.6), 1.30-1.10 (m, 2), 1.07 (d, 3, *J* = 6.7), 1.03 (t, 3, *J* = 6.7).

Imine **20** slowly tautomerized to the enamine analogous to **19** in $CDCl_3$. The mixture equilibrated over time to give a 2.5:1 mixture of imine **20** and the enamine: ^{1}H NMR (enamine, partial) 3.43 (dd, 1, *J* = 4.8, 4.8), 2.86 (br d, 1, *J* = 12.2), 0.79 (d, 3, *J* = 6.7), 0.48 (t, 3, *J* = 7.3).

To a 2.5:1 mixture of imine **20** and the enamine (4.4 mg, 17.4 μmol) in 1 mL of $CDCl_3$ at 25 °C was added 20 μL of 10% TFA in CH_2Cl_2. After stirring for 5 min, the solvent was removed under reduced pressure. Any residual TFA was removed at 0.2 Torr to give 6.0 mg (100%) of iminium trifluoroacetate salt **21** as a yellow oil: ^{1}H NMR 7.37-7.24 (m, 5, H-13 to H-18), 5.87 (br d, 1, *J* = 9.8, H-11), 5.80 (ddd, 1, *J* = 9.6, 4.8, 2.4, H-10), 3.76-3.69 (m, 2, H-1 and H-12), 3.22 (br d, 1, *J* = 13.4, H-6b), 2.53 (dd, 1, *J* = 10.8, 10.0, H-4), 2.45 (ddd, 1, J = 13.4, 12.9, 6.1, H-6a), 2.35 (br dd, 1, *J* = 12.4, 10.8, H-9), 2.22 (br d, 1, J = 12.9, H-7b), 2.12 (dd, 1, *J* = 12.4, 2.5, H-8b), 2.02 (ddd, 1, *J* = 12.8, 10.0, 4.8, H-3), 1.97-1.85 (m, 1, H-20a), 1.79 (ddddd, 1, *J* = 12.9, 12.9, 12.9, 3.8, 3.8, H-7a), 1.57 (dddd, 1, *J* = 12.9, 12.9, 12.4, 3.6, H-8a), 1.50-1.38 (m, 2, H-2 and H-20b), 1.17 (d, 3, *J* = 6.7, H-19), 1.10 (t, 3, *J* = 7.3, H-21); ^{13}C NMR 188.0, 161.8 (TFA), 137.6, 130.6, 130.1, 130.0 (2 C), 128.6 (2 C), 127.7, 59.6, 43.3, 42.8, 41.7, 38.2, 33.3, 30.6, 30.2, 25.2, 24.3, 14.4, 10.5, one carbon of the trifluoroacetate was not observed; IR (neat) 2924, 1693, 1199, 1129; HRMS (DCI/NH_3) Calcd for $C_{21}H_{28}N$ (MH^+) 294.2221, found 294.2224. The ^{1}H NMR spectrum of **21** is pH sensitive. When >1 eq of TFA was added, the chemical shift of H-1 and H-6a shifted further downfield.

The numbering corresponds to that previously used for symbioimine.[1a] In a 2D NOESY experiment, NOEs were observed between H-4 at δ 2.53 and H-2 at δ 1.50-1.38, the phenyl proton at δ 7.37-7.24, H-6b at δ 2.45, and H-8a at δ 1.57, between H-3 at δ 2.02 and H-12 at δ 3.76-3.69, the methyl proton at δ 1.17, and H-9 at δ 2.35, between H-9 at δ 2.35 and H-7a at δ 1.79, between H-7a at δ 1.79 and both H-8b at δ 2.12 and H-6a at δ 3.22, and between H-7b at δ 2.22 and H-6b at δ 2.45. Selected NOE correlations are drawn below.



Ethyl 6-(1,3)-Dioxolan-2-yl-3-(2-ethoxycarbonyl-propylamino)-2-hexenoate (24). To a solution of ketoester **22**[15] (1.15 g, 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 amine **23**[16] (655 mg, 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% K_2CO_3 solution. The mixture was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (20:1 CH_2Cl_2/MeOH) gave 1.65 g (96%) of enamine **24** as a colorless oil: R_f = 0.30 (20:1 CH_2Cl_2/MeOH); ^{1}H NMR 8.70 (br t, 1, NH), 4.87 (t, 1, J = 4.2), 4.47 (s, 1), 4.16 (q, 2, J = 7.0), 4.08 (q, 2, J = 7.0), 4.00-3.80 (m, 4), 3.48 (ddd, 1, J = 13.4, 6.8, 6.8), 3.26 (ddd, 1, J = 13.4, 6.8, 6.8), 2.64 (ddq, 1, J = 6.8, 6.8, 6.8), 2.30-2.17 (m, 2), 1.76-1.60 (m, 4), 1.28-1.21 (m, 9); ^{13}C NMR 174.5, 170.6, 164.7, 104.0, 82.3, 64.8 (2 C), 60.8, 58.3, 45.3, 40.8, 33.0, 31.9, 22.1, 14.8, 14.5, 14.1; IR (neat) 1734, 1655, 1608, 1141; HRMS (DCI/NH_3) calcd for $C_{17}H_{30}NO_6$ (MH^+) 344.2073, found 344.2063.

