Supporting Information for:

Preparation of Hexahydro-benzo[*f*]isoquinolines Using a Vinylogous Pictet-Spengler Cyclization.

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General Comments

In most cases, a general procedure for product isolation and purification was utilized that involved quenching the reaction in an aqueous solution, exhaustive extraction with an organic solvent, drying over an anhydrous salt, filtration, evaporation under reduced pressure and flash chromatography. Such a workup is indicated by the phrase "product isolation" (which is then followed, in parentheses, by a listing of quenching agent, extraction solvent and drying agent if not $MgSO_4$, which is not listed) and "purification" (which is followed, in parentheses, by the elution solvent used in the flash chromatography).

All reactions were performed under a dry (Drierite) argon atmosphere. Unless otherwise specified, reagents and solvents used in this study were obtained from commercial sources, (Aldrich, Strem, or Fluka), and are used without further purification. Temperatures refer to that of the reaction bath. Dimethylformamide was dried with barium hydroxide and distilled from and stored over 4Å molecular sieves. Methanol and butanol were distilled from magnesium activated with iodine and stored over 3Å molecular sieves. Hexanes were distilled from $CaSO_4$ before use in flash chromatography.

Reaction progress was monitored using analytical thin-layer chromatography (TLC) on 0.25 mm Merck F-254 silica gel glass plates. Visualization was achieved using potassium permanganate or UV illumination. Flash chromatography was performed according to the literature method[1] with Woelm silica gel (0.040-0.063 mm) packing.

^{1}H and ^{13}C NMR spectra were recorded on a U400 or U500 Varian FT-NMR spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) downfield from internal tetramethylsilane or by reference to proton resonances resulting from incomplete deuteration of the NMR solvent. Low resolution electron impact (EI) mass spectra were

[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

obtained on a Finnigan MAT CH5 or VG Instruments 70-VSE spectrometer. High resolution EI mass spectra were obtained on a Finnigan MAT 731 spectrometer. Both high and low resolution chemical ionization (CI) mass spectra were obtained on a VG Instruments 70-VSE spectrometer. Elemental and DSC analyses were performed by the Microanalytical Service Laboratory of the University of Illinois.

Procedures

Nearly all of the substrates used in this study are available from commercial sources. However, in the case of compounds **6**[2] and **10**[3], we followed the syntheses reported in the literature. All enamines could be isolated via column chromatography, yet we found that to avoid decomposition of these intermediates, their prompt use following isolation was preferred. The mixture of isomers obtained in the formation of compound **8** made rigorous assignments of the quaternary carbons chemical shifts difficult. Therefore, we have listed resonances only for those carbon atoms which could be assigned unambiguously.

Typical Experimental Procedure for the Vinylogous Pictet-Spengler Reaction. Conditions A. Amine (**1**) (100 mg, 0.42 mmol) was dissolved in butanol (3 mL) and the corresponding ketone (0.63 mmol) was added. The solution was then refluxed for the specified time. Product isolation (sat. $NaHCO_3$, EtOAc) and purification afforded the desired compound.

Typical Experimental Procedure for the Vinylogous Pictet-Spengler Reaction. Conditions B. Amine (**1**) (100 mg, 0.42 mmol) was dissolved in DMF (1 mL) and cooled to 0 ˚C. Triethylamine (64 μL, 0.46 mmol), was added and triethylammonium chloride immediately precipitated from the solution. The appropriate ketone or alkyne (0.50 mmol) was then added neat, (or as a solution in a minimal amount

[2] Luettrinhaus, A. *Justus. Liebigs. Ann. Chem.* **1963**, *661*, 84.
[3] D'Angelo, J.; Gomez-Pardo, D. *Tetrahedron Lett.* **1991**, *32*, 3063.

of DMF), and the reaction mixture was warmed to room temperature and stirred for the specified time. Product isolation (sat. LiCl, EtOAc) and purification through a silica plug to remove unreacted amine, afforded the corresponding enamine which was used without further purification: ^{1}H NMR data for the enamines is given. The neat enamine was then cooled to 0 ˚C and treated with anhydrous TFA (2 mL). After 30 min, the solution was diluted with EtOAc and neutralized with saturated $NaHCO_3$. Product isolation (H_2O, EtOAc) and purification afforded the desired product.

