Synthesis and Biological Evaluation of Benzocyclooctene-based and Indene-based Anticancer Agents that Function as Inhibitors of Tubulin Polymerization

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4. Experimental Section

4.1 General Materials and Methods

Tetrahydrofuran (THF), CH_2Cl_2, ethanol, methanol, dimethylformamide (DMF), and acetonitrile were used in their anhydrous forms. Reactions were performed under nitrogen gas. 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). Intermediates and products synthesized were characterized on the basis of their ^{1}H NMR (500 or 600 MHz) and ^{13}C NMR (125 or 150 MHz) spectroscopic data using a Varian VNMRS 500 MHz or a Bruker Ascend 600 MHz instrument. Spectra were recorded in $CDCl_3$ and D_2O. All chemical shifts are expressed in ppm (δ), coupling constants (J) are presented in Hz, and peak patterns are reported as singlet (s), doublet (d), triplet (t), quartet (q), pentet (p), septet (sept), and multiplet (m).

Purity of the target 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 A: solvent A, acetonitrile, solvent B, H_2O; gradient, 10% A/90% B to 100% A/0% B or method B: solvent A, acetonitrile, solvent B, 0.1% TFA in H_2O over 0 to 40 min; post-time 10 min; flow rate 1.0 mL/min; injection volume 20 μL; monitored at wavelengths of 210, 254, 230, 280, and 360 nm. Mass spectrometry was carried out under positive ESI (electrospray ionization) using a Thermo Scientific LTQ Orbitrap

Discovery instrument.

4.1.1. 6-(2′,3′-Dimethoxyphenyl)hex-5-enoic acid (1).[7] To a well-stirred solution of 4-(carboxybutyl)triphenyl phosphonium bromide (13.47 g, 30.39 mmol) dissolved in THF (500 mL) at rt was added potassium *tert*-butoxide (7.43 g, 66.2 mmol). After 1 h, 2,3-dimethoxybenzaldehyde (5.02 g, 30.1 mmol) dissolved in THF (100 mL) was added to the original reaction mixture, and stirring at room temperature was continued. After 12 h, the THF was evaporated under reduced pressure, and the resulting material was quenched with 2 M HCl (100 mL) and extracted with EtOAc (2 x 100 mL). The combined organic layers were evaporated under reduced pressure. Purification by flash column chromatography using a pre-packed 100 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 10%A / 90%B (1 CV), 10%A / 90%B → 50%A / 50%B (10 CV), 50%A / 50%B (2 CV); flow rate: 40 mL/min; monitored at 254 and 280 nm] afforded compound **1** (3.61 g, 14.4 mmol, 48%) as a yellow oil. NMR characterization was determined after the next step.

4.1.2. 6-(2′,3′-Dimethoxyphenyl)hexanoic acid (3). [7] To a well-stirred solution of carboxylic acid **1** (3.61 g, 14.4 mmol) dissolved in MeOH (150 mL) was added 10% Pd on carbon (0.74 g) and H_2 gas (balloon), and the reaction was stirred at room temperature for 12 h. The reaction mixture was then filtered through Celite®, the Celite® was washed with EtOAc (3 x 50 mL), and the filtrate (MeOH and EtOAc) was evaporated under reduced pressure. The 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: 40 mL/min; monitored at 254 and 280 nm] to afford carboxylic acid **3** (3.63 g, 14.4

mmol, quantitative) as a colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 11.83 (1H, s), 7.01 (1H, t, *J* = 9.5 Hz), 6.80 (2H, *J* = 10 Hz), 3.88 (3H, s), 3.86 (3H, s), 2.68 (2H, t, *J* = 9 Hz), 2.39 (2H, t, *J* = 16 Hz), 1.70 (4H, m), 1.46 (2H, p, *J* = 9.5 Hz). ^{13}C NMR ($CDCl_3$, 150 Hz) δ 180.1, 152.7, 147.1, 136.2, 123.8, 121.9, 110.2, 60.5, 55.5, 34.0, 30.4, 29.6, 28.9, 24.5.

4.1.3. 1,2-Dimethoxy-benzocylcooct-5-one (5). [7] To carboxylic acid **3** (4.40 g, 17.4 mmol) was added Eaton's reagent (35 mL, 3 g per mmol of compound **3**), and the mixture was stirred at room temperature for 12 h, at which time it was poured over ice, which was allowed to melt, and the solution was neutralized with sodium bicarbonate. The organic layer was extracted with EtOAc (3 x 50 mL), dried over sodium sulfate, evaporated under reduced pressure, and 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: 40 mL/min; monitored at 254 and 280 nm] to afford ketone **5** (0.58 g, 2.5 mmol, 14 %) as a yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.35 (1H, d, *J* = 8.4 Hz), 6.65 (1H, d, *J* = 9 Hz), 3.69 (3H, s), 3.59 (3H, s), 2.94 (2H, t, *J* = 6.6 Hz), 2.73 (2H, t, *J* = 6.6 Hz), 1.59 (4H, m), 1.27 (2H, p, *J* = 6.6 Hz). ^{13}C NMR ($CDCl_3$, 150 Hz) δ 204.9, 155.5, 146.2, 134.7, 133.5, 124.8, 109.6, 60.7, 55.6, 43.9, 27.0, 25.4, 24.7, 24.1.

4.1.4. [TMAH][Al_2Cl_7].[70] To dry CH_2Cl_2 (150 mL) was added $AlCl_3$ (19.84 g, 149.08 mmol), which was stirred and cooled to 0 °C. Trimethylamine hydrochloride (7.11 g, 74.54 mmol) was added, and the mixture was stirred for 2 h at room temperature. The resulting liquid was stored at room temperature under nitrogen.

4.1.5. 1-Hydroxy-2-methoxy-benzocyclooct-5-one (13). To ketone **5** (0.57 g, 2.3 mmol) in a 20 mL microwave vial was added [TMAH][Al_2Cl_7] (7.54 mL, 4.69 mmol), and the mixture was reacted in a microwave for 1 h at 80 °C. The solution was poured into water (50 mL), extracted with EtOAc (3 x 25 mL), dried over sodium sulfate, and evaporated under reduced pressure. The crude reaction mixture 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 / 40%B (2 CV); flow rate: 50 mL/min; monitored at 254 and 280 nm] affording phenol **13** (0.28 g, 1.3 mmol, 54%) as a clear oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.23 (1H, d, *J* = 8.4 Hz), 6.73 (1H, d, *J* = 8.4 Hz), 6.11 (1H, s) 3.85 (3H, s), 3.06 (2H, t, *J* = 6.6 Hz), 2.88 (2H, t, *J* = 6.6 Hz), 1.75 (4H, m), 1.49 (2H, p, *J* = 6 Hz). ^{13}C NMR ($CDCl_3$, 150 Hz) δ 206.4, 148.7, 142.9, 133.7, 126.7, 120.1, 107.9, 56.0, 44.4, 25.9, 25.7, 25.3, 23.9.

4.1.6. 1-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-benzocyclooct-5-one (14). Phenol **13** (0.22 g, 1.0 mmol) was dissolved in DMF (50 mL). TBSCl (0.30 g, 2.0 mmol) and DIPEA (0.52 mL, 3.0 mmol) were added, and the reaction was stirred for 12 h at room temperature. The reaction mixture was washed with water (50 mL), extracted with EtOAc (5 x 30 mL), dried over sodium sulfate, and evaporated under reduced pressure. The crude reaction mixture was purified by flash chromatography using a pre-packed 25 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 2%A / 98%B (1 CV), 2%A / 98%B → 20%A / 80%B (10 CV), 20%A / 80%B (2 CV); flow rate: 50 mL/min; monitored at 254 and 280 nm] affording TBS-protected ketone **14** (0.31 g, 0.93 mmol, quantitative) as a white solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.04 (1H, d, *J* =8.4 Hz), 6.56 (1H, d, *J* = 9 Hz), 3.62 (3H, s), 2.87 (2H, t, *J* = 6 Hz), 2.69 (2H, t, *J* = 7.2 Hz), 1.58

(4H, m), 1.33 (2H, p, J = 3 Hz), 0.81 (9H, s), 0.00 (6H, s). ^{13}C NMR ($CDCl_3$, 150 Hz) δ 207.1, 151.9, 141.9, 133.7, 131.5, 120.9, 108.5, 54.5, 44.5, 26.2, 26.0, 25.8, 25.5, 23.7, 18.8, -3.9.

4.1.7. 1-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-5-(3′,4′,5′- trimethoxyphenyl)-benzocyclooctan-5-ol (19). To an oven dried flask containing THF (50 mL) was added 3,4,5-trimethoxyphenyl bromide (0.20 g, 0.81 mmol), and the solution was cooled to -78 °C. *n*-BuLi (1.3 mL, 0.85 mmol) was slowly added to the reaction mixture, which was then stirred at -78 °C for 1 h. TBS-protected **14** (0.20 g, 0.60 mmol) was added dropwise to the flask, and the reaction mixture was stirred while warming from -78 °C to room temperature over 12 h, at which time the reaction mixture was washed with water, extracted with EtOAc (3 x 50 mL), dried over sodium sulfate, and evaporated under reduced pressure. The organic material was purified by flash chromatography using a pre-packed 25 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 2%A / 98%B (1 CV), 2%A / 98%B → 20%A / 80%B (10 CV), 20%A / 80%B (2 CV); flow rate: 50 mL/min; monitored at 254 and 280 nm] affording tertiary alcohol **19** (0.044 g, 0.088 mmol, 15%) as a yellow oil. NMR characterization was performed after the next step.

4.1.8. 1-((*tert*-Butyldimethylsilyl)oxy)-2-methoxy-5-(3′,4′,5′-trimethoxyphenyl)benzocyclooct-5-ene (22). Acetic acid (10 mL) was added to tertiary alcohol **19** (0.044 g, 0.088 mmol), and the reaction mixture was stirred for 12 h at room temperature, at which time the mixture was washed with water (50 mL), extracted with EtOAc (3 x 30 mL), and dried over sodium sulfate. The organic phase was evaporated under reduced pressure, and the crude reaction mixture was purified by flash

chromatography using a pre-packed 10 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 2%A / 98%B (1 CV), 2%A / 98%B → 20%A / 80%B (10 CV), 20%A / 80%B (2 CV); flow rate: 12 mL/min; monitored at 254 and 280 nm] affording TBS-protected **22** (0.022 g, 0.045 mmol, 52%) as a clear oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.68 (1H, d, *J* = 8.4 Hz), 6.56 (1H, d, *J* = 8.4 Hz), 6.42 (2H, s), 6.19 (1H, t, *J* = 7.8 Hz), 3.84, (3H, s), 3.80 (3H, s), 3.78 (6H, s), 3.27 (1H, overlapping doublets, *J* = 12.6 Hz), 2.23 (1H, m), 1.96 (1H, m), 1.75 (1H, m), 1.66 (1H, q, *J* = 22 Hz), 1.37 (2H, m), 1.02 (9H, s), 0.27 (3H, s), 0.24 (3H, s).

4.1.9. 1-Hydroxy-2-methoxy-5-(3′,4′,5′- trimethoxyphenyl)-benzocyclooct-5-ene (23). [7] TBS-protected benzocyclooctene **22** (0.022 g, 0.045 mmol) was dissolved in THF (10 mL), TBAF (0.031 g, 0.099 mmol) was added, and the reaction mixture was stirred at room temperature for 12 h. The solution was washed with water (50 mL), extracted with EtOAc (3 x 30 mL), dried over sodium sulfate, and evaporated under reduced pressure. The crude reaction mixture was purified by flash chromatography using a pre-packed 10 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 3%A / 97%B (1 CV), 3%A / 97%B → 30%A / 70%B (10 CV), 30%A / 70%B (2 CV); flow rate: 36 mL/min; monitored at 254 and 280 nm] affording benzocyclooctene **23** (0.0053 g, 0.014 mmol, 33%) as a white solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.70 (1H, d, *J* = 8.4 Hz), 6.53 (1H, d, *J* = 8.4 Hz), 6.43 (2H, s), 6.21 (1H, t, *J* = 8.4 Hz), 5.76 (1H, s), 3.92 (3H, s), 3.84 (3H, s), 3.78 (6H, s), 3.25 (1H, dd, *J* = 12.6, 7.8 Hz), 2.30 (2H, m), 2.03 (1H, m), 1.79 (1H, m), 1.68 (1H, dt, *J* = 22.2, 11.4 Hz), 1.45 (1H, qd, *J* = 13.2, 4.8 Hz), 1.34 (1H, qd, *J* = 13.2, 4.8 Hz) ^{13}C NMR ($CDCl_3$, 150 MHz) δ 152.8, 145.3, 142.7, 139.7, 139.1, 137.1, 132.3, 129.8, 129.7, 120.3, 107.8, 104.6, 60.9, 56.1, 56.0, 28.3, 26.5, 25.8, 24.7. HRMS:

Obsvd 393.1693 [M + Na^+], Calcd for $C_{22}H_{26}O_5Na$: 393.1672. HPLC: 16.61 min.

4.1.10. Sodium 2-methoxy-5-(3′,4′,5′- trimethoxyphenyl)-benzocyclooct-5-en-1-yl phosphate (24). Phosphorus oxychloride (0.18 mL, 1.9 mmol) was cooled to 0 °C in CH_2Cl_2 (10 mL) and triethylamine (0.68 mL, 4.9 mmol) was added, and the reaction mixture was stirred for 5 min. Benzocyclooctene **23** (0.14 g, 0.38 mmol) in CH_2Cl_2 (5 mL) was added to the reaction dropwise, and the reaction mixture was stirred at 0 °C for 1 h and then warmed to room temperature over 12 h. The mixture was then evaporated under reduced pressure. CH_2Cl_2 (10 mL) was added to the resulting residue, and the resulting solution was again evaporated under reduced pressure. This was repeated two more times. The resulting solid was dissolved in a mixture of THF and water (2:1, 6 mL total) and stirred for 1 h. The solution was then cooled to 0 °C, and 0.1 M NaOH was added until a pH of 10 was achieved. The solution was then evaporated under reduced pressure, and the crude product was purified by a C18 30 g reversed phase column [solvent A: acetonitrile; solvent B: water; gradient: 10%A / 90%B (1 CV), 10%A / 90%B → 100%A / 0%B (10 CV), 100%A / 0%B (2 CV); flow rate: 25 mL/min; monitored at 254 and 280 nm] to afford phosphate salt **24** (0.06 g, 0.12 mmol, 32%) as a brown solid. ^{1}H NMR (D_2O, 600 MHz) δ 6.69 (1H, d, *J* = 8.4 Hz), 6.52 (2H, s), 6.47 (1H, d, *J* = 8.4 Hz), 6.20 (1H, t, *J* = 7.4 Hz), 3.72 (3H, s), 3.67 (6H, s), 3.63 (3H, s), 3.45 (1H, dd, *J* = 13.2, 8.4 Hz), 2.14 (1H, dt, *J* = 13.8, 8.4), 2.05 (1H, t, *J* = 12 Hz), 1.91 (1H, m), 1.63 (1H, m), 1.43 (1H, dt, *J* = 22.2, 12 Hz), 1.30 (1H, qd, *J* = 13.2, 4.8 Hz), 1.16 (1H, qd, *J* = 13.2, 4.8 Hz). ^{13}C NMR (D_2O, 150 MHz) δ 152.2, 151.4 (d, *J* = 2.25 Hz), 141.1 (d, *J* = 6.75 Hz), 140.0, 138.8, 138.0 (d, *J* = 3.38 Hz), 135.8, 131.5, 131.2, 123.8, 109.5, 104.9, 60.9, 56.0, 55.6, 28.1, 26.6, 26.3, 23.8. ^{31}P NMR (D_2O, 242 MHz) δ -0.25. HRMS: Obsvd

495.1249 [M + H], Calcd for $C_{22}H_{26}O_8Na_2P^+$: 495.1155 HPLC: 5.46 min.

4.1.11. 1,2-Dimethoxy-5-(3′,4′,5′- trimethoxyphenyl)-benzocyclooctan-5-ol (17). To an oven dried flask, THF (50 mL) and 3,4,5-trimethoxyphenyl bromide (0.26 g, 1.0 mmol) were added, and the solution was cooled to -78 °C. *n*-BuLi (0.44 mL, 1.1 mmol) was slowly added to the reaction mixture, which was then stirred at -78 °C for 1 h. Benzocyclooctone **5** (0.18 g, 0.77 mmol) was added dropwise to the flask, and the reaction was stirred while warming from -78 °C to room temperature over 12 h, at which time the reaction mixture was washed with water (50 mL), extracted with EtOAc (3 x 50 mL), dried over sodium sulfate, and evaporated under reduced pressure. The crude product was purified by flash chromatography using a pre-packed 25 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 / 40%B (2 CV); flow rate: 50 mL/min; monitored at 254 and 280 nm] affording tertiary alcohol **17** (0.15 g, 0.37 mmol, 48%) as a clear oil. NMR characterization was performed after the next step.

4.1.12. 1,2-Dimethoxy-5-(3′,4′,5′- trimethoxyphenyl)-benzocyclooct-5-ene (20). Acetic acid (20 mL) was added to tertiary alcohol **17** (0.15 g, 0.37 mmol), and the reaction mixture was stirred for 12 h at room temperature, at which time the mixture was washed with water (50 mL), extracted with EtOAc (3 x 30 mL), and dried over sodium sulfate. The organic phase was evaporated under reduced pressure, and the crude organic product was purified by flash chromatography using a pre-packed 10 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 / 40%B (2 CV); flow rate: 12 mL/min; monitored at 254 and 280 nm] affording benzocyclooctene **20** (0.082 g, 0.213 mmol, 59%) as a white solid.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.74 (1H, d, *J* = 8.5 Hz), 6.72 (1H, d, *J* = 8 Hz), 6.41 (2H, s), 6.21 (1H, dd, *J* = 10.8, 9 Hz), 3.93 (3H, s), 3.88 (3H, s), 3.84 (3H, s), 3.78 (6H, s), 3.24 (1H, dd, *J* = 15, 9.6 Hz), 2.27 (2H, m), 2.06 (1H, m), 1.77 (1H, m), 1.65 (1H, dt, *J* = 25.2, 12.6 Hz), 1.37 (2H, m). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 152.8, 151.8, 146.3, 139.7, 139.0, 137.5, 137.2, 131.9, 129.7, 124.8, 109.5, 104.7, 60.9, 60.7, 56.1, 55.6, 28.3, 27.8, 26.0, 24.6. HRMS: Obsvd 407.1859 [M + Na^+], Calcd for $C_{19}H_{28}O_2Na$: 407.1829. HPLC: 18.53 min.

4.1.13. 6-(3′-Methoxyphenyl)hex-5-enoic acid (2). [80] To a well-stirred solution of 4-(carboxybutyl)triphenyl phosphonium bromide (16.29 g, 36.75 mmol) dissolved in THF (500 mL) at rt was added potassium *tert*-butoxide (9.09 g, 81.0 mmol). After 1 h, 2,3-dimethoxybenzaldehyde (4.47 mL, 36.8 mmol) dissolved in THF (100 mL) was added to the original reaction mixture, and the resulting reaction mixture was stirred at room temperature for 12 h. The THF was evaporated under reduced pressure, and the resulting material was quenched with 2 M HCl (100 mL) and extracted with EtOAc (2 x 100 mL). The combined organic layer was evaporated under reduced pressure and purified by flash chromatography using a pre-packed 100 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 10%A / 90%B (1 CV), 10%A / 90%B → 80%A / 20%B (10 CV), 80%A / 20%B (2 CV); flow rate: 40 mL/min; monitored at 254 and 280 nm] affording carboxylic acid **2** (8.01 g, 36.7 mmol, 99%) as a yellow oil. NMR characterization was performed after the next step.

4.1.14. 6-(3′-Methoxyphenyl)hexanoic acid (4). [81,82] To dissolved carboxylic acid **2** (8.01 g, 36.7 mmol) in MeOH (150 mL) was added 10% Pd on carbon (0.46 g) and H_2 gas (balloon). The reaction mixture was stirred at room temperature for 12 h. The mixture

was then filtered through Celite®, the Celite® was washed with EtOAc (3 x 50 mL), and the filtrate (MeOH and EtOAc) was evaporated under reduced pressure. The combined 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 → 60%A / 40%B (10 CV), 60%A / 40%B (2 CV); flow rate: 40 mL/min; monitored at 254 and 280 nm] to afford carboxylic acid **4** (7.53 g, 33.9 mmol, 93%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.21 (1H, t, J = 10.2 Hz), 6.78 (1H, d, J = 9.6 Hz), 6.76 (2H, m), 3.81 (3H), 2.62 (2H, t, J = 9 Hz), 2.38 (2H, t, J = 9 Hz), 1.67 (4H, overlapping pentets, J = 9 Hz), 1.41 (2H, p, J = 9.6 Hz).

4.1.15. 2-Methoxy-benzocyclooct-5-ene (6). [69,82–84] Carboxylic acid **4** (7.53 g, 33.9 mmol) was dissolved in CH_2Cl_2 (100 mL) and cooled to 0 °C. Eaton's reagent (68 mL, 3 g per mmol of compound **4**) was added, and the mixture was stirred while warming to room temperature over 12 h, at which time it was poured over ice, which was allowed to melt, and the solution was neutralized with $NaHCO_3$. The organic layer was extracted with EtOAc (3 x 50 mL), dried over sodium sulfate, evaporated under reduced pressure, and purified by flash chromatography using a pre-packed 100 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 5%A / 95%B (1 CV), 5%A / 95%B → 40%A / 60%B (10 CV), 40%A / 60%B (2 CV); flow rate: 40 mL/min; monitored at 254 and 280 nm] to afford ketone **6** (0.45 g, 2.2 mmol, 7 %) as a yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.81 (1H, d, J = 9 Hz), 6.63 (1H, dd, J = 9, 2.4 Hz), 6.51 (1H, d, J = 3 Hz), 3.65 (3H, s), 2.94 (2H, t, J = 6.6 Hz), 2.81 (2H, t, J = 7.2 Hz), 1.67 (2H, p, J = 7.2 Hz), 1.61 (2H, p, J = 6.6 Hz), 1.26 (2H, p, J = 6 Hz). ^{13}C NMR ($CDCl_3$, 150 Hz) δ 202.4, 162.8, 143.1, 132.2, 131.4, 116.5, 111.5, 55.1, 42.6, 35.3, 27.6, 24.5, 23.0.

4.1.16. 2-Methoxy-5-(3′,4′,5′-trimethoxyphenyl)-benzocyclooctan-5-ol (18). To an oven dried flask containing THF (50 mL) was added 3,4,5-trimethoxyphenyl bromide (0.73 g, 3.0 mmol), and the solution was cooled to -78 °C. *n*-BuLi (4.9 mL, 3.1 mmol) was slowly added to the reaction mixture, which was then stirred at -78 °C for 1 h. Ketone **6** (0.45 g, 2.2 mmol) was then added dropwise to the flask, and the reaction mixture was stirred while warming from -78 °C to room temperature over 12 h, at which time the reaction mixture was washed with water, extracted with EtOAc (3 x 50 mL), dried over sodium sulfate, and evaporated under reduced pressure. The crude reaction mixture was purified by flash chromatography using a pre-packed 25 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 / 40%B (2 CV); flow rate: 50 mL/min; monitored at 254 and 280 nm] to afford tertiary alcohol **18** (0.18 g, 0.48 mmol, 22%) as a yellow oil. NMR characterization was performed after the next step.

4.1.17. 2-Methoxy-5-(3′,4′,5′-trimethoxyphenyl)-benzocyclooct-5-ene (21). Acetic acid (10 mL) was added to tertiary alcohol **18** (0.18 g, 0.48 mmol), and the reaction mixture was stirred for 12 h at rt, at which time the mixture was washed with water (50 mL), extracted with EtOAc (3 x 30 mL), and dried over sodium sulfate. The organic phase was evaporated under reduced pressure, and the crude reaction mixture was purified by flash chromatography using a pre-packed 10 g silica column [solvent A: EtOAc; solvent B: hexanes; gradient: 5%A / 95%B (1 CV), 5%A / 95%B → 40%A / 60%B (10 CV), 40%A / 60%B (2 CV); flow rate: 12 mL/min; monitored at 254 and 280 nm] to afford benzocyclooctene **21** (0.089 g, 0.25 mmol, 52%) as a white solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.95 (1H, d, J = 8.4 Hz), 6.85 (1H, d, J = 2.4 Hz), 6.73 (1H, dd, J =

6.4, 2.4 Hz), 6.44 (2H, s), 6.24 (1H, dd, *J* = 9, 7.8 Hz), 3.863 (3H, s), 3.857 (3H, s), 3.80 (6H, s), 2.83 (1H, dd, *J* = 13.2, 7.8 Hz), 2.56 (1H, t, *J* = 12.6 Hz), 2.29 (1H, dt, *J* = 13.8, 7.8 Hz), 2.07 (1H, m), 1.80 (1H, m) 1.64 (1H, dt, *J* = 21, 10.8 Hz), 1.41 (1H, qd, *J* = 12.6, 4.8 Hz), 1.34 (1H, qd, *J* = 13.2, 5.4 Hz). ^{13}C NMR ($CDCl_3$, 150 Hz) δ 159.0, 152.8, 144.6, 139.7, 139.0, 137.1, 130.7, 129.3, 114.0, 111.4, 104.6, 60.9, 56.1, 55.2, 33.5, 28.8, 28.3, 24.9. HRMS: Obsvd 377.1724 [M + Na^+], Calcd for $C_{22}H_{26}O_4Na$: 377.1723. HPLC: 19.29 min.

4.1.18. 3-(2´,3´-Dimethoxyphenyl)propanoic acid (9).[85,86] *Trans*-2,3-dimethoxycinnamic acid **(7)** (5.00 g, 24.0 mmol) was dissolved in MeOH (100 mL), 10% Pd on carbon (0.82 g) was added, and the mixture was stirred for 12 h under H_2 (balloon). The mixture was then filtered through Celite®, the Celite® was washed with EtOAc (2 x 50 mL). The organic layer (EtOAc and MeOH) was dried over sodium sulfate, concentrated and purified by flash chromatography using a prepacked 100 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 7%A/ 93%B (1 CV), 7%A/ 93%B → 60%A/ 40%B (10 CV), 60%A/40%B (2 CV); flow rate: 40 mL/min; monitored at 254 nm and 280 nm] to afford carboxylic acid **9** (4.34 g, 20.6 mmol, 86%) as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 11.91 (1H, s), 6.97 (1H, t, *J* = 8 Hz), 6.78 (2H, d, *J* = 8 Hz), 3.85 (3H, s), 3.80 (3H, s), 2.98 (2H, t, *J* = 7.5 Hz), 2.67 (2H, t, *J* = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 179.4, 152.7, 147.1, 133.9, 124.0, 121.7, 111.0, 60.4, 55.5, 34.7, 25.3.

4.1.19. 4,5-Dimethoxy-2,3-dihydro-1*H*-inden-1-one (11).[85,87] Carboxylic acid **9** (4.99 g, 23.7 mmol) was mixed with Eaton's reagent (47.5 mL, 3 g per mmol of carboxylic acid **9**) and stirred for 72 h at room temperature. The mixture was then poured over ice,

neutralized, and extracted with EtOAc (3 x 75 mL). The organic layer was dried over sodium sulfate, concentrated and purified by flash chromatography using a prepacked 100 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 7%A/93%B (1 CV), 7%A/ 93%B → 60%A/ 40%B (10 CV), 60%A/ 40%B (2 CV); flow rate: 40 mL/min; monitored at 254 nm and 280 nm] to afford ketone **11** (2.01 g, 10.5 mmol, 44%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.06 (1H, d, *J* = 8.4 Hz), 6.62 (1H, d, *J* =8.4 Hz), 3.61 (3H, s), 3.57 (3H, s), 2.70 (2H, t, *J* = 5.4 Hz), 2.25 (2H, t, *J* = 5.4 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 204.6, 157.1, 147.4, 145.0, 130.7, 119.4, 112.0, 59.8, 55.8, 36.0, 22.1.

4.1.20. 4-Hydroxy-5-methoxy-2,3-dihydro-1*H*-inden-1-one (15).[70,88,89] Ketone **11** (0.70 g, 3.2 mmol) was added to a 20 mL microwave vial with [TMAH][Al_2Cl_7] (10.0 mL, 7.26 mmol) and microwaved for 1 h at 80 °C. The mixture was poured into water, extracted with CH_2Cl_2 (3 x 30 mL), dried over sodium sulfate and purified by flash chromatography using a prepacked 50 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 12%A/ 88%B (1 CV), 12%A/ 88%B → 100%A/ 0%B (10 CV), 100%A/ 0%B (2 CV); flow rate: 50 mL/min; monitored at 254 nm and 280 nm] to afford phenol **15** (0.42 g, 2.36 mmol, 72%) as a brown solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.35 (1H, d, *J* = 10.2 Hz), 6.92 (1H, d, *J* = 10.2 Hz), 5.81 (1H, s), 3.97 (3H, s), 3.07 (2H, t, *J* = 6.6 Hz), 2.69 (2H, t, *J* = 6.6 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 206.0, 150.9, 142.1, 140.5, 131.4, 116.1, 110.4, 56.4, 36.5, 21.9.

4.1.21. 4-((*tert*-Butyldimethylsilyl)oxy)-5-methoxy-2,3-dihydro-1*H*-inden-1-one (16). Phenol **15** (0.90 g, 5.1 mmol) was dissolved in DMF (25 mL), and TBSCl (0.71 g, 4.7 mmol) was added, followed by the addition of DIPEA (1.24 mL, 7.08 mmol). The

mixture was stirred for 12 h at room temperature, washed with water, and extracted with EtOAc (5 x 50 mL). The organic layer was dried over sodium sulfate, concentrated and purified by flash chromatography using a prepacked 50 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 7%A/ 93%B (1 CV), 7%A/ 93%B → 60%A/ 40%B (10 CV), 60%A/ 40%B (2 CV); flow rate: 50 mL/min; monitored at 254 nm and 280 nm] to afford TBS-protected **16** (0.63 g, 2.2 mmol, 91%) as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.30 (1H, d, *J* = 8.5 Hz), 6.83 (1H, d, *J* = 8.5 Hz), 3.81 (3H, s), 2.94 (2H, t, *J* = 6 Hz), 2.56 (2H, t, *J* = 6 Hz), 0.95 (9H, s), 0.12 (6H s). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 205.8, 155.0, 146.3, 141.4, 131.1, 117.4, 111.5, 55.4, 36.4, 25.9, 22.9, 18.6, -4.1.

4.1.22. 4-((*tert*-Butyldimethylsilyl)oxy)-5-methoxy-1-(3′,4′,5′-trimethoxyphenyl)-2,3-dihydro-1*H*-inden-1-ol (27). 5-Bromo-1,2,3-trimethoxybenzene (0.51 g, 2.1 mmol) was dissolved in THF (25 mL) and cooled to -78 °C. *n*-BuLi (1.22 mL, 3.05 mmol) was added dropwise, and the reaction mixture was stirred for 1 h. TBS-protected **16** (0.43 g, 1.53 mmol) was dissolved in THF (10 mL) and added dropwise to the reaction flask, and the mixture was stirred for 12 h while warming to room temperature, at which time it was washed with water, extracted with EtOAc (3 x 30 mL), dried over sodium sulfate, concentrated, and purified by flash chromatography using a prepacked 50 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 7%A/ 93%B (2 CV), 7%A/ 93%B → 60%A/ 40%B (10 CV), 60%A/40%B (2 CV); flow rate: 50 mL/min; monitored at 254 nm and 280 nm] to afford tertiary alcohol **27** (0.37 g, 0.80 mmol, 37%) as a yellow oil. NMR characterization was performed after the next step.