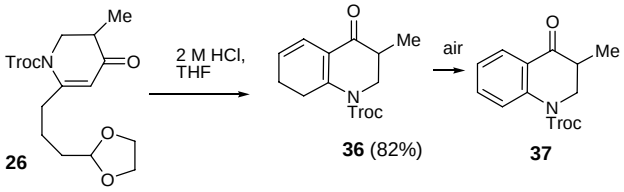
Ethyl 2-(3-(1,3-Dioxolan-2-yl)-propyl)-1,4,5,6-tetrahydro-5-methyl-4-oxopyridine-3-carboxylate (25). To a solution of enamine **24** (1.72 g, 5 mmol) in 20 mL of dry THF at 25 °C was added NaH (60% in mineral oil, 0.6 g, 15 mmol) in one portion. The resulting mixture was

heated to reflux for 3 h and cooled to 25 °C. Saturated NH_4Cl solution (10 mL) was carefully added and the layers were separated. The aqueous phase was extracted with Et_2O (3 × 20 mL), and the combined organic layers were washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (20:1 CH_2Cl_2/MeOH) gave 1.45 g (97%) of dihydropyridinone **25** as a tan oil: R_f = 0.20 (20:1 CH_2Cl_2/MeOH); ^{1}H NMR 6.12 (br s, NH), 4.85 (t, 1, *J* = 4.2), 4.25 (q, 2, *J* = 7.0), 4.00-3.85 (m, 4), 3.57 (ddd, 1, *J* = 13.4, 6.2, 3.7), 3.22 (ddd, 1, *J* = 13.4, 11.0, 2.4), 2.70-2.59 (m, 2), 2.51-2.41 (m, 1), 1.85-1.73 (m, 4), 1.32 (t, 3, *J* = 7.0), 1.13 (d, 3, *J* = 7.0); ^{13}C NMR 191.5, 168.1, 167.1, 104.3, 102.9, 64.8 (2 C), 60.1, 46.9, 38.2, 33.2, 32.0, 22.6, 14.3, 13.2; IR (neat) 3263, 1694, 1565, 1289; HRMS (DCI/NH_3) calcd for $C_{15}H_{24}NO_5$ (MH^+) 298.1654, found 298.1649.

6-(3-(1,3-Dioxolan-2-yl)propyl)-2,3-dihydro-3-methylpyridin-4(1*H*)-one. To a solution of dihydropyridinone **25** (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 12 h. After the mixture was cooled to 25 °C, 10 mL of saturated NH_4Cl solution was added. The solution was extracted with CH_2Cl_2 (5 × 20 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (20:1 CH_2Cl_2/MeOH) afforded 634 mg (94%) of the dihydropyridinone as a tan oil: R_f = 0.20 (20:1 CH_2Cl_2/MeOH); ^{1}H NMR 5.53 (br s, NH), 4.98 (s, 1), 4.85 (br t, 1, *J* = 4.2), 4.00-3.85 (m, 4), 3.56 (ddd, 1, *J* = 12.8, 5.5, 3.0), 3.21 (ddd, 1, *J* = 12.8, 10.0, 2.2), 2.44-2.34 (m, 1), 2.28-2.23 (m, 2), 1.80-1.65 (m, 4), 1.12 (d, 3, *J* = 6.8); ^{13}C NMR 196.1, 165.9, 104.0, 97.2, 64.8 (2 C), 48.1, 38.0, 34.3, 32.3, 22.0, 13.7; IR (neat) 2926, 1606, 1548, 1139; HRMS (DCI/NH_3) calcd for $C_{12}H_{20}NO_3$ (MH^+) 226.1443, found 226.1439.

2,2,2-Trichloroethyl 6-(3-(1,3-Dioxolan-2-yl)propyl)-3,4-dihydro-3-methyl-4-oxopyridine-1(2*H*)-carboxylate (26). To a solution of the above dihydropyridinone (450 mg, 2 mmol) in 20.0 mL of THF at -78 ºC 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 μL, 445 mg, 2.1 mmol) in 2 mL of THF was added dropwise via cannula over 5 min. The reaction was stirred for 30

min at -78 °C, warmed to 25 °C over 20 min, treated with 10 mL of saturated $NaHCO_3$, and stirred at 25 °C for 20 min. The reaction mixture was extracted with EtOAc (3 × 20 mL), and the combined organic layers were washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography on silica gel (4:1 hexanes/EtOAc) afforded 767 mg (96%) of dihydropyridinone **26** as a colorless oil: R_f = 0.20 (4:1 hexanes/EtOAc); ^{1}NMR 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 (4, m), 1.15 (d, 3, J = 6.8); ^{13}C NMR 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/NH_3) calcd for $C_{15}H_{21}Cl_3NO_5$ (MH^+) 400.0485, found 400.0485.



