SUPPLEMENTARY DATA FILE

Efficient Synthetic Methodology for the Construction of Dihydronaphthalene and Benzosuberene Molecular Frameworks

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General Materials and Methods

Tetrahydrofuran (THF), carbon tetrachloride, dichloromethane, methanol, dimethylformamide (DMF), and acetonitrile were used in their anhydrous forms. Reactions were performed under nitrogen gas, unless otherwise specified. Thin-layer chromatography (TLC) plates (precoated glass plates with silica gel 60 F254, 0.25 mm thickness) were used to monitor reactions. Purification of intermediates and products was carried out with a Biotage Isolera flash purification system using silica gel (200-400 mesh, 60 Å) or RP-18 pre-packed columns or manually in glass columns. Intermediates and products synthesized were characterized on the basis of their ^{1}H NMR (500 or 600 MHz), ^{13}C NMR (125 or 150 MHz) spectroscopic data using a Varian VNMRS 500 MHz or Bruker DPX 600 MHz instrument. Spectra were recorded in $CDCl_3$, D_2O, $(CD_3)_2CO$, or CD_3OD. All chemicals shifts are expressed in ppm (δ), and peak patterns are reported as broad (br), singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), sextet (sext), septet (sept), double doublet (dd), double double doublet (ddd), and multiplet (m).

Purity of the final compounds was further analyzed at 25 °C using an Agilent 1200 HPLC system with a diode-array detector (λ = 190−400 nm), a Zorbax XDB-C18 HPLC column (4.6 mm Å~ 150 mm, 5 μm), and a Zorbax reliance cartridge guard-column; Method: solvent A, acetonitrile, solvent B, H_2O; gradient, 10% A/ 90% B to 100% A/ 0% B over 0 to 40 min; post-time 10 min; flow rate 1.0mL/min; injection volume 20 μL; monitored at wavelengths of 210, 230, 254, 280, and 320 nm. Mass spectrometry was carried out under positive or negative ESI (electrospray ionization) using a Thermo Scientific LTQ Orbitrap Discovery instrument.

2-Isopropoxy-3-methoxybenzaldehyde (6, NHC_3_94). To a well-stirred solution of 2-hydroxy-3-methoxybenzaldehyde (5.00 g, 32.9 mmol) in DMF (100 mL) was added K_2CO_3 (14.97 g, 98.58 mmol) and 2-iodopropane (6.54 mL, 65.7 mmol). After heating at 50 °C for 20 h,

DMF was removed under reduced pressure, and the resulting material was washed with water (100 mL) to remove the excess salt and extracted with EtOAc (3 x 100 mL). The combined organic phase was dried over sodium sulfate and concentrated to afford protected aldehyde **6** (6.24 g, 32.2 mmol, 98%) as a colorless oil without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.44 (1H, s), 7.41 (1H, d, J = 7.8 Hz), 7.10 (2H, m), 4.62 (1H, m), 3.86 (3H, s), 1.31 (6H, d, J = 6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 191.0, 153.4, 150.7, 131.0, 123.7, 119.0, 118.0, 76.3, 56.1, 22.4.

5-(2-Isopropoxy-3-methoxyphenyl)pentanoic acid (7, NHC_5_114/118). 3-(Carboxypropyl)triphenyl phosphonium bromide (11.54 g, 26.89 mmol) was dissolved in DMF (350 mL) followed by the addition of potassium *tert*-butoxide (8.08 g, 71.7 mmol). The resultant reaction mixture was stirred at room temperature for 45 min. Aldehyde **6** (3.48 g, 17.9 mmol) in THF (50 mL) was added slowly, and the reaction mixture was stirred at room temperature for an additional 24 h. The solvent was removed under reduced pressure, and the resulting material was acidified with 2 M HCl (70 mL) and extracted with EtOAc (3 x 100 mL). The combined organic layer was evaporated under reduced pressure, and the crude product was dissolved in CH_3OH (60 mL) without further purification. 10% palladium on carbon (1.9 g) and hydrogen gas were introduced, and the reaction mixture was stirred for 24 h at room temperature followed by filtration through Celite®, and the Celite® was further washed with EtOAc (3 x 50 mL). The combined organic phase (CH_3OH and EtOAc) was evaporated under reduced pressure. The resulting organic material was purified by flash chromatography using a pre-packed 100 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → 40%A / 60%B (10 CV), 40%A / 60%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford carboxylic acid **7** (4.51 g, 16.9 mmol, 94%) as a yellow oil. ^{1}H NMR (600

MHz, $CDCl_3$) δ 6.95 (1H, t, *J* = 7.8 Hz), 6.77 (1H, d, *J* = 7.8 Hz), 6.75 (1H, d, *J* = 7.8 Hz), 4.46 (1H, sept, *J* = 6 Hz), 2.66 (2H, t, *J* = 7.8 Hz), 2.38 (2H, 7.2 Hz), 1.66 (4H, m), 1.27 (6H, d, *J* = 6 Hz) ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.9, 153.0, 145.0, 136.6, 123.3, 121.8, 110.1, 74.6, 55.7, 34.0, 29.9, 29.8, 24.7, 22.8.

1-Isopropoxy-2-methoxy-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (8, NHC_5_121).[1] To a solution of carboxylic acid **7** (0.92 g, 3.5 mmol) in CH_2Cl_2 (20 mL) was added DMF (0.15 mL) and oxalyl chloride (1.51 mL, 17.3 mmol). The solution was stirred at room temperature for 2 h. The solvent and excess reagent were removed under reduced pressure to afford the acyl chloride as a yellow solid. The acyl chloride was dissolved in CH_2Cl_2 (20 mL), and $SnCl_4$ (3.80 mL, 1 M, 3.80 mmol) was added to the solution at -10 °C, and the reaction mixture was stirred for 40 min. The reaction mixture was quenched by the addition of water (30 mL) followed by extraction with CH_2Cl_2 (3 x 40 mL). The combined organic phase was dried over sodium sulfate and concentrated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 2%A / 98%B (1 CV), 2%A / 98%B → 40%A / 60%B (10 CV), 40%A / 60%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford ketone **8** (0.65 g, 2.6 mmol, 75%) as a clear oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (1H, d, *J* = 9 Hz), 6.78 (1H, d, *J* = 9 Hz), 4.38 (1H, sept, *J* = 6.6 Hz), 3.83 (3H, s), 2.99 (2H, t, *J* = 6 Hz), 2.65 (2H, m), 1.75 (4H, m), 1.25 (6H, d, *J* = 6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.9, 156.1, 143.7, 136.2, 132.8, 124.8, 109.5, 74.9, 55.6, 40.6, 24.8, 23.8, 22.5, 21.0.

4-Isopropoxy-3-methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulene (9, NHC_5_122/124).[1] To an oven dried flask, THF (50 mL) and 1,2,3-trimethoxy phenyl bromide (1.00 g, 4.05 mmol) were added, and the solution was cooled to -78 °C. *n*-BuLi (1.63 mL, 2.5 M,

4.05 mmol) was slowly added to the reaction mixture, which was then stirred at -78 °C for 30 min. Ketone **8** (0.51 g, 2.0 mmol) in THF (20 mL) was added dropwise to the flask, and the reaction mixture was stirred while warming from -78 °C to room temperature over 16 h. The reaction mixture was washed with 2 M HCl (30 mL) for 30 min and extracted with EtOAc (3 x 50 mL). The combined organic phase was dried over sodium and evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 98%B → 40%A / 60%B (10 CV), 40%A / 60%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford benzosuberene **9** (0.68 g, 1.7 mmol, 84%) as a yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.73 (2H, s), 6.47 (2H, s), 6.32 (1H, t, *J* = 7.2 Hz), 4.50 (1H, sept, 6H), 3.85 (3H, s), 3.84 (3H, s), 3.79 (6H, s), 2.77 (2H, t, J = 7.2 Hz), 2.13 (3H, m), 1.95 (2H, m), 1.33 (6H, d, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.9, 151.8, 143.9, 143.0, 138.7, 137.4, 136.6, 133.8, 127.1, 125.0, 109.4, 105.4, 74.8, 61.0, 56.2, 55.7, 34.4, 25.8, 24.5, 22.8.

3-Methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-ol (1, NHC_5_128, KGP18).[1,2] To a solution of isopropyl-protected phenol **9** (0.52 g, 1.3 mmol) in CH_2Cl_2 (15 mL) was added BCl_3 (1.44 mL, 1 M, 1.44 mmol) at 0 °C. The solution was stirred for 2 h, followed by the addition of water, and subsequent extraction with CH_2Cl_2 (3 x 30 mL). The combined organic phase was dried over sodium sulfate, and evaporated under reduced pressure. The crude reaction product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 2%A / 98%B (1 CV), 2%A / 98%B → 30%A / 70%B (10 CV), 30%A / 70%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford phenol **1** (0.42 g, 1.2 mmol, 92%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.71 (1H, d, *J* = 8.4 Hz), 6.57 (1H, d, *J* = 8.4 Hz), 6.50 (2H, s), 6.33 (1H, t, *J* = 7.2 Hz),

3.91 (3H, s), 3.86 (3H, s), 3.80 (6H, s), 2.76 (2H, t, J = 7.2 Hz), 2.14 (2H, m), 1.97 (2H, m). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.9, 145.2, 142.5, 138.6, 137.4, 134.4, 127.9, 127.3, 120.9, 61.0, 56.2, 56.1, 33.7, 25.8, 23.7. HRMS: Obsvd 379.1517 [M + Na^+], Calcd for $C_{21}H_{24}O_5Na$: 379.1516, HPLC: 9.52 min.

3-Methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-yl trifluoromethanesulfonate (10, NHC_5_149). To a solution of phenol **1** (0.13 g, 0.36 mmol) in CH_2Cl_2 (20 mL) was added TEA (0.056 mL, 0.72 mmol) and triflic anhydride (0.051 mL, 0.54 mmol). The reaction mixture was stirred at 0 °C for 5 h, followed by the addition of water and subsequent extraction with CH_2Cl_2 (3 x 20 mL). The combined organic phase was dried over sodium sulfate and evaporated under reduced pressure. The resulting material was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 12%A / 88%B (1 CV), 12%A / 88%B → 50%A / 50%B (10 CV), 50%A / 50%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford triflic product **10** (0.15 g, 0.31 mmol, 84%) as a yellow solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.04 (1H, d, J = 8.4 Hz), 6.87 (1H, d, J = 8.4 Hz), 6.47 (2H, s), 6.43 (1H, t, J = 7.2 Hz), 3.93 (3H, s), 3.89 (3H, s), 3.83 (6H, s), 2.79 (2H, m), 2.25 (2H, p, J = 7.2 Hz), 2.00 (2H, m). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.1, 150.0, 141.8, 137.8, 136.7, 136.4, 134.4, 130.0, 129.8, 128.5, 110.5, 110.0, 105.4, 61.0, 56.3, 56.1, 34.1, 25.5, 25.4. ^{19}F NMR (564 MHz, $CDCl_3$) δ -72.94.

3-Methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-amine (2, DM30901, KGP156).[3] A toluene solution (15 mL) of triflate **10** (0.74 g, 1.5 mmol), $Pd(OAc)_2$ (34 mg, 0.15 mmol), *rac*-BINAP (0.14 g, 0.23 mmol), benzophenone imine (0.254 mL, 2.27 mmol) and Cs_2CO_3 (740 mg, 2.27 mmol) was degassed (bubbling nitrogen) for 15 min. The reaction mixture was then heated at 110 °C for 36 h. The reaction mixture was cooled to room

temperature and diluted with EtOAc and quenched with water. The organic phase was separated and dried over sodium sulfate. Solvent was removed and the crude was dissolved in THF and treated with aqueous 2 M HCl to pH 2-3 followed by stirring for 1 h. A NaOH solution (1 M) was added to the reaction to achieve basic pH. The reaction solution was extracted with EtOAc (3 x 30 mL) and the combined organic phase was dried over sodium sulfate and evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 100 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → 60%A / 40%B (10 CV), 60%A / 80%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford amine **2** (500 mg, 1.41 mmol, 93%) as a greenish solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.67 (1H, d, *J* = 8.5 Hz), 6.52 (2H, s), 6.48 (1H, d, *J* = 8.5 Hz), 6.30 (1H, t, *J* = 7 Hz), 3.87 (3H, s), 3.86 (3H, s), 3.80 (6H, s), 2.59 (2H, t, *J* = 7 Hz), 2.12 (2H, p, *J* = 7 Hz), 1.95 (2H, m). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.9, 146.5, 143.7, 138.7, 137.4, 133.7, 132.6, 126.9, 126.4, 119.9, 107.7, 105.4, 61.0, 56.3, 55.7, 33.4, 25.7, 25.4. HRMS: Obsvd 378.1677 [M + Na^+], Calcd for $C_{21}H_{25}NO_4Na$: 378.1676, HPLC: 20.20 min.

(3-Hydroxypropyl)triphenylphosphonium bromide (12, NHC_5_115). To a solution of PPh_3 (7.55 g, 28.8 mmol) in toluene (60 mL) was added 3-bromo-1-propanol **11** (5.2 mL, 58 mmol), and the reaction mixture was stirred and heated to reflux for 24 h. The toluene and unreacted 3-bromo-1-propanol were removed under reduced pressure. The solid residue was washed with diethyl ether to remove unreacted triphenylphosphine. The ether suspension was filtered and rinsed with diethyl ether (2 x 50 mL) to afford Wittig salt **12** as a white solid (11.06 g, 27.56 mmol, 96%), which was advanced without further purification.

4-(2-Isopropoxy-3-methoxyphenyl)butan-1-ol (13, NHC_5_117/123). To a solution of Wittig salt **12** (9.3 g, 23 mmol) in THF (50 mL) was added *n*-BuLi (18.53 mL, 2.5 M, 46.33 mmol)

slowly, and the solution was stirred at 0 °C for 15 min. TMS-Cl (2.94 mL, 23.2 mmol) was added to the reaction mixture which was stirred for 30 min. Aldehyde **6** (3.00 g, 15.5 mmol) was added slowly, the reaction mixture was stirred at 0 °C for 1 h, and then at room temperature for 2 h. 2 M HCl (50 mL) was added, followed by stirring for 30 min at room temperature and subsequent extraction with EtOAc (3 x 50 mL). The combined organic layer was dried over sodium sulfate and concentrated under reduced pressure. The resulting crude material was dissolved in CH_3OH (60 mL), and Pd/C (1.63 g) and H_2 balloons were introduced. The reaction mixture was stirred for 24 h at room temperature followed by filtration through Celite®. The Celite® was washed with EtOAc (3 x 50 mL). The combined organic phase (CH_3OH and EtOAc) was evaporated under reduced pressure to afford saturated alcohol **13** (3.39 g, 14.2 mmol, 92%), which was advanced to the next step without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.96 (1H, t, 7.8 Hz), 6.78 (1H, d, 7.8 Hz), 6.75 (1H, d, 7.8 Hz), 4.48 (1H, m), 3.83 (3H, s), 3.66 (2H, m), 2.69 (2H, t, J = 7.2 Hz), 1.67 (2H, m), 1.60 (2H, m), 1.29 (6H, d, 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.9, 144.8, 136.9, 123.3, 121.8, 110.0, 74.7, 62.8, 55.7, 32.5, 29.8, 26.6, 22.7.

4-(2-Isopropoxy-3-methoxyphenyl)butanoic acid (14, NHC_5_127/130). To a solution of alcohol **13** (0.60 g, 2.5 mmol) dissolved in water/ acetonitrile (75 mL/ 120 mL) was added Oxone® (2.32 g, 3.78 mmol) and 2-Iodoxybenzoic acid (IBX) (0.21 g, 0.76 mmol). The reaction mixture was stirred at 70 °C for 20 h, and the solvent was removed under reduced pressure. The residue was washed with 2 M HCl (20 mL) and extracted with EtOAc (3 x 30 mL). The combined organic phase was dried over sodium sulfate and evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 12%A / 88%B (1 CV), 12%A / 88%B →

50%A / 50%B (10 CV), 50%A / 50%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford carboxylic **14** (0.29 g, 1.2 mmol, 46%) as a brown oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.47 (1H, t, *J* = 7.8 Hz), 6.77 (2H, m), 4.48 (1H, m), 3.82 (3H, s), 2.72 (2H, m), 2.38 (2H, t, *J* = 7.2 Hz), 1.95 (2H, m), 1.26 (6H, d, *J* = 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 179.8, 152.9, 144.9, 135.7, 123.3, 121.9, 110.3, 74.5, 55.6, 33.5, 29.4, 25.2, 22.6.

5-Isopropoxy-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (15, NHC_5_132). To a solution of carboxylic acid **14** (0.29 g, 1.2 mmol) in CH_2Cl_2 (20 mL) was added oxalyl chloride (0.51 mL, 5.8 mmol) and DMF (0.15 mL). The reaction mixture was stirred at room temperature for 2 h. The excessed solvent and oxalyl chloride were removed under reduced pressure. The resulting acyl chloride was dissolved in CH_2Cl_2 (30 mL), and $SnCl_4$ (1.29 mL, 1 M, 1.29 mmol) was added to the solution at -10 °C. The reaction mixture was stirred for 40 min and washed with water and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phase was dried over sodium sulfate, evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → 40%A / 60%B (10 CV), 40%A / 60%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford ketone **15** (0.25 g, 1.1 mmol, 92%) as a pale yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (1H, d, *J* = 8.4 Hz), 6.85 (1H, d, *J* = 8.4 Hz), 4.44 (1H, m), 3.88 (3H, s), 2.94 (2H, t, *J* = 6 Hz), 2.57 (2H, t, *J* = 6.6 Hz), 2.05 (2H, m), 1.28 (6H, d, *J* = 6.6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.8, 157.1, 143.3, 139.5, 126.8, 124.1, 110.0, 74.8, 55.8, 38.9, 24.3, 23.1, 22.7.

8-Isopropoxy-7-methoxy-4-(3,4,5-trimethoxyphenyl)-1,2-dihydronaphthalene (16, NHC_5_134). To an oven-dried flask, THF (30 mL) and 3,4,5-trimethoxyphenyl bromide (0.34 g, 1.4 mmol) were added, and the solution was cooled to -78 °C. *n*-BuLi (0.55 mL, 1.4 mmol)

was slowly added to the reaction mixture, which was then stirred at -78 °C for 30 min. Ketone **15** (0.16 g, 0.68 mmol) was then added dropwise to the flask, and the reaction mixture was stirred while warming from -78 °C to room temperature over 16 h. The reaction mixture was washed with water and extracted with EtOAc (3 x 50 mL). The combined organic phase was dried over sodium sulfate and evaporated under reduced pressure. The crude reaction product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → 60%A / 40%B (10 CV), 60%A / 80%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford dihydronaphthalene **16** (0.17 g, 0.44 mmol, 65%) as a yellow oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.76 (1H, d, J = 8.4 Hz), 6.64 (1H, d, J = 8.4 Hz), 6.57 (2H, s), 5.96 (1H, t, J = 4.8 Hz), 4.41 (1H, m), 3.89 (3H, s), 3.86 (3H, s), 3.84 (6H, s), 2.89 (2H, t, J = 7.8 Hz), 2.32 (2H, m), 1.32 (6H, d, J = 6 Hz). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.0, 143.7, 139.8, 137.0, 131.6, 128.9, 125.3, 123.7, 121.3, 109.0, 106.0, 105.3, 75.0, 61.0, 56.2, 55.7, 23.2, 22.8, 22.0.

2-Methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-ol (3, NHC_5_135, Oxi6196).[4] To a solution of **16** (0.16 g, 0.41 mmol) in CH_2Cl_2 (20 mL) was added BCl_3 (0.46 mL, 1 M, 0.46 mmol). The reaction mixture was stirred at 0 °C for 3 h. The solution was washed with water and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic phase was dried over sodium sulfate, evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → 60%A / 40%B (10 CV), 60%A / 80%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford phenol **3** (0.12 g, 0.35 mmol, 85%) as a white solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.62 (1H, d, J = 8.4 Hz), 6.60 (1H, d, J = 8.4 Hz), 6.56 (2H, s), 5.97 (1H, t, J = 4.8 Hz), 3.88(8) (3H, s), 3.88(5) (3H, s), 3.84 (6H, s), 2.88

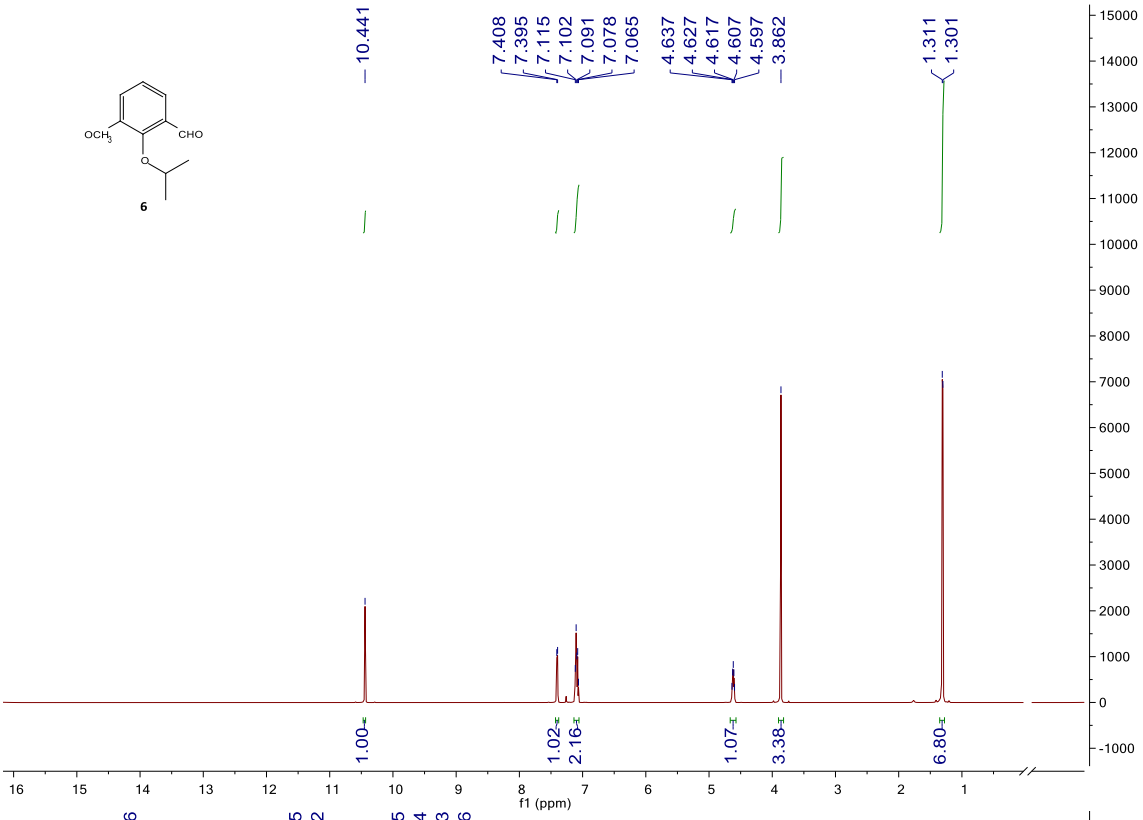
(2H, t, J = 7.8 Hz), 2.38 (2H, m). ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.0, 146.0, 142.1, 139.7, 137.2, 137.0, 129.1, 125.5, 122.4, 107.4, 106.1, 61.1, 56.3, 23.0, 20.4. HRMS: Obsvd 365.1363 [M + Na^+], Calcd for $C_{20}H_{22}O_5Na$: 365.1359, HPLC: 19.41 min.

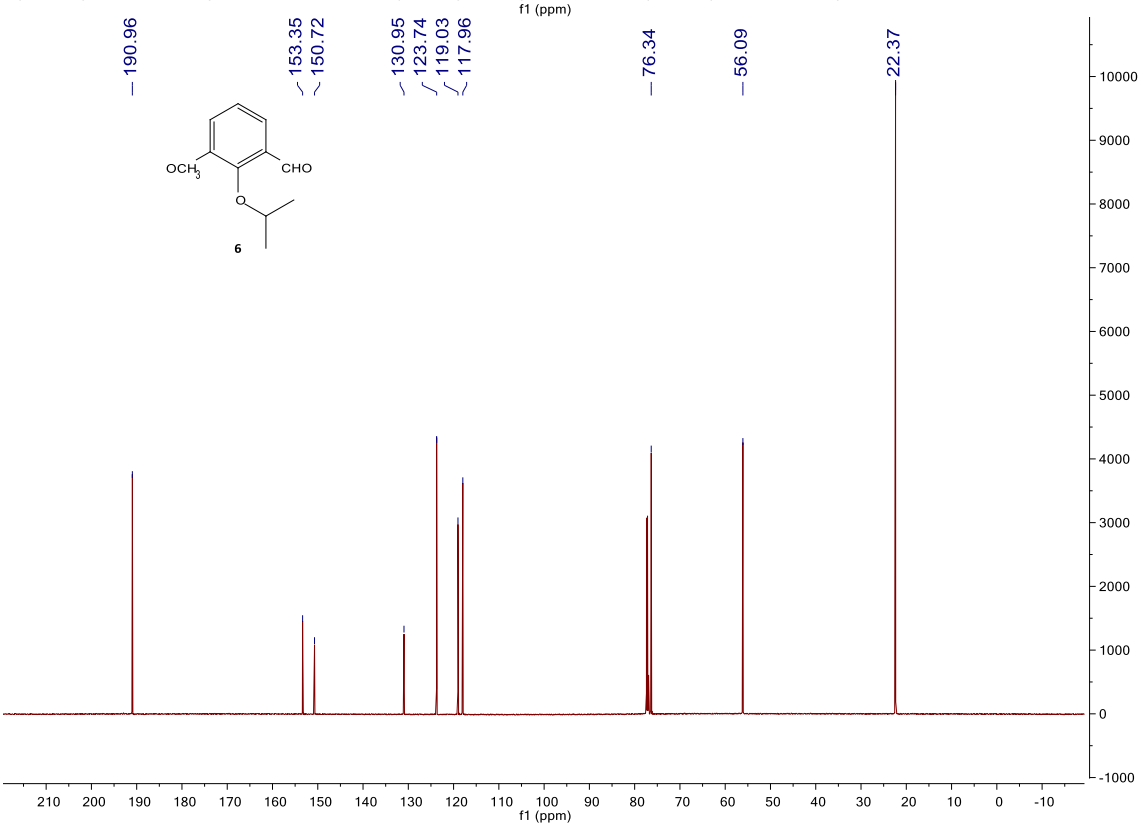
2-Methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-yl trifluoromethanesulfonate (17, NHC_5_144). To a solution of phenol **3** (46 mg, 0.13 mmol) in CH_2Cl_2 (20 mL) was added TEA (0.037 mL, 0.26 mmol) and triflic anhydride (0.034 mL, 0.20 mmol) at 0 °C. The reaction mixture was stirred for 5 h while warming from 0 °C to room temperature. The solution was washed with water and extracted with CH_2Cl_2 (3 x 30 mL). The organic phase was dried over sodium sulfate and evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 50 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → 60%A / 40%B (10 CV), 60%A / 80%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford triflic compound **17** (64 mg, 0.20 mmol, 100%) as a brown solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.01 (1H, d, J = 9 Hz), 6.75 (1H, d, J = 9 Hz), 6.53 (2H, s), 6.03 (1H, t, J = 4.2 Hz), 3.89 (3H, s), 3.88 (3H, s), 3.85 (6H, s), 2.91 (2H, t, J = 7.8 Hz), 2.39 (2H, m). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.3, 150.3, 139.0, 137.5, 136.5, 136.0, 131.2, 129.5, 125.9, 125.8, 109.7, 105.9, 61.1, 56.3, 56.2, 22.5, 22.1. ^{19}F NMR (564 MHz, $CDCl_3$) δ -73.35.