2-(6-Methoxy-3,4-dihydronaphthalen-1-yl)-ethylamine hydrochloride (1). Diethyl cyanomethylphosphonate (9.71 mL, 60 mmol) is slowly added to a stirred suspension of sodium hydride (2.80 g, 70.0 mmol) in THF (100 mL) at room temperature. Following completion of hydrogen gas evolution, 6-methoxy-1-tetralone (8.81 g, 50.0 mmol) was added as a solution in THF (20 mL) dropwise over 1 h using a syringe pump. After being stirred for 1 h at room temperature, the solution was heated to reflux for 4 h. Product isolation (ice-H_2O, Et_2O) and purification (R_f 0.30 in benzene) afforded (6-Methoxy-3,4-dihydro-2*H*-naphthalen-1-ylidene)-acetonitrile as a colorless liquid which exists as a mixture of *E*/*Z* isomers. Recrystallization from EtOAc/Hexanes afforded colorless crystals (8.40 g, 84%) of a single isomer. Mp: 63.2-66.6 ˚C (lit.[4] 58.9-60.4 ˚C). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.51, (d, 1H, J = 8.74 Hz), 6.76 (dd, 1H, J = 8.74, 2.74 Hz), 6.67 (d, 1H, J = 2.80 Hz), 5.58 (t, 1H, J = 1.43 Hz), 3.82 (s, 3H), 2.85, (ddd, 2H, J = 7.73, 5.20, 1.69 Hz), 2.84 (t, 2H, J = 6.17 Hz), 1.91, (quin, 2H, 6.30 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 161.4, 158.6, 141.4, 125.9, 124.4, 118.4, 113.4, 113.3, 88.1, 55.3, 30.8, 30.5, 22.6. MS (EI, 70 eV): *m/z* (relative intensity) 199(M^+, 100), 184(12) 159(9), 128(11), 115(10). Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.28; H, 6.44; N, 7.03.

[4] Geier, M.; Hesse, M. *Synthesis* **1990**, 56.

Aluminum chloride (2.21 g, 16.6 mmol) was carefully dissolved in Et_2O (20 mL), and the resulting solution was added dropwise to a suspension of lithium aluminum hydride (629 mg, 16.6 mmol) at room temperature. The slurry was cooled to -20 ˚C, and a solution of the nitrile (3.00 g, 15.1 mmol) as a solution in Et_2O (10 mL) was added dropwise. The reaction mixture was warmed to room temperature and stirred for 2 h. The mixture was then cooled to 0 ˚C, and water was added dropwise. After 30 mL water had been added, the mixture was allowed to stir at room temperature until gas evolution ceased. Product isolation (1 N NaOH, EtOAc) and purification (R_f 0.17 in 1%TEA/5%MeOH/94%CH_2Cl_2) afforded a yellow oil as the endocyclic olefin isomer exclusively. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.53 (d, 1H, J = 8.60 Hz), 6.71 (dd, 1H, J = 8.69, 2.85 Hz), 6.61 (d, 1H, J = 2.73 Hz), 5.93 (tt, 1H, J = 6.70, 1.68 Hz), 3.78 (s, 3H), 3.47 (d, 2H, J = 6.59 Hz), 2.75 (t, 2H, J = 6.24 Hz), 2.47 (t, 2H, J = 6.32 Hz), 1.81 (quin, 2H, J = 6.27 Hz). This oil was diluted with Et_2O, cooled to 0 ˚C and treated with excess 1 M HCl in Et_2O. The Et_2O was removed in vacuo, and the yellow solid was recrystallized from ethanol/hexanes to afford colorless needles (3.00 g, 83%). This product proved to be the endocyclic olefin isomer. Mp: 169.9-171.1 ˚C. ^{1}H NMR (CD_3OD, 500 MHz): δ 7.20 (d, 2H, J = 8.81 Hz), 6.76 (m, 2H), 5.88 (tt, 1H, J = 4.51, 1.08 Hz), 3.78 (s, 3H), 3.03 (dd, 2H, J = 8.18, 6.92 Hz), 2.79 (td, 2H, J = 7.59, 1.19 Hz), 2.73 (t, 2H, J = 8.13 Hz), 2.25 (tdt, 2H, J = 8.03, 4.45, 1.32 Hz). ^{13}C NMR (CD_3OD, 125 MHz): δ 160.6, 140.2, 132.9, 127.7, 126.7, 124.7, 115.3, 112.3, 55.8, 31.9, 29.6, 24.2. MS (EI, 70 eV): *m/z* (relative intensity) 203(M-HCl, 43), 174(100), 159(54), 128(18), 115(22). Anal. Calcd for $C_{13}H_{18}ClNO$: C, 65.13; H, 7.57; Cl, 14.79; N, 5.84. Found: C, 64.96; H, 7.46; Cl, 14.76; N, 5.80.

