

Supporting Information

***Exo*-Selective and Enantioselective Photoenolization/Diels–Alder Reaction**

Min Hou,^{a†} Mengmeng Xu,^{a†} Baochao Yang,^a Haibing He,^{*b} Shuanhu Gao^{*a,b}

^a Shanghai Key Laboratory of Green Chemistry and Chemical Processes, School of Chemistry and Molecular Engineering, East China Normal University, 3663N Zhongshan Road, Shanghai 200062, China.

^b Shanghai Engineering Research Center of Molecular Therapeutics and New Drug Development, East China Normal University, 3663N Zhongshan Road, Shanghai 200062, China.

Corresponding Author: Haibing He^{*} and Shuanhu Gao^{*}

E-mail: hbbe@chem.ecnu.edu.cn, shgao@chem.ecnu.edu.cn

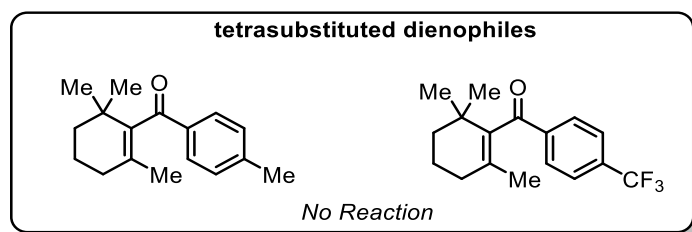
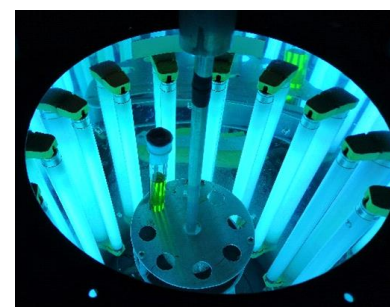
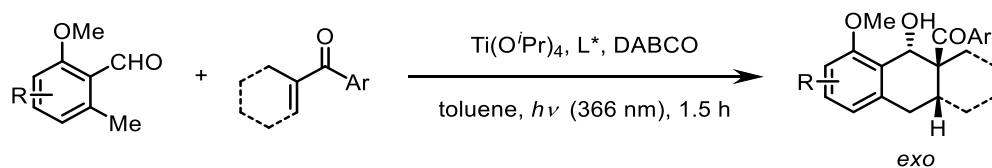
Contents

I.	General Information	S3
II.	General Procedures for the enantioselective PEDA reaction	S4
III.	Crystal data and structure refinement for 7	S14
IV.	Crystal data and structure refinement for 7a	S16
V.	Crystal data and structure refinement for 9	S18
VI.	NMR and HPLC Spectra	S20

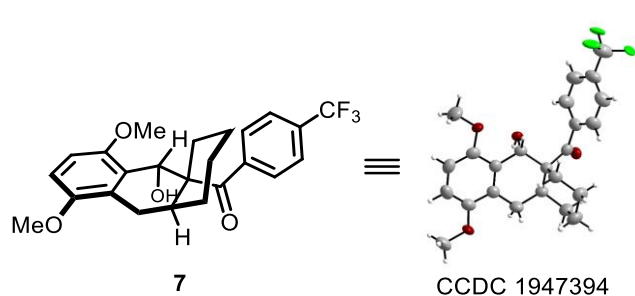
I. General Information

General Experimental Procedures. All reactions were carried out under nitrogen except noted. Anhydrous dichloromethane, toluene, acetonitrile and dimethylformamide were purified by the PS-MD5 (Innovative Technology) solvent purification system. Tetrahydrofuran and anhydrous diethyl ether were distilled from sodium-benzophenone ketyl. All other commercial reagents were used as received. Flash column chromatography was performed as described by Still, employing Qingdao Haiyang silica gel 60 (200–300 mesh). TLC analyses were performed on EMD 250 μm Silica Gel HSGF254 plates and visualized by quenching of UV fluorescence ($\lambda_{\text{max}} = 254 \text{ nm}$), or by staining ceric ammonium molybdate, phosphomolybdic acid, or potassium permanganate. ^1H and ^{13}C NMR spectra were recorded on a Bruker 500, 400 spectrometer. Chemical shifts for ^1H and ^{13}C NMR spectra are reported in ppm (δ) relative to residue protium in the solvent (CDCl_3 : δ 7.26, 77.0 ppm, and the multiplicities are presented as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad single. High-resolution mass spectra (HRMS) were acquired on Thermo Scientific, Q Exactive Focus (Orbitrap). The $[\alpha]_D^{25}$ was recorded using Anton Paar MCP 5500. Infrared (IR) spectra were obtained using a Shimadzu IRTracer-100 fourier transform infrared spectroscopy (FTIR). HPLC analysis on chiral stationary phase was performed on an Agilent 1200-series instrument, employing Daicel Chiralpak OD-H, AS-H, OJ-H and IG chiral columns. Single-crystal X-ray diffraction data were collected on a X-ray Diffractometer (XtaLAB P2000). The photo reactor used for this photolysis is Rayonet RPR-200 (Southern New England Ultraviolet Company). The irradiation vessel of the photo reaction is quartz glass tube, 10 cm from the light source.

II. General Procedures for Asymmetric Photoenolization/Diels–Alder Reaction (APEDA)

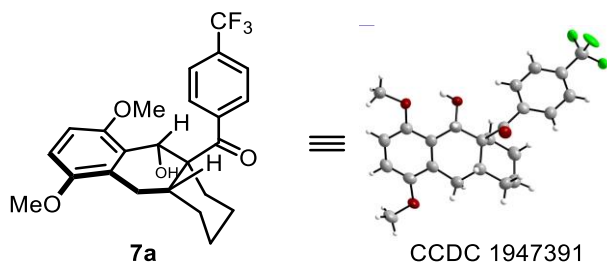


To a solution of aromatic aldehyde (0.3 mmol, 1.0 equiv.), chiral ligand (0.15 mmol, 0.5 equiv.) and 1,4-diazabicyclo[2.2.2]octane (DABCO) (0.3 mmol, 1.0 equiv.) in anhydrous toluene (30 mL, 0.01 M) was added dienophile (0.45 mmol, 1.5 equiv.) (if the dienophile was solid, it was added before the addition of solvent) under N_2 , in quartz tube sealed with rubber plug. Then, titanium (IV) isopropoxide ($\text{Ti}(\text{O}i\text{-Pr})_4$, 0.3 mmol, 1.0 equiv.) was added, after homogeneous mixing, the solution was photolyzed at room temperature in a Rayonet chamber reactor (16 lamps) at $\lambda_{\text{max}} = 366$ nm for 1.5 h. Then the reaction mixture was poured into saturated sodium bicarbonate and stirred over 30 min, the above mixture was extracted three times with ethyl acetate, the combined organic phases were washed twice with brine and dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography to give the corresponding cycloadducts, and the ligand could be recovered over 95% yield.



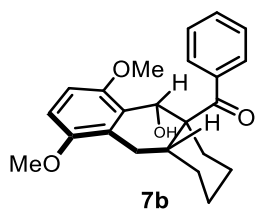
7 (50 mg, dr > 20:1) was prepared according to general procedure in 38% yield (in the presence of $\text{Ti}(\text{O}i\text{-Pr})_4$, (0.9 mmol, 3.0 equiv.), without ligand and DABCO). The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid; $R_f = 0.3$ (20% ethyl acetate-petroleum ether); and it was recrystallized from dichloromethane /hexane (V/V = 1/4), slowly volatilize for several days at 25 °C, to obtain colorless crystals, CCDC (1947394). ^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, $J = 8.0$ Hz, 2H), 7.67 (d, $J = 8.1$ Hz, 2H), 6.75 (d, $J = 8.8$ Hz, 1H), 6.71 (d, $J = 8.9$ Hz, 1H), 5.10 (d, $J = 3.3$ Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 2.95 – 2.80 (m, 2H), 2.72 – 2.61 (m, 2H), 1.95 (d, $J = 12.0$ Hz, 1H), 1.62 – 1.42 (m, 5H), 1.31 – 1.21 (m, 2H). ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 208.6, 151.5, 151.1, 144.7, 132.0 (q, $J = 32.6$ Hz, 1C), 127.8 (2C), 125.7, 125.6, 125.2, 124.9 (q, $J = 3.8$ Hz, 1C), 122.5, 108.9, 107.2, 69.1, 55.64, 55.60, 55.1, 27.4, 27.2, 26.5, 24.7, 22.8, 19.6 ppm; IR ν_{max} 2949, 1481,

1325, 1305, 1255, 1166, 1126, 1066, 742 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{25}\text{O}_4\text{F}_3\text{Na}$, 457.1597; found, 457.1594.



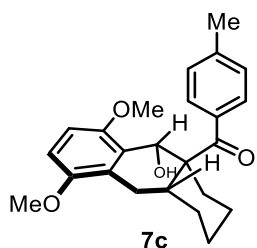
7a (102 mg, dr = 3.6:1) was prepared according to general procedure in 78% yield. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.6 (20% ethyl acetate-petroleum ether); m.p. 142 – 144 $^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20}$ -70.2 (c

1.24, DCM); and it was recrystallized from dichloromethane /hexane (V/V = 1/4), slowly volatilize for several days at 25 $^{\circ}\text{C}$, to obtain colorless crystals, CCDC (1947391). ^1H NMR (400 MHz, CDCl_3) δ 8.06 (d, J = 8.1 Hz, 2H), 7.66 (d, J = 8.1 Hz, 2H), 6.72 (s, 2H), 5.23 (s, 1H), 4.81 (d, J = 1.5 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 2.88 – 2.64 (m, 3H), 2.44 (dt, J = 14.6, 2.9 Hz, 1H), 1.75 – 1.65 (m, 1H), 1.60 – 1.39 (m, 5H), 1.05 – 0.90 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 211.9, 151.8, 151.3, 144.7, 131.9 (q, J = 32.5 Hz, 1C), 127.9 (2C), 126.7, 125.9, 125.2, 124.9 (q, J = 3.8 Hz, 1C), 122.5, 108.2, 108.1, 73.5, 55.8, 55.7, 55.6, 33.4, 27.6, 24.3, 21.8, 21.6, 19.1 ppm; IR ν_{max} 2949, 1481, 1325, 1305, 1255, 1166, 1126, 1066, 742 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{25}\text{O}_4\text{F}_3\text{Na}$, 457.1597; found, 457.1594; Enantiomeric excess: 99.1%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 $^{\circ}\text{C}$, 230 nm): t_{R} = 10.883 min (major), t_{R} = 17.052 min (minor).

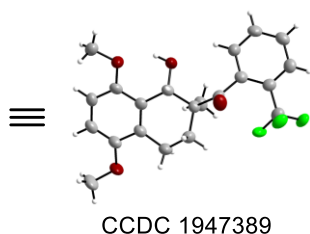
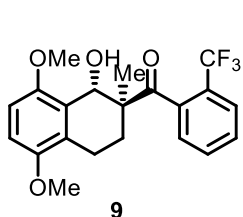


7b (42 mg, dr = 5.3:1) was prepared according to general procedure in 38% yield. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a yellow oil: R_f = 0.5 (20% ethyl acetate-petroleum ether); $[\alpha]_{\text{D}}^{20}$ -77.4 (c 0.25, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.96 – 7.91 (m, 2H), 7.48 – 7.36 (m, 3H), 6.71 (s, 2H), 5.30 (d, J = 1.6

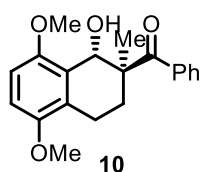
Hz, 1H), 4.69 (d, J = 1.7 Hz, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 2.88 – 2.74 (m, 2H), 2.74 – 2.61 (m, 1H), 2.52 (dt, J = 14.7, 3.8 Hz, 1H), 1.72 – 1.51 (m, 4H), 1.49 – 1.42 (m, 1H), 1.42 – 1.34 (m, 1H), 1.08 (dt, J = 13.4, 4.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 211.9, 151.9, 151.2, 141.3, 130.3, 127.8, 127.6 (2C), 127.0 (2C), 126.0, 108.1, 107.9, 73.0, 55.8 (d, J = 2.4 Hz, 1C), 55.6 (d, J = 2.4 Hz, 1C), 55.3, 33.6, 27.6, 24.3, 21.8, 21.7, 19.3 ppm; IR ν_{max} 1371, 1282, 1267, 1180, 1141, 744, 707 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{23}\text{H}_{26}\text{O}_4\text{Na}$, 389.1723; found, 389.1719; Enantiomeric excess: 99.3%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 $^{\circ}\text{C}$, 230 nm): t_{R} = 8.594 min (minor), t_{R} = 16.710 min (major).



7c (65 mg, dr = 7.3:1) was prepared according to general procedure in 58% yield. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a yellow solid: R_f = 0.55 (20% ethyl acetate-petroleum ether); m.p. 130 – 132 °C; $[\alpha]_D^{20}$ -103 (c 0.26, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.87 (d, J = 8.2 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 6.71 (s, 2H), 5.30 (d, J = 1.7 Hz, 1H), 4.66 (d, J = 1.8 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 2.88 – 2.76 (m, 2H), 2.69 (q, J = 12.0 Hz, 1H), 2.54 (dt, J = 14.9, 3.7 Hz, 1H), 2.39 (s, 3H), 1.71 – 1.60 (m, 1H), 1.56 – 1.31 (m, 5H), 1.10 (dt, J = 13.3, 4.5 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 211.1, 151.9, 151.1, 140.7, 138.4, 128.4 (2C), 127.9 (2C), 127.0, 126.1, 108.0, 107.8, 72.7, 55.7 (d, J = 2.2 Hz, 1C), 55.5 (d, J = 2.1 Hz, 1C), 55.2, 33.6, 27.5, 24.3, 21.82, 21.78, 21.4, 19.3 ppm; IR ν_{max} 3003, 1604, 1342, 1203, 1147, 1066, 1016, 827, 742, 702 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{24}\text{H}_{28}\text{O}_4\text{Na}$, 403.1880; found, 403.1876; Enantiomeric excess: 96%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.673 min (minor), t_R = 15.138 min (major).

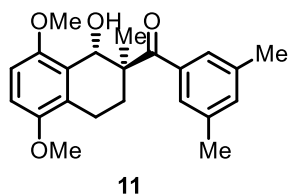


9 (73.2 mg) was prepared according to general procedure in 62% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.33 (20% ethyl acetate-petroleum ether); m.p. 118 - 120; $[\alpha]_D^{20}$ -20.6 (c 0.73, DCM); and it was recrystallized from dichloromethane /hexane (V/V = 1/4), slowly volatilize for several days at 25 °C, to obtain colorless crystals, CCDC (1947389). ^1H NMR (500 MHz, CDCl_3) δ 7.81 – 7.77 (m, 1H), 7.69 – 7.66 (m, 1H), 7.58 – 7.53 (m, 1H), 7.51 – 7.46 (m, 1H), 6.73 (d, J = 8.9 Hz, 1H), 6.69 (d, J = 8.9 Hz, 1H), 5.37 (s, 1H), 4.43 (s, 1H), 3.84 (s, 3H), 3.78 (s, 3H), 2.81 – 2.70 (m, 1H), 2.68 – 2.57 (m, 1H), 2.22 – 2.12 (m, 1H), 2.04 – 1.94 (m, 1H), 1.22 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 212.0, 152.1, 151.3, 139.6 (q, J = 1.9 Hz, 1C), 131.0, 128.7, 127.7, 126.7, 126.6 (q, J = 31.7 Hz, 1C), 126.4 (q, J = 4.5 Hz, 1C), 126.2, 123.6 (q, J = 273.7 Hz, 1C), 108.3, 108.2, 71.5, 55.8, 55.5, 51.5, 29.7, 20.5, 16.1 ppm; IR ν_{max} 3055, 1697, 1280, 1107, 802, 744 cm^{-1} ; HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{21}\text{H}_{21}\text{F}_3\text{O}_4$, 394.1392; found, 394.1395; Enantiomeric excess: 97%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 13.027 min (major), t_R = 15.067 min (minor).

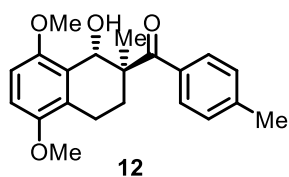


10 (86.9 mg) was prepared according to general procedure in 92% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a yellow solid: R_f = 0.34 (20% ethyl acetate-petroleum ether); m.p. 96 - 98; $[\alpha]_D^{20}$ +56.2 (c 0.24, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.65 – 7.59 (m, 2H), 7.46 – 7.41 (m, 1H), 7.38 – 7.31 (m, 2H), 6.66 (s, 2H), 5.43 (s, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 2.81 – 2.66 (m, 2H), 2.50 – 2.29 (m, 2H), 2.14

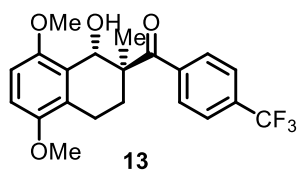
– 2.03 (m, 1H), 1.58 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 207.3, 151.6, 151.2, 138.8, 130.8, 128.2, 128.0 (2C), 127.5 (2C), 125.9, 108.6, 107.9, 66.8, 55.8, 55.5, 51.2, 27.5, 21.1, 20.8 ppm; IR ν_{max} 3691, 3055, 1697, 1265, 1107, 744 cm^{-1} ; HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{20}\text{H}_{22}\text{O}_4$, 326.1518; found, 326.1512; Enantiomeric excess: 79%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, $T = 25\text{ }^\circ\text{C}$, 230 nm): $t_{\text{R}} = 13.843$ min (major), $t_{\text{R}} = 16.134$ min (minor).



11 (101.1 mg, dr = 5:1) was prepared according to general procedure in 81% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a colorless oil: $R_f = 0.27$ (20% ethyl acetate-petroleum ether); $[\alpha]_{\text{D}}^{20} +91.1$ (c 0.77, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.14 (s, 2H), 7.05 (s, 1H), 6.67 (s, 2H), 5.41 (s, 1H), 3.79 (s, 3H), 3.74 (s, 3H), 2.77 – 2.65 (m, 2H), 2.53 – 2.40 (m, 1H), 2.29 (s, 6H), 2.13 – 2.01 (m, 1H), 1.54 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 208.0, 151.6, 151.3, 139.1, 137.5 (2C), 132.2, 128.3, 126.1, 125.0 (2C), 108.6, 107.8, 66.8, 55.8, 55.5, 51.3, 27.4, 21.3 (2C), 21.1, 21.0 ppm; IR ν_{max} 2889, 1685, 1267, 1049, 744 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{O}_4\text{Na}$, 377.1723; found, 377.1719; Enantiomeric excess: 82%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, $T = 25\text{ }^\circ\text{C}$, 230 nm): $t_{\text{R}} = 26.115$ min (major), $t_{\text{R}} = 31.599$ min (minor).



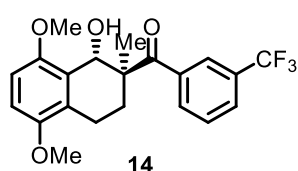
12 (72.7 mg) was prepared according to general procedure in 71% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a colorless oil: $R_f = 0.18$ (20% ethyl acetate-petroleum ether); $[\alpha]_{\text{D}}^{20} +122$ (c 0.49, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.62 (d, $J = 8.1$ Hz, 2H), 7.16 (d, $J = 8.1$ Hz, 2H), 6.68 (d, $J = 8.9$ Hz, 1H), 6.65 (d, $J = 8.9$ Hz, 1H), 5.46 (s, 1H), 3.81 (s, 3H), 3.72 (s, 3H), 2.78 – 2.66 (m, 2H), 2.44 – 2.31 (m, 5H), 2.18 – 2.07 (m, 1H), 1.59 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 206.2, 151.7, 151.2, 141.5, 135.7, 128.7, 128.5 (2C), 128.0 (2C), 125.9, 108.6, 107.9, 66.78, 66.75, 55.9, 55.5, 51.0, 27.7, 21.2, 21.1 ppm; IR ν_{max} 3055, 2889, 1676, 1315, 1267, 1051, 744 cm^{-1} ; HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{21}\text{H}_{24}\text{O}_4$, 340.1675; found, 340.1680; Enantiomeric excess: 85%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, $T = 25\text{ }^\circ\text{C}$, 230 nm): $t_{\text{R}} = 33.565$ min (major), $t_{\text{R}} = 38.586$ min (minor).



13 (80.5 mg, dr = 3.5:1) was prepared according to general procedure in 68% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a colorless oil: $R_f = 0.15$ (20% ethyl acetate-petroleum ether); $[\alpha]_{\text{D}}^{20} +81.9$ (c 0.19, DCM); ^1H NMR (500 MHz, CDCl_3) δ 7.60 (s, 4H), 6.68 (d, $J = 8.8$ Hz, 1H), 6.65 (d, $J = 8.8$ Hz, 1H), 5.35 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 2.94 (s, 1H), 2.80 – 2.68 (m, 1H), 2.57 – 2.46 (m, 1H), 2.34 – 2.23 (m, 1H), 2.10 – 2.04 (m, 1H), 1.53 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ

207.5, 151.6, 151.3, 142.5, 132.1 (q, $J = 32.6$ Hz, 1C), 127.7, 127.4 (2C), 125.9, 125.0 (q, $J = 3.7$ Hz, 2C), 123.7 (d, $J = 272.3$ Hz, 1C), 108.7, 107.9, 66.9, 55.7, 55.5, 51.5, 27.4, 20.9, 20.3 ppm; IR ν_{\max} 3055, 1697, 1280, 1265, 1107, 744 cm^{-1} ; HRMS–EI (m/z): $[M]^+$ calcd for $\text{C}_{21}\text{H}_{21}\text{F}_3\text{O}_4$, 394.1392; found, 394.1387; Enantiomeric excess: 99.5%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, $T = 25$ °C, 230 nm): $t_R = 8.402$ min (major), $t_R = 9.827$ min (minor). For the 1 mmol scale reaction, two 50 ml quartz glass tubes are used (0.5 mmol for each), after the reaction is complete, combine the two reaction solutions for treatment, the same yield and ee value was obtained.

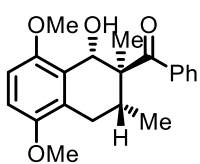
For the 1 mmol scale reaction, two 50 ml quartz glass tubes are used (0.5 mmol for each): aromatic aldehyde (0.5 mmol, 1.0 equiv.), chiral ligand (0.25 mmol, 0.5 equiv.), dienophile (0.75 mmol, 1.5 equiv.) and 1,4-diazabicyclo[2.2.2]octane (DABCO) (1.0 mmol, 2.0 equiv.) was added in a 50 ml quartz glass tube sealed with rubber plug, then add anhydrous toluene (50 mL, 0.01 M) to dissolve the reactants under N_2 . Then, titanium (IV) isopropoxide ($\text{Ti}(\text{O}i\text{-Pr})_4$, 0.5 mmol, 1.0 equiv.) was added, after homogeneous mixing, the solution was photolyzed at room temperature in a Rayonet chamber reactor (16 lamps) at $\lambda_{\max} = 366$ nm for 1.5 h. After the reaction is complete, combine the two reaction solutions for treatment. The reaction mixture was poured into saturated sodium bicarbonate and stirred over 30 min, the above mixture was extracted three times with ethyl acetate, the combined organic phases were washed twice with brine and dried over anhydrous sodium sulfate. The dried solution was filtered and the filtrate was concentrated under vacuum. The residue was purified by silica gel column chromatography to give the corresponding cycloadducts 268 mg (68%, dr = 3.5:1, 99.5% ee).



14

14 (109.1 mg) was prepared according to general procedure in 85% yield. Ligand **L10** (0.24 mmol, 0.8 equiv.), DABCO (0.96 mmol, 3.2 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a

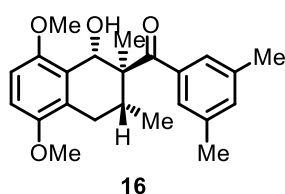
colorless oil: $R_f = 0.32$ (20% ethyl acetate-petroleum ether); $[\alpha]_D^{20} +60.6$ (c 0.86, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.80 – 7.65 (m, 3H), 7.54 – 7.45 (m, 1H), 6.68 (d, $J = 8.9$ Hz, 1H), 6.66 (d, $J = 8.9$ Hz, 1H), 5.36 (s, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 2.84 (s, 1H), 2.79 – 2.69 (m, 1H), 2.56 – 2.45 (m, 1H), 2.35 – 2.26 (m, 1H), 2.16 – 2.03 (m, 1H), 1.55 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 206.7, 151.5, 151.3, 139.6, 130.5 (2C), 128.6 (2C), 127.7, 127.2, 125.9, 124.1, 108.8, 107.8, 66.8, 55.7, 55.51, 51.46, 27.3, 21.0, 20.6 ppm; IR ν_{\max} 2889, 1685, 1267, 1089, 1051, 881 cm^{-1} ; HRMS–EI (m/z): $[M]^+$ calcd for $\text{C}_{21}\text{H}_{21}\text{F}_3\text{O}_4$, 394.1392; found, 394.1388; Enantiomeric excess: 98%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, $T = 25$ °C, 230 nm): $t_R = 8.494$ min (major), $t_R = 10.672$ min (minor).



15

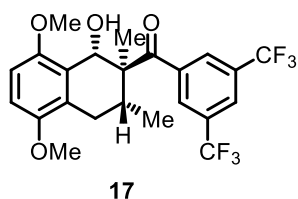
15 (63.8 mg) was prepared according to general procedure in 62% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: $R_f = 0.46$ (20% ethyl acetate-petroleum ether); m.p. 88 - 90 °C; $[\alpha]$

²⁰_D -23.4 (c 0.37, DCM); ¹H NMR (500 MHz, CDCl₃) δ 7.66 – 7.61 (m, 2H), 7.46 – 7.36 (m, 3H), 6.72 (d, *J* = 8.9 Hz, 1H), 6.68 (d, *J* = 8.9 Hz, 1H), 5.43 (s, 1H), 4.73 (d, *J* = 1.3 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 2.79 (dd, *J* = 17.9, 5.0 Hz, 1H), 2.55 – 2.44 (m, 1H), 2.38 – 2.26 (m, 1H), 1.19 (s, 3H), 1.06 (d, *J* = 6.7 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ 212.5, 152.2, 151.1, 141.4, 129.8, 127.9 (2C), 127.4, 126.5 (2C), 126.1, 108.3, 108.1, 74.1, 55.8, 55.7, 55.5, 33.4, 29.5, 16.6, 9.9 ppm; IR ν_{max} 3055, 2306, 1676, 1317, 1265, 740 cm⁻¹; HRMS–ESI (*m/z*): [M+Na]⁺ calcd for C₂₁H₂₄O₄Na, 363.1567; found, 363.1562; Enantiomeric excess: 96%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.985 min (minor), t_R = 13.200 min (major).



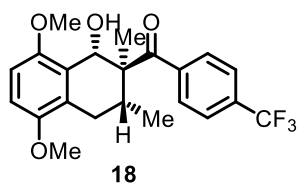
16 (47.5 mg) was prepared according to general procedure in 43% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.5 (20% ethyl acetate-petroleum ether);

m.p. 142 – 144 °C; [α]_D²⁰ -25.2 (c 0.58, DCM); ¹H NMR (500 MHz, CDCl₃) δ 7.22 (s, 2H), 7.06 (s, 1H), 6.72 (d, *J* = 8.9 Hz, 1H), 6.69 (d, *J* = 8.9 Hz, 1H), 5.44 (s, 1H), 4.69 (d, *J* = 1.3 Hz, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 2.78 (dd, *J* = 18.0, 5.1 Hz, 1H), 2.55 – 2.46 (m, 1H), 2.36 – 2.29 (m, 7H), 1.18 (s, 3H), 1.06 (d, *J* = 6.7 Hz, 3H) ppm; ¹³C NMR (125 MHz, CDCl₃) δ 212.8, 152.3, 151.1, 141.5, 137.4 (2C), 131.5, 127.6, 126.2, 124.2 (2C), 108.3, 108.0, 74.1, 55.8, 55.7, 55.5, 33.5, 29.5, 21.4 (2C), 16.6, 10.0 ppm; IR ν_{max} 3055, 1685, 1483, 1267, 1111, 746 cm⁻¹; HRMS–ESI (*m/z*): [M+Na]⁺ calcd for C₂₃H₂₈O₄Na, 391.1880; found, 391.1874; Enantiomeric excess: 99%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.099 min (major), t_R = 11.419 min (minor).

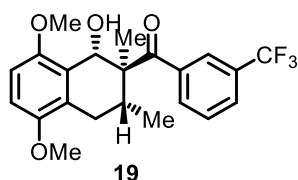


17 (97.7 mg) was prepared according to general procedure in 68% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a colorless oil: R_f = 0.5 (20% ethyl acetate-petroleum ether);

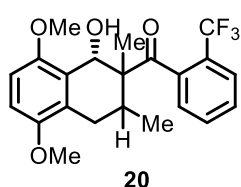
[α]_D²⁰ +45.3 (c 0.52, DCM); ¹H NMR (400 MHz, CDCl₃) δ 8.30 (s, 2H), 7.95 (s, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 1H), 5.06 (d, *J* = 3.0 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.00 (dd, *J* = 18.5, 5.8 Hz, 1H), 2.88 – 2.79 (m, 1H), 2.75 (d, *J* = 3.0 Hz, 1H), 2.18 (dd, *J* = 18.5, 11.6 Hz, 1H), 1.10 (s, 3H), 0.89 (d, *J* = 6.5 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 206.7, 151.7, 150.8 (2C), 143.0 (2C), 131.3 (q, *J* = 33.6 Hz, 2C), 128.0, 125.9, 125.5, 123.5, 123.1 (q, *J* = 272.8 Hz, 1C), 109.1, 107.5, 70.4, 70.3, 55.6, 54.5, 29.5, 26.9, 16.8, 14.1 ppm; IR ν_{max} 3055, 1751, 1707, 1483, 1267, 1109, 746 cm⁻¹; HRMS–ESI (*m/z*): [M+Na]⁺ calcd for C₂₃H₂₂F₆O₄Na, 499.1314; found, 499.1308; Enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 95/5, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.018 min (major), t_R = 11.141 min (minor).



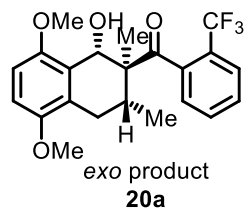
18 (74.3 mg) was prepared according to general procedure in 61% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.5 (20% ethyl acetate-petroleum ether); m.p. 86 - 88 °C; $[\alpha]_D^{20}$ -24.1 (c 0.30, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.71 (d, J = 8.2 Hz, 2H), 7.66 (d, J = 8.2 Hz, 2H), 6.73 (d, J = 8.9 Hz, 1H), 6.69 (d, J = 8.9 Hz, 1H), 5.34 (s, 1H), 4.83 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 2.80 (dd, J = 17.8, 5.0 Hz, 1H), 2.53 – 2.39 (m, 1H), 2.31 (dd, J = 17.8, 11.9 Hz, 1H), 1.16 (s, 3H), 1.06 (d, J = 6.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 212.3, 152.2, 151.2, 144.9, 131.5 (q, J = 32.5 Hz, 1C), 127.1, 126.7 (2C), 126.0, 125.0 (q, J = 3.8 Hz, 2C), 122.5, 108.5, 108.2, 74.3, 56.0, 55.8, 55.6, 33.3, 29.5, 16.6, 9.8 ppm; IR ν_{max} 3055, 1751, 1483, 1267, 1085, 744, 677 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{23}\text{F}_3\text{O}_4\text{Na}$, 431.1441; found, 431.1436; Enantiomeric excess: 99%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 7.497 min (minor), t_R = 9.044 min (major).