4.1.23. *tert*-Butyl((6-methoxy-3-(3′,4′,5′-trimethoxyphenyl)-1*H*-inden-7-yl)oxy)dimethylsilane (30). Acetic acid (15 mL) was added to tertiary alcohol **27** (0.37

g, 0.80 mmol), and the reaction mixture was stirred at room temperature for 12 h, at which time it was washed with water and extracted with EtOAc (3 x 30 mL). The combined organic layer was dried over sodium sulfate, concentrated, and purified by flash chromatography using a prepacked 25 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 7%A/ 93%B (1 CV), 7%A/ 93%B → 60%A/40%B (10 CV), 60%A/40%B (2 CV); flow rate: 25 mL/min; monitored at 254 nm and 280 nm] to afford TBS-protected **30** (0.14 g, 0.32 mmol, 39%) as a clear oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.92 (1H, d, J = 6.5 Hz), 6.64 (1H, d, J = 7 Hz), 6.59 (2H, s), 6.19 (1H, t, J = 2 Hz), 3.69 (9H, s), 3.62 (3H, s), 3.23 (2H, d, J = 2 Hz), 0.84 (9H, s), 0.00 (6H, s). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 153.3, 148.8, 144.9, 141.2, 138.2, 137.5, 135.7, 132.1, 128.8, 113.2, 110.3, 104.7, 61.0, 56.2, 55.6, 35.9, 26.1, 18.7, -4.1.

4.1.24. 6-Methoxy-3-(3′,4′,5′-trimethoxyphenyl)-1*H*-inden-7-ol (31).[7] TBS-protected **30** (0.46 g, 1.0 mmol) was dissolved in THF (5 mL), TBAF (5.2 mL, 5.2 mmol) was added, and the reaction mixture was stirred at room temperature for 12 h, at which time the mixture was washed with water, extracted with EtOAc (3 x 40 mL), dried with sodium sulfate, evaporated under reduced pressure, and purified by flash chromatography using a prepacked 25 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 12%A/ 88%B (1 CV), 12%A/ 88%B → 100%A/ 0%B (10 CV), 100%A/ 0%B (2 CV); flow rate: 25 mL/min; monitored at 254 nm and 280 nm] to afford indene **31** (0.23 g, 0.70 mmol, 68%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.08 (1H, d, J = 7.8 Hz), 6.87 (1H, d, J = 7.8 Hz), 6.80 (2H, s), 6.46 (1H, t, J = 2.4 Hz), 5.78 (1H, s), 3.94 (3H, s), 3.91 (9H, s), 3.48 (2H, d, J = 2.4 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 153.3, 144.9, 144.8, 141.8, 139.7, 138.7, 137.6, 131.9, 129.37, 139.35, 111.7, 109.2, 104.8, 61.0, 56.5, 56.2,

34.8. HRMS: Obsvd 351.1203 $[M+Na]^+$, calcd for $C_{19}H_{20}O_5Na$: 351.1208. HPLC: 12.84 min.

4.1.25. Sodium 6-methoxy-3-(3′,4′,5′-trimethoxyphenyl)-1*H*-inden-7-yl phosphate (32). $POCl_3$ (0.26 mL, 2.8 mmol) was cooled to 0 °C in CH_2Cl_2 (10 mL). Indene **31** (0.23 g, 0.70 mmol) and pyridine (0.20 mL, 2.5 mmol) in CH_2Cl_2 (5 mL) was added to the reaction mixture dropwise, and the reaction mixture was stirred at 0 °C for 1 h. The mixture was then warmed to room temperature over 12 h. The mixture was then evaporated under reduced pressure. CH_2Cl_2 (10 mL) was added to the resulting residue, and the mixture was again evaporated under reduced pressure. This was repeated two more times. The resulting solid was dissolved in a mixture of THF and water (2:1, 6 mL total) and stirred for 1 h. The solution was then cooled to 0 °C, and 0.1 M NaOH was added until a pH of 10 was achieved. The solution was then evaporated under reduced pressure, and the crude product was purified by a C18 30 g reversed phase column [solvent A: acetonitrile; solvent B: water; gradient: 10%A / 90%B (1 CV), 10%A / 90%B → 100%A / 0%B (10 CV), 100%A / 0%B (2 CV); flow rate: 25 mL/min; monitored at 254 and 280 nm] to afford phosphate salt **32** (0.09 g, 0.20 mmol, 28%) as a light brown solid. ^{1}H NMR (600 MHz, D_2O) δ 6.98 (1H, d, J = 8.4 Hz), 6.81 (1H, d, J = 7.8 Hz), 6.67 (2H, s), 6.39 (1H, t, J = 1.8 Hz), 3.79 (3H, s), 3.68 (6H, s), 3.65 (3H, s), 3.58 (2H, s). ^{13}C NMR (150 MHz, D_2O) δ 152.4, 150.0 (d, J = 3 Hz), 142.8, 139.5 (d, J = 6.4 Hz), 138.2 (d, J = 2.5 Hz), 137.4, 136.0, 132.4, 130.8, 115.0, 111.1, 104.8, 60.9, 56.3, 55.9, 36.3. ^{31}P NMR (242 MHz, D_2O) δ 0.60. HRMS: Obsvd 453.0687 [M + H], Calcd for $C_{19}H_{20}O_8Na_2P^+$: 453.0686 HPLC: 4.04 min.

4.1.26. 4,5-Dimethoxy-1-(3′,4′,5′-trimethoxyphenyl)-2,3-dihydro-1*H*-inden-1-ol (25). 5-Bromo-1,2,3-trimethoxybenzene (1.60 g, 6.47 mmol) was dissolved in THF (50 mL) and cooled to -78 °C. *n*-BuLi (2.7 mL, 6.8 mmol) was added dropwise, and the reaction mixture was stirred for 1 h. Ketone **11** (0.92 g, 4.79 mmol) was dissolved in THF (10 mL) and added dropwise to the reaction flask, and the mixture was stirred for 12 h while warming to room temperature, at which time it was washed with water, extracted with EtOAc (3 x 30 mL), dried over sodium sulfate, concentrated, and purified by flash chromatography using a prepacked 50 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 10%A/ 90%B (1 CV), 10%A/ 90%B → 80%A/ 20%B (10 CV), 80%A/ 20%B (1 CV); flow rate: 50 mL/min; monitored at 254 nm and 280 nm] to afford tertiary alcohol **25** (1.221 g, 3.39 mmol, 71%) as an orange oil. NMR data was collected after the subsequent step.

4.1.27. 6,7-Dimethoxy-3-(3′,4′,5′-trimethoxyphenyl)-1*H*-indene (28). Acetic acid (25 mL) was added to tertiary alcohol **25** (1.22 g 3.39 mmol), and the mixture was stirred at room temperature for 12 h. The mixture was washed with water, extracted with EtOAc (3 x 30 mL), dried over sodium sulfate, concentrated under reduced pressure, and purified by flash chromatography using a prepacked 50 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 7%A/ 93%B (1 CV), 7%A/ 93%B → 60%A/ 40%B (10 CV), 60%A/ 40%B (2 CV); flow rate: 40 mL/min; monitored at 254 nm and 280 nm] to afford indene **28** (0.56 g, 1.64 mmol, 48%) as a brown solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.28 (1H, d, J = 8 Hz), 6.93 (1H, d, J = 8.5 Hz), 6.83 (2H, s), 6.44 (1H, s), 3.99 (3H, s), 3.93 (3H, s), 3.91 (9H, s), 3.53 (2H, s). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 153.1, 150.2, 145.2,

144.5, 138.2, 137.4, 136.4, 131.6, 128.6, 115.2, 110.9, 104.5, 60.6, 59.8, 56.0, 55.8, 35.2. HRMS: Obsvd 365.1385 $[M+Na]^+$, calcd for $C_{20}H_{22}O_5Na$: 365.1359. HPLC: 14.96 min.

4.1.28. 3-(3′-Methoxyphenyl)propanoic acid (10).[90] 3-methoxycinnamic acid **(8)** (3.56 g, 19.98 mmol) was dissolved in MeOH (100 mL), and 10% Pd on carbon (0.44 g) was added. The mixture was stirred for 12 h at room temperature under H_2 (balloon). The reaction mixture was then filtered through Celite®, and the Celite® was washed with EtOAc (3 x 30 mL). The filtrate (EtOAc and MeOH) was evaporated under reduced pressure resulting in carboxylic acid **10** (3.59 g, 19.7 mmol, quantitative). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 11.93 (1H, s), 7.27 (1H, t, J = 7.5 Hz), 6.88 (2H, m), 6.83 (1H, d, J = 8 Hz), 3.79 (3H, s), 2.99 (2H, t, J = 7 Hz), 2.73 (2H, t, J = 7 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 179.2, 159.9, 142.0, 129.6, 120.7, 114.2, 111.6, 54.9, 35.5, 30.6.

4.1.29. 5-Methoxy-2,3-dihydro-1*H*-inden-1-one (12).[8,91] Eaton's reagent (43 mL, 3 g/mmol of carboxylic acid **10**) was added to carboxylic acid **10** (3.95 g, 21.9 mmol), and the reaction mixture was stirred at room temperature for 72 h. It was then poured over ice, neutralized, and extracted with EtOAc (3 x 50 mL). The organic layer was dried over sodium sulfate, concentrated, and purified by flash chromatography using a prepacked 100 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 12%A/ 88%B (1 CV), 12%A/ 88%B → 100%A/ 0%B (10 CV), 100%A/ 0%B (10 CV); flow rate: 50 mL/min; monitored at 254 nm and 280 nm] to afford ketone **12** (2.26 g, 13.9 mmol, 64%) as a green solid. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.49 (1H, d, J = 7.5 Hz), 6.72 (2H, m), 3.72 (3H, s), 2.91 (2H, t, J = 6 Hz), 2.48 (2H, t, J = 5.5 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 205.0, 165.1, 158.1, 130.2, 125.0, 115.2, 109.6, 55.5, 36.3, 25.7.

4.1.30. 5-Methoxy-1-(3′,4′,5′-trimethoxyphenyl)-2,3-dihydro-1*H*-inden-1-ol (26). [8] 5-Bromo-1,2,3-trimethoxybenzene (1.95 g, 7.91 mmol) was dissolved in THF (50 mL), and the mixture was cooled to -78 °C. *n*-BuLi (3.3 mL, 8.3 mmol) was added dropwise, and the reaction mixture was stirred for 1 h. Ketone **12** (0.95 g, 5.86 mmol) was dissolved in THF (10 mL) and added dropwise to the reaction flask, and the mixture was stirred for 12 h warming to room temperature, at which time it was washed with water, extracted with EtOAc (3 x 30 mL), dried over sodium sulfate, concentrated under reduced pressure, and purified by flash chromatography using a prepacked 100 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 10%A/ 90%B (1 CV), 10%A/ 90%B → 80%A/ 20%B (10 CV), 80%A/ 20%B (2 CV); flow rate: 50 mL/min; monitored at 254 nm and 280 nm] to afford tertiary alcohol **26** (1.45 g, 4.39 mmol, 75%) as a yellow oil. NMR data was collected after the subsequent step.

4.1.30. 6-Methoxy-3-(3′,4′,5′-trimethoxyphenyl)-1*H*-indene (29).[8] Acetic acid (25 mL) was added to tertiary alcohol **26** (1.45 g 4.39 mmol) and stirred at room temperature for 12 h. The mixture was washed with water, extracted with EtOAc (3 x 30 mL), dried over sodium sulfate, concentrated, and purified by flash chromatography using a prepacked 100 g silica column [solvent A: EtOAc; solvent B: hexane; gradient: 7%A/ 93%B (1 CV), 7%A/93%B → 60%A/ 40%B (10 CV), 60%A/ 40%B (1 CV); flow rate: 50 mL/min; monitored at 254 nm and 280 nm] to afford indene **29** (1.30 g, 4.16 mmol, 95%) as a red-yellow oil. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.47 (1H, d, J = 8.5 Hz), 7.08 (1H, d, J = 2 Hz), 6.86 (1H, dd, J = 10.5, 2 Hz), 6.81 (2H, s), 6.38 (1H, t, J = 2 Hz), 3.90 (3H, s), 3.87 (6H, s), 3.79 (3H, s), 3.40 (2H, d, J = 1 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 150.1, 153.3, 146.7, 144.6, 137.6, 136.8, 132.0, 128.4, 120.5, 111.8, 110.6, 104.7, 60.8, 56.1, 55.4,

38.0. HRMS: Obsvd 335.1281 $[M+Na]^+$, calcd for $C_{19}H_{20}O_4Na$: 335.1254. HPLC: 15.95 min.

4.2. Biological Evaluations

4.2.1. SRB Assay. [92,93] Inhibition of growth of human cancer cells was assessed using the sulforhodamine B assay (SRB), as previously described.[92] Cancer cell lines (DU-145, SK-OV-3, and NCI-H460) were plated at 7500-8000 cells/well into 96-well plates using DMEM supplemented with 5% fetal bovine serum/ 1% gentamicin sulfate and incubated for 24 h at 37°C in a humidified incubator. Compound serial dilutions were then added. After 48 h treatment, the cells were fixed with trichloroacetic acid (10% final concentration), washed, dried, stained with sulforhodamine B dye (Acid red 52), washed to remove excess dye, and dried. SRB dye was solubilized, and absorbances were measured at wavelength 540 nm and normalized to values at wavelength 630 nm using an automated Biotek plate reader. A growth inhibition of 50% (GI_{50} or the drug concentration causing 50% reduction in the net protein increase) was calculated from the absorbance data.

4.2.2. Colchicine Binding Assay. Inhibition of [^{3}H]colchicine binding to tubulin was measured using reaction mixtures (100 μL each) containing 1.0 μM tubulin, 5.0 μM [^{3}H]colchicine (from Perkin-Elmer), 5% (v/v) dimethyl sulfoxide, potential inhibitors at 5.0 μM, and components that stabilize the colchicine binding activity of tubulin [94] (1.0 M monosodium glutamate [adjusted to pH 6.6 with HCl in a 2.0 M stock solution], 0.5 mg/mL bovine serum albumin, 0.1 M glucose-1-phosphate, 1.0 mM $MgCl_2$, and 1.0 mM GTP). Incubation was for 10 min at 37 °C, a time point selected because the binding

reaction in control reaction mixtures is 40-60% complete. Reactions were stopped with 2.0 mL of ice-cold water, and the reaction mixtures were placed on ice. Each sample was poured onto a stack of two DEAE-cellulose filters (from Whatman), followed by 6 mL of ice-cold water. The samples were aspirated under reduced vacuum. The filters were washed three times with 2 mL water and placed into vials containing 5 mL of Biosafe II scintillation cocktail. Samples were counted 18 h later in a Beckman scintillation counter. Samples with inhibitors were compared to samples with no inhibitor, and percent inhibition was determined. All samples were corrected for the amount of radiolabel bound to the filters in the absence of tubulin.

4.2.3. Inhibition of Tubulin Polymerization.Tubulin polymerization experiments were performed in 0.25 mL reaction mixtures (final volume).[95] The mixtures contained 1 mg/mL (10 μM) purified bovine brain tubulin, 0.8 M monosodium glutamate (pH 6.6), 4% (v/v) dimethyl sulfoxide, 0.4 mM GTP, and different compound concentrations. All reaction components except GTP were preincubated for 15 min at 30 °C in 0.24 mL. The mixtures were cooled to 0 °C, and 10 μL of 10 mM GTP were added. Reaction mixtures were transferred to cuvettes held at 0 °C in Beckman DU-7400 and DU-7500 spectrophotometers equipped with electronic temperature controllers. The temperature was jumped to 30 °C, taking about 30 s, and polymerization was followed at 350 nm for 20 min. The IC_{50} was defined as the compound concentration that inhibited extent of polymerization by 50% after 20 min.

4.2.4. *In Vivo* Tumor Model. Human breast cancer cells, MCF7-luc-GFP-mCherry (ATCC), were transfected sequentially with a lentivirus containing firefly luciferase reporter, GFP and mCherry reporter genes, as described previously.[78] Highly expressing

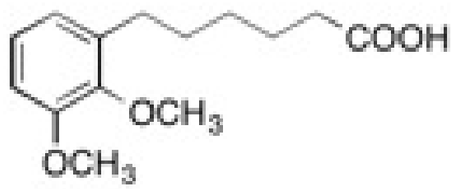
stable clones were isolated. Induction of tumors was carried out by injecting 10^6 cells mixed with 50% Matrigel™ (BD Biosciences, San Jose, CA) into the right upper ventral mammary fat pads of female SCID-NOD mice (UTSW breeding colony). Tumors were allowed to grow to a size of 10-12 mm in diameter, determined by calipers, before selection for BLI. All animal procedures were approved by the University of Texas Southwestern Medical Center Institutional Animal Care and Use Committee.

4.2.5. *In Vivo* Bioluminescence Imaging (BLI). BLI was carried out as described previously.[78] Briefly, anesthetized, tumor bearing mice (O_2, 2% isoflurane, Henry Schein Inc., Melville, NY) were injected subcutaneously in the fore-back neck region with 80 µL of a solution of luciferase substrate, *D*-luciferin (sodium salt, 120 mg/kg, in saline, Gold Biotechnology, St. Louis, MO). Mice were maintained under anesthesia (2% isoflurane in oxygen, 1 dm^3/min) while baseline BLI was performed using a Caliper Xenogen IVIS® Spectrum (Perkin-Elmer, Alameda, CA). A series of BLI images was collected over 35 min using the following settings: auto exposure time, f-stop = 2, Field of view = D, binning = 4 (medium). Light intensity-time curves obtained from these images were analyzed using Living Image® software and light emission compared based on area under the light emission curve. Mice were injected intraperitoneally with either 120 µL of saline (vehicle), **CA4P** (provided by Mateon Therapeutics, Inc.; 120 mg/kg in saline as used previously[54] or analogue **24** (120 mg/kg) in saline immediately after baseline BLI. BLI was repeated, with new luciferin injections, 4, 24, and 48 h later.

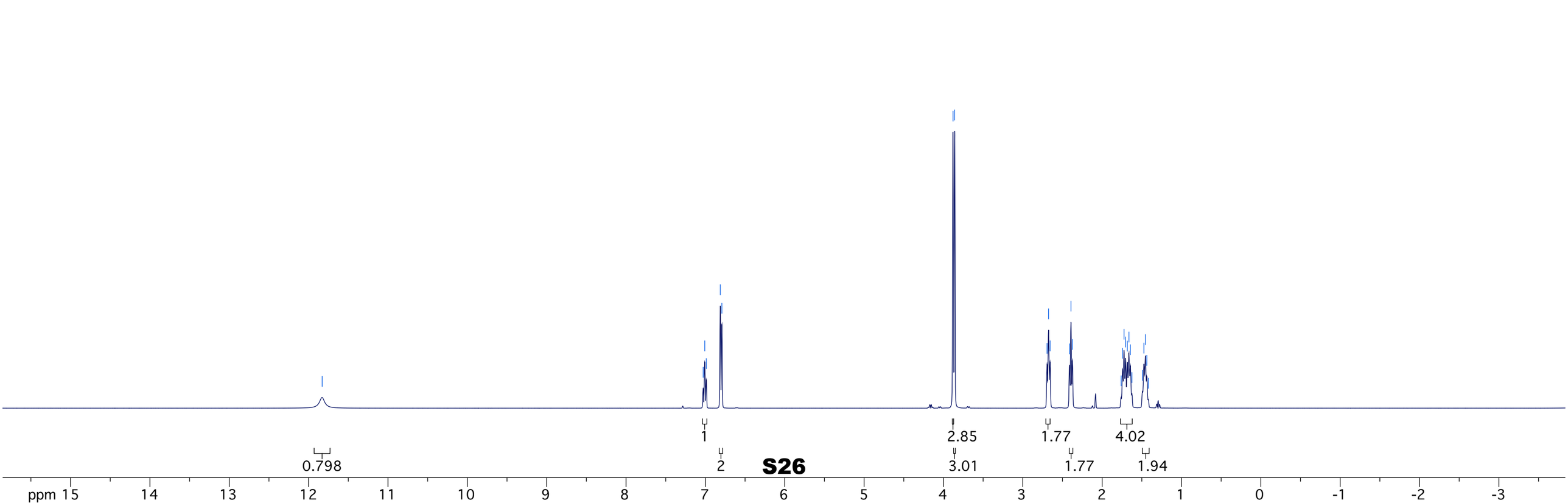
4.2.6. Histology. Following the 48 h BLI data acquisition, the tumors were excised, bisected and fixed in 4% paraformaldehyde solution. Tumor tissue was processed for paraffin embedding, sectioned and stained by routine methods. H&E staining was

performed on one cross section from each tumor. Whole mount high resolution microscopy was obtained using a Zeiss Axioscan Z1 digital slide scanner.


11.830
7.027
7.008
6.989
6.812
6.792
3.879
3.858
2.694
2.676
2.656
2.411
2.393
2.374
1.760
1.742
1.724
1.704
1.683
1.662
1.644
1.625
1.492
1.474
1.455
1.437
1.418


COOH
OCH3
OCH3

3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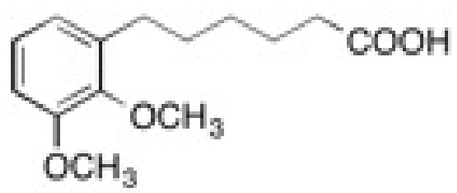
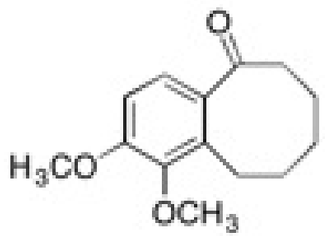
1
2
2.85
3.01
1.77
1.77
4.02
1.94
ppm 15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3


COOH
OCH3
OCH3

3

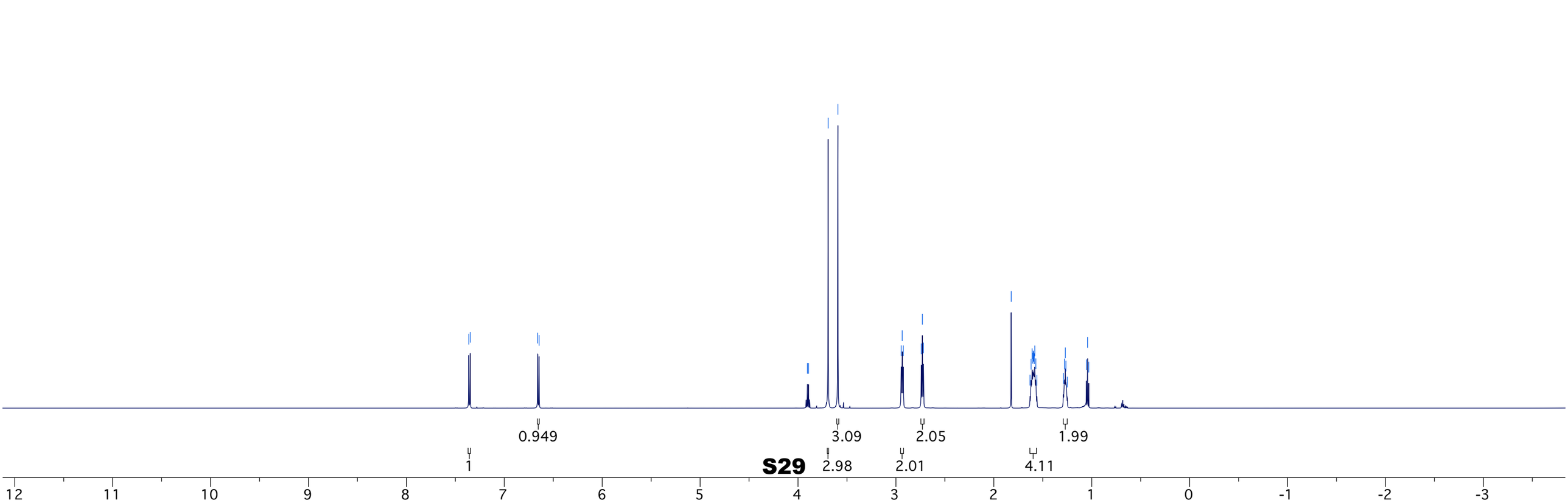
180.149
152.704
147.075
136.167
123.758
121.890
110.188
60.452
55.536
33.967
30.380
29.625
28.902
24.537
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

4


O
H3CO
OCH3

5

7.362
7.348
6.659
6.644
3.904
3.892
3.692
3.592
2.947
2.936
2.925
2.741
2.730
2.718
1.822
1.630
1.619
1.609
1.602
1.598
1.592
1.587
1.581
1.571
1.560
1.290
1.279
1.270
1.264
1.250
1.054
1.042
1.031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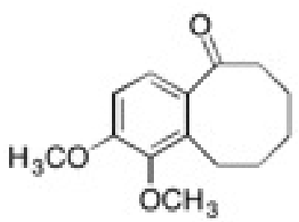
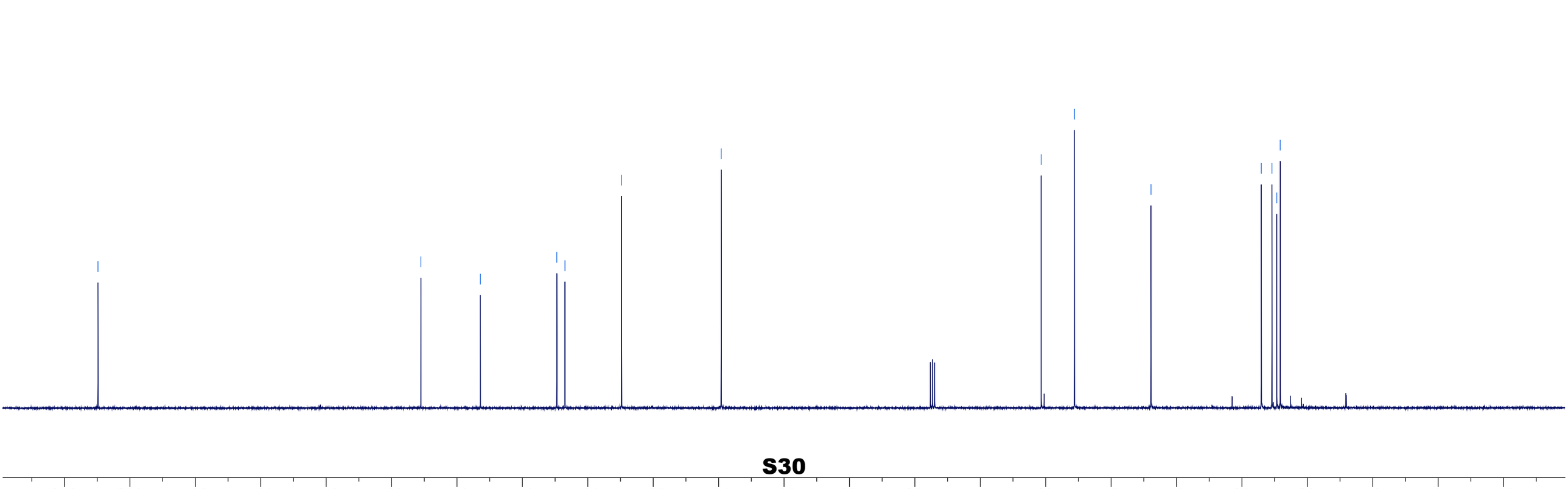
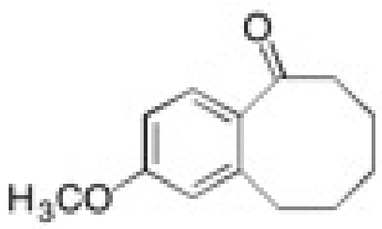
3.09
2.05
1.99
1
2.98
2.01
4.11
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3


O
H3CO
OCH3

5

204.885
155.521
146.423
134.743
133.489
124.835
109.605
60.686
55.604
43.902
27.040
25.406
24.669
24.146

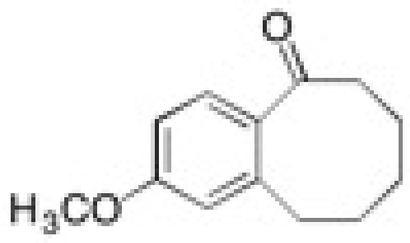

ppm 210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


O
H3CO

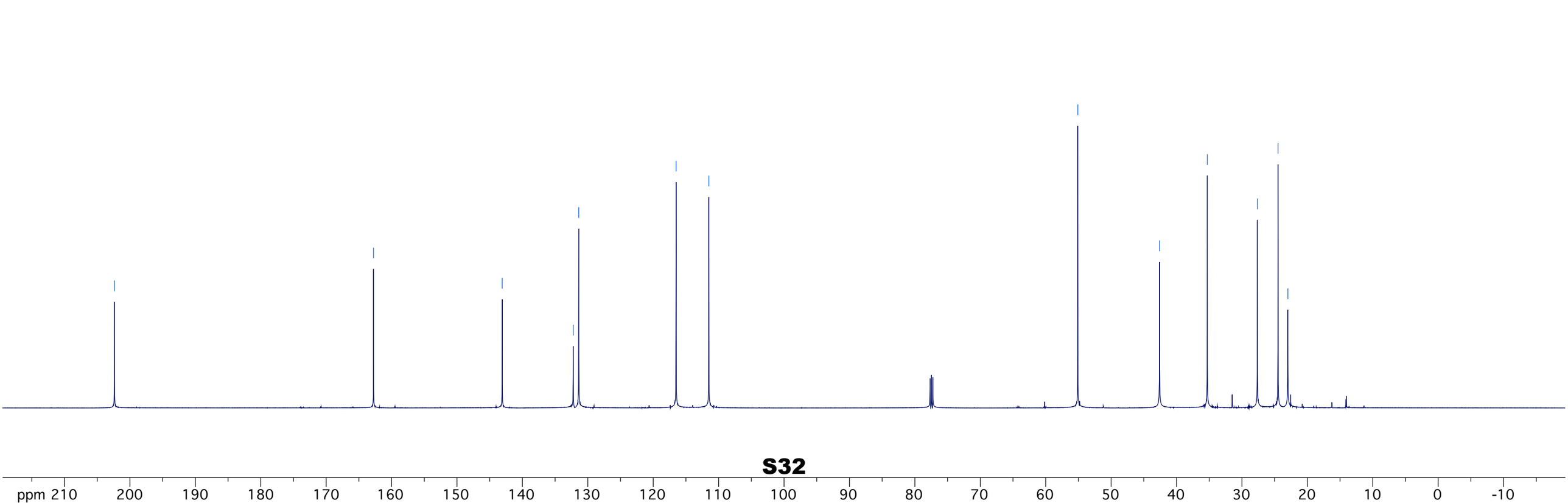
6

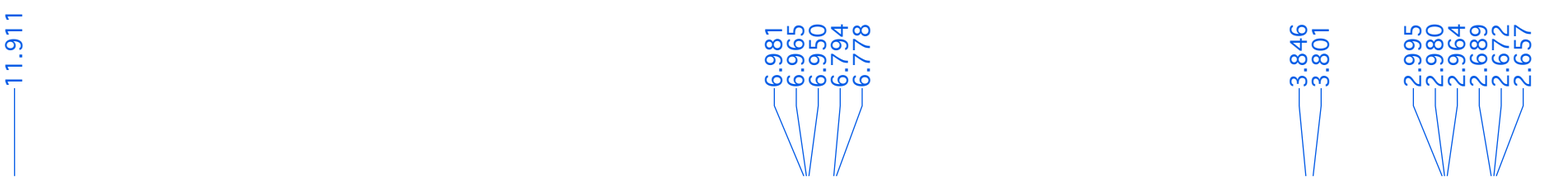
7.824
7.809
6.638
6.634
6.624
6.619
6.517
6.512
3.650
2.958
2.947
2.935
2.827
2.815
2.803
1.694
1.682
1.672
1.661
1.649
1.635
1.624
1.614
1.603
1.592
1.276
1.266
1.255
1.245
1.235
1
1.04
1.96
2.04
1.99
-0.0123
1.02
3.26
1.99
1.98
ppm
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3