2,2,2-Trichloroethyl 3,4,7,8-Tetrahydro-3-methyl-4-oxoquinoline-1(2*H*)-carboxylate (36) and 2,2,2-Trichloroethyl 3,4-Dihydro-3-methyl-4-oxoquinoline-1(2*H*)-carboxylate (37). To a solution of dihydropyridinone **26** (200 mg, 0.5 mmol) in 15 mL of anhydrous THF at 25 °C was added 5 mL of 1 M HCl. The resulting solution was stirred at 25 °C for 4 h. The reaction was neutralized with saturated $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined ether extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 154 mg of 90% pure tetrahydroquinoline **36** (82%) as a colorless liquid: R_f = 0.20 (20:1 hexanes/EtOAc); ^{1}H NMR 6.55 (d, 1, J = 9.8), 5.79 (dt, 1, J = 9.8, 4.3), 4.90 (d, 1, J = 12.0), 4.85 (d, 1, J = 12.0), 4.30 (dd, 1, J = 12.8, 4.4), 3.77 (dd, 1, J = 12.8, 9.6), 2.95-2.76 (m, 2), 2.64-2.55 (m, 1), 2.32-2.36 (m, 2), 1.17 (d, 3, J = 7.3).

Tetrahydroquinoline **36** was unstable and gradually oxidized to give the corresponding dihydroquinoline **37**, which can be readily purified by flash chromatography on silica gel (20:1

hexanes/Et_2O): R_f = 0.25 (20:1 hexanes/EtOAc); ^{1}H NMR 8.04 (dd, 1, *J* = 7.9, 1.8), 7.89 (br d, 1, *J* = 8.3), 7.55 (ddd, 1, *J* = 8.3, 8.3, 1.8), 7.24 (dd, 1, *J* = 8.3, 7.9, 1.2), 4.96 (d, 1, *J* = 12.2), 4.88 (d, 1, *J* = 12.2), 4.46 (dd, 1, *J* = 13.4, 4.9), 3.85 (d, 1, *J* = 13.4, 10.1), 2.83 (ddq, 1, *J* = 10.1, 4.9, 6.7), 1.28 (d, 3, *J* = 6.7); ^{13}C NMR 196.2, 152.2, 142.6, 134.1, 127.8, 124.9, 124.5, 123.4, 94.9, 75.5, 50.8, 42.5, 12.7; IR (neat) 1227, 1693, 1602, 1482, 1393, 1209, 1150.

2,2,2-Trichloroethyl 3,4-Dihydro-6-(4,4-dimethoxybutyl)-3-methyl-4-oxopyridine-1(2*H*)-carboxylate (27). To a solution of dihydropyridinone **26** (400 mg, 1.0 mmol) in 15 mL of anhydrous MeOH at 25 °C was added PPTS (62.5 mg, 0.25 mmol) in one portion. The resulting solution was stirred overnight at 65 °C, cooled, and concentrated. The residue was dissolved in 20 mL of Et_2O. The solution was washed with 10 mL of saturated $NaHCO_3$, and the aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give 383 mg (95%) of dimethyl acetal **27** as a colorless oil, which was used for the next step without further purification: R_f = 0.20 (4:1 hexanes/EtOAc); ^{1}H NMR 5.49 (s, 1), 4.87 (br s, 2), 4.37 (t, 1, *J* = 4.9), 4.28 (dd, 1, *J* = 12.8, 4.2), 3.73 (dd, 1, *J* = 12.8, 10.0), 3.31 (s, 6), 2.92-2.69 (m, 2), 2.59-2.49 (m, 1), 1.66-1.54 (m, 4), 1.15 (d, 3, *J* = 7.3); ^{13}C NMR 197.2, 159.3, 151.4, 113.5, 104.0, 94.6, 75.5, 52.9 (2 C), 52.8, 40.6, 34.7, 31.9, 22.9, 12.5.

2,2,2-Trichloroethyl 6-(4-oxobutyl)-3,4-dihydro-3-methyl-4-oxopyridine-1(2*H*)-carboxylate (28). A solution of dimethyl acetal **27** (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 55 °C for 3 h, cooled to 25 °C and concentrated. The residue was dissolved in 25 mL of Et_2O. The solution was washed with 10 mL of saturated $NaHCO_3$, and the aqueous phase was extracted with Et_2O (2 × 10 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography on silica gel (4:1 hexanes/EtOAc) afforded 140 mg (87%) of aldehyde **28** as a colorless oil: R_f = 0.15 (4:1 hexanes/EtOAc); ^{1}H NMR 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); ^{13}C NMR 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/NH_3) calcd for $C_{13}H_{17}Cl_3NO_4$ (MH^+) 358.0194, found 358.0198.