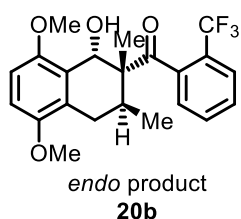
19 (57.2 mg) was prepared according to general procedure in 47% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.38 (20% ethyl acetate-petroleum ether); m.p. 108 - 110 °C; $[\alpha]_D^{20}$ -26.8 (c 0.04, DCM); ^1H NMR (500 MHz, CDCl_3) δ 7.89 (s, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.53 (t, J = 7.8 Hz, 1H), 6.73 (d, J = 8.9 Hz, 1H), 6.69 (d, J = 8.9 Hz, 1H), 5.35 (s, 1H), 4.83 (d, J = 1.2 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 2.80 (dd, J = 18.1, 5.2 Hz, 1H), 2.52 – 2.42 (m, 1H), 2.38 – 2.24 (m, 1H), 1.17 (s, 3H), 1.06 (d, J = 6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 211.9, 152.2, 151.1, 142.1, 130.3 (q, J = 32.3 Hz, 1C), 129.7, 128.5, 127.1, 126.5 (q, J = 4.0 Hz, 1C), 126.0, 123.5 (q, J = 4.0 Hz, 1C), 122.8, 108.5, 108.2, 74.4, 55.9, 55.8, 55.6, 33.5, 29.5, 16.6, 10.0 ppm; IR ν_{max} 3055, 1751, 1707, 1483, 1109, 746 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{23}\text{F}_3\text{O}_4\text{Na}$, 431.1441; found, 431.1435; Enantiomeric excess: 99%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 7.045 min (major), t_R = 9.123 min (minor).



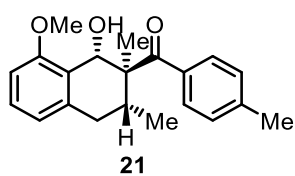
20 (57.2 mg, dr = 1.8:1) was prepared according to general procedure in 54% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) to give **20a** (20.4 mg, 19%) and **20b** (36.8 mg, 35%) as a yellow solid.



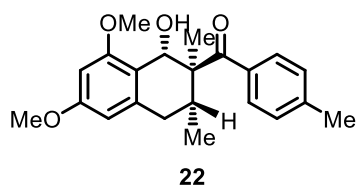
20a (the relative configuration was determined by NOESY spectra) R_f = 0.33 (20% ethyl acetate-petroleum ether); m.p. 99 - 101 °C; $[\alpha]_D^{20}$ -8.2 (c 0.056, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.78 – 7.69 (m, 2H), 7.57 – 7.46 (m, 2H), 6.71 (d, J = 9.5 Hz, 1H), 6.69 (d, J = 9.5 Hz, 1H), 5.24 (s, 1H), 4.49 (d, J = 1.6 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 2.78 (dd, J = 16.8, 3.6 Hz, 1H), 2.49 – 2.33 (m, 2H), 1.21 (s, 3H), 1.11 (d, J = 6.3 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 210.6, 152.0, 150.9, 130.5, 129.4, 129.1, 128.1, 127.9 (q, J = 32.1 Hz, 1C), 127.6, 127.4 (q, J = 4.9 Hz, 1C), 126.5, 126.2, 108.11, 108.07, 73.7, 56.1, 55.61, 55.56, 33.7, 29.5, 16.6, 10.7 ppm; IR ν_{max} 3055, 1707, 1483, 1421, 1317, 1111, 746 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{23}\text{F}_3\text{O}_4\text{Na}$, 431.1441; found, 431.1432; Enantiomeric excess: 98%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 7.302 min (major), t_R = 9.260 min (minor).



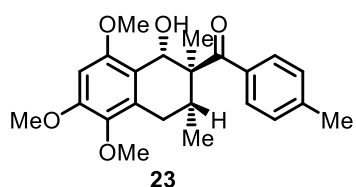
20b (the relative configuration was determined by NOESY spectra) R_f = 0.18 (20% ethyl acetate-petroleum ether); m.p. 120 - 122 °C; $[\alpha]_D^{20}$ -13.1 (c 0.19, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.73 – 7.66 (m, 2H), 7.52 (t, J = 7.6 Hz, 1H), 7.35 (t, J = 7.7 Hz, 1H), 6.75 (s, 2H), 5.12 (d, J = 2.3 Hz, 1H), 4.34 (dd, J = 12.2, 5.5 Hz, 1H), 3.86 (s, 3H), 3.76 (s, 3H), 3.55 (s, 1H), 3.15 (dd, J = 18.5, 5.5 Hz, 1H), 2.81 (dd, J = 18.5, 12.2 Hz, 1H), 1.78 (s, 3H), 1.32 (s, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 213.1, 151.9, 150.7, 143.4, 131.6, 129.3 (q, J = 28.9 Hz, 1C), 128.8, 126.6 (q, J = 6.1 Hz, 1C), 126.5, 126.2, 125.5, 124.4 (d, J = 274.4 Hz, 1C), 109.1, 108.3, 70.3, 56.0, 55.5, 54.8, 33.6, 30.5, 27.5, 16.3 ppm; IR ν_{max} 3055, 1707, 1483, 1421, 1317, 1111, 746 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{23}\text{F}_3\text{O}_4\text{Na}$, 431.1441; found, 431.1432; Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 16.068 min (minor), t_R = 30.321 min (major).



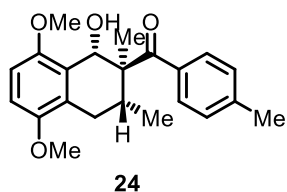
21 (46 mg) was prepared according to general procedure in 47% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.55 (20% ethyl acetate-petroleum ether); m.p. 120 – 122 °C; $[\alpha]_D^{20}$ -5.58 (c 0.74, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.59 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.15 (t, J = 8.0 Hz, 1H), 6.78 – 6.71 (m, 2H), 5.49 (s, 1H), 4.50 (d, J = 1.5 Hz, 1H), 3.85 (s, 3H), 2.74 – 2.66 (m, 2H), 2.65 – 2.53 (m, 1H), 2.38 (s, 3H), 1.24 (s, 3H), 1.02 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 211.2, 158.5, 140.4, 138.2, 137.3, 128.6 (2C), 127.6, 127.0 (2C), 126.4, 121.5, 108.3, 73.7, 56.1, 55.4, 34.9, 33.9, 21.4, 16.4, 10.3 ppm; IR ν_{max} 2964, 1583, 1469, 1257, 1083, 1016, 744 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{24}\text{O}_3\text{Na}$, 347.1618; found, 347.1613; Enantiomeric excess: 99.7%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 75/25, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 19.337 min (major), t_R = 27.734 min (minor).



22 (46.5 mg) was prepared according to general procedure in 44% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.52 (30% ethyl acetate-petroleum ether); m.p. 74 - 76 °C; $[\alpha]_D^{20}$ -14.8 (c 0.42, DCM); ^1H NMR (500 MHz, CDCl_3) δ 7.58 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 7.9 Hz, 2H), 6.33 (d, J = 2.3 Hz, 1H), 6.26 (d, J = 2.3 Hz, 1H), 5.43 (s, 1H), 4.32 (d, J = 1.4 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 2.67 – 2.53 (m, 3H), 2.38 (s, 3H), 1.22 (s, 3H), 1.00 (d, J = 6.3 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 211.2, 159.5, 159.2, 140.4, 138.2, 138.0, 128.6 (2C), 127.1 (2C), 119.1, 104.4, 97.1, 73.3, 56.2, 55.5, 55.3, 35.3, 33.9, 21.4, 16.4, 10.4 ppm; IR ν_{max} 3053, 2964, 1670, 1610, 1456, 1267, 1149, 833, 738 cm^{-1} ; HRMS–EI (m/z): $[\text{M}]^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{O}_4$, 354.1831; found, 354.1835; Enantiomeric excess: 99.9%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 20.989 min (major), t_R = 33.791 min (minor).



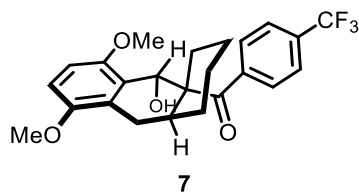
23 (48.7 mg) was prepared according to general procedure in 42% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a white solid: R_f = 0.42 (30% ethyl acetate-petroleum ether); m.p. 95 - 97 °C; $[\alpha]_D^{20}$ -21.4 (c 0.38, DCM); ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 7.9 Hz, 2H), 6.42 (s, 1H), 5.42 (s, 1H), 4.40 (d, J = 1.4 Hz, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.76 (s, 3H), 2.83 (dd, J = 16.9, 4.1 Hz, 1H), 2.54 – 2.41 (m, 2H), 2.38 (s, 3H), 1.20 (s, 3H), 1.03 (d, J = 6.3 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 211.4, 154.7, 151.5, 140.3, 140.2, 138.3, 131.2, 128.6 (2C), 127.0 (2C), 119.1, 95.5, 73.5, 60.1, 56.0, 55.9, 55.8, 33.6, 29.5, 21.4, 16.5, 10.2 ppm; IR ν_{max} 3053, 2303, 1610, 1492, 1236, 1124, 744 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{23}\text{H}_{28}\text{O}_5\text{Na}$, 407.1829; found, 407.1822; Enantiomeric excess: 99.8%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 26.250 min (major), t_R = 31.271 min (minor).



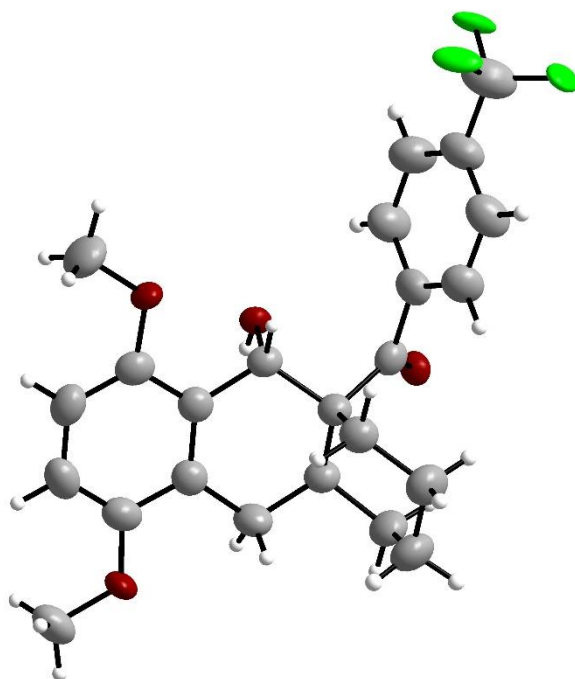
24 (71.9 mg) was prepared according to general procedure in 68% yield. DABCO (0.60 mmol, 2.0 equiv.) was used. The reaction time was 90 min under 366 nm light. The product was isolated through silica gel column chromatography (6% to 20% ethyl acetate-petroleum ether) as a colorless oil: R_f = 0.45 (20% ethyl acetate-petroleum ether); $[\alpha]_D^{20}$ -20.2 (c 0.16, DCM); ^1H NMR (500 MHz, CDCl_3) δ 7.58 (d, J = 8.2 Hz, 2H), 7.20 (d, J = 7.9 Hz, 2H), 6.71 (d, J = 8.9 Hz, 1H), 6.68 (d, J = 8.9 Hz, 1H), 5.47 (s, 1H), 4.68 (d, J = 1.3 Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 2.81 – 2.74 (m, 1H), 2.56 – 2.47 (m, 1H), 2.38 (s, 3H), 2.37 – 2.29 (m, 1H), 1.21 (s, 3H), 1.04 (d, J = 6.7 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl_3) δ 211.6, 152.2, 151.1, 140.2, 138.3, 128.5 (2C), 127.5, 126.9 (2C), 126.2, 108.3, 108.0, 73.9, 55.8, 55.7, 55.5, 33.5, 29.5, 21.4, 16.5, 10.0 ppm; IR ν_{max} 3055, 1672,

1309, 1267, 1122, 740 cm^{-1} ; HRMS–ESI (m/z): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{22}\text{H}_{26}\text{O}_4\text{Na}$, 377.1723; found, 377.1717; Enantiomeric excess: 97%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, $T = 25\text{ }^\circ\text{C}$, 230 nm): $t_{\text{R}} = 10.124\text{ min}$ (minor), $t_{\text{R}} = 12.489\text{ min}$ (major).

III. Crystal data and structure refinement for 7



CCDC 1947394

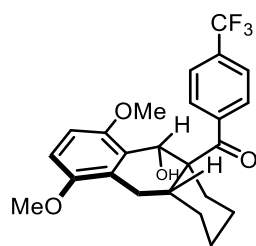


(ellipsoid contour at 50% probability level)

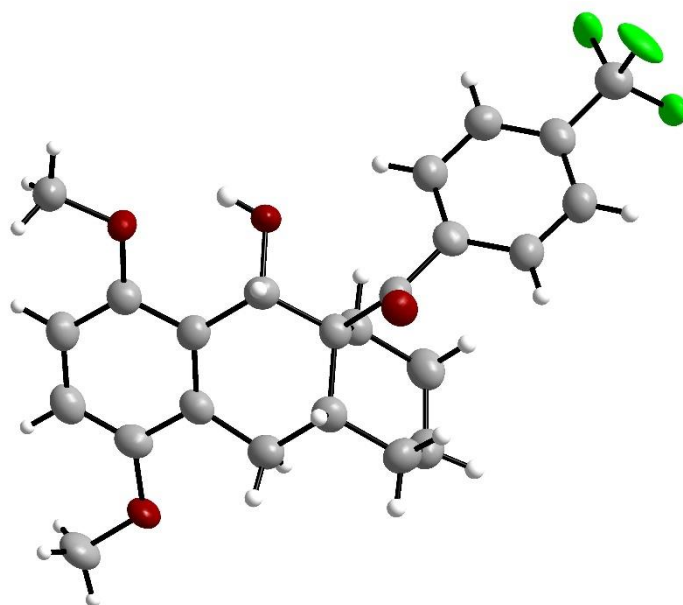
Crystal data and structure refinement for 7

Identification code	7
Empirical formula	C ₂₄ H ₂₅ F ₃ O ₄
Formula weight	434.44
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	10.2397(2)
b/Å	10.3182(2)
c/Å	10.7297(3)
α /°	74.853(2)
β /°	74.200(2)
γ /°	69.720(2)
Volume/Å ³	1005.55(4)
Z	2
ρ calc/g/cm ³	1.435
μ /mm ⁻¹	0.971
F(000)	456.0
Crystal size/mm ³	0.43 × 0.38 × 0.36
Radiation	CuK α (λ = 1.54184)
2 θ range for data collection/°	8.716 to 148.936
Index ranges	-12 ≤ h ≤ 12, -12 ≤ k ≤ 12, -12 ≤ l ≤ 12
Reflections collected	21252
Independent reflections	4008 [R _{int} = 0.0337, R _{sigma} = 0.0195]
Data/restraints/parameters	4008/0/283
Goodness-of-fit on F ²	1.041
Final R indexes [I ≥ 2 σ (I)]	R ₁ = 0.0357, wR ₂ = 0.0899
Final R indexes [all data]	R ₁ = 0.0372, wR ₂ = 0.0910
Largest diff. peak/hole / e Å ⁻³	0.26/-0.25

IV. Crystal data and structure refinement for 7a



7a
CCDC 1947391

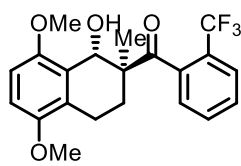


(ellipsoid contour at 50% probability level)

Crystal data and structure refinement for 7a

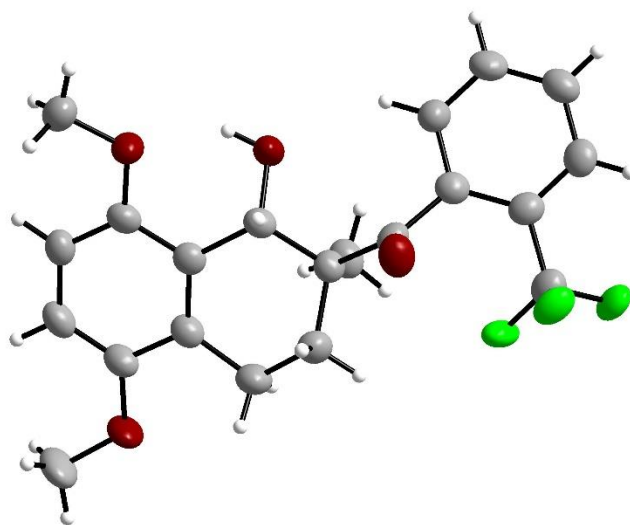
Identification code	7a
Empirical formula	C ₂₄ H ₂₅ F ₃ O ₄
Formula weight	434.44
Temperature/K	100.00(10)
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	7.45280(10)
b/Å	12.18510(10)
c/Å	22.5826(2)
α /°	90
β /°	90
γ /°	90
Volume/Å ³	2050.80(4)
Z	4
ρ_{calc} /cm ³	1.407
μ /mm ⁻¹	0.953
F(000)	912.0
Crystal size/mm ³	0.38 × 0.26 × 0.22
Radiation	CuK α (λ = 1.54184)
2 Θ range for data collection/°	7.83 to 148.952
Index ranges	-8 ≤ h ≤ 8, -15 ≤ k ≤ 15, -27 ≤ l ≤ 28
Reflections collected	49662
Independent reflections	4111 [R_{int} = 0.1197, R_{sigma} = 0.0406]
Data/restraints/parameters	4111/0/284
Goodness-of-fit on F ²	1.063
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0370, wR_2 = 0.0966
Final R indexes [all data]	R_1 = 0.0390, wR_2 = 0.0982
Largest diff. peak/hole / e Å ⁻³	0.25/-0.22
Flack parameter	-0.17(7)

V. Crystal data and structure refinement for **9**



9

CCDC 1947389



(ellipsoid contour at 50% probability level)

Crystal data and structure refinement for **9**

Identification code	9
Empirical formula	C ₂₁ H ₂₁ F ₃ O ₄
Formula weight	394.38
Temperature/K	100.00(10)
Crystal system	orthorhombic
Space group	P2 ₁ 2 ₁ 2 ₁
a/Å	7.01890(10)
b/Å	10.7355(2)
c/Å	24.6659(3)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90
Volume/Å ³	1858.61(5)
Z	4
$\rho_{\text{calc}}/\text{cm}^3$	1.409
μ/mm^{-1}	0.992
F(000)	824.0
Crystal size/mm ³	0.48 × 0.28 × 0.22
Radiation	CuK α (λ = 1.54184)
2 Θ range for data collection/ $^\circ$	8.984 to 149.184
Index ranges	-8 ≤ h ≤ 8, -13 ≤ k ≤ 13, -30 ≤ l ≤ 30
Reflections collected	41677
Independent reflections	3767 [R_{int} = 0.1067, R_{sigma} = 0.0365]
Data/restraints/parameters	3767/0/260
Goodness-of-fit on F ²	1.050
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0435, wR_2 = 0.1124
Final R indexes [all data]	R_1 = 0.0446, wR_2 = 0.1134
Largest diff. peak/hole / e Å ⁻³	0.32/-0.27
Flack parameter	0.02(7)

VI. NMR and HPLC Spectra

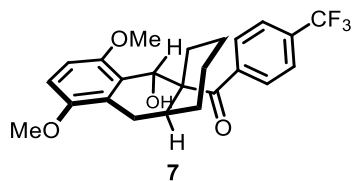
HM-VI-93C-1. 10. fid
HM-VI-93C-1

7.93
7.91
7.68
7.66
6.76
6.74
6.72
6.70

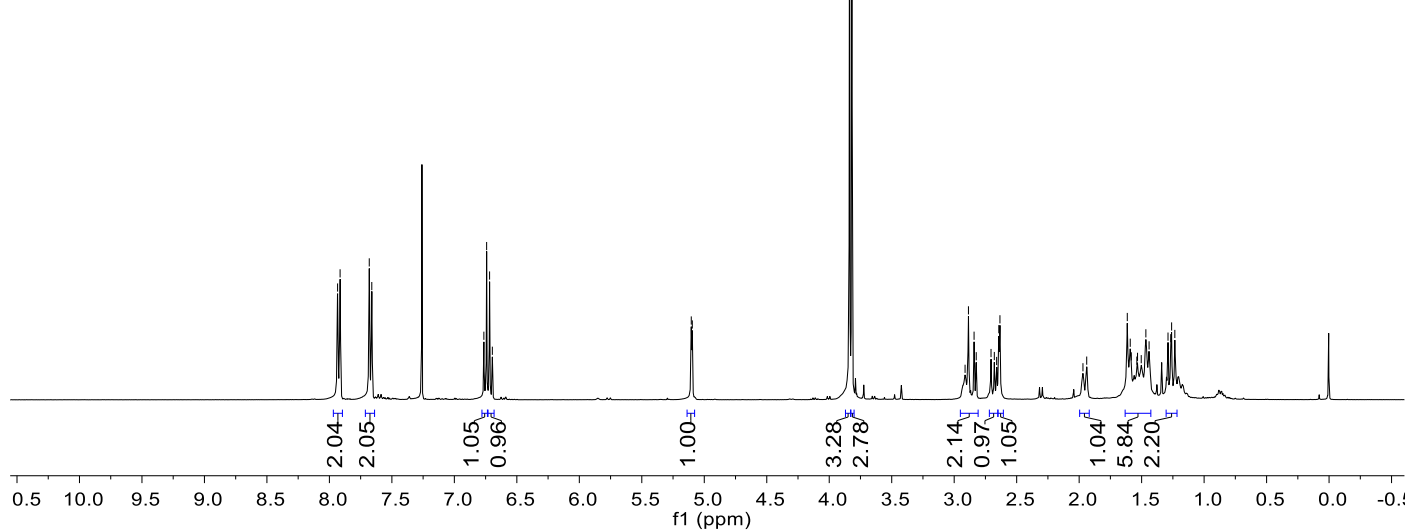
5.10
5.10

3.84
3.82
2.91
2.89
2.84
2.82
2.71
2.68
2.66
2.64
2.63

1.94
1.61
1.59
1.58
1.54
1.53
1.50
1.47
1.44
1.29
1.27
1.26
1.23



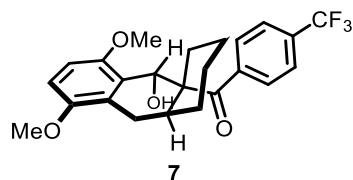
Chemical Formula: $C_{24}H_{25}F_3O_4$
400 MHz, $CDCl_3$



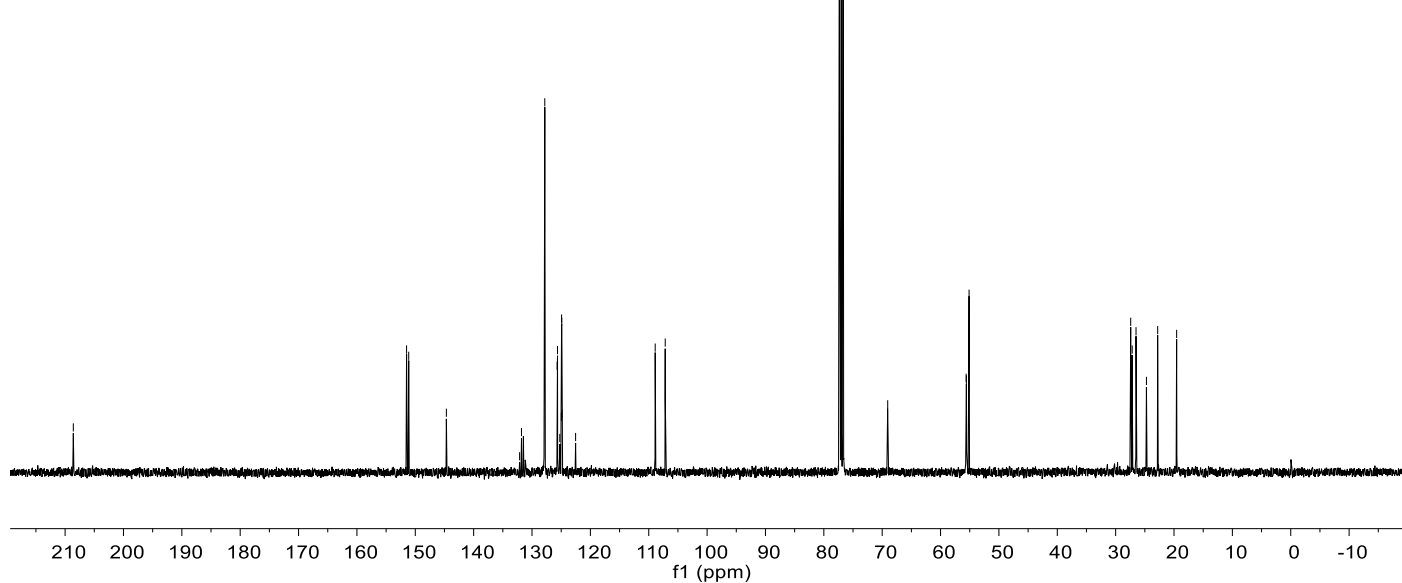
HM-VI-93C-1 C. 12. fid
HM-VI-93C-1 C

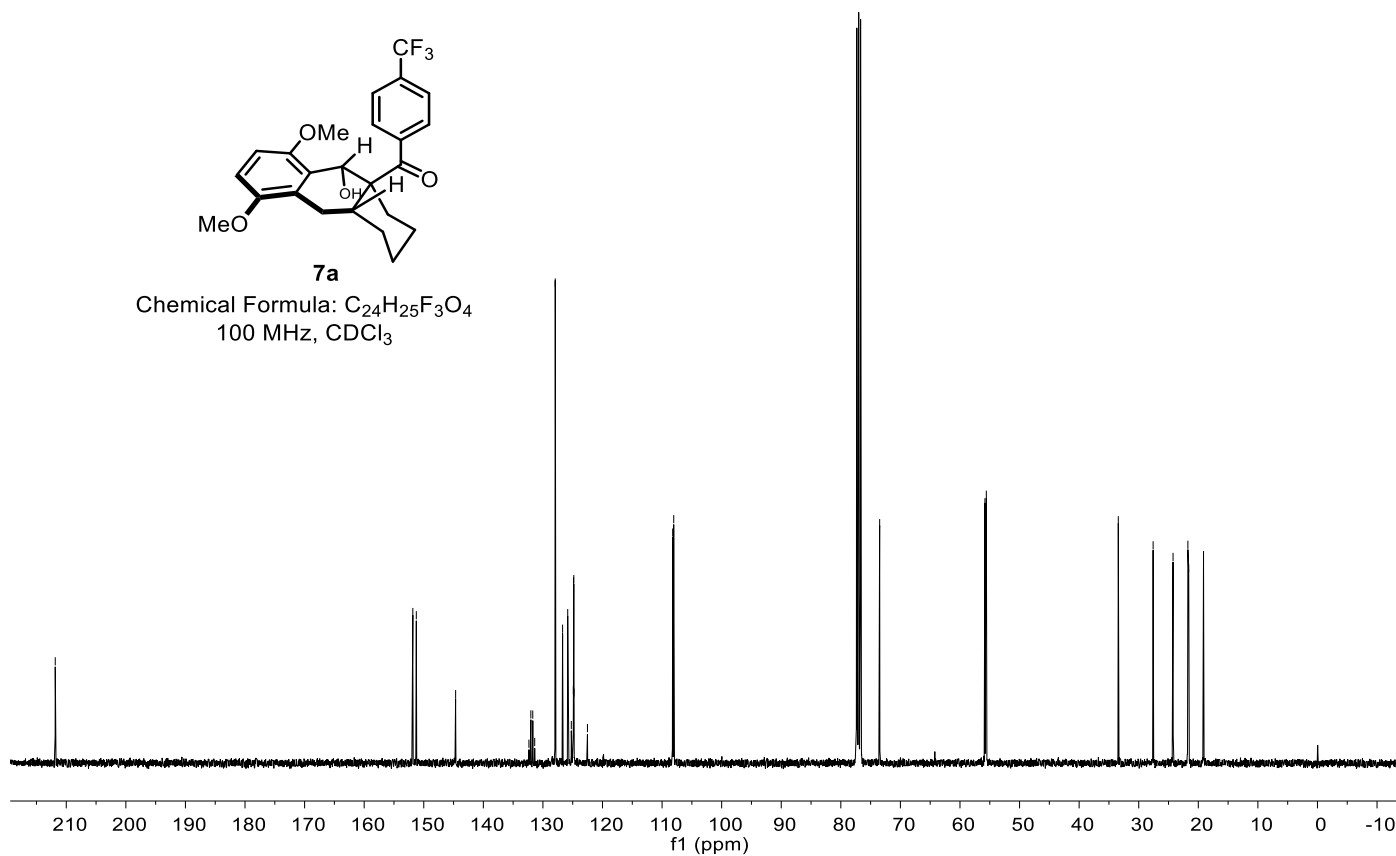
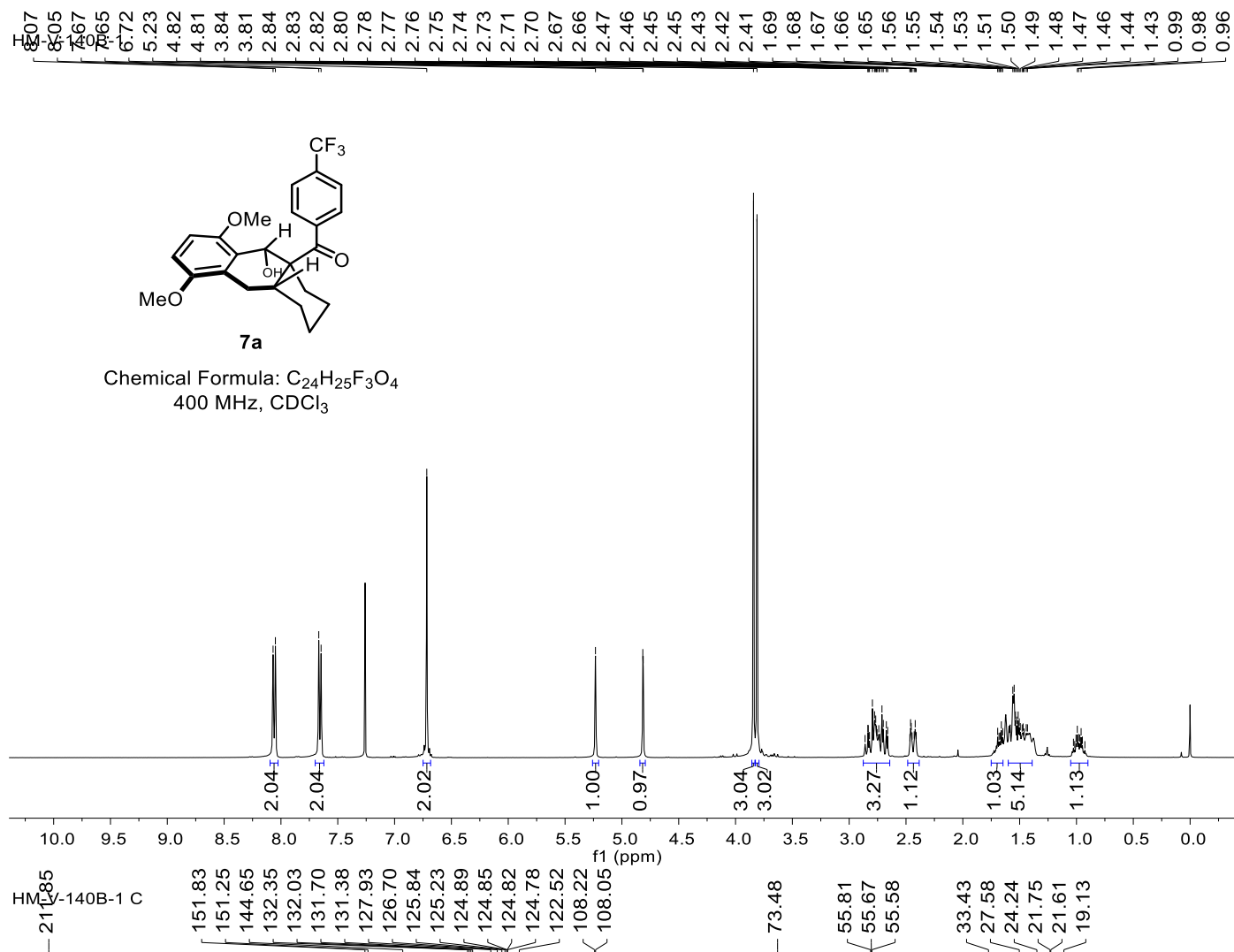
208.59