2-Methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-amine (4, DM40511, KGP05).[4] To toluene (20 mL) in a pressure vial was added triflate **17** (0.96 g, 2.0 mmol), $Pd(OAc)_2$ (45 mg, 0.20 mmol), *rac*-BINAP (0.19 g, 0.30 mmol), benzophenone imine (0.51 mL) and Cs_2CO_3 (989 mg, 3.04 mmol). The solution was degassed (bubbling nitrogen) for 15 min. After heating at 110 °C for 36 h, the reaction mixture was cooled to room temperature and diluted with EtOAc and quenched with water. The organic layer was separated and dried over

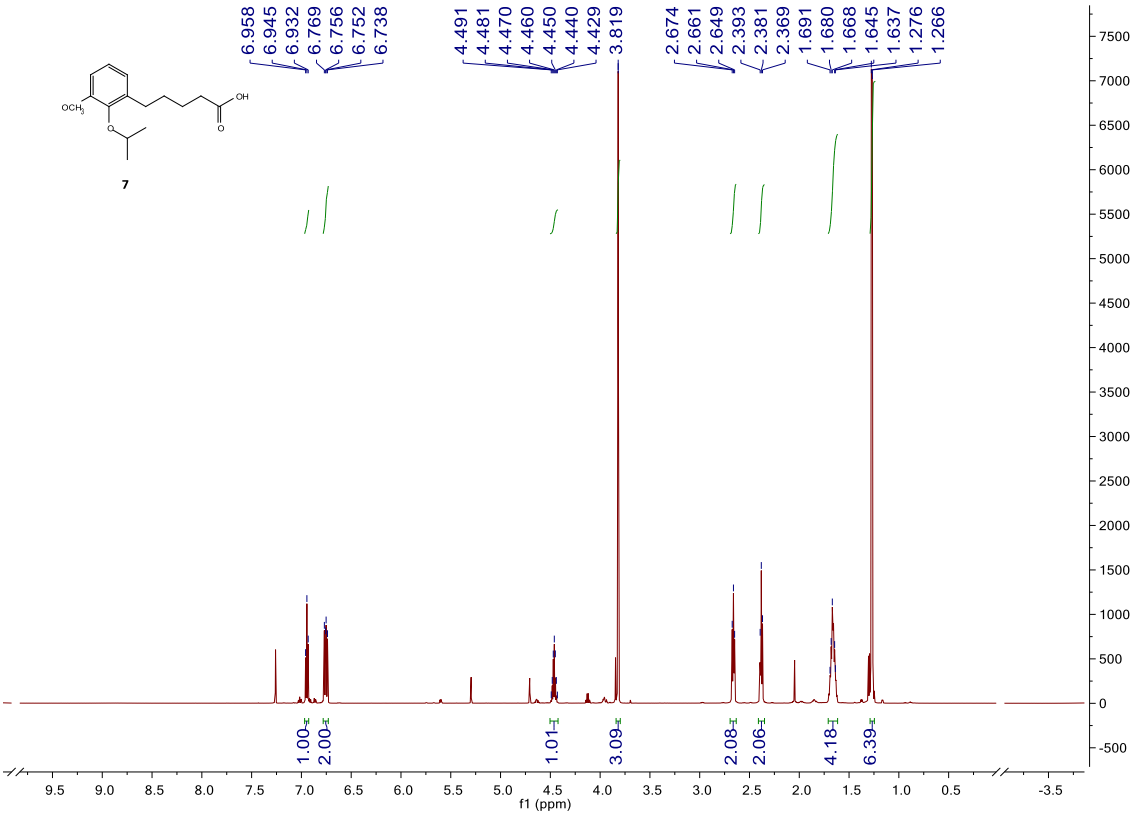
anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude product was dissolved in THF (20 mL) and treated with 2 M HCl until pH 2-3 was achieved, followed by stirring for 1 h. A 1 M NaOH solution was added to the reaction to achieve basic pH. The solution was extracted with EtOAc (3 x 30 mL) and the combined organic layers were dried over sodium sulfate and evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 100 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 7%A / 93%B (1 CV), 7%A / 93%B → 60%A / 40%B (10 CV), 60%A / 80%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford amine **4** (500 mg, 1.46 mmol, 72%) as a white crystal solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.60 (1H, d, *J* = 8.5 Hz), 6.56 (2H, s), 6.51 (1H, d, *J* = 8.5 Hz), 5.92 (1H, t, *J* = 4.5 Hz), 3.89 (3H, s), 3.86 (3H, s), 3.84 (6H, s), 2.67 (2H, t, *J* = 8 Hz), 2.42 (2H, m). ^{13}C NMR (150 MHz, $CDCl_3$) δ 152.8, 147.1, 140.0, 137.2, 137.0, 132.7, 128.2, 124.0, 121.1, 116.6, 107.1, 106.1, 60.9, 56.1, 55.6, 23.0, 21.6. HRMS: Obsvd 364.1522 [M + Na^+], Calcd for $C_{22}H_{23}NO_4Na$: 364.1519, HPLC: 19.07 min.

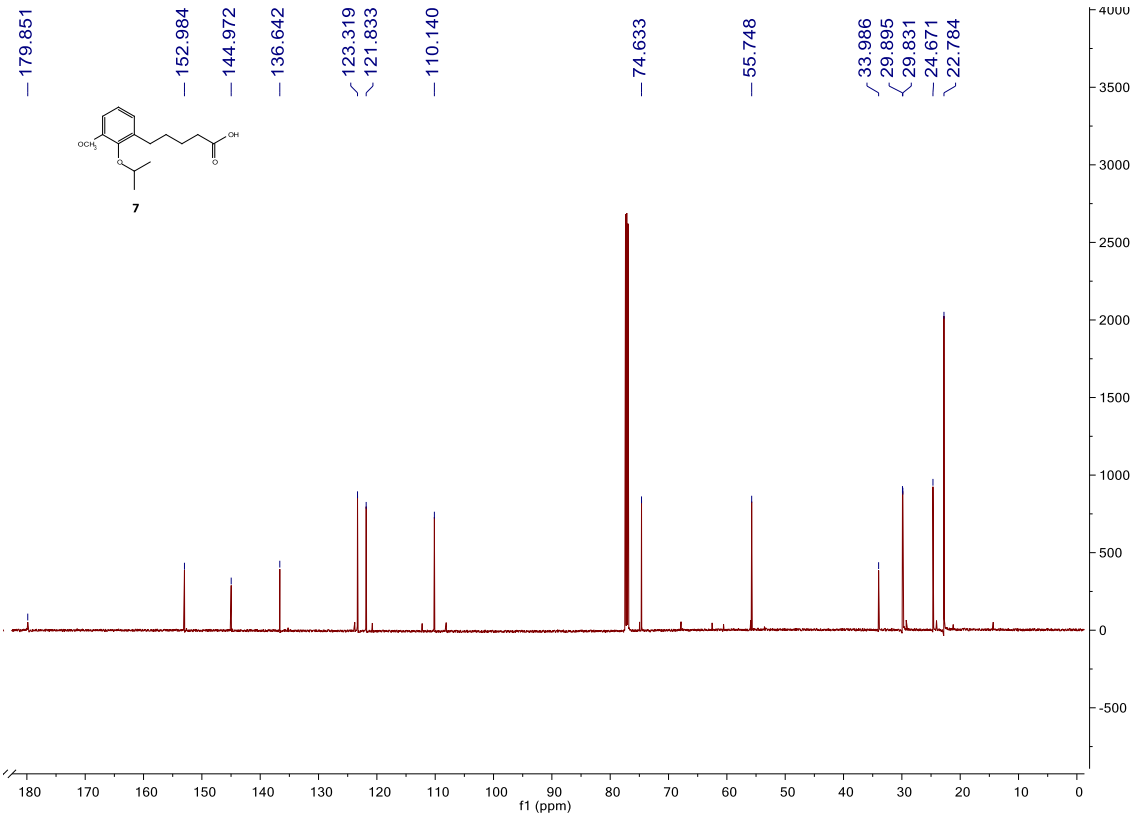
2-isopropoxy-3-methoxybenzaldehyde



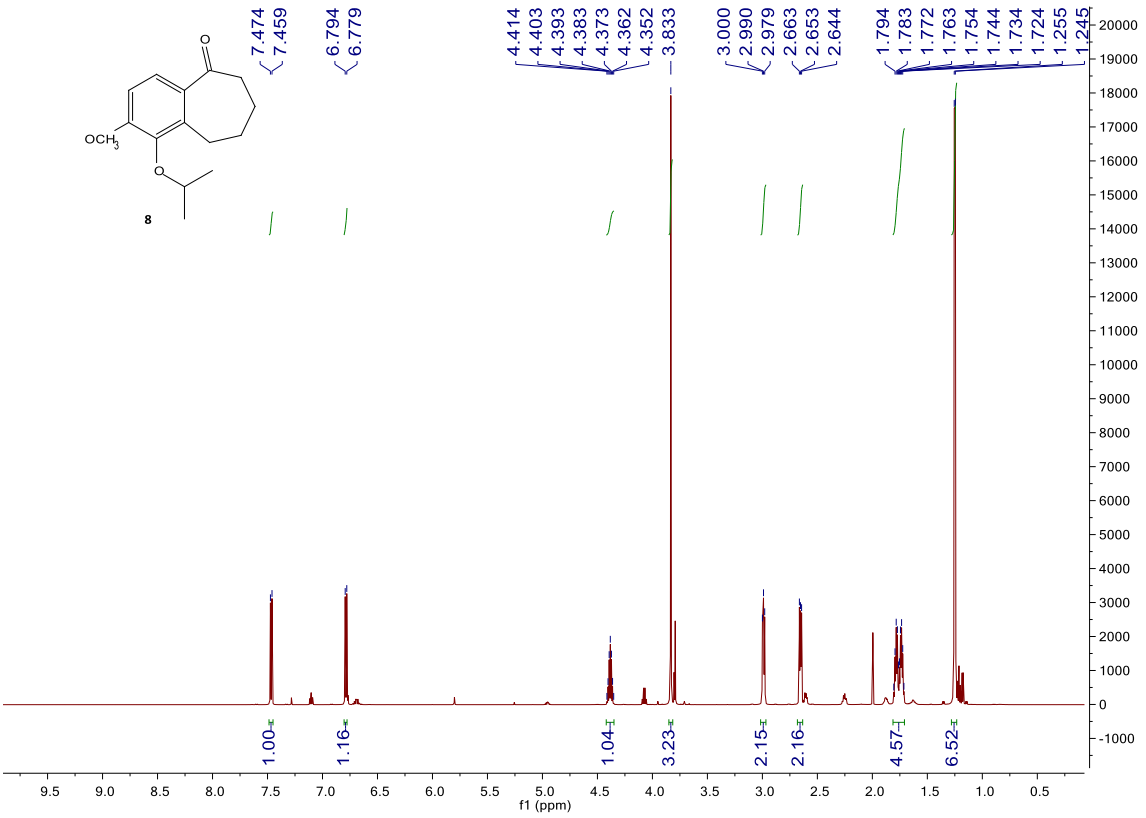


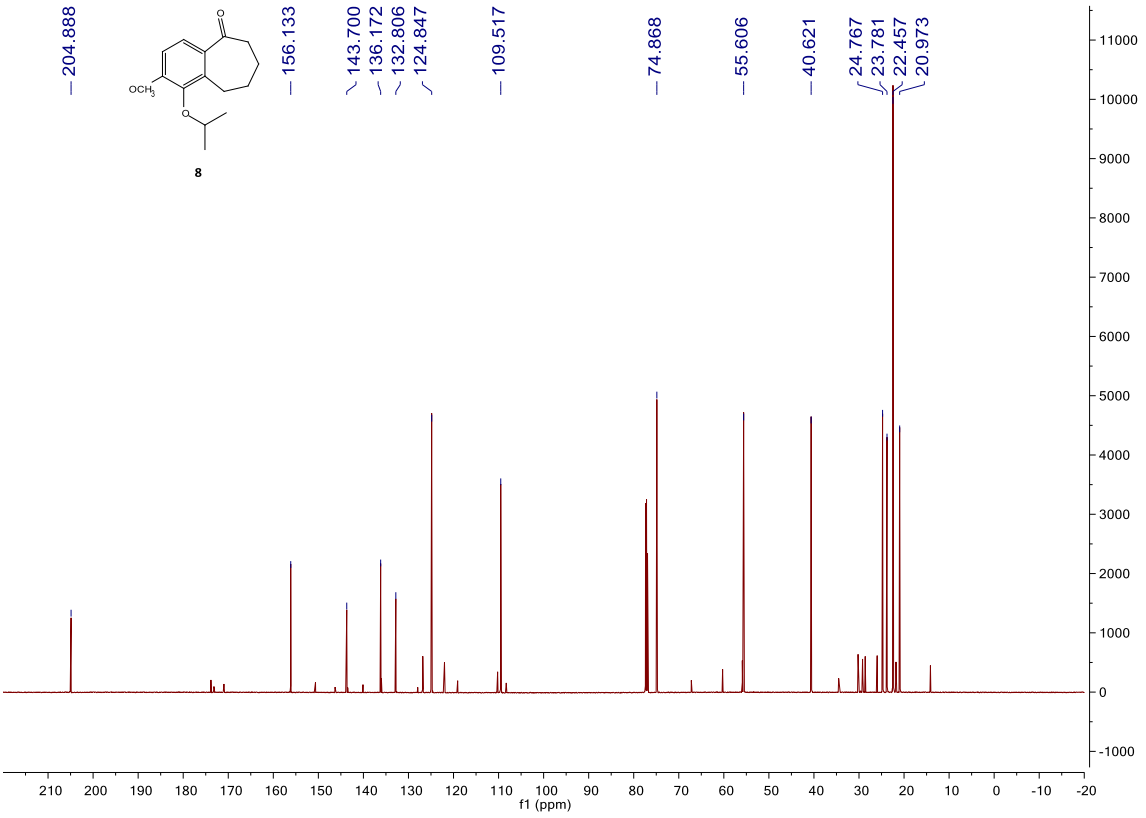
5-(2-isopropoxy-3-methoxyphenyl)pentanoic acid



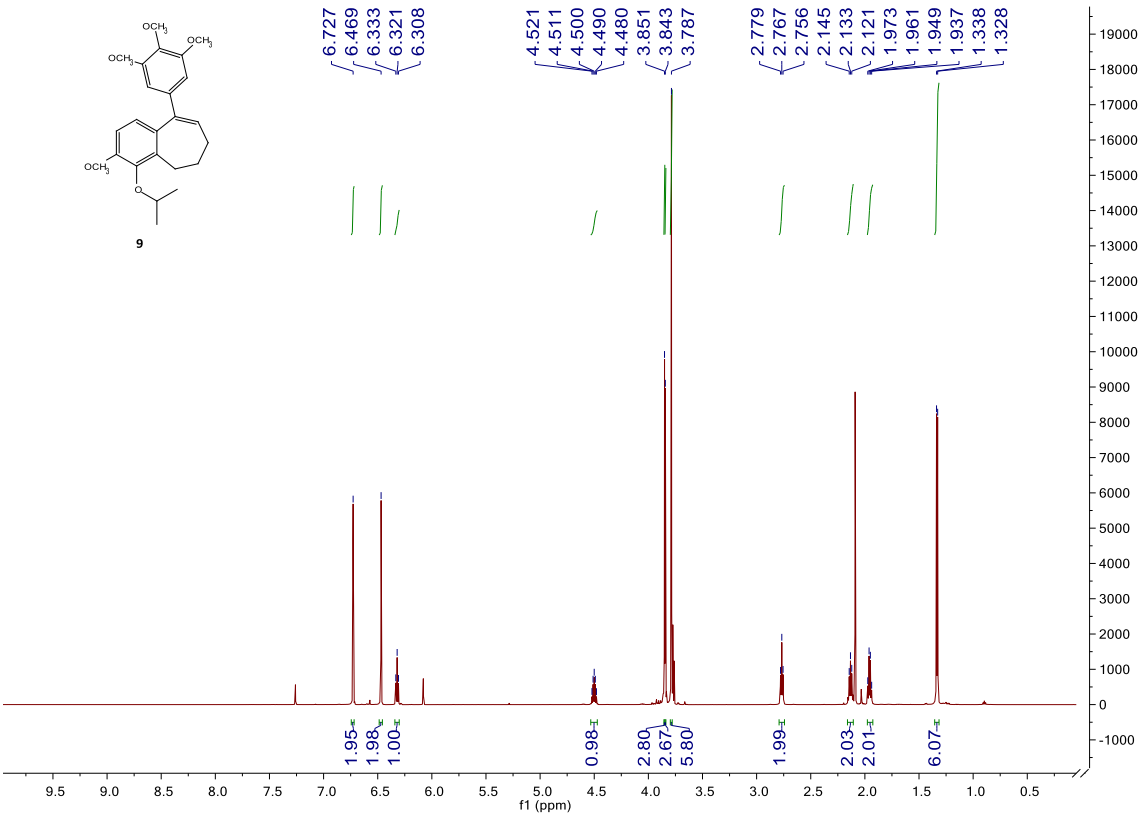


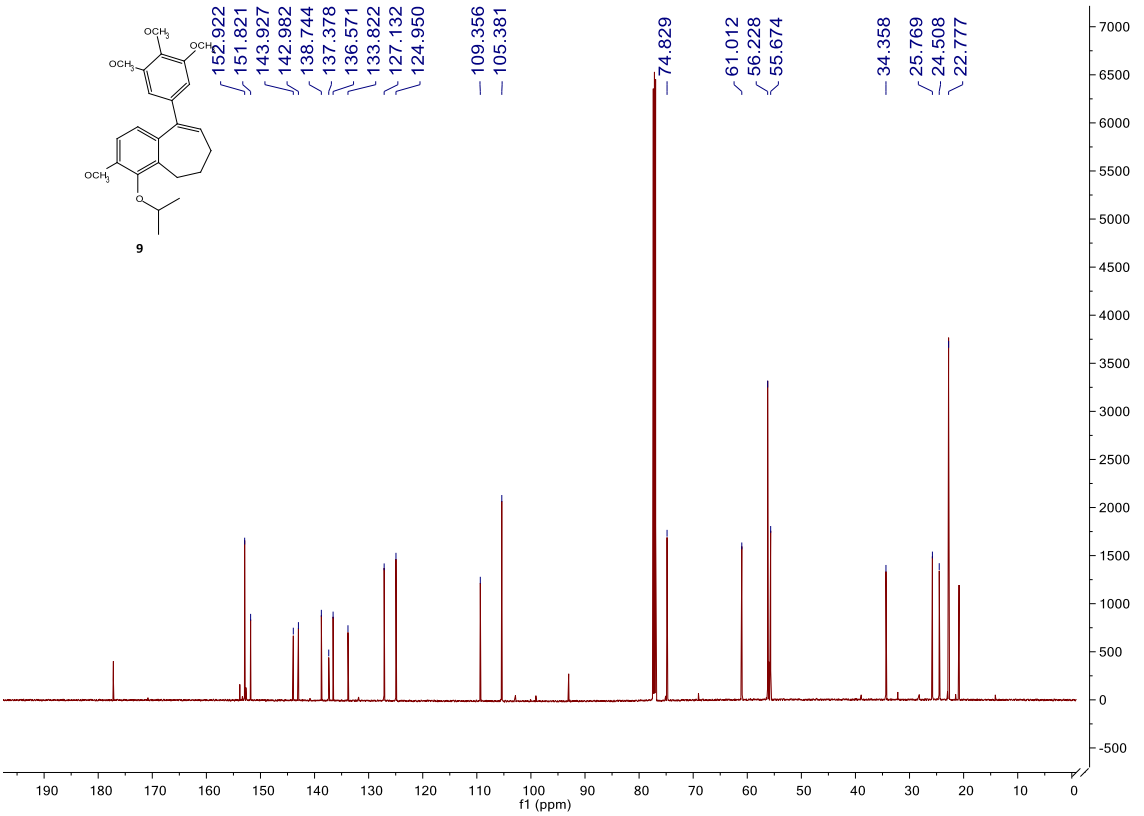
1-isopropoxy-2-methoxy-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one





4-isopropoxy-3-methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulene





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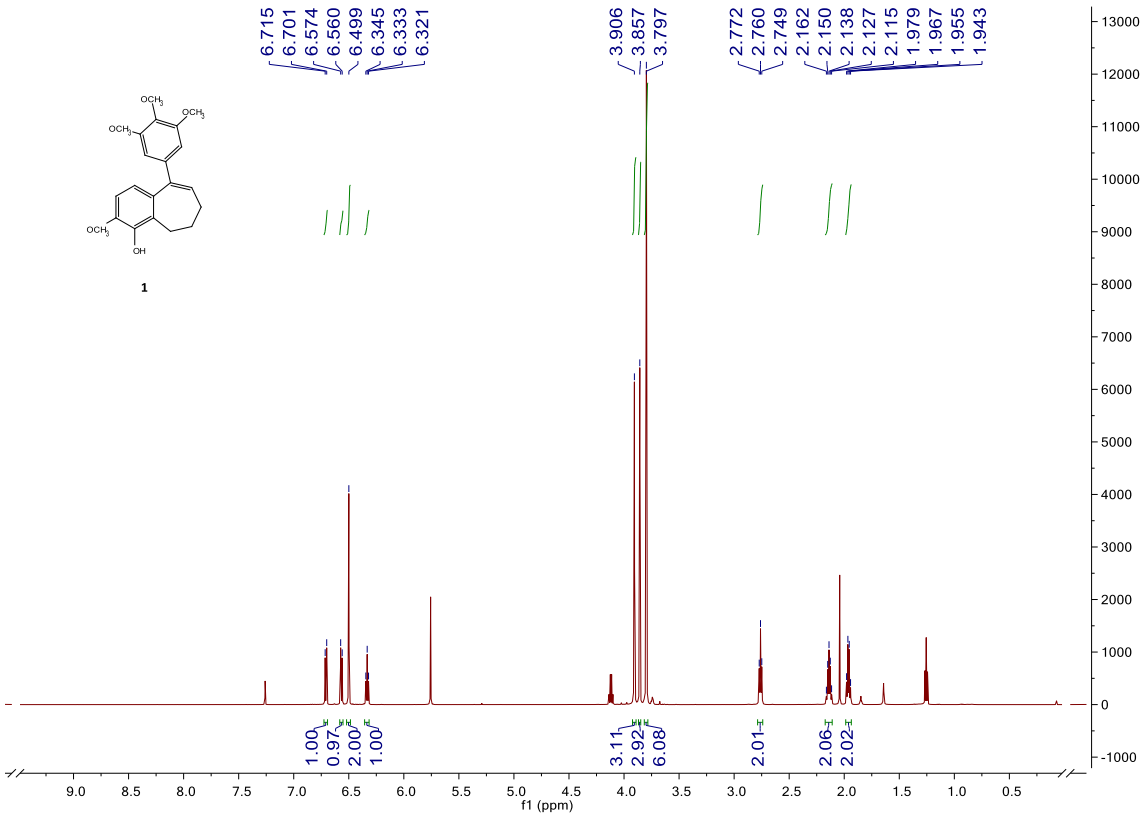

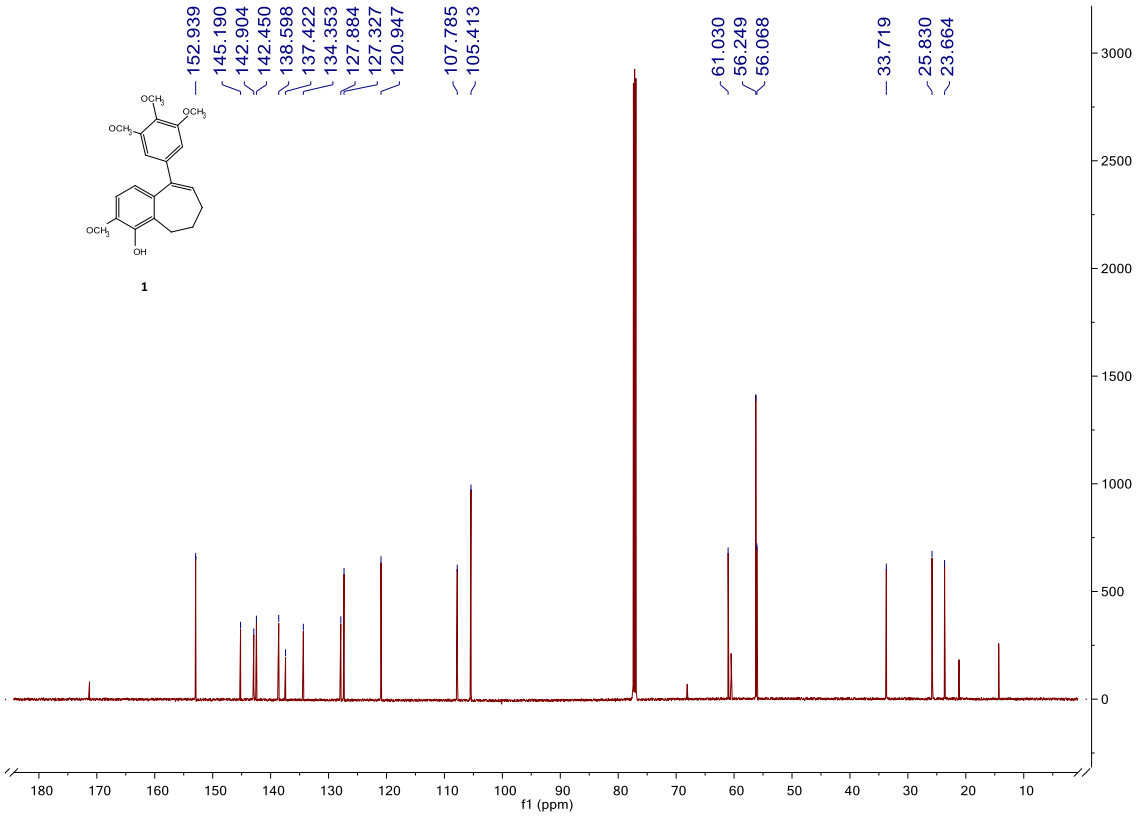

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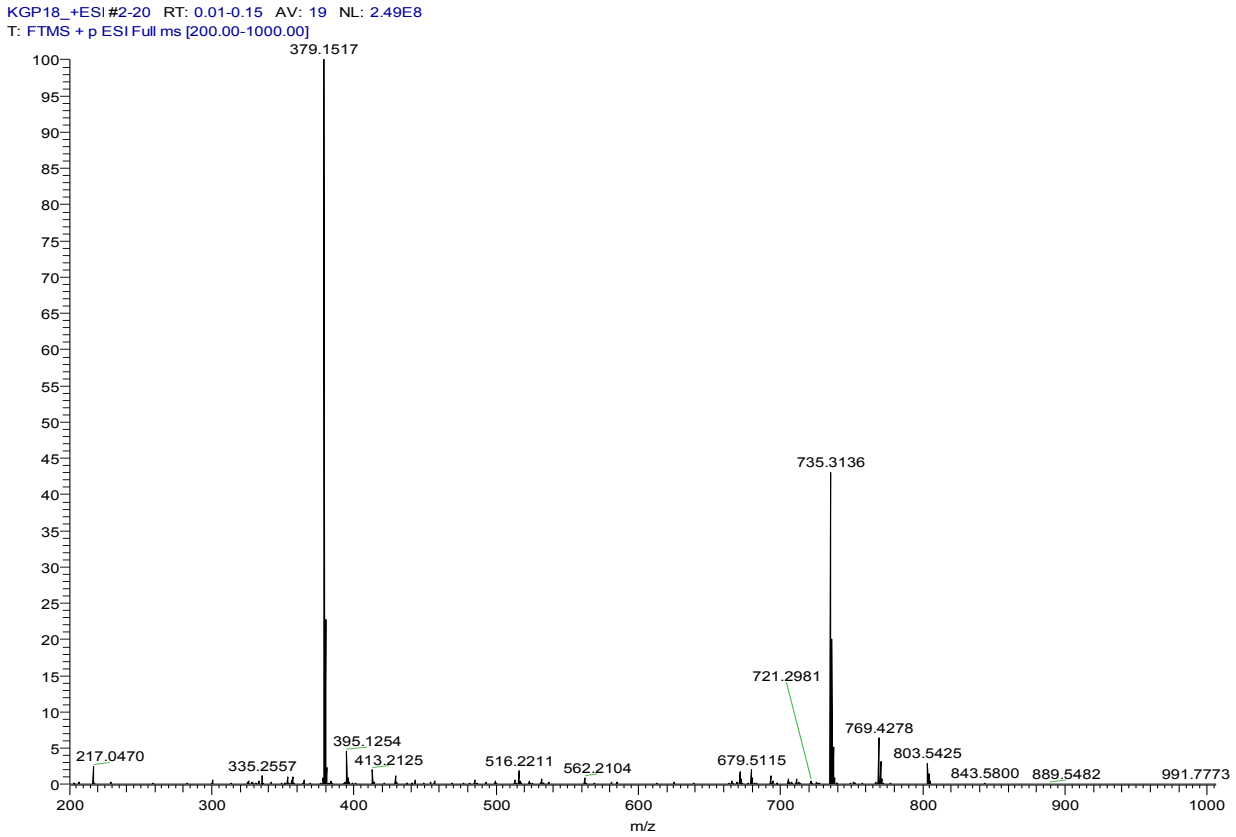