8-Methoxy-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinoline-4-carboxylic acid ethyl ester (2). Conditions A. Reflux for 24 h. R_f 0.05 in 5% MeOH/$CHCl_3$. Yellow oil (120 mg, 84%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.12 (d, 1H, J = 8.50 Hz), 6.72 (dd, 1H, J = 8.28, 2.81 Hz), 6.69 (d, 1H, J = 2.73 Hz), 4.24 (m, 2H), 4.19 (bs, 1H), 3.30 (ddd,

1H, *J* = 12.94, 8.70, 4.82 Hz), 3.20 (ddd, 1H, *J* = 12.32, 5.52, 4.63 Hz), 2.76 (m, 2H), 2.54 (m, 1H), 2.45 (m, 1H), 2.39 (m, 1H), 2.56 (m, 1H), 1.30 (t, 3H, *J* = 7.20 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.9, 158.7, 137.4, 128.5, 128.0, 125.3, 123.3, 113.5, 111.0, 61.5, 59.3, 55.2, 40.3, 28.4, 26.2, 24.5, 14.1. MS (CI, CH_4): *m/z* (relative intensity) 288(M+1, 56), 259(38), 214(100). HRMS Calcd for $C_{17}H_{21}NO_3$: 287.1521. Found: 287.1518.

8-Methoxy-2,3,5,6-tetrahydro-1*H*-benzo[*f*]isoquinoline-4,4-dicarboxylic acid diethyl ester (3).[5] Conditions A. Reflux for 24 h. R_f 0.10 in 30% EtOAc/Hexanes. Colorless oil (50.0 mg, 65%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.15 (d, 1H, *J* = 8.20 Hz), 6.71 (dd, 1H, *J* = 8.40, 2.68 Hz), 6.83 (d, H, *J* = 2.66 Hz), 4.25, (ABq, 4H, J_{AB} = 10.74 Hz, J_q = 7.12 Hz), 3.79 (s, 3H), 3.09 (t, 2H, *J* = 5.80 Hz), 2.76 (dd, 2H, *J* = 8.13, 7.09 Hz), 2.46 (tt, 2H, *J* = 5.78, 1..93 Hz), 2.38 (tt, 2H, *J* = 7.56, 1.91 Hz), 1.28 (t, 6H, *J* = 7.13 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.4, 158.7, 138.1, 130.7, 128.3, 125.5, 123.7, 113.2, 110.9, 70.8, 61.9, 55.1, 40.1, 28.7, 25.8, 25.2, 14.0. MS (EI, 70 eV): *m/z* (relative intensity) 359(M^+, 4), 286(100), 258(10), 212(30). HRMS Calcd for $C_{20}H_{25}NO_5$: 359.1733. Found: 359.1730.

8-Methoxy-4-(4-oxa-spirocyclohexa)-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinoline (4). Conditions A. Reflux for 72 h. R_f 0.33 in 20% MeOH/$CHCl_3$. Brown solid (105 mg, 88%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.12 (d, 1H, *J* = 8.34 Hz), 6.73 (dd, 1H, *J* = 8.37, 2.73 Hz), 6.69 (d, 1H, *J* = 2.64 Hz), 3.85 (td, 2H, *J* = 11.58, 1.85 Hz), 3.80 (s, 3H), 3.76 (dd, 2H, *J* = 11.36, 5.15 Hz), 3.06 (t, 2H, *J* = 5.80 Hz), 2.69 (dd, 2H, *J* = 8.26, 7.35 Hz), 2.37 (tt, 2H, *J* = 5.35, 1..52 Hz), 2.21 (tt, 2H, *J* = 7.65, 2.08 Hz), 2.08 (dd, 2H, *J* = 13.67, 12.56, 5.16 Hz), 2.66 (d, 2H, *J* = 13.63 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.2, 137.2, 137.1, 129.3, 126.8, 123.1, 113.1, 111.0, 63.2, 55.2, 52.8, 38.0, 33.3, 29.1, 26.8, 24.1. MS (EI, 70 eV): *m/z* (relative intensity)

[5] Diethylketomalonate has previously been employed in Pictet-Spengler cyclizations: cf. Narayanan, K.; Schindler, L; Cook, J. M. *J. Org. Chem.* **1991**, *56*, 359.