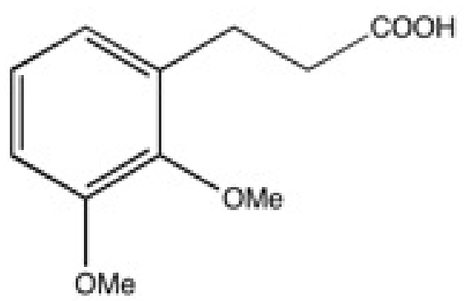
202.376
162.760
143.089
132.227
131.383
116.503
111.494
55.087
42.599
35.294
27.640
24.480
22.976



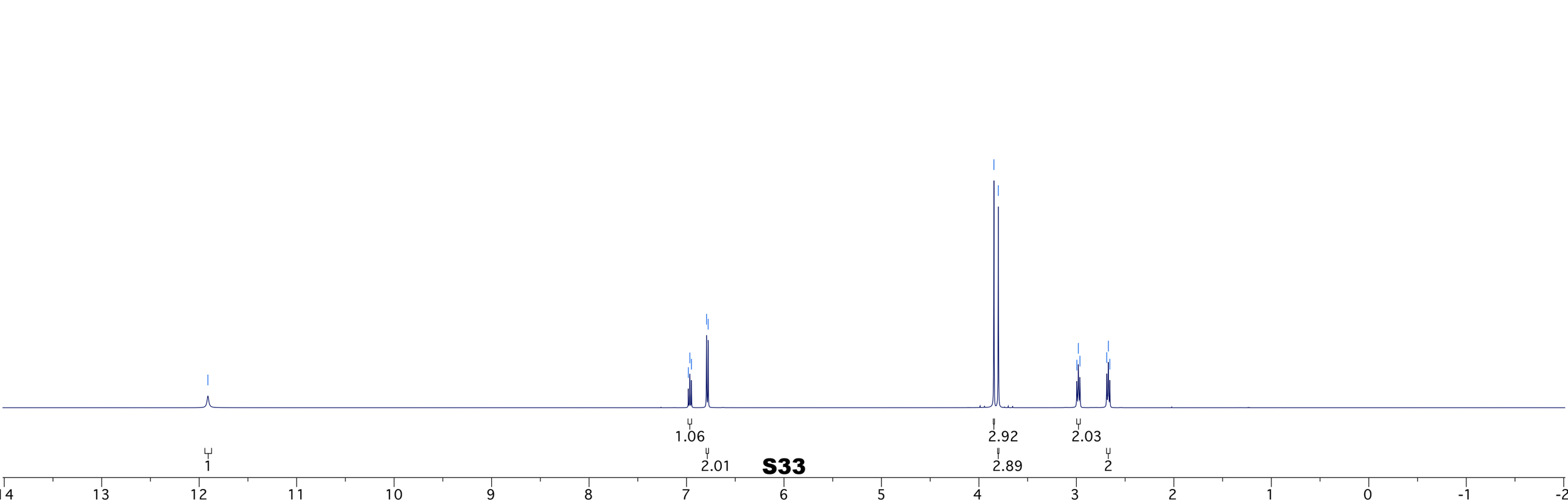
6

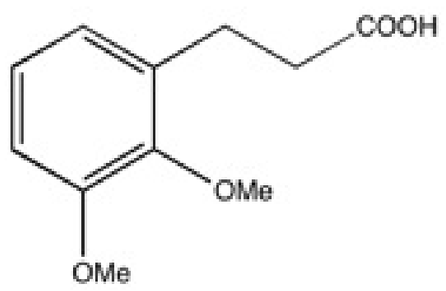



11.911
6.981
6.965
6.950
6.794
6.778
3.846
3.801
2.995
2.980
2.964
2.689
2.672
2.657


COOH
OMe
OMe

9


1.06
2.92
2.03
1
2.01
2.89
2
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2



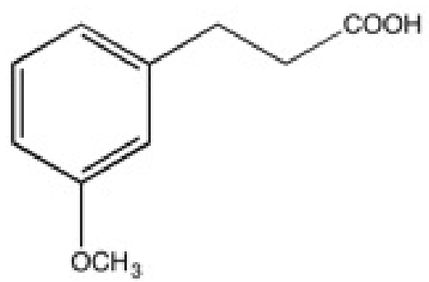
9

179.390
152.715
147.134
133.903
123.999
121.678
111.001
60.375
55.510
34.669
25.291

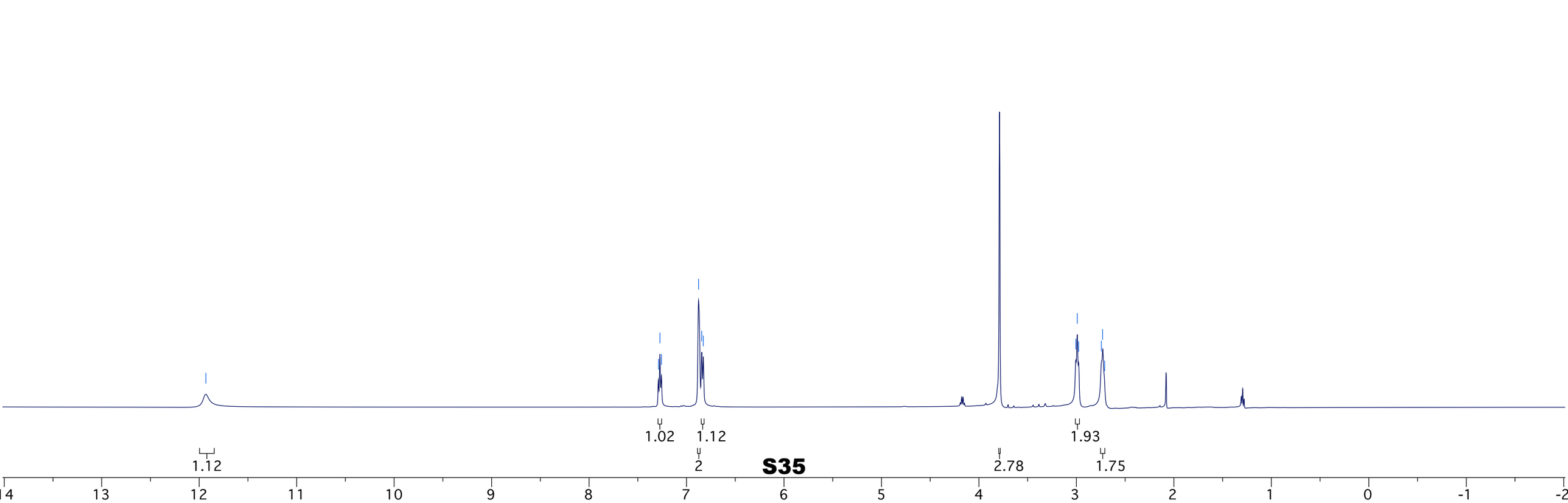
11.931

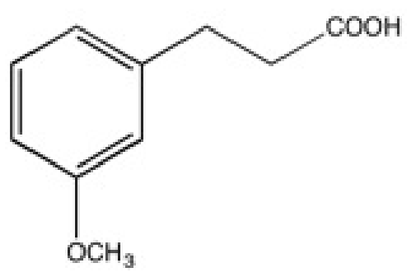
7.288
7.273
7.257
6.876
6.844
6.828

3.005
2.992
2.977
2.744
2.731
2.710



10





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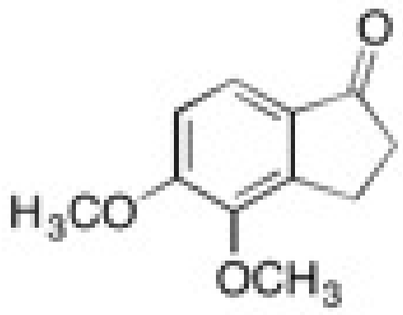
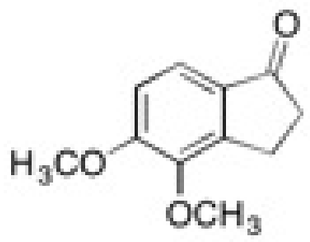
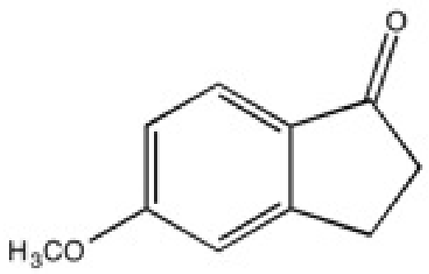


11



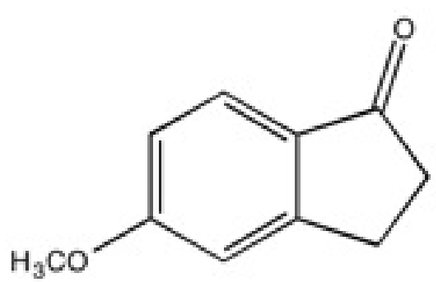
11


O
H3CO

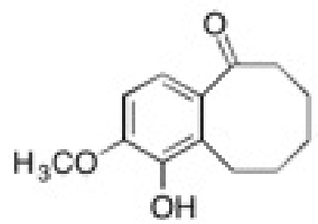
12

7.498
7.483
6.739
6.723
6.719
3.724
2.918
2.906
2.894
2.492
2.481
2.469
2.06
2.08
1
3.27
2.07
ppm 12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2

204.996
165.084
158.097
130.169
124.963
115.167
109.552
55.495
36.267
25.721



12



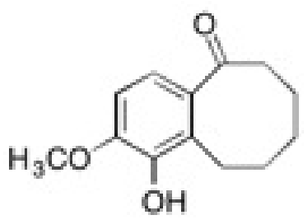
13

7.237
7.223
6.739
6.725
6.110
4.092
4.080
3.849
3.070
3.059
3.048
2.888
2.877
2.866
1.796
1.784
1.779
1.775
1.767
1.764
1.756
1.753
1.749
1.746
1.735
1.503
1.496
1.492
1.488
1.482
1.477
1.472
1.462

1.04
3.19
1.99
1.91
1
0.996
2.14
4.15

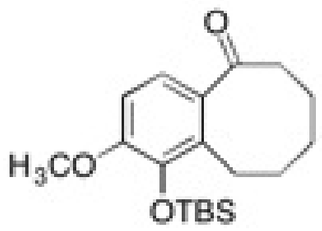
ppm 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3

206.445
148.748
142.907
133.655
126.663
120.112
107.917
55.976
44.381
25.904
25.742
25.298
23.853



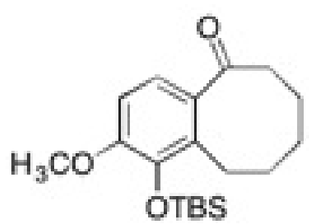
13

ppm 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10



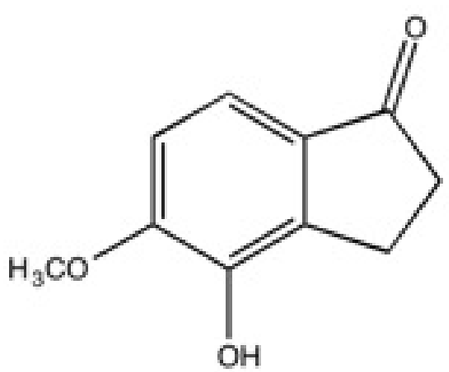
14

207.075
151.854
141.937
133.698
131.543
120.902
108.544
77.160
76.948
76.735
54.509
44.478
26.167
25.982
25.846
25.522
23.667
18.800
-3.865



14

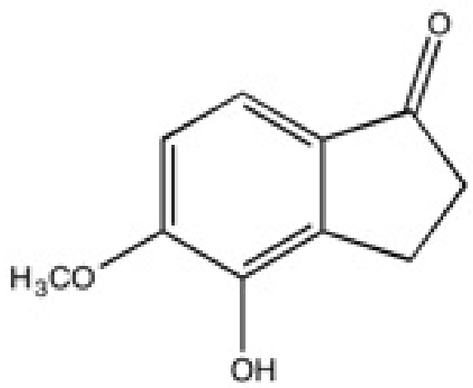
ppm 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10


O
H3CO
OH

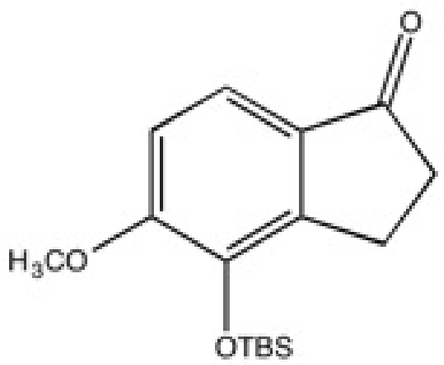
15

7.363
7.346
6.931
6.914
5.805
3.968
3.079
3.068
3.056
2.696
2.685
2.673
1.1
3.13
2.23
1
0.728
2.15
ppm 11
10
9
8
7
6
5
4
3
2
1
0
-1
-2

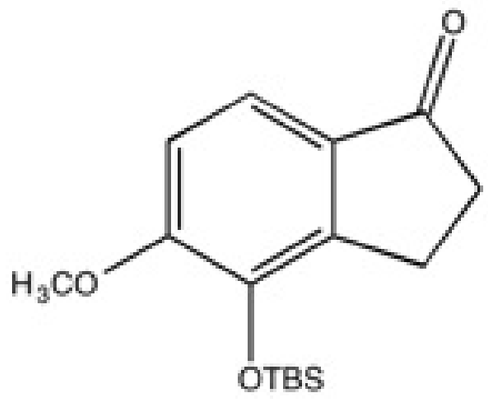
206.014
150.904
142.118
140.525
131.404
116.137
110.447
56.417
36.519
21.882



15



16


O
H3CO
OTBS

16

205.806
155.049
146.275
141.383
131.071
117.413
111.454
55.359
36.390
25.827
22.921
18.574
4.145
230
220
210
200
190
180
170
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140
130
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100
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60
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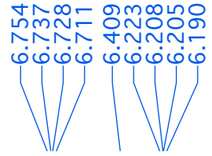
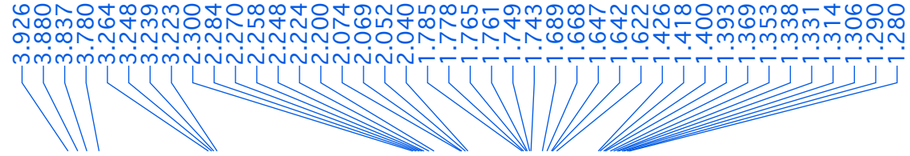
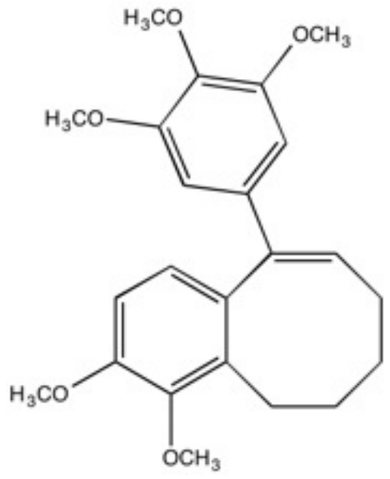
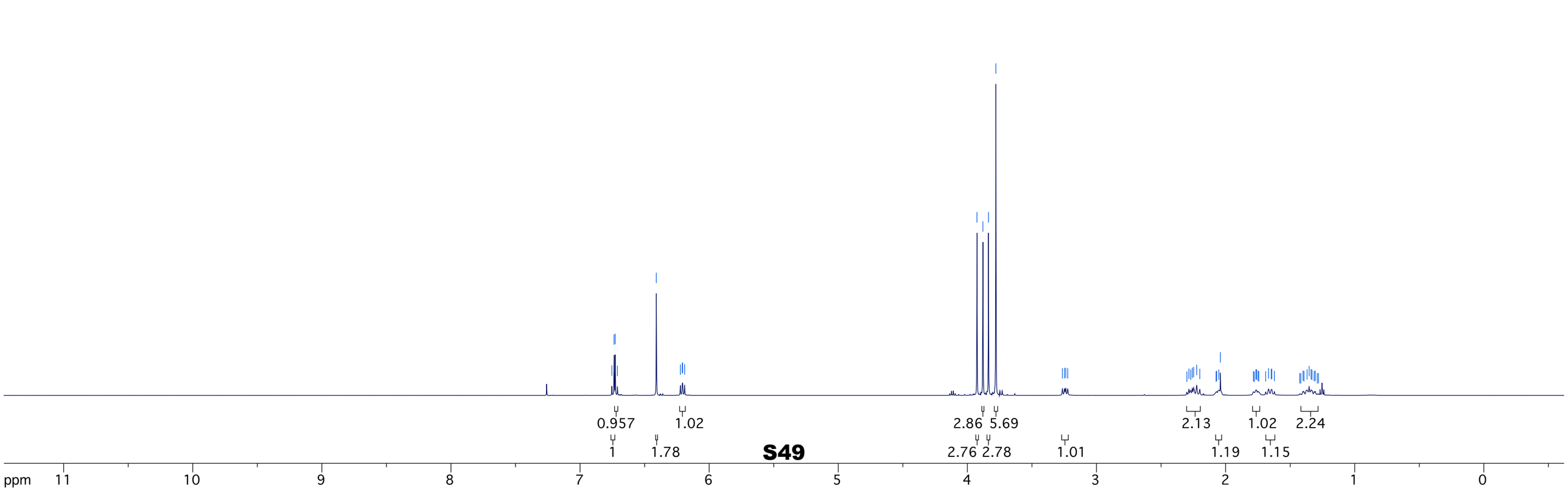
0
-10


6.754
6.737
6.728
6.711
6.409
6.223
6.208
6.205
6.190


3.926
3.880
3.837
3.780
3.264
3.248
3.239
3.223
2.300
2.284
2.270
2.258
2.248
2.224
2.200
2.074
2.069
2.052
2.040
1.785
1.778
1.765
1.761
1.749
1.743
1.689
1.668
1.647
1.642
1.622
1.426
1.418
1.400
1.393
1.369
1.353
1.338
1.331
1.314
1.306
1.290
1.280


H3CO
OCH3
H3CO
H3CO
OCH3

20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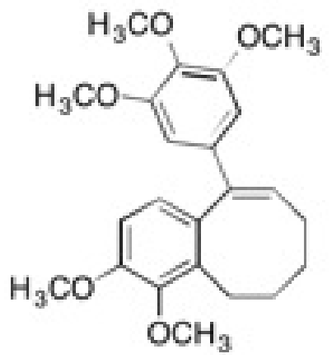
1.02
2.86
5.69
2.13
1.02
2.24
1
1.78
2.76
2.78
1.01
1.19
1.15
ppm
11
10
9
8
7
6
5
4
3
2
1
0


H3CO
OCH3
H3CO
H3CO
OCH3

20

152.787
151.823
146.337
139.702
139.031
137.543
137.172
131.899
129.719
124.765
109.506
104.672
60.868
60.716
56.112
55.551
28.348
27.838
26.046
24.621

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_4_88000001.D
Sample Name: CAH_4_88

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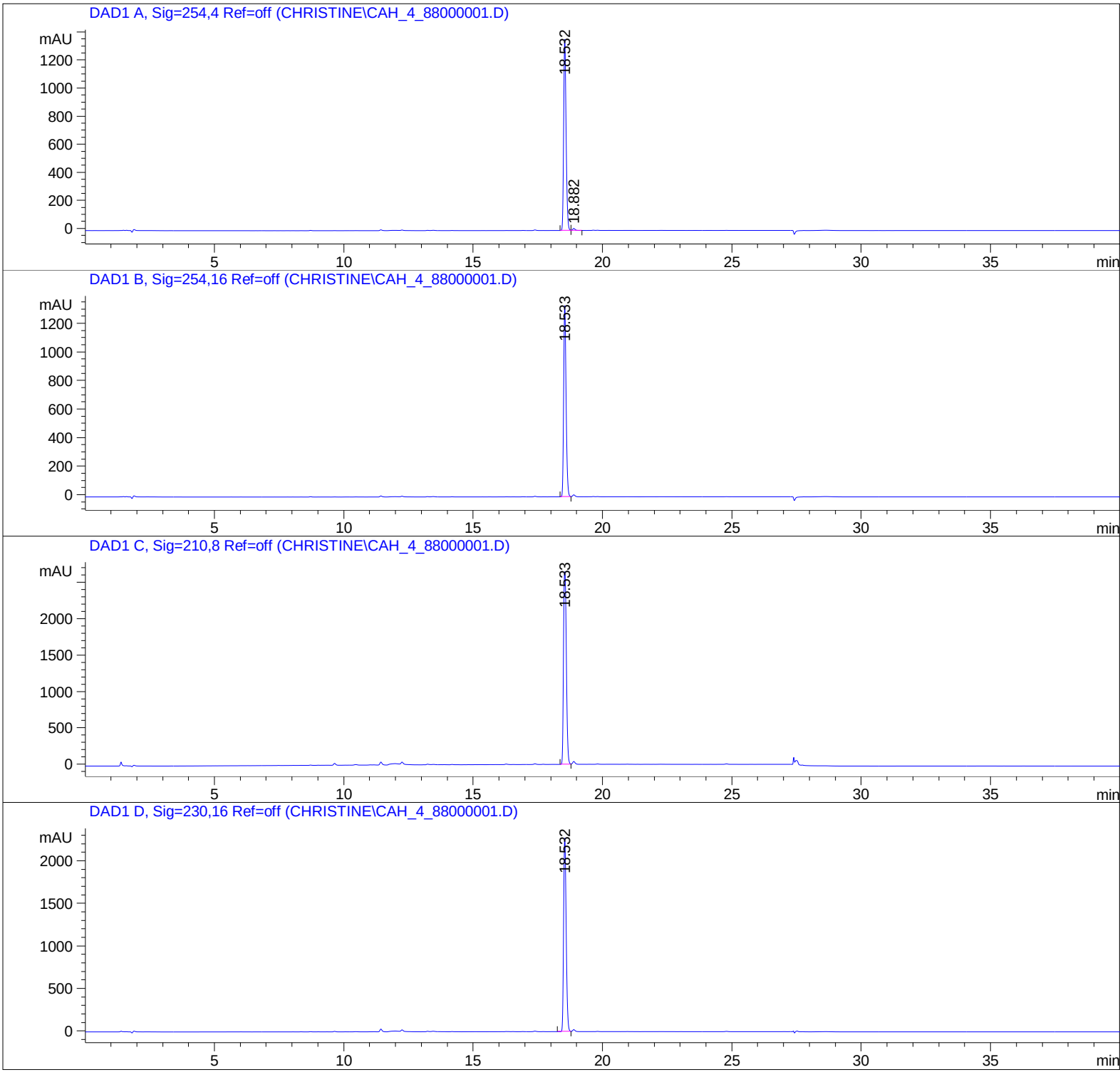
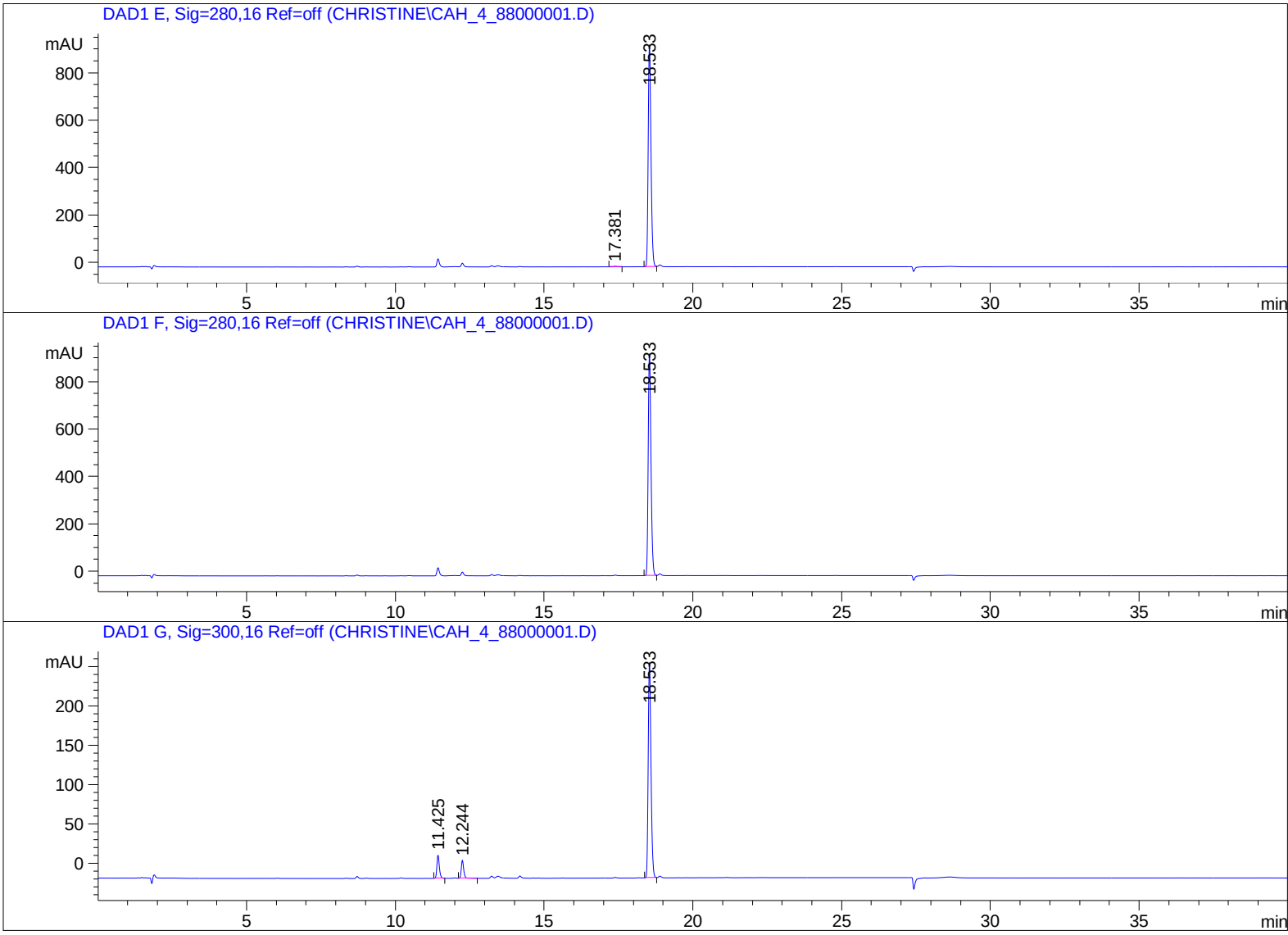
Acq. Operator : Christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 9/23/2014 8:51:24 AM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 9/23/2014 8:17:01 AM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CAH_4_88000001.D\DA.M (MASTERMETHOD.M)
Last changed : 9/23/2014 9:45:13 AM by Christine



Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_4_88000001.D
Sample Name: CAH_4_88



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Area Percent Report

==========

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

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.532	BV	0.0995	8838.96289	1365.10266	98.9235
2	18.882	VB	0.1004	96.18368	14.31833	1.0765

Totals : 8935.14657 1379.42099

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_4_88000001.D
Sample Name: CAH_4_88

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.533	BV	0.0995	8683.92773	1341.87500	100.0000
Totals :				8683.92773	1341.87500	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.533	BV	0.1233	2.02628e4	2646.86206	100.0000
Totals :				2.02628e4	2646.86206	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.532	BV	0.1082	1.56791e4	2280.01855	100.0000
Totals :				1.56791e4	2280.01855	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.381	BB	0.1023	16.08844	2.39759	0.2640
2	18.533	BV	0.0995	6078.18750	939.42749	99.7360
Totals :				6094.27594	941.82508	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.533	BV	0.0995	6078.18750	939.42749	100.0000

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_4_88000001.D
Sample Name: CAH_4_88

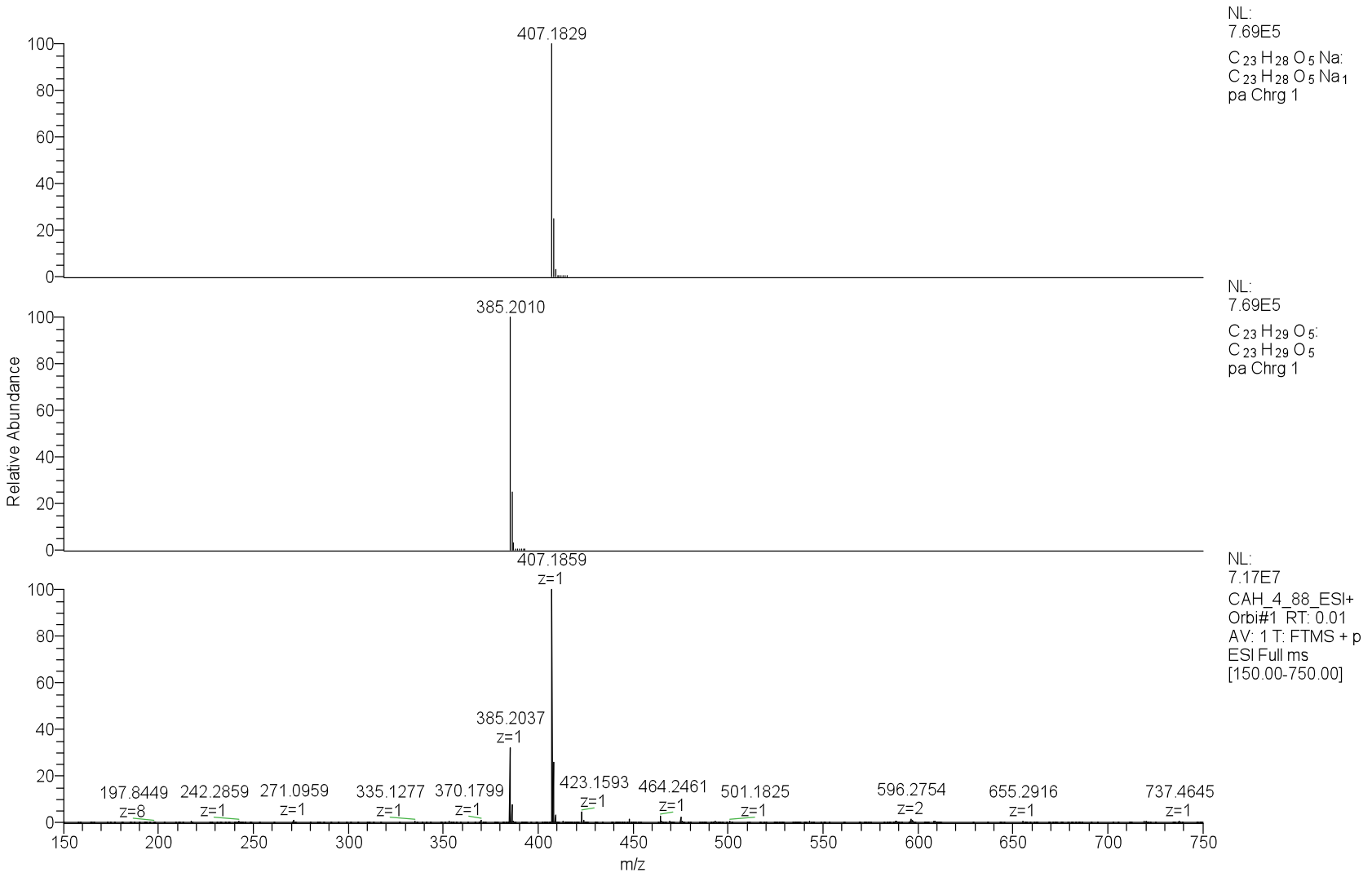
Totals : 6078.18750 939.42749

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.425	BB	0.0866	167.73837	29.38750	8.0605
2	12.244	VB	0.0884	130.17458	22.87446	6.2554
3	18.533	BV	0.0998	1783.07324	274.61212	85.6840