2,2,2-Trichloroethyl 3,4-Dihydro-3-methyl-4-oxo-6-((4*E*,6*E*)-7-phenylhepta-4,6-dienyl)pyridine-1(2*H*)-carboxylate (29*E*) and 2,2,2-Trichloroethyl 3,4-Dihydro-3-methyl-4-oxo-6-((4*Z*,6*E*)-7-phenylhepta-4,6-dienyl)pyridine-1(2*H*)-carboxylate (29*Z*). To a solution of (*E*)-cinnamyltriphenylphosphonium chloride[22] (212 mg, 0.5 mmol) in 10 mL of THF at 0 °C was added *n*-BuLi (1.6 M in hexanes, 313 μL, 0.5 mmol) dropwise over 5 min under N_2. After stirring at 0 °C for 1 h, the orange ylide solution was cooled to -78 °C and treated with a solution of aldehyde **28** (180 mg, 0.5 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 $NaHCO_3$ and extracted with Et_2O (3 × 20 mL). The combined ether extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (10:1 hexanes/EtOAc) gave 190 mg (83%) of an inseparable 2:1 mixture of diene **29*E*** and **29*Z*.**

The 2:1 mixture of Dienes **29*E*** and **29*Z*** was dissolved in 15 mL of dry CH_2Cl_2. The solution was treated with 5 mg of I_2 and stirred at 25 °C for 1 h. The solution was treated with 5 mL of 10% $NaHSO_3$ to reduce the I_2. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated to afford 190 mg (100%) of an inseparable 6:1 mixture of **29*E*** and **29*Z***: R_f = 0.25 (10:1 hexanes/EtOAc); ^{1}H NMR (**29*E***) 7.36 (d, 2, *J* = 7.3), 7.30 (t, 2, *J* = 7.3), 7.20 (t, 1, *J* = 7.3), 6.73 (dd,1, *J* = 15.3, 10.4), 6.46 (d, 1, *J* = 15.3), 6.21 (dd, 1, *J* = 15.3, 10.4), 5.77 (dt, 1, *J* = 15.3, 7.3), 5.50 (s, 1), 4.88 (s, 2), 4.29 (dd, 1, *J* = 12.8, 4.4), 3.72 (dd, 1, *J* = 12.8, 10.0), 2.88 (dt, 1, *J* = 15.2, 7.3), 2.74 (dt, 1, *J* = 15.2, 7.3), 2.55 (ddq, 1, *J* = 10.0, 4.4, 7.3), 2.19 (dt, 2, *J* = 7.3, 7.3), 1.67 (tt, 2, *J* = 7.3, 7.3), 1.15 (d, 3, *J* = 7.3); ^{1}H NMR (**29*Z***) 7.37 (d, 2, *J* = 7.3), 7.31 (t, 2, *J* = 7.3), 7.21 (t, 1, *J* = 7.3), 7.00 (dd, 1, *J* = 15.3, 10.4), 6.54 (d, 1, *J* = 15.3), 6.19 (dd, 1, *J* = 10.4, 10.4), 5.49 (s, 1), 5.49 (dt, 1, *J* = 10.4, 7.3), 4.85 (s, 2), 4.28 (dd, 1, *J* =

12.8, 4.4), 3.73 (dd, 1, *J* = 12.8, 10.0), 2.89 (dt, 1, *J* = 15.2, 7.3), 2.75 (dt, 1, *J* = 15.2, 7.3), 2.54 (ddq, 1, *J* = 10.0, 4.4, 7.3), 2.33 (dt, 2, *J* = 7.3, 7.3), 1.67 (tt, 2, *J* = 7.3, 7.3), 1.14 (d, 3, *J* = 7.3); ^{13}C NMR (**29*E***) 197.2, 159.5, 151.5, 137.4, 133.9, 131.5, 130.7, 128.9, 128.5 (2 C), 127.2, 126.2 (2 C), 113.6, 94.7, 75.6, 52.8, 40.7, 34.5, 32.2, 27.5, 12.5; IR (neat, mixture) 2932, 1735, 1674, 1592, 1441, 1392, 1341, 1170, 1030, 833, 782, 717; HRMS (DCI/NH_3) calcd for $C_{22}H_{28}Cl_3N_2O_3$ (MNH_4^+) 473.1165, found 473.1167.