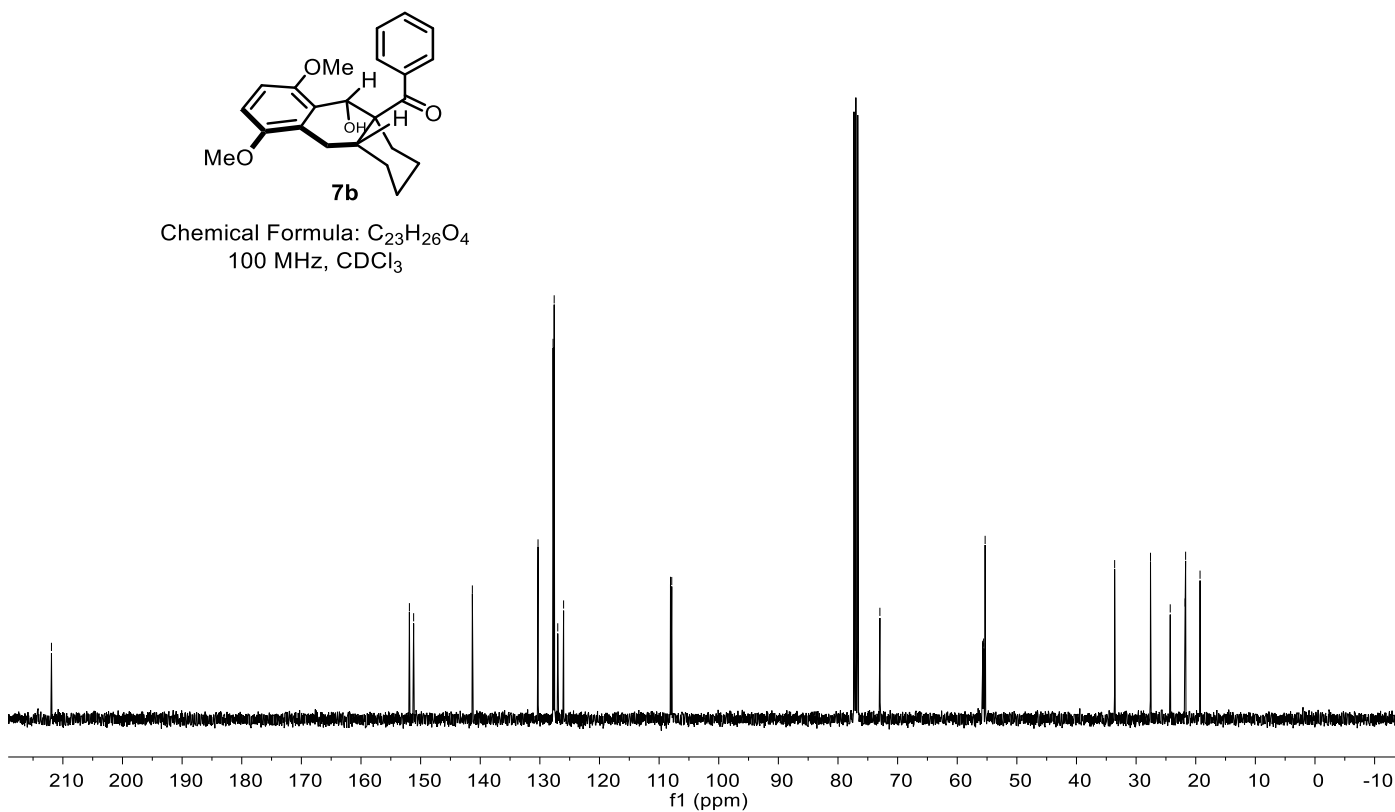
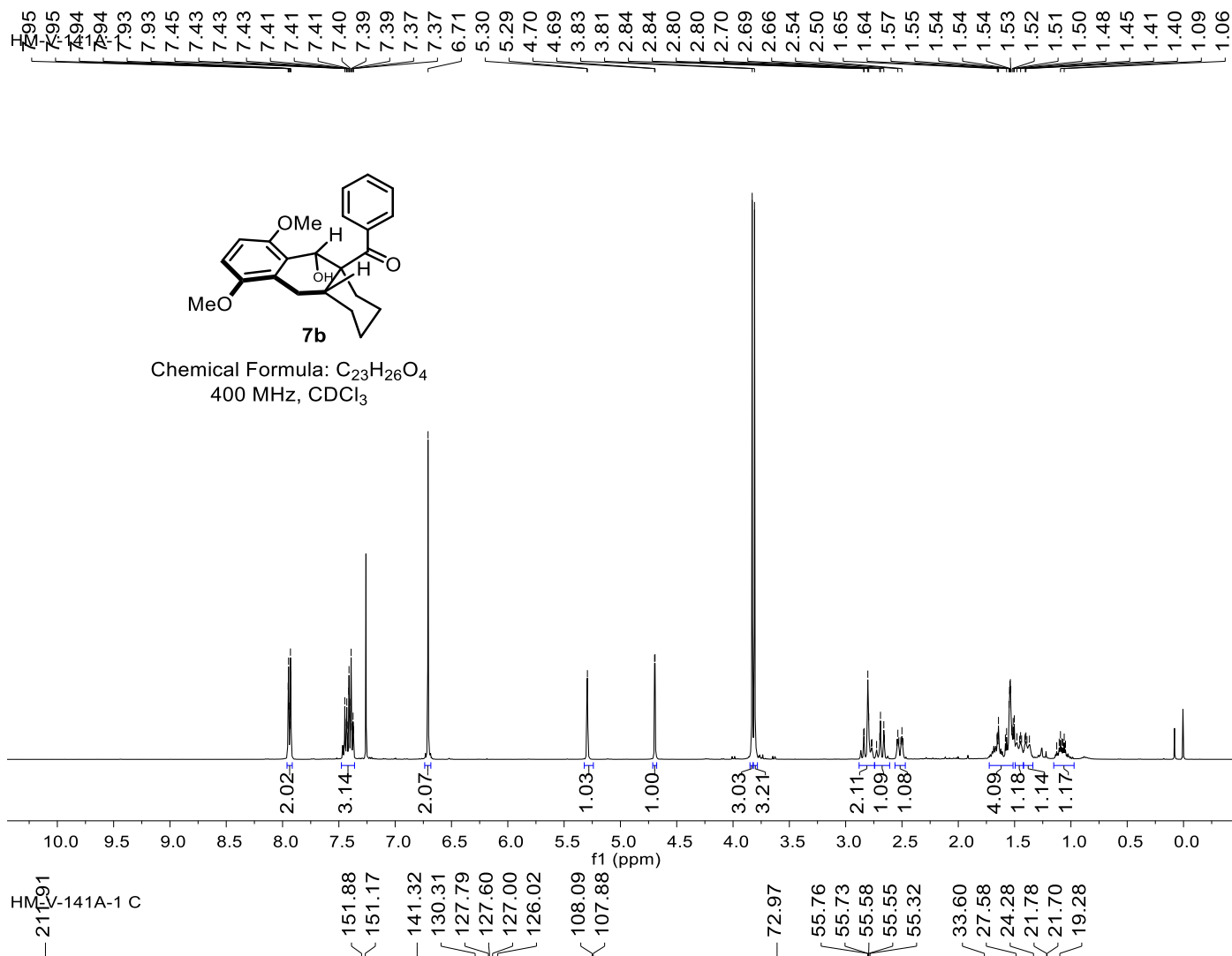
151.49
151.13
144.67
132.13
131.80
127.81
125.70
125.63
125.24
124.97
124.93
124.90
124.86
122.53
108.89
107.18
69.06
55.62
55.57
55.12
27.42
27.17
26.51
24.72
22.80
19.55

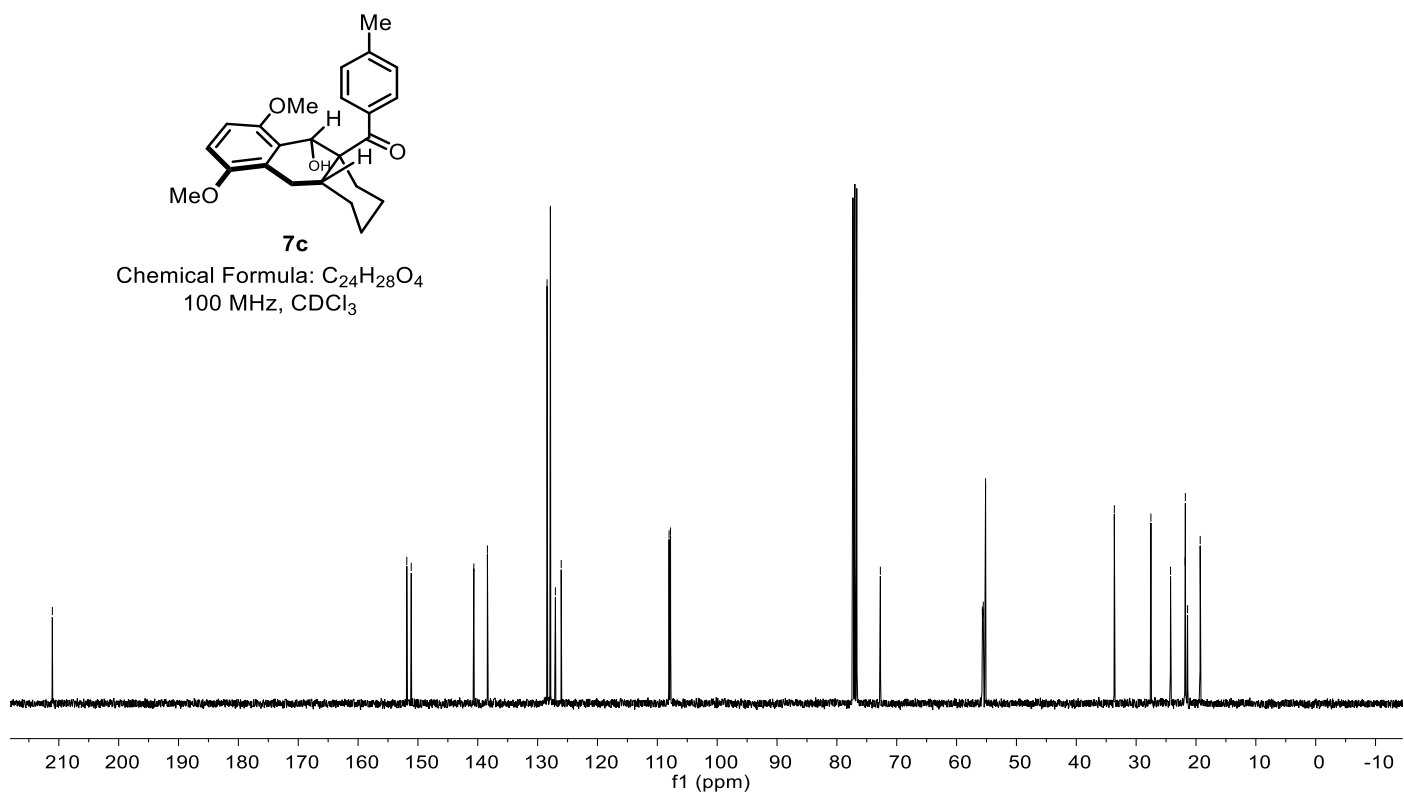
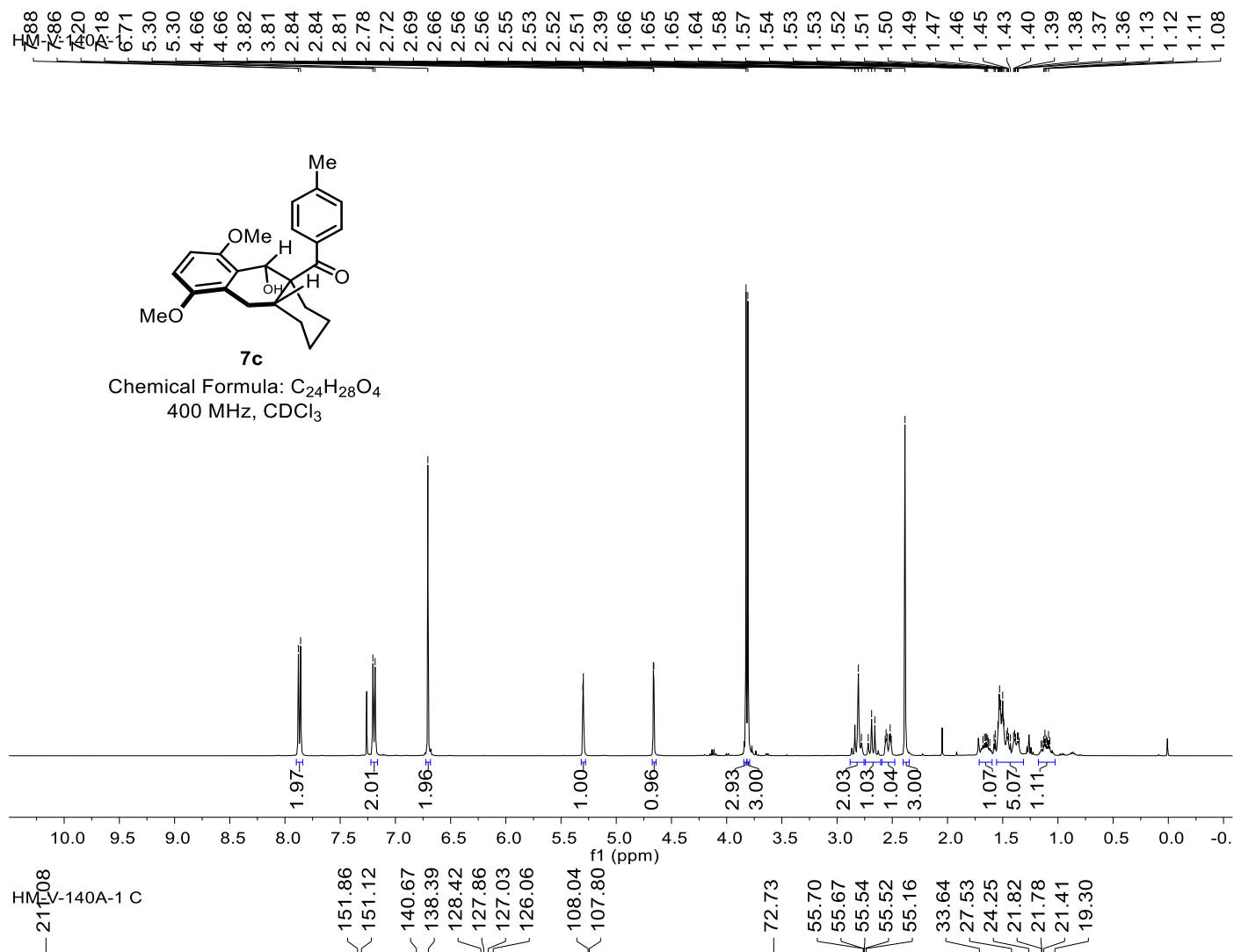


Chemical Formula: $C_{24}H_{25}F_3O_4$
100 MHz, $CDCl_3$

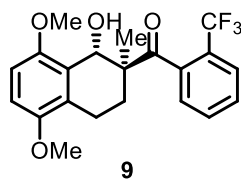




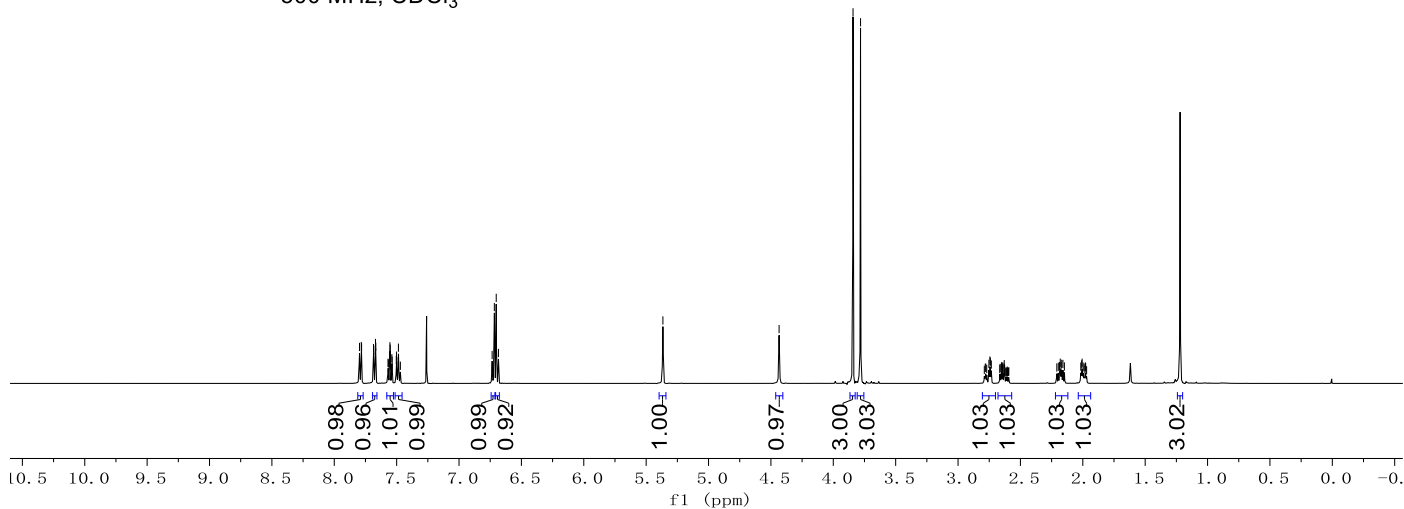




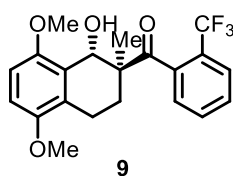
7.80
7.78
7.76
7.69
7.68
7.67
7.57
7.57
7.55
7.55
7.54
7.54
7.50
7.50
7.50
7.49
7.47
6.73
6.72
6.70
6.68
5.37
4.43
3.84
3.78
2.78
2.75
2.74
2.74
2.73
2.65
2.64
2.63
2.63
2.21
2.20
2.19
2.18
2.17
2.17
2.16
2.15
2.02
2.01
2.01
2.00
1.98
1.98
1.22



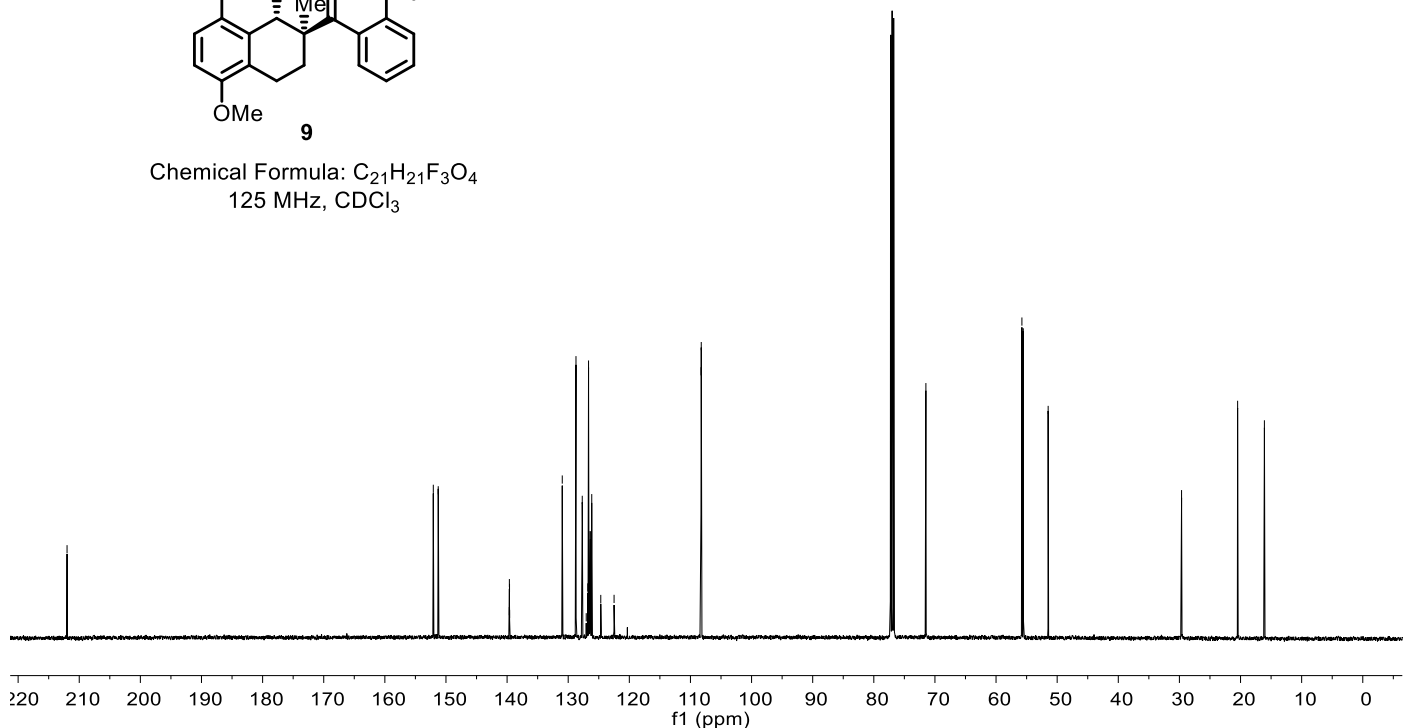
Chemical Formula: C₂₁H₂₁F₃O₄
500 MHz, CDCl₃

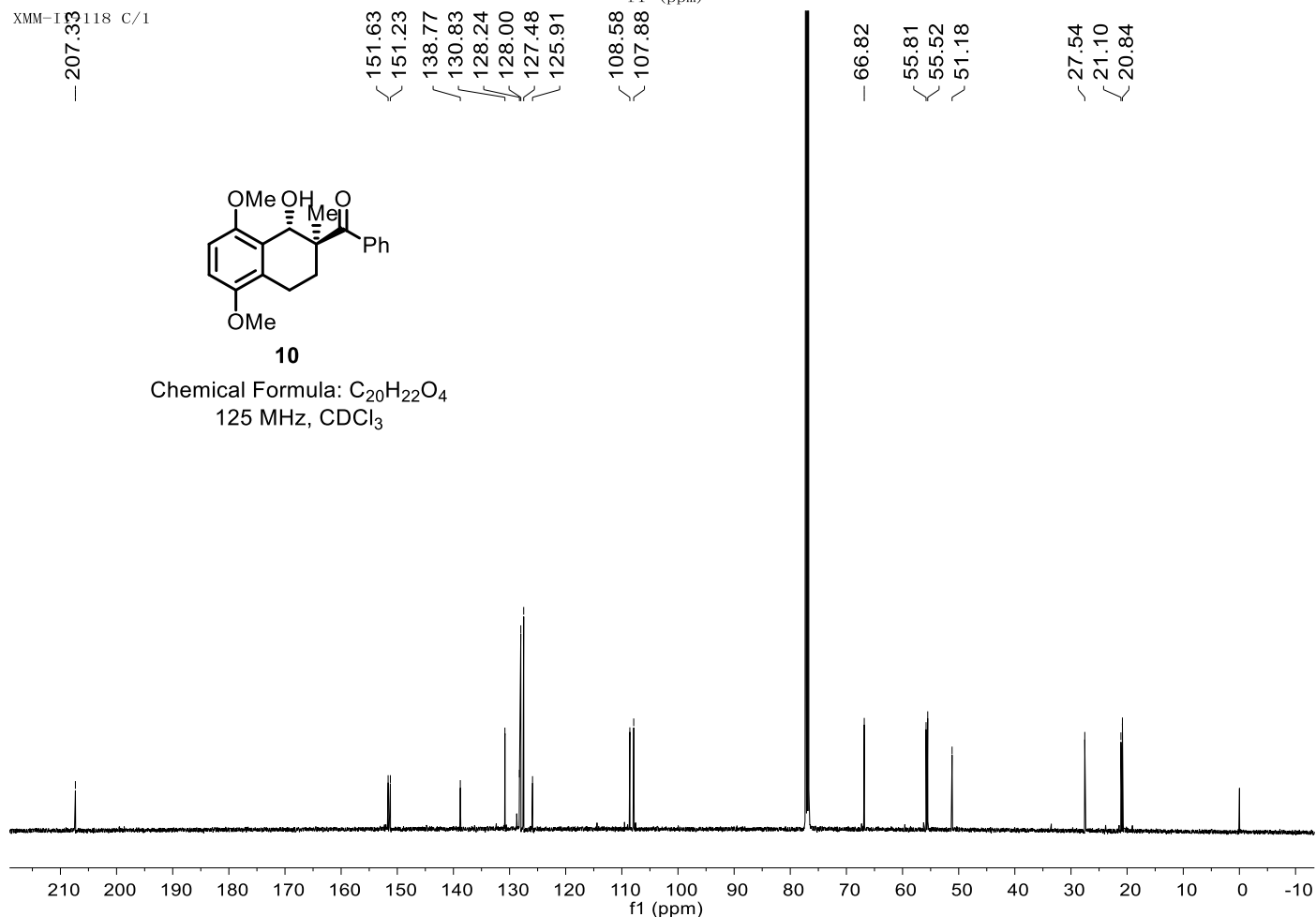
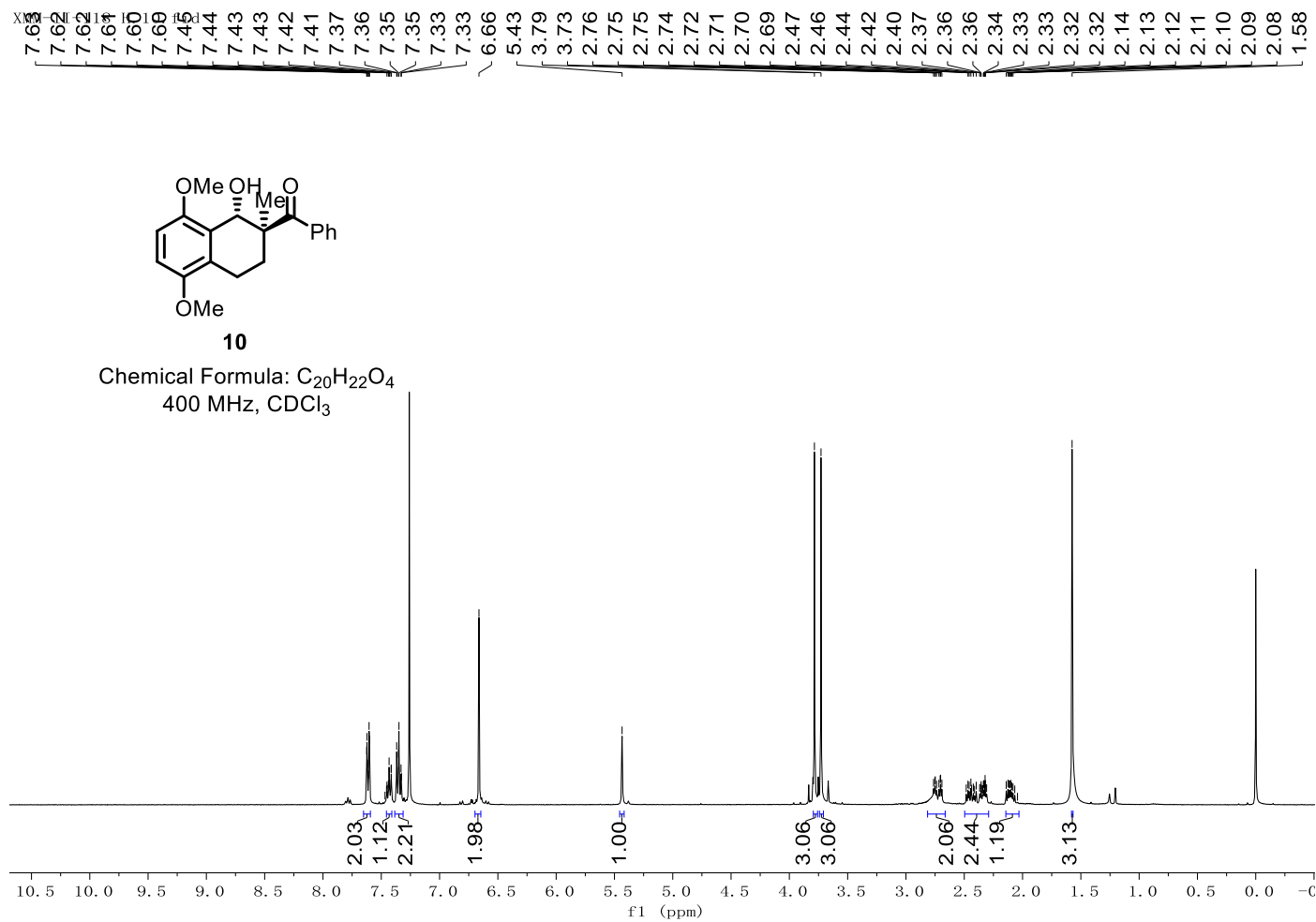