Totals : 2080.98619 326.87408

*** End of Report ***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7.69E5
C 23 H 28 O 5 Na:
C 23 H 28 O 5 Na 1
pa Chrg 1
385.2010
NL:
7.69E5
C 23 H 29 O 5:
C 23 H 29 O 5
pa Chrg 1
Relative Abundance
407.1859
z=1
NL:
7.17E7
CAH_4_88_ESI+
Orbi#1 RT: 0.01
AV: 1 T: FTMS + p
ESI Full ms
[150.00-750.00]
385.2037
z=1
197.8449
z=8
242.2859
z=1
271.0959
z=1
335.1277
z=1
370.1799
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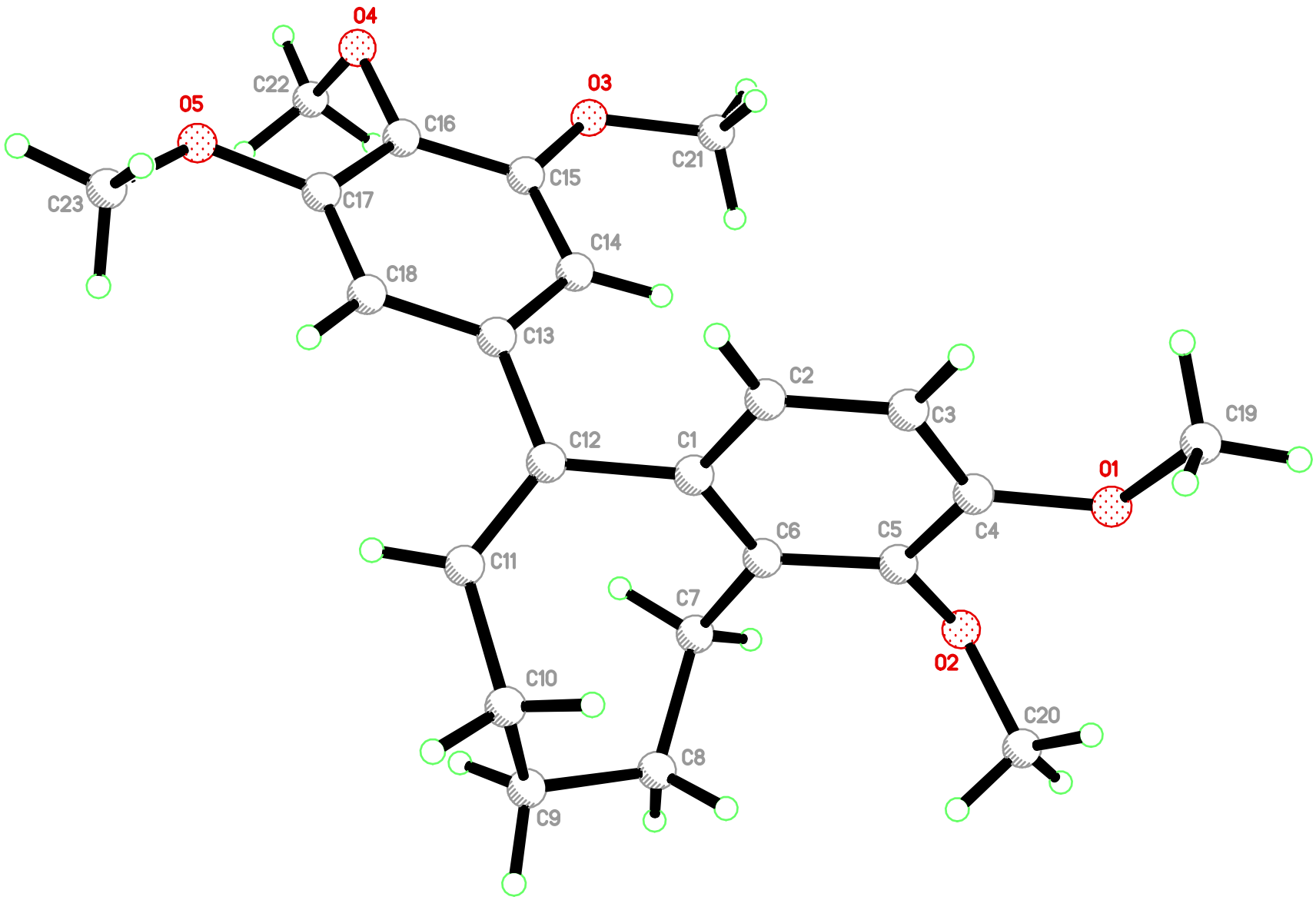
423.1593
z=1
464.2461
z=1
501.1825
z=1
596.2754
z=2
655.2916
z=1
737.4645
z=1
m/z


O4
C22
O5
C16
O3
C21
C23
C17
C15
C14
C18
C13
C2
C3
C19
C12
C1
O1
C6
C5
C4
C11
C7
O2
C10
C20
C8
C9

X-ray Crystallographic Analysis:

X-ray crystallographic analysis of compound **20**. Crystallographic data were collected on a crystal of **20** with dimensions 0.257 x 0.138 x 0.039 mm^3. Data were collected at 150 K on a Bruker X8 Apex using Mo KR radiation (λ = 0.71073 Å). The structure was solved by direct methods after correction of the data using SADABS. Crystallographic data and definement details for the complex mentioned herein is found in the Supporting Information (Table S1-S4). All data were processed using the Bruker AXS SHELXTL software, version 6.10.

Table 1. Crystal data and structure refinement for Compound 20.

Identification code	Compound 20	
Empirical formula	C23 H28 O5	
Formula weight	384.45	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 11.7350(5) Å	a= 90°.
	b = 9.4232(5) Å	b= 102.544(2)°.
	c = 18.5619(10) Å	g = 90°.
Volume	2003.60(17) $Å^3$	
Z	4	
Density (calculated)	1.275 Mg/m^3	
Absorption coefficient	0.089 mm^{-1}	
F(000)	824	
Crystal size	0.257 x 0.138 x 0.039 mm^3	
Theta range for data collection	2.436 to 29.679°.	
Index ranges	-16<=h<=12, -12<=k<=13, -25<=l<=23	
Reflections collected	13077	
Independent reflections	5627 [R(int) = 0.0336]	
Completeness to theta = 25.242°	99.3 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.902 and 0.885
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5627 / 0 / 253
Goodness-of-fit on F^2	1.025
Final R indices [I>2sigma(I)]	R1 = 0.0541, wR2 = 0.1131
R indices (all data)	R1 = 0.0879, wR2 = 0.1267
Extinction coefficient	n/a
Largest diff. peak and hole	0.344 and -0.242 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Compound 20. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3173(1)	14383(1)	4025(1)	30(1)
O(2)	4861(1)	13357(1)	3412(1)	29(1)
O(3)	857(1)	9497(1)	770(1)	28(1)
O(4)	251(1)	6770(1)	589(1)	23(1)
O(5)	819(1)	4899(1)	1700(1)	27(1)
C(1)	3180(1)	10093(2)	3481(1)	20(1)
C(2)	2272(1)	10643(2)	3767(1)	23(1)
C(3)	2252(1)	12049(2)	3979(1)	24(1)
C(4)	3134(1)	12951(2)	3878(1)	22(1)
C(5)	4042(1)	12422(2)	3577(1)	21(1)
C(6)	4094(1)	10996(2)	3387(1)	19(1)
C(7)	5115(1)	10470(2)	3087(1)	24(1)
C(8)	6151(1)	9948(2)	3694(1)	30(1)
C(9)	6098(1)	8424(2)	3958(1)	32(1)
C(10)	4997(1)	8045(2)	4242(1)	28(1)
C(11)	3994(1)	7669(2)	3619(1)	24(1)
C(12)	3176(1)	8564(2)	3272(1)	21(1)
C(13)	2289(1)	8107(2)	2605(1)	21(1)
C(14)	1906(1)	9084(2)	2043(1)	21(1)
C(15)	1226(1)	8632(2)	1370(1)	21(1)
C(16)	907(1)	7212(2)	1263(1)	20(1)
C(17)	1222(1)	6255(2)	1844(1)	21(1)
C(18)	1921(1)	6696(2)	2514(1)	22(1)
C(19)	2327(2)	14928(2)	4397(1)	36(1)
C(20)	5700(1)	13882(2)	4028(1)	35(1)
C(21)	948(2)	10986(2)	893(1)	32(1)
C(22)	963(1)	6307(2)	95(1)	28(1)
C(23)	1023(2)	3932(2)	2307(1)	36(1)

Table 3. Bond lengths [Å] and angles [°] for Compound 20.

O(1)-C(4)	1.3749(19)
O(1)-C(19)	1.4217(19)
O(2)-C(5)	1.3859(17)
O(2)-C(20)	1.426(2)
O(3)-C(15)	1.3706(18)
O(3)-C(21)	1.4221(19)
O(4)-C(16)	1.3838(16)
O(4)-C(22)	1.4353(17)
O(5)-C(17)	1.3686(18)
O(5)-C(23)	1.428(2)
C(1)-C(2)	1.390(2)
C(1)-C(6)	1.410(2)
C(1)-C(12)	1.492(2)
C(2)-C(3)	1.384(2)
C(3)-C(4)	1.384(2)
C(4)-C(5)	1.399(2)
C(5)-C(6)	1.394(2)
C(6)-C(7)	1.5094(19)
C(7)-C(8)	1.547(2)
C(8)-C(9)	1.523(2)
C(9)-C(10)	1.539(2)
C(10)-C(11)	1.5015(19)
C(11)-C(12)	1.334(2)
C(12)-C(13)	1.4964(19)
C(13)-C(14)	1.392(2)
C(13)-C(18)	1.397(2)
C(14)-C(15)	1.3947(19)
C(15)-C(16)	1.392(2)
C(16)-C(17)	1.393(2)
C(17)-C(18)	1.3957(19)
C(4)-O(1)-C(19)	117.05(13)
C(5)-O(2)-C(20)	115.76(12)
C(15)-O(3)-C(21)	117.25(12)

C(16)-O(4)-C(22)	112.51(10)
C(17)-O(5)-C(23)	116.68(12)
C(2)-C(1)-C(6)	119.28(14)
C(2)-C(1)-C(12)	120.02(13)
C(6)-C(1)-C(12)	120.69(12)
C(3)-C(2)-C(1)	121.86(13)
C(2)-C(3)-C(4)	119.33(13)
O(1)-C(4)-C(3)	124.69(13)
O(1)-C(4)-C(5)	115.74(13)
C(3)-C(4)-C(5)	119.51(14)
O(2)-C(5)-C(6)	119.14(12)
O(2)-C(5)-C(4)	119.07(14)
C(6)-C(5)-C(4)	121.62(13)
C(5)-C(6)-C(1)	118.33(12)
C(5)-C(6)-C(7)	119.47(13)
C(1)-C(6)-C(7)	122.20(14)
C(6)-C(7)-C(8)	113.40(12)
C(9)-C(8)-C(7)	116.92(13)
C(8)-C(9)-C(10)	115.17(13)
C(11)-C(10)-C(9)	111.52(13)
C(12)-C(11)-C(10)	125.74(15)
C(11)-C(12)-C(1)	121.55(13)
C(11)-C(12)-C(13)	121.10(14)
C(1)-C(12)-C(13)	117.06(12)
C(14)-C(13)-C(18)	119.84(13)
C(14)-C(13)-C(12)	118.93(13)
C(18)-C(13)-C(12)	121.00(13)
C(13)-C(14)-C(15)	119.92(14)
O(3)-C(15)-C(16)	115.38(12)
O(3)-C(15)-C(14)	124.30(14)
C(16)-C(15)-C(14)	120.30(14)
O(4)-C(16)-C(15)	119.85(13)
O(4)-C(16)-C(17)	120.45(13)
C(15)-C(16)-C(17)	119.67(12)
O(5)-C(17)-C(16)	115.50(12)
O(5)-C(17)-C(18)	124.35(13)

C(16)-C(17)-C(18)	120.14(14)
C(17)-C(18)-C(13)	119.88(14)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Compound 20. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

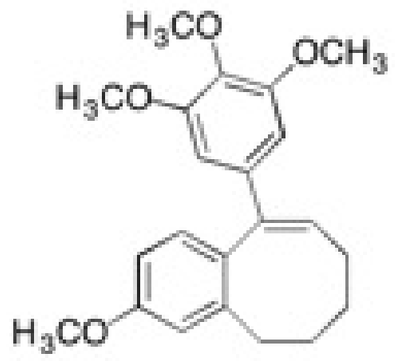
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	34(1)	23(1)	36(1)	-4(1)	14(1)	1(1)
O(2)	33(1)	28(1)	29(1)	-2(1)	14(1)	-12(1)
O(3)	35(1)	24(1)	20(1)	0(1)	-4(1)	0(1)
O(4)	18(1)	30(1)	19(1)	-8(1)	-1(1)	0(1)
O(5)	29(1)	22(1)	26(1)	-4(1)	0(1)	-6(1)
C(1)	20(1)	24(1)	14(1)	1(1)	0(1)	-3(1)
C(2)	18(1)	30(1)	21(1)	0(1)	2(1)	-6(1)
C(3)	18(1)	30(1)	22(1)	-1(1)	4(1)	0(1)
C(4)	24(1)	22(1)	20(1)	-1(1)	3(1)	1(1)
C(5)	20(1)	24(1)	18(1)	2(1)	4(1)	-4(1)
C(6)	19(1)	24(1)	14(1)	0(1)	2(1)	-1(1)
C(7)	24(1)	26(1)	24(1)	-2(1)	9(1)	-2(1)
C(8)	19(1)	34(1)	37(1)	-3(1)	5(1)	-2(1)
C(9)	23(1)	35(1)	33(1)	-2(1)	-3(1)	3(1)
C(10)	28(1)	28(1)	23(1)	3(1)	-4(1)	-2(1)
C(11)	27(1)	23(1)	21(1)	-1(1)	0(1)	-5(1)
C(12)	21(1)	24(1)	17(1)	-1(1)	2(1)	-6(1)
C(13)	18(1)	25(1)	18(1)	-4(1)	2(1)	-2(1)
C(14)	21(1)	21(1)	20(1)	-3(1)	2(1)	-2(1)
C(15)	19(1)	25(1)	18(1)	-1(1)	2(1)	1(1)
C(16)	16(1)	25(1)	18(1)	-6(1)	1(1)	0(1)
C(17)	18(1)	20(1)	24(1)	-5(1)	4(1)	-2(1)
C(18)	22(1)	24(1)	20(1)	-1(1)	1(1)	-2(1)
C(19)	39(1)	33(1)	39(1)	-10(1)	14(1)	5(1)
C(20)	29(1)	34(1)	42(1)	-8(1)	10(1)	-12(1)
C(21)	40(1)	24(1)	27(1)	0(1)	-2(1)	0(1)

C(22)	27(1)	34(1)	23(1)	-8(1)	6(1)	-2(1)
C(23)	52(1)	24(1)	30(1)	0(1)	3(1)	-11(1)

Crystallographic data for structure **20** (deposition number CCDC 1046343) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

6.959 6.945 6.850 6.846 6.742 6.738 6.728 6.724 6.444 6.256 6.243 6.241 6.228

3.863 3.857 3.798 2.849 2.836 2.827 2.815 2.581 2.560 2.541 2.320 2.307 2.297 2.295 2.285 2.272 2.082 2.078 2.065 2.063 2.057 2.050 1.820 1.813 1.804 1.800 1.791 1.786 1.670 1.652 1.635 1.614 1.456 1.448 1.435 1.428 1.414 1.407 1.393 1.387 1.376 1.369 1.355 1.349 1.335 1.328 1.315 1.306



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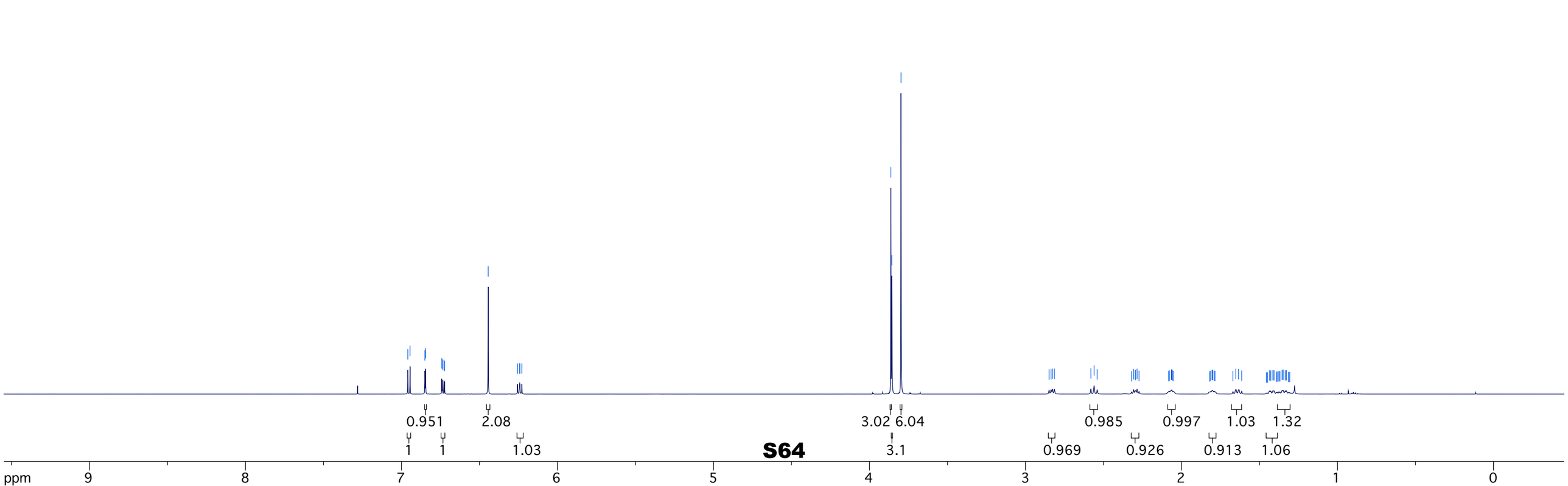

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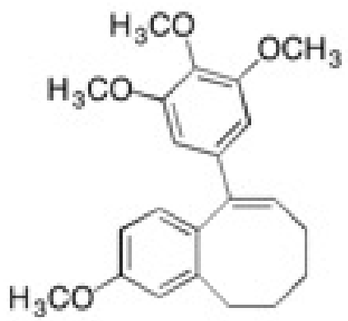

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Sample Name: CAH_5_67

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Acq. Instrument : Instrument 1 Location : -
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Last changed : 5/26/2015 12:40:08 PM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CAH_5_67000001.D\DA.M (MASTERMETHOD.M)
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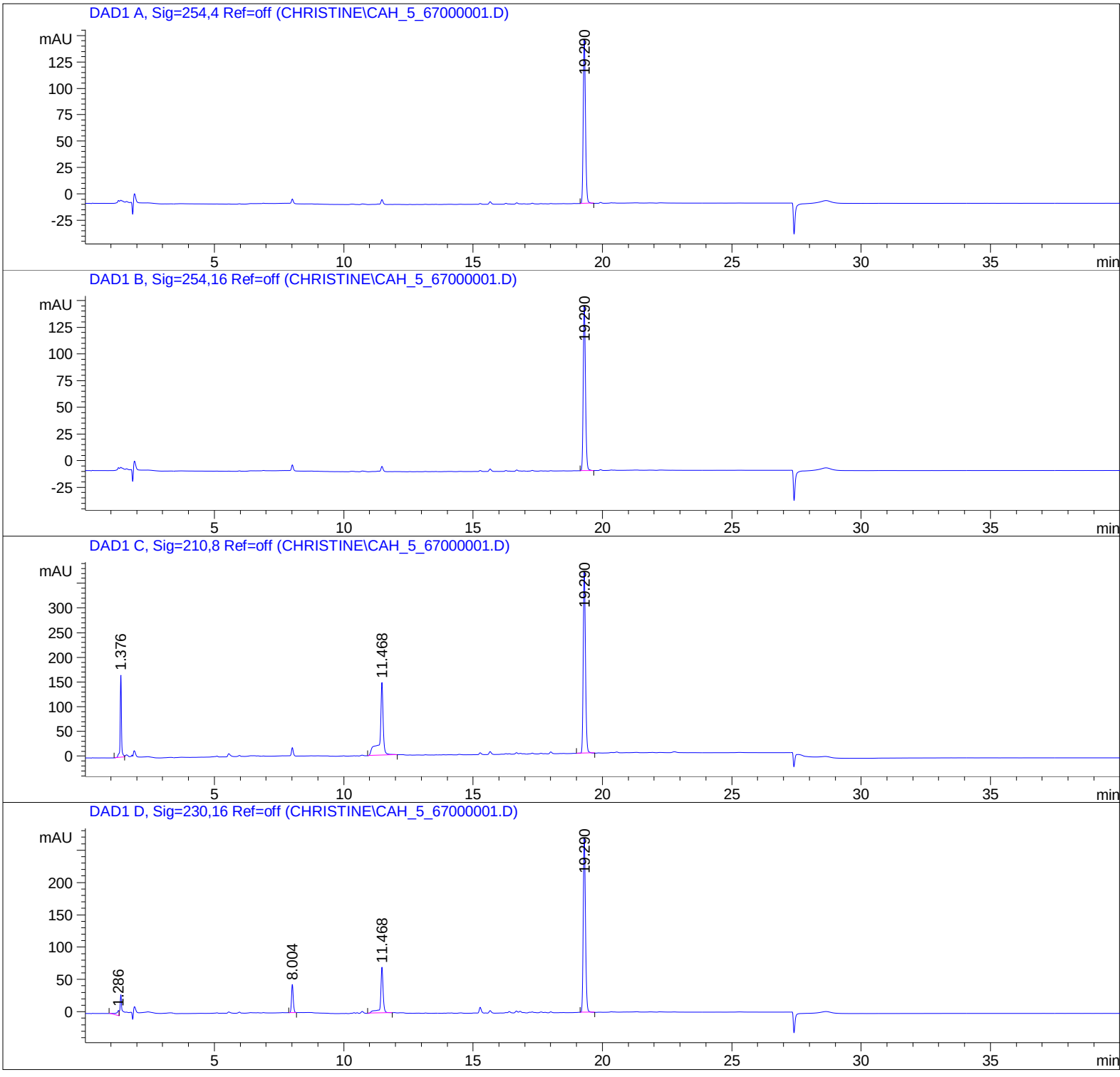

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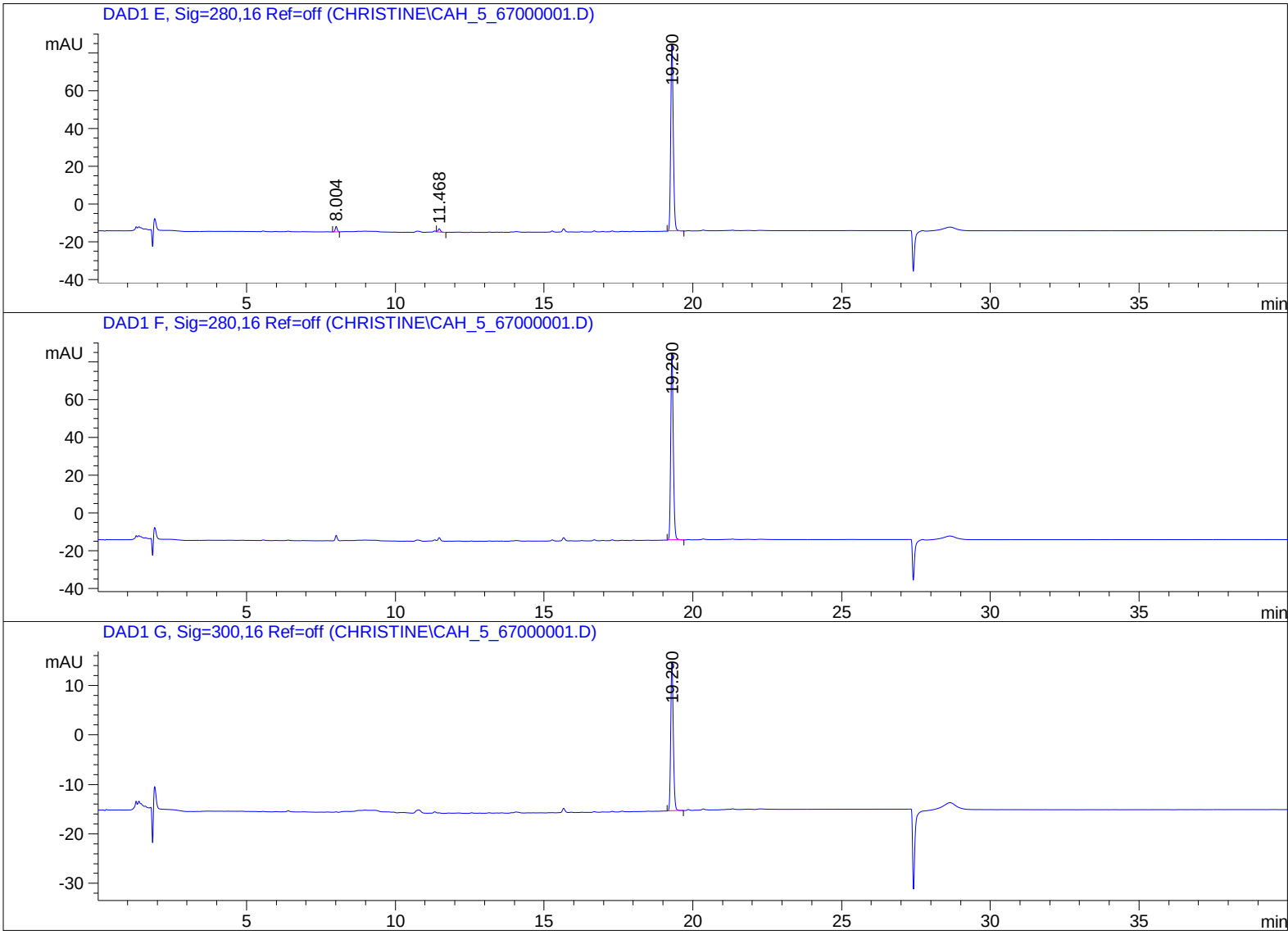

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Area Percent Report

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

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.290	BB	0.0924	939.05951	155.64803	100.0000

Totals : 939.05951 155.64803

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_5_67000001.D
Sample Name: CAH_5_67

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.290	BB	0.0924	933.50537	154.77390	100.0000
Totals :				933.50537	154.77390	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.376	BV	0.0514	566.59003	167.64386	13.7716
2	11.468	BB	0.1247	1325.44922	147.65602	32.2164
3	19.290	BB	0.0945	2222.16187	367.52441	54.0120
Totals :				4114.20111	682.82430	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.286	BV	0.1040	63.83619	8.09134	2.6688
2	8.004	BB	0.0727	205.53131	43.84377	8.5927
3	11.468	BB	0.1019	497.50229	70.89946	20.7993
4	19.290	BB	0.0923	1625.05005	269.84534	67.9392
Totals :				2391.91984	392.67990	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.004	BB	0.0713	12.97011	2.83754	2.0930
2	11.468	VB	0.0893	11.36858	1.91306	1.8346
3	19.290	BB	0.0924	595.34033	98.72345	96.0724
Totals :				619.67902	103.47405	

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_5_67000001.D
Sample Name: CAH_5_67

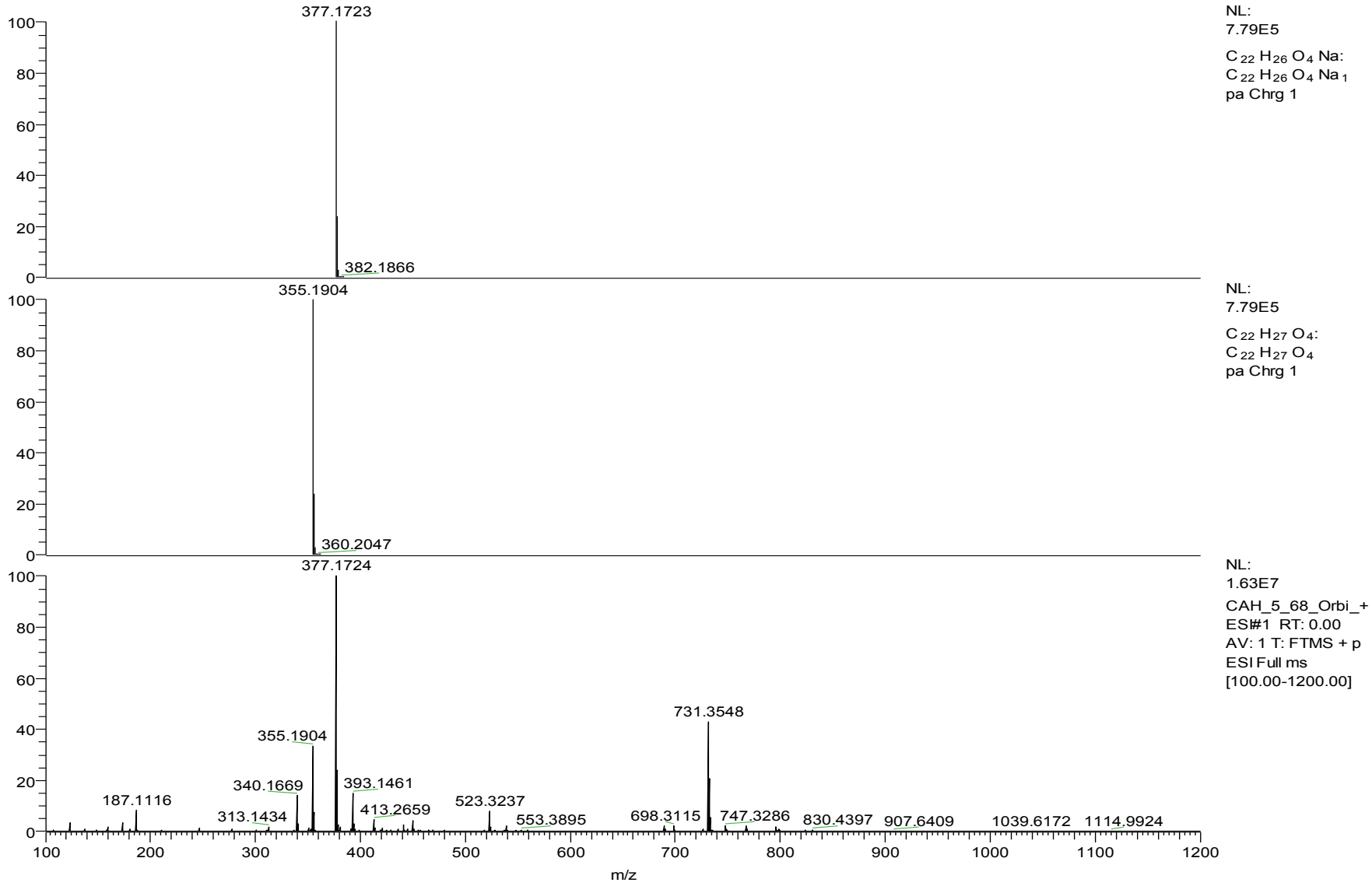
Signal 6: DAD1 F, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.290	BB	0.0924	595.34247	98.72340	100.0000
Totals :				595.34247	98.72340	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	19.290	BB	0.0925	181.02713	29.95630	100.0000
Totals :				181.02713	29.95630	