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Sample Info     : WASH
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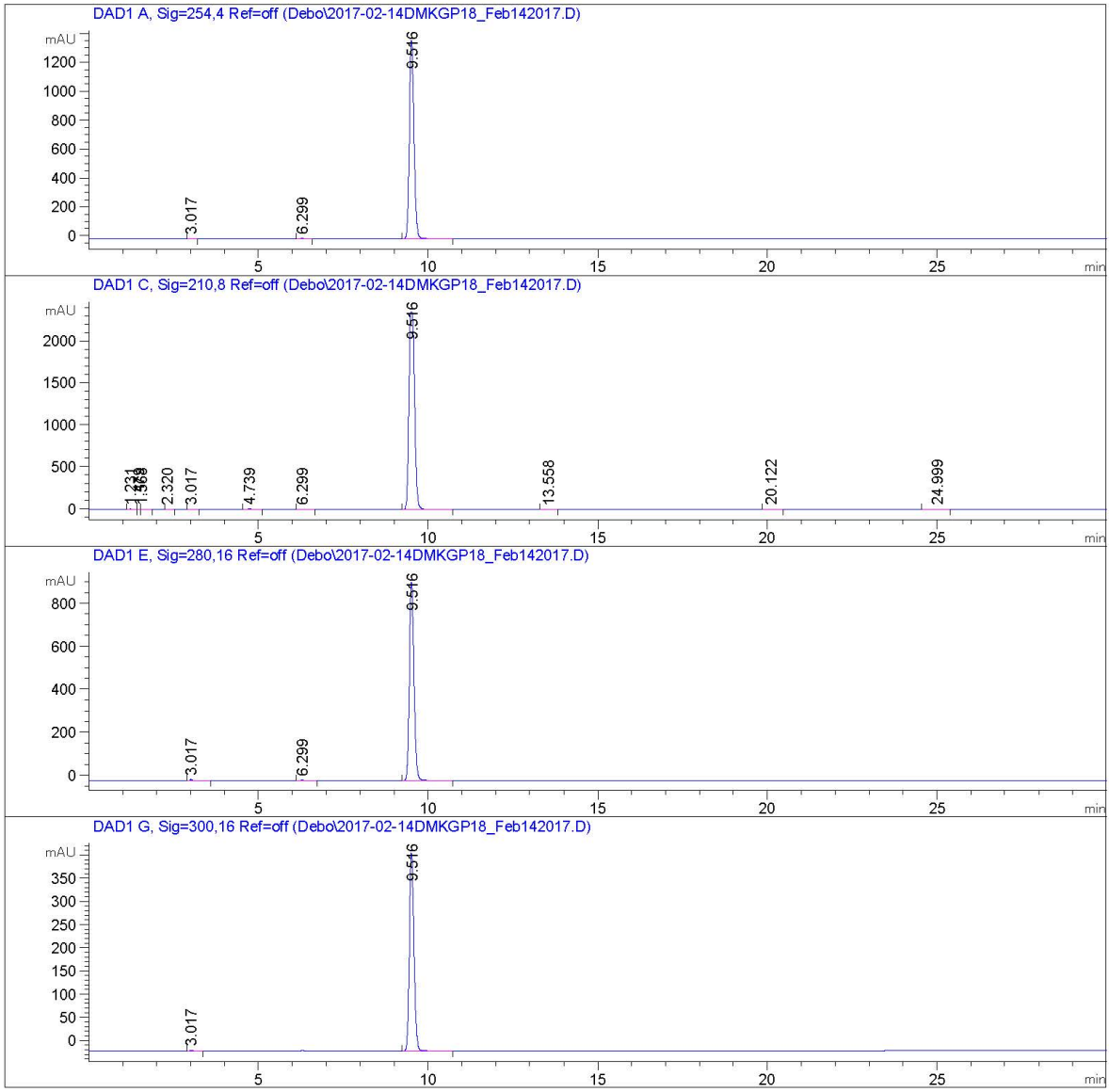

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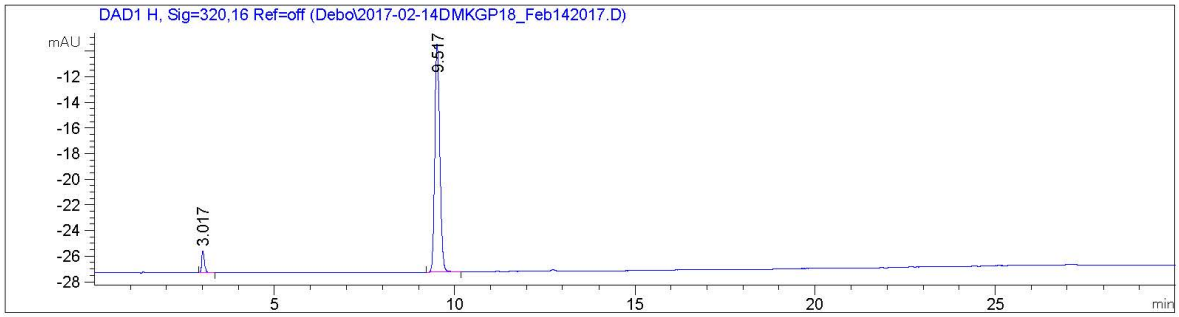
Sample Name: DMKGP18_Feb142017

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                    Area Percent Report
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Sorted By             :      Signal
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Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   3.017 BB    0.0809    7.92427    1.51895   0.0613
   2   6.299 BB    0.1177   18.41172    2.39434   0.1425
   3   9.516 BB    0.1457 1.28930e4  1370.82507  99.7962

Totals :                  1.29193e4  1374.73836



Signal 2: DAD1 C, Sig=210,8 Ref=off

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   1.231 BV    0.1239   67.62749    7.31446   0.2446
   2   1.479 VV    0.0687   24.06869    5.13172   0.0870
   3   1.568 VB    0.0880   21.89349    3.45356   0.0792
   4   2.320 BB    0.0914   23.63717    3.75622   0.0855
   5   3.017 BB    0.0815   33.52399    6.36371   0.1212
   6   4.739 BB    0.1053   77.87326   11.18089   0.2816
   7   6.299 BB    0.1225   51.40400    6.34442   0.1859
   8   9.516 BB    0.1848 2.72540e4  2359.50000  98.5700
   9  13.558 BB    0.1699   11.40957    1.04072   0.0413
  10  20.122 BB    0.1840   30.95074    2.61644   0.1119
  11  24.999 BB    0.2012   52.99282    4.03620   0.1917

Totals :                  2.76494e4  2410.73835
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Data File C:\Chem32\1\Data\Debo\2017-02-14DMKGP18_Feb142017.D
Sample Name: DMKGP18_Feb142017

Signal 3: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.017	BB	0.0826	20.04528	3.73385	0.2313
2	6.299	BB	0.1186	12.28080	1.58086	0.1417
3	9.516	BB	0.1453	8635.64453	921.89136	99.6271
Totals :				8667.97061	927.20607	

Signal 4: DAD1 G, Sig=300,16 Ref=off

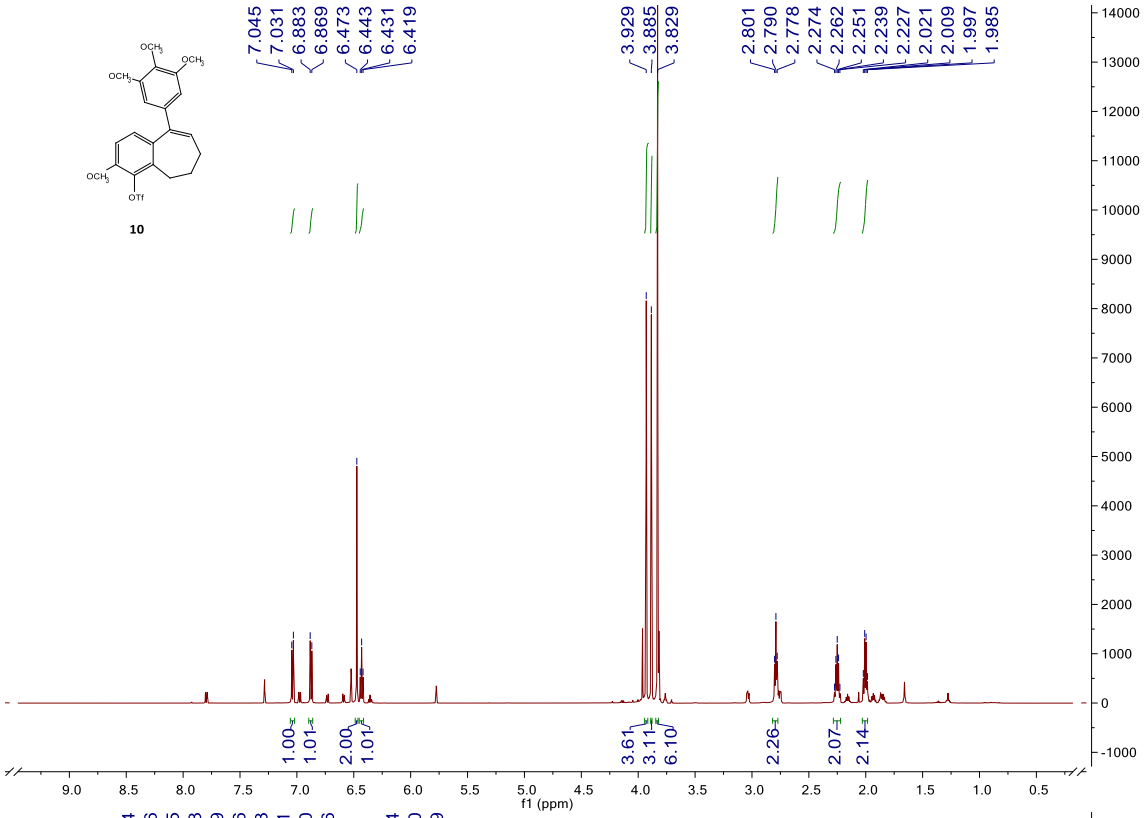
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.017	BB	0.0811	12.90936	2.46527	0.3210
2	9.516	BB	0.1454	4008.43823	427.41019	99.6790
Totals :				4021.34760	429.87545	

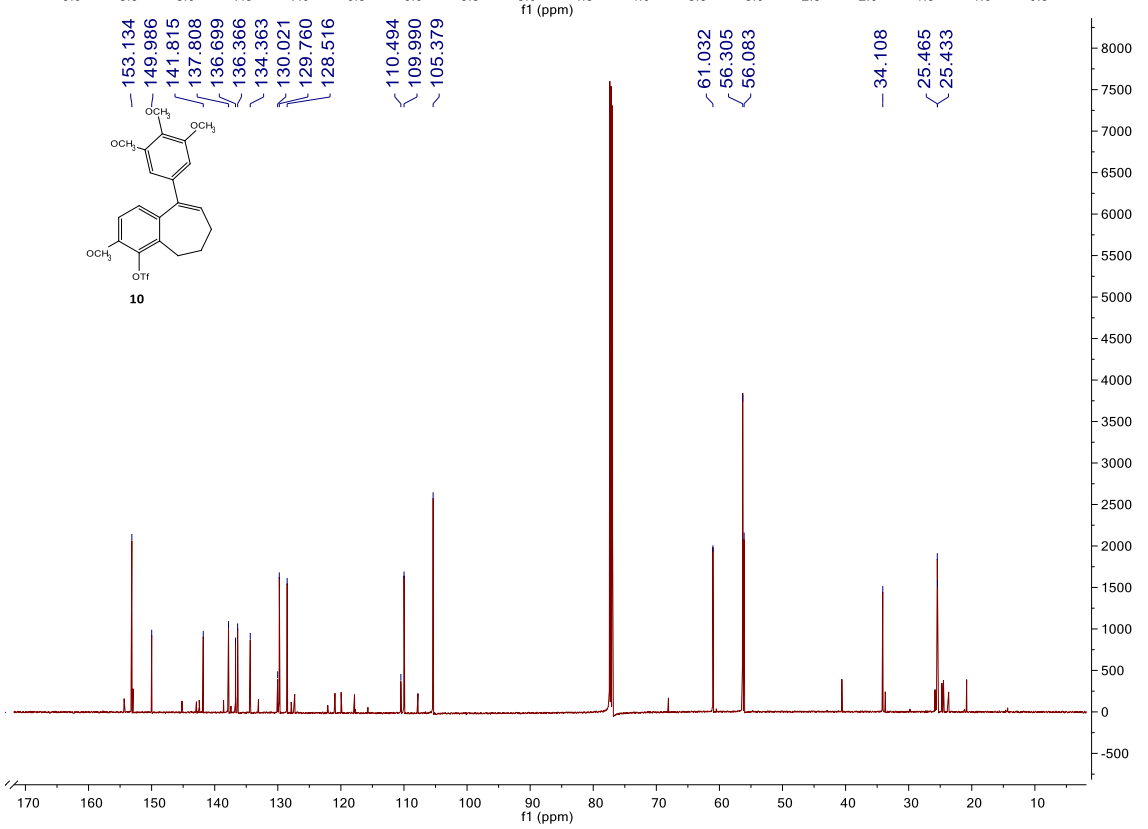
Signal 5: DAD1 H, Sig=320,16 Ref=off

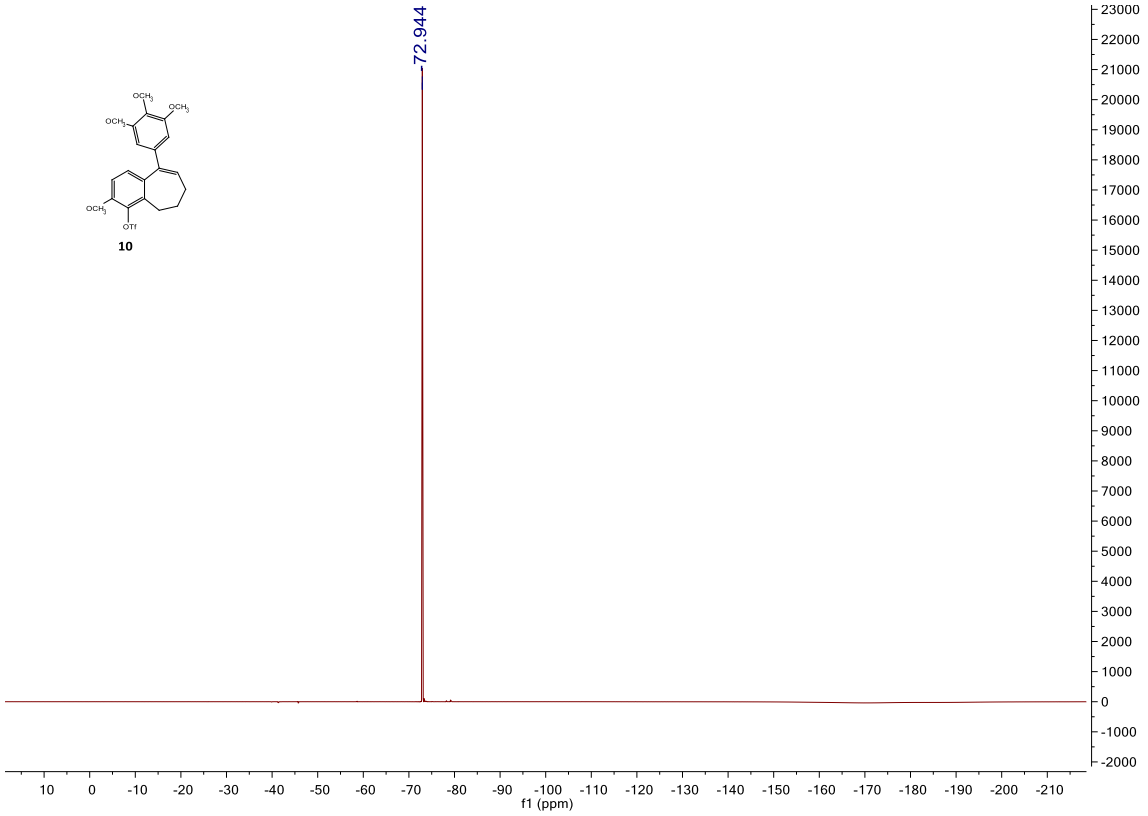
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.017	BB	0.0812	8.83565	1.68324	4.8729
2	9.517	BB	0.1512	172.48602	17.77163	95.1271
Totals :				181.32167	19.45487	

*** End of Report ***

3-methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-yl trifluoromethanesulfonate



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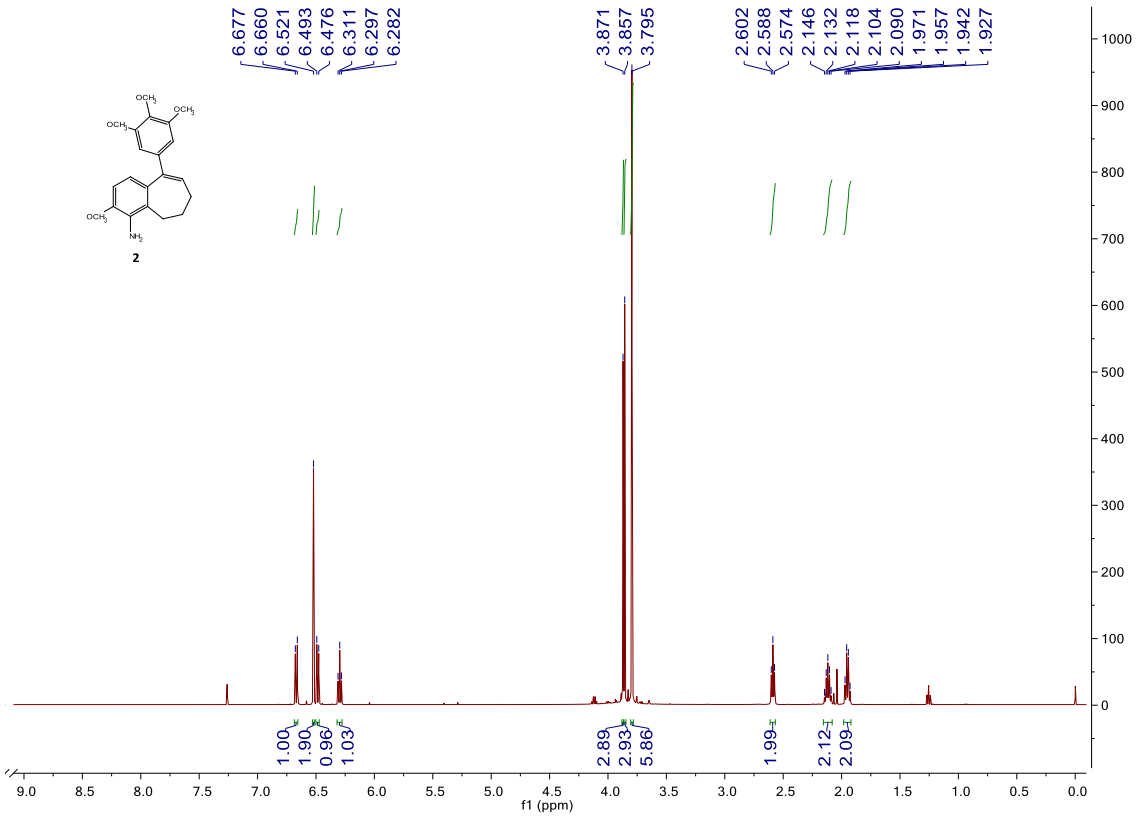
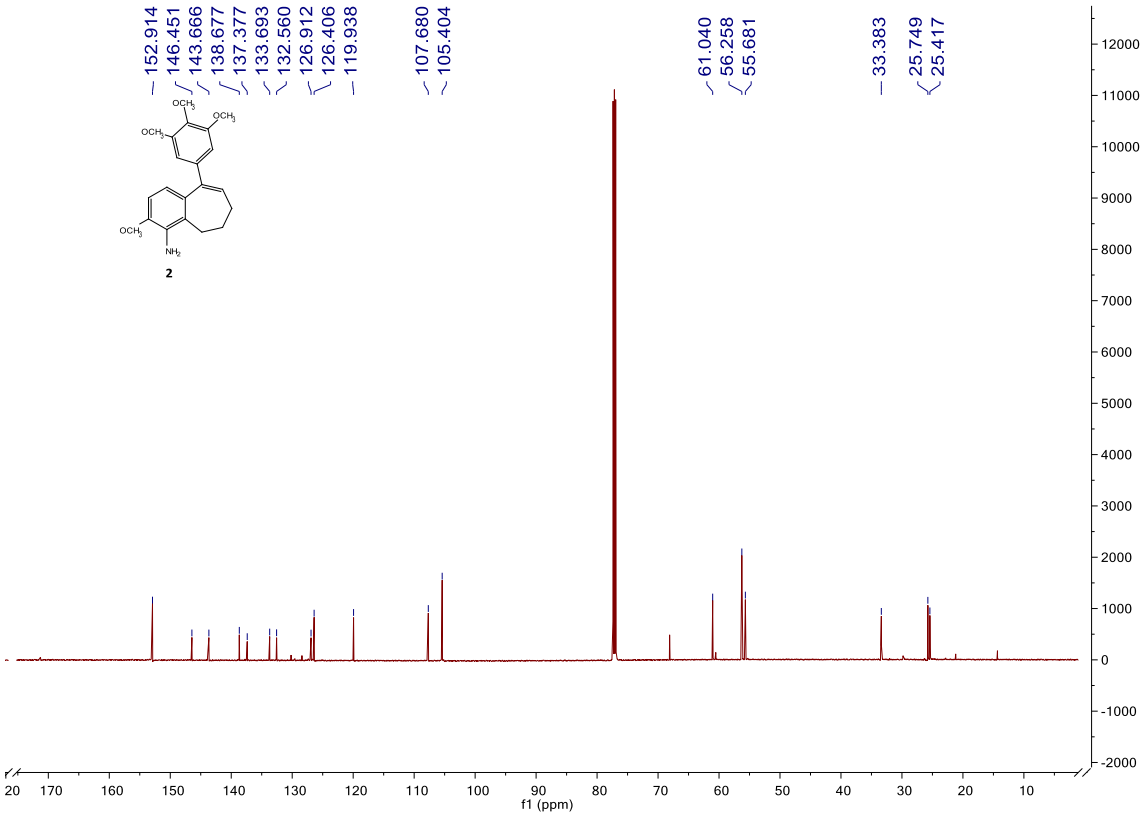
f1 (ppm)

3-methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-amine





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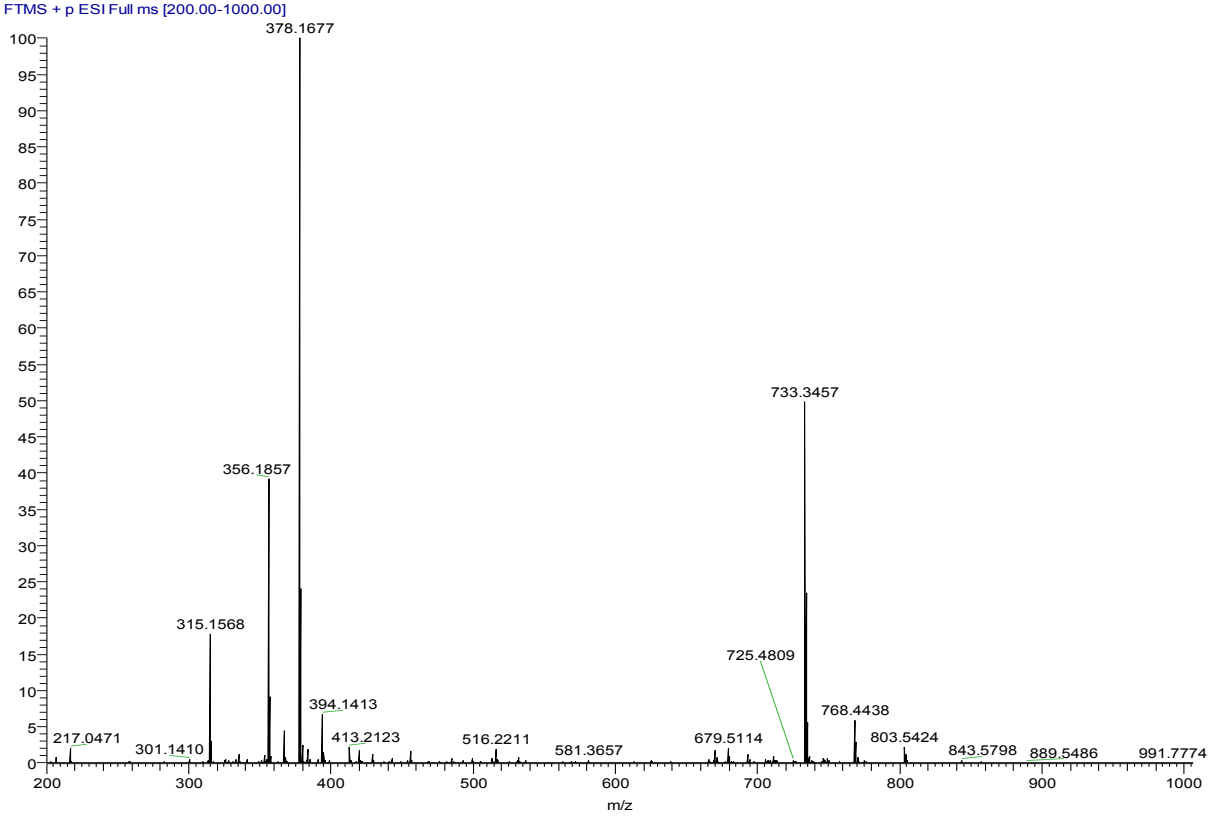
T: FTMS + p ESI Full ms [200.00-1000.00]