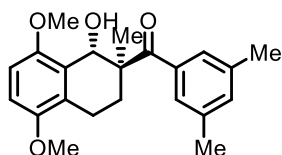
HM-V52B-1
HM-V52B-1
211.99
152.07
151.26
139.64
139.62
139.60
139.59
130.97
128.73
127.70
127.05
126.80
126.67
126.54
126.46
126.43
126.39
126.35
126.15
124.67
122.50
108.27
108.23
71.48
55.77
55.54
51.47
29.65
20.48
16.09



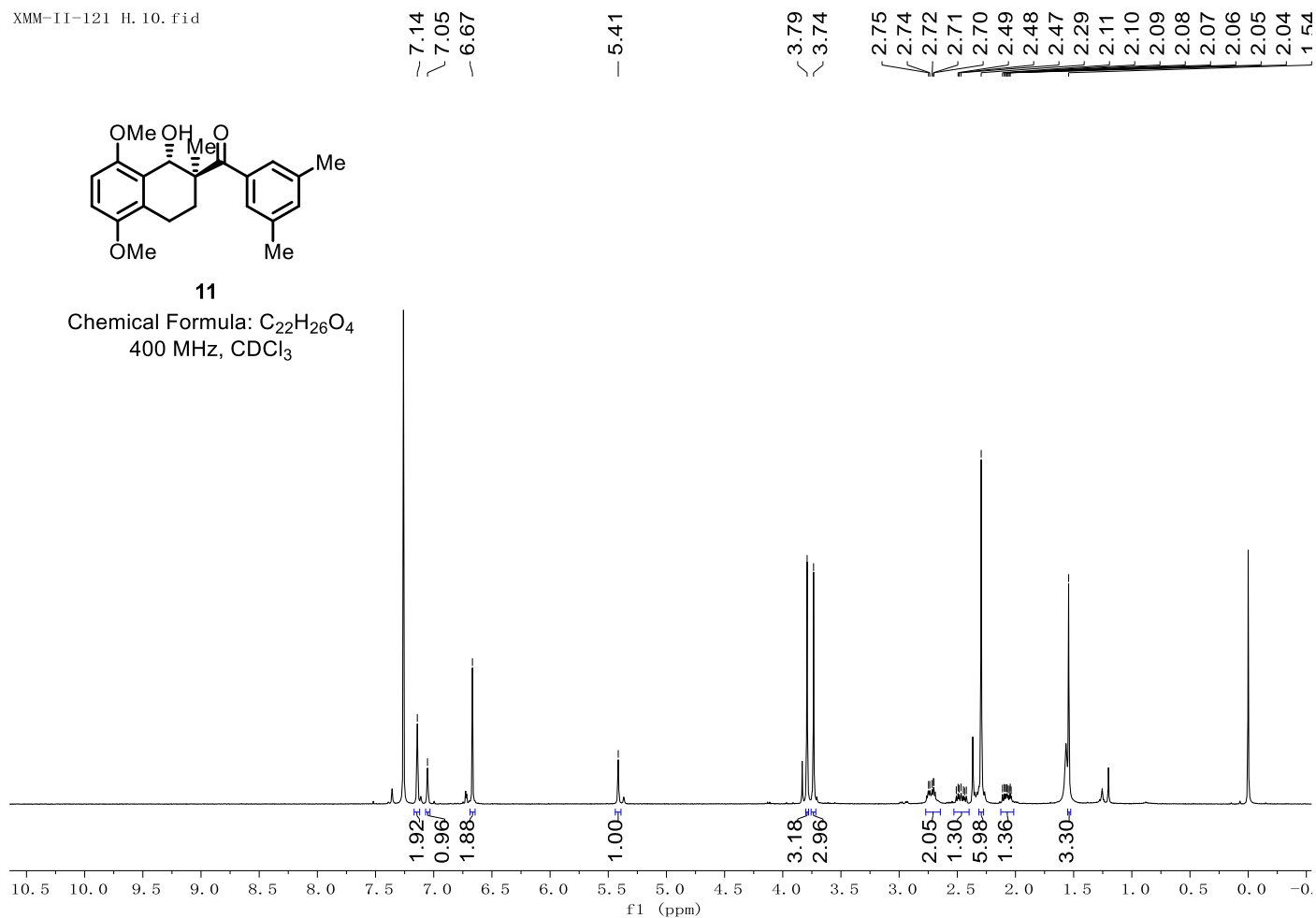
Chemical Formula: C₂₁H₂₁F₃O₄
125 MHz, CDCl₃



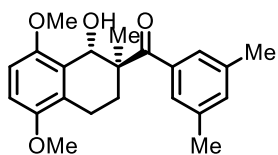


**11**

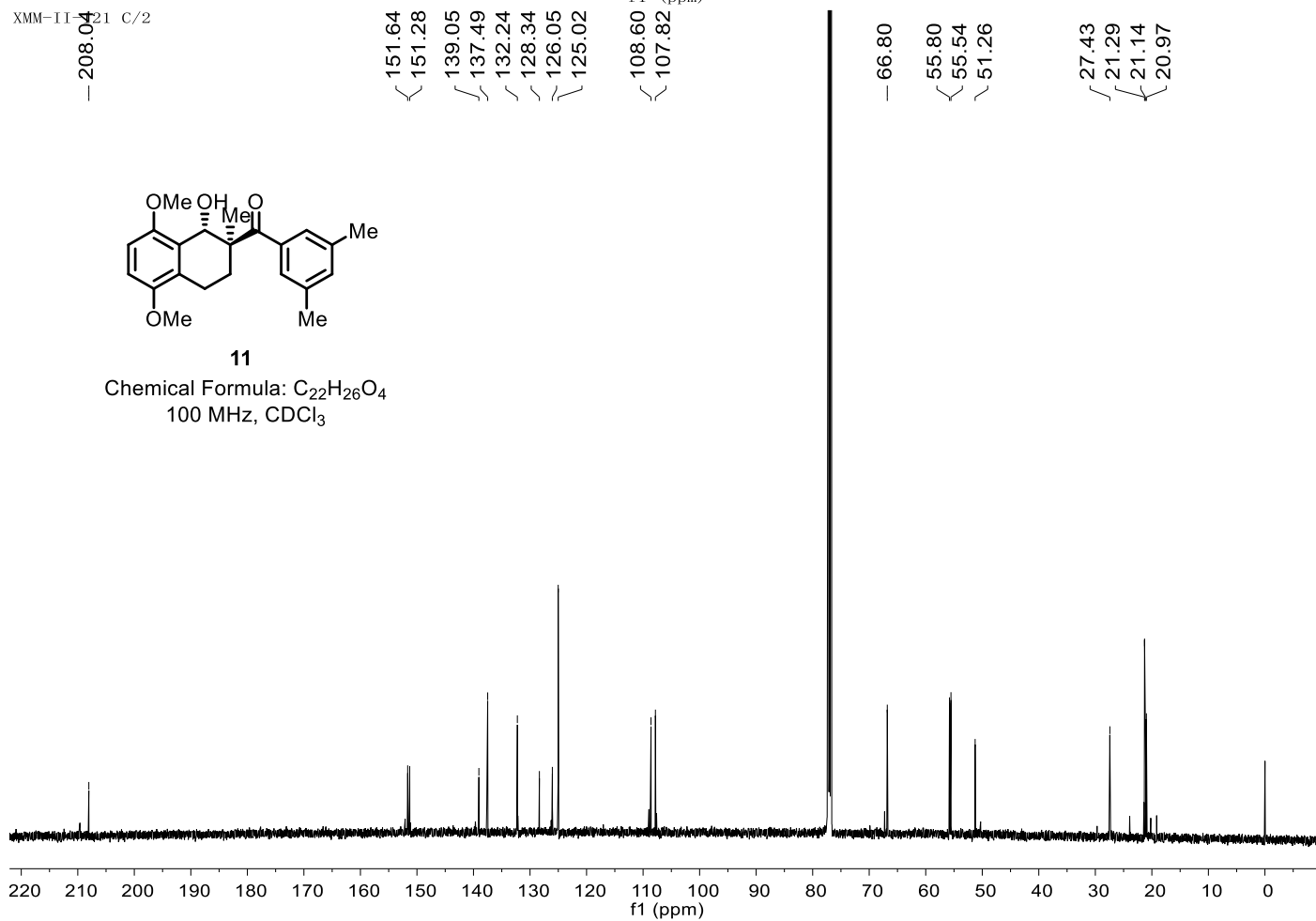
Chemical Formula: C₂₂H₂₆O₄
400 MHz, CDCl₃

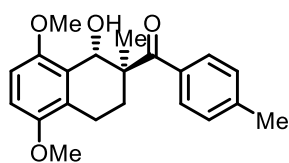


XMM-II-121 C/2

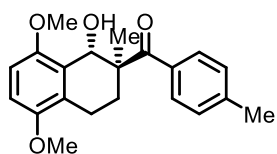
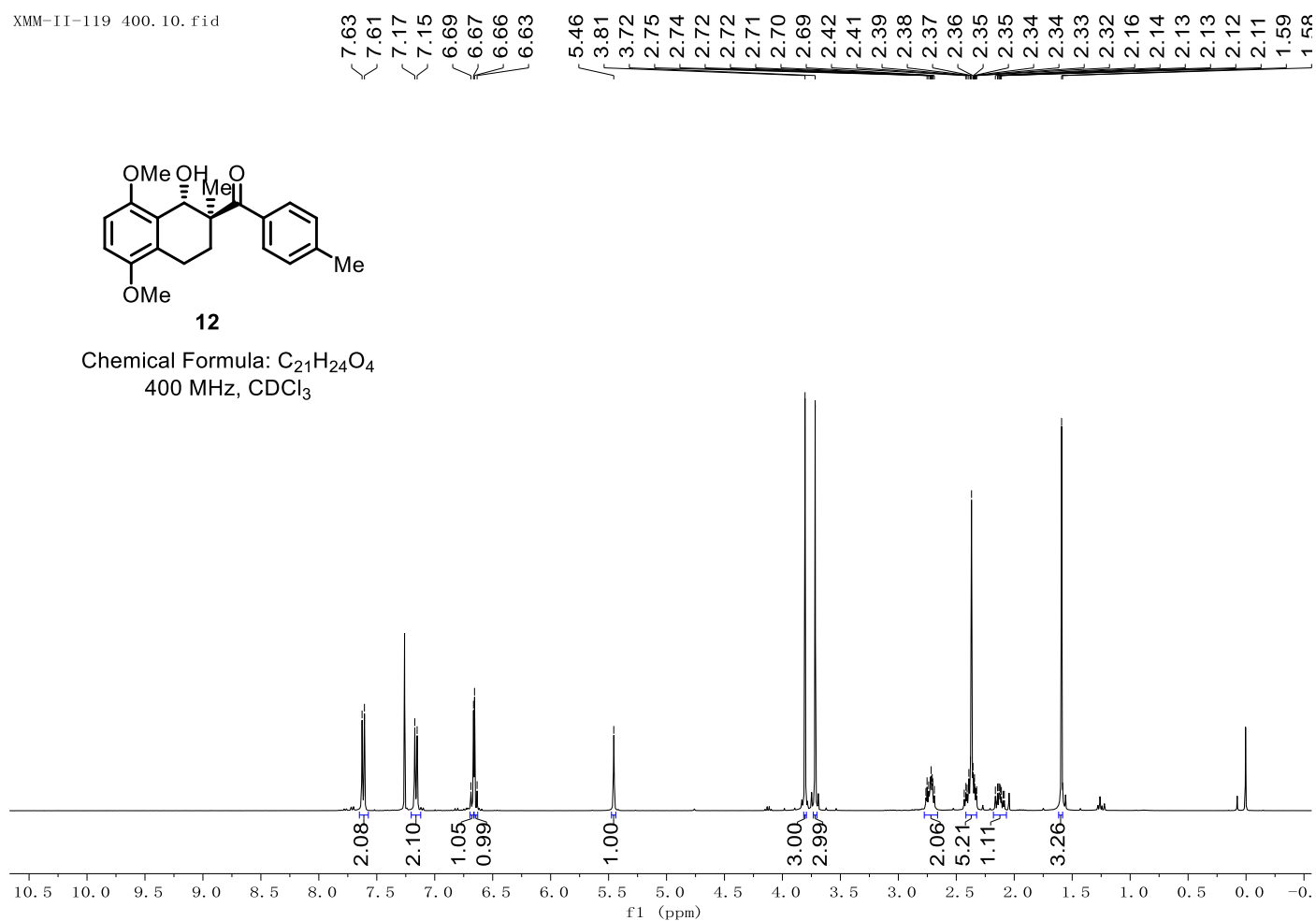
**11**

Chemical Formula: C₂₂H₂₆O₄
100 MHz, CDCl₃

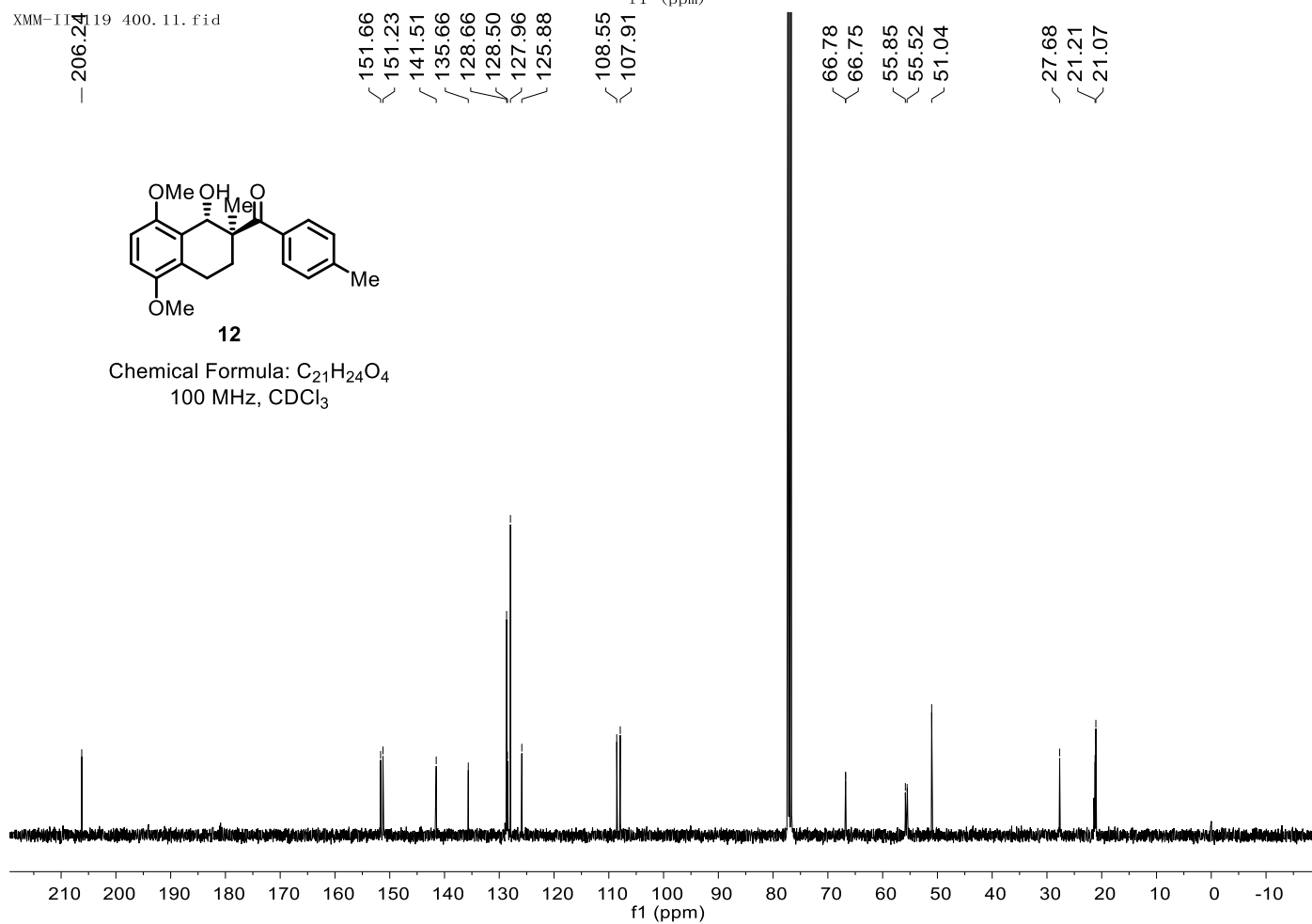


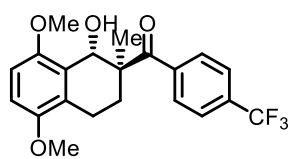
**12**

Chemical Formula: C₂₁H₂₄O₄
400 MHz, CDCl₃

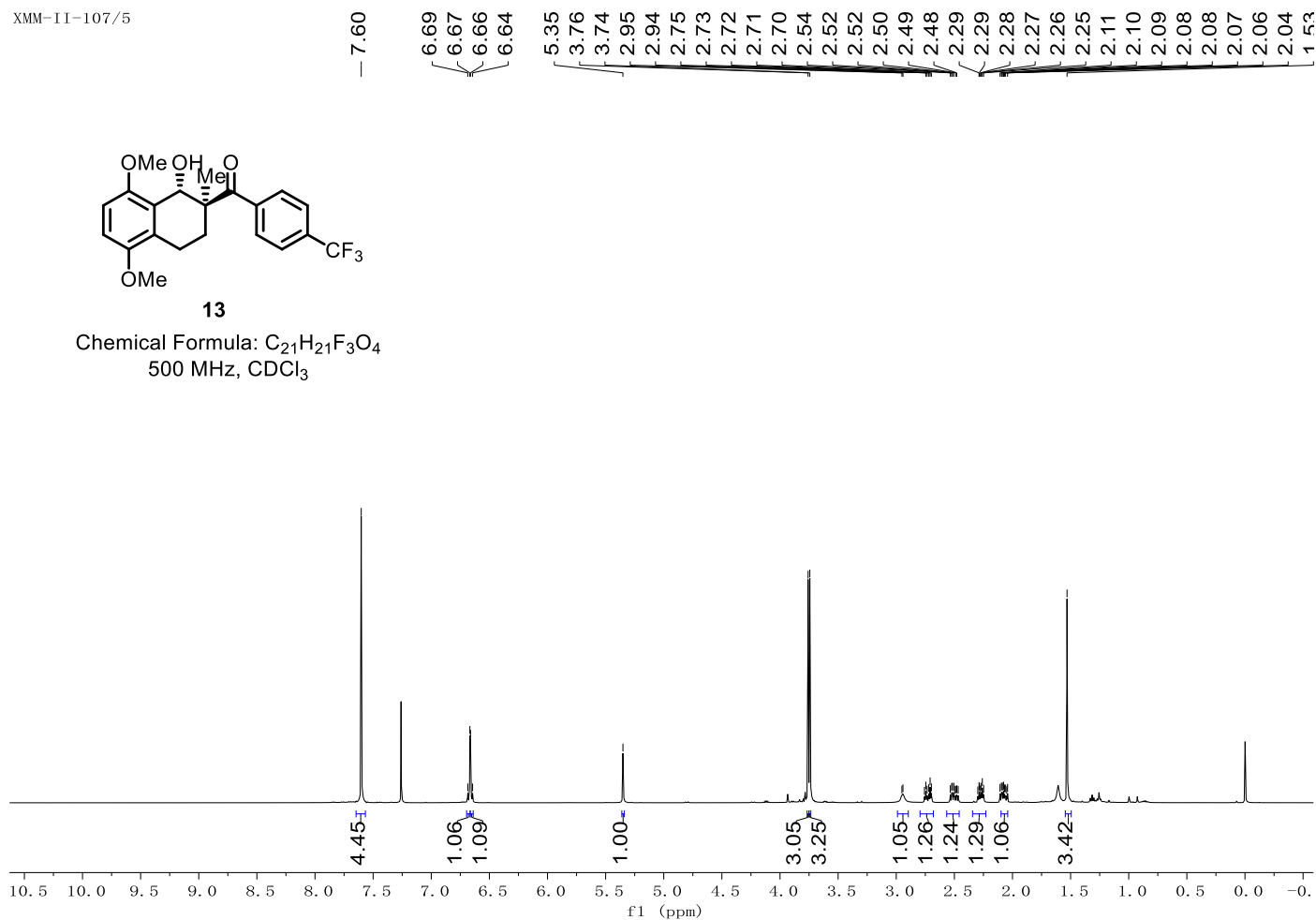
**12**

Chemical Formula: C₂₁H₂₄O₄
100 MHz, CDCl₃

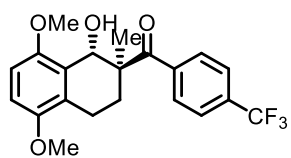


**13**

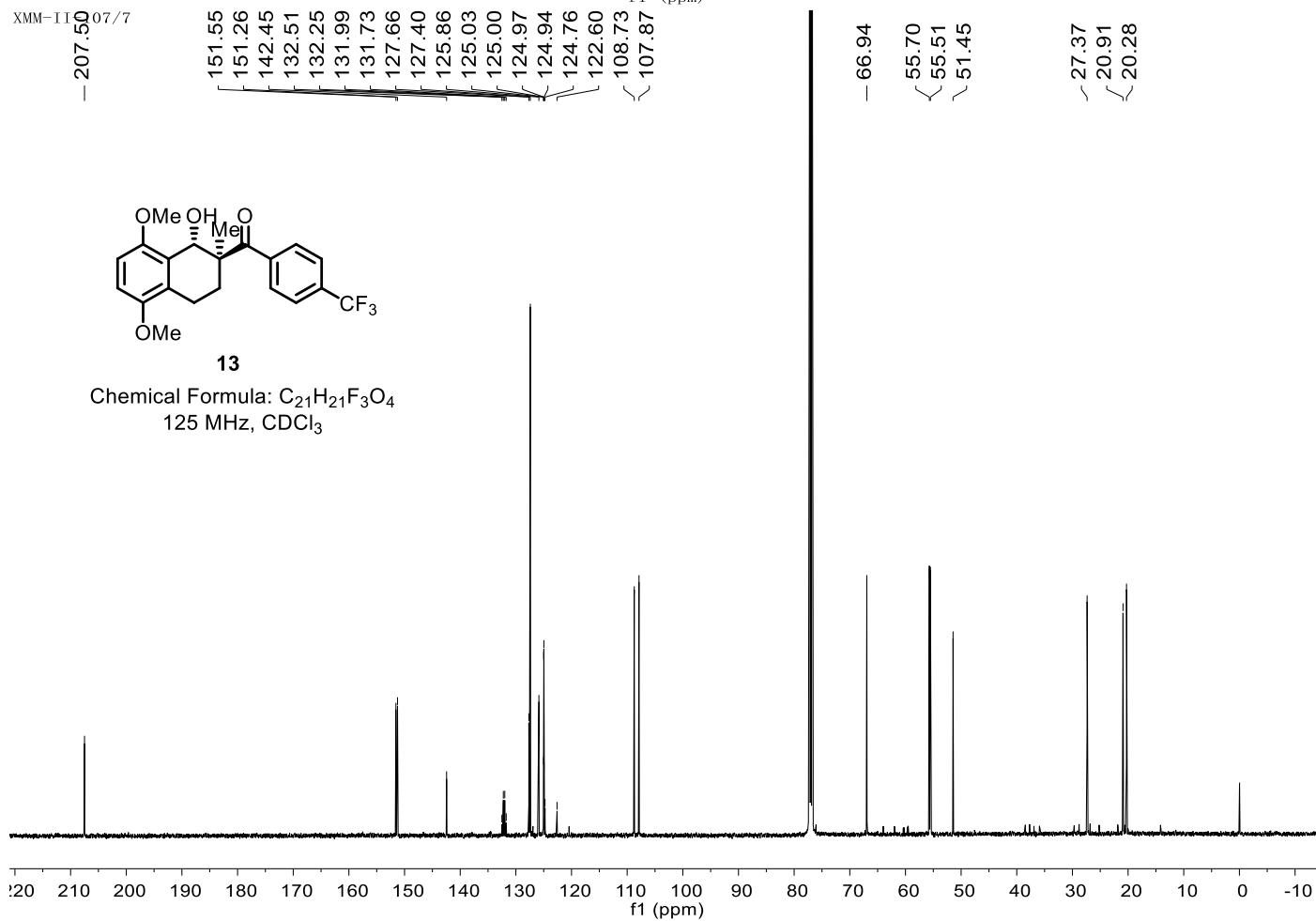
Chemical Formula: $C_{21}H_{21}F_3O_4$
500 MHz, $CDCl_3$



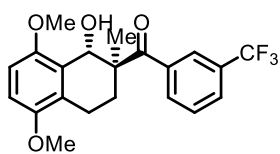
XMM-II-107/7

**13**

Chemical Formula: $C_{21}H_{21}F_3O_4$
125 MHz, $CDCl_3$

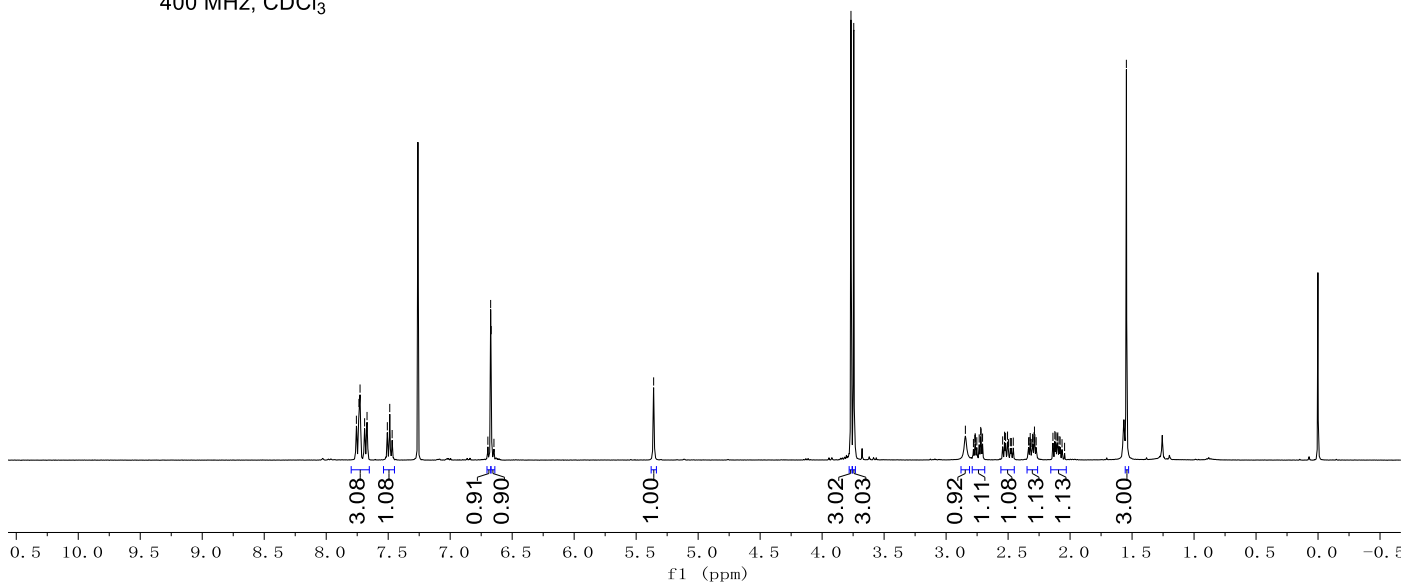


7.76
7.74
7.73
7.69
7.67
7.58
7.49
7.47
6.70
6.67
6.67
6.65
5.36
3.77
3.74
2.84
2.78
2.77
2.77
2.76
2.75
2.73
2.72
2.72
2.71
2.54
2.53
2.52
2.50
2.48
2.47
2.46
2.33
2.32
2.32
2.32
2.31
2.30
2.30
2.29
2.29
2.28
2.27
2.14
2.12
2.11
2.10
2.10
2.09
2.08
1.55