*** End of Report ***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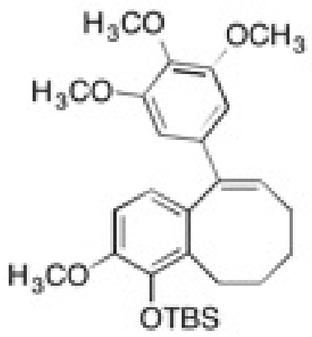
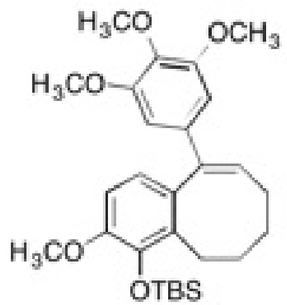
NL:
7.79E5
C 22 H 27 O 4:
C 22 H 27 O 4
pa Chrg 1
377.1724
731.3548
355.1904
340.1669
393.1461
187.1116
313.1434
413.2659
523.3237
553.3895
698.3115
747.3286
830.4397
907.6409
1039.6172
1114.9924
NL:
1.63E7
CAH_5_68_Orbi_+
ES#1 RT: 0.00
AV: 1 T: FTMS + p
ESI Full ms
[100.00-1200.00]
m/z



22


H3CO
OCH3
H3CO
H3CO
OTBS

22

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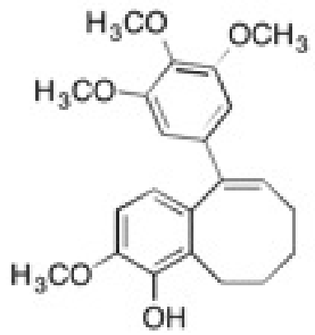
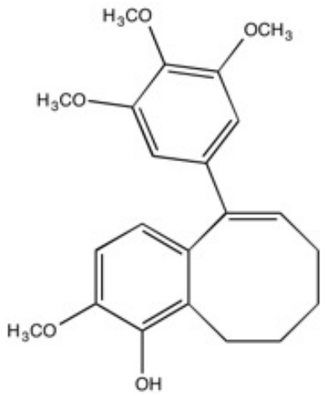
141.982
140.145
139.196
137.066
135.021
131.928
129.523
121.632
108.439
104.576
60.915
56.107
54.562
31.633
29.091
28.334
27.441
26.340
24.715
19.137
11.481
3.237
3.512

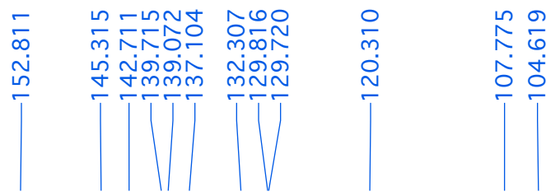

H3CO
OCH3
H3CO
H3CO
OH

23

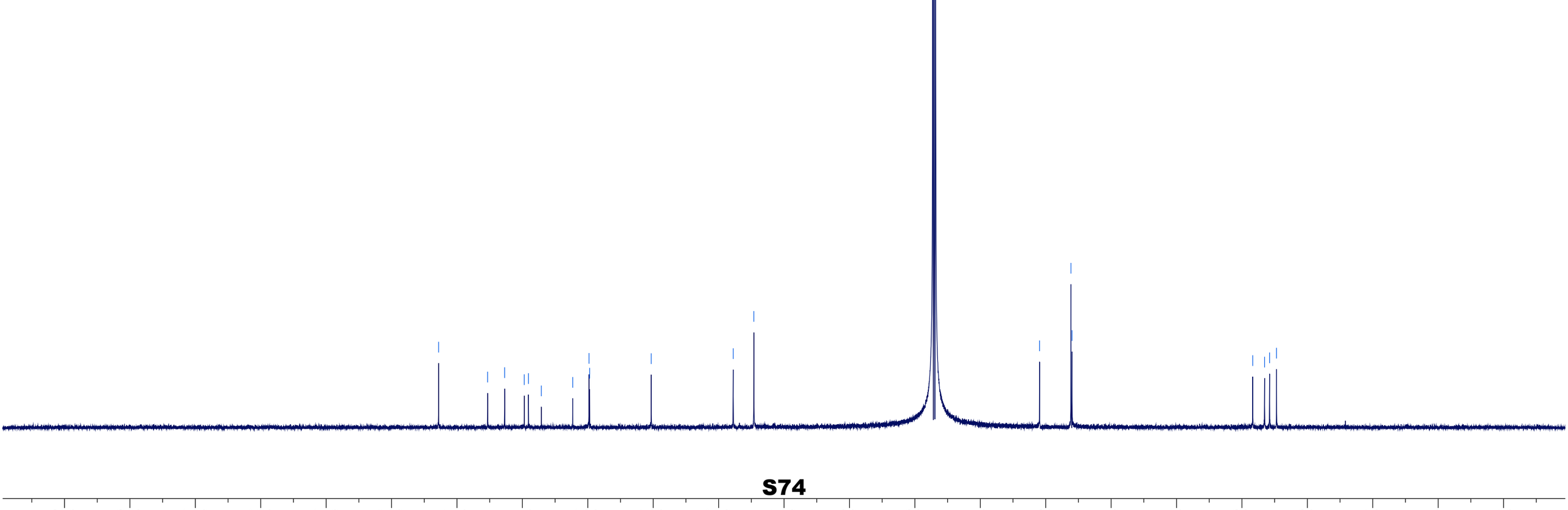
7.260
6.712
6.698
6.542
6.528
6.433
6.226
6.212
6.198
5.756
3.915
3.841
3.784
3.247
3.234
3.225
3.212
2.297
2.277
2.259
2.038
2.026
2.015
1.786
1.776
1.765
1.691
1.672
1.654
1.634
1.473
1.466
1.452
1.445
1.430
1.425
1.410
1.403
1.381
1.374
1.360
1.354
1.339
1.332
1.319
1.310
1.252
0.809
1.11
3.04
6.09
1.71
1.05
1.2
0.993
2.01
1.02
1
0.959
1.29
1.25
ppm 11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3


H3CO
OCH3
H3CO
H3CO
OH

23


152.811
145.315
142.711
139.715
139.072
137.104
132.307
129.816
129.720
120.310
107.775
104.619


60.943
56.137
55.975
28.349
26.541
25.774
24.715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200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-5-15000002.D
Sample Name: cah-5-15

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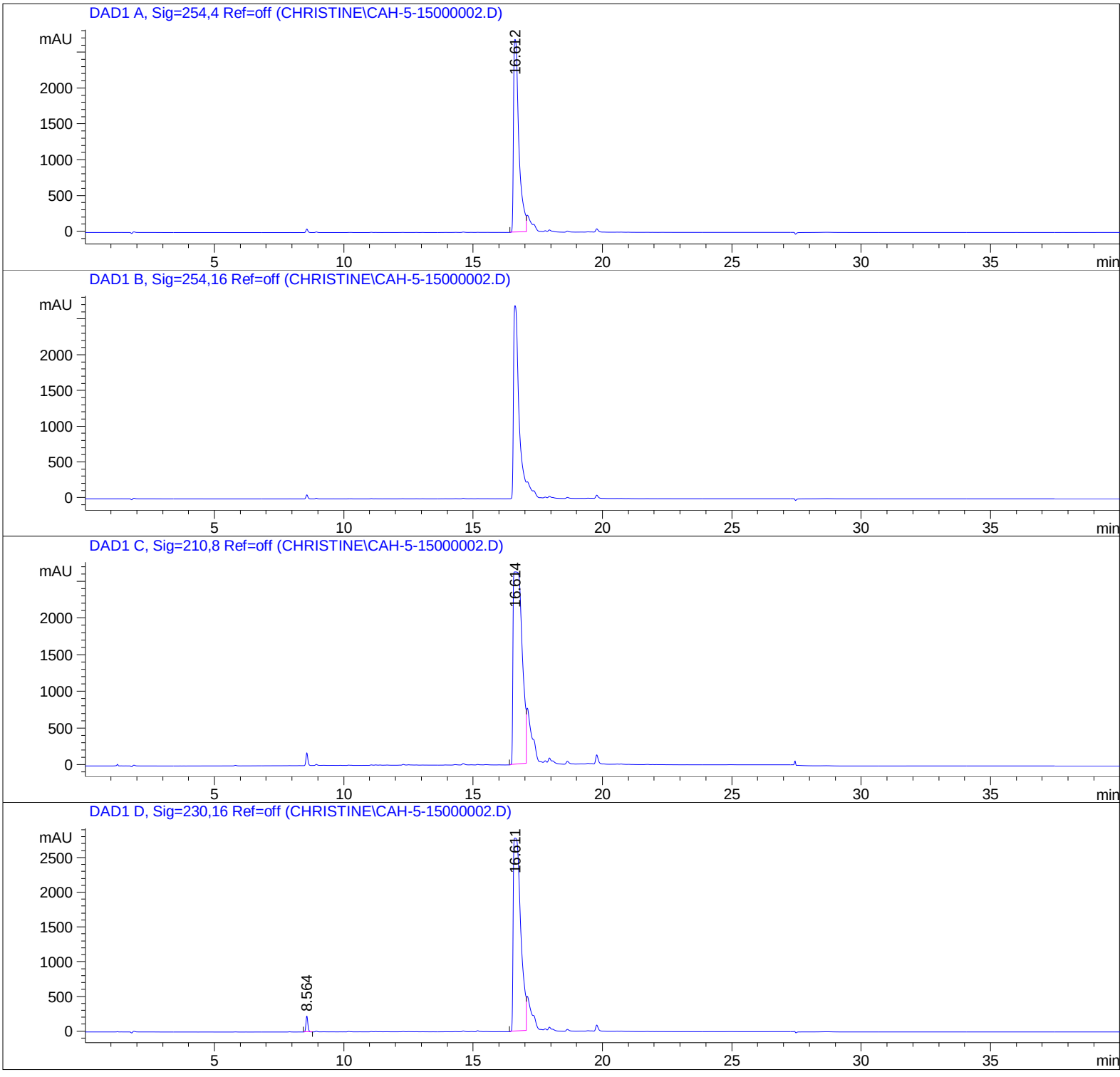
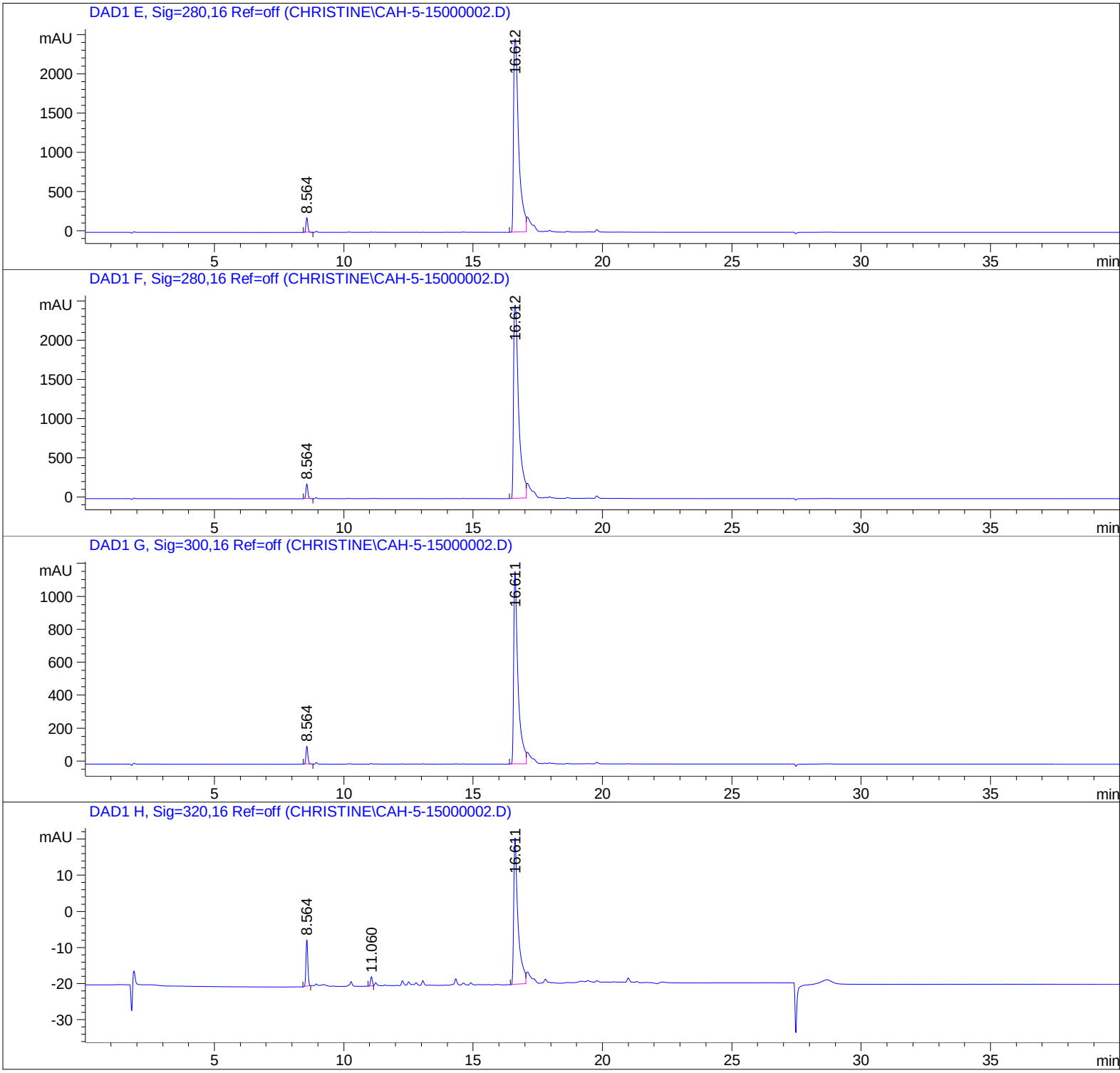
Acq. Instrument : Instrument 1 Location : -
Injection Date : 1/28/2015 12:58:55 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 1/28/2015 12:55:13 PM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CAH-5-15000002.D\DA.M (MASTERMETHOD.M)
Last changed : 1/28/2015 1:50:44 PM by Christine



Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-5-15000002.D
Sample Name: cah-5-15



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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\CHRISTINE\CAH-5-15000002.D
Sample Name: cah-5-15

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.612	BV	0.2164	3.88516e4	2691.22314	100.0000
Totals :				3.88516e4	2691.22314	

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

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.614	BV	0.3761	6.34811e4	2625.34521	100.0000
Totals :				6.34811e4	2625.34521	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.564	BB	0.0771	1163.02673	229.77750	2.0414
2	16.611	BV	0.3100	5.58100e4	2782.44800	97.9586
Totals :				5.69730e4	3012.22549	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.564	BV	0.0773	953.32397	187.54671	2.7213
2	16.612	BV	0.2055	3.40785e4	2462.50952	97.2787
Totals :				3.50318e4	2650.05623	

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-5-15000002.D
Sample Name: cah-5-15

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.564	BV	0.0773	953.32397	187.54671	2.7213
2	16.612	BV	0.2055	3.40785e4	2462.50952	97.2787
Totals :				3.50318e4	2650.05623	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.564	BV	0.0773	555.76282	109.26016	3.9560
2	16.611	BV	0.1668	1.34929e4	1167.44519	96.0440
Totals :				1.40486e4	1276.70535	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.564	BB	0.0763	64.41962	12.88749	11.7453
2	11.060	BV	0.0800	13.31195	2.58971	2.4271
3	16.611	BV	0.1653	470.73935	40.60112	85.8276
Totals :				548.47093	56.07832	

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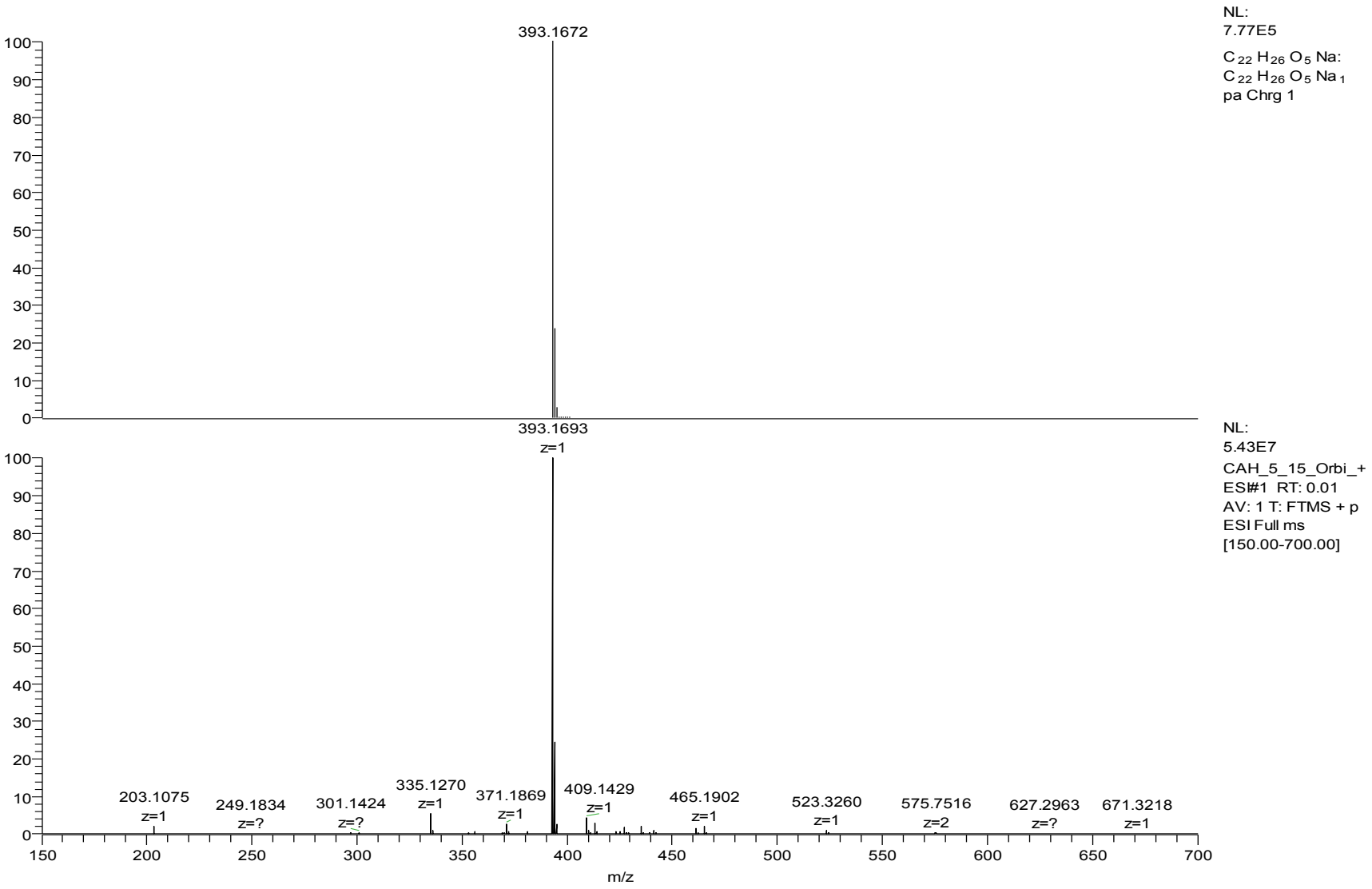
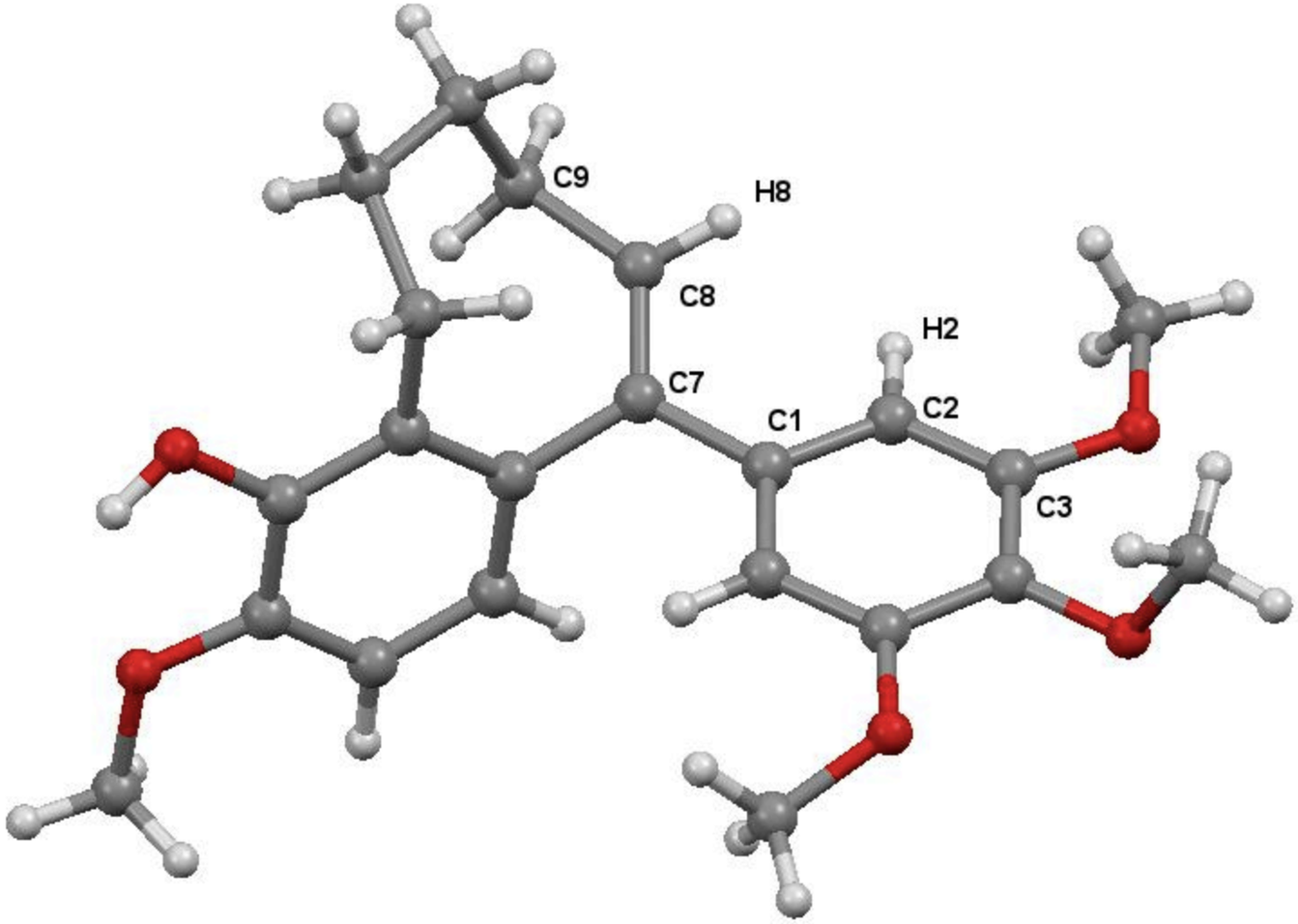
*** End of Report ***


393.1672
NL:
7.77E5
C 22 H 26 O 5 Na:
C 22 H 26 O 5 Na 1
pa Chrg 1
393.1693
z=1
NL:
5.43E7
CAH_5_15_Orbi_+
ESI#1 RT: 0.01
AV: 1 T: FTMS + p
ESI Full ms
[150.00-700.00]
203.1075
z=1
249.1834
z=?
301.1424
z=?
335.1270
z=1
371.1869
z=1
409.1429
z=1
465.1902
z=1
523.3260
z=1
575.7516
z=2
627.2963
z=?
671.3218
z=1
m/z


C9
H8
C8
H2
C7
C1
C2
C3

X-ray Crystallographic Analysis:

X-ray crystallographic analysis of compound **23**. Crystallographic data

were collected on a crystal of **23** with dimensions 0.171 x 0.130 x 0.089 mm^3. Data were collected at 150 K on a Bruker X8 Apex using Mo KR radiation (λ = 0.71073 Å). The structure was solved by direct methods after correction of the data using SADABS. Crystallographic data and definement details for the complex mentioned herein is found in the Supporting Information (Table S5-S9). All data were processed using the Bruker AXS SHELXTL software, version 6.10.

Table 5. Crystal data and structure refinement for Compound 23.

Identification code	Compound 23	
Empirical formula	C22 H26 O5	
Formula weight	370.43	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P b c a	
Unit cell dimensions	a = 16.6410(12) Å	a= 90°.
	b = 11.1239(8) Å	b= 90°.
	c = 20.5570(13) Å	g = 90°.
Volume	3805.4(5) $Å^3$	
Z	8	
Density (calculated)	1.293 Mg/m^3	
Absorption coefficient	0.091 mm^{-1}	
F(000)	1584	
Crystal size	0.171 x 0.130 x 0.089 mm^3	
Theta range for data collection	2.963 to 26.370°.	
Index ranges	-20<=h<=20, -13<=k<=13, -25<=l<=24	
Reflections collected	80769	
Independent reflections	3865 [R(int) = 0.0567]	
Completeness to theta = 25.242°	99.7 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.966 and 0.959
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3865 / 0 / 252
Goodness-of-fit on F^2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.0365, wR2 = 0.0902
R indices (all data)	R1 = 0.0476, wR2 = 0.0964
Extinction coefficient	n/a
Largest diff. peak and hole	0.264 and -0.179 e.$Å^{-3}$

Table 6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Compound 23. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6253(1)	3752(1)	2758(1)	33(1)
O(2)	6709(1)	1740(1)	2161(1)	32(1)
O(3)	2132(1)	2432(1)	1252(1)	30(1)
O(4)	1339(1)	3655(1)	318(1)	32(1)
O(5)	2058(1)	5446(1)	-342(1)	33(1)
C(1)	5933(1)	3482(1)	2159(1)	25(1)
C(2)	6161(1)	2438(1)	1831(1)	25(1)
C(3)	5839(1)	2181(1)	1226(1)	28(1)
C(4)	5304(1)	2991(1)	949(1)	28(1)
C(5)	5079(1)	4044(1)	1265(1)	25(1)
C(6)	5379(1)	4281(1)	1893(1)	25(1)
C(7)	5110(1)	5342(1)	2301(1)	29(1)
C(8)	5675(1)	6433(1)	2275(1)	34(1)
C(9)	5567(1)	7256(1)	1691(1)	36(1)
C(10)	5583(1)	6606(1)	1029(1)	33(1)
C(11)	4779(1)	6077(1)	857(1)	29(1)
C(12)	4546(1)	4933(1)	936(1)	26(1)
C(13)	3728(1)	4541(1)	739(1)	26(1)
C(14)	3345(1)	3609(1)	1070(1)	26(1)
C(15)	2548(1)	3322(1)	933(1)	25(1)
C(16)	2122(1)	3961(1)	463(1)	26(1)
C(17)	2516(1)	4872(1)	119(1)	26(1)
C(18)	3313(1)	5152(1)	249(1)	27(1)
C(19)	6957(1)	652(1)	1853(1)	39(1)
C(20)	2608(1)	1511(1)	1544(1)	31(1)
C(21)	761(1)	4440(2)	613(1)	37(1)
C(22)	2446(1)	6392(1)	-692(1)	36(1)

Table 7. Bond lengths [Å] and angles [°] for Compound 23.