285(M^+ 82), 256(54), 240(79), 226(100), 186(82), 118(45). HRMS Calcd for $C_{18}H_{23}NO_2$: 285.1729. Found: 285.1722.

4-Spirocyclopenta-8-methoxy-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinoline (5). Conditions A. Reflux for 72 h. R_f 0.19 in 20% MeOH/$CHCl_3$. White solid (60.4 mg, 54%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.10 (d, 1H, J = 8.45 Hz), 6.72 (dd, 1H, J = 8.40, 2.75 Hz), 6.68 (d, 1H, J = 2.80 Hz), 3.80 s, 3H), 3.09 (t, 2H, J = 5.82 Hz), 2.69 (dd, 2H, J = 7.95, 7.10 Hz), 2.40 (tt, 2H, J = 5.81, 2.02 Hz), 2.34 (bs, 1H), 2.15 (tt, 2H, J = 7.55, 1.96 Hz), 1.85 (m, 4H), 1.68 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.2, 158.6, 136.6, 127.9, 125.7, 123.5, 113.2, 111.1, 67.0, 55.2, 38.4, 37.0, 28.8, 25.7, 24.1, 23.3. MS (EI, 70 eV): *m/z* (relative intensity) 269(M^+, 50), 240(100), 226(25). HRMS Calcd for $C_{18}H_{23}NO$: 269.1780. Found: 269.1780.

2-(4-Methoxyphenyl)-[1,3]dithian-5-one (6). *p*-Anisaldehyde (5.00 mL, 41.1 mmol) and mercapto-acetic acid ethyl ester (9.46 mL, 86.3 mmol) were dissolved in benzene (4 mL) at room temperature. Several drops of concentrated HCl were then added and stirring was continued overnight at room temperature. Product isolation (sat $NaHCO_3$), and purification (R_f 0.09 in 10% EtOAc/Hexanes) afforded a colorless oil (13.7 g, 93%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38 (AA' of AA'XX', 2H, J_{AX} = 8.74 Hz, J_{AA} = 2.62 Hz), 6.81 (XX' of AA'XX', 2H, J_{AX} = 8.67 Hz, J_{XX} = 2.59 Hz), 5.32 (s 1H), 4.15 (q, 4H, J = 7.13 Hz), 3.80 (s, 3H), 3.28 (AB, 4H, J_{AB} = 15.11 Hz), 1.27 (t, 5H, J = 7.14 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.9, 159.6, 130.3, 129.1, 114.0, 61.4, 55.3, 52.9, 34.0, 14.1. MS (EI, 70 eV): *m/z* (relative intensity) 358(M^+, 0.1), 313(5), 271(3), 239(100), 211(3), 165(10), 151(18), 137(12) 95(120), 83(42). HRMS Calcd for $C_{16}H_{22}O_3S_2$: 358.0909. Found: 357.0837.

Sodium hydride (117 mg, 2.93 mmol) is suspended in THF (2 mL) and then warmed to 60 ˚C. The above dithioacetal (500 mg, 1.39 mmol) is then added dropwise as a solution in THF (350 μL). The reaction mixture turned yellow and hydrogen gas evolved. The reaction is heated to reflux for 3 h then cooled to room temperature and