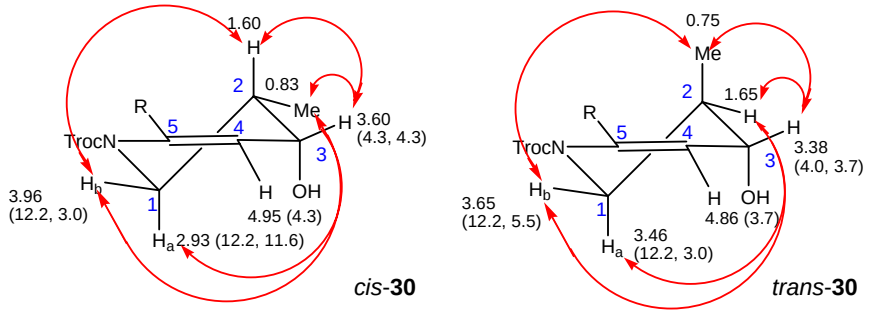
Luche Reduction (*cis*- and *trans*-30). To a stirred solution of dihydropyridinone **29** (6:1 mixture of **29*E***/**29*Z***, 90 mg, 0.2 mmol) and $CeCl_3$•$7H_2O$ (89 mg, 0.24 mmol) in 2 mL of MeOH was added $NaBH_4$ (7.2 mg, 0.2 mmol) in one portion at -78 °C. After stirring at -78 °C for 30 min, the reaction was stirred at 0 °C for 30 min and treated with saturated $NaHCO_3$. The MeOH was removed under reduced pressure and the mixture was extracted with Et_2O (4 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Flash chromatography of the residue on silica gel (6:1 hexanes/EtOAc) afforded 87.8 mg (95%) of an inseparable 3:1 mixture of *cis*- and *trans*-**30,** each as a 6:1 mixture of *E*/*Z* isomers.

Data for *cis*-**30** *E* isomer were determined from the mixture: R_f = 0.25 (4:1 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$) 7.29 (d, 2, *J* = 7.3), 7.21 (t, 2, *J* = 7.3), 7.11 (t, 1, *J* = 7.3), 6.69 (dd, 1, *J* = 15.9, 10.4), 6.36 (d, 1, *J* = 15.9), 6.13 (dd, 1, *J* = 15.3, 10.4), 5.75 (dt, 1, *J* = 15.3, 7.3), 5.12 (d, 1, *J* = 4.3), 4.81 (d, 1, *J* = 12.2), 4.66 (d, 1, *J* = 12.2), 3.95-3.85 (m, 2), 2.89 (dd, 1, *J* = 12.8, 12.8), 2.81 (dt, 1, *J* = 14.6, 7.3), 2.31 (dt, 1, *J* = 14.6, 7.3), 2.06 (dt, 2, *J* = 7.3, 7.3), 1.86-1.76 (m, 1), 1.49 (tt, 2, *J* = 7.3, 7.3), 0.94 (d, 3, *J* = 7.3); ^{1}H NMR (C_6D_6) 7.28 (d, 2, *J* = 7.3), 7.15 (t, 2, *J* = 7.3), 7.04 (t, 1, *J* = 7.3), 6.78 (dd, 1, *J* = 15.3, 10.4), 6.42 (d, 1, *J* = 15.3), 6.23 (dd, 1, *J* = 14.7, 10.4), 5.73 (dt, 1, *J* = 14.7, 7.3), 4.95 (d, 1, *J* = 4.3), 4.71 (d, 1, *J* = 12.2), 4.47 (d, 1, *J* = 12.2), 3.96 (dd, 1, *J* = 12.2, 3.0), 3.60 (br s, 1, after adding D_2O, dd, *J* = 4.3, 4.3), 3.06 (dt, 1, *J* = 14.7, 7.3), 2.93 (dd, 1, *J* = 12.2, 11.6), 2.44 (dt, 1, *J* = 14.7, 7.3), 2.12 (dt, 2, *J* = 7.3, 7.3), 1.67-1.52 (m, 3), 0.83 (d, 3, *J* = 6.7); ^{13}C NMR (C_6D_6) 152.6, 141.7, 138.6, 135.6, 132.3, 131.5, 130.2, 129.5 (2 C), 128.0, 127.2 (2 C), 115.9, 96.6, 75.8, 65.5, 48.0, 35.8, 35.1, 33.2, 28.7,

13.3; IR (neat) 3411, 1722, 1398, 1199, 1116; HRMS (DCI/NH_3) calcd for $C_{22}H_{25}Cl_3NO_2$ (MH^+-H_2O) 440.0951, found 440.0988.