O(1)-C(1)	1.3737(16)
O(2)-C(2)	1.3762(16)
O(2)-C(19)	1.4259(17)
O(3)-C(15)	1.3756(16)
O(3)-C(20)	1.4281(16)
O(4)-C(16)	1.3796(16)
O(4)-C(21)	1.4350(18)
O(5)-C(17)	1.3722(16)
O(5)-C(22)	1.4294(17)
C(1)-C(6)	1.3917(19)
C(1)-C(2)	1.3966(19)
C(2)-C(3)	1.3834(19)
C(3)-C(4)	1.3894(19)
C(4)-C(5)	1.3902(19)
C(5)-C(6)	1.4090(18)
C(5)-C(12)	1.4902(19)
C(6)-C(7)	1.5153(18)
C(7)-C(8)	1.537(2)
C(8)-C(9)	1.521(2)
C(9)-C(10)	1.540(2)
C(10)-C(11)	1.505(2)
C(11)-C(12)	1.340(2)
C(12)-C(13)	1.4863(18)
C(13)-C(14)	1.3940(19)
C(13)-C(18)	1.3977(19)
C(14)-C(15)	1.3936(19)
C(15)-C(16)	1.3930(19)
C(16)-C(17)	1.3984(19)
C(17)-C(18)	1.3885(19)
C(2)-O(2)-C(19)	116.88(11)
C(15)-O(3)-C(20)	115.89(11)
C(16)-O(4)-C(21)	113.03(11)
C(17)-O(5)-C(22)	116.09(11)

O(1)-C(1)-C(6)	118.07(12)
O(1)-C(1)-C(2)	120.53(12)
C(6)-C(1)-C(2)	121.40(12)
O(2)-C(2)-C(3)	125.67(12)
O(2)-C(2)-C(1)	114.33(11)
C(3)-C(2)-C(1)	120.00(12)
C(2)-C(3)-C(4)	118.93(12)
C(3)-C(4)-C(5)	121.79(12)
C(4)-C(5)-C(6)	119.35(12)
C(4)-C(5)-C(12)	120.49(12)
C(6)-C(5)-C(12)	120.13(12)
C(1)-C(6)-C(5)	118.41(12)
C(1)-C(6)-C(7)	118.32(12)
C(5)-C(6)-C(7)	123.24(12)
C(6)-C(7)-C(8)	114.57(11)
C(9)-C(8)-C(7)	115.49(12)
C(8)-C(9)-C(10)	114.38(12)
C(11)-C(10)-C(9)	112.05(12)
C(12)-C(11)-C(10)	126.89(13)
C(11)-C(12)-C(13)	120.66(13)
C(11)-C(12)-C(5)	120.88(12)
C(13)-C(12)-C(5)	118.32(12)
C(14)-C(13)-C(18)	119.23(12)
C(14)-C(13)-C(12)	120.18(12)
C(18)-C(13)-C(12)	120.46(12)
C(15)-C(14)-C(13)	120.36(12)
O(3)-C(15)-C(16)	116.20(12)
O(3)-C(15)-C(14)	123.22(12)
C(16)-C(15)-C(14)	120.56(12)
O(4)-C(16)-C(15)	120.31(12)
O(4)-C(16)-C(17)	120.79(12)
C(15)-C(16)-C(17)	118.82(12)
O(5)-C(17)-C(18)	123.93(12)
O(5)-C(17)-C(16)	115.24(12)
C(18)-C(17)-C(16)	120.83(12)
C(17)-C(18)-C(13)	120.11(13)

Symmetry transformations used to generate equivalent atoms:

Table 8. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for Compound 23. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	36(1)	37(1)	24(1)	-7(1)	-8(1)	10(1)
O(2)	32(1)	32(1)	31(1)	-6(1)	-4(1)	9(1)
O(3)	28(1)	27(1)	35(1)	3(1)	-3(1)	-2(1)
O(4)	26(1)	37(1)	34(1)	-2(1)	-8(1)	-4(1)
O(5)	31(1)	41(1)	26(1)	7(1)	-8(1)	-2(1)
C(1)	23(1)	32(1)	21(1)	-4(1)	1(1)	0(1)
C(2)	22(1)	28(1)	26(1)	-1(1)	2(1)	1(1)
C(3)	28(1)	29(1)	26(1)	-6(1)	3(1)	0(1)
C(4)	28(1)	33(1)	22(1)	-3(1)	-2(1)	-3(1)
C(5)	20(1)	31(1)	24(1)	-1(1)	2(1)	-2(1)
C(6)	20(1)	31(1)	24(1)	-4(1)	2(1)	0(1)
C(7)	27(1)	36(1)	24(1)	-4(1)	0(1)	7(1)
C(8)	29(1)	39(1)	35(1)	-14(1)	-4(1)	4(1)
C(9)	31(1)	34(1)	42(1)	-8(1)	2(1)	-5(1)
C(10)	30(1)	36(1)	34(1)	-1(1)	2(1)	-4(1)
C(11)	27(1)	34(1)	27(1)	0(1)	-1(1)	0(1)
C(12)	24(1)	33(1)	21(1)	-2(1)	0(1)	0(1)
C(13)	25(1)	29(1)	23(1)	-5(1)	0(1)	2(1)
C(14)	26(1)	27(1)	24(1)	-1(1)	-3(1)	4(1)
C(15)	27(1)	25(1)	23(1)	-3(1)	1(1)	0(1)
C(16)	24(1)	29(1)	24(1)	-7(1)	-4(1)	-1(1)
C(17)	29(1)	31(1)	19(1)	-3(1)	-4(1)	2(1)
C(18)	29(1)	30(1)	22(1)	-1(1)	0(1)	-2(1)
C(19)	39(1)	34(1)	43(1)	-10(1)	-4(1)	11(1)
C(20)	37(1)	27(1)	30(1)	1(1)	-2(1)	2(1)
C(21)	25(1)	48(1)	38(1)	7(1)	-4(1)	2(1)
C(22)	42(1)	33(1)	31(1)	5(1)	-11(1)	-3(1)

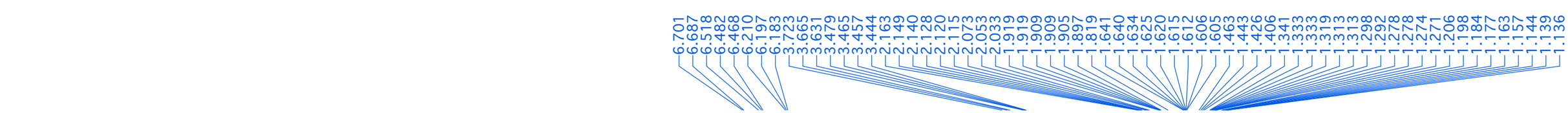
Table 9. Hydrogen bonds for Compound 23 [Å and °].

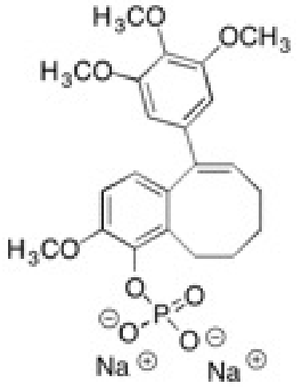
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(2)	0.879(19)	2.202(18)	2.6623(14)	112.3(15)
O(1)-H(1)...O(3)#1	0.879(19)	2.152(19)	2.9046(14)	143.3(16)

Symmetry transformations used to generate equivalent atoms:

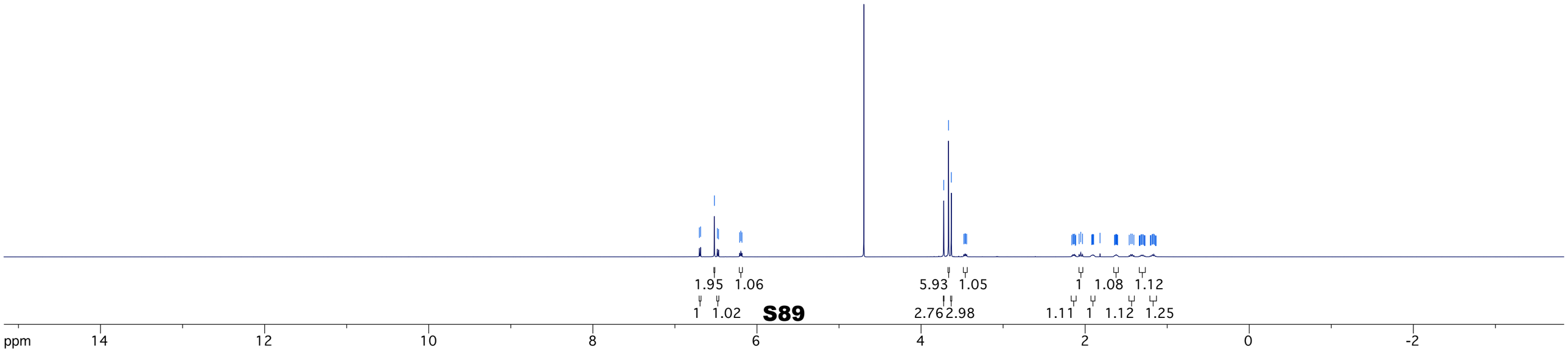
#1 x+1/2,y,-z+1/2

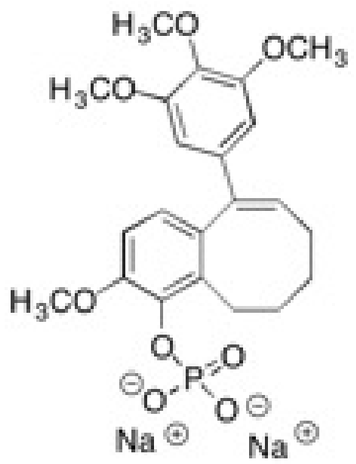
Crystallographic data for structure **23** (deposition number CCDC 1046344) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0) 1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).


6.701
6.687
6.518
6.482
6.468
6.210
6.197
6.183
3.723
3.665
3.631
3.479
3.465
3.457
3.444
2.163
2.149
2.140
2.128
2.120
2.115
2.073
2.053
2.033
1.919
1.919
1.909
1.909
1.905
1.897
1.819
1.641
1.640
1.634
1.625
1.620
1.615
1.612
1.606
1.605
1.463
1.443
1.426
1.406
1.341
1.333
1.333
1.319
1.313
1.313
1.298
1.292
1.278
1.278
1.274
1.271
1.206
1.198
1.184
1.177
1.163
1.157
1.144
1.139
1.136


H3CO
OCH3
H3CO
H3CO
O
O
P
O
O
O
Na
Na

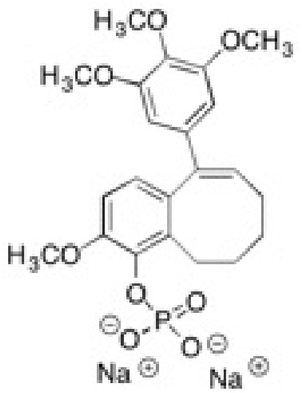
24


1.95
1.06
1
1.02
5.93
1.05
2.76
2.98
1
1.08
1.12
1.11
1
1.12
1.25
ppm
14
12
10
8
6
4
2
0
-2


H3CO
OCH3
H3CO
H3CO
O
O
P
O
O
O
Na
Na

24

152.167
151.416
151.398
141.124
141.070
139.993
138.849
138.029
138.002
135.799
131.540
131.235
123.808
109.506
104.941
60.889
55.970
55.562
28.078
26.631
26.346
23.798
ppm
200
180
160
140
120
100
80
60
40
20
0

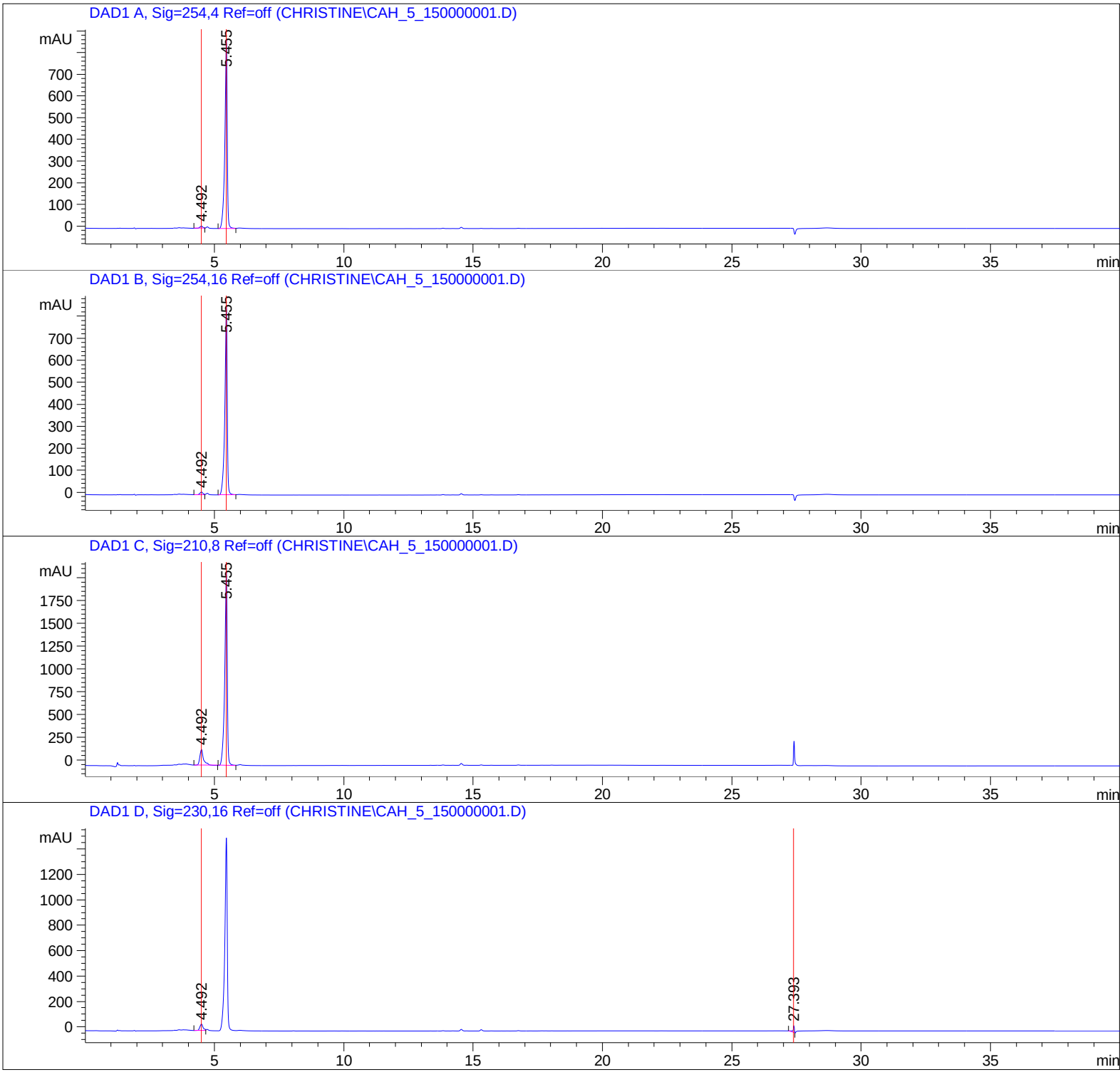


24

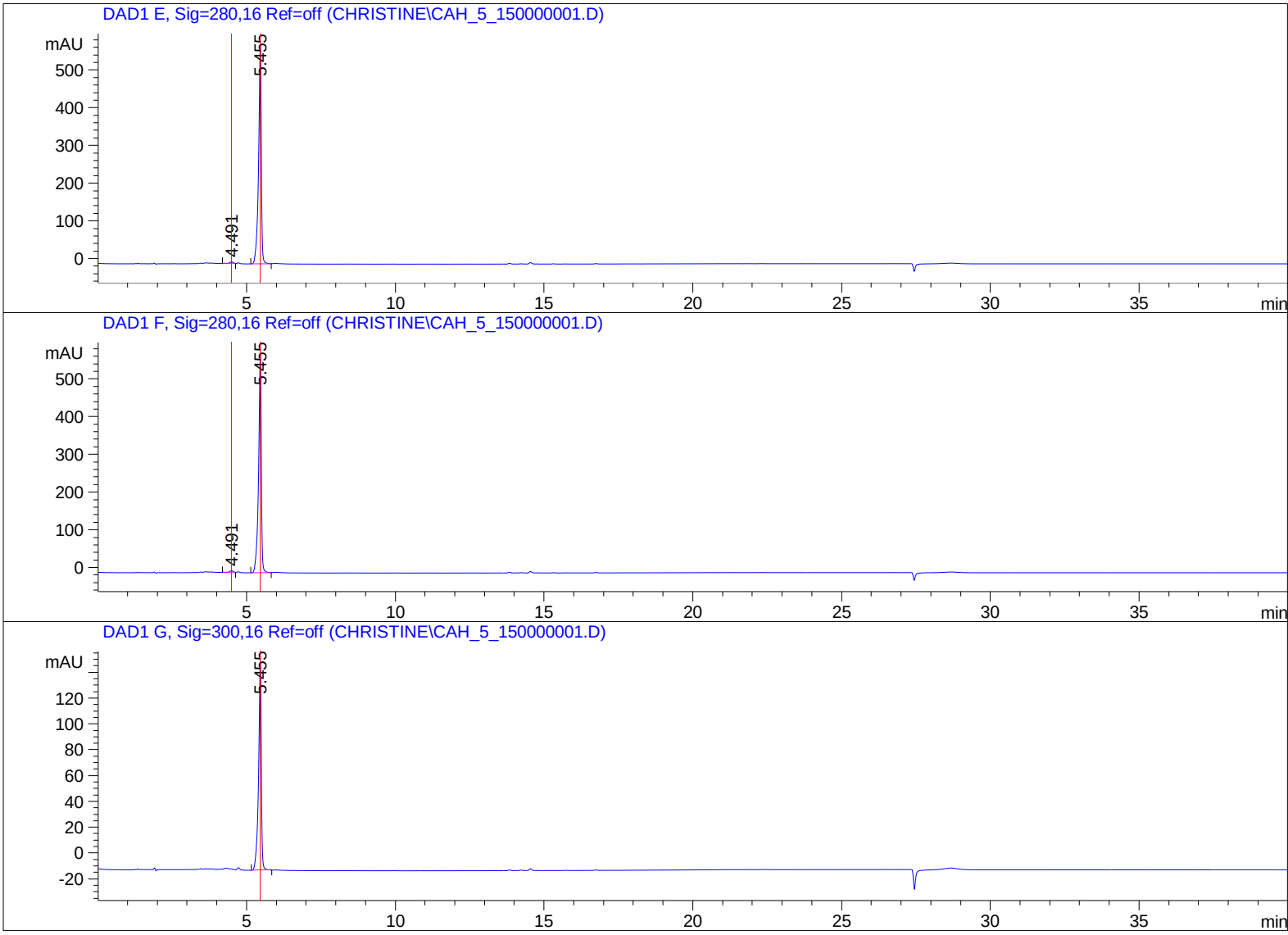
Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_5_150000001.D
Sample Name: CAH_5_150

==========

Acq. Operator : christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 1/19/2016 1:07:33 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 1/19/2016 1:04:30 PM by christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CAH_5_150000001.D\DA.M (MASTERMETHOD.M)
Last changed : 1/19/2016 1:58:42 PM by christine



Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_5_150000001.D
Sample Name: CAH_5_150



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Area Percent Report

==========

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

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.492	BV	0.1295	91.48150	10.72987	1.5876
2	5.455	BV	0.0955	5670.79883	876.42407	98.4124

Totals : 5762.28033 887.15394

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_5_150000001.D
Sample Name: CAH_5_150

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.492	BV	0.1298	105.85542	12.38030	1.8594
2	5.455	BV	0.0955	5587.14062	863.45483	98.1406
Totals :				5692.99605	875.83513	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.492	BB	0.1491	1733.28137	172.71095	10.5676
2	5.455	BV	0.1022	1.46685e4	2132.77539	89.4324
Totals :				1.64018e4	2305.48634	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.492	BV	0.1383	472.28870	51.84144	70.2817
2	27.393	BB	0.0564	199.70493	52.48211	29.7183
Totals :				671.99362	104.32355	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.491	BV	0.1358	47.16594	5.10381	1.2332
2	5.455	BV	0.0956	3777.51514	583.23889	98.7668
Totals :				3824.68107	588.34271	

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_5_150000001.D
Sample Name: CAH_5_150

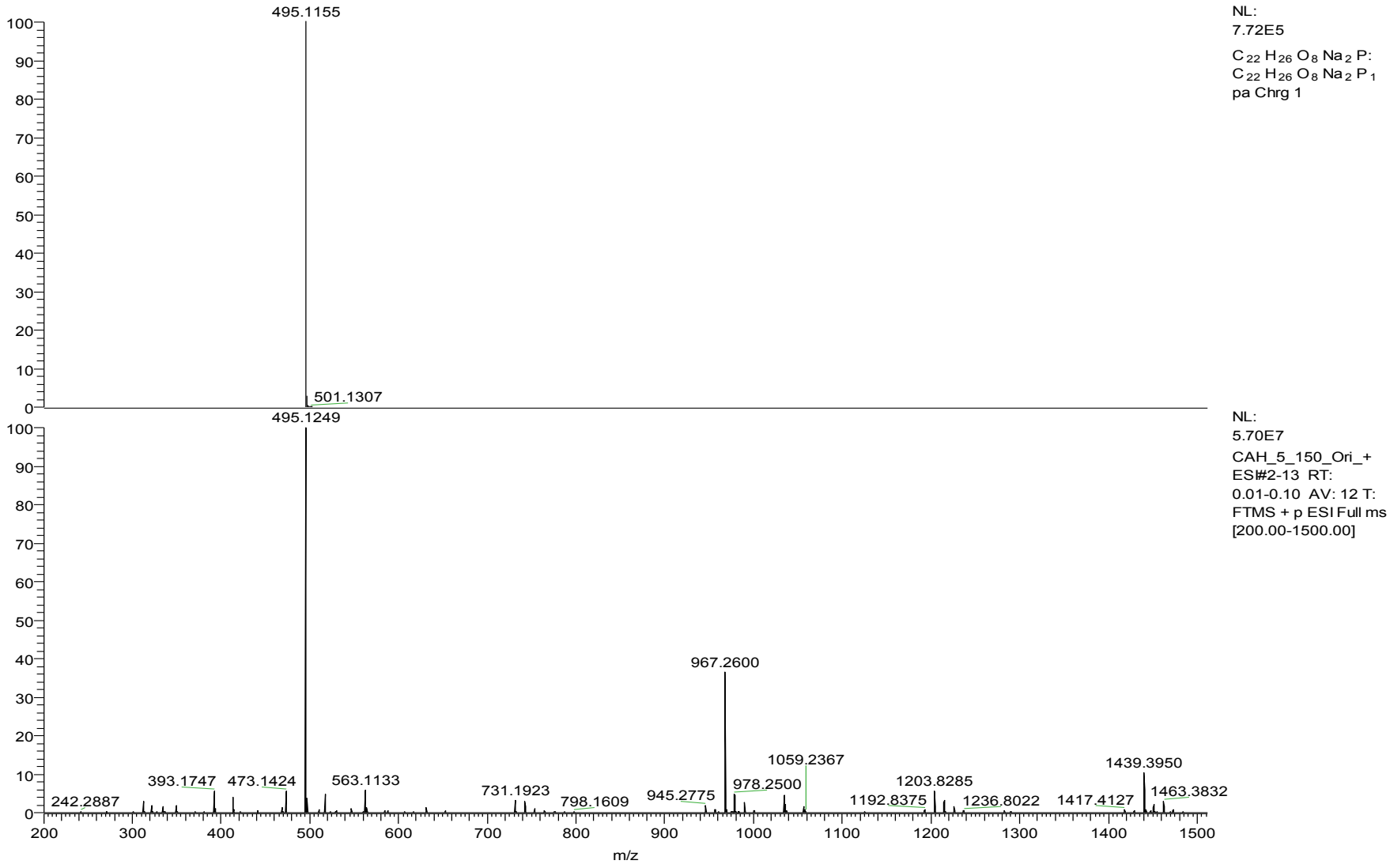
Signal 6: DAD1 F, Sig=280,16 Ref=off

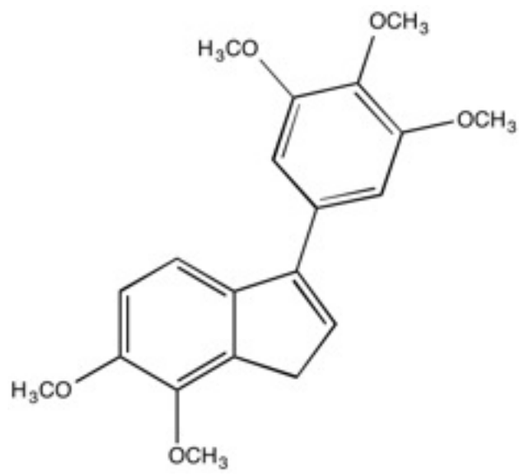
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.491	BV	0.1358	47.16594	5.10381	1.2332
2	5.455	BV	0.0956	3777.51514	583.23889	98.7668
Totals :				3824.68107	588.34271	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.455	BB	0.0960	1050.76099	161.39412	100.0000
Totals :				1050.76099	161.39412	

*** End of Report ***


495.1155
501.1307
NL:
7.72E5
C22 H26 O8 Na2 P:
C22 H26 O8 Na2 P1
pa Chrg 1
495.1249
967.2600
1059.2367
1439.3950
393.1747
473.1424
563.1133
978.2500
1203.8285
731.1923
798.1609
945.2775
1192.8375
1236.8022
1417.4127
1463.3832
242.2887
NL:
5.70E7
CAH_5_150_Ori_+
ESI#2-13 RT:
0.01-0.10 AV: 12 T:
FTMS + p ESI Full ms
[200.00-1500.00]
m/z

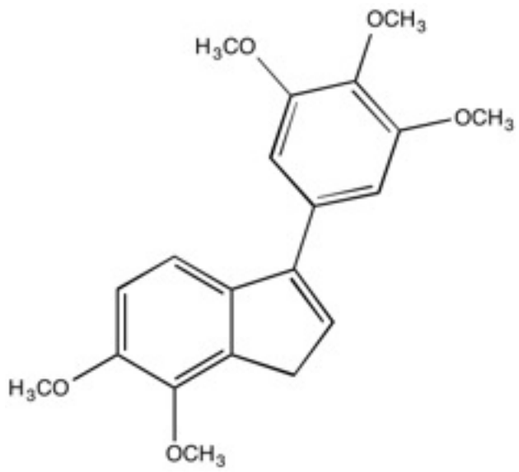


28

7.286
7.270
6.940
6.923
6.828
6.441
4.124
4.110
3.989
3.926
3.913
3.533
2.042
1.274
1.260
1.246

1.05
1.03
3.15
2.1
1
2.03
2.95
9.13

11 10 9 8 7 6 5 4 3 2 1 0 -1



28

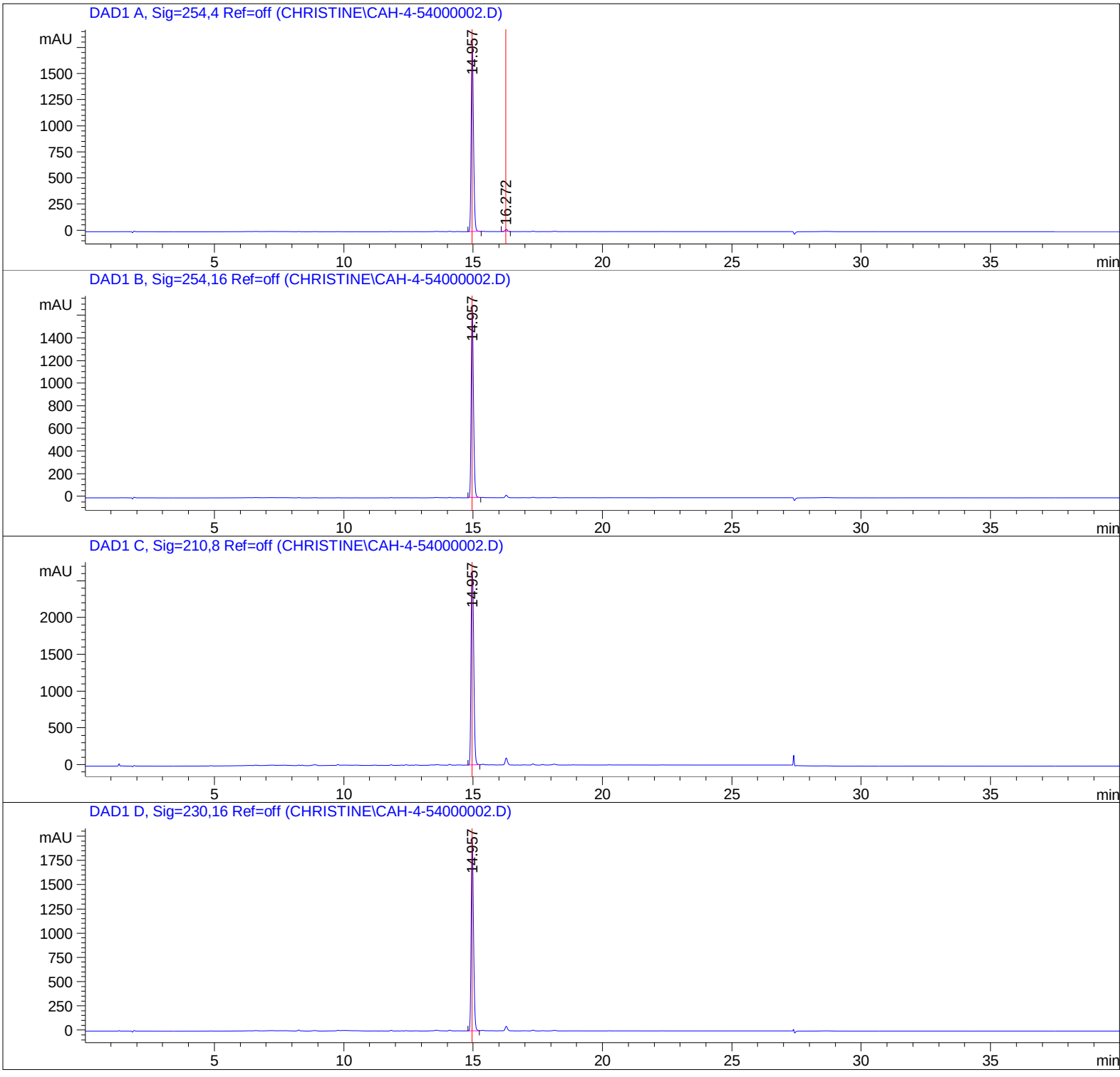
153.103
150.249
145.243
144.490
138.170
137.366
136.357
131.583
128.640
115.179
110.941
104.496
60.607
59.833
55.994
55.849
35.211

ppm 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

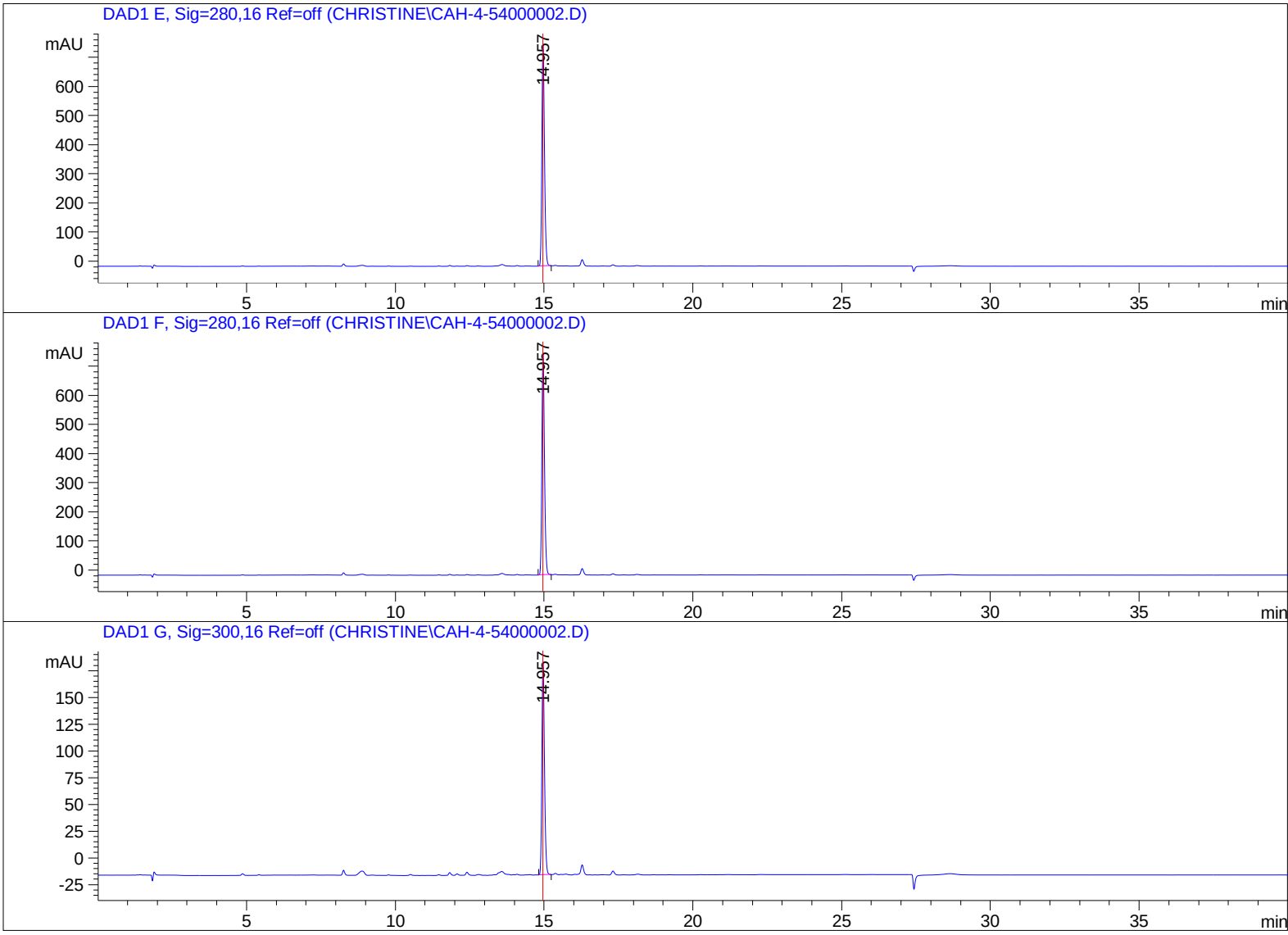
Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-4-54000002.D
Sample Name: CAH-4-54