stirred overnight. Several drops of absolute ethanol are then added to quench any remaining sodium hydride. Product isolation (sat $NaHCO_3$, EtOAc), and purification (10% EtOAc/Hexanes) afforded an orange oil. This oil was immediately taken up in 2 N H_2SO_4 and heated to reflux for 12 h to effect decarboxylation. Product isolation (sat $NaHCO_3$, Et_2O), and purification (R_f 0.10 in 10% EtOAc/Hexanes) afforded a white solid (121 mg, 36% for two steps). Recrystallization from EtOAc/pet ether afforded colorless needles. Mp: 139.4-141.3 ˚C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48 (AA' of AA'XX', 2H, J_{AX} = 8.81 Hz, J_{AA} = 2.74 Hz), 6.88 (XX' of AA'XX', 2H, J_{AX} = 8.77 Hz, J_{XX} = 2.66 Hz), 5.61 (s, 1H), 3.81 (s, 3H), 3.56 (AB, 4H, J_{AB} = 14.62 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 201.8, 159.9, 129.2, 128.8, 114.2, 55.3, 48.6, 38.5. MS (EI, 70 eV): *m/z* (relative intensity) 240(M^+, 13), 176(24), 152(42), 134(15), 84(80), 66(100). HRMS Calcd for $C_{11}H_{12}O_2S_2$: 240.0279. Found: 240.0284.

Thioacetic acid *S*-(3-acetylsulfanyl-2-oxo-propyl) ester (7). To a solution of *n*-Bu_4NSAc (3.00 g, 9.45 mmol) in THF (30 mL) was added a solution of 1,3-dichloroacetone (400 mg, 3.15 mmol) in THF (10 mL) dropwise at room temperature. The solution turned from yellow to red as it stirred overnight. Product isolation (H_2O, Et_2O) and purification (R_f 0.09 in 10% EtOAc/Hexanes) afforded a red oil which solidified upon standing 520 mg, 80%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 3.87 (s, 4H), 2.89 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 197.8, 194.2, 38.2, 30.1. MS (CI, CH_4): *m/z* (relative intensity) 207(M+1, 13), 165(100), 147(10), 131(12), 117(23), 77(25). Anal. Calcd for $C_7H_{10}O_3S_2$: C, 40.76; H, 4.89; S, 31.09. Found: C, 40.71; H, 4.66; S, 31.16.

4-(5-Spiro-2-(4-methoxy-phenyl)-[1,3]dithiane)-8-methoxy-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinoline (8). Conditions A. Reflux for 72 h. R_f 0.21 in 4% MeOH:CH_2Cl_2. White solid (90 mg, 51%). ^{1}H NMR ($CDCl_3$, 500 MHz): $\Delta^{8(9)}$ isomer. δ 7.44 (AA' of AA'XX', 2H, J_{AX} = 8.71 Hz, J_{AA} = 2.61 Hz), 7.17 (d, 1H, J = 8.76 Hz), 6.88 (XX' of AA'XX', 2H, J_{AX} = 8.80 Hz, J_{XX} = 2.58 Hz), 6.75 (dd, 1H, J = 8.58, 2.08

Hz), 6.70 (d, 1H, J = 2.64 Hz), 5.03 (s, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.49 (AB, 2H, J_{AB} = 13.96 Hz), 3.10 (t, 2H, J = 5.73 Hz), 3.79 (AB, 2H, J = 14.09 Hz), 2.73 (dd, 2H, J = 7.95, 7.41 Hz), 2.55 (tt, 2H, J = 5.87, 2.00 Hz), 2.27 (tt, 2H, J = 7.76, 2.02 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.7, 158.5, 136.9, 130.2, 128.9, 123.7, 114.1, 113.2, 111.2, 55.3, 55.2, 49.5, 46.4, 39.3, 37.5, 29.0, 26.8, 23.7. MS (EI, 70 eV): *m/z* (relative intensity) 425(M^+, 5), 378(12), 272(13), 258(13), 227(100). HRMS Calcd for $C_{24}H_{27}NO_2S_2$: 425.1483. Found: 425.1474.