Data File C:\Chem32\1\Data\NHC\KGP156_NewRoute.D
Sample Name: KGP156_NewRoute

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Last changed    : 12/2/2015 12:37:42 PM by Eric Lin
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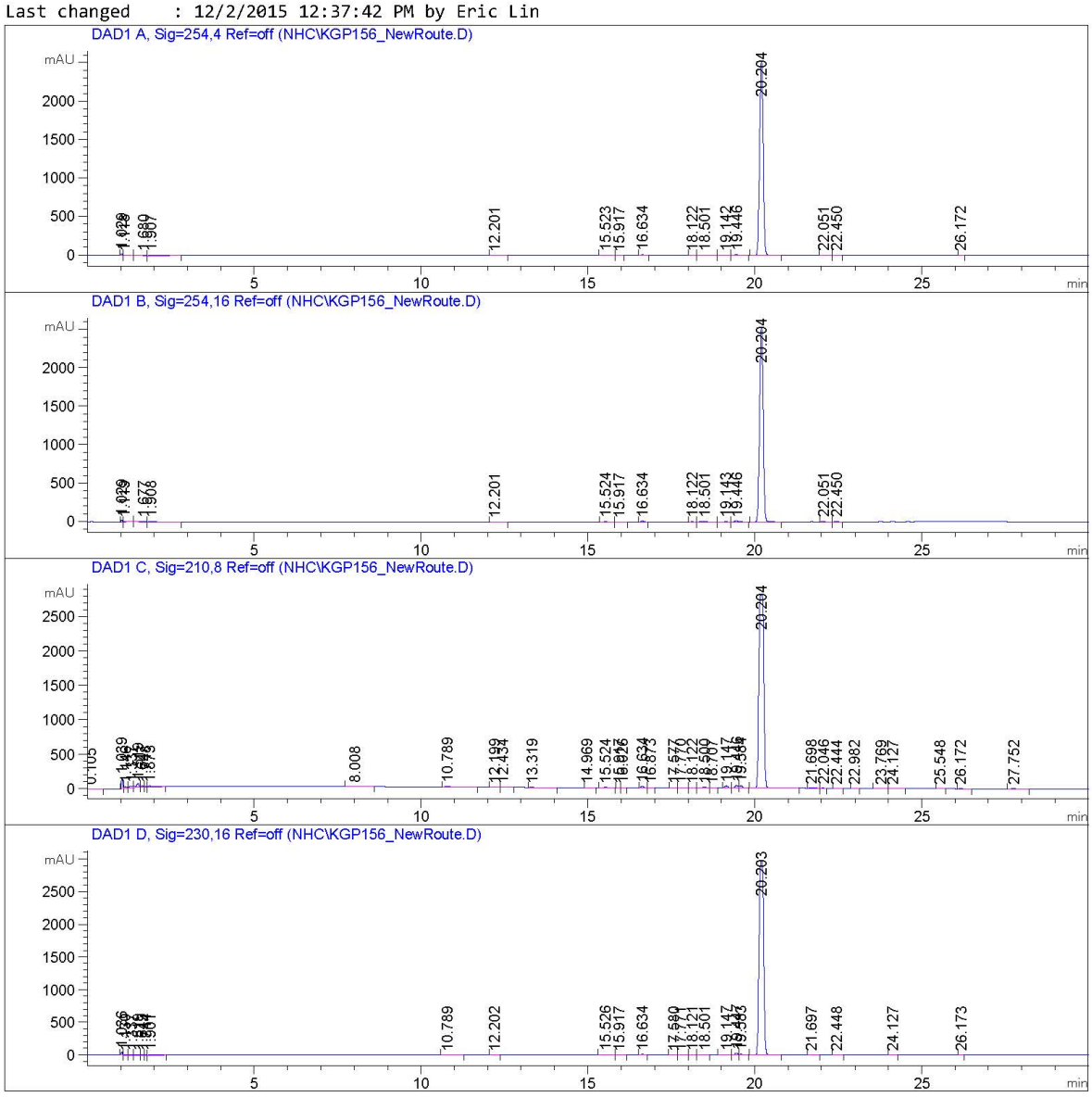

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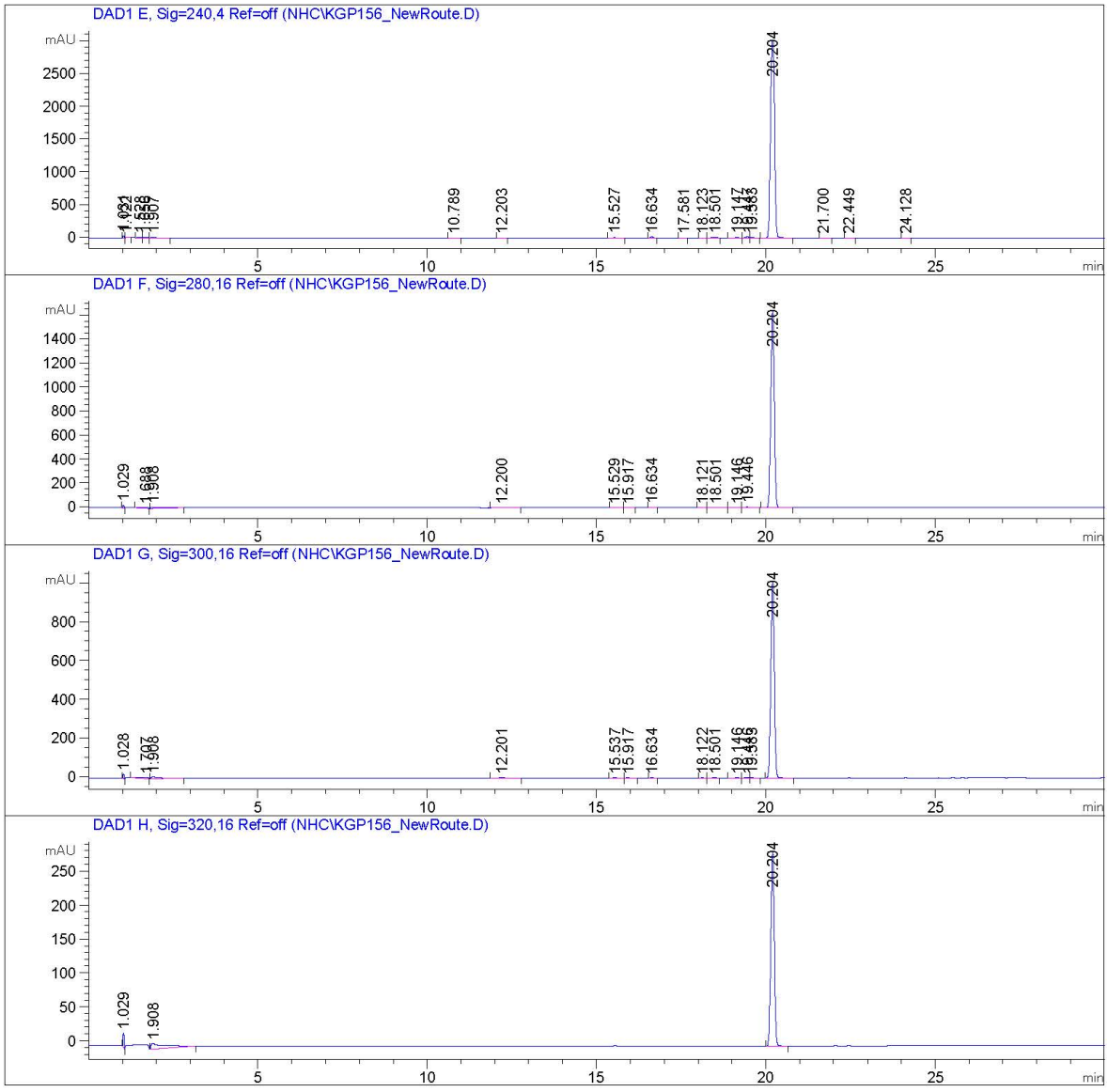
Sample Name: KGP156_NewRoute



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Data File C:\Chem32\1\Data\NHC\KGP156_NewRoute.D
Sample Name: KGP156_NewRoute

Signal 1: DAD1 A, Sig=254,4 Ref=off

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2	1.118	BB	0.1385	42.81089	4.36124	0.2219
3	1.680	BB	0.2278	138.07449	8.95691	0.7158
4	1.907	BB	0.3133	325.06317	13.97761	1.6851
5	12.201	BB	0.1674	14.90917	1.40945	0.0773
6	15.523	BV	0.1072	20.49548	2.87480	0.1062
7	15.917	VB	0.0940	6.14189	1.02298	0.0318
8	16.634	BB	0.0874	58.33884	10.41444	0.3024
9	18.122	BB	0.0885	12.03194	2.11179	0.0624
10	18.501	BB	0.1652	61.16386	5.88928	0.3171
11	19.142	BB	0.1032	10.32391	1.55925	0.0535
12	19.446	BB	0.1064	91.89568	13.01069	0.4764
13	20.204	BB	0.1149	1.84236e4	2530.97681	95.5080
14	22.051	VV	0.1250	10.32810	1.19292	0.0535
15	22.450	VB	0.1052	13.72154	2.02115	0.0711
16	26.172	BB	0.0798	5.39494	1.05173	0.0280
Totals :				1.92901e4	2624.71211	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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2	1.119	BB	0.1389	41.82282	4.24751	0.2161
3	1.677	BB	0.2294	136.65419	8.79058	0.7061
4	1.908	BB	0.3125	320.27887	13.81122	1.6549
5	12.201	BB	0.1691	15.84175	1.47786	0.0819
6	15.524	BV	0.1078	20.49586	2.85384	0.1059
7	15.917	VB	0.0940	6.49141	1.05227	0.0335
8	16.634	BB	0.0872	55.58357	9.94209	0.2872
9	18.122	BV	0.0888	12.16264	2.12407	0.0628
10	18.501	VB	0.1679	60.18542	5.75875	0.3110
11	19.143	BV	0.1057	13.06765	1.86512	0.0675
12	19.446	VB	0.1100	93.51012	12.68323	0.4832
13	20.204	BB	0.1151	1.84998e4	2535.37988	95.5880
14	22.051	VV	0.1257	9.69743	1.11286	0.0501
15	22.450	VB	0.1071	13.17622	1.94355	0.0681
Totals :				1.93537e4	2627.15918	

Data File C:\Chem32\1\Data\NHC\KGP156_NewRoute.D
Sample Name: KGP156_NewRoute

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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2	1.039	BV	0.0426	435.94681	165.97623	1.4097
3	1.146	VV	0.1043	155.01181	21.97941	0.5013
4	1.337	VV	0.1198	213.80933	24.02304	0.6914
5	1.519	VB	0.0853	289.87567	50.21970	0.9374
6	1.647	BV	0.0672	84.60459	19.26048	0.2736
7	1.748	VB	0.0580	49.05077	13.01072	0.1586
8	1.873	BB	0.1706	178.12035	15.91610	0.5760
9	8.008	BB	0.2266	37.89616	2.24884	0.1225
10	10.789	VB	0.1108	102.47525	14.43470	0.3314
11	12.199	BV	0.1615	30.62111	3.04053	0.0990
12	12.434	VB	0.1266	12.30986	1.34753	0.0398
13	13.319	BB	0.1477	11.35693	1.08865	0.0367
14	14.969	VB	0.1036	11.77649	1.72702	0.0381
15	15.524	BB	0.1160	48.63016	6.16380	0.1573
16	15.917	BV	0.0831	11.59196	2.14212	0.0375
17	16.026	VB	0.0814	8.38063	1.59134	0.0271
18	16.634	VV	0.0878	116.36454	20.63740	0.3763
19	16.873	VB	0.0894	14.29773	2.47631	0.0462
20	17.577	BV	0.1248	8.98047	1.15382	0.0290
21	17.770	VB	0.0997	16.80680	2.58943	0.0543
22	18.122	BV	0.0928	41.97680	6.91610	0.1357
23	18.500	VV	0.1642	125.87863	11.82832	0.4071
24	18.707	VB	0.1129	11.68607	1.49987	0.0378
25	19.147	VV	0.0992	194.16022	30.93661	0.6279
26	19.446	VV	0.0920	232.49939	38.72795	0.7518
27	19.584	VB	0.0982	241.77089	36.99688	0.7818
28	20.204	BB	0.1620	2.80380e4	2820.07422	90.6674
29	21.698	BV	0.1452	17.81673	1.74420	0.0576
30	22.046	VB	0.0909	6.75678	1.17809	0.0218
31	22.444	BB	0.1132	8.46806	1.18758	0.0274
32	22.982	BV	0.1003	11.69455	1.78918	0.0378
33	23.769	BV	0.1963	15.29358	1.00057	0.0495
34	24.127	VV	0.1256	16.37481	1.88088	0.0530
35	25.548	BB	0.1049	35.16088	5.19697	0.1137
36	26.172	BB	0.1060	13.36985	1.85652	0.0432
37	27.752	BB	0.1713	60.69699	5.39515	0.1963
Totals :				3.09240e4	3341.38136	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.036	BV	0.0407	124.66803	50.76436	0.4319
2	1.130	VV	0.1155	55.39950	7.06510	0.1919
3	1.337	VV	0.1235	92.19374	9.82043	0.3194
4	1.519	VV	0.1310	130.97940	13.77194	0.4537

Data File C:\Chem32\1\Data\NHC\KGP156_NewRoute.D
Sample Name: KGP156_NewRoute

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
5	1.649	VV	0.0919	88.31196	13.57421	0.3059
6	1.744	VB	0.0647	55.18219	13.22710	0.1912
7	1.901	BB	0.2079	208.21948	14.63946	0.7213
8	10.789	BB	0.1151	25.48580	3.41192	0.0883
9	12.202	BB	0.1523	29.56805	3.18566	0.1024
10	15.526	BV	0.1148	41.98088	5.39564	0.1454
11	15.917	VB	0.1161	12.78415	1.58488	0.0443
12	16.634	VB	0.0876	91.07066	16.19882	0.3155
13	17.580	BV	0.1186	10.71600	1.41125	0.0371
14	17.771	VB	0.1056	7.44635	1.03965	0.0258
15	18.121	BB	0.0887	28.08753	4.90946	0.0973
16	18.501	BV	0.1604	82.86704	8.16548	0.2871
17	19.147	BB	0.1000	66.43429	10.47385	0.2301
18	19.447	BV	0.0948	162.44650	26.75455	0.5627
19	19.583	VB	0.0930	84.30189	13.47432	0.2920
20	20.203	BB	0.1493	2.74223e4	2980.54883	94.9922
21	21.697	BV	0.1498	22.20905	2.09263	0.0769
22	22.448	BB	0.1091	11.10630	1.59686	0.0385
23	24.127	BB	0.0930	8.46844	1.39141	0.0293
24	26.173	BB	0.0784	5.73531	1.18555	0.0199
Totals :				2.88680e4	3205.68335	

Signal 5: DAD1 E, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.031	BB	0.0393	71.64593	30.66300	0.2831
2	1.122	BB	0.0965	18.19417	2.92825	0.0719
3	1.528	BV	0.1112	34.13404	4.46297	0.1349
4	1.656	VB	0.1628	106.91344	8.61382	0.4224
5	1.907	BB	0.2242	215.12267	13.77413	0.8499
6	10.789	BB	0.1084	10.86397	1.53786	0.0429
7	12.203	BB	0.1524	24.73338	2.66176	0.0977
8	15.527	BB	0.1114	28.84837	3.94067	0.1140
9	16.634	BB	0.0870	63.05199	11.31498	0.2491
10	17.581	BV	0.1177	9.20557	1.22497	0.0364
11	18.123	BB	0.0884	10.59986	1.86338	0.0419
12	18.501	BV	0.1628	68.30199	6.70673	0.2698
13	19.147	BV	0.1050	35.05600	5.17687	0.1385
14	19.447	VV	0.0960	85.96707	13.92544	0.3396
15	19.583	VB	0.0942	47.76067	7.51296	0.1887
16	20.204	BB	0.1308	2.44483e4	3008.89478	96.5902
17	21.700	BV	0.1403	14.35606	1.46525	0.0567
18	22.449	BB	0.1070	11.76523	1.73853	0.0465
19	24.128	BB	0.0921	6.53606	1.08784	0.0258
Totals :				2.53114e4	3129.49417	

Data File C:\Chem32\1\Data\NHC\KGP156_NewRoute.D
Sample Name: KGP156_NewRoute

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.029	BB	0.0374	52.70672	22.45042	0.4345
2	1.688	BB	0.2298	115.93475	7.44116	0.9557
3	1.908	BB	0.3154	258.82291	11.04414	2.1337
4	12.200	BB	0.1866	21.54193	1.76230	0.1776
5	15.529	BV	0.1054	14.69091	2.10641	0.1211
6	15.917	VB	0.0933	14.84133	2.49962	0.1223
7	16.634	BB	0.0869	30.46751	5.47958	0.2512
8	18.121	BV	0.0907	17.59917	2.99044	0.1451
9	18.501	VB	0.1643	31.84293	3.03732	0.2625
10	19.146	BV	0.1049	15.22276	2.19395	0.1255
11	19.446	VB	0.1141	62.17640	8.05141	0.5126
12	20.204	BB	0.1095	1.14944e4	1646.40137	94.7582
Totals :				1.21302e4	1715.45812	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.028	BB	0.0386	47.62583	20.87785	0.6285
2	1.707	BB	0.2639	122.55516	6.68573	1.6174
3	1.908	BB	0.3223	212.69646	8.85409	2.8070
4	12.201	BB	0.1833	23.09685	1.93406	0.3048
5	15.537	BV	0.1115	14.68926	2.00552	0.1939
6	15.917	VB	0.0906	7.55386	1.28497	0.0997
7	16.634	BB	0.0863	10.32639	1.87303	0.1363
8	18.122	BB	0.0900	6.61254	1.13526	0.0873
9	18.501	BB	0.1577	11.69376	1.17887	0.1543
10	19.146	BV	0.1051	8.64193	1.24296	0.1140
11	19.446	VV	0.0988	18.63790	2.90577	0.2460
12	19.583	VB	0.0961	8.74240	1.34089	0.1154
13	20.204	BB	0.1091	7084.46484	1018.61517	93.4954
Totals :				7577.33718	1069.93420	

Signal 8: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.029	BB	0.0366	48.09990	21.09005	2.1064
2	1.908	BB	0.3984	238.60016	7.81096	10.4490
3	20.204	BB	0.1091	1996.76819	287.26431	87.4445
Totals :				2283.46825	316.16533	

Data File C:\Chem32\1\Data\NHC\KGP156_NewRoute.D
Sample Name: KGP156_NewRoute

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*** End of Report ***

3-Methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-amine (**2**)

X-ray crystallographic data has been deposited with the Cambridge Crystallographic Data Centre. Deposition number: CCDC 1868223. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk).

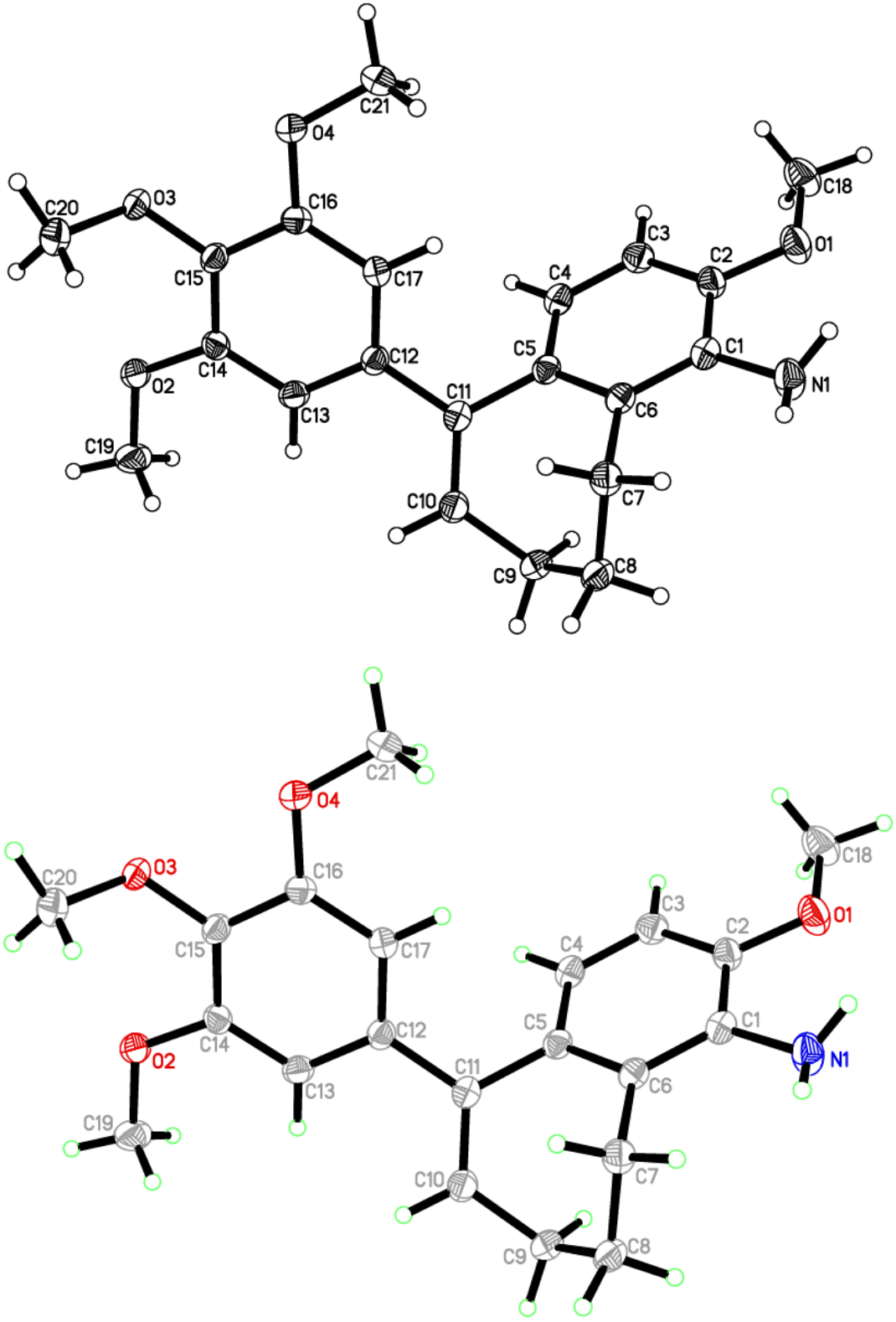


Table 1

Identification code	KP84	
Empirical formula	C21 H25 N O4	
Formula weight	355.42	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 10.6830(3) Å	α= 90°.
	b = 19.4724(6) Å	β= 113.1761(10)°.
	c = 9.4948(3) Å	γ = 90°.
Volume	1815.75(10) $Å^3$	
Z	4	
Density (calculated)	1.300 Mg/m^3	
Absorption coefficient	0.090 mm^{-1}	
F(000)	760	
Crystal size	0.532 x 0.209 x 0.139 mm^3	
Theta range for data collection	2.323 to 28.346°.	
Index ranges	-14<=h<=14, -25<=k<=25, -12<=l<=12	
Reflections collected	21293	
Independent reflections	4523 [R(int) = 0.0362]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.915 and 0.883	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4523 / 0 / 247	
Goodness-of-fit on F^2	1.022	
Final R indices [I>2sigma(I)]	R1 = 0.0438, wR2 = 0.1038	
R indices (all data)	R1 = 0.0616, wR2 = 0.1134	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.297 and -0.215 $e.Å^{-3}$	

Table 2

(x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)

for KP84. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	10011(1)	5280(1)	12206(1)	30(1)
O(2)	4071(1)	7011(1)	1615(1)	25(1)
O(3)	4411(1)	5660(1)	1233(1)	25(1)
O(4)	6162(1)	4907(1)	3470(1)	28(1)
N(1)	11554(1)	6150(1)	11520(1)	28(1)
C(1)	10182(1)	6119(1)	10519(1)	21(1)
C(2)	9341(1)	5659(1)	10896(1)	22(1)
C(3)	7972(1)	5601(1)	9980(2)	24(1)
C(4)	7408(1)	6012(1)	8686(2)	22(1)
C(5)	8202(1)	6480(1)	8296(1)	19(1)
C(6)	9612(1)	6531(1)	9212(1)	20(1)
C(7)	10482(1)	7011(1)	8720(2)	23(1)
C(8)	10275(1)	7776(1)	8969(2)	25(1)
C(9)	8754(1)	7952(1)	8445(2)	24(1)
C(10)	7877(1)	7597(1)	6977(2)	22(1)
C(11)	7583(1)	6923(1)	6906(1)	19(1)
C(12)	6692(1)	6589(1)	5440(1)	19(1)
C(13)	5746(1)	6976(1)	4258(2)	21(1)
C(14)	5012(1)	6673(1)	2848(1)	20(1)
C(15)	5178(1)	5979(1)	2596(1)	20(1)
C(16)	6080(1)	5588(1)	3794(1)	20(1)
C(17)	6839(1)	5891(1)	5200(1)	20(1)
C(18)	9216(2)	4802(1)	12634(2)	34(1)
C(19)	3877(2)	7721(1)	1781(2)	35(1)
C(20)	4581(2)	5918(1)	-95(2)	28(1)
C(21)	6863(2)	4469(1)	4739(2)	39(1)

Table 3

KP84.