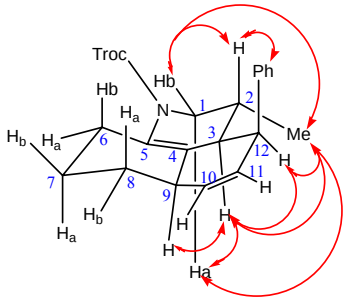
Partial data for *trans*-**30** *E* isomer were determined from mixture: ^{1}H NMR ($CDCl_3$) 7.29 (d, 2, *J* = 7.3), 7.21 (t, 2, *J* = 7.3), 7.11 (t, 1, *J* = 7.3), 6.69 (dd, 1, *J* = 15.9, 10.4), 6.36 (d, 1, *J* = 15.9), 6.13 (dd, 1, *J* = 15.3, 10.4), 5.75 (dt, 1, *J* = 15.3, 7.3), 5.02 (d, 1, *J* = 3.7), 4.80-4.60 (m, 2), 3.95-3.85 (m, 2), 3.45 (dd, 1, *J* = 12.8, 3.1), 2.06 (dt, 2, *J* = 7.3, 7.3), 1.86-1.76 (m, 1), 1.49 (tt, 2, *J* = 7.3, 7.3), 0.84 (d, 3, *J* = 7.3); ^{1}H NMR (C_6D_6), 7.28 (d, 2, *J* = 7.3), 7.15 (t, 2, *J* = 7.3), 7.04 (t, 1, *J* = 7.3), 6.78 (dd, 1, *J* = 15.3, 10.4), 6.42 (d, 1, *J* = 15.3), 6.23 (dd, 1, *J* = 14.7, 10.4), 5.73 (dt, 1, *J* = 14.7, 7.3), 4.86 (d, 1, *J* = 3.7), 4.64 (d, 1, *J* = 12.2), 4.49 (d, 1, *J* = 12.2), 3.65 (dd, 1, *J* = 12.2, 5.5), 3.46 (dd, 1, *J* = 12.2, 3.0), 3.38 (br s, 1, after adding D_2O, dd, *J* = 4.0, 3.7), 2.93 (dt, 1, *J* = 14.7, 7.3), 2.55 (dt, 1, *J* = 14.7, 7.3), 2.26 (dt, 2, *J* = 7.3, 7.3), 1.67-1.52 (m, 3), 0.75 (d, 3, *J* = 6.7).

The stereochemistry of the isomers of **30** was established by a 2D NOESY experiment in C_6D_6. For *cis*-**30**, NOEs were observed between H-1a at δ 2.93 and the methyl protons at δ 0.83, but not H-2 at δ 1.60, between H-1b at δ 3.96 and both H-2 at δ 1.60 and the methyl protons at δ 0.83, between H-2 at δ 1.67-1.52 and H-3 at δ 3.60, between H-3 at δ 3.60 and both the methyl protons at δ 0.83 and H-4 at δ 4.95. For *trans*-**30**, NOEs were observed between H-1a at δ 3.46 and H-2 at δ 1.65 but not the methyl protons at δ 0.75, between H-1b at δ 3.65 and both H-2 at δ 1.65 and the methyl protons at δ 0.75, between H-3 at δ 3.38 and both the methyl protons at δ 0.75 and H-2 at δ 1.65. Selected NOE correlations are drawn below.



Diels-Alder Adduct 33. To a solution of a 3:1 mixture of *cis*- and *trans*-**30** (*E*/*Z* = 6:1, 45.8 mg, 0.1 mmol,) in 3 mL of CH_2Cl_2 at -78 °C was added BF_3•OEt_2 (110 μL, 1.0 M in CH_2Cl_2, 0.11 mmol) dropwise under N_2. The resulting mixture was stirred at –78 °C for 10 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 $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 × 5 mL), the combined extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography on silica gel (100:1 hexanes/EtOAc) gave 11.6 mg (31% based on 4*E* diene) of pure **33** as a colorless oil: R_f = 0.85 (20:1 hexanes/EtOAc); ^{1}H NMR 7.21 (t, 2, *J* = 7.3), 7.13 (t, 1, *J* = 7.3), 7.05 (d, 2, *J* = 7.3), 5.74 (ddd, 1, *J* = 9.6, 4.8, 2.4), 5.67 (br d, 1, *J* = 9.6), 4.79 (d, 1, *J* = 12.0), 4.37 (br d, 1, *J* = 12.0), 3.84-3.72 (br, 1), 3.62 (dd, 1, *J* = 5.3, 4.8), 3.00-2.88 (m, 2), 2.72-2.58 (m, 1), 2.29 (br dd, 1, *J* = 5.3, 9.3), 2.14-1.92 (m, 3), 1.68-1.34 (m, 3), 0.97 (d, 3, *J* = 6.7); ^{13}C NMR 141.0, 130.3, 129.4 (2 C), 128.4, 128.0 (2 C), 126.5, 122.9, 95.5 (br), 74.9 (br), 50.5, 45.8, 37.6, 32.2, 30.5, 29.7, 22.9, 17.3, (two tertiary carbons and one other carbon were not observed due to slow rotation about the carbamate CO-N bond); IR (neat) 2929, 1721, 1401, 1196, 1156, 1122; HRMS (DCI/NH_3) Calcd for $C_{22}H_{25}NO_2Cl_3$ (MH^+) 440.0945, found 440.0938.

The stereochemistry of **33** was established by a 2D NOESY experiment. The numbering corresponds to that previously used for symbioimine.[1a] NOEs were observed between H-1a at δ 2.65 and both H-3 at δ 2.29 and the methyl protons at δ 0.97, between H-1b at δ 3.77 and both H-2 at δ 1.40 and the methyl protons at δ 0.97, between the methyl protons at δ 0.97 and H-3 at δ 2.29, between H-2 at δ 1.40 and the phenyl protons at δ 7.21, between H-3 at δ 2.29 and both H-9 at δ 2.94 and H-12 at δ 3.62. Selected NOE correlations are drawn below.