14

Chemical Formula: $C_{21}H_{21}F_3O_4$
400 MHz, $CDCl_3$



XMM-117 500/5

206.75

151.47
151.27

139.64

130.46

128.59

127.66

127.15

125.87

124.12

108.80

107.83

66.84

55.67

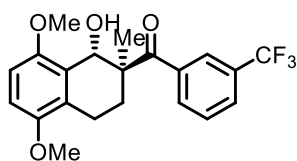
55.51

51.46

27.30

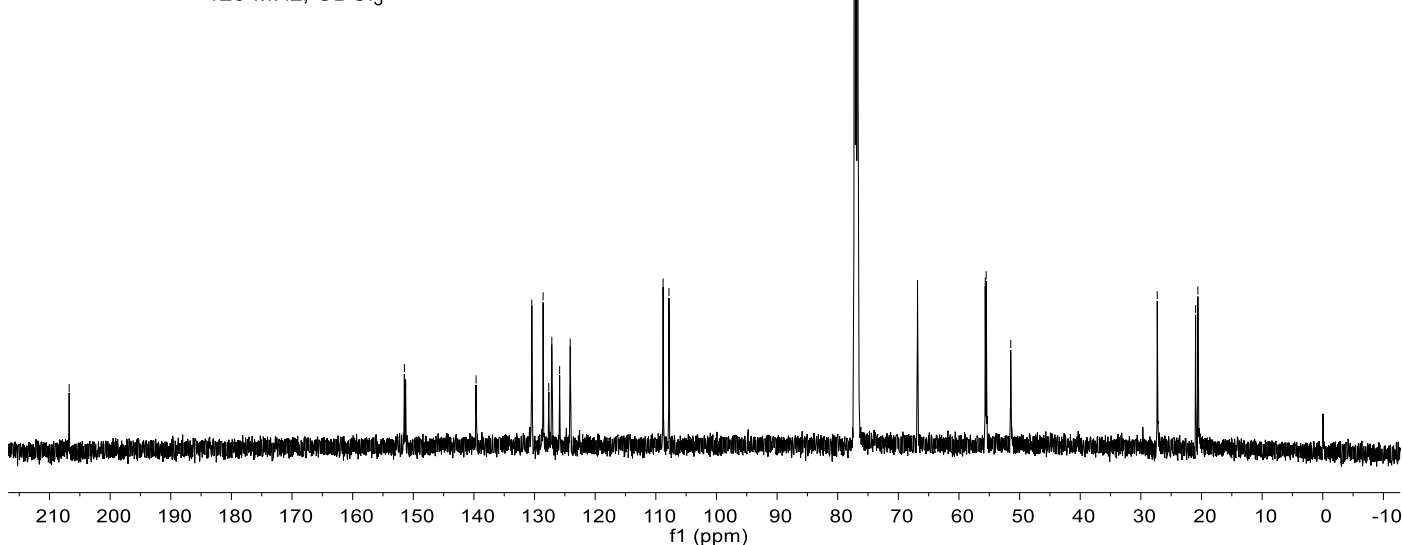
20.97

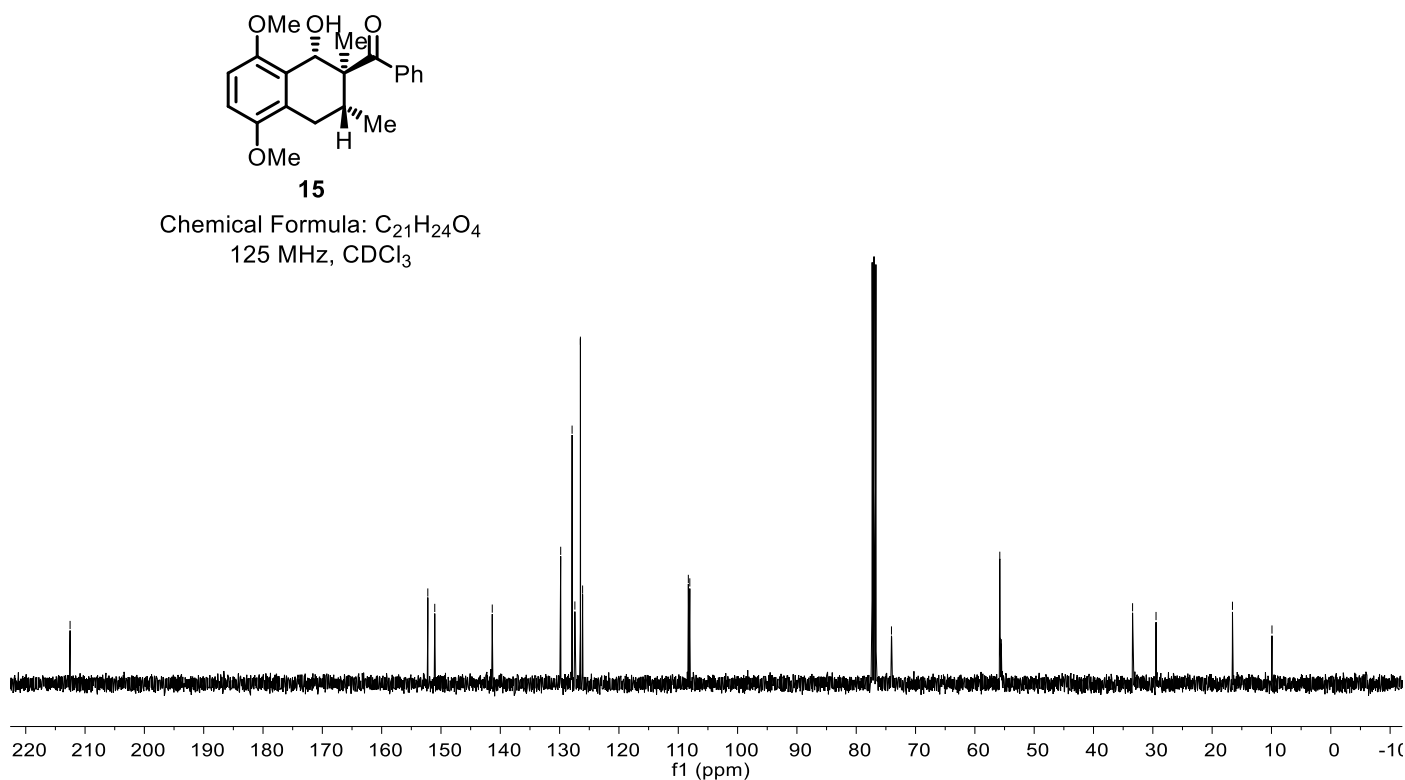
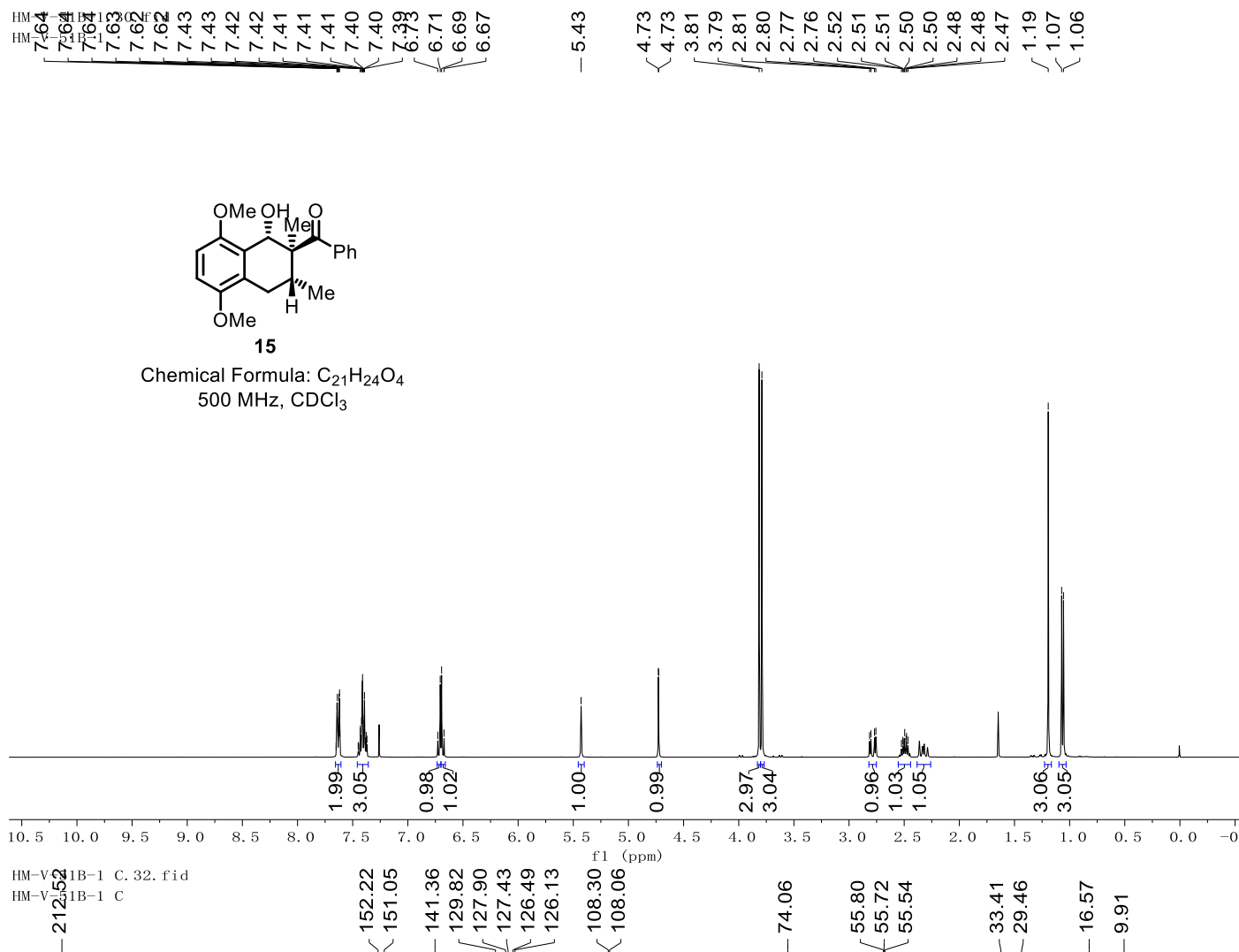
20.60

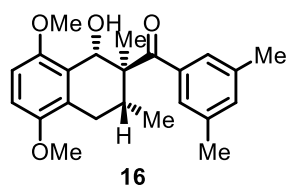


14

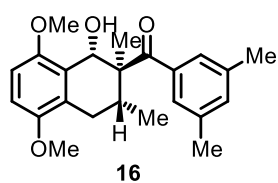
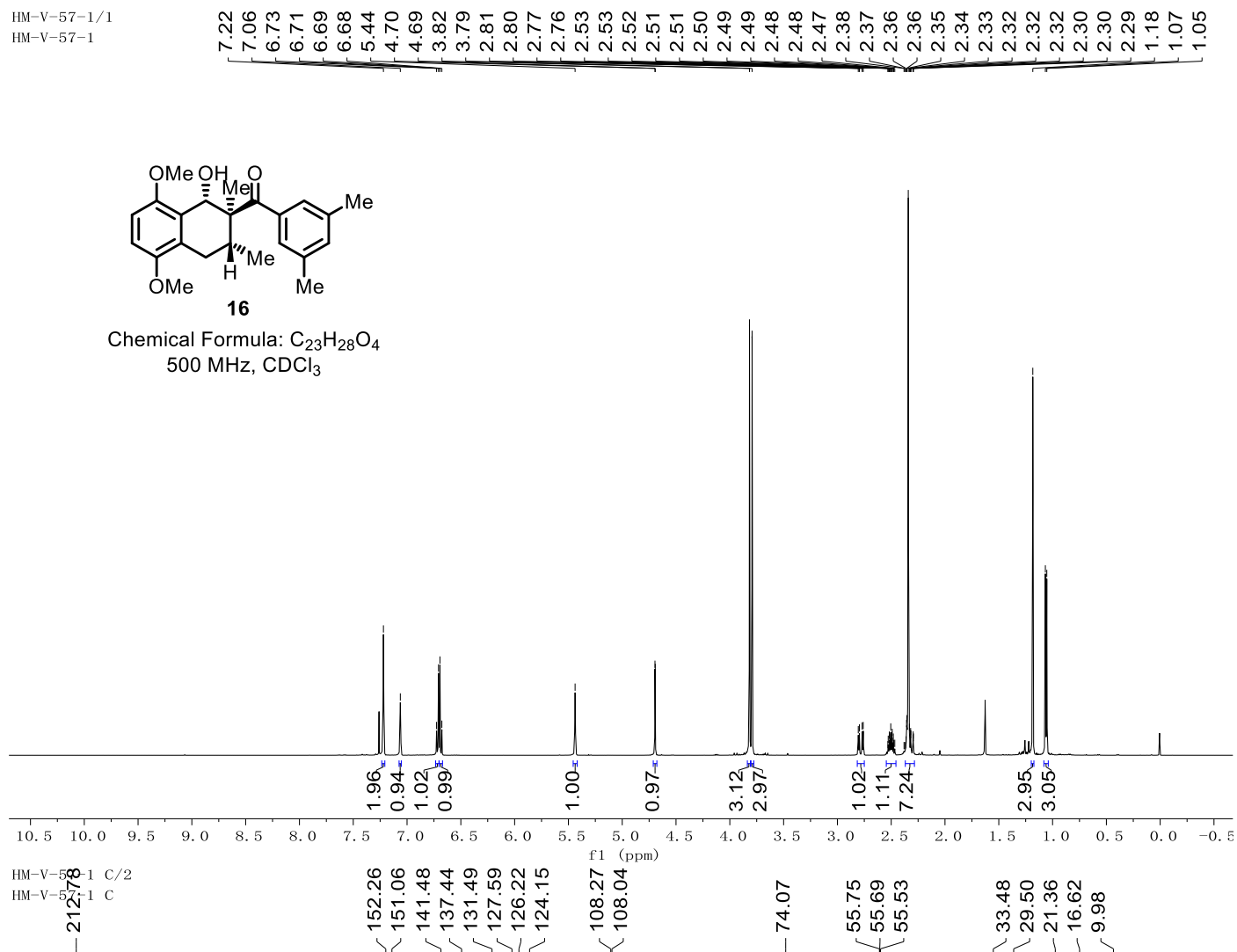
Chemical Formula: $C_{21}H_{21}F_3O_4$
125 MHz, $CDCl_3$



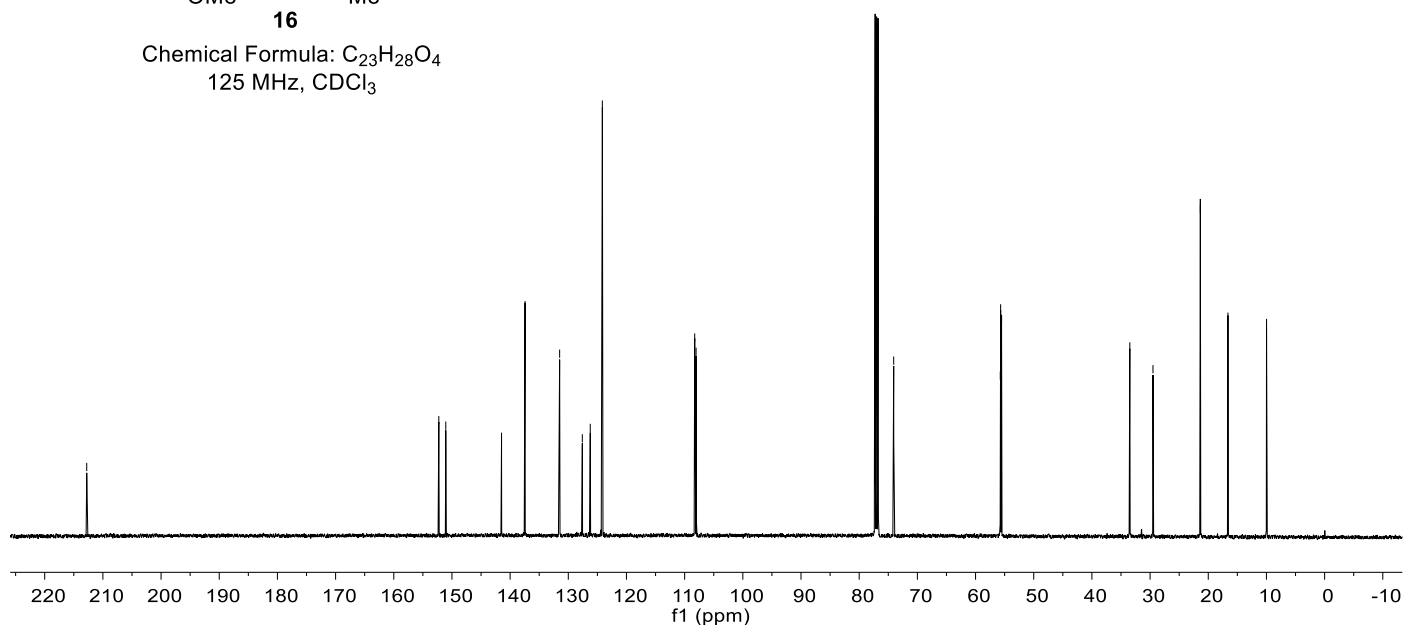




Chemical Formula: $C_{23}H_{28}O_4$
500 MHz, $CDCl_3$



Chemical Formula: $C_{23}H_{28}O_4$
125 MHz, $CDCl_3$

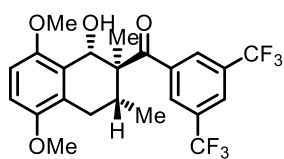


8.30
7.95

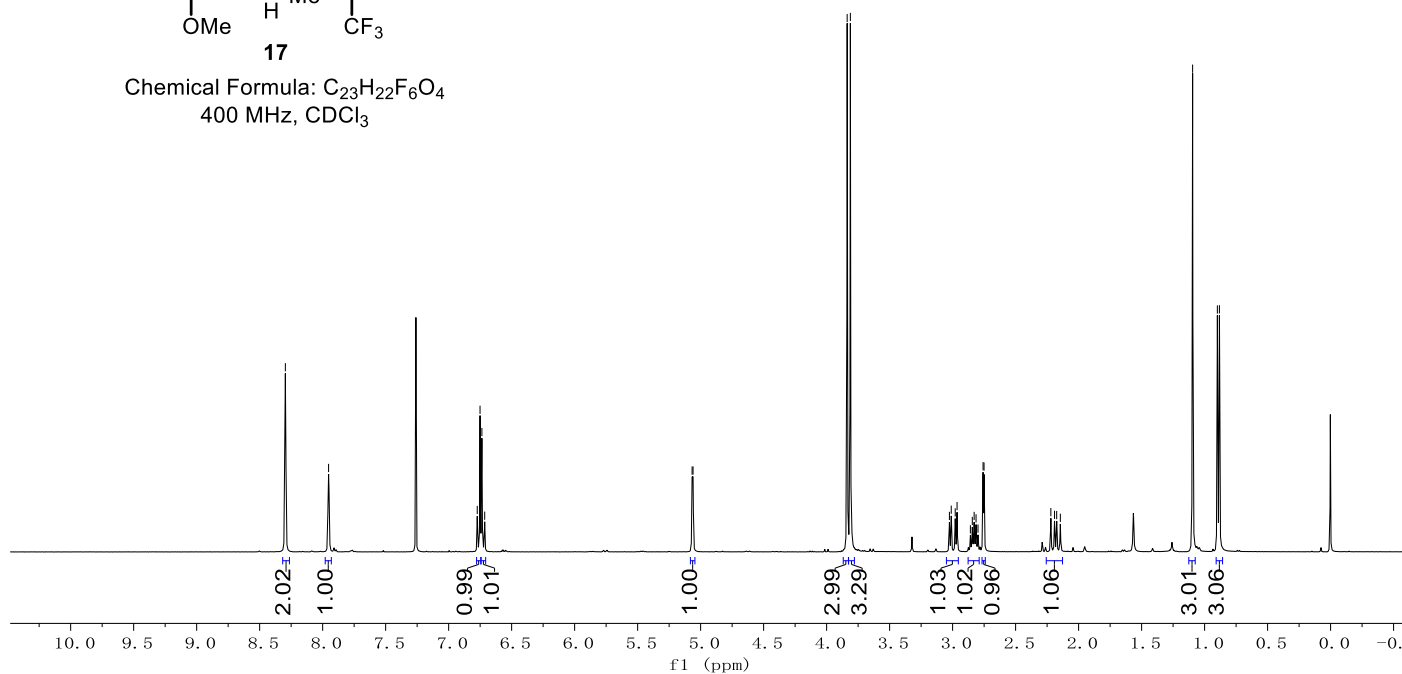
6.77
6.75
6.74
6.71

5.07
5.06

3.84
3.81
3.03
3.01
2.98
2.96
2.86
2.84
2.83
2.81
2.80
2.76
2.75
2.22
2.19
2.17
2.14
1.10
0.90
0.88



Chemical Formula: $C_{23}H_{22}F_6O_4$
400 MHz, $CDCl_3$



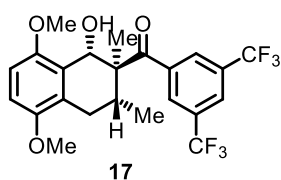
xmm-II-110-C 400.12.fid

206.70

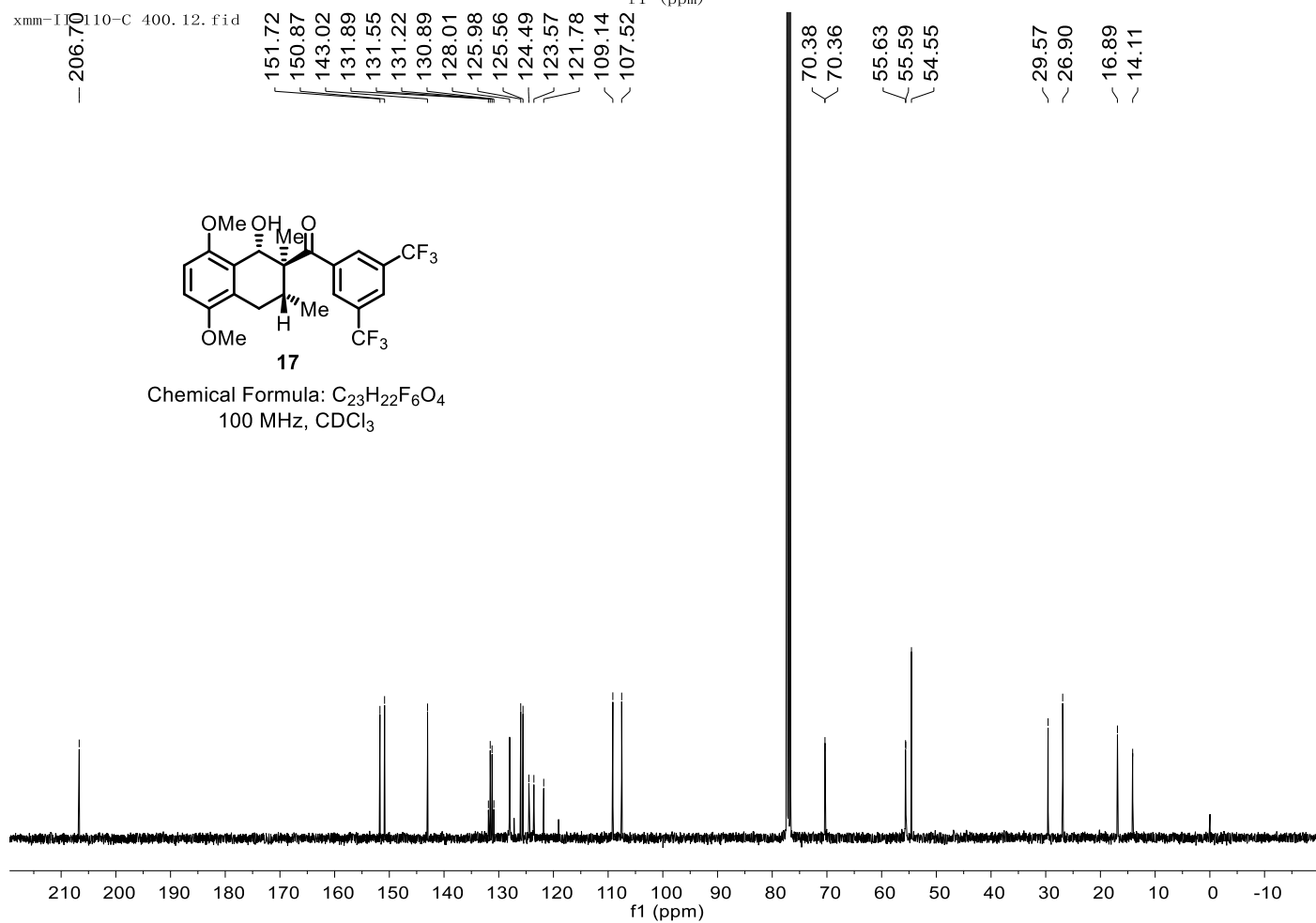
151.72
150.87
143.02
131.89
131.55
131.22
130.89
128.01
125.98
125.56
124.49
123.57
121.78
109.14
107.52

70.38
70.36
55.63
55.59
54.55

29.57
26.90
16.89
14.11



Chemical Formula: $C_{23}H_{22}F_6O_4$
100 MHz, $CDCl_3$



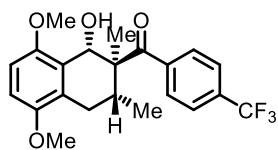
XMM-II-115-HC 400.10.fid

7.72
7.70
7.67
7.65
6.74
6.72
6.70
6.68

5.34

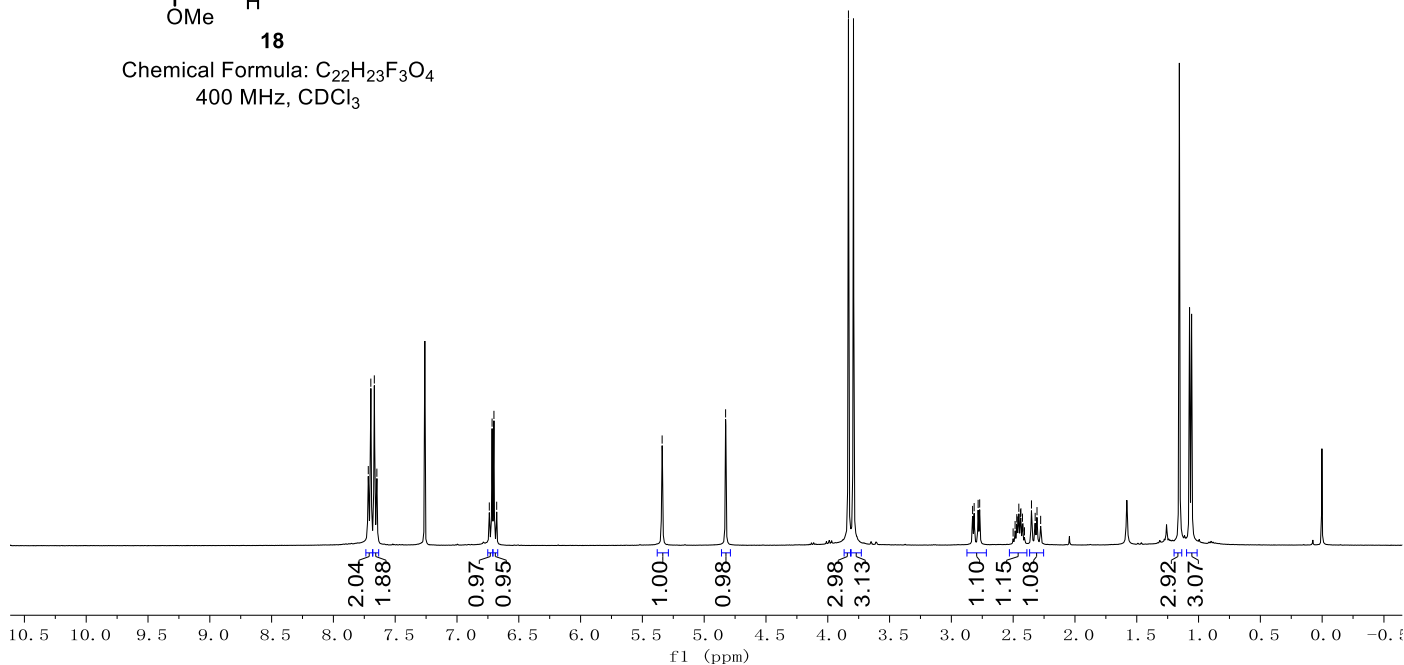
4.83

3.83
3.79
2.83
2.82
2.78
2.77
2.50
2.48
2.47
2.47
2.45
2.44
2.44
2.42
2.42
2.41
2.35
2.32
2.31
2.28



18

Chemical Formula: C₂₂H₂₃F₃O₄
400 MHz, CDCl₃



XMM-II-115-HC 400.11.fid

212.33

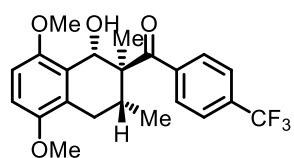
152.23
151.15
144.92
131.63
131.30
127.10
126.65
126.00
124.99
124.96
122.50
108.50
108.24