O(1)-C(2)	1.3792(16)
O(1)-C(18)	1.4236(18)
O(2)-C(14)	1.3737(15)
O(2)-C(19)	1.4168(17)
O(3)-C(15)	1.3772(15)
O(3)-C(20)	1.4335(16)
O(4)-C(16)	1.3719(16)
O(4)-C(21)	1.4250(17)
N(1)-C(1)	1.3996(17)
C(1)-C(6)	1.4005(18)
C(1)-C(2)	1.4109(19)
C(2)-C(3)	1.3813(19)
C(3)-C(4)	1.3888(19)
C(4)-C(5)	1.3920(19)
C(5)-C(6)	1.4160(18)
C(5)-C(11)	1.4949(17)
C(6)-C(7)	1.5145(18)
C(7)-C(8)	1.5378(19)
C(8)-C(9)	1.540(2)
C(9)-C(10)	1.5065(17)
C(10)-C(11)	1.3443(19)
C(11)-C(12)	1.4914(17)
C(12)-C(13)	1.3971(18)
C(12)-C(17)	1.3973(18)
C(13)-C(14)	1.3883(17)
C(14)-C(15)	1.3960(18)
C(15)-C(16)	1.3917(18)
C(16)-C(17)	1.3917(17)
C(2)-O(1)-C(18)	116.82(11)
C(14)-O(2)-C(19)	117.55(10)
C(15)-O(3)-C(20)	115.77(10)

C(16)-O(4)-C(21)	116.69(10)
N(1)-C(1)-C(6)	123.38(12)
N(1)-C(1)-C(2)	117.16(12)
C(6)-C(1)-C(2)	119.43(12)
O(1)-C(2)-C(3)	124.73(12)
O(1)-C(2)-C(1)	114.35(11)
C(3)-C(2)-C(1)	120.91(12)
C(2)-C(3)-C(4)	119.57(13)
C(3)-C(4)-C(5)	121.03(12)
C(4)-C(5)-C(6)	119.65(12)
C(4)-C(5)-C(11)	120.59(11)
C(6)-C(5)-C(11)	119.75(11)
C(1)-C(6)-C(5)	119.38(12)
C(1)-C(6)-C(7)	121.43(12)
C(5)-C(6)-C(7)	119.15(11)
C(6)-C(7)-C(8)	113.99(11)
C(7)-C(8)-C(9)	111.31(11)
C(10)-C(9)-C(8)	112.92(11)
C(11)-C(10)-C(9)	122.79(12)
C(10)-C(11)-C(12)	121.53(12)
C(10)-C(11)-C(5)	120.34(11)
C(12)-C(11)-C(5)	118.07(11)
C(13)-C(12)-C(17)	118.98(11)
C(13)-C(12)-C(11)	120.63(12)
C(17)-C(12)-C(11)	120.31(11)
C(14)-C(13)-C(12)	120.12(12)
O(2)-C(14)-C(13)	124.41(12)
O(2)-C(14)-C(15)	114.64(11)
C(13)-C(14)-C(15)	120.95(11)
O(3)-C(15)-C(16)	119.08(11)
O(3)-C(15)-C(14)	121.91(11)
C(16)-C(15)-C(14)	118.87(11)
O(4)-C(16)-C(15)	115.47(11)
O(4)-C(16)-C(17)	124.07(11)
C(15)-C(16)-C(17)	120.46(12)
C(16)-C(17)-C(12)	120.55(12)

Table 4

($Å^2 x\ 10^3$) for KP84. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	28(1)	34(1)	26(1)	11(1)	8(1)	0(1)
O(2)	24(1)	19(1)	23(1)	1(1)	-1(1)	2(1)
O(3)	29(1)	23(1)	16(1)	-2(1)	4(1)	-8(1)
O(4)	39(1)	17(1)	21(1)	-2(1)	3(1)	2(1)
N(1)	20(1)	37(1)	25(1)	7(1)	5(1)	-1(1)
C(1)	18(1)	24(1)	20(1)	-2(1)	7(1)	0(1)
C(2)	25(1)	23(1)	18(1)	2(1)	7(1)	1(1)
C(3)	24(1)	24(1)	24(1)	1(1)	10(1)	-4(1)
C(4)	19(1)	26(1)	21(1)	-2(1)	6(1)	-2(1)
C(5)	20(1)	20(1)	17(1)	-3(1)	7(1)	0(1)
C(6)	20(1)	21(1)	18(1)	-2(1)	8(1)	-1(1)
C(7)	20(1)	27(1)	21(1)	1(1)	8(1)	-2(1)
C(8)	25(1)	26(1)	22(1)	-2(1)	7(1)	-7(1)
C(9)	27(1)	21(1)	22(1)	-4(1)	7(1)	-2(1)
C(10)	22(1)	22(1)	20(1)	-1(1)	6(1)	1(1)
C(11)	18(1)	22(1)	18(1)	-2(1)	6(1)	1(1)
C(12)	18(1)	21(1)	18(1)	-1(1)	7(1)	-2(1)
C(13)	21(1)	17(1)	23(1)	-2(1)	7(1)	0(1)
C(14)	16(1)	20(1)	20(1)	2(1)	4(1)	-1(1)
C(15)	19(1)	22(1)	17(1)	-2(1)	6(1)	-4(1)
C(16)	22(1)	17(1)	21(1)	0(1)	9(1)	-1(1)
C(17)	21(1)	20(1)	17(1)	1(1)	6(1)	1(1)
C(18)	37(1)	34(1)	34(1)	12(1)	16(1)	1(1)
C(19)	31(1)	19(1)	39(1)	1(1)	-3(1)	3(1)
C(20)	36(1)	30(1)	20(1)	-1(1)	10(1)	0(1)
C(21)	51(1)	19(1)	31(1)	3(1)	0(1)	2(1)

Table 5

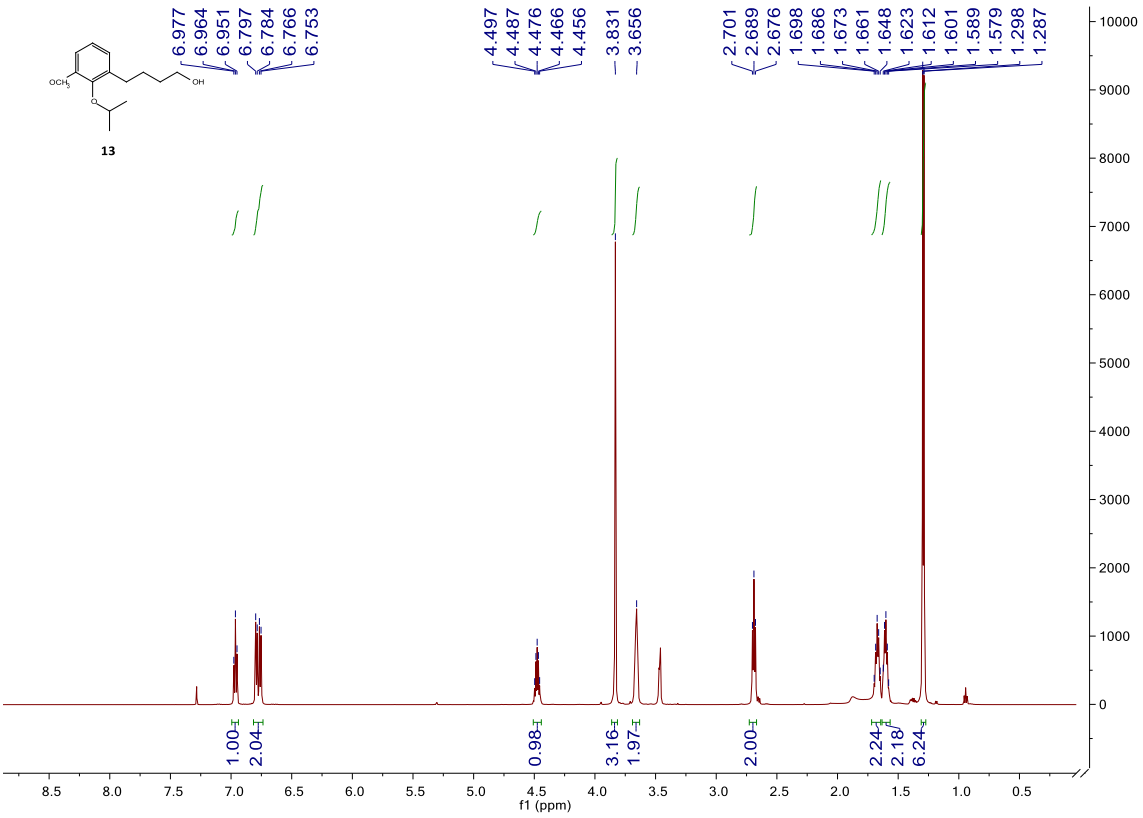
[Å and °].

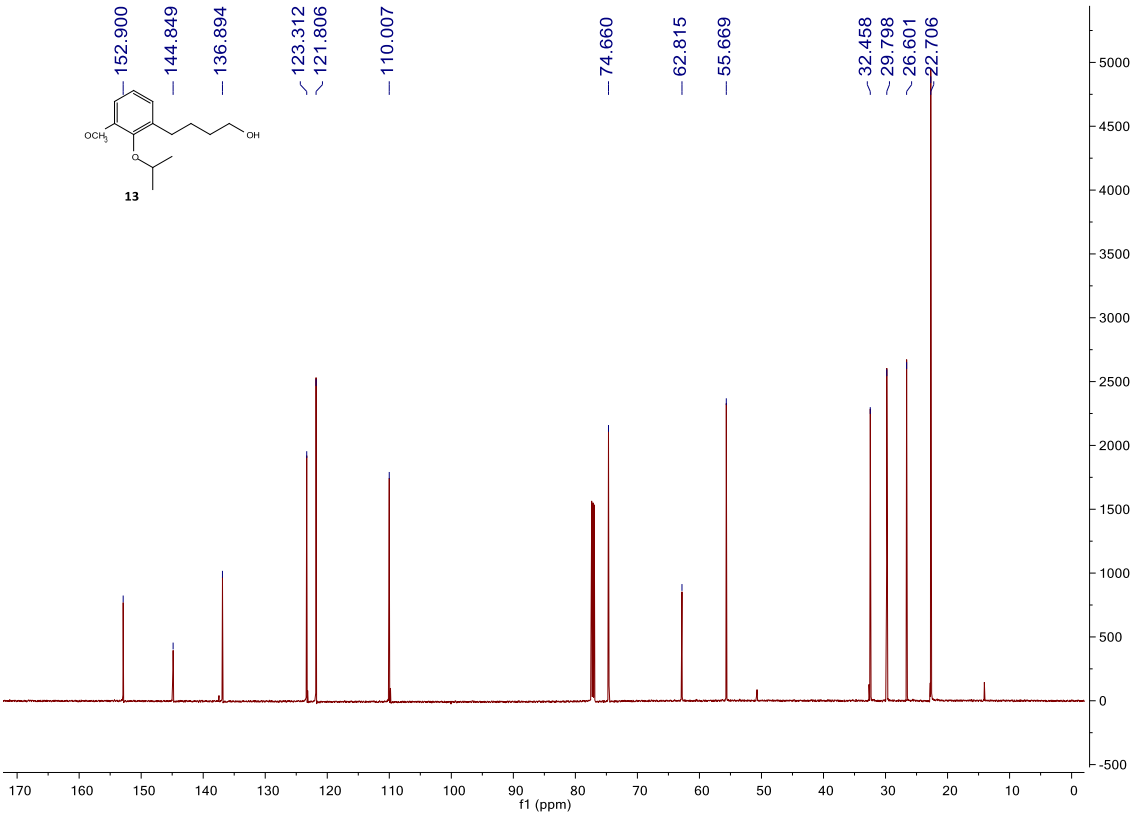
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1)...O(2)#1	0.88(2)	2.37(2)	3.1393(17)	147.0(16)

Symmetry transformations used to generate equivalent atoms:

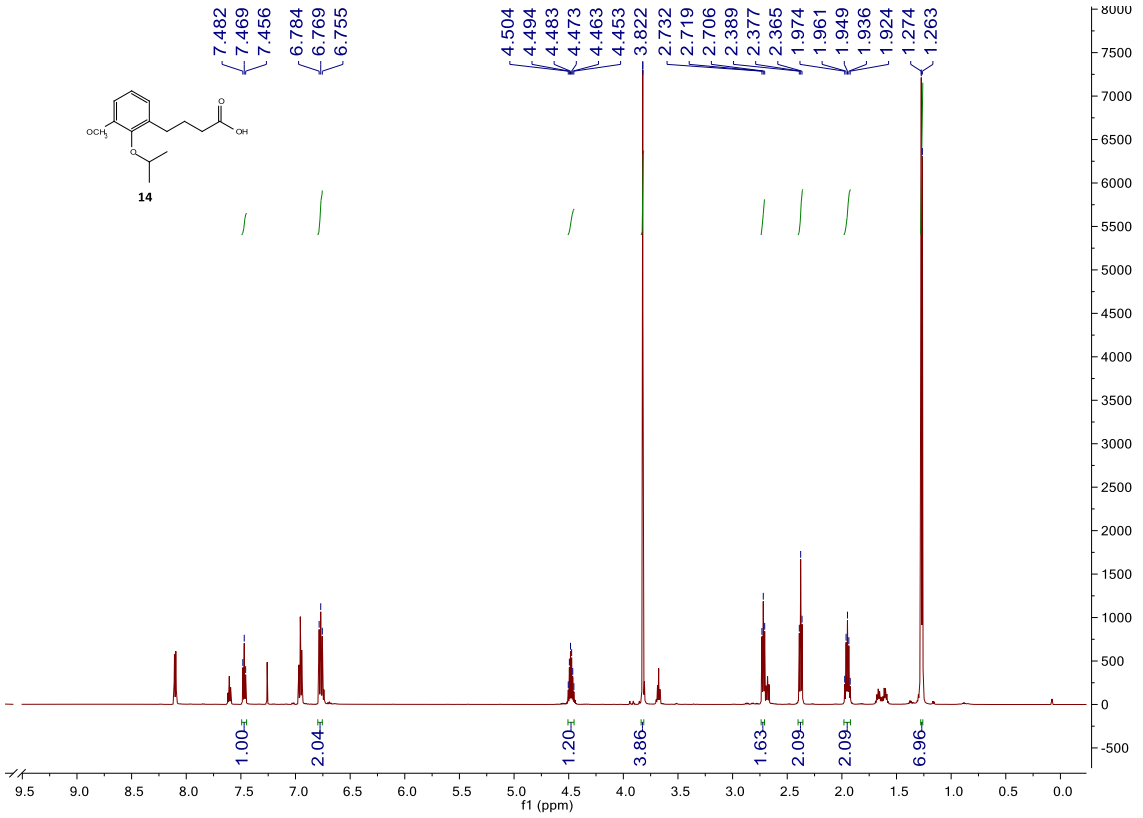
#1 x+1,y,z+1

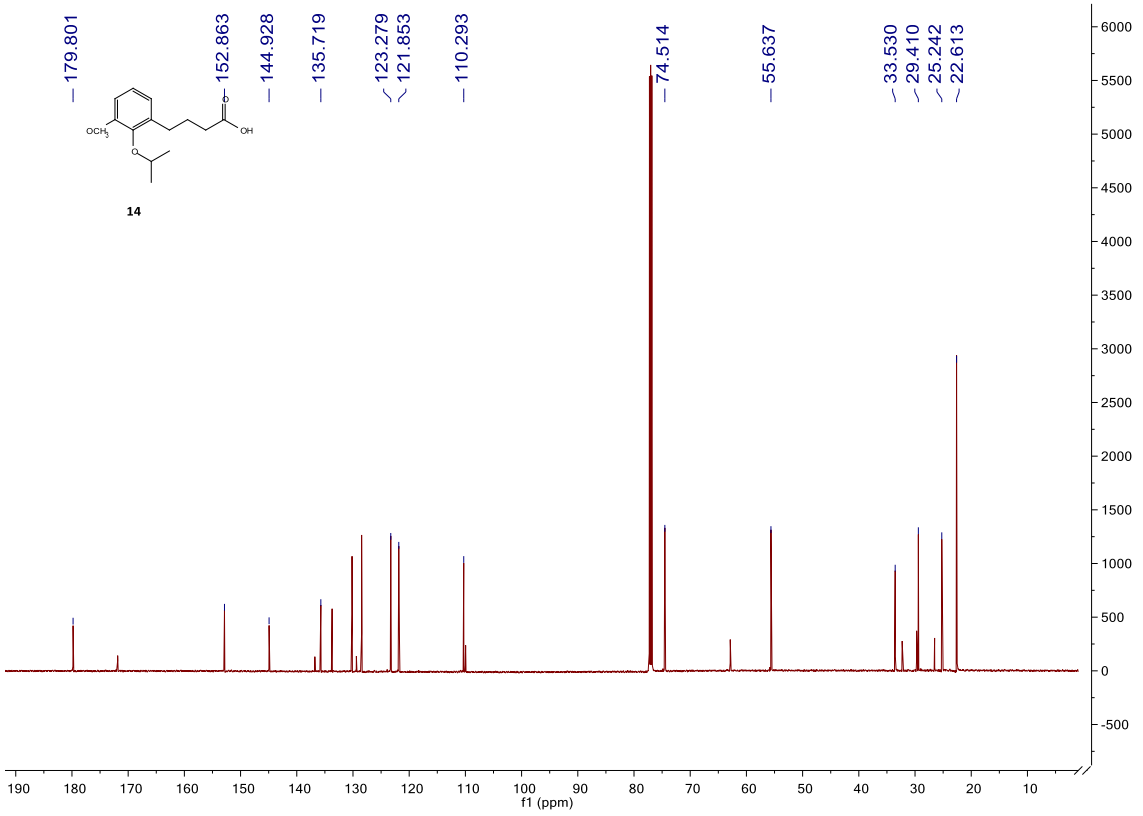
4-(2-isopropoxy-3-methoxyphenyl)butan-1-ol



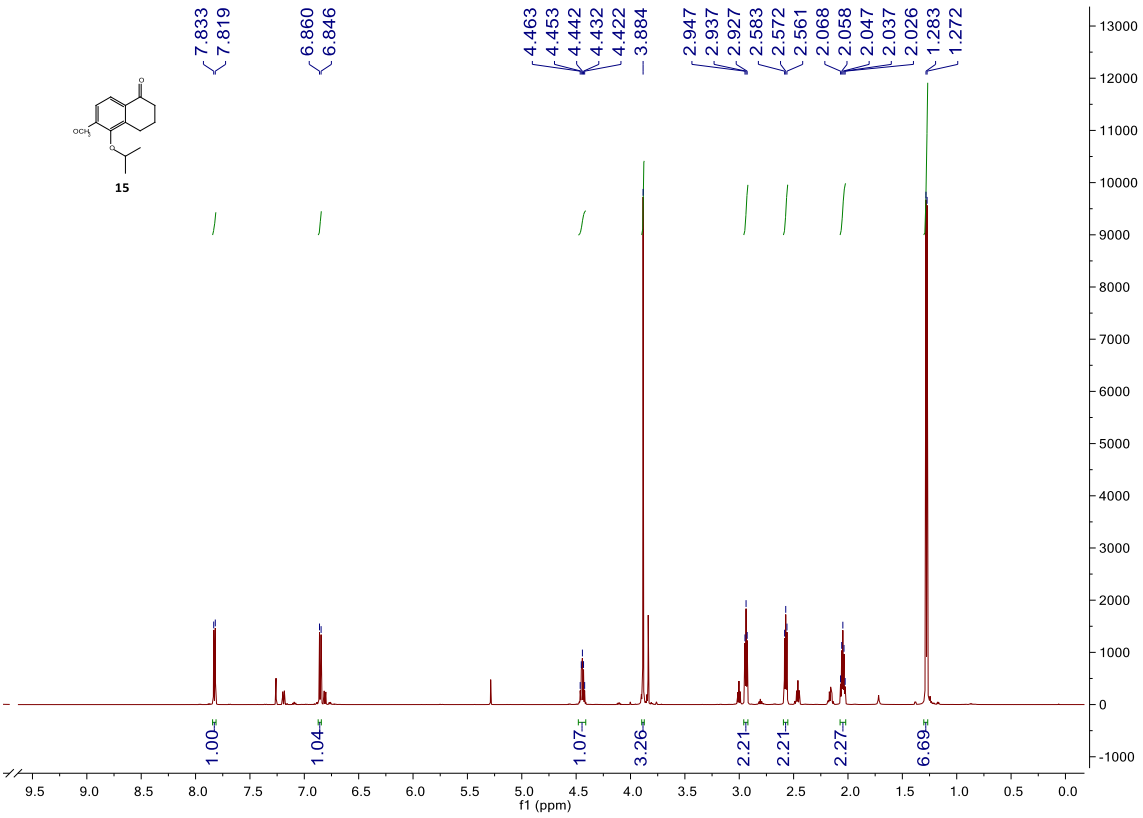


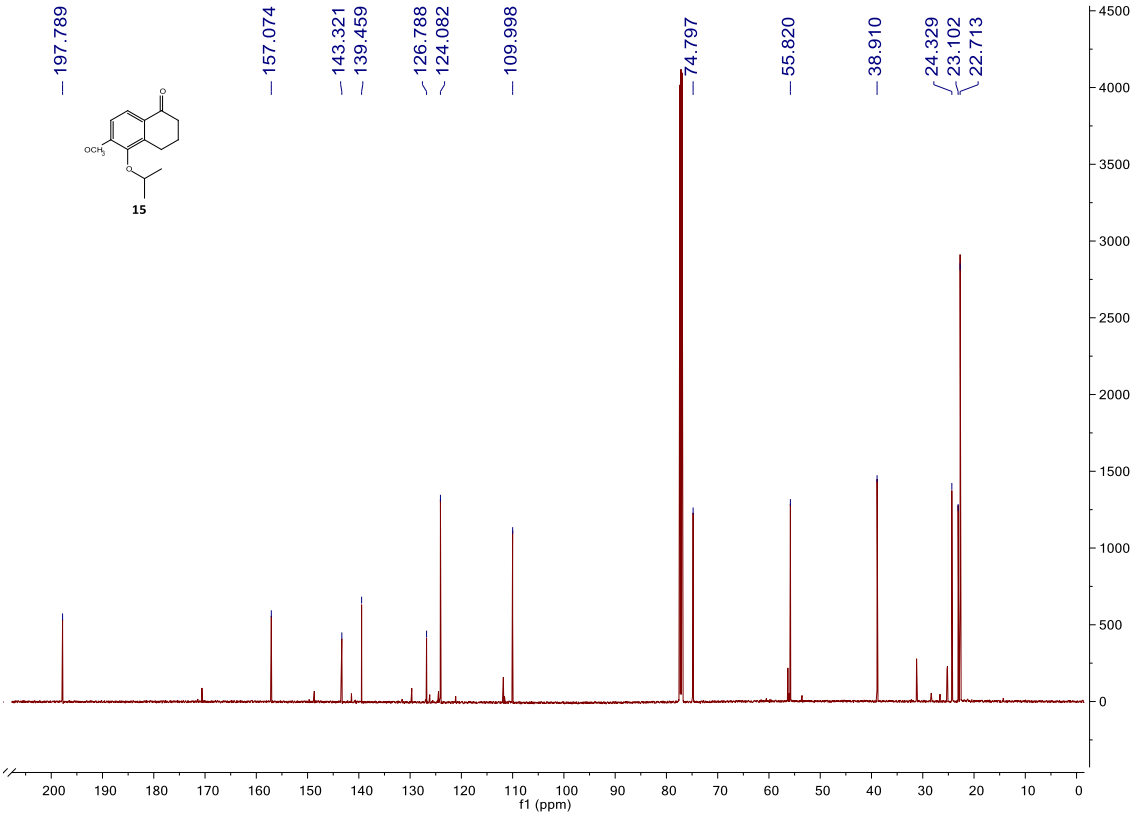
4-(2-isopropoxy-3-methoxyphenyl)butanoic acid



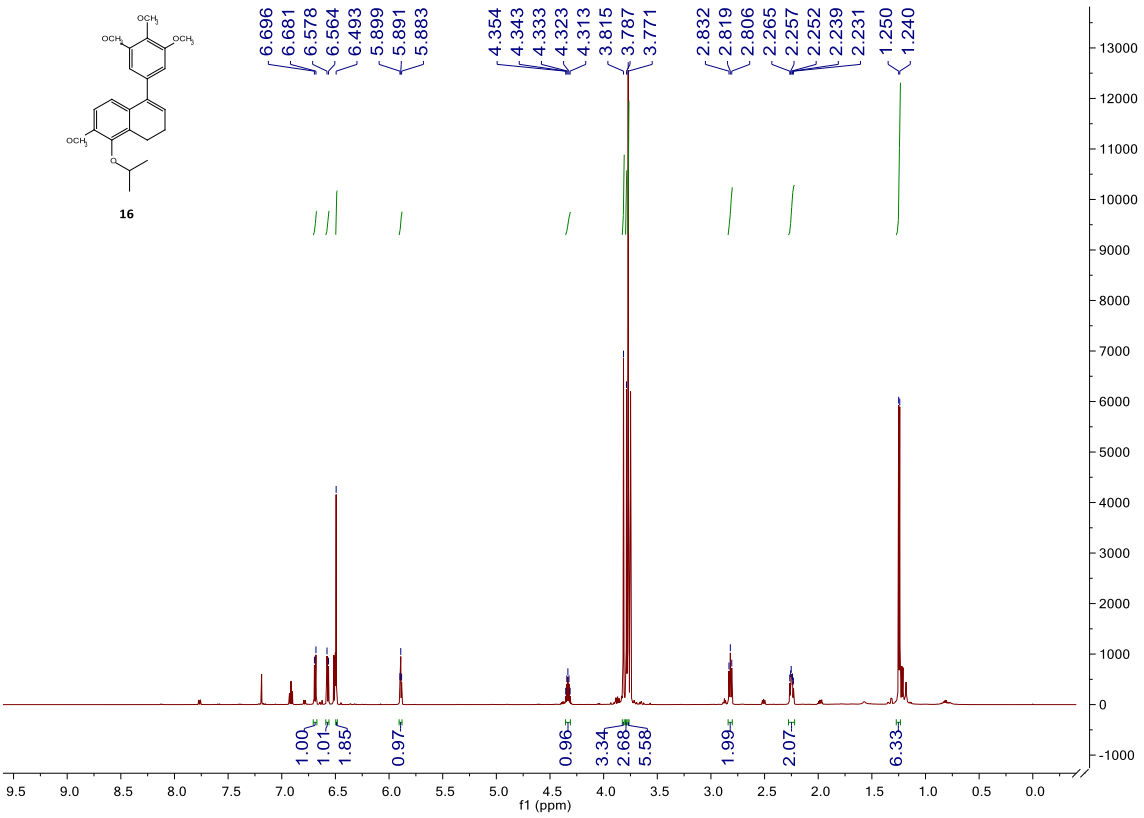


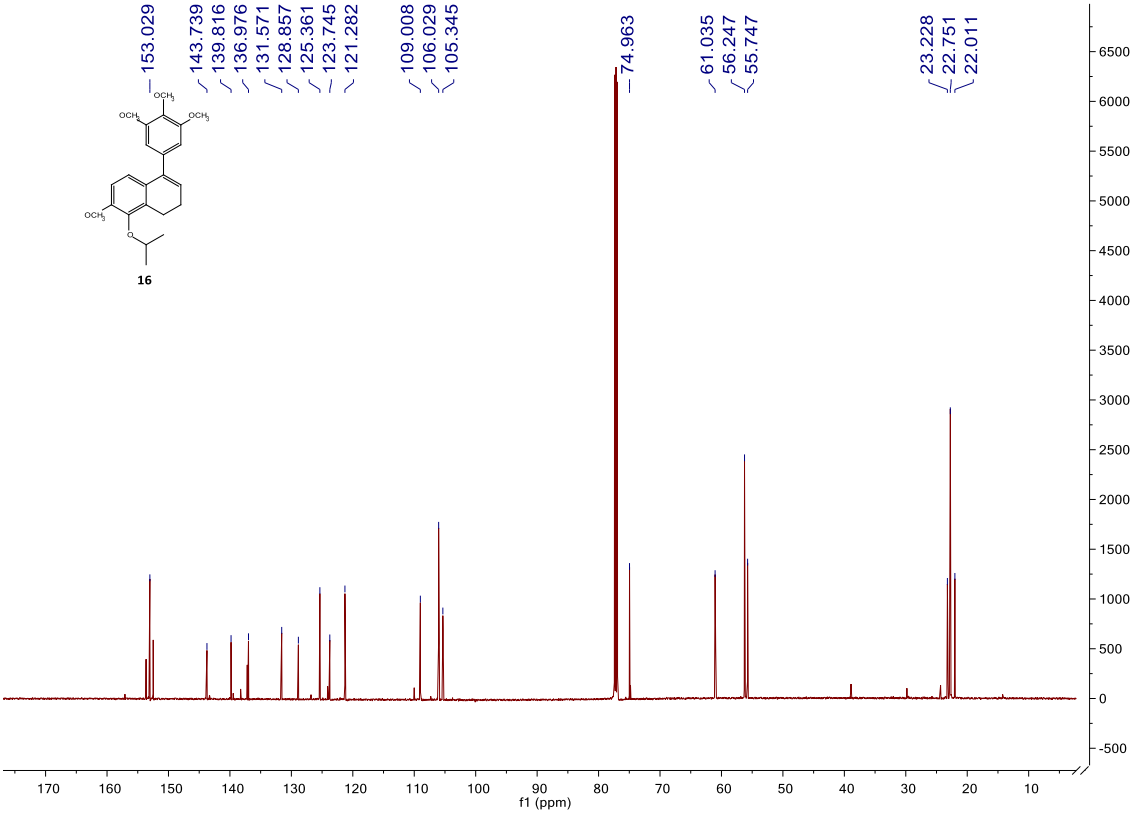
5-isopropoxy-6-methoxy-3,4-dihydronaphthalen-1(2H)-one