==========

Acq. Operator : christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 7/21/2014 2:36:52 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 7/21/2014 2:31:17 PM by christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CAH-4-54000002.D\DA.M (MASTERMETHOD.M)
Last changed : 7/21/2014 4:13:46 PM by christine



Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-4-54000002.D
Sample Name: CAH-4-54



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Area Percent Report

==========

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

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.957	BV	0.0962	1.14170e4	1843.72681	98.7691
2	16.272	BV	0.0979	142.28862	22.46073	1.2309

Totals : 1.15593e4 1866.18753

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-4-54000002.D
Sample Name: CAH-4-54

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.957	BV	0.0960	1.05029e4	1702.27014	100.0000
Totals :				1.05029e4	1702.27014	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.957	BV	0.1179	1.93357e4	2627.26172	100.0000
Totals :				1.93357e4	2627.26172	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.957	BV	0.0977	1.25838e4	1992.09021	100.0000
Totals :				1.25838e4	1992.09021	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.957	BB	0.0951	4634.12646	760.19556	100.0000
Totals :				4634.12646	760.19556	

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

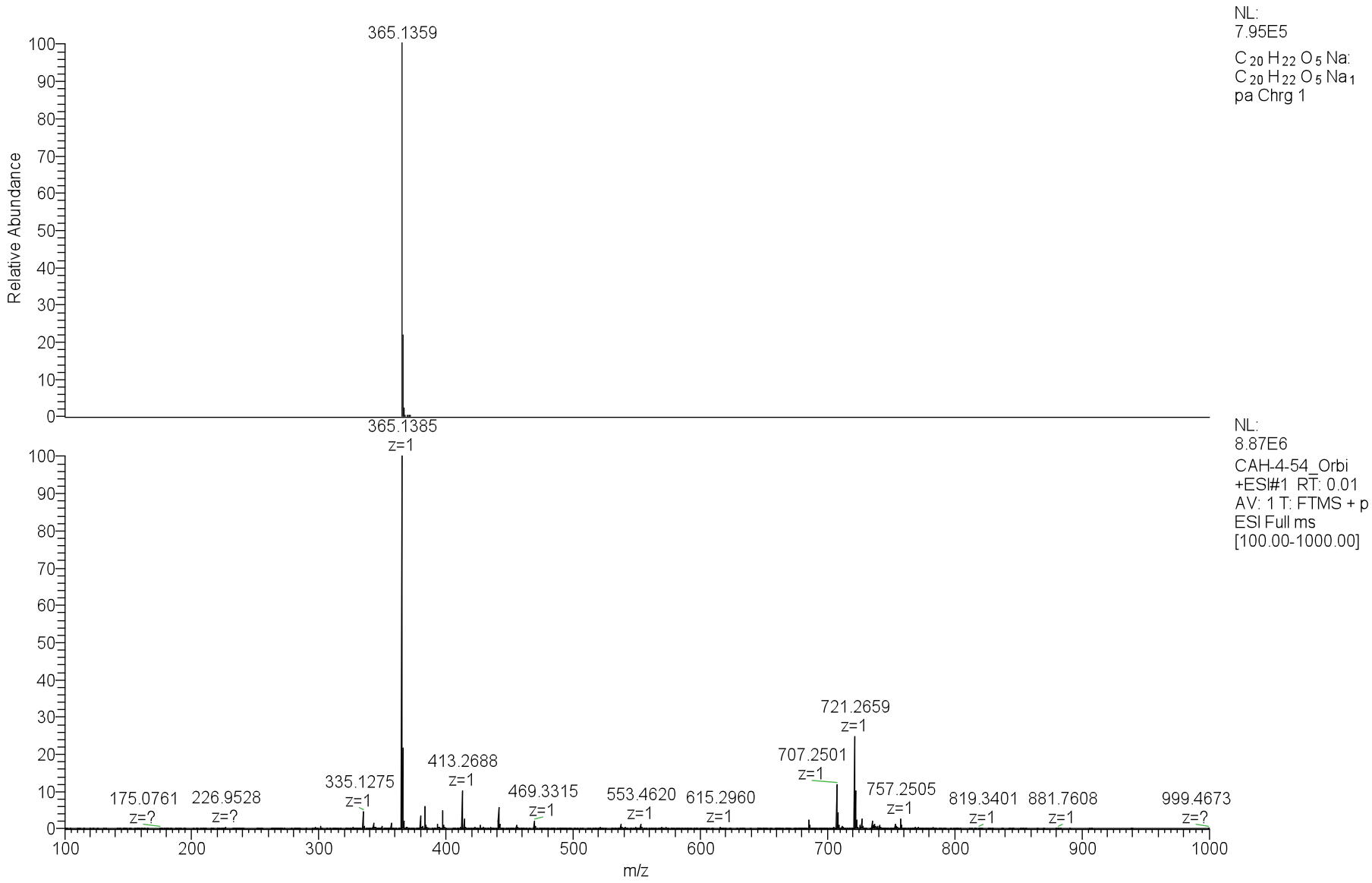
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.957	BB	0.0951	4634.12646	760.19556	100.0000
Totals :				4634.12646	760.19556	

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-4-54000002.D
Sample Name: CAH-4-54

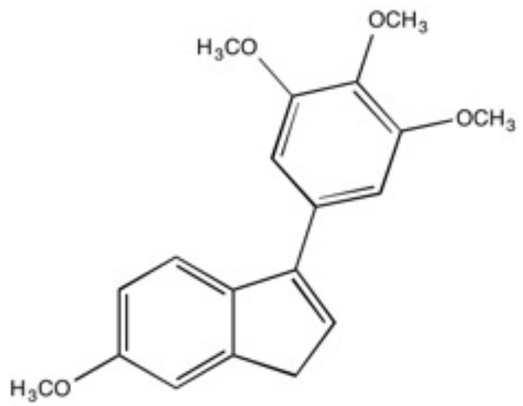
Signal 7: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.957	BB	0.0952	1213.09326	198.69473	100.0000
Totals :				1213.09326	198.69473	

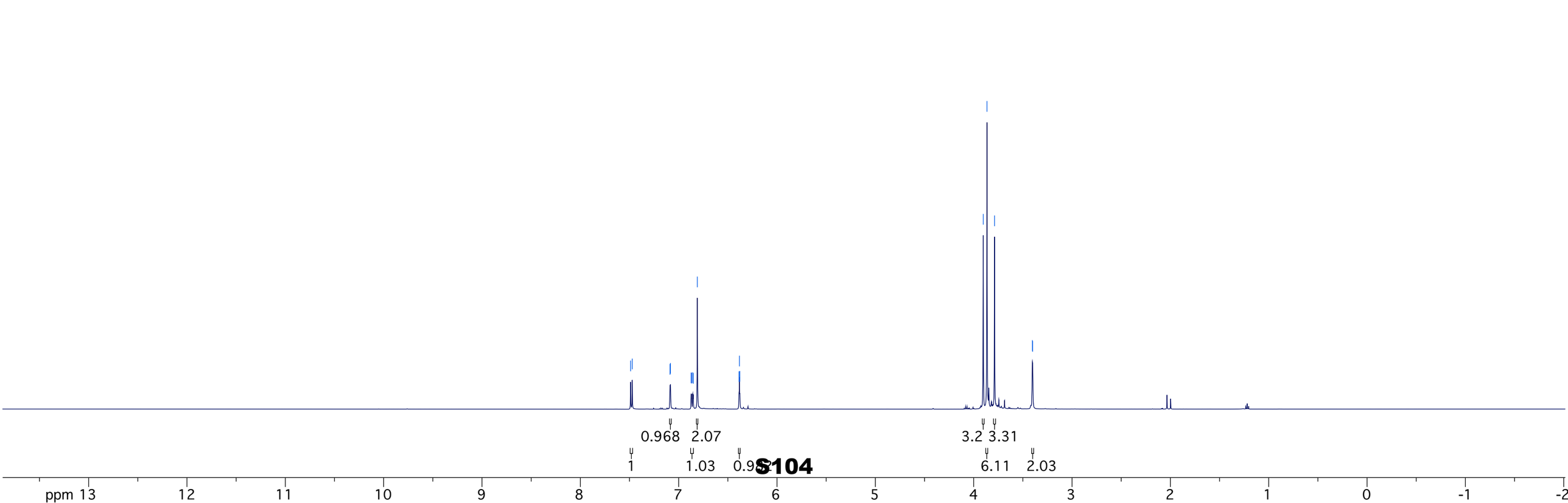
*** End of Report ***


365.1359
NL:
7.95E5
C 20 H 22 O 5 Na:
C 20 H 22 O 5 Na 1
pa Chrg 1
Relative Abundance
365.1385
z=1
NL:
8.87E6
CAH-4-54_Orbi
+ESI#1 RT: 0.01
AV: 1 T: FTMS + p
ESI Full ms
[100.00-1000.00]
175.0761
z=?
226.9528
z=?
335.1275
z=1
413.2688
z=1
469.3315
z=1
553.4620
z=1
615.2960
z=1
707.2501
z=1
721.2659
z=1
757.2505
z=1
819.3401
z=1
881.7608
z=1
999.4673
z=?
m/z

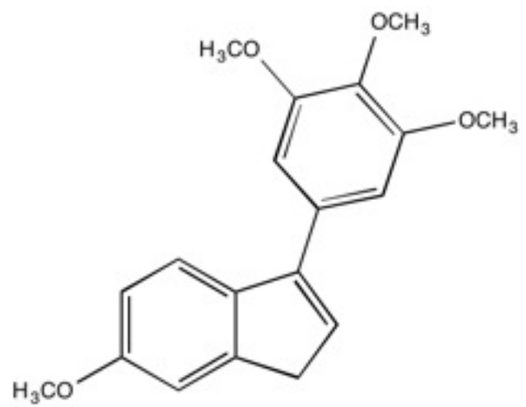

7.489
7.472
7.088
7.084
6.873
6.869
6.857
6.852
6.810
6.386
6.382
6.378
3.903
3.865
3.788
3.403
3.401


OCH3
H3CO
OCH3
H3CO

29


0.968
2.07
3.2
3.31
1
1.03
6.11
2.03
ppm 13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2

158.084
153.333
146.664
144.617
137.567
136.827
132.018
128.384
120.508
111.820
110.569
104.671
60.817
56.050
55.385
37.962



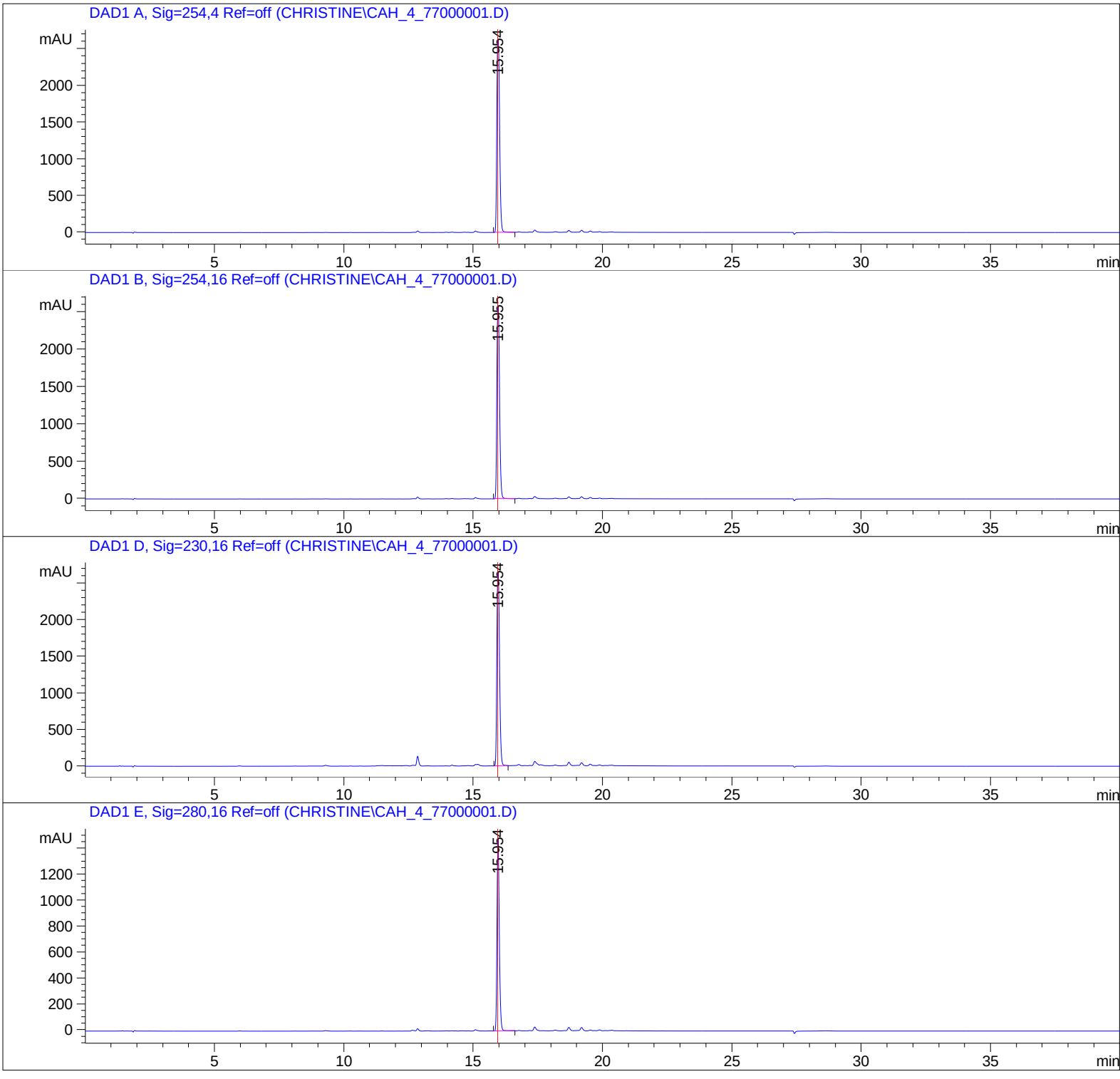
29

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

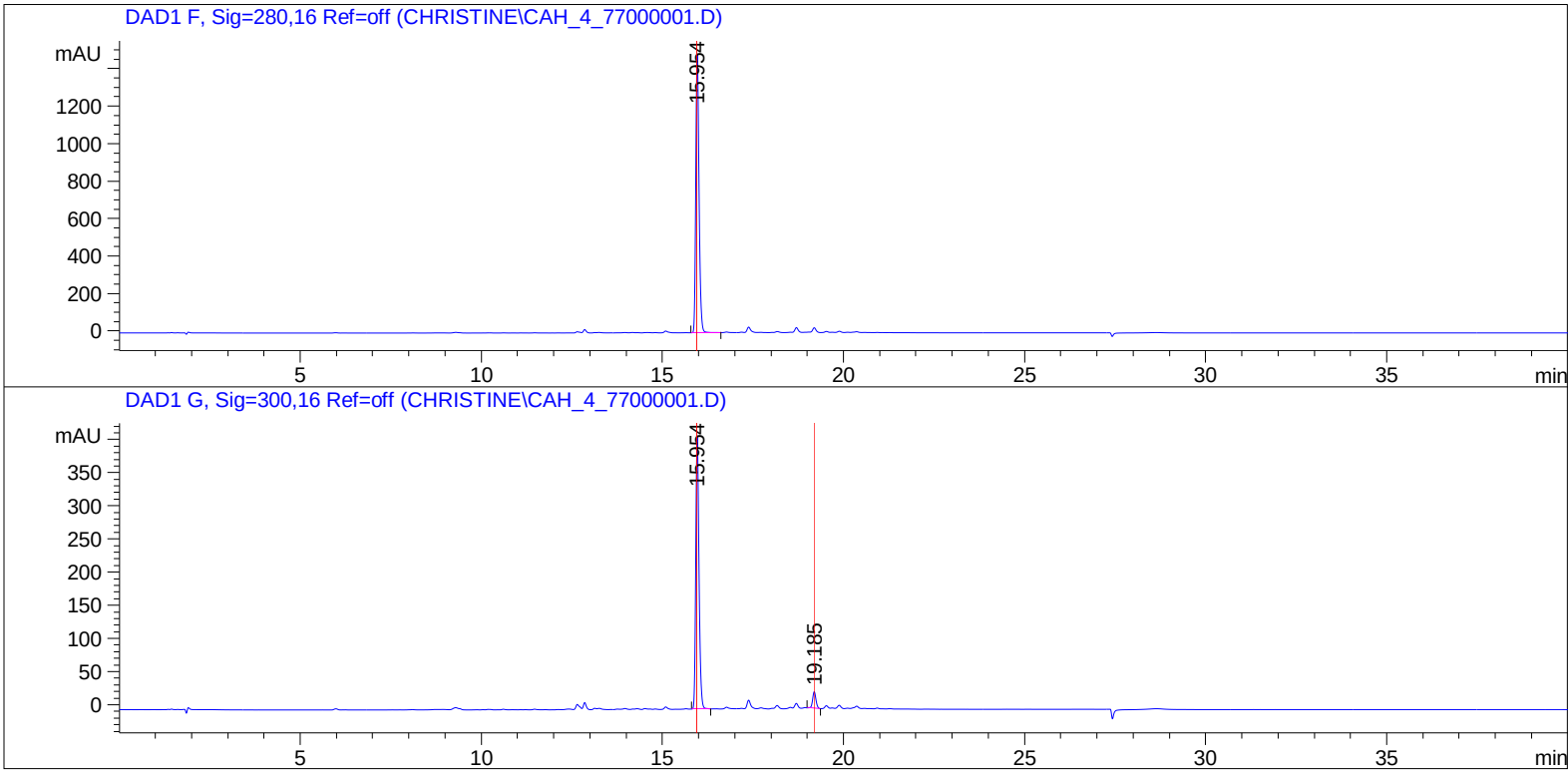
Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_4_77000001.D
Sample Name: CAH_4_77

==========

Acq. Operator : Christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 8/20/2014 12:17:48 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 8/20/2014 10:28:06 AM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CAH_4_77000001.D\DA.M (MASTERMETHOD.M)
Last changed : 8/20/2014 1:08:14 PM by Christine



Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_4_77000001.D
Sample Name: CAH_4_77



==========

Area Percent Report

==========

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

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.954	BV	0.1202	1.98992e4	2632.82886	100.0000
Totals :				1.98992e4	2632.82886	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.955	BV	0.1145	1.87492e4	2588.72656	100.0000
Totals :				1.87492e4	2588.72656	

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH_4_77000001.D
Sample Name: CAH_4_77

Signal 3: DAD1 D, Sig=230,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.954	BV	0.1145	1.91852e4	2648.36694	100.0000
Totals :				1.91852e4	2648.36694	

Signal 4: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.954	BV	0.0965	9237.36035	1485.50195	100.0000
Totals :				9237.36035	1485.50195	

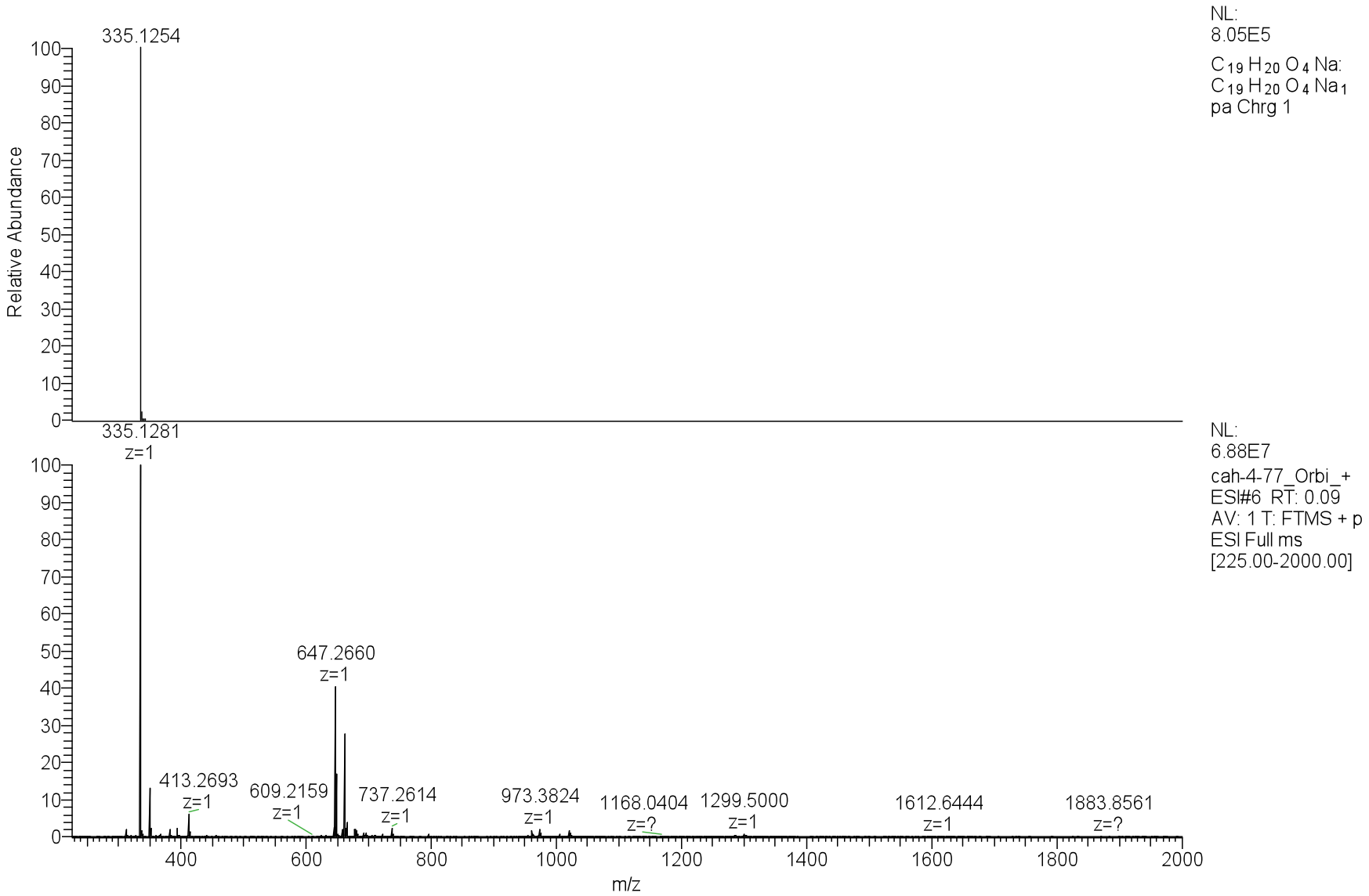
Signal 5: DAD1 F, Sig=280,16 Ref=off

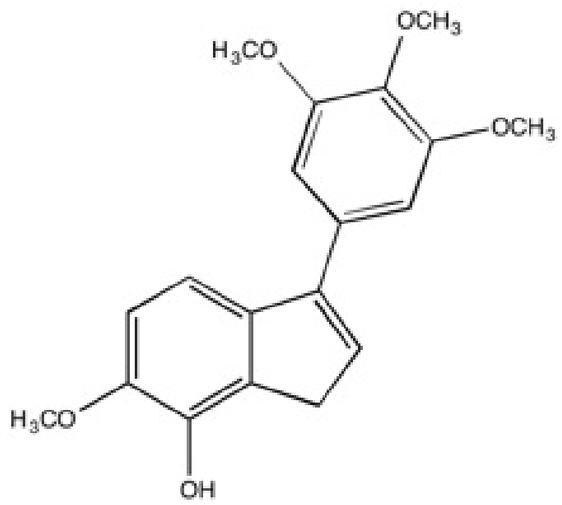
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.954	BV	0.0965	9237.36035	1485.50195	100.0000
Totals :				9237.36035	1485.50195	

Signal 6: DAD1 G, Sig=300,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.954	BB	0.0942	2545.80176	411.13858	94.1161
2	19.185	BB	0.0984	159.15662	24.96513	5.8839
Totals :				2704.95837	436.10371	

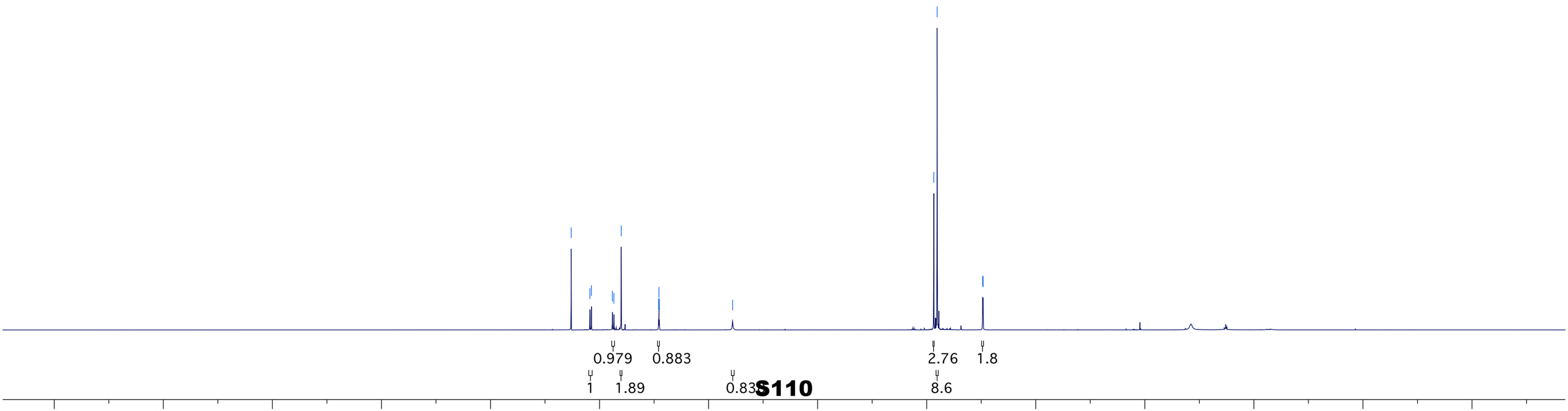
*** End of Report ***

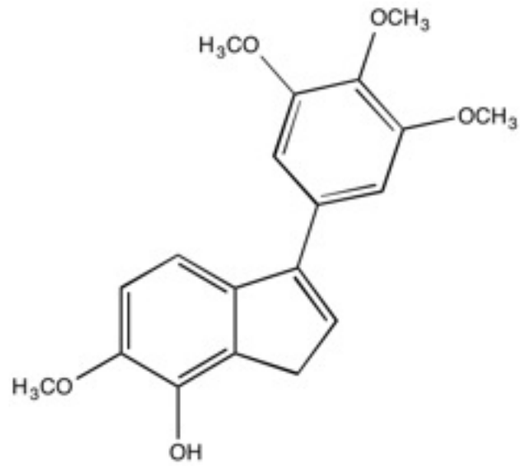

335.1254
NL:
8.05E5
C19 H20 O4 Na:
C19 H20 O4 Na1
pa Chrg 1
Relative Abundance
335.1281
z=1
NL:
6.88E7
cah-4-77_Orbi_+
ESI#6 RT: 0.09
AV: 1 T: FTMS + p
ESI Full ms
[225.00-2000.00]
647.2660
z=1
413.2693
z=1
609.2159
z=1
737.2614
z=1
973.3824
z=1
1168.0404
z=?
1299.5000
z=1
1612.6444
z=1
1883.8561
z=?
m/z


OCH3
H3CO
OCH3
H3CO
OH


7.260
7.088
7.075
6.882
6.869
6.801
6.459
6.455
6.451
5.780
3.935
3.905
3.487
3.483

31


0.979
0.883
2.76
1.8
1
1.89
0.83
8.6
ppm 12
11
10
9
8
7
6
5
4
3
2
1
0
-1



31

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137.586
131.936
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111.741
109.204
104.839
60.980
56.536
56.195
34.819
129.349
129.40 129.38 129.36 129.34 129.32

ppm 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

Data File C:\CHEM32\1\DATA\CHRISTINE\JVL_1_103000001.D
Sample Name: JVL_1_103

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Acq. Operator : christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 9/2/2015 11:49:32 AM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 9/2/2015 11:46:00 AM by christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\JVL_1_103000001.D\DA.M (MASTERMETHOD.M)
Last changed : 9/2/2015 1:22:35 PM by christine
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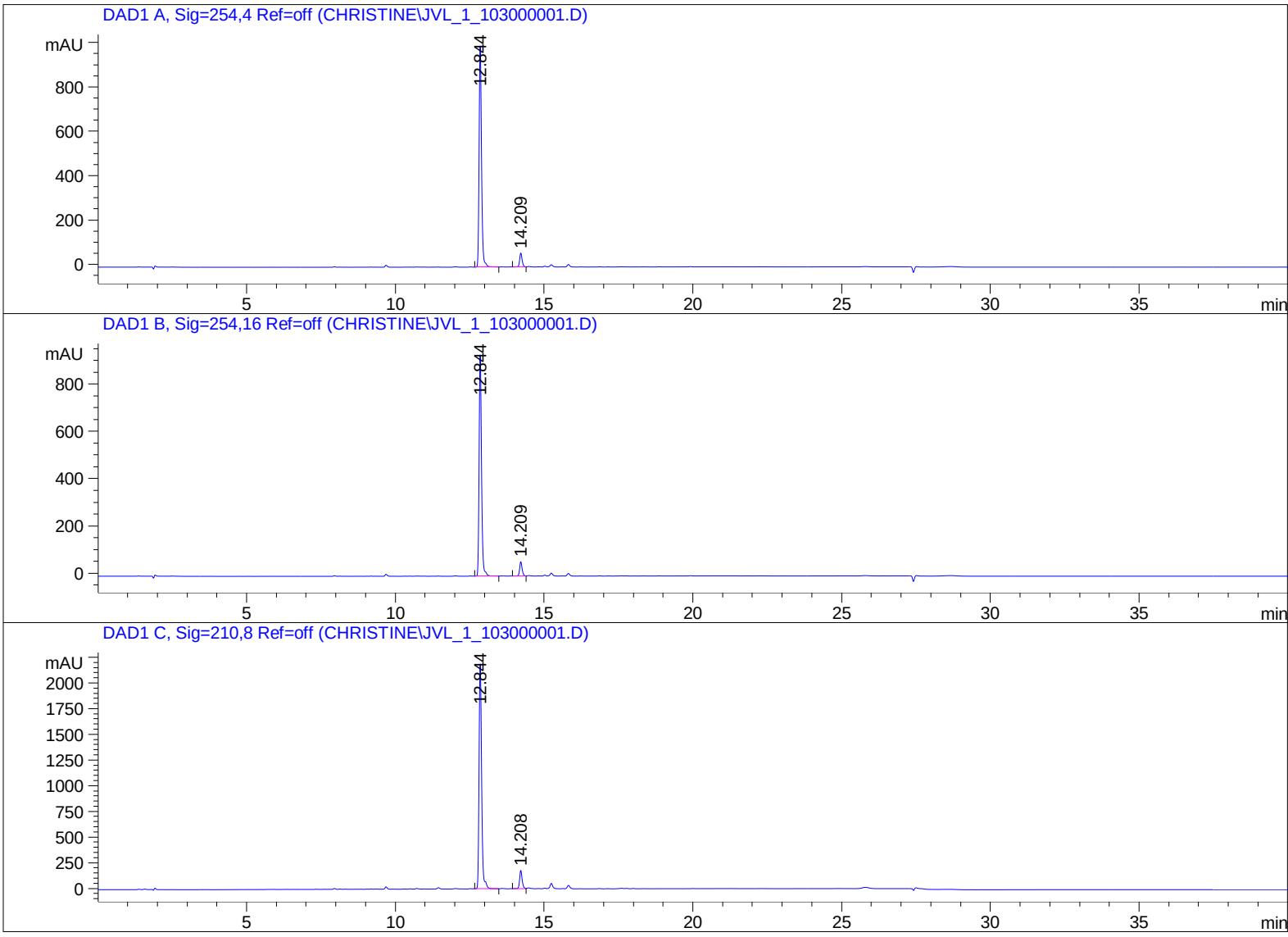