(4-Ethoxycarbonylmethyl-8-methoxy-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinolin-4-yl)-acetic acid ethyl ester (9). Conditions B. Diethyl 1,3-acetonedicarboxylate (91 μL, 0.50 mmol). Stir for 24 h. R_f 0.25 in 20% EtOAc/Hexanes. Colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.58 (bs, 1H), 7.12 (d, 1H, J = 8.77 Hz), 6.71 (m, 2H), 5.81 (t, 1H, J = 4.54 Hz), 4.48 (s, 1H), 4.14 (q, 2H, J = 7.13 Hz), 4.09 (q, 2H, J = 7.15 Hz), 3.80 (s, 3H), 3.38 (td, 2H, J = 7.22, 6.02 Hz), 3.13 (s, 2H), 2.72 (t, 2H, J = 7.94 Hz), 2.67, (t, 2H, J = 7.20 Hz), 2.24 (tdt, 2H, J = 7.93, 4.62, 1.15 Hz). R_f 0.23 in 40% EtOAc/Hexanes. Colorless oil (3.00 g, 96% for two steps). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.12 (d, 1H, J = 8.20 Hz), 6.72 (dd, 1H, J = 8.36, 2.66 Hz), 6.67 (d, 1H, J = 2.92 Hz), 4.09 (ABq, 4H, J_{AB} = 10.95 Hz, J_q = 7.13 Hz), 3.80 (s, 3H), 3.08 (t, 2H, J = 5.83 Hz), 2.77 (AB, 4H, J_{AB} = 14.30 Hz), 2.70 (dd, 2H, J = 8.19, 7.50 Hz), 2.36 (tt, 2H, J = 5.77, 1.93 Hz), 2.18 (tt, 2H, J = 7.64, 1.96 Hz), 1.19 (t, 6H, J = 7.06 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.3, 158.3, 137.2, 133.1, 128.8, 128.4, 123.5, 113.1, 111.0, 60.4, 57.9, 55.2, 42.2, 38.4, 28.7, 25.9, 24.3, 14.1. MS (CI, CH_4): *m/z* (relative intensity) 388(M+1, 11), 328(11), 300(67), 254(45), 89(76), 61(100). Anal. Calcd for $C_{22}H_{29}NO_5$: C, 68.20; H, 7.54; N, 3.61. Found: C, 67.90; H, 7.53; N, 3.32.

8-Methoxy-4-(4-tetrahydropyran-2-one)-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinoline (11). Conditions B. Dihydro-pyran-2,4-dione (48 mg, 0.42 mmol). Stir for 24 h. R_f 0.21 in 5% MeOH/$CHCl_3$. Yellow solid. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.13 (d, 1H, J = 9.32 Hz), 6.73 (d, 1H, J = 2.33 Hz), 6.73 (dd, 1H, J = 9.24,

2.74 Hz), 5.79 (tt, 1H, J = 4.67, 1.21 Hz), 4.73 (s, 1H), 4.56 (bs, 1H), 4.27 (dd, 2H, J = 6.45, 5.87 Hz), 3.80 (s, 3H), 3.26 (td, 2H, J = 6.77, 5.29 Hz), 2.72 (td, 2H, J = 6.80, 1.10 Hz), 2.72 (dd, 2H, J = 9.06, 6.96 Hz), 2.38 (t, 2H, J = 6.24 Hz), 2.26 (tdt, 2H, J = 8.07, 4.52, 1.22 Hz). R_f 0.13 in 20% Acetone/CH_2Cl_2. Colorless oil (34 mg, 27% for two steps). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.13 (d, 1H, J = 8.38 Hz), 6.74 (dd, 1H, J = 8.45, 2.81 Hz), 6.69 (d, 1H, J = 2.61 Hz), 4.61 (td, 1H, J = 11.27, 3.81 Hz), 4.35 (ddd, 1H, J = 11.26, 5.31, 3.62 Hz), 3.80 (s, 3H), 3.09 (tt, 1H, J = 13.69, 5.58 Hz), 3.05 (ddd, 1H, J = 13.82, 6.72, 5.29 Hz), 2.75 (AB, 1H, J_{AB} = 16.50 Hz), 2.72 (dd, 2H, J = 7.86, 6.87 Hz), 2.53 (ABd, 1H, J_{AB} = 16.20, J_d = 1.73 Hz), 2.38 (m, 2H), 2.21 (ddd, 1H, J = 14.77, 10.93, 5.27 Hz), 2.17 (ddt, 2H, J = 9.34, 6.10, 2.18 Hz), 1.80 (dtd, 1H J = 14.65, 3.57, 1.74 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.3, 158.6, 136.8, 134.0, 128.4, 127.9, 123.4, 113.3, 111.3, 65.7, 55.3, 54.6, 40.5, 38.3, 32.4, 28.8, 26.1, 24.2. MS (EI, 70 eV): *m/z* (relative intensity) 299(M^+, 58), 256(25), 238(93), 226(100), 212(38). HRMS Calcd for $C_{19}H_{21}NO_3$: 299.1521. Found: 299.1518.