74.34

55.98
55.82
55.58

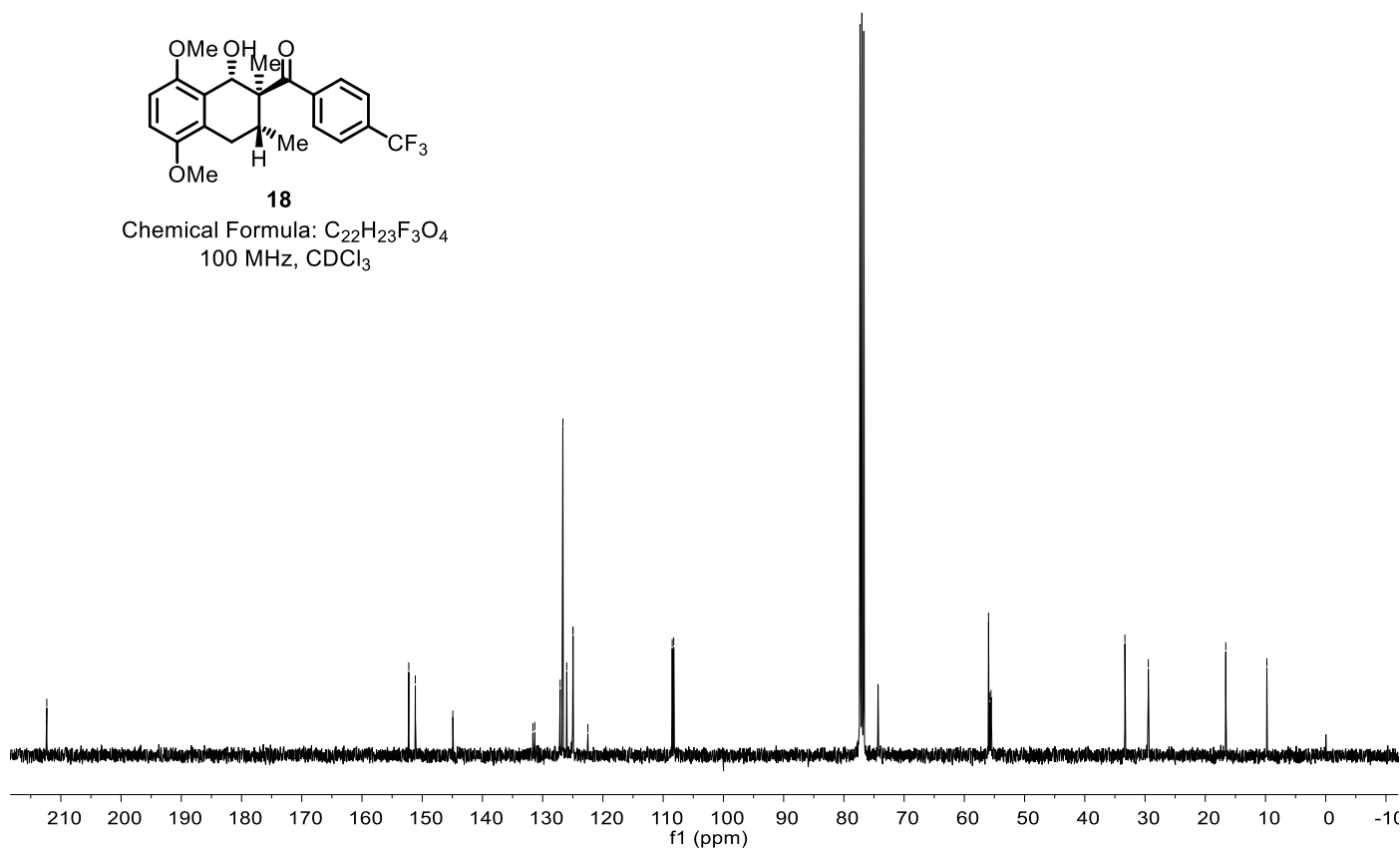
33.34
29.46

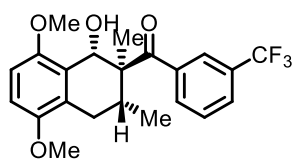
16.60
9.77



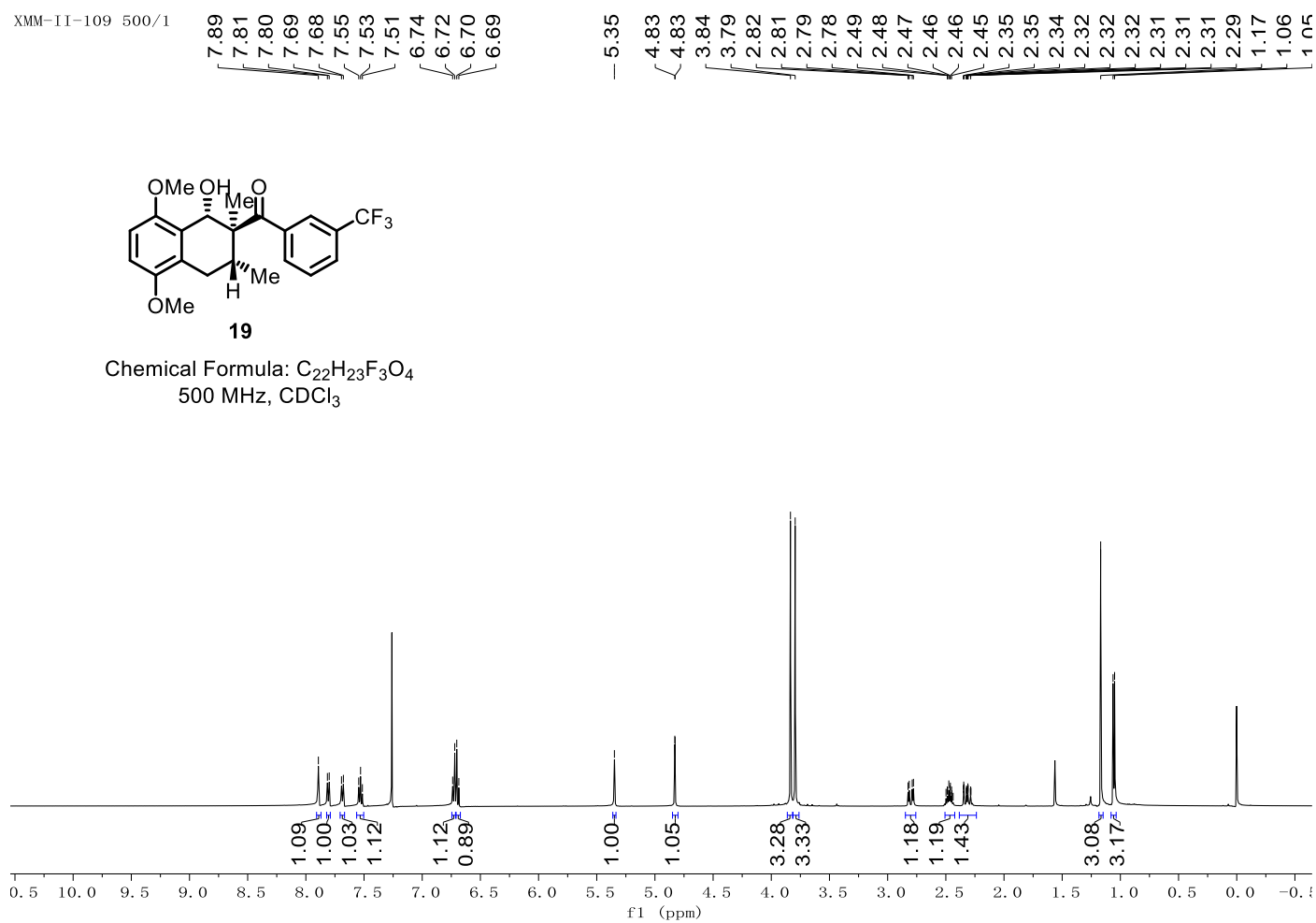
18

Chemical Formula: C₂₂H₂₃F₃O₄
100 MHz, CDCl₃

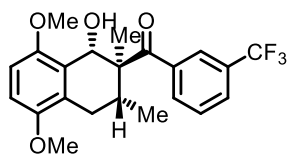


**19**

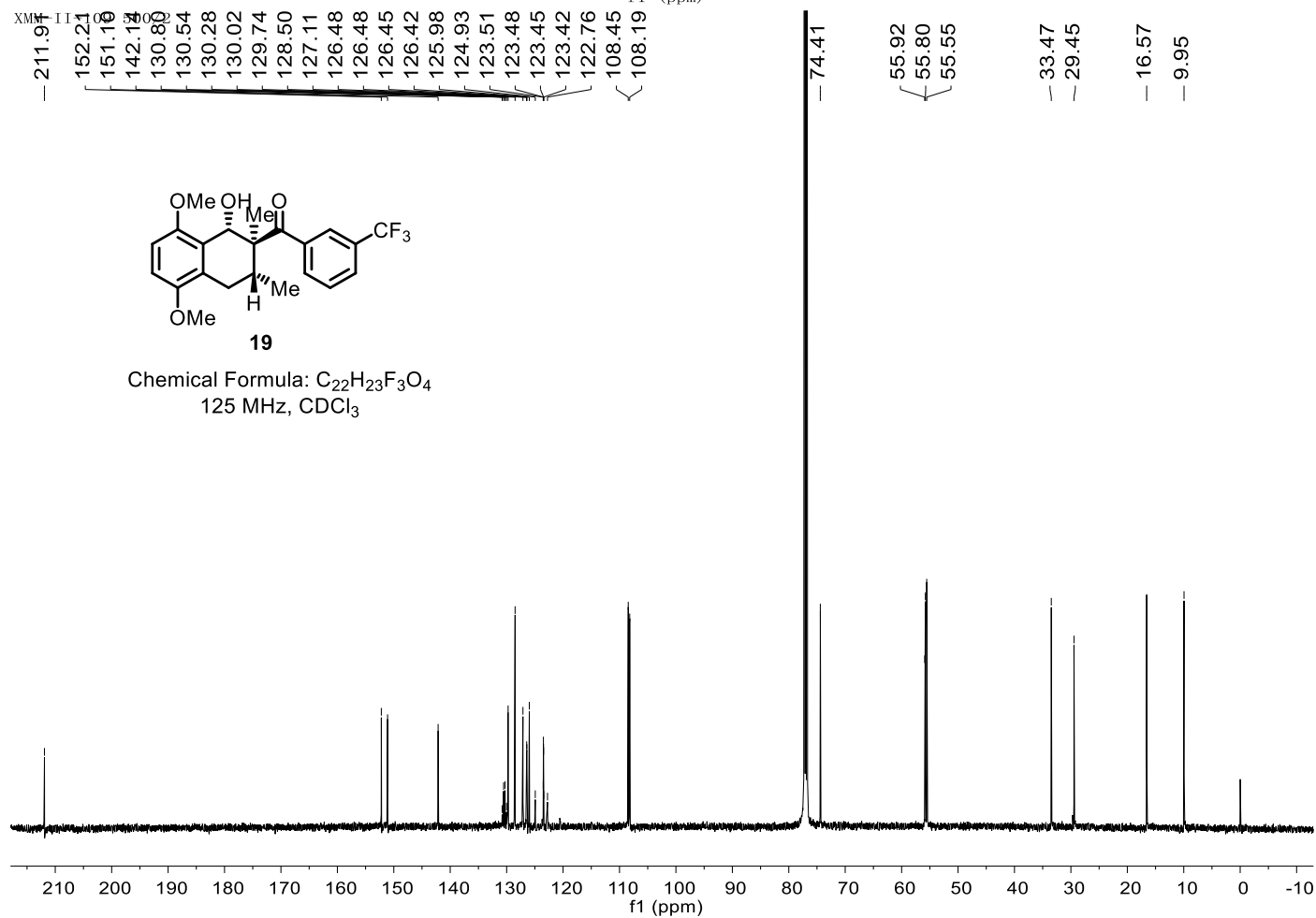
Chemical Formula: $C_{22}H_{23}F_3O_4$
500 MHz, $CDCl_3$

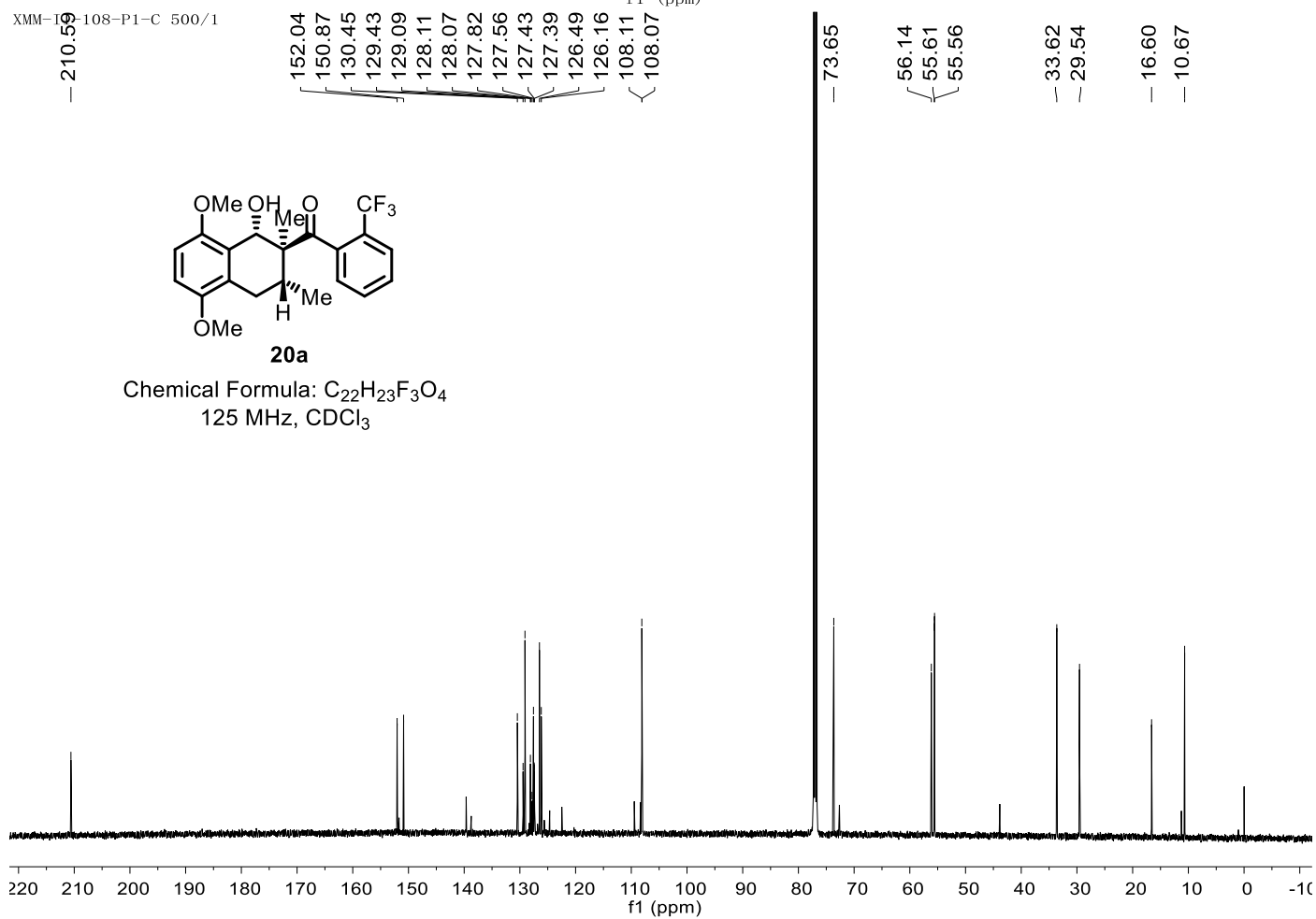
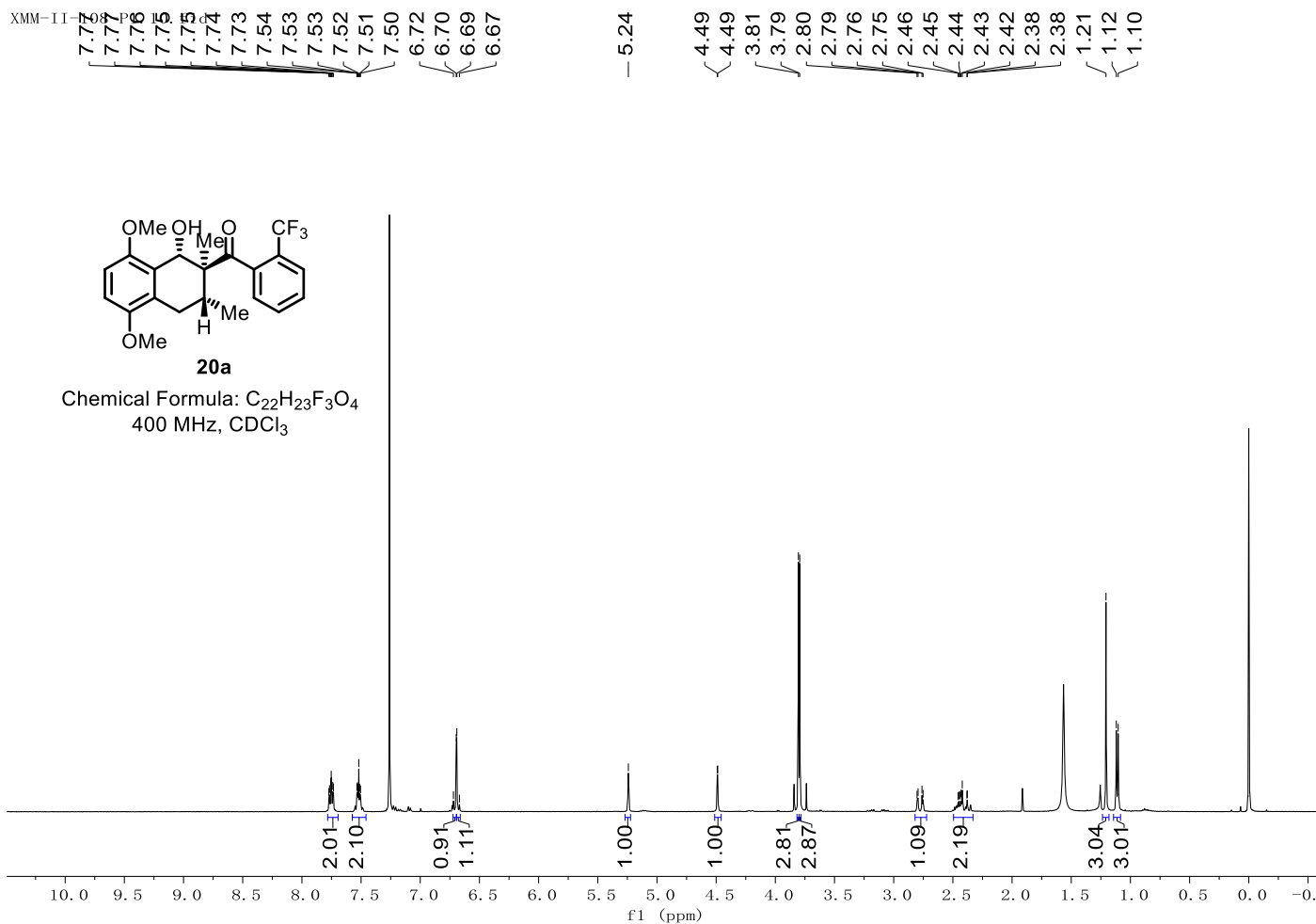


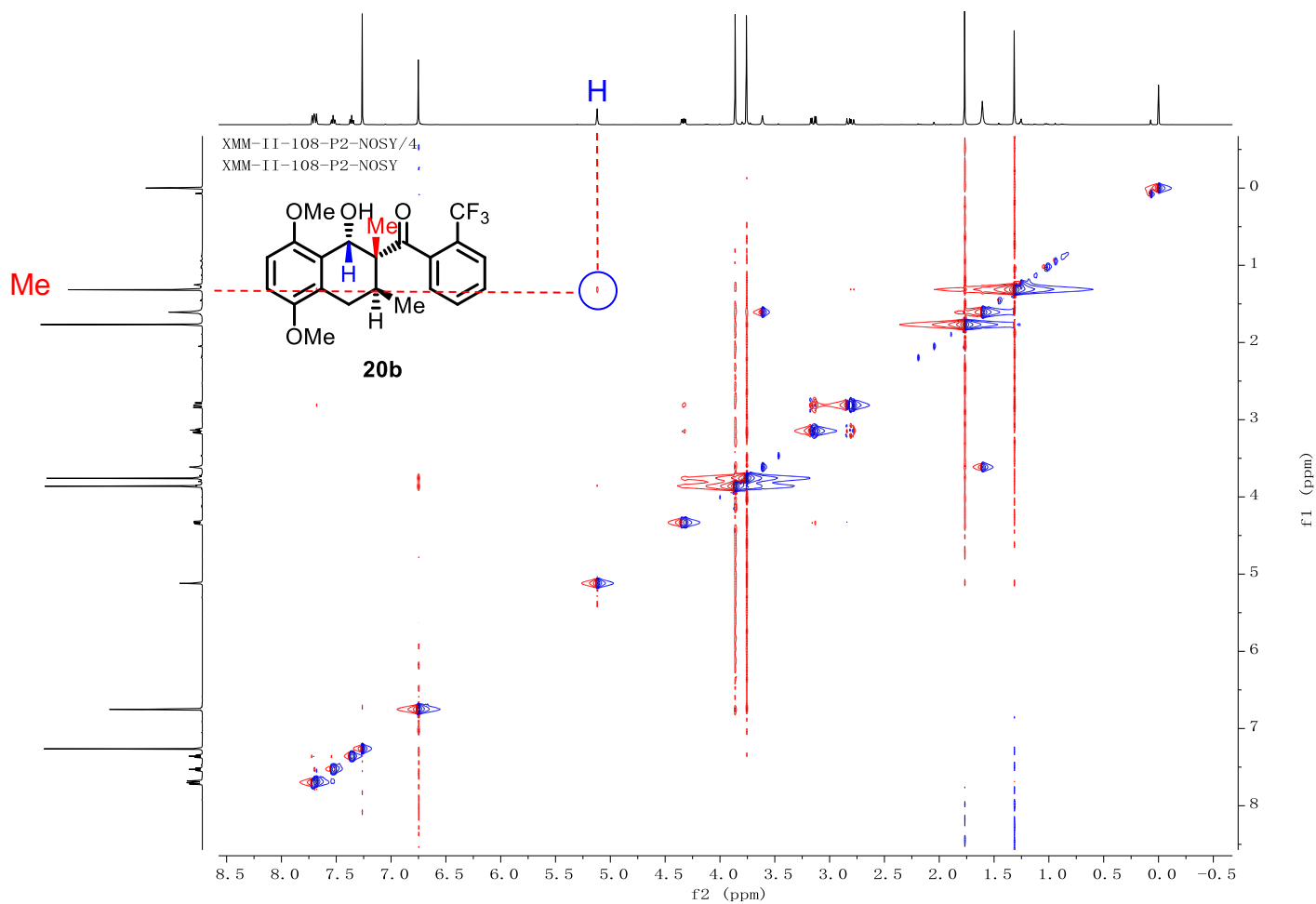
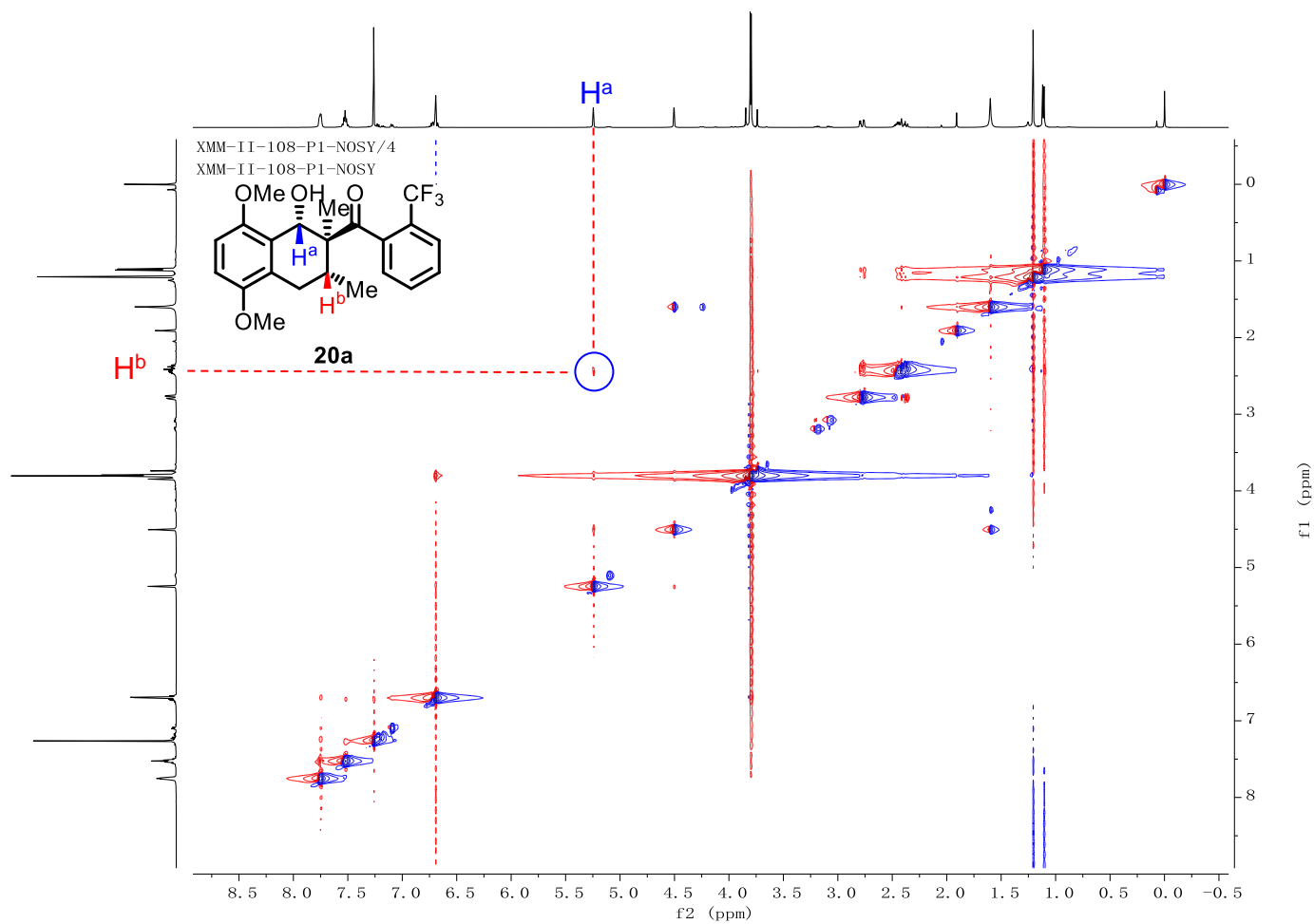
XMM-II-109

**19**

Chemical Formula: $C_{22}H_{23}F_3O_4$
125 MHz, $CDCl_3$

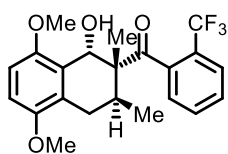






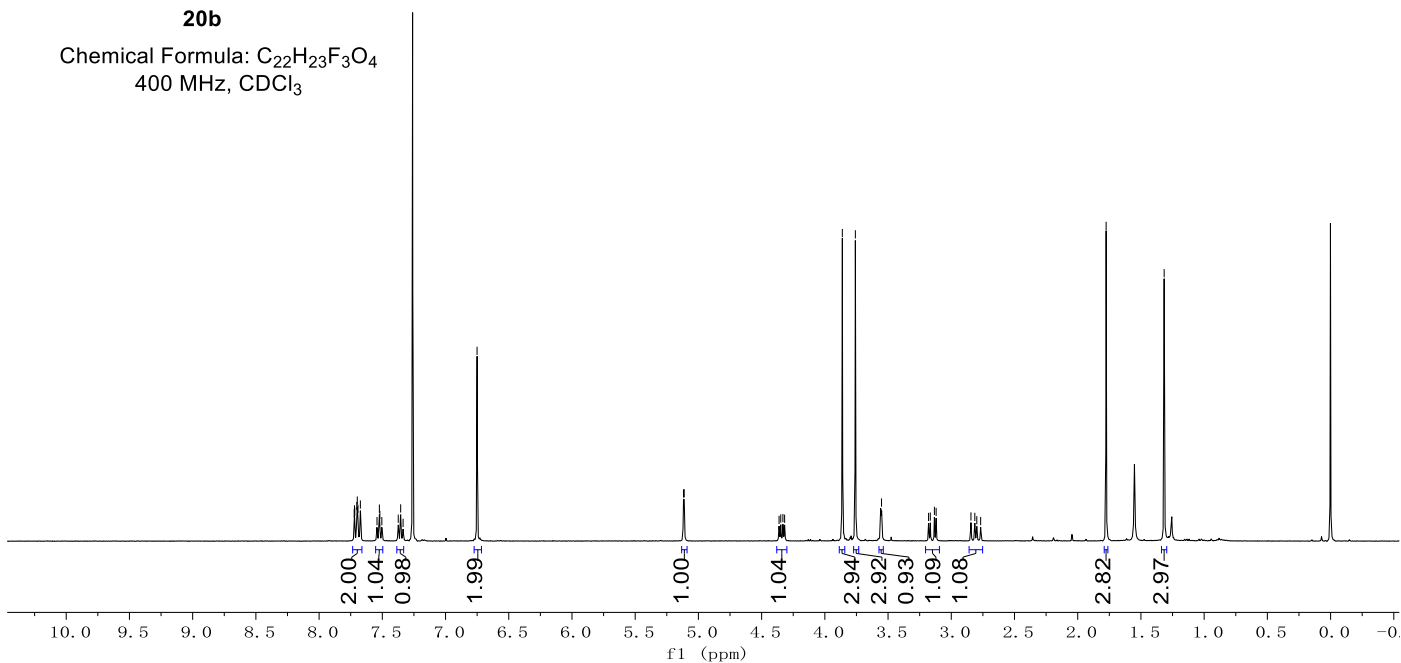
XMM-11-188-P2-C 500
 7.72
 7.72
 7.72
 7.70
 7.69
 7.67
 7.54
 7.52
 7.52
 7.50
 7.37
 7.35
 7.34
 6.75

5.12
 5.11
 4.36
 4.35
 4.33
 4.32
 3.86
 3.76
 3.55
 3.18
 3.17
 3.13
 3.12
 2.84
 2.81
 2.80
 2.77
 1.78
 1.32