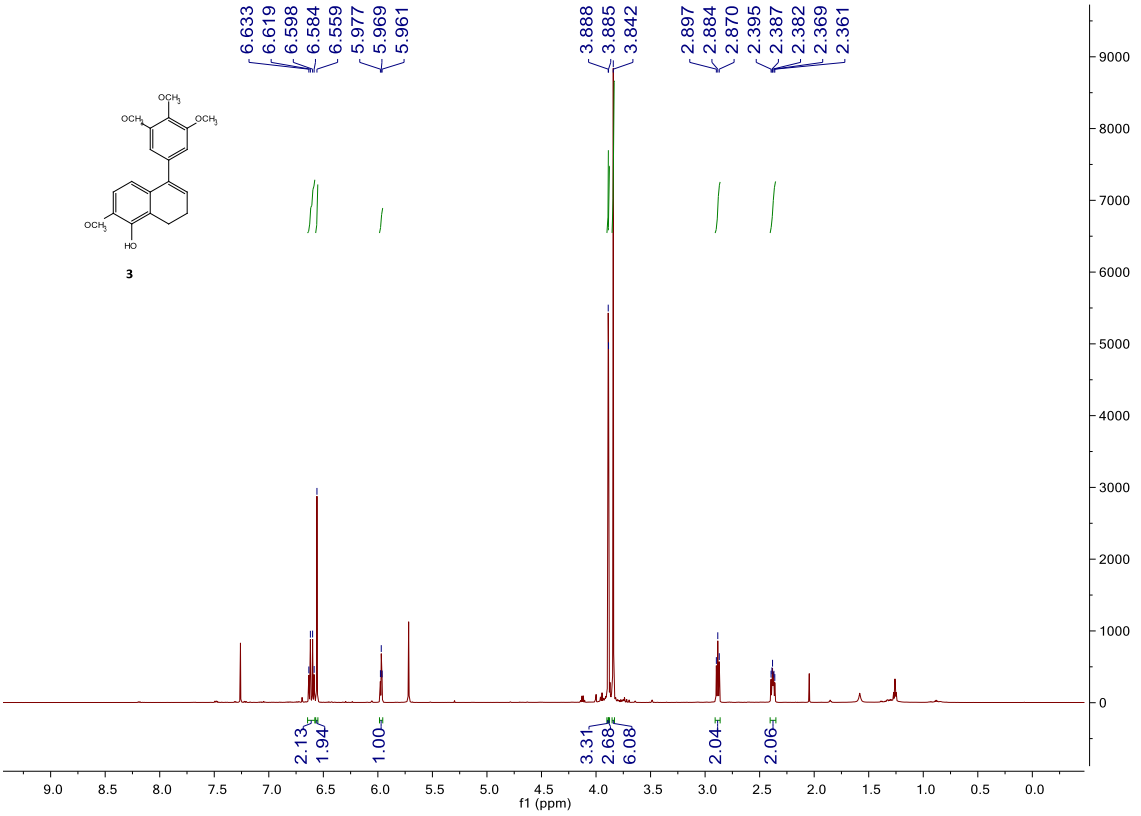


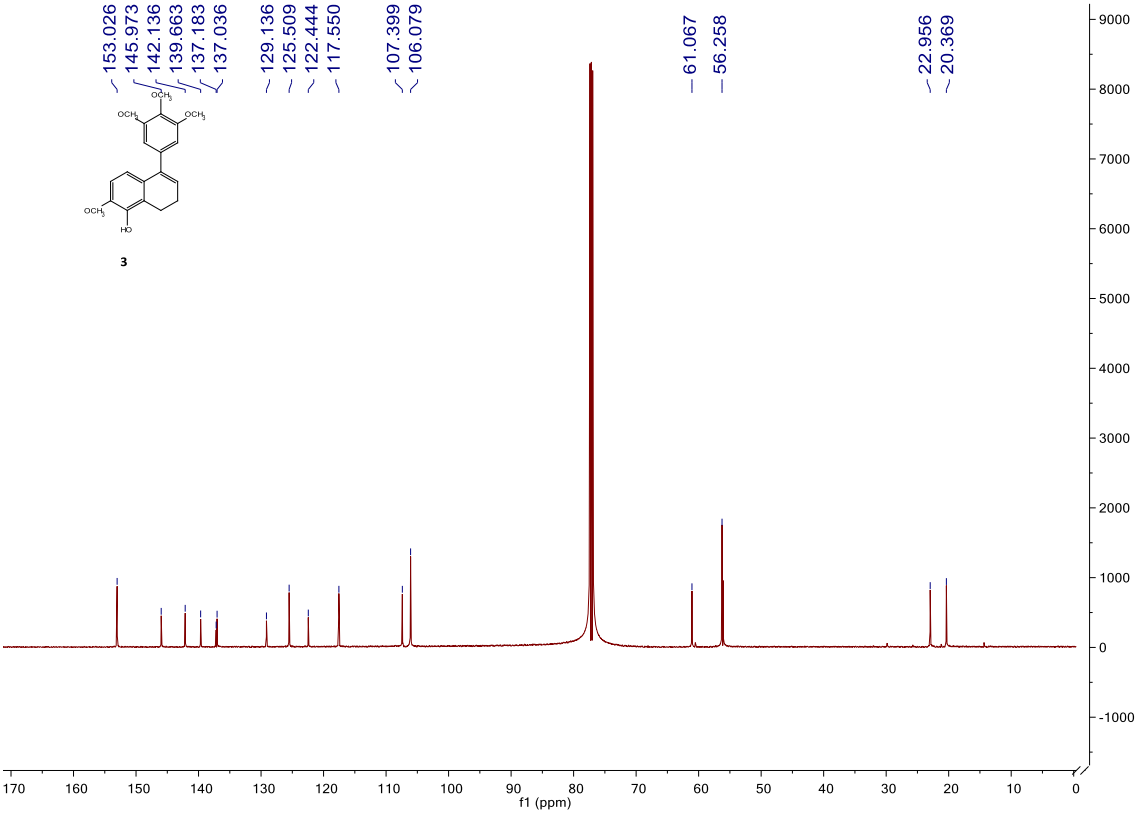
8-isopropoxy-7-methoxy-4-(3,4,5-trimethoxyphenyl)-1,2-dihydronaphthalene





2-methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-ol





C:\Xcalibur\...\21-Feb-2018\Oxi6196_+ESI 2/21/2018 8:14:30 AM

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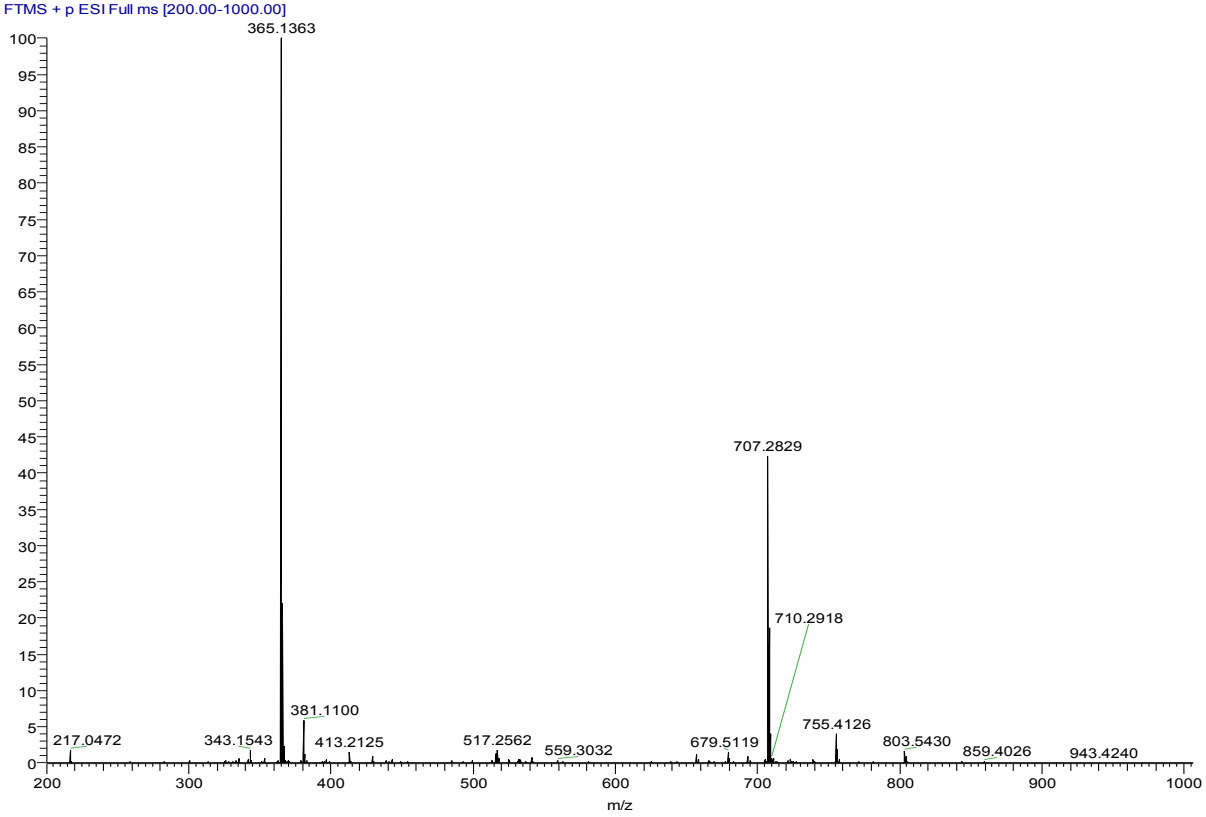
T: FTMS + p ESI Full ms [200.00-1000.00]



Data File C:\Chem32\1\Data\NHC\Oxi6196_NewRoute_Concentrated.D
Sample Name: Oxi6196_NewRoute_Concentrated

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Sample Operator : SYSTEM
Acq. Instrument : 1200 HPLC                    Location :   1
Injection Date  : 2/23/2018 2:00:43 PM
                                             Inj Volume : No inj
Acq. Method     : C:\CHEM32\1\METHODS\MASTERMETHOD2.M
Last changed    : 12/2/2015 12:37:42 PM by Eric Lin
Analysis Method : C:\Users\CHEMISTRY\Desktop\CHRISTINE\VANIHINGEDPHEN1.D\ACQ.M
Last changed    : 6/18/2014 3:18:53 PM by Christine
Additional Info : Peak(s) manually integrated
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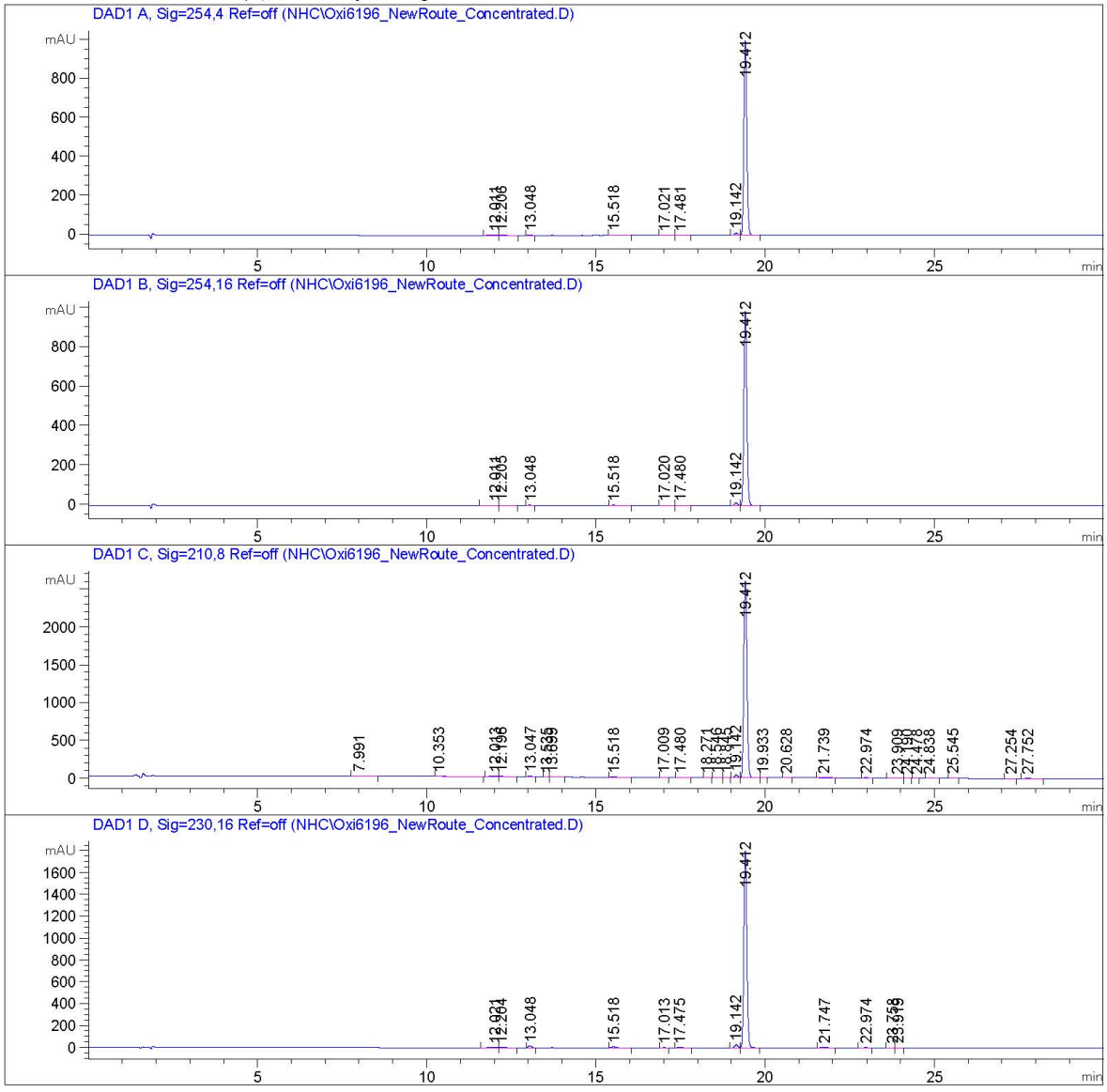
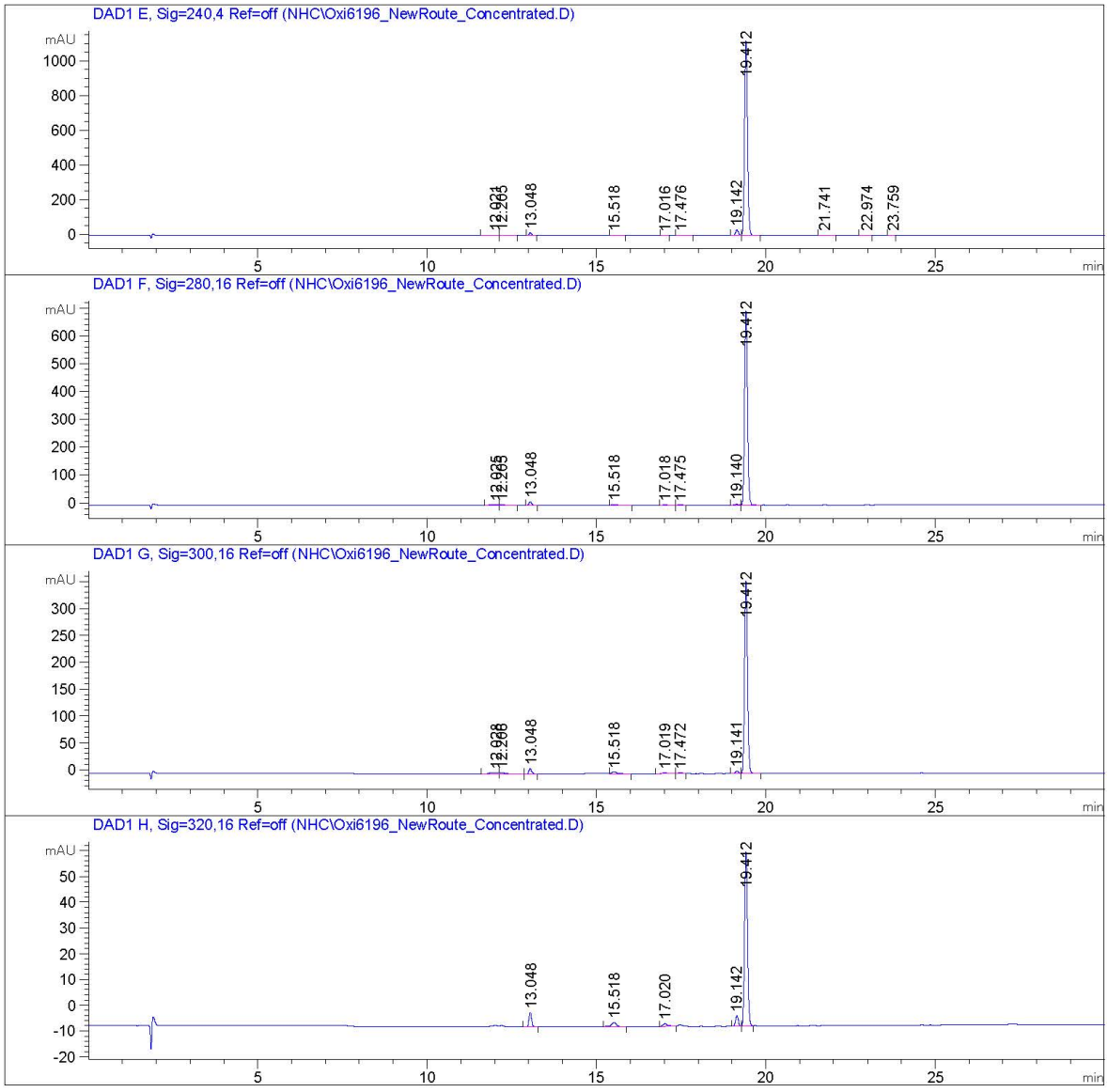


Data File C:\Chem32\1\Data\NHC\Oxi6196_NewRoute_Concentrated.D
Sample Name: Oxi6196_NewRoute_Concentrated



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Data File C:\Chem32\1\Data\NHC\Oxi6196_NewRoute_Concentrated.D
Sample Name: Oxi6196_NewRoute_Concentrated

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.011	BV	0.2356	25.94462	1.54712	0.4153
2	12.206	VB	0.1592	15.38476	1.45636	0.2463
3	13.048	BB	0.0815	14.16903	2.68909	0.2268
4	15.518	BB	0.1419	22.86301	2.51919	0.3660
5	17.021	BV	0.1589	13.92447	1.28000	0.2229
6	17.481	VB	0.1641	19.77390	1.92113	0.3165
7	19.142	BV	0.0931	69.27430	11.69412	1.1089
8	19.412	VB	0.0930	6065.64063	997.05682	97.0972
Totals :				6246.97471	1020.16384	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.011	BV	0.2370	28.48997	1.65403	0.4590
2	12.205	VB	0.1612	16.67857	1.55450	0.2687
3	13.048	BB	0.0816	18.67237	3.53612	0.3009
4	15.518	BB	0.1403	23.33660	2.61046	0.3760
5	17.020	BV	0.1597	13.83091	1.26343	0.2228
6	17.480	VB	0.1620	20.06612	1.98399	0.3233
7	19.142	BV	0.0931	85.47532	14.42553	1.3772
8	19.412	VB	0.0930	5999.91992	986.17603	96.6720
Totals :				6206.46979	1013.20409	

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.991	BB	0.2184	35.31418	2.18658	0.1932
2	10.353	BB	0.1655	20.85667	1.62749	0.1141
3	12.013	BV	0.2216	59.31018	3.72882	0.3244
4	12.196	VB	0.1565	32.59122	3.15524	0.1783
5	13.047	VB	0.0823	86.97964	16.30069	0.4758
6	13.535	BV	0.0798	12.35308	2.40875	0.0676
7	13.699	VB	0.0836	15.58864	2.85865	0.0853
8	15.518	VB	0.1527	59.03706	5.90197	0.3229
9	17.009	BV	0.1354	15.70359	1.80748	0.0859
10	17.480	BB	0.1542	45.39658	4.71963	0.2483
11	18.271	VB	0.0972	8.59195	1.37032	0.0470
12	18.546	BV	0.1449	10.00587	1.05247	0.0547
13	18.845	VB	0.0950	14.51705	2.38708	0.0794
14	19.142	BV	0.0930	220.43597	37.28934	1.2058
15	19.412	VB	0.1060	1.73615e4	2596.37451	94.9662

Data File C:\Chem32\1\Data\NHC\Oxi6196_NewRoute_Concentrated.D
Sample Name: Oxi6196_NewRoute_Concentrated

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
16	19.933	BB	0.0897	6.82932	1.21207	0.0374
17	20.628	BB	0.0967	9.46331	1.51932	0.0518
18	21.739	BB	0.1556	49.15228	4.42618	0.2689
19	22.974	BB	0.0936	44.94076	7.53022	0.2458
20	23.909	BV	0.1532	29.23256	2.63901	0.1599
21	24.190	VB	0.1091	10.51668	1.47666	0.0575
22	24.478	BV	0.0971	7.24885	1.12658	0.0397
23	24.838	BB	0.1045	9.10787	1.32030	0.0498
24	25.545	BB	0.1035	37.75469	5.68167	0.2065
25	27.254	BB	0.1038	8.03404	1.14575	0.0439
26	27.752	BB	0.1672	71.31586	6.53935	0.3901
Totals :				1.82818e4	2717.78615	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.021	BV	0.2296	62.34489	3.75715	0.5322
2	12.204	VB	0.1584	37.81323	3.54563	0.3228
3	13.048	BB	0.0815	91.62273	17.37372	0.7821
4	15.518	VB	0.1497	57.70858	5.92378	0.4926
5	17.013	BB	0.1243	9.67194	1.25019	0.0826
6	17.475	BB	0.1260	33.38165	3.89394	0.2849
7	19.142	BV	0.0934	169.20265	28.44065	1.4443
8	19.412	VV	0.0985	1.11758e4	1798.08618	95.3932
9	21.747	VV	0.2146	43.50099	2.97559	0.3713
10	22.974	BB	0.0951	17.62972	2.89247	0.1505
11	23.758	BV	0.0988	6.95548	1.05711	0.0594
12	23.919	VV	0.1050	9.87603	1.42280	0.0843
Totals :				1.17155e4	1870.61921	

Signal 5: DAD1 E, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.021	BV	0.2334	52.25179	3.11979	0.7127
2	12.205	VB	0.1585	31.45958	2.94728	0.4291
3	13.048	BB	0.0817	84.91316	16.04879	1.1582
4	15.518	VB	0.1429	41.86513	4.56853	0.5710
5	17.016	BB	0.1222	7.97453	1.03152	0.1088
6	17.476	BB	0.1287	25.47445	2.89384	0.3475
7	19.142	BV	0.0929	191.41354	32.41834	2.6108
8	19.412	VB	0.0931	6850.16895	1123.72144	93.4336
9	21.741	BB	0.2086	26.25027	1.86012	0.3580
10	22.974	BB	0.0966	11.58485	1.81287	0.1580
11	23.759	BV	0.1015	8.23751	1.23984	0.1124

Data File C:\Chem32\1\Data\NHC\Oxi6196_NewRoute_Concentrated.D
Sample Name: Oxi6196_NewRoute_Concentrated

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
Totals :				7331.59376	1191.66235	

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.025	BV	0.2307	30.08454	1.80283	0.6769
2	12.205	VB	0.1615	18.88387	1.75569	0.4249
3	13.048	BB	0.0822	66.79344	12.53245	1.5029
4	15.518	VB	0.1409	24.04367	2.67373	0.5410
5	17.018	BB	0.1511	12.90658	1.26475	0.2904
6	17.475	BB	0.1151	12.46462	1.63150	0.2805
7	19.140	BV	0.0975	27.22408	4.32105	0.6126
8	19.412	VB	0.0930	4251.80273	698.98523	95.6707
Totals :				4444.20353	724.96722	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.028	BV	0.2298	33.37157	1.98810	1.4075
2	12.206	VB	0.1653	22.04439	1.95810	0.9298
3	13.048	BB	0.0824	47.94264	8.96929	2.0221
4	15.518	VB	0.1414	31.09973	3.44276	1.3117
5	17.019	BV	0.1497	15.24822	1.51207	0.6431
6	17.472	VB	0.1131	12.22469	1.63713	0.5156
7	19.141	BV	0.0955	29.54172	4.82335	1.2460
8	19.412	VB	0.0930	2179.48535	357.97537	91.9242
Totals :				2370.95831	382.30618	

Signal 8: DAD1 H, Sig=320,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.048	BB	0.0825	29.69995	5.54493	6.0118
2	15.518	BB	0.1560	16.48550	1.60261	3.3370
3	17.020	BB	0.1423	10.87157	1.12949	2.2006
4	19.142	BV	0.0916	23.17568	4.00192	4.6912
5	19.412	VB	0.0932	413.79181	67.79539	83.7594
Totals :				494.02451	80.07434	

Data File C:\Chem32\1\Data\NHC\Oxi6196_NewRoute_Concentrated.D
Sample Name: Oxi6196_NewRoute_Concentrated