(8-Methoxy-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinolin-4-yl)-acetic acid methyl ester (12). Conditions B. Methyl propiolate (45 μL, 0.50 mmol). Stir for 120 h. R_f 0.20 in 20% EtOAc/Hexanes. Colorless oil. Mixture of *E:Z* isomers in a 3:1 ratio by integration of vinyl signals. R_f 0.20 in 5% MeOH/$CHCl_3$. Yellow oil (29 mg, 24% for two steps). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.11 (d, 1H, J = 8.39 Hz), 6.72 (dd, 1H, J = 8.37, 2.74 Hz), 6.69 (d, 1H, J = 2.79 Hz), 3.90 (bd, 1H, J = 10.61 Hz), 3.80 (s, 3H), 3.71 (s, 3H), 3.16 (dt, 1H, J = 12.24, 5.55 Hz), 3.02 (ddd, 1H, J = 12.06, 6.99, 4.90 Hz), 2.77 (ddd, 1H, J = 15.24, 11.78, 6.64 Hz), 2.71 (dd, 1H, J = 15.90, 2.90 Hz), 2.70 (dt, 1H, J = 15.50, 6.50 Hz), 2.47 (m, 1H), 2.46 (dd, 1H, J = 15.90, 10.20 Hz), 2.33 (m, 1H), 2.19 (m, 1H), 2.07 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 173.1, 158.2, 136.8, 131.1, 128.8, 127.4, 122.9, 113.3, 110.9, 55.2, 53.9, 51.7, 40.2, 37.4, 28.5, 25.8, 25.5. MS (CI, CH_4): *m/z* (relative intensity) 288(M+1, 44), 259(20), 240(20), 212(100), 75(63). HRMS Calcd

for $C_{17}H_{22}NO_3$: 288.1600. Found: 288.1596.

8-Methoxy-4-methoxycarbonylmethyl-1,2,3,4,5,6-hexahydro-benzo[*f*]isoquinoline-4-carboxylic acid methyl ester (13). Conditions B. Dimethyl acetylenedicarboxylate (61 μL, 0.50 mmol). Stir for 24 h. R_f 0.37 in 20% EtOAc/Hexanes. Colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.09 (bs, 1H), 7.12 (d, 1H, J = 9.20 Hz), 6.71 (m, 2H), 5.79 (tt, 1H, J = 4.44, 1.12 Hz), 5.04 (s, 1H), 3.80 (s, 3H), 3.71 (s, 3H), 3.67 (s, 3H), 3.52 (dt, 2H, J = 6.97, 6.97 Hz), 2.73 (dd, 2H, J = 8.35, 7.73 Hz), 2.67 (td, 2H, J = 7.14, 1.09 Hz), 2.24 (dddt, 2H, J = 12.52, 7.99, 4.56, 1.08 Hz). R_f 0.10 in 30% EtOAc/Hexanes. Colorless oil (127 mg, 35% for two steps). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.16 (d, 1H, J = 8.31 Hz), 6.73 (dd, 1H, J = 8.46, 2.76 Hz), 6.68 (d, 1H, J = 2.55 Hz), 3.80 (s, 3H), 3.77 (s, 3H), 3.67 (s, 3H), 3.37 (ddd, 1H, J = 12.24, 9.16, 4.58 Hz), 3.23 (AB, 1H, J_{AB} = 16.39 Hz), 3.11 (ddd, 1H, J = 12.31, 5.80, 4.26 Hz), 2.69 (dd, 2H, J = 8.79, 6.27 Hz), 2.61 (AB, 1H, J_{AB} = 16.37 Hz), 2.55 (m, 1H), 2.36 (m, 1H), 2.21 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 174.6, 172.2, 159.0, 137.6, 130.8, 128.8, 127.8, 124.0, 113.4, 111.4, 63.2, 55.5, 52.8, 52.1, 41.6, 39.6, 28.9, 25.8, 24.0. MS (CI, CH_4): *m/z* (relative intensity) 346(M+1, 100), 317(18), 286(71), 272(36). HRMS Calcd for $C_{19}H_{24}NO_5$: 346.1654. Found: 346.1659.