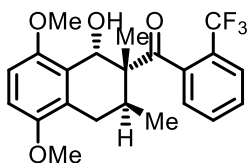


20b

Chemical Formula: $C_{22}H_{23}F_3O_4$
 400 MHz, $CDCl_3$

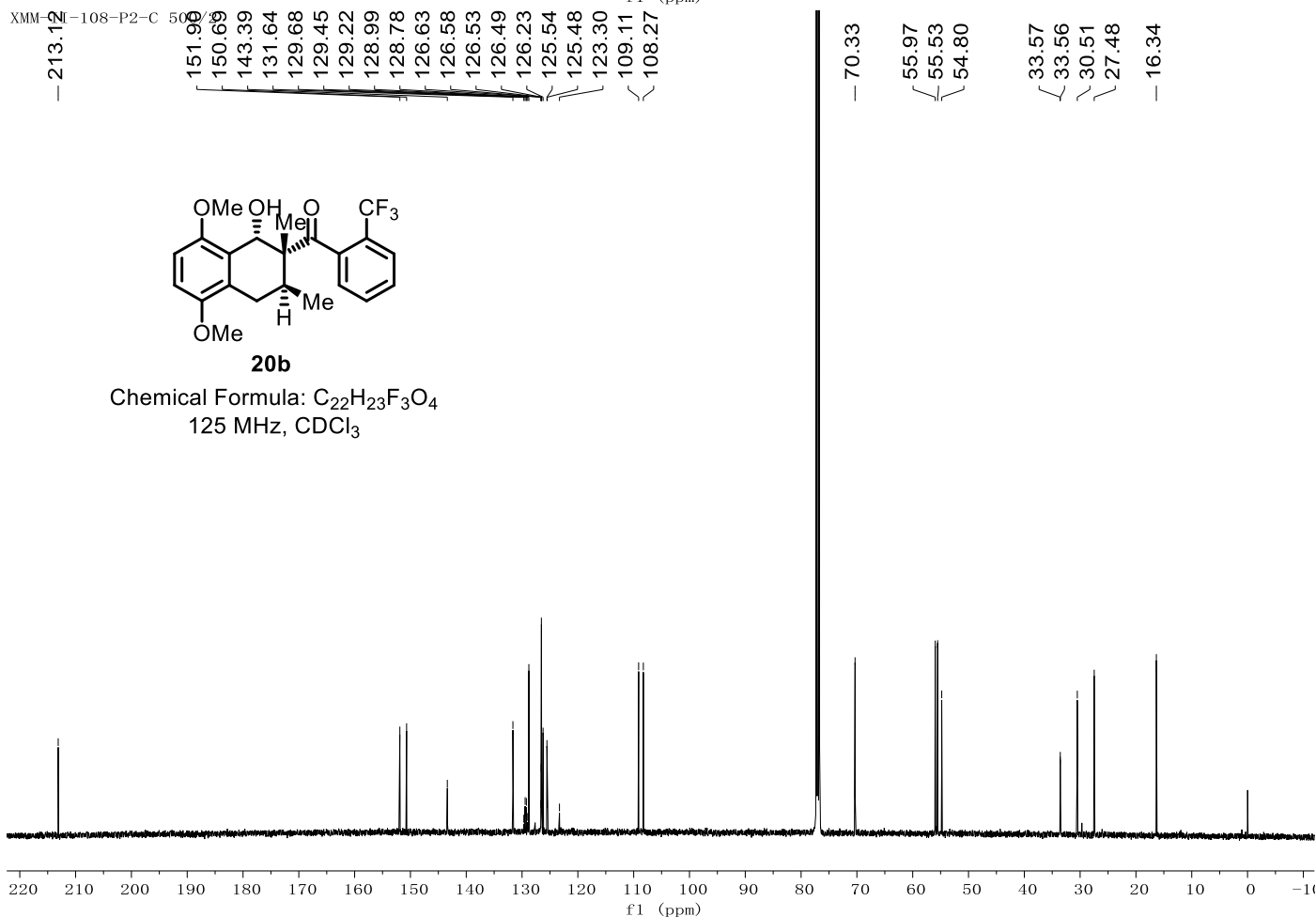


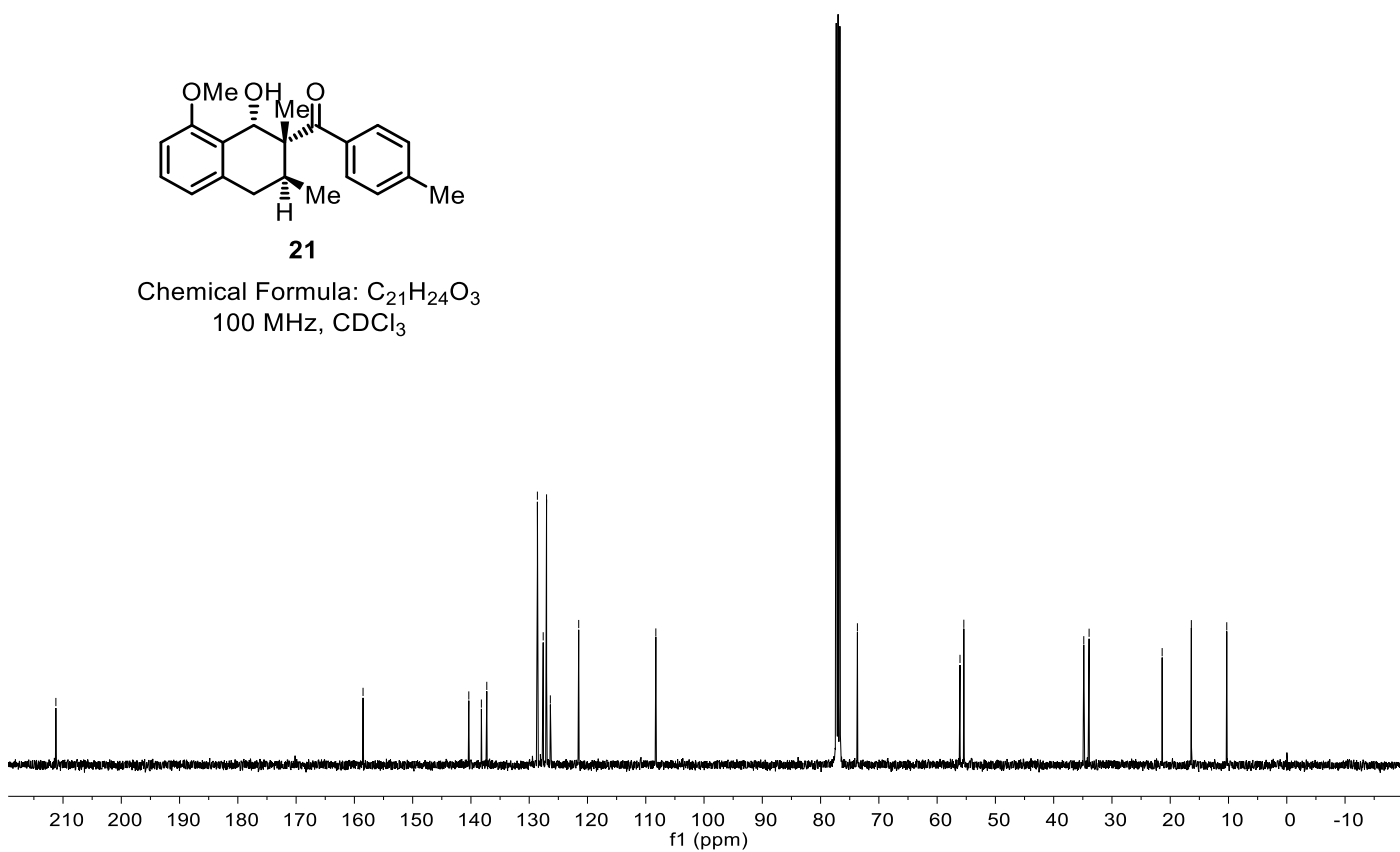
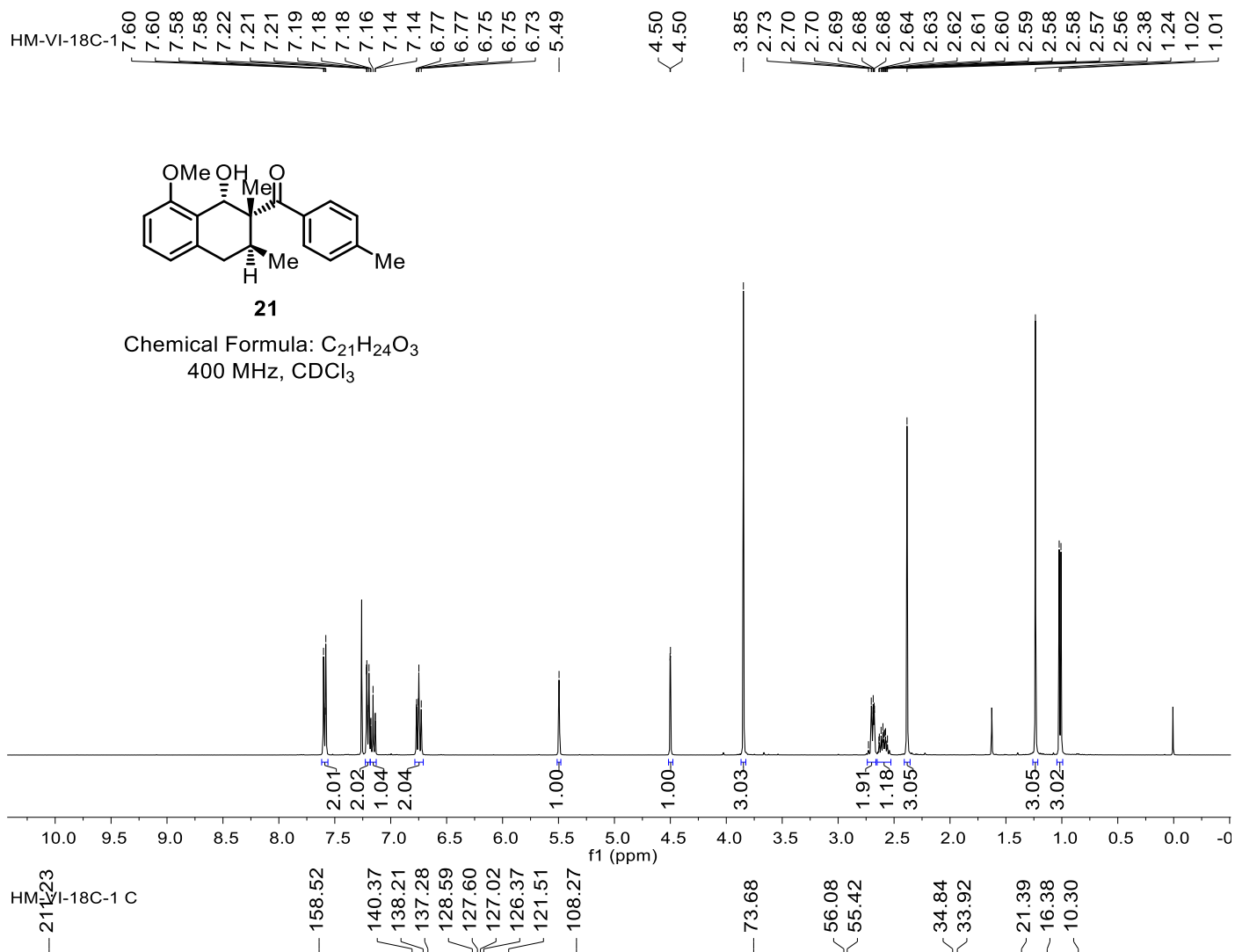
XMM-11-108-P2-C 500
 213.12
 151.99
 150.69
 143.39
 131.64
 129.68
 129.45
 129.22
 128.99
 128.78
 126.63
 126.58
 126.53
 126.49
 126.23
 125.54
 125.48
 123.30
 109.11
 108.27
 70.33
 55.97
 55.53
 54.80
 33.57
 33.56
 30.51
 27.48
 16.34

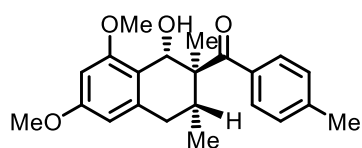


20b

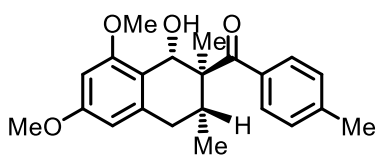
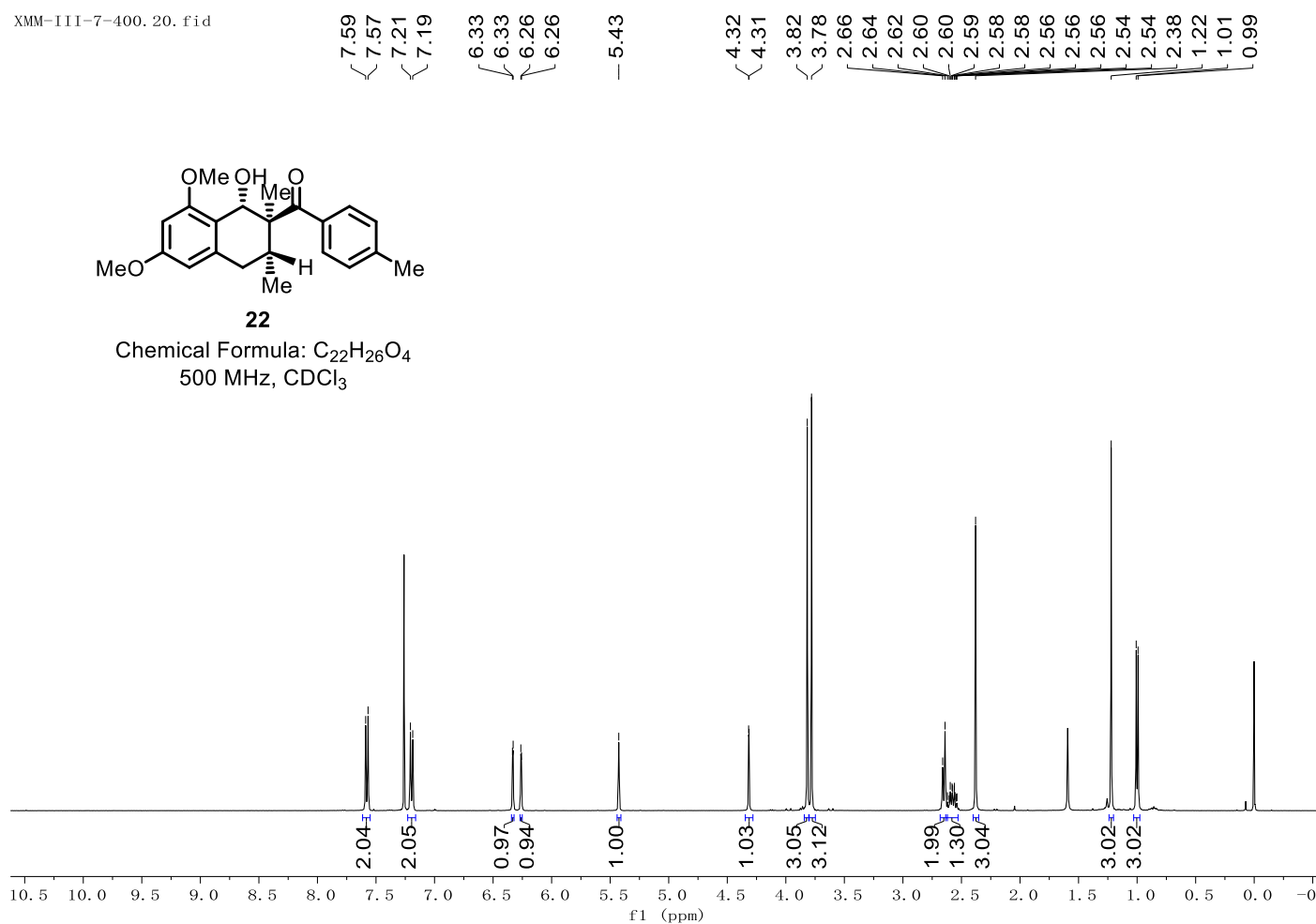
Chemical Formula: $C_{22}H_{23}F_3O_4$
 125 MHz, $CDCl_3$



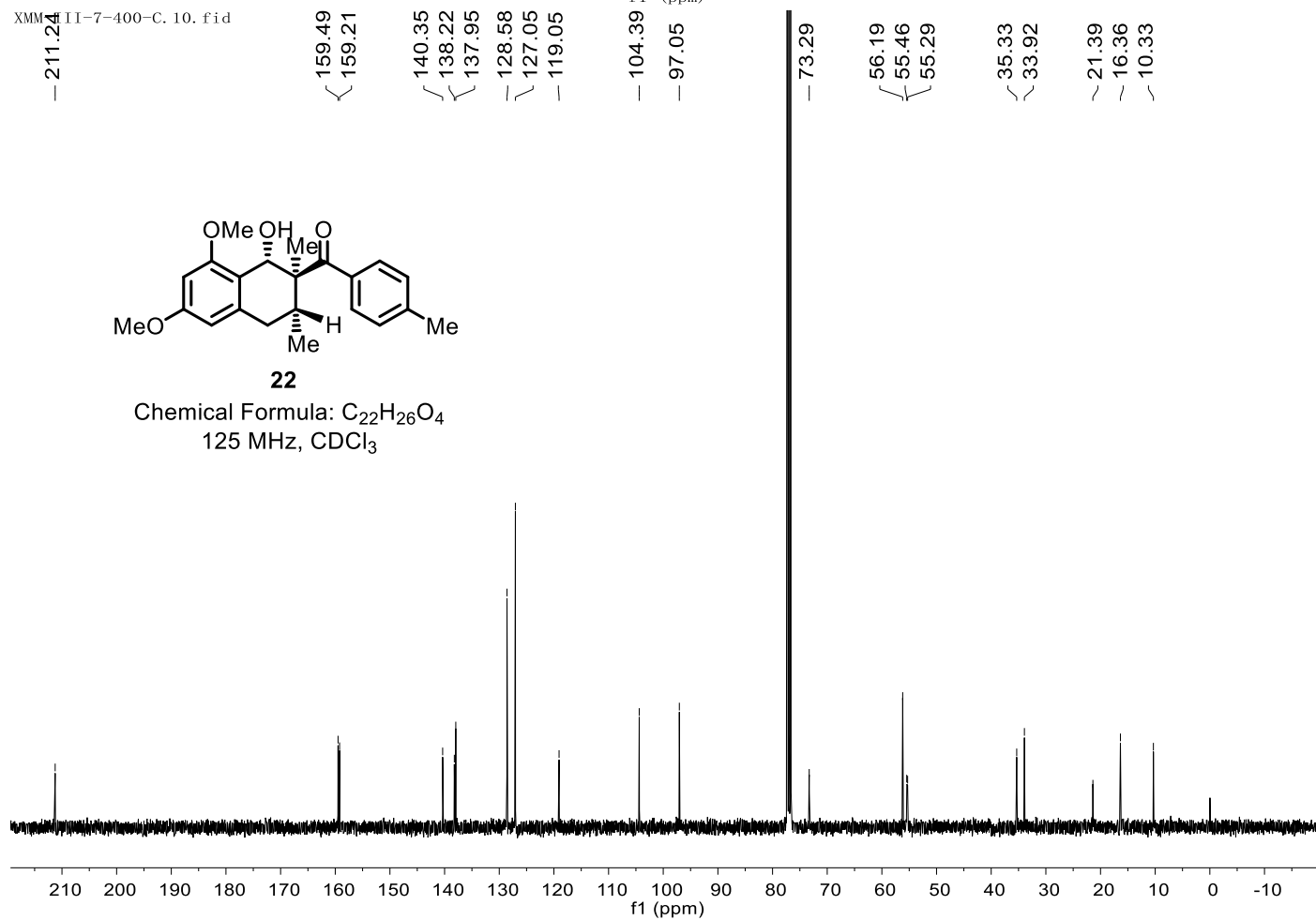


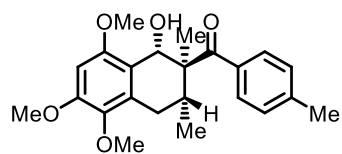
**22**

Chemical Formula: $C_{22}H_{26}O_4$
500 MHz, $CDCl_3$

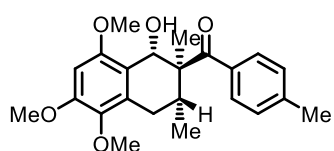
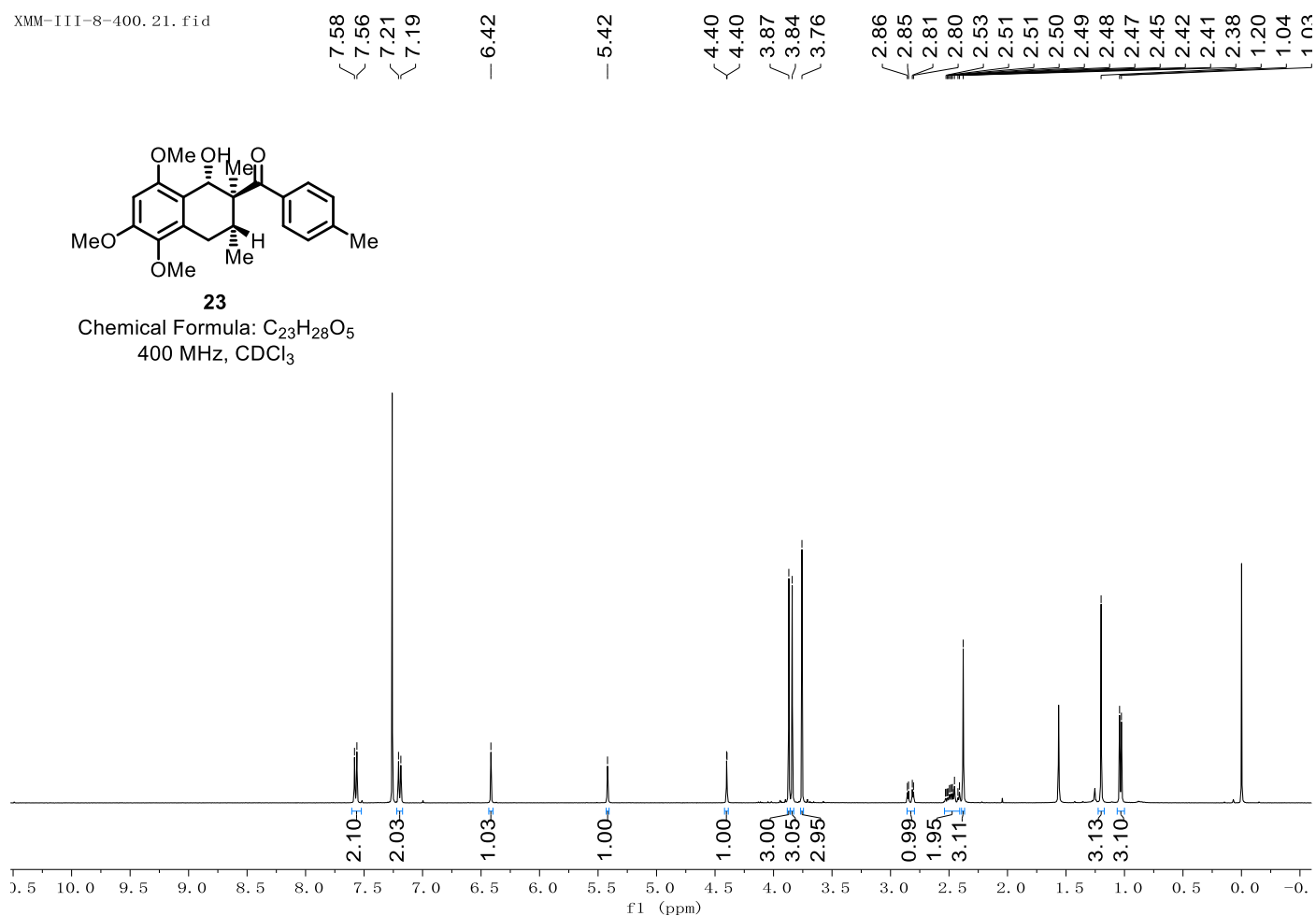
**22**

Chemical Formula: $C_{22}H_{26}O_4$
125 MHz, $CDCl_3$

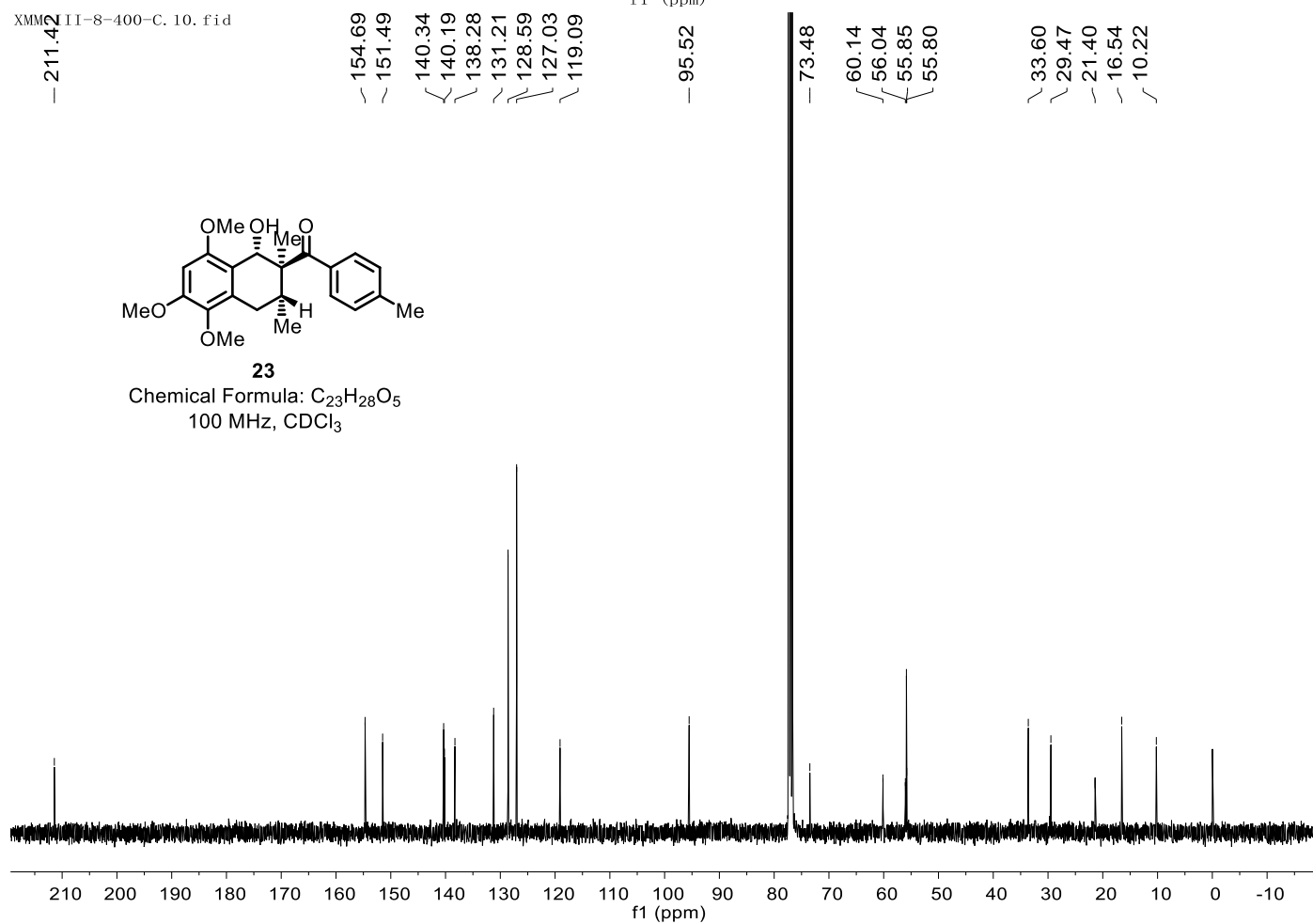


**23**

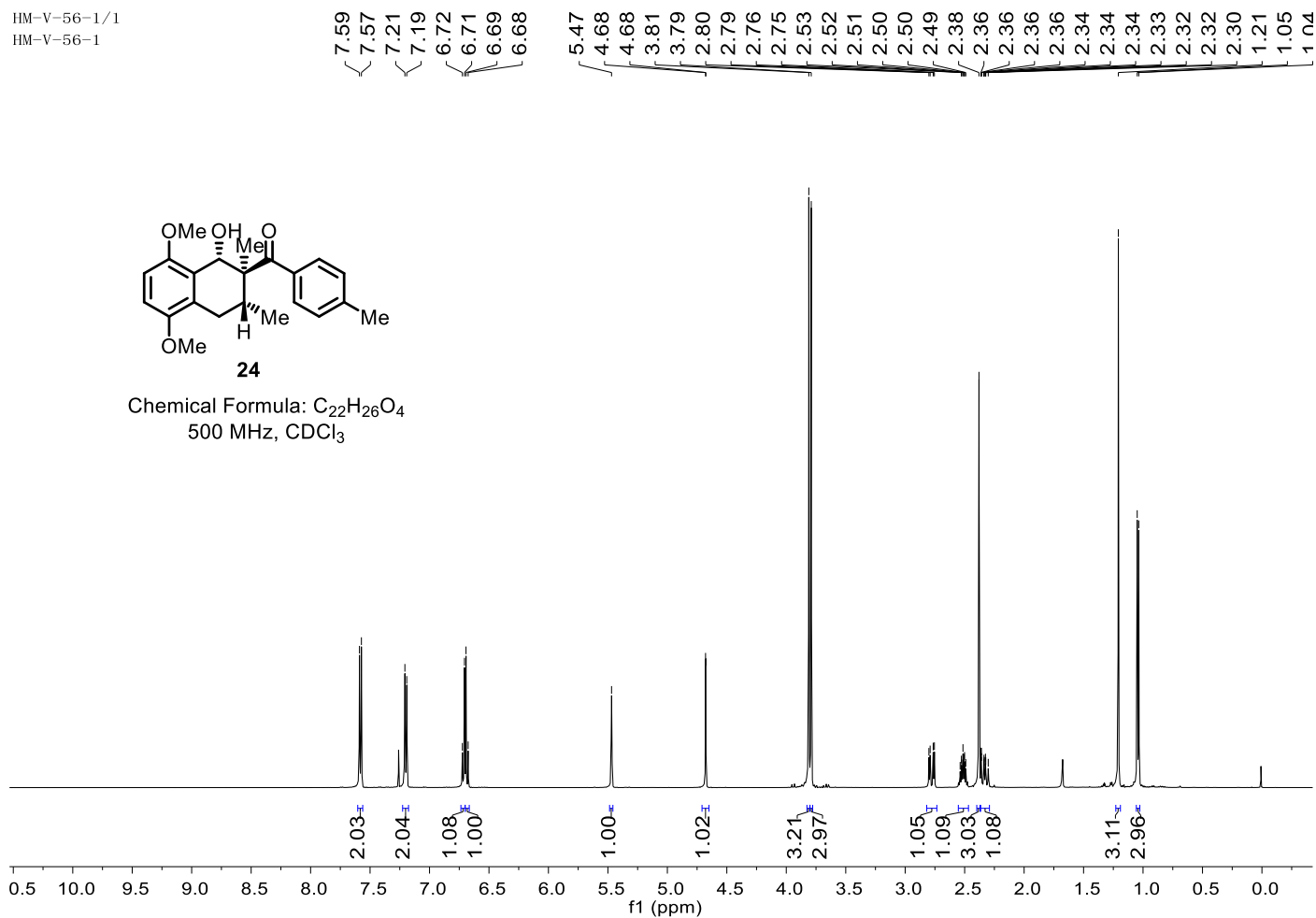
Chemical Formula: C₂₃H₂₈O₅
400 MHz, CDCl₃

**23**

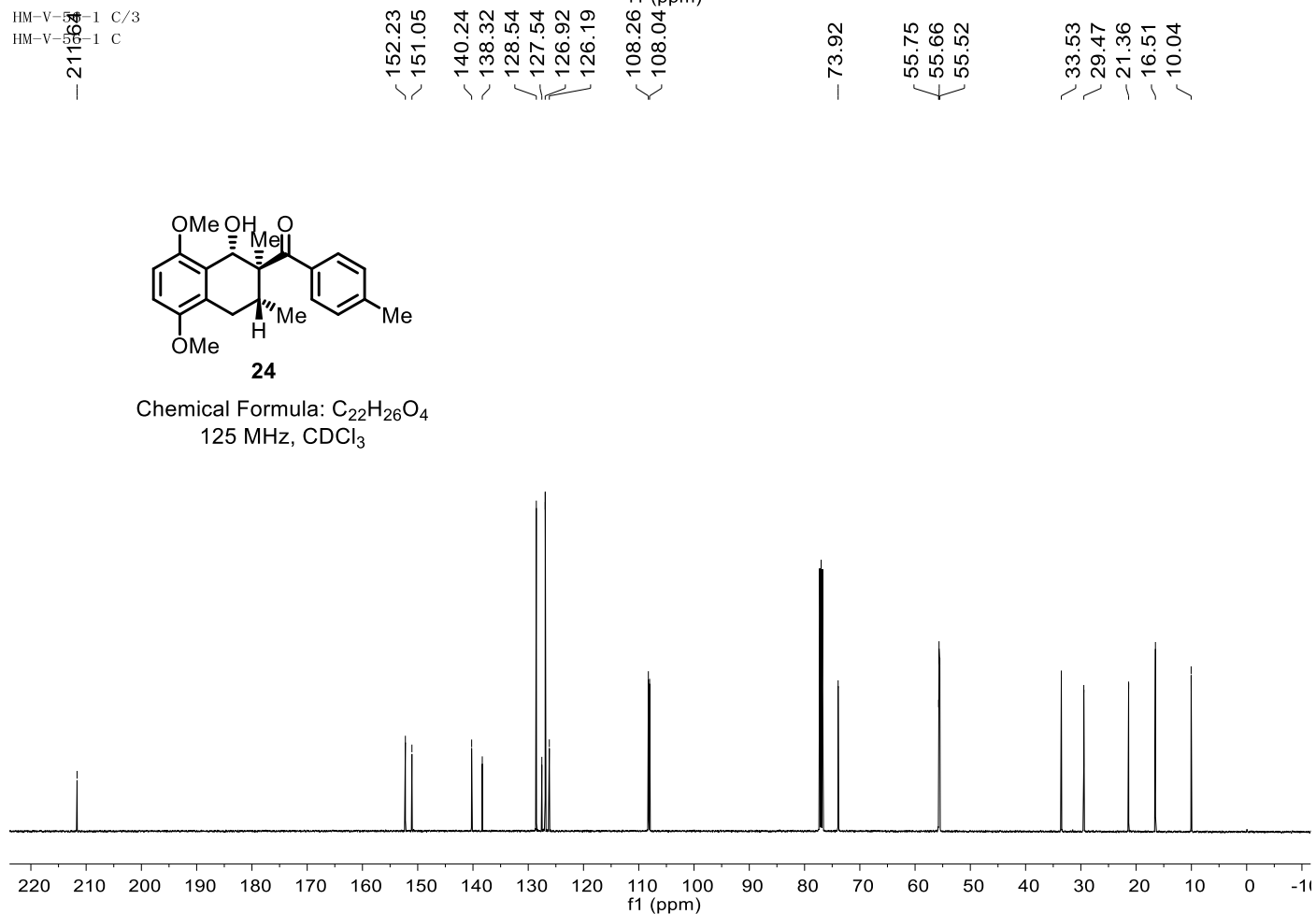
Chemical Formula: C₂₃H₂₈O₅
100 MHz, CDCl₃