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*** End of Report ***

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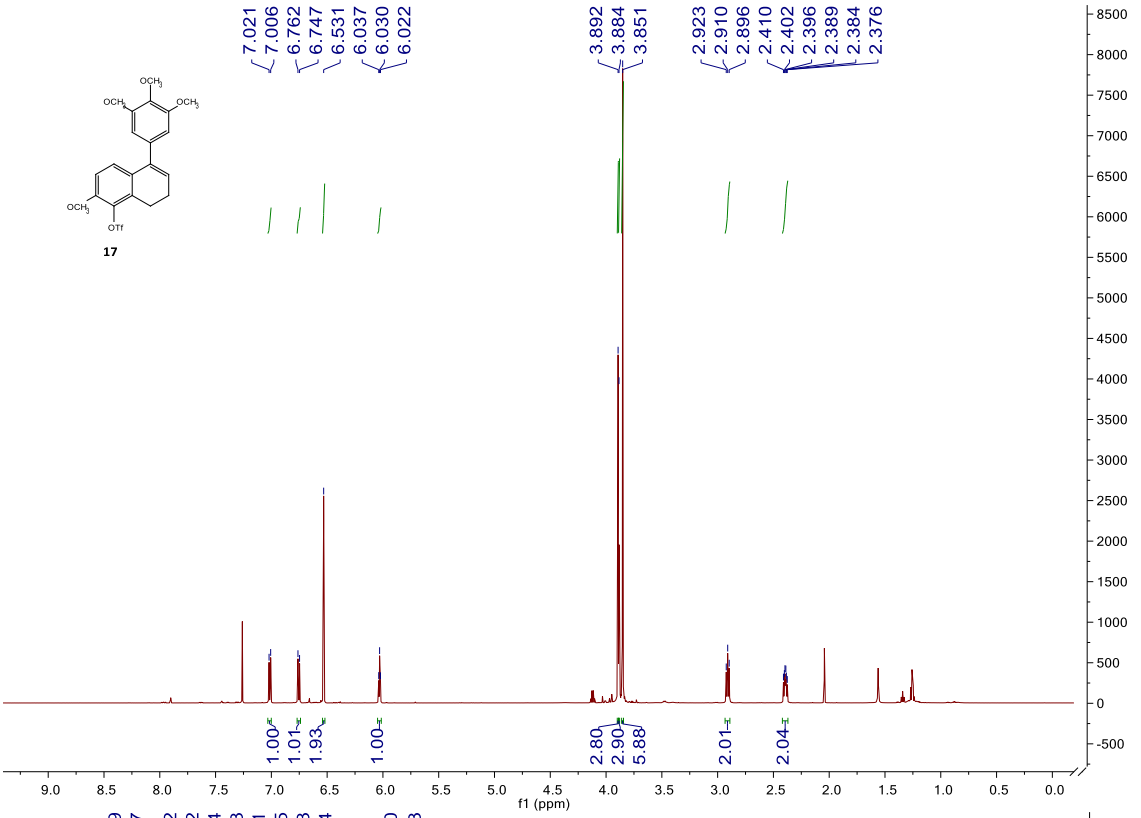

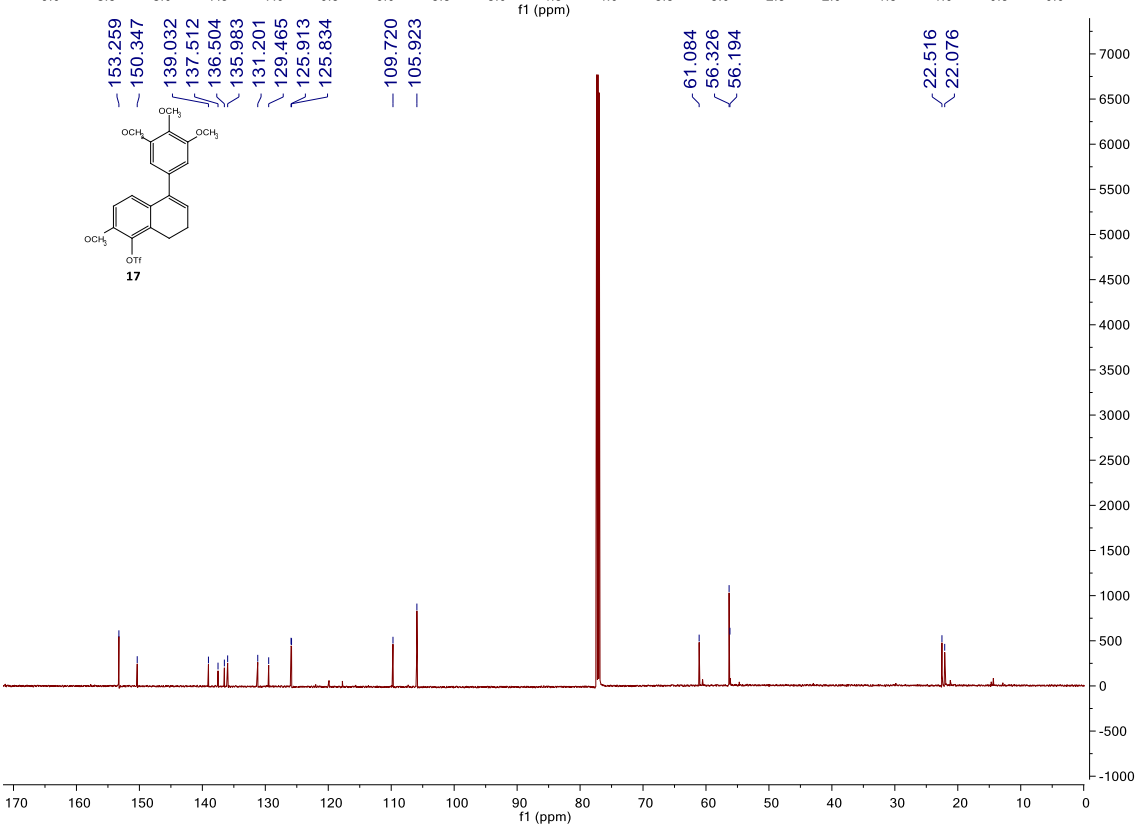

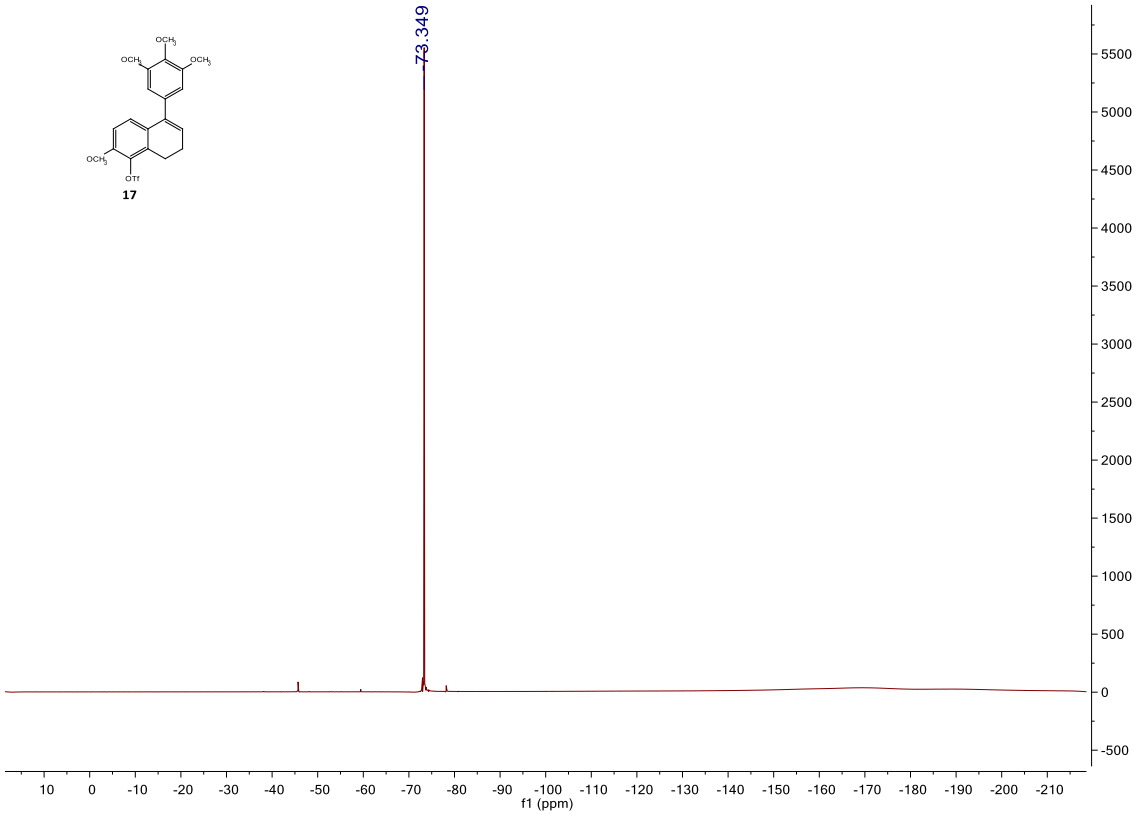
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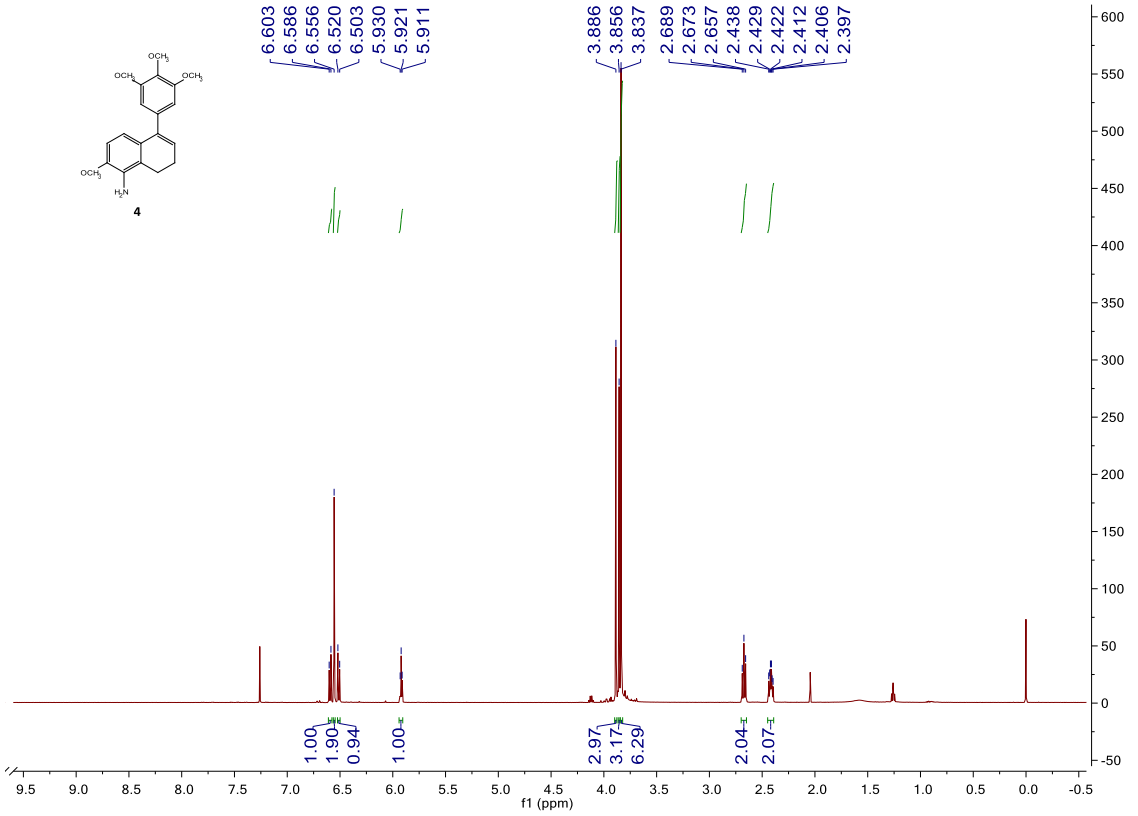
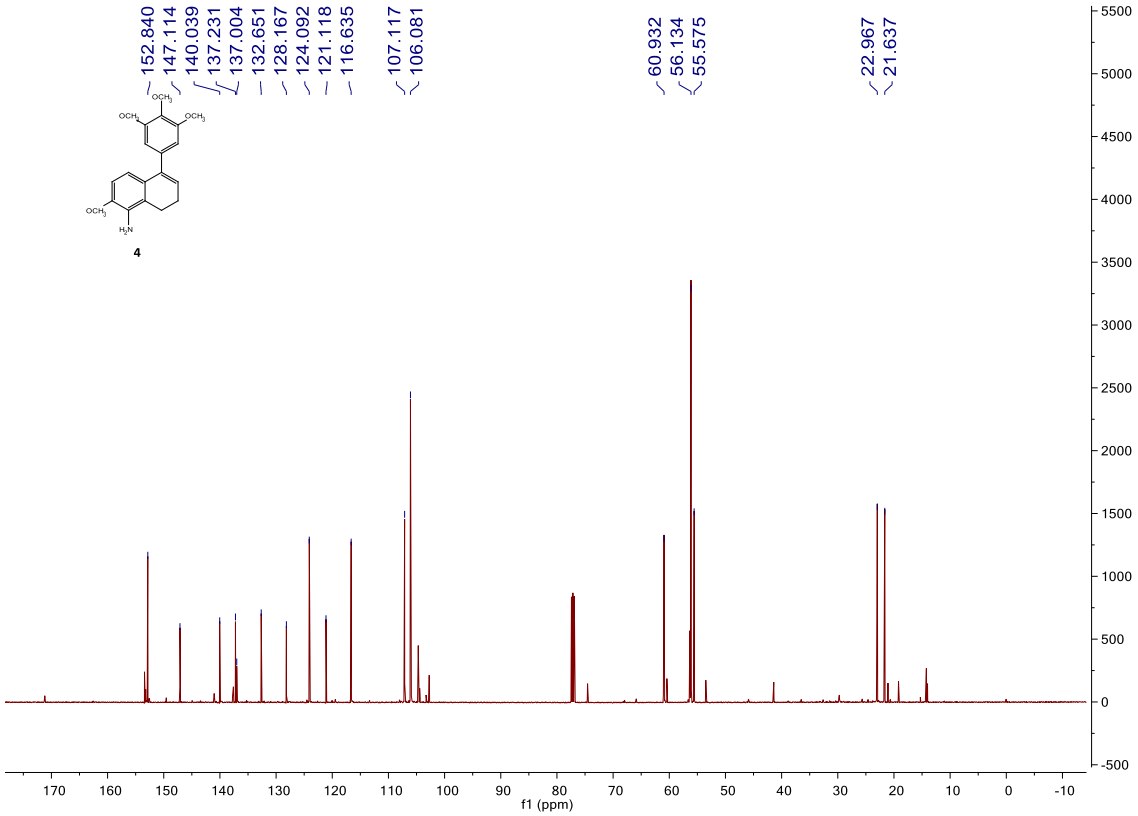
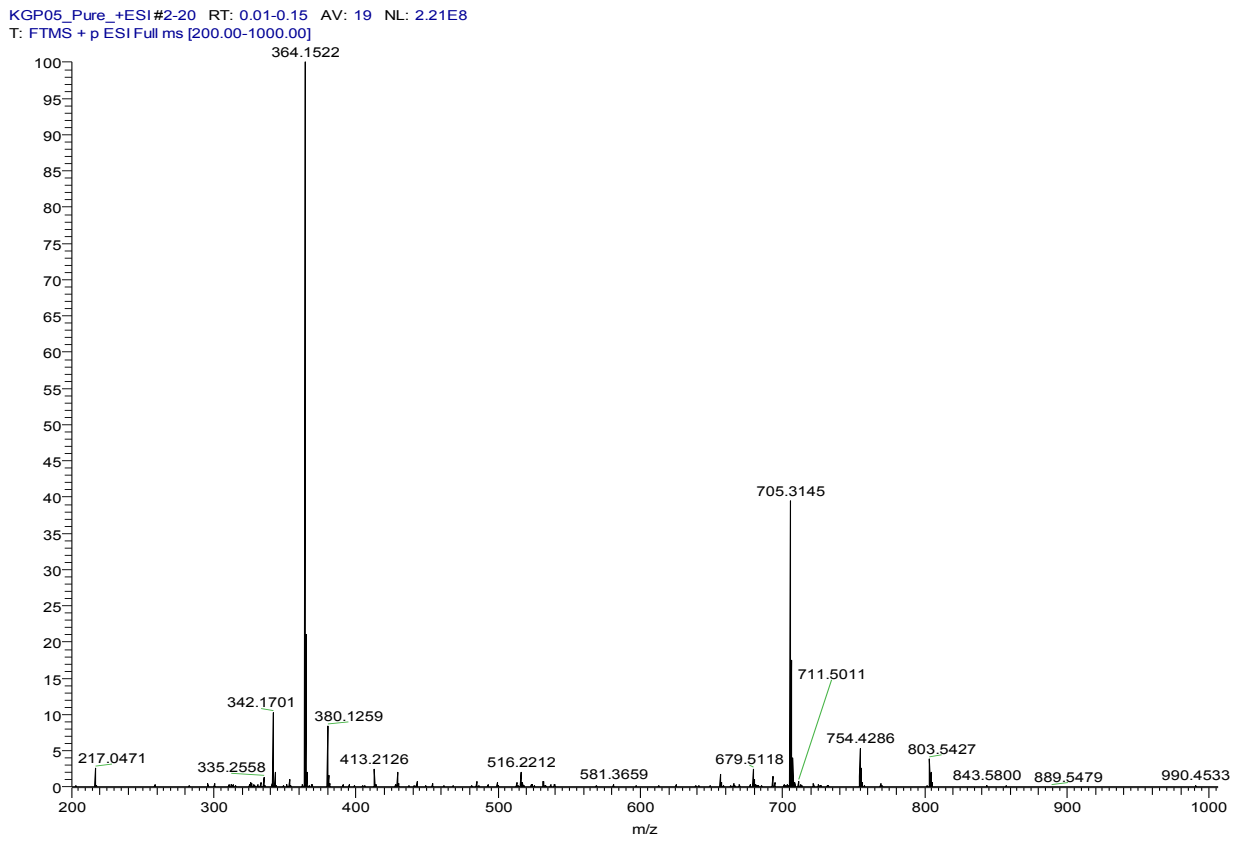
f1 (ppm)

2-methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-amine



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Data File C:\Chem32\1\Data\NHC\KGP05_NewRoute.D
Sample Name: KGP05_NewRoute

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Acq. Operator   : SYSTEM
Sample Operator : SYSTEM
Acq. Instrument : 1200 HPLC                    Location :   1
Injection Date  : 2/23/2018 4:37:30 PM
                                             Inj Volume : No inj
Acq. Method     : C:\CHEM32\1\METHODS\MASTERMETHOD2.M
Last changed    : 12/2/2015 12:37:42 PM by Eric Lin
Analysis Method : C:\Users\CHEMISTRY\Desktop\CHRISTINE\VANIHINGEDPHEN1.D\ACQ.M
Last changed    : 6/18/2014 3:18:53 PM by Christine
Additional Info : Peak(s) manually integrated
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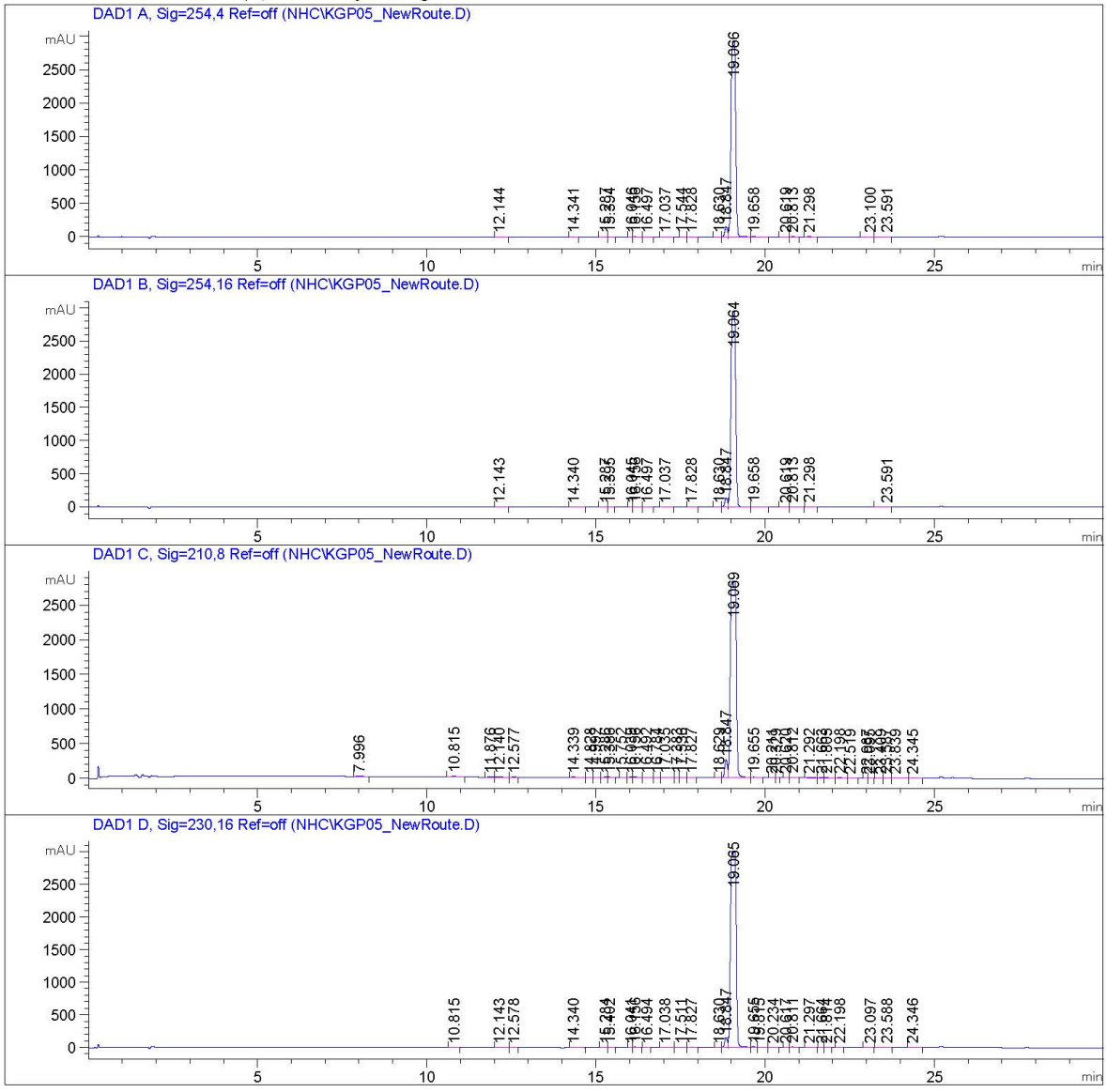
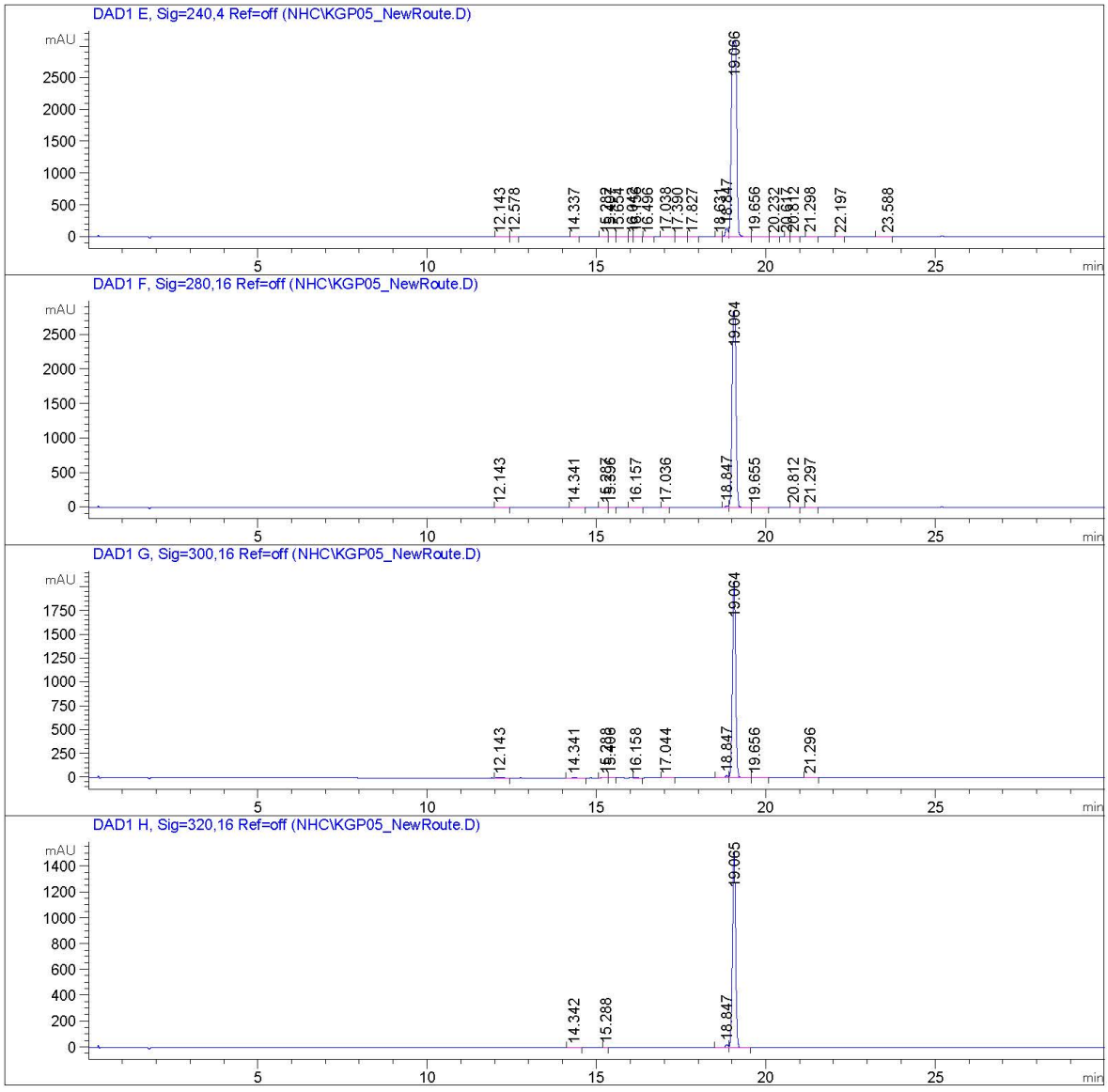


Data File C:\Chem32\1\Data\NHC\KGP05_NewRoute.D
Sample Name: KGP05_NewRoute



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Area Percent Report

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Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Data File C:\Chem32\1\Data\NHC\KGP05_NewRoute.D
Sample Name: KGP05_NewRoute

Signal 1: DAD1 A, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.144	BB	0.1456	11.43589	1.26316	0.0407
2	14.341	BB	0.0934	10.43205	1.75395	0.0371
3	15.287	BV	0.0885	21.39037	3.53788	0.0760
4	15.394	VB	0.1050	12.59640	1.90868	0.0448
5	16.046	BV	0.0705	9.21967	1.97350	0.0328
6	16.156	VB	0.0902	28.19130	4.68357	0.1002
7	16.497	BV	0.1267	9.51598	1.10252	0.0338
8	17.037	BB	0.1121	23.20277	3.07219	0.0825
9	17.544	VB	0.1076	7.16592	1.00014	0.0255
10	17.828	BB	0.0900	8.81138	1.46926	0.0313
11	18.630	BV	0.0927	18.56085	3.15008	0.0660
12	18.847	VV	0.0875	859.45300	153.07661	3.0555
13	19.066	VV	0.1513	2.69622e4	2932.58545	95.8548
14	19.658	VB	0.1475	50.49631	4.77099	0.1795
15	20.619	BV	0.1211	14.90903	1.82944	0.0530
16	20.813	VB	0.1103	24.79796	3.43096	0.0882
17	21.298	BB	0.1054	33.80489	4.84669	0.1202
18	23.100	BB	0.1118	7.52187	1.02297	0.0267
19	23.591	BV	0.1596	14.44914	1.22530	0.0514
Totals :				2.81281e4	3127.70334	