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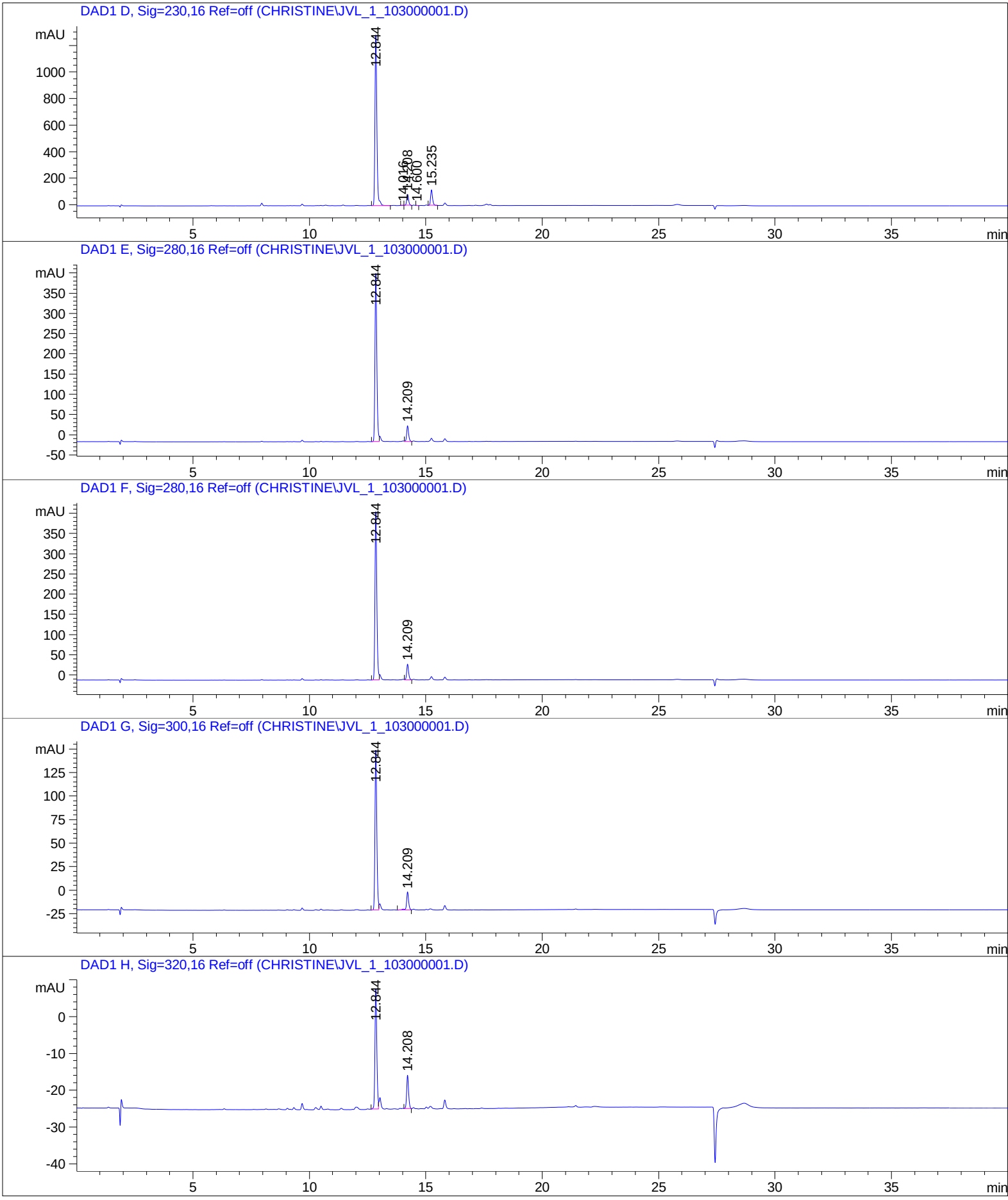
Sample Name: JVL_1_103



Data File C:\CHEM32\1\DATA\CHRISTINE\JVL_1_103000001.D
Sample Name: JVL_1_103

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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

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	VB	0.0879	5636.32080	997.72461	93.8211
2	14.209	VV	0.0889	371.19644	62.86393	6.1789
Totals :				6007.51724	1060.58854	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	VB	0.0880	5292.54199	935.98364	93.6462
2	14.209	VV	0.0893	359.09149	60.48515	6.3538
Totals :				5651.63348	996.46879	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	VV	0.0925	1.32413e4	2191.42236	92.4869
2	14.208	VV	0.0904	1075.65198	178.37202	7.5131
Totals :				1.43170e4	2369.79439	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	VV	0.0891	7398.26025	1285.71204	86.1586
2	14.016	VV	0.0917	9.59935	1.60752	0.1118

Data File C:\CHEM32\1\DATA\CHRISTINE\JVL_1_103000001.D
Sample Name: JVL_1_103

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
3	14.208	VB	0.0880	488.34366	83.83261	5.6871
4	14.600	VB	0.0731	5.42998	1.14918	0.0632
5	15.235	VB	0.0880	685.15985	117.48914	7.9792
Totals :				8586.79310	1489.79048	

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	BV	0.0868	2311.47363	416.20947	90.9454
2	14.209	VV	0.0889	230.13258	38.96600	9.0546
Totals :				2541.60622	455.17548	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	BV	0.0868	2311.47461	416.20947	90.9454
2	14.209	VV	0.0889	230.13316	38.96600	9.0546
Totals :				2541.60777	455.17548	

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

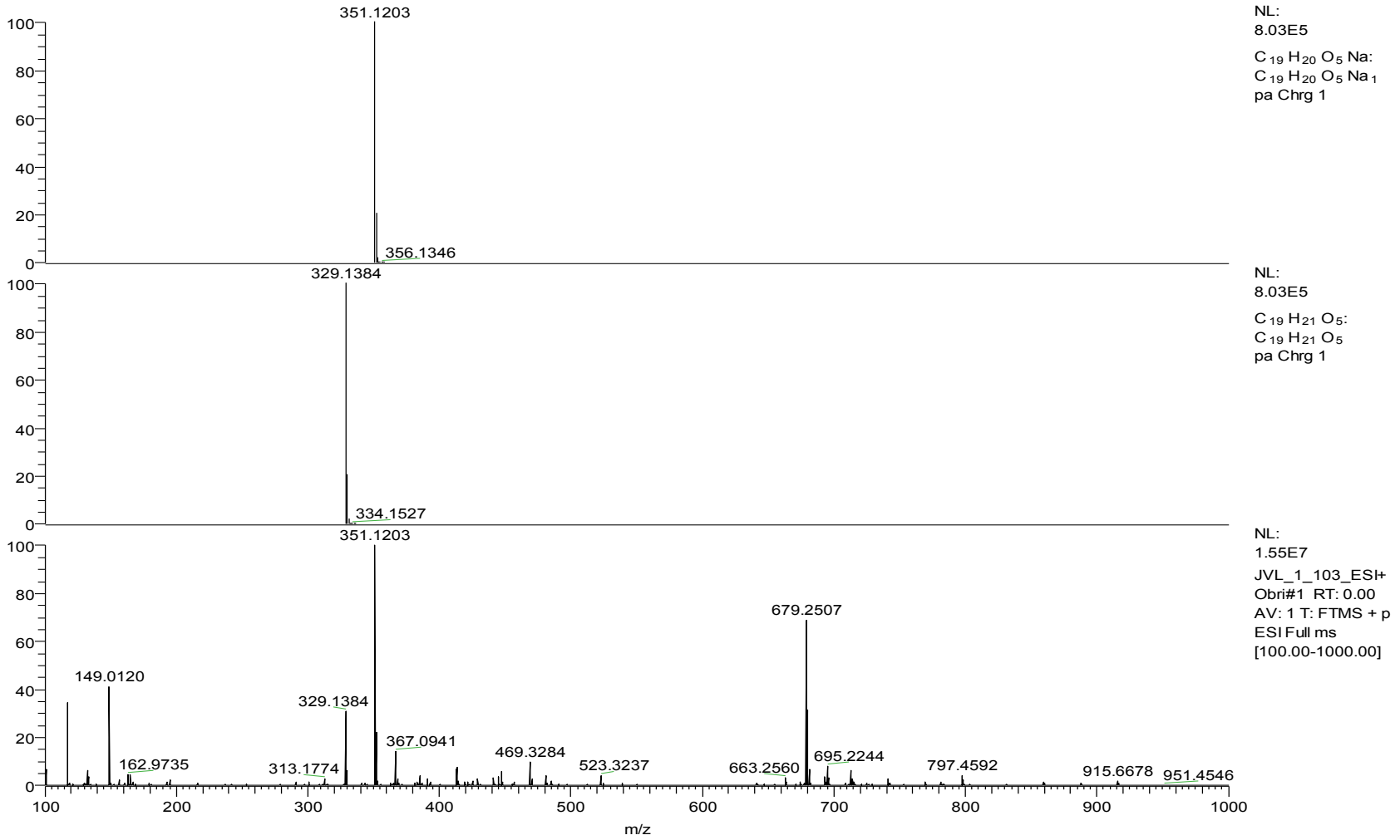
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	BV	0.0868	944.62726	170.05644	88.5016
2	14.209	BV	0.0946	122.72880	19.20041	11.4984
Totals :				1067.35606	189.25686	

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

Data File C:\CHEM32\1\DATA\CHRISTINE\JVL_1_103000001.D
Sample Name: JVL_1_103

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.844	BV	0.0875	183.99568	32.77533	77.8242
2	14.208	BB	0.0874	52.42920	9.07247	22.1758
Totals :				236.42488	41.84780	

*** End of Report ***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8.03E5
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C 19 H 20 O 5 Na 1
pa Chrg 1
329.1384
334.1527
NL:
8.03E5
C 19 H 21 O 5:
C 19 H 21 O 5
pa Chrg 1
351.1203
679.2507
149.0120
329.1384
367.0941
469.3284
162.9735
313.1774
523.3237
663.2560
695.2244
797.4592
915.6678
951.4546
NL:
1.55E7
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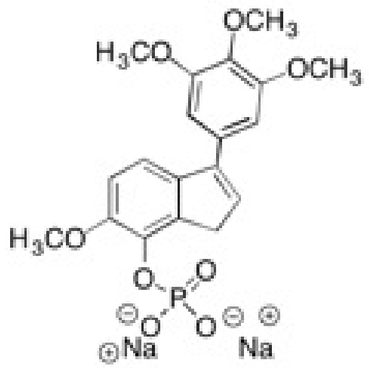
Obri#1 RT: 0.00
AV: 1 T: FTMS + p
ESI Full ms
[100.00-1000.00]
m/z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OCH3
H3CO
O
P
O
O
O
Na
Na

32

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6.392
6.389
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3.678
3.648
3.580
1.07
1.03
6.18
1.8
1
2.1
3.17
3.15
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12
10
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6
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2
0
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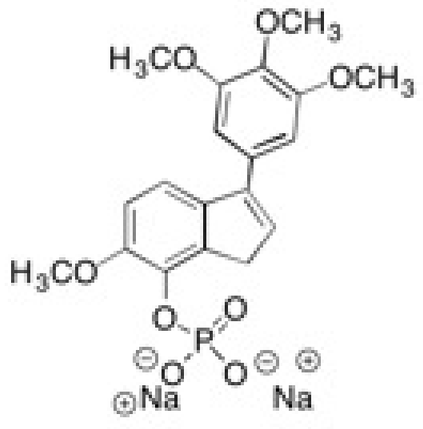

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60.866
56.282
55.882
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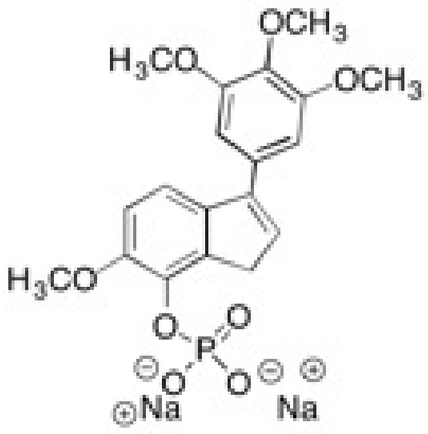

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Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-6-24000001.D
Sample Name: CAH-6-24

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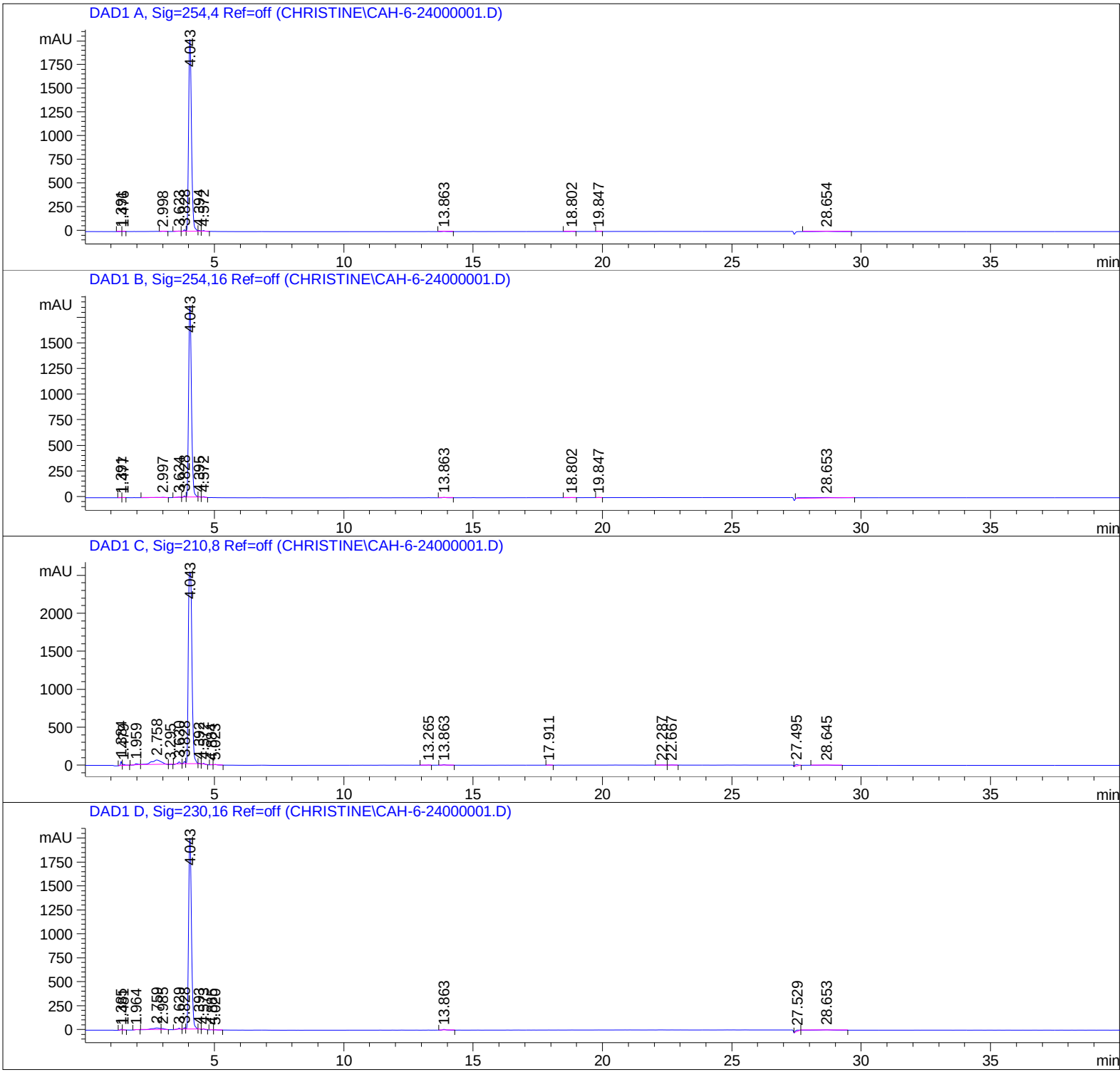
Acq. Operator : Christine
Acq. Instrument : Instrument 1 Location : -
Injection Date : 4/26/2016 12:43:48 PM
Acq. Method : C:\CHEM32\1\METHODS\MASTERMETHOD.M
Last changed : 4/26/2016 12:31:15 PM by Christine
Analysis Method : C:\CHEM32\1\DATA\CHRISTINE\CAH-6-24000001.D\DA.M (MASTERMETHOD.M)
Last changed : 4/26/2016 1:57:20 PM by Christine



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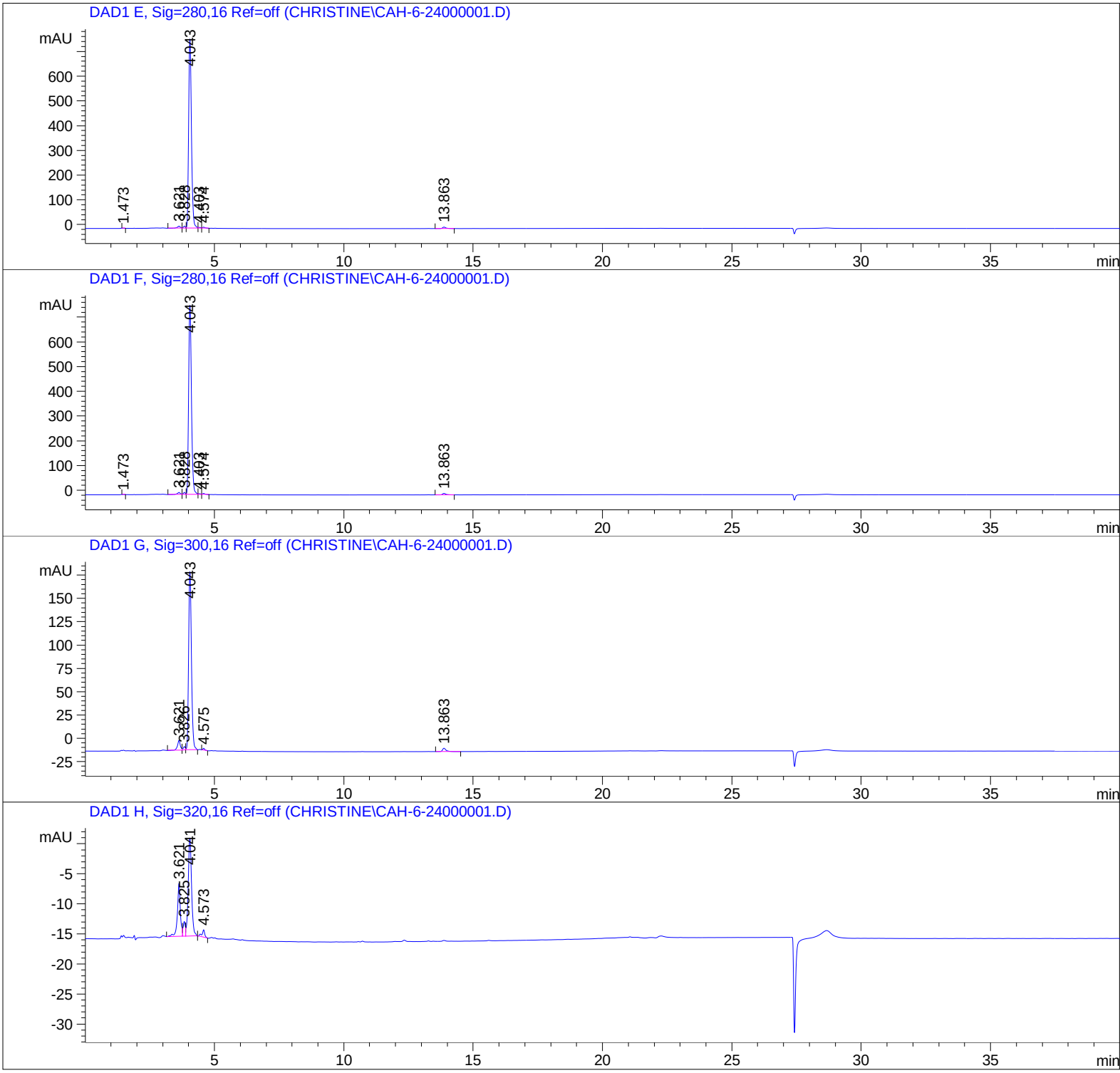
Sample Name: CAH-6-24



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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\CHRISTINE\CAH-6-24000001.D
Sample Name: CAH-6-24

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.391	BV	0.0610	7.81049	1.85999	0.0488
2	1.476	VV	0.0836	10.12844	1.74734	0.0633
3	2.998	BB	0.1245	17.02232	1.97571	0.1064
4	3.623	BB	0.1181	25.76275	3.19316	0.1611
5	3.828	BV	0.0699	68.47198	14.82507	0.4281
6	4.043	VV	0.1199	1.56188e4	2025.83167	97.6627
7	4.394	VV	0.0885	55.33225	8.90629	0.3460
8	4.572	VB	0.1021	62.22238	8.63247	0.3891
9	13.863	BB	0.1367	25.87182	2.77756	0.1618
10	18.802	BB	0.1071	9.02090	1.29729	0.0564
11	19.847	BB	0.0948	8.76622	1.44499	0.0548
12	28.654	BB	0.4623	83.38203	2.58484	0.5214
Totals :				1.59925e4	2075.07638	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.391	BV	0.0591	7.21573	1.78816	0.0476
2	1.477	VV	0.0799	9.09765	1.66187	0.0601
3	2.997	BB	0.2996	70.14854	2.96901	0.4631
4	3.624	BB	0.1172	27.39253	3.42800	0.1808
5	3.828	BV	0.0679	59.99481	13.48118	0.3960
6	4.043	VV	0.1190	1.42912e4	1872.98071	94.3370
7	4.395	VB	0.0709	22.35714	4.74763	0.1476
8	4.572	BB	0.0769	27.41272	5.42608	0.1810
9	13.863	BB	0.1386	30.36974	3.26277	0.2005
10	18.802	BB	0.1084	8.06718	1.14245	0.0533
11	19.847	BB	0.0949	8.07938	1.32921	0.0533
12	28.653	BB	1.2066	587.76019	6.16329	3.8798
Totals :				1.51491e4	1918.38036	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.384	BV	0.0515	181.29756	53.53682	0.6562
2	1.479	VB	0.0908	101.26290	15.37472	0.3665
3	1.959	BV	0.1503	171.36317	16.61413	0.6203

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-6-24000001.D
Sample Name: CAH-6-24

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
4	2.758	VB	0.3937	1774.10779	62.39947	6.4215
5	3.295	BB	0.0764	12.51878	2.33929	0.0453
6	3.630	BB	0.1072	200.15843	28.07985	0.7245
7	3.828	BV	0.0671	138.52396	31.64297	0.5014
8	4.043	VV	0.1570	2.44912e4	2527.73950	88.6480
9	4.392	VB	0.0686	47.80655	10.59979	0.1730
10	4.572	BB	0.0760	63.74675	12.82641	0.2307
11	4.884	BV	0.0744	8.96094	1.85477	0.0324
12	5.023	VB	0.0880	45.50289	7.58052	0.1647
13	13.265	BB	0.1017	15.46335	2.20867	0.0560
14	13.863	BB	0.1410	53.45221	5.61953	0.1935
15	17.911	BB	0.0924	8.66976	1.47981	0.0314
16	22.287	BV	0.2091	18.72872	1.19320	0.0678
17	22.667	VV	0.1811	23.63048	1.95335	0.0855
18	27.495	BB	0.1340	202.18147	23.12298	0.7318
19	28.645	BB	0.4029	68.88494	2.55251	0.2493
Totals :				2.76275e4	2808.71828	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.385	BV	0.0537	35.52041	9.92666	0.2130
2	1.481	VB	0.0696	20.23402	4.24269	0.1213
3	1.964	BB	0.1094	26.49018	3.53564	0.1588
4	2.759	BV	0.3117	411.25793	18.47796	2.4656
5	2.985	VB	0.1213	112.17307	12.91943	0.6725
6	3.629	BB	0.1126	93.04063	12.53667	0.5578
7	3.828	BV	0.0669	73.80240	16.90789	0.4425
8	4.043	VV	0.1205	1.54928e4	1996.45898	92.8845
9	4.393	VB	0.0699	25.51955	5.52837	0.1530
10	4.573	BB	0.0735	34.24681	7.19496	0.2053
11	4.885	BV	0.0784	10.15930	2.02997	0.0609
12	5.020	VB	0.0851	14.67683	2.55004	0.0880
13	13.863	BB	0.1415	70.21961	7.34801	0.4210
14	27.529	BB	0.1549	158.54309	15.29897	0.9505
15	28.653	BB	0.4906	100.96045	2.97006	0.6053
Totals :				1.66797e4	2117.92632	

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-6-24000001.D
Sample Name: CAH-6-24

Signal 5: DAD1 E, Sig=280,16 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.473	VB	0.0704	5.48779	1.13574	0.0911
2	3.621	BV	0.1263	76.58023	8.56689	1.2716
3	3.828	VV	0.0811	48.96879	8.78171	0.8131
4	4.043	VV	0.1181	5779.64941	765.73773	95.9686
5	4.403	VV	0.1005	24.02273	3.48107	0.3989
6	4.574	VB	0.1010	32.78029	4.60598	0.5443
7	13.863	BB	0.1385	54.94780	5.91066	0.9124
Totals :				6022.43705	798.21977	

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.473	VB	0.0704	5.48760	1.13574	0.0911
2	3.621	BV	0.1263	76.57832	8.56689	1.2716
3	3.828	VV	0.0811	48.96640	8.78171	0.8131
4	4.043	VV	0.1181	5779.65039	765.73773	95.9687
5	4.403	VV	0.1005	24.02216	3.48060	0.3989
6	4.574	VB	0.1010	32.77953	4.60598	0.5443
7	13.863	BB	0.1385	54.94532	5.91063	0.9123
Totals :				6022.42972	798.21928	

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

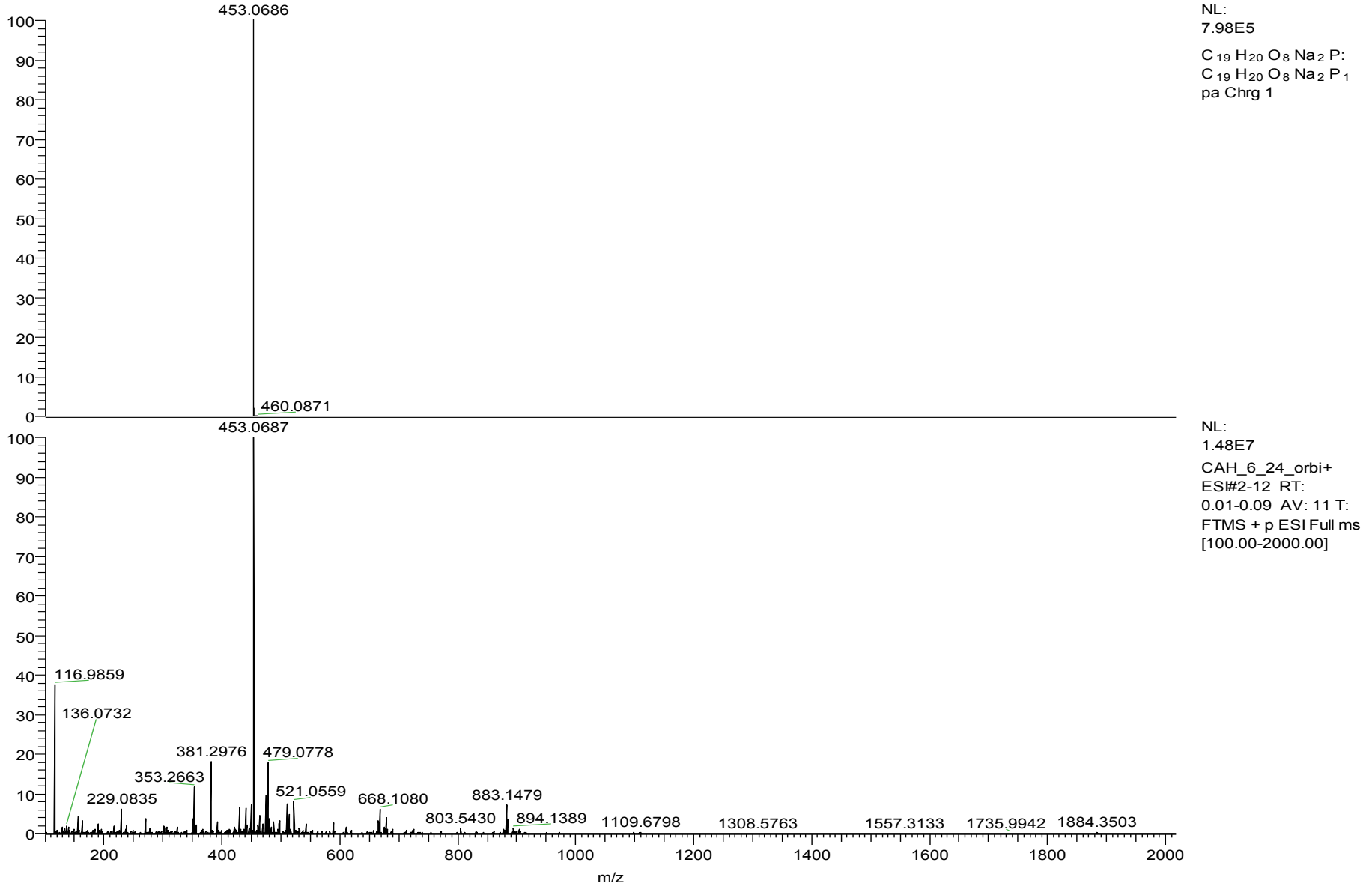
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.621	BV	0.1131	83.12932	10.64792	5.1879
2	3.826	VV	0.0800	20.97679	3.82476	1.3091
3	4.043	VB	0.1186	1452.70459	191.39255	90.6600
4	4.575	VB	0.0810	11.73287	2.17350	0.7322
5	13.863	BB	0.1406	33.82201	3.56693	2.1108
Totals :				1602.36558	211.60565	

Data File C:\CHEM32\1\DATA\CHRISTINE\CAH-6-24000001.D
Sample Name: CAH-6-24

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

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.621	BV	0.1166	71.65930	8.83325	29.4579
2	3.825	VV	0.0844	14.51530	2.47418	5.9670
3	4.041	VB	0.1372	147.71956	16.38952	60.7250
4	4.573	BB	0.1057	9.36575	1.24525	3.8501
Totals :				243.25991	28.94220	

*** End of Report ***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