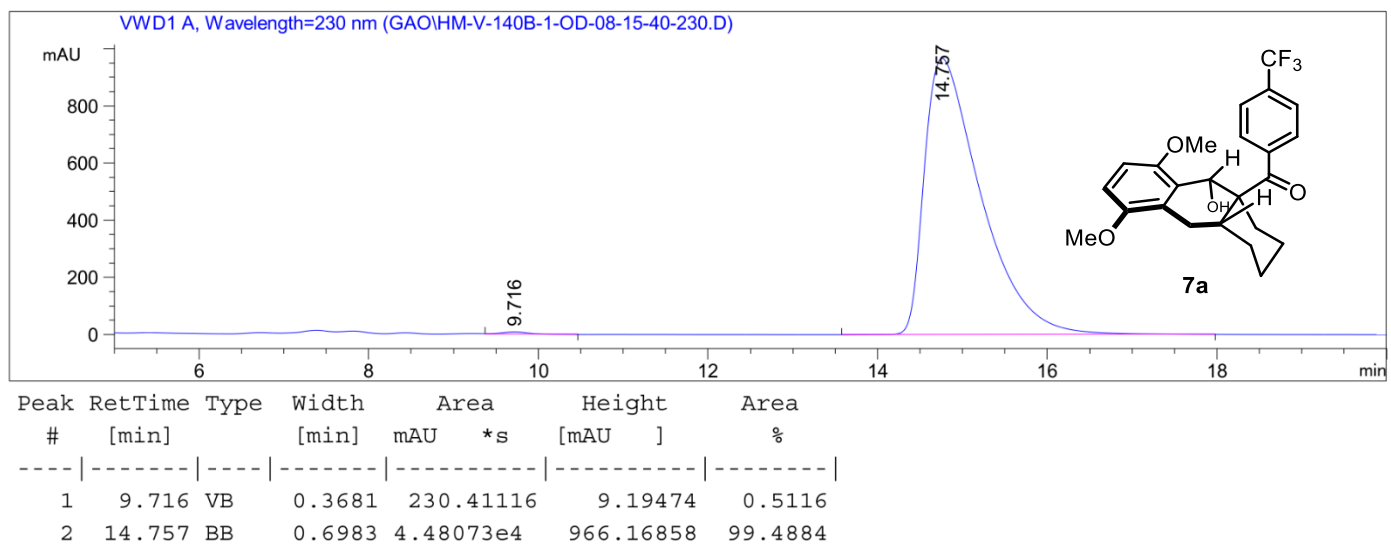
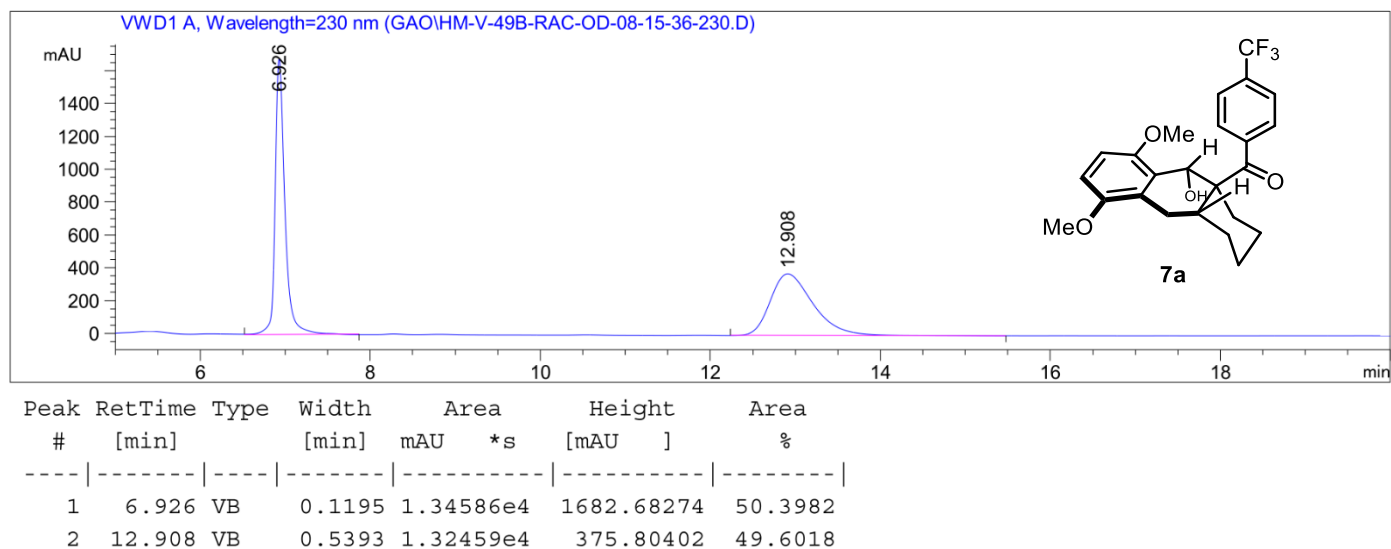


HM-V-56-1/1
HM-V-56-1

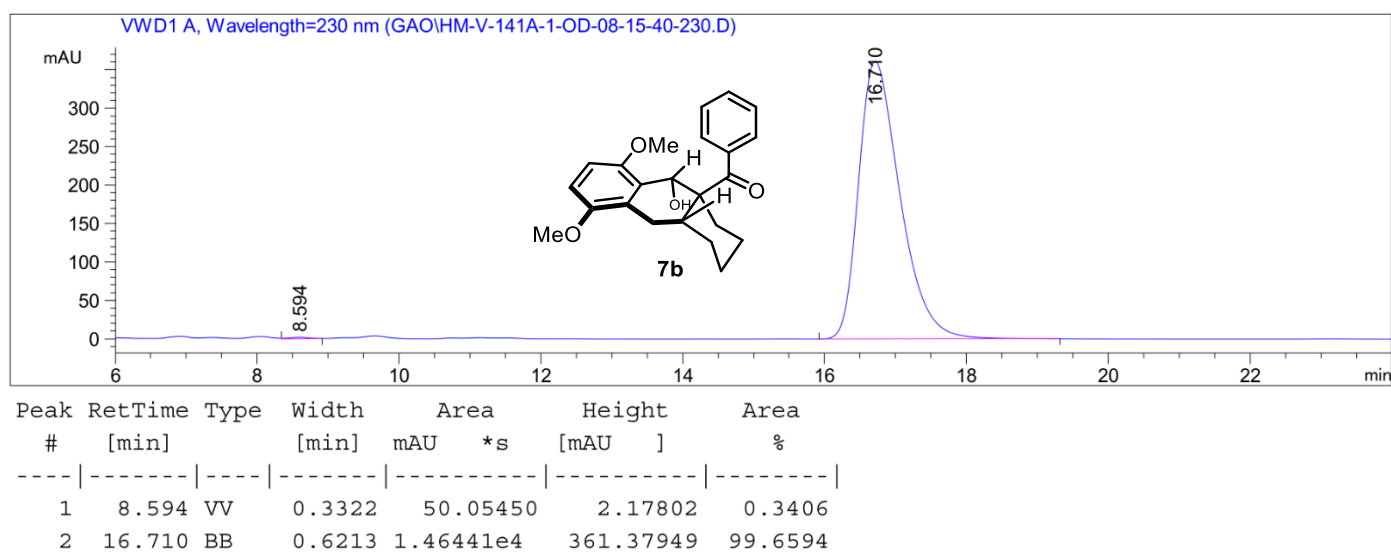
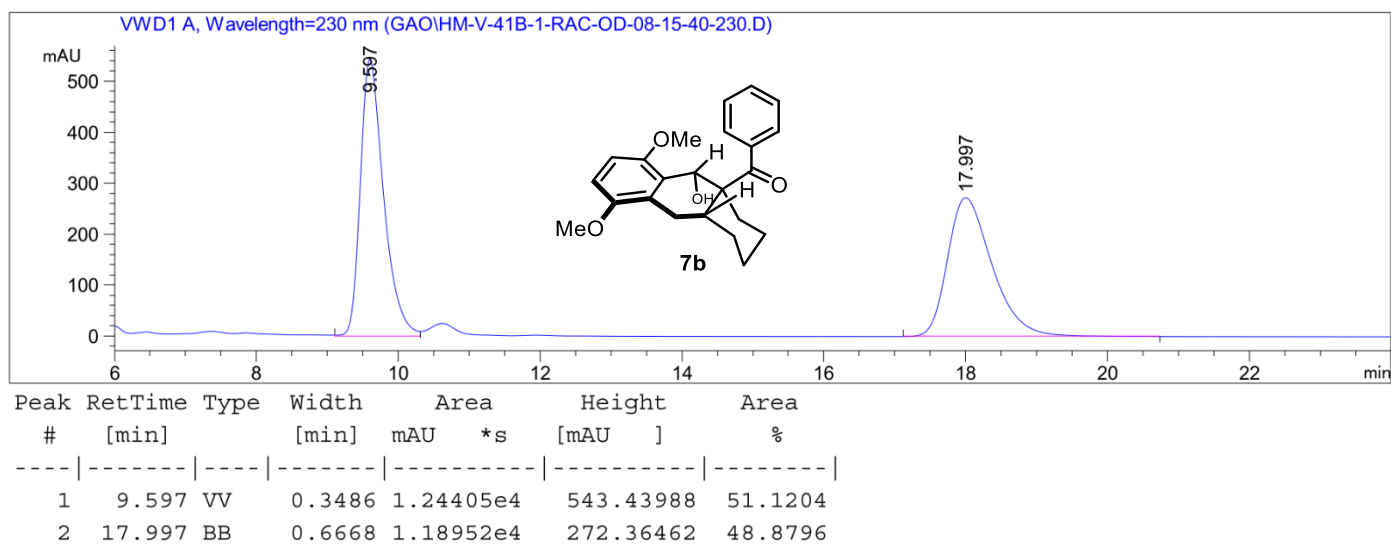


HM-V-56-1 C/3
HM-V-56-1 C

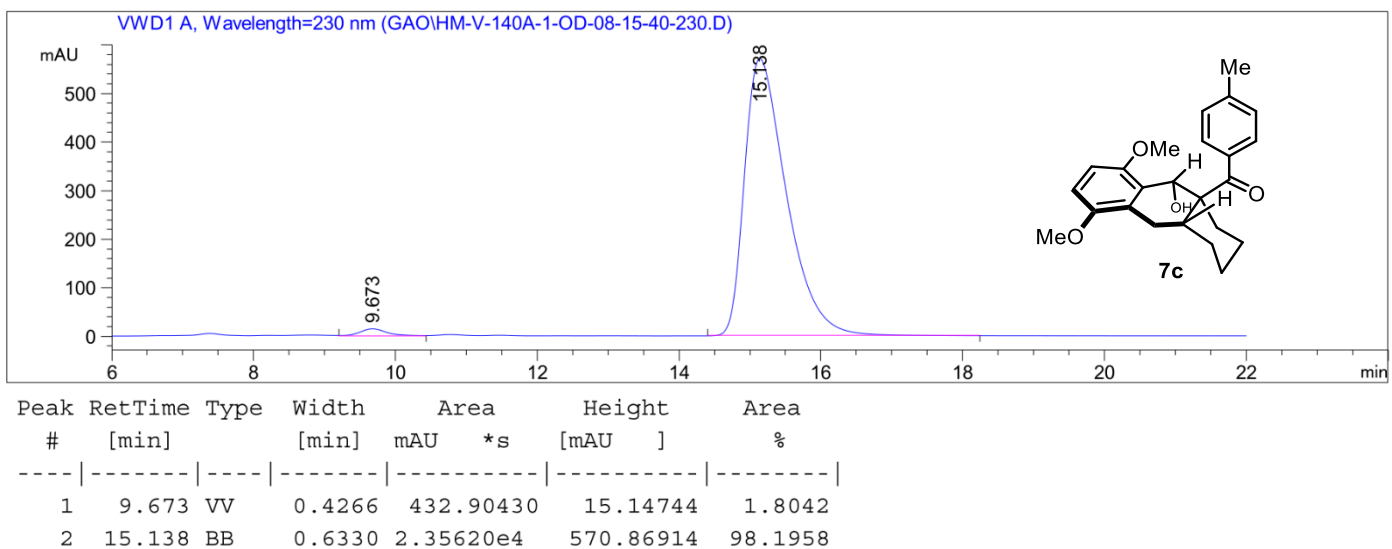
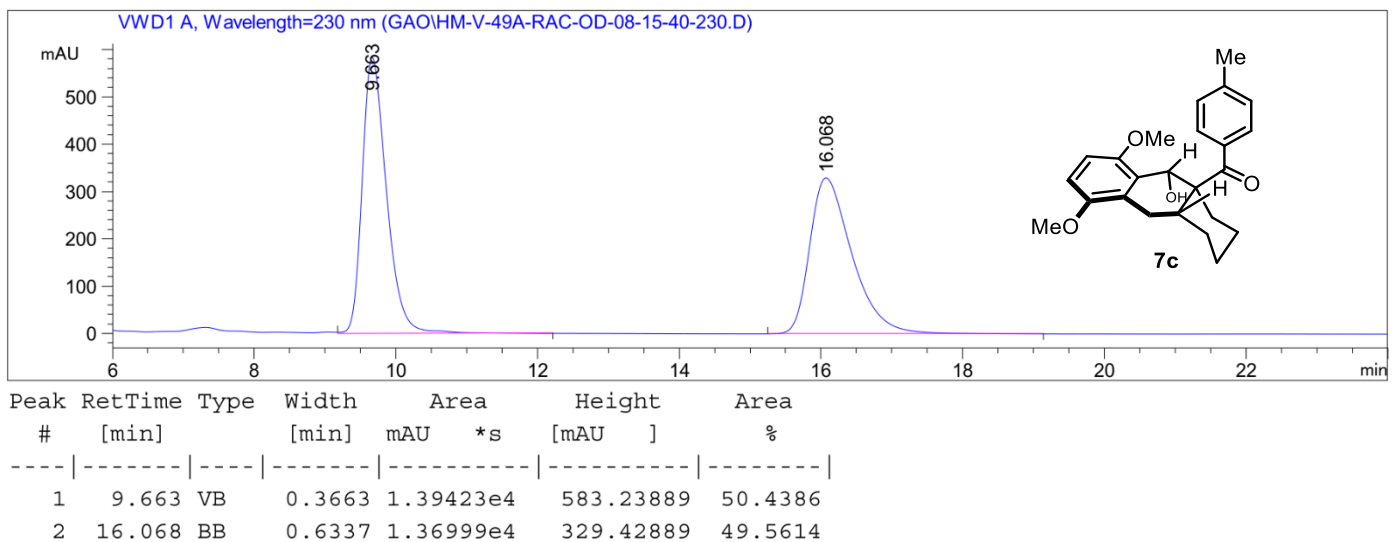




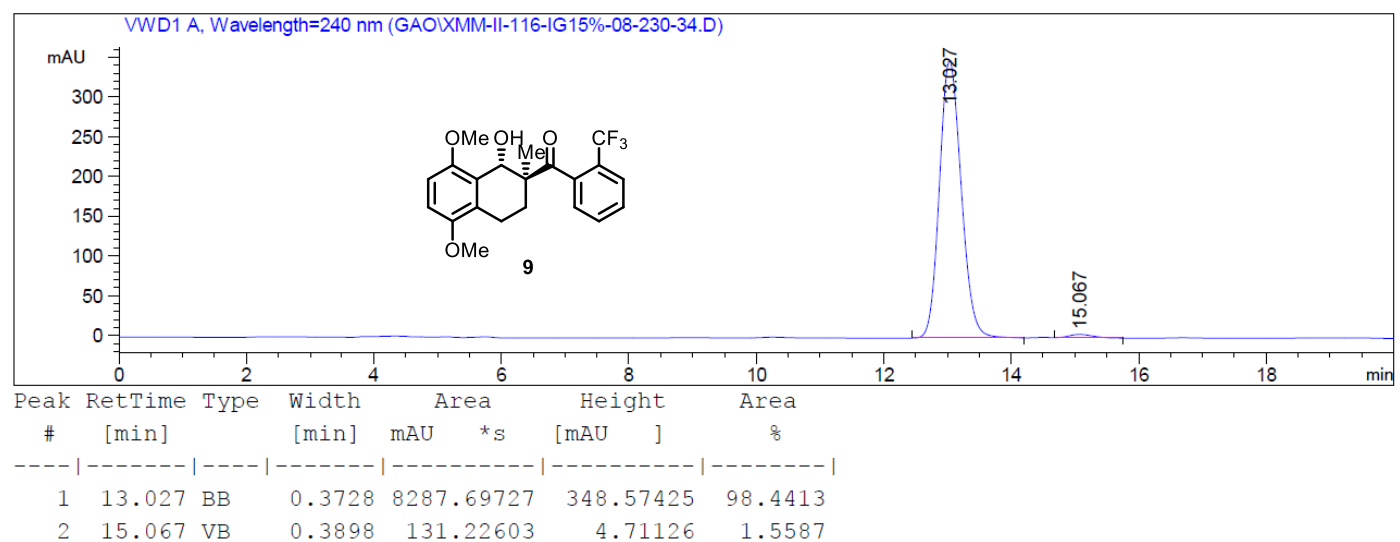
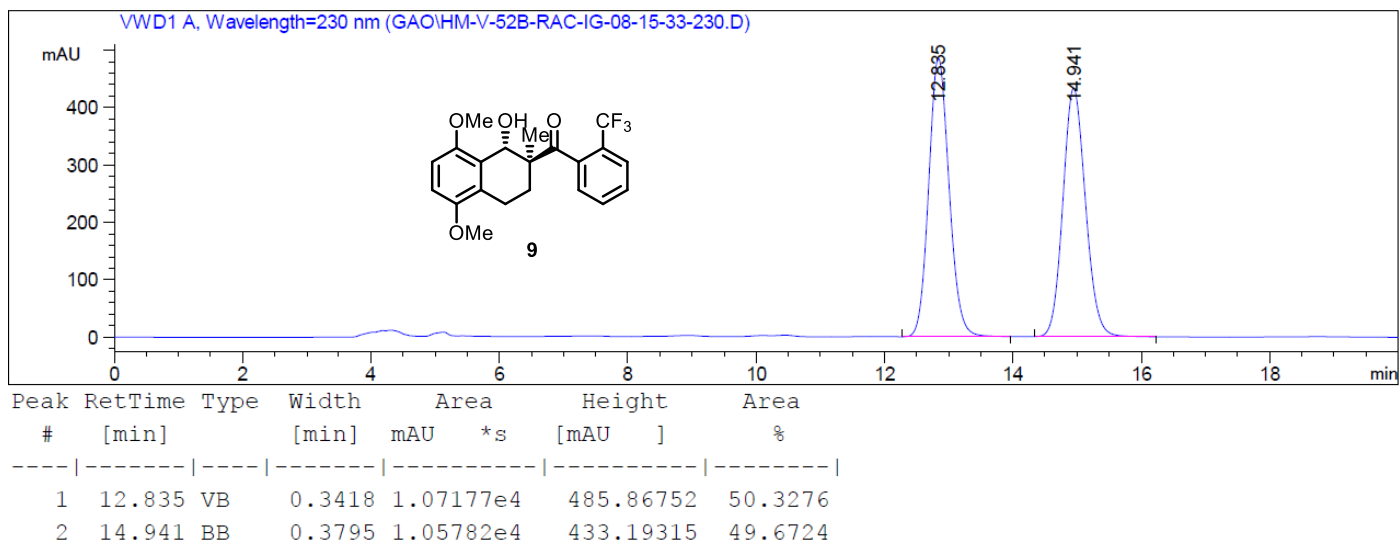
Enantiomeric excess: 99%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 10.883min (major), t_R = 17.052 min (minor).



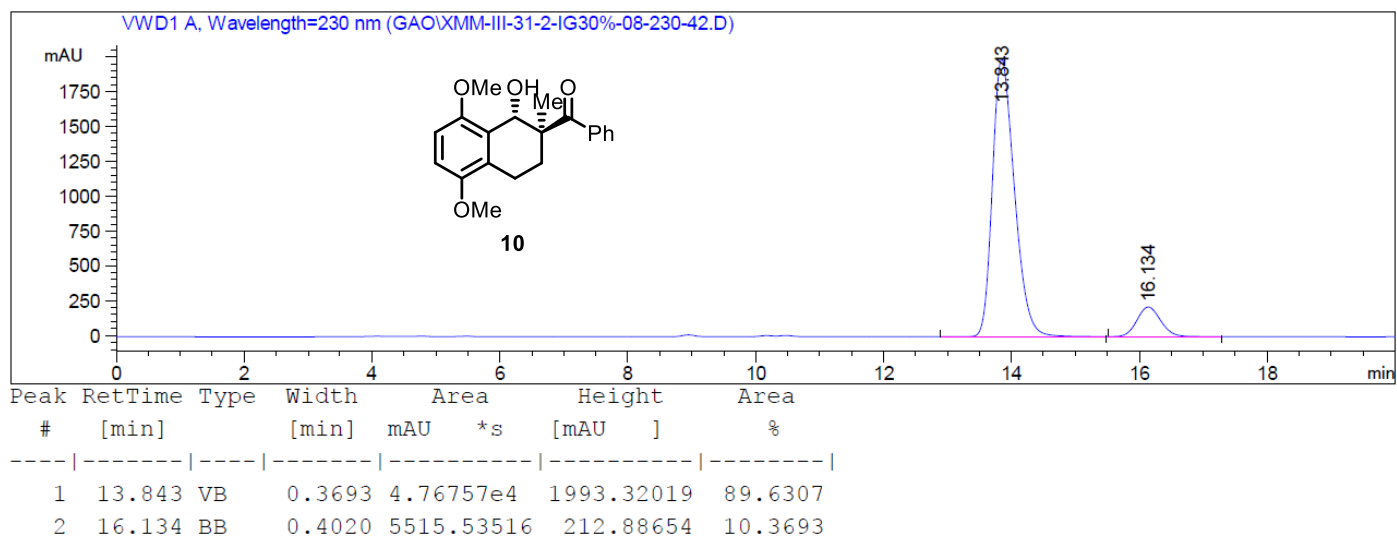
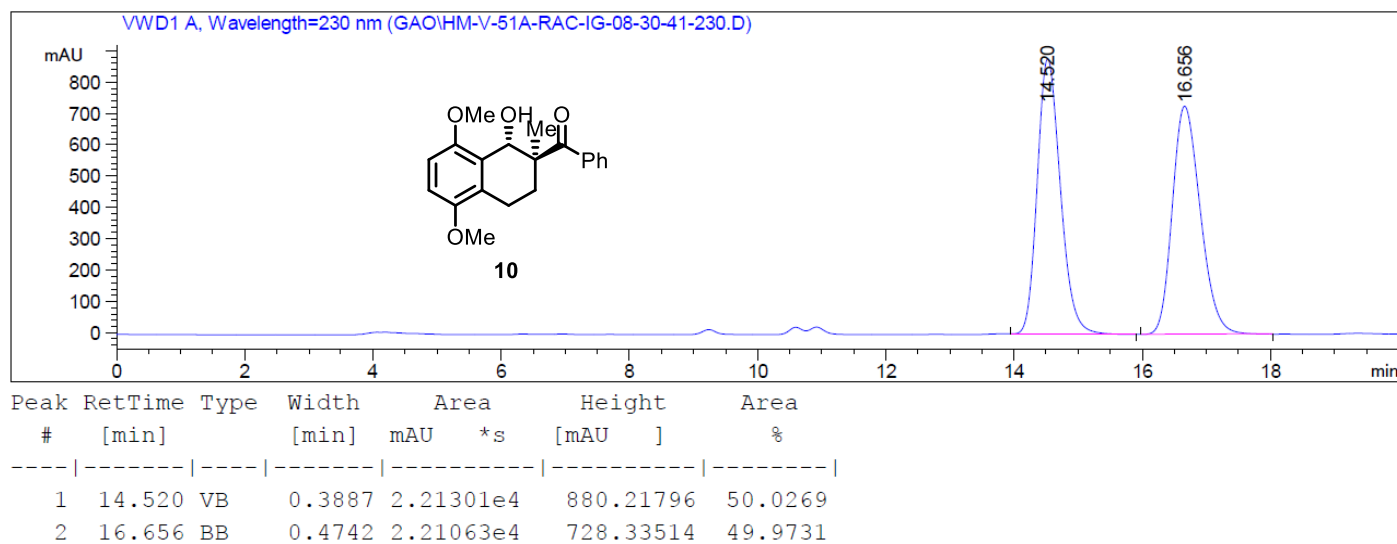
Enantiomeric excess: 99.3%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 8.594min (minor), t_R = 16.710 min (major).



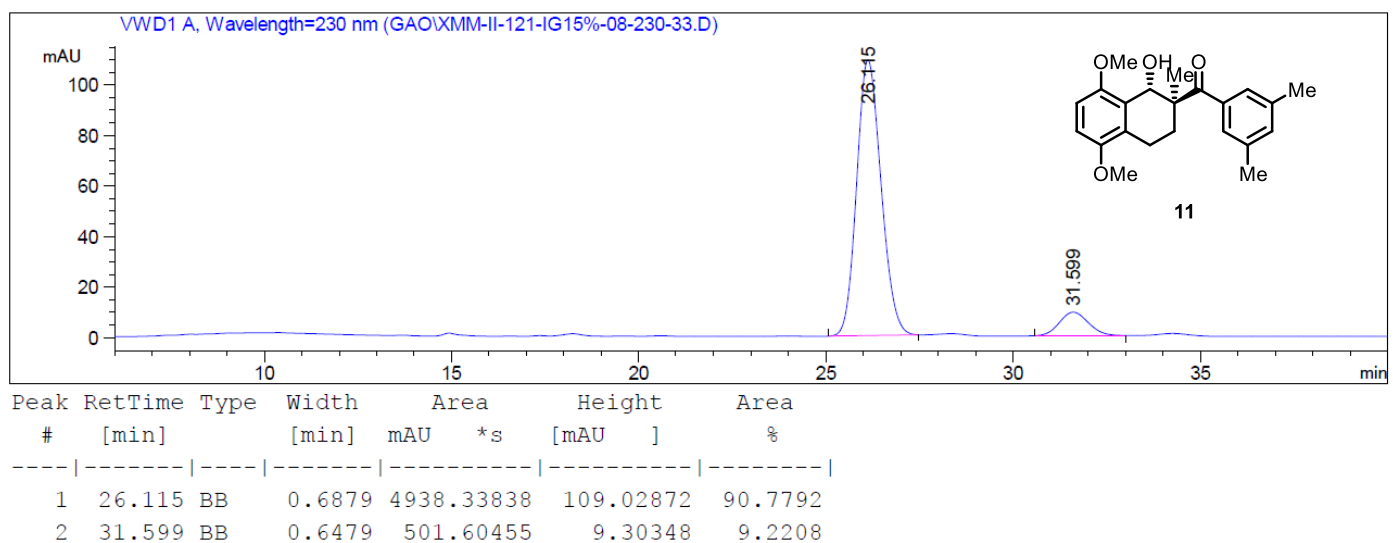
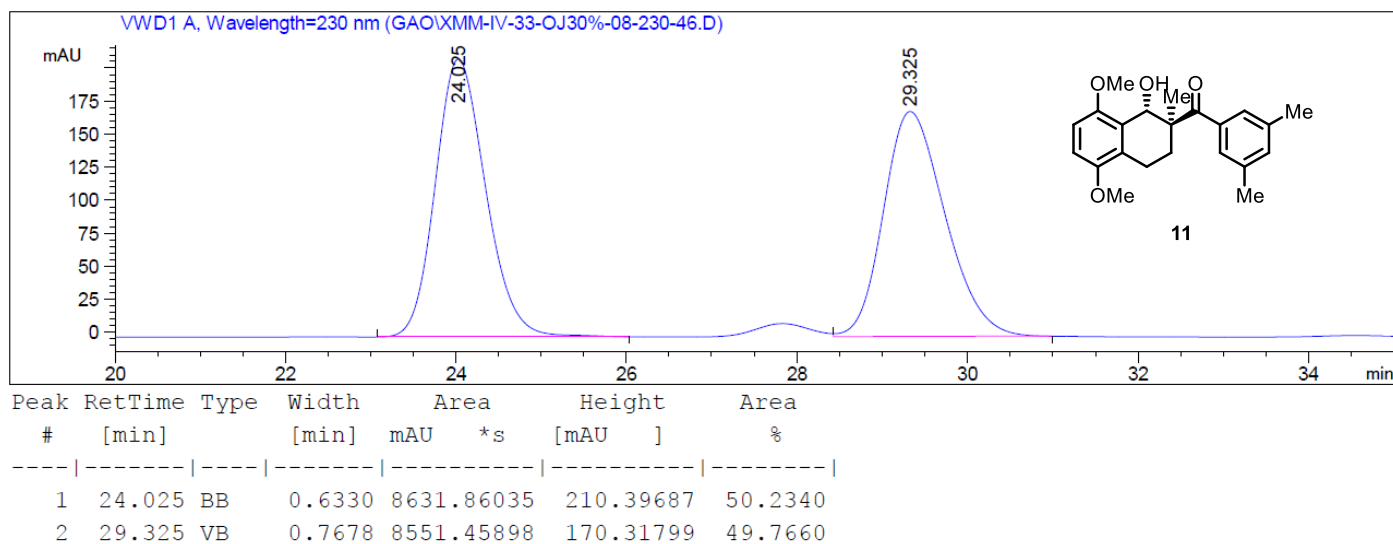
Enantiomeric excess: 96%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.673min (minor), t_R = 15.138 min (major).



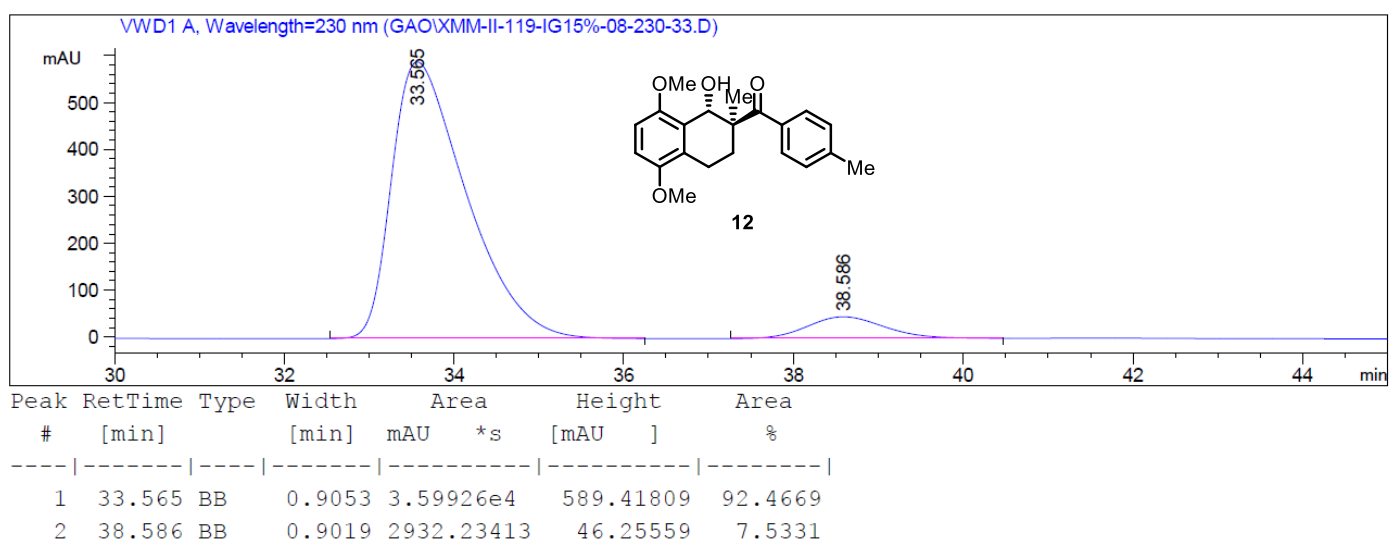