Deoxysymbioimine (35). Powdered zinc was activated by washing sequentially with 3 M HCl, water, EtOH, and ether and drying under reduced pressure.[14] To a solution of tricyclic adduct **33** (8.8 mg, 20 μmol) in 1 mL of MeOH was added activated zinc (200 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 2 mL of 5% aqueous NaOH, and the solution was extracted with Et_2O (5 × 5 mL). The combined ether extracts were washed with brine, dried over anhydrous K_2CO_3, and concentrated under reduced pressure. Flash chromatography on silica gel (1:1 hexanes/Et_2O to pure Et_2O) gave 4.0 mg (75%) of imine **34** as a viscous oil: ^{1}H NMR 7.31-7.20 (m, 5), 5.78 (br d, 1, *J* = 9.8), 5.68 (ddd, 1, *J* = 9.8, 4.9, 2.4), 3.72 (dd, 1, *J* = 4.9, 4.9), 3.57 (br d, 1, *J* = 17.1), 3.04-2.94 (m, 1), 2.37 (br d, 1, *J* = 14.0), 2.15 (br dd, 1, *J* = 14.0, 14.0), 2.09-1.92 (m, 4), 1.72-1.34 (m, 4), 1.02 (d, 3, *J* = 6.7).

To the solution of imine **34** (3.0 mg, 11.3 μmol) in 1 mL of $CDCl_3$ at 25 °C was added 20 μL of 10% TFA in CH_2Cl_2. The solution was stirred for 5 min and concentrated under reduced pressure. Any residual TFA was removed at 0.2 Torr to give iminium trifluoroacetate salt **35** (4.1 mg, 100%) as a yellow oil: ^{1}H NMR ($CDCl_3$) 7.36 (t, 2, *J* = 7.3, H-15/17), 7.31 (t, 1, *J* = 7.3, H-16), 7.25 (d, 2, *J* = 7.3, H-14/18), 5.87 (br d, 1, *J* = 9.8, H-11), 5.80 (ddd, 1, *J* = 9.8, 4.9, 2.4, H-10), 3.85 (dd, 1, *J* = 4.9, 4.9, H-12), 3.70 (br d, 1, *J* = 14.6, H-1b), 3.20 (dd, 1, *J* = 14.6, 12.3, H-1a), 3.03 (br d, 1, *J* = 15.2, H-6b), 2.52-2.38 (m, 3, H-4, H-6a, H-9), 2.22 (br d, 1, *J* = 12.9, H-7b), 2.13 (ddd, 1, *J* = 13.2, 3.1, 2.0, H-8b), 1.85 (ddd, 1, *J* = 11.6, 9.8, 5.5, H-3), 1.81 (ddddd, 1, *J* = 12.9, 12.9, 12.9, 4.3, 3.7, H-7a), 1.57 (dddd, 1, *J* = 12.9, 12.9, 12.9, 3.0, H-8a), 1.39-1.24 (m, 1, H-2), 1.20 (d, 3, *J* = 6.7, H-19); ^{1}H NMR (CD_3OD) 7.39-7.25 (m, 5, H-14 to H-18), 5.88 (ddd, 1, *J* = 9.8, 1.8, 1.2, H-11), 5.77 (ddd, 1, *J* = 9.8, 4.9, 2.4, H-10), 3.86 (dddd, 1, *J* = 5.5, 4.9, 1.8, 1.8, H-12), 3.60 (dd, 1, *J* = 15.8, 4.9, H-1b), 3.21 (dd, 1, *J* = 15.8, 12, H-1a), 2.75-2.66 (m, 2, H-6a and H-6b), 2.70 (br dd, 1, *J* = 12.2, 10.4, H-4), 2.50 (dddd, 1, *J* = 12.8, 12.2, 2.4, 2.4, H-9), 2.19 (ddddd, 1, *J* = 12.2, 3.7, 3.7, 3.7, 3.7, H-7b), 2.08 (dddd, 1, *J* = 12.8, 3.7, 3.1, 2.4, H-8b), 1.95 (ddd, 1, *J* = 11.6, 10.4, 5.5, H-3), 1.89-1.77 (m, 1, H-7a), 1.64 (dddd, 1, *J* = 12.8, 12.8, 12.8,