Signal 2: DAD1 B, Sig=254,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.143	BB	0.1473	11.92598	1.32108	0.0418
2	14.340	BB	0.0962	11.70246	1.83920	0.0410
3	15.287	BV	0.0896	20.99781	3.42119	0.0736
4	15.395	VB	0.1063	13.13152	1.95703	0.0460
5	16.045	BV	0.0734	9.74003	2.05064	0.0341
6	16.156	VB	0.0901	27.60028	4.59181	0.0968
7	16.497	BV	0.1270	9.36268	1.08142	0.0328
8	17.037	BB	0.1116	23.83972	3.17631	0.0836
9	17.828	BB	0.0897	8.39291	1.40479	0.0294
10	18.630	BV	0.0929	18.01997	3.05347	0.0632
11	18.847	VV	0.0874	788.60284	140.69543	2.7645
12	19.064	VV	0.1522	2.74400e4	2959.95923	96.1916
13	19.658	VB	0.1477	52.16078	4.91813	0.1829
14	20.619	BV	0.1234	14.76134	1.76743	0.0517
15	20.813	VB	0.1194	28.83435	3.60152	0.1011
16	21.298	BB	0.1057	32.89208	4.69830	0.1153
17	23.591	BV	0.1607	14.42984	1.21414	0.0506
Totals :				2.85264e4	3140.75114	

Data File C:\Chem32\1\Data\NHC\KGP05_NewRoute.D
Sample Name: KGP05_NewRoute

Signal 3: DAD1 C, Sig=210,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.996	BB	0.1789	20.50076	1.60581	0.0581
2	10.815	BB	0.1378	80.69191	9.43467	0.2287
3	11.876	BV	0.1140	19.06164	2.36648	0.0540
4	12.140	VB	0.1610	30.95048	3.03506	0.0877
5	12.577	BV	0.0994	28.59613	4.42572	0.0810
6	14.339	BB	0.0931	64.45770	10.57556	0.1827
7	14.828	BV	0.1045	9.47881	1.44551	0.0269
8	14.992	VB	0.0802	7.09835	1.33060	0.0201
9	15.286	BV	0.0895	49.88937	7.91920	0.1414
10	15.386	VB	0.1010	39.10905	5.92893	0.1108
11	15.752	VB	0.0983	9.28196	1.34815	0.0263
12	16.039	BV	0.0786	44.58123	8.58206	0.1263
13	16.156	VB	0.0914	69.80530	11.73819	0.1978
14	16.492	BV	0.1244	24.18276	2.86794	0.0685
15	16.784	VB	0.0898	8.85806	1.52453	0.0251
16	17.035	BB	0.1076	53.45822	7.46132	0.1515
17	17.383	BV	0.0842	7.50770	1.32349	0.0213
18	17.536	VB	0.1088	13.63358	1.83327	0.0386
19	17.827	BB	0.0855	22.02780	3.92107	0.0624
20	18.629	BB	0.0876	22.91023	4.20579	0.0649
21	18.847	BV	0.0864	1410.23096	255.45058	3.9963
22	19.069	VB	0.1914	3.28838e4	2832.92188	93.1865
23	19.655	BB	0.1186	56.15527	6.92900	0.1591
24	20.211	BV	0.1190	15.61918	2.09467	0.0443
25	20.329	VB	0.0747	6.53818	1.39390	0.0185
26	20.620	VV	0.1015	19.41312	2.92372	0.0550
27	20.812	VB	0.1085	75.65466	10.69636	0.2144
28	21.292	BB	0.1286	32.07181	3.57759	0.0909
29	21.663	BV	0.0972	11.49804	1.78341	0.0326
30	21.805	VV	0.1605	12.49424	1.03746	0.0354
31	22.198	VB	0.1137	21.77303	2.83249	0.0617
32	22.519	BB	0.1441	11.18503	1.05162	0.0317
33	22.987	BV	0.0868	10.11540	1.76788	0.0287
34	23.095	VB	0.0956	11.63191	1.84484	0.0330
35	23.409	BV	0.1091	7.58604	1.04029	0.0215
36	23.587	VV	0.1210	27.26513	3.27857	0.0773
37	23.839	VV	0.1833	33.10796	2.45590	0.0938
38	24.345	VB	0.1378	15.94666	1.66357	0.0452
Totals :				3.52881e4	3227.61707	

Signal 4: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.815	BB	0.1322	17.49115	2.12184	0.0501
2	12.143	VB	0.1618	34.99557	3.40943	0.1002
3	12.578	BB	0.0924	8.26647	1.36915	0.0237

Data File C:\Chem32\1\Data\NHC\KGP05_NewRoute.D
Sample Name: KGP05_NewRoute

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
4	14.340	BB	0.0933	32.15208	5.26187	0.0921
5	15.284	BV	0.0996	31.51141	4.39869	0.0902
6	15.402	VB	0.1169	29.66775	3.98250	0.0850
7	16.041	BV	0.0767	24.80235	4.92773	0.0710
8	16.156	VB	0.0918	49.38046	8.25542	0.1414
9	16.494	BB	0.0990	11.40789	1.82433	0.0327
10	17.038	BV	0.1062	46.27760	6.41281	0.1325
11	17.511	VB	0.2209	19.82826	1.27894	0.0568
12	17.827	BB	0.0888	8.86393	1.50347	0.0254
13	18.630	BB	0.0878	17.55673	3.21131	0.0503
14	18.847	BV	0.0854	835.78552	153.77007	2.3937
15	19.065	VV	0.1816	3.34704e4	3012.69092	95.8599
16	19.655	VV	0.1208	65.31109	7.87023	0.1871
17	19.815	VB	0.1162	27.41306	3.39404	0.0785
18	20.234	BB	0.1351	26.04231	2.94681	0.0746
19	20.617	VV	0.0984	12.42971	1.89863	0.0356
20	20.811	VB	0.1065	38.75175	5.61653	0.1110
21	21.297	BB	0.1256	40.54931	4.65598	0.1161
22	21.664	BV	0.0925	7.74135	1.28087	0.0222
23	21.814	VB	0.1090	7.54903	1.03594	0.0216
24	22.198	BB	0.0971	10.70251	1.70707	0.0307
25	23.097	BB	0.1351	10.33754	1.08587	0.0296
26	23.588	BV	0.1476	21.00341	1.98295	0.0602
27	24.346	BB	0.1324	9.74102	1.06806	0.0279
Totals :				3.49160e4	3248.96144	

Signal 5: DAD1 E, Sig=240,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.143	VB	0.1620	29.70107	2.88745	0.0873
2	12.578	BV	0.0947	6.29699	1.01039	0.0185
3	14.337	BB	0.0949	9.40256	1.54804	0.0276
4	15.282	BV	0.1071	22.32708	2.86076	0.0656
5	15.407	VB	0.1181	21.85952	2.89563	0.0643
6	15.654	BB	0.1347	10.17704	1.03514	0.0299
7	16.042	BV	0.0790	17.95292	3.54973	0.0528
8	16.156	VB	0.0920	32.44355	5.41095	0.0954
9	16.496	BV	0.1284	11.59169	1.32064	0.0341
10	17.038	BV	0.1073	37.76653	5.16427	0.1110
11	17.390	VB	0.1910	17.01636	1.14761	0.0500
12	17.827	BB	0.0892	6.73428	1.13587	0.0198
13	18.631	BB	0.0873	16.19819	2.98691	0.0476
14	18.847	BV	0.0856	761.83679	139.77220	2.2395
15	19.066	VV	0.1739	3.28191e4	3091.19092	96.4752
16	19.656	VB	0.1552	79.47507	7.06691	0.2336
17	20.232	BB	0.1443	18.28837	1.89934	0.0538
18	20.617	VV	0.0982	9.57039	1.46446	0.0281
19	20.812	VB	0.1064	34.06365	4.94172	0.1001
20	21.298	BB	0.1153	37.82603	4.83226	0.1112

Data File C:\Chem32\1\Data\NHC\KGP05_NewRoute.D
Sample Name: KGP05_NewRoute

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
21	22.197	BB	0.0993	7.62234	1.21290	0.0224
22	23.588	BB	0.1314	10.93429	1.18751	0.0321
Totals :				3.40182e4	3286.52160	

Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.143	BB	0.1510	14.55555	1.55749	0.0639
2	14.341	BB	0.0907	23.32549	3.95847	0.1024
3	15.287	BV	0.0912	20.25547	3.22794	0.0889
4	15.396	VB	0.1091	14.11893	2.03223	0.0620
5	16.157	BB	0.1109	24.37087	3.19886	0.1070
6	17.036	BB	0.0927	11.58850	1.96765	0.0509
7	18.847	BV	0.0825	147.43117	27.53336	0.6472
8	19.064	VV	0.1280	2.24666e4	2848.95654	98.6314
9	19.655	VB	0.1484	29.81342	2.79708	0.1309
10	20.812	VB	0.1156	12.89520	1.71737	0.0566
11	21.297	BB	0.1081	13.38892	1.85670	0.0588
Totals :				2.27784e4	2898.80370	

Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.143	BB	0.1519	16.23135	1.72349	0.1208
2	14.341	BB	0.0925	16.34811	2.70358	0.1216
3	15.288	BV	0.0894	17.85512	2.91646	0.1328
4	15.406	VB	0.1166	16.62880	2.23992	0.1237
5	16.158	VB	0.0944	7.35675	1.18523	0.0547
6	17.044	BB	0.1317	9.73999	1.03621	0.0725
7	18.847	BV	0.0868	110.88705	19.97747	0.8250
8	19.064	VV	0.1007	1.32208e4	2065.10962	98.3655
9	19.656	VB	0.1580	15.93034	1.36678	0.1185
10	21.296	BB	0.1127	8.71391	1.14643	0.0648
Totals :				1.34405e4	2099.40518	

Signal 8: DAD1 H, Sig=320,16 Ref=off

Data File C:\Chem32\1\Data\NHC\KGP05_NewRoute.D
Sample Name: KGP05_NewRoute

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.342	BB	0.0916	6.79143	1.13817	0.0700
2	15.288	BB	0.0668	5.60983	1.34069	0.0579
3	18.847	BV	0.0881	143.93456	25.39465	1.4846
4	19.065	VV	0.0972	9539.15430	1519.85461	98.3875
Totals :				9695.49011	1547.72812	

*** End of Report ***

Scale-up Experimental Section:

2-Isopropoxy-3-methoxybenzaldehyde (6, DM 08/24/2016 P77). A homogeneous mixture of 2-hydroxy-3-methoxybenzaldehyde (14.7 g, 96.6 mmol) and K_2CO_3 (20.0 g, 145 mmol) in DMF (193 mL) was stirred at room temperature for 30 min. 2-Iodopropane (19.3 mL, 193 mmol) was added and the reaction mixture was stirred at 50 °C for 20 h, subsequently returned to room temperature, and diluted with EtOAc and water. The organic layer was separated, and the aqueous layer was washed two more times with EtOAc. The combined organic layer was washed twice with brine and dried over anhydrous sodium sulfate. Purification by flash chromatography (Biotage Isolera, silica gel column using 0-5% EtOAc-hexane) afforded aldehyde **6** (17.7 g, 91.1 mmol, 95%) as an oily liquid.

5-(2-Isopropoxy-3-methoxyphenyl)pentanoic acid (7, DM21541, 06/16/2016). To an ice-cold solution of potassium *tert*-butoxide (12.13 g, 108.1 mmol) in DMF (154.0 mL), 3-carboxypropyltriphenylphosphonium bromide (19.89 g, 46.34 mmol) was added and the reaction mixture was stirred for 10 min. A DMF (10.0 mL) solution of aldehyde **6** (6.00 g, 30.9 mmol) was added to the generated ylide, and the reaction mixture was stirred at room temperature for 20 h, followed by the addition of deionized (DI) water to obtain a clear solution. DMF and water were removed under reduced pressure and the crude residue was taken up in EtOAc and water to which the aqueous layer was acidified (pH ~ 1-2) with HCl (2 M). The organic layer was separated, and the aqueous layer was washed twice with EtOAc. The combined organic layer was dried over sodium sulfate, filtered [round bottom flask (250.0 mL)], and concentrated under reduced pressure to obtain the crude intermediate alkene (both *E* and *Z*) as an oil. The mixture of alkene geometrical isomers was dissolved in CH_3OH (61.6 mL) followed by the slow and careful addition of Pd-C (10 wt%, 1.643 g, 1.544 mmol) under nitrogen to avoid the risk of fire. The

resultant heterogeneous mixture was stirred under a hydrogen atmosphere (balloon filled with hydrogen) at room temperature for 24 h. Pd/C was filtered by passage through a Celite® bed. The filtrate was collected and the solvent was removed under reduced pressure to obtain an oily liquid. Purification by flash chromatography (Biotage Isolera, silica gel column 0-25% EtOAc-hexane) afforded carboxylic acid **7** (7.80 g, 29.3 mmol, 95%) as an oily liquid.

1-Isopropoxy-2-methoxy-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (8, DM 02/14/2017 P26). To a solution of carboxylic acid **7** (8.17 g, 30.7 mmol) and oxalyl chloride (5.20 mL, 61.4 mmol) in CH_2Cl_2 (30.0 mL), DMF (236 μL, 0.307 mmol) was added dropwise. The reaction mixture was stirred for 2 h at room temperature. Excess oxalyl chloride was removed under reduced pressure (rotary evaporation) and trace amounts of remaining oxalyl chloride were removed by repeated evaporation with toluene. The crude acyl chloride solution in CH_2Cl_2 (306 mL) was cooled (ice bath) and $SnCl_4$ (1 M in CH_2Cl_2, 36.8 mL, 36.8 mmol). The reaction mixture was stirred for 30 min at -10 ^oC, and subsequently quenched with DI water, followed by the addition of HCl (1 M) to dissolve the white emulsion. The organic layer was separated, and the aqueous layer was washed twice with dichloromethane. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to generate a crude oily liquid. Purification by flash chromatography (Biotage Isolera, silica gel column using 0-10% EtOAc-hexane) afforded ketone **8** (5.10 g, 20.5 mmol, 67%) as an oily liquid.

4-Isopropoxy-3-methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulene (9, DM 08/17/2016 P72). A solution of 1, 2, 3-trimethoxy-5-bromobenzen (10.5 g, 42.7 mmol) in

THF (213 mL) was cooled to -78 °C, followed by the addition of *n*-BuLi (2.5 M in hexane, 17.1 mL, 42.7 mmol). The reaction mixture was stirred for 30 min. A solution of ketone **8** (5.30 g, 21.3 mmol) in THF (10 mL) was added (via cannula) to the generated organometallic reagent. The reaction mixture was stirred at -78 °C for 5 h and subsequently stirred at room temperature for an additional 15 h. The reaction mixture was diluted with EtOAc, quenched with water, and the aqueous solution was adjusted to slightly acidic (pH ~ 3-4) with HCl (2 M). The organic layer was separated, and the aqueous layer was further washed twice with EtOAc. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to yield a crude oily liquid. Purification by flash chromatography (Biotage Isolera, silica gel column using 0-10% EtOAc-hexane) afforded compound **9** (7.17 g, 18.0 mmol, 84%) as a white solid.

3-Methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-ol (1, DM 08/22/2016 P74, KGP18). To an ice-cold solution of compound **9** (7.15 g, 17.9 mmol) in CH_2Cl_2 (89.5 mL), was added (slowly) boron trichloride (1 M in CH_2Cl_2, 19.7 mL, 19.7 mmol). After stirring for 4 h at 0 ^oC, the reaction mixture was quenched with DI water and further acidified (2 M HCl) to obtain clear phases. The organic layer was separated, and the aqueous layer was further washed twice with dichloromethane. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain a crude white solid. Purification by flash chromatography (Biotage Isolera, silica gel column using 0-15% EtOAc-hexane) afforded phenol **1** (5.50 g, 15.4 mmol, 86%) as a white solid.

3-Methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-yl

trifluoromethanesulfonate (10, DM 08/25/2016 P78). To an ice-cold solution of phenol **1** (2.4 g, 6.7 mmol) and DMAP (82 mg, 0.67 mmol) in CH_2Cl_2 (67.3 mL), was added triethylamine (TEA) (1.0 mL, 7.4 mmol) and the reaction mixture was stirred for 15 min. Triflic anhydride (2.2 mL, 13 mmol) was added slowly and the reaction mixture was stirred at room temperature for 18 h, and subsequently quenched with water. The organic layer was separated, and the aqueous layer was washed twice with CH_2Cl_2. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain a crude white solid. Purification by flash chromatography (Biotage Isolera, silica gel column using 0-10% EtOAc-hexane) afforded triflate **10** (2.54 g, 5.20 mmol, 77%) as a white solid.

3-Methoxy-9-(3,4,5-trimethoxyphenyl)-6,7-dihydro-5H-benzo[7]annulen-4-amine (2, DM 08/29/2016 P79, KGP156). A solution of triflate **10** (1.74 g, 3.56 mmol), $Pd(OAc)_2$ (80 mg, 0.36 mmol), BINAP (332 mg, 0.534 mmol), benzophenone imine (896 μL, 5.34 mmol), and Cs_2CO_3 (1.74 g, 5.34 mmol) in toluene (14 mL) was degassed by bubbling nitrogen through the solution for 15 min in a sealed tube with a needle outlet. The reaction mixture was heated at 110 °C for 36 h, and subsequently returned to room temperature, diluted with EtOAc, and quenched with water. The organic layer was separated, and the aqueous layer was washed further twice with EtOAc. .The solution was collected in a round bottom flask and solvent was evaporated to yield crude intermediate imine compound. The crude imine was dissolved in THF (35.0 mL) and treated with aqueous 2 M HCl to maintain pH ~ 1-2 and stirred at room temperature for 3 h. The solvent (THF) was removed under reduced pressure, and EtOAc and $NaHCO_3$ (saturated aqueous solution to neutralize the acid) were added to the residue. The organic layer was separated, and the aqueous layer was washed twice with EtOAc. The combined organic layer

was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to yield a crude solid. Purification by flash chromatography (Biotage Isolera, silica gel column using 5-20% EtOAc-hexane) afforded amine **2** (1.00 g, 2.81 mmol, 79% as a slightly greenish-white crystalline solid.

(3-Hydroxypropyl)triphenylphosphonium bromide (12, DM 05/17/2017 P66). A solution of 3-bromo-1-propanol (14.0 mL, 155 mmol) and triphenylphosphine (20.3 g, 77.4 mmol) in toluene (77.4 mL) was heated at reflux for 24 h. Toluene was removed under vacuum. To the solid residue, diethyl ether was added and resultant solution was sonicated to dissolve trace amounts of triphenylphosphine. The diethyl ether layer was decanted. This step was repeated twice and the white solid was dried under vacuum to afford highly pure bromide **12** (28.1 g, 70.0 mmol, 90%) as a white solid.

4-(2-Isopropoxy-3-methoxyphenyl)butan-1-ol (13, DM 02/06/2017 P22). To an ice-cold suspension of Wittig salt **12** (13.1 g, 32.7 mmol) in THF (374 mL) was slowly added *n*-BuLi (2.5 M in hexane, 26.1 mL, 65.4 mmol). The reaction mixture was stirred for 15 min at which point the suspension dissolved to reveal a bright orange colored solution. To this solution was added TMSCl (4.10 mL, 32.7 mmol) and the resultant reaction mixture was stirred for an additional 30 min. Subsequently, a solution of aldehyde **6** [4.23 g, 21.8 mmol in THF (10.0 mL)] was added to the generated ylide. The reaction mixture was stirred at 0 °C for 1 h and subsequently at room temperature for 1 h. The solvent (THF) was removed under reduced pressure to afford a concentrated crude reaction mixture, which was diluted with EtOAc and quenched with HCl (2 M to maintain pH 1-2). The biphasic solution was stirred for 15 min to obtain a clear solution.

The organic layer was then separated and the aqueous layer was washed twice with EtOAc. The combined organic layer was dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resultant crude product was dissolved in CH_3OH (43.4 mL), and stirred under a hydrogen atmosphere (via balloon) in the presence of Pd/C [10 wt% (2.32 g, 2.20 mmol)] at room temperature for 24 h. The Pd/C was removed by Celite® filtration. The solvent (CH_3OH) was removed under reduced pressure to afford the crude intermediate, which was subsequently dissolved in THF (43.4 mL) and treated with TBAF (1 M in THF, 32.7 mL, 32.7 mmol). The reaction mixture was stirred for 1 h, and subsequently quenched with aqueous 2 M HCl (12 mL). The solvent (THF) was removed under reduced pressure, and the crude product was diluted with EtOAc and water was added. The biphasic solution was stirred for 15 min. The organic layer was separated, and the aqueous layer was washed twice with EtOAc. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to afford the product as a crude liquid. Purification by flash chromatography (Biotage Isolera, silica gel column using 5-30% EtOAc-hexane) afforded alcohol **13** (4.78 g, 20.1 mmol, 92%) as an oily liquid.

4-(2-Isopropoxy-3-methoxyphenyl)butanoic acid (14, NHC_5_138). To a solution of alcohol **13** (2.47 g, 10.4 mmol) dissolved in water/acetonitrile (150 mL/300 mL) was added Oxone® (9.55 g, 15.5 mmol) and 2-Iodoxybenzoic acid (IBX) (0.87 g, 3.1 mmol). The reaction mixture was stirred at 70 °C for 20 h, and the solvent was removed under reduced pressure. The residue was washed with 2 M HCl (100 mL) and extracted with EtOAc (3 x 50 mL). The combined organic phase was dried over sodium sulfate and evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 100 g silica column [solvent

A: EtOAc; solvent B: hexanes; gradient: 12%A / 88%B (1 CV), 12%A / 88%B → 50%A / 50%B (10 CV), 50%A / 50%B (2 CV); flow rate: 100 mL/min; monitored at 254 and 280 nm] to afford carboxylic acid **14** (1.85 g, 7.38 mmol, 71%) as a brown oil.

5-Isopropoxy-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (15, DM 03/10/2017 P45). To a solution of carboxylic acid **14** (2.85 g, 11.3 mmol) and oxalyl chloride (1.9 mL, 23 mmol) in CH_2Cl_2 (22.4 mL), DMF (87 µL, 1.1 mmol) was added dropwise. The reaction mixture was stirred for 2 h. Excess oxalyl chloride (and solvent CH_2Cl_2) was removed under vacuum. Remaining trace amounts of oxalyl chloride was removed by repeated evaporation with toluene. The resulting acyl chloride was dissolved in CH_2Cl_2 (112 mL), cooled to 0 ^oC, and $SnCl_4$ (1 M in CH_2Cl_2, 13.5 mL, 13.5 mmol) was added. After stirring for 30 min, the reaction was quenched with DI water, and HCl aqueous 2 M) was added to dissolve the white emulsion. The organic layer was separated, and the aqueous layer was washed twice with CH_2Cl_2. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain a crude liquid. Purification by flash chromatography (Biotage Isolera, silica gel column using 5-10% EtOAc-hexane) afforded ketone **15** (2.25 g, 9.6 mmol, 84%).

8-Isopropoxy-7-methoxy-4-(3,4,5-trimethoxyphenyl)-1,2-dihydronaphthalene (16, DM 03/14/2017 P47). A solution of 1, 2, 3-trimethoxy-5-bromobenzene (6.54 g, 26.5 mmol) in THF (101 mL) was cooled to -78 °C followed by the slow addition of *n*-BuLi (2.5 M in hexane, 10.6 mL, 26.5 mmol). After stirring for 30 min, a solution of ketone **15** (3.10 g, 13.2 mmol) in THF (5.0 mL) was added (via cannula) to the generated organolithium reagent. The reaction mixture was stirred at cold for 5 h and stirred at room temperature for 15 h. The reaction mixture was

diluted with EtOAc, quenched with DI water, and the aqueous solution was acidified (pH ~ 1-2) with HCl aqueous 2 M) and stirred for 1 h. The organic layer was separated, and the aqueous layer was washed twice with EtOAc. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure to obtain a crude liquid. Purification by flash chromatography (Biotage Isolera, silica gel column using 2-15% EtOAc-hexane) afforded compound **16** (3.30 g, 8.58 mmol, 65%) as a viscous liquid.

2-Methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-ol (3, DM 03/17/2017 P48, Oxi6196). A solution of compound **16** (3.10 g, 8.06 mmol) in CH_2Cl_2 (80 mL) was cooled (ice-bath) and BCl_3 (1 M in CH_2Cl_2, 8.87 mL, 8.87 mmol) was added slowly over a 30 min period. The reaction mixture was stirred for 3 h at 0 °C and for an additional 3 h at room temperature. The reaction was quenched with DI water and further acidified with aqueous 2 M HCl (pH ~ 1-2). The organic layer was separated, and the aqueous layer was washed twice with CH_2Cl_2. Purification by flash chromatography (Biotage Isolera, silica gel column using 5-15% EtOAc-hexnae) afforded phenol **3** (2.30 g, 6.72 mmol, 83%) as a white solid.

2-Methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-yl trifluoromethanesulfonate (17, DM 03/23/2017 P50). To a solution of phenol **3** (1.00 g, 2.92 mmol) in CH_2Cl_2 (29 mL), trimethylamine (615 μL, 4.38 mmol) was added and resultant reaction mixture was stirred for 15 min at room temperature, followed by the addition of triflic anhydride (736 μL, 4.38 mmol). After stirring at room temperature for 6 h, the reaction was quenched with DI water and neutralized by a saturated $NaHCO_3$ solution. The organic layer was separated and aqueous layer was washed twice with CH_2Cl_2. The combined organic layer was

dried over sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash chromatography (Biotage Isolera, silica gel column using 5-10% EtOAc-hexane) afforded triflic compound **17** (1.15 g, 2.42 mmol, 83%) as a white solid.

2-Methoxy-5-(3,4,5-trimethoxyphenyl)-7,8-dihydronaphthalen-1-amine (4, DM 03/29/2017 KGP05). To toluene (20 mL) in a pressure vial (sealed tube) was added triflate **17** (0.96 g, 2.0 mmol), $Pd(OAc)_2$ (45 mg, 0.20 mmol), *rac*-BINAP (0.19 g, 0.30 mmol), benzophenone imine (0.51 mL), and Cs_2CO_3 (989 mg, 3.04 mmol). The solution was degassed (bubbling nitrogen) for 15 min. After heating at 110 °C for 36 h, the reaction mixture was cooled to room temperature, diluted with EtOAc, and quenched with DI water. The organic layer was separated, and the aqueous layer was washed further twice with EtOAc. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The crude product was dissolved in THF (20 mL) and treated with aqueous 2 M HCl until pH 2-3 was achieved, followed by stirring for 6 h. The solvent (THF) was removed under reduced pressure, and to the residue, EtOAc and a saturated aqueous $NaHCO_3$ solution was added to neutralize the acid. The organic layer was separated, and the aqueous layer was washed twice with EtOAc. The combined organic layer was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. Purification by flash chromatography (Biotage Isolera, silica gel column using 5-20% EtOAc-hexane) afforded amine **4** (500 mg, 1.46 mmol, 72%) as a white crystalline solid.

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