3.7, H-8a), 1.44-1.28 (m, 1, H-2), 1.17 (d, 3, J = 6.1, H-19); ^{1}H NMR (DMSO-d_6) 12.93 (br s, 1, NH), 7.40-7.30 (m, 4, H-14/H-18 and H-15/H-17), 7.24-7.30 (m, 1, H-16), 5.81 (br d, 1, J = 9.8, H-11), 5.67 (ddd, 1, J = 9.8, 4.9, 2.4, H-10), 3.78 (dd, 1, J = 5.5, 4.8, H-12), 3.58 (dd, 1, J = 14.3, 4.3, H-1b), 3.15 (dd, 1, J = 14.3, 12.6, H-1a), 2.73-2.64 (m, 2, H-6a and H-6b), 2.62 (br dd, 1, J = 11.9, 11.0, H-4), 2.43 (dd, 1, J = 11.9, 11.6, H-9), 2.07-2.00 (m, 1, H-7b), 1.95 (br d, 1, J = 12.4, H-8b), 1.86 (ddd, 1, J = 11.0, 11.0, 5.5, H-3), 1.74-1.61 (m, 1, H-7a), 1.53 (dddd, 1, J = 12.8, 12.4, 11.6, 4.2, H-8a), 1.27-1.12 (m, 1, H-2), 1.02 (d, 3, J = 6.1, H-19); ^{13}C NMR ($CDCl_3$) 190.6, 160.1 (TFA), 137.5, 130.1, 130.0, 129.8 (2 C), 128.7 (2 C), 127.8, 50.3, 42.9, 42.3, 42.0, 41.2, 34.1, 30.4, 26.3, 24.8, 15.8 (one carbon of the trifluoroacetate was not observed); ^{13}C NMR (CD_3OD) 193.8, 140.0, 131.32, 131.30 (2 C), 131.2, 129.5 (2 C), 128.4, 51.2, 43.9, 43.6, 42.9, 42.5, 35.0, 31.3, 27.7, 25.9, 15.9, (two carbons of the trifluoroacetate were not observed); ^{13}C NMR (DMSO-d_6) 189.7, 138.9, 130.4, 130.0 (2 C), 129.7, 128.2 (2 C), 127.0, 49.2, 41.9, 41.3, 40.7, 40.4, 33.1, 29.5, 26.1, 24.3, 15.2, (two carbons of the trifluoroacetate were not observed); IR (neat) 2924, 1693, 1199, 1129; HRMS (DEI) Calcd for $C_{19}H_{23}N$ (M^+) 265.1831, found 265.1823.

The stereochemistry of **35** was established by 2D NOESY experiments in $CDCl_3$, CD_3OD, and DMSO-d_6. The numbering corresponds to that previously used for symbioimine.[1a] Proton assignments are indicated in the spectral list above. NOEs were observed between H-4 and H-2, H-Ph, H-6b and H-8a, between H-3 and H-12, H-Me, and H-9, between H-9 and H-7a, between H-7a and both H-8b and H-6a, between H-7b and H-6b. Selected NOE correlations are drawn below.

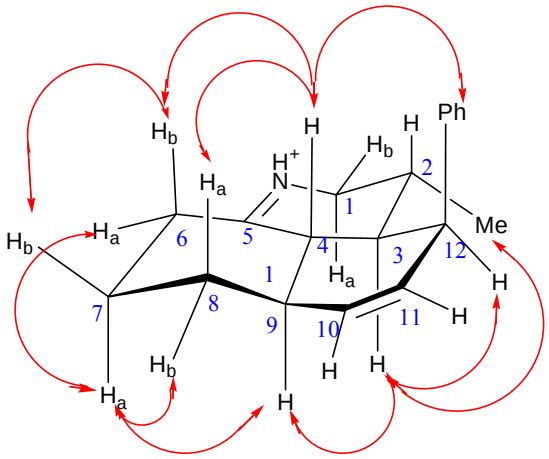
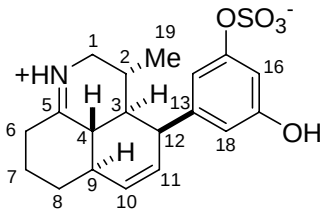
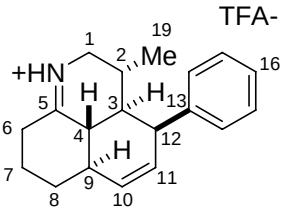

Hb
Ha
Hb
Ha
H
H+
N
Hb
H
Ph
2
1
Me
6
5
4
3
12
1
Ha
H
7
8
9
10
11
H
Hb
H
H
Ha
H

Table 1. Comparison of ^{13}C NMR spectra of Symbioimine (**1)** in DMSO-d_6 with those of **35** in DMSO-d_6, $CDCl_3$, and CD_3OD.





	(DMSO-d_6, 200MHz)	(DMSO-d_6)	($CDCl_3$)	(CD_3OD)
1	50.0	49.2	50.3	51.2
2	26.2	26.1	26.3	27.7
3	40.8	40.7	42.0	42.9
4	40.1	40.4	41.2	42.5
5	188.0	189.7	190.6	193.8
6	33.8	33.1	34.0	35.0
7	24.4	24.3	24.8	25.9
8	29.8	29.5	30.4	31.3
9	41.4	41.3	42.3	43.6
10	130.4	130.1	130.1	131.3
11	129.5	129.7	129.9	131.2
12	41.7	41.9	42.9	43.9
13	139.8	138.9	137.5	140.0
14	112.8	128.2	128.7	131.3
15	154.1	130.0	129.8	129.5
16	105.8	127.0	127.8	128.4
17	157.2	130.0	129.8	129.5
18	111.7	128.2	128.7	131.3
19	15.6	15.2	15.9	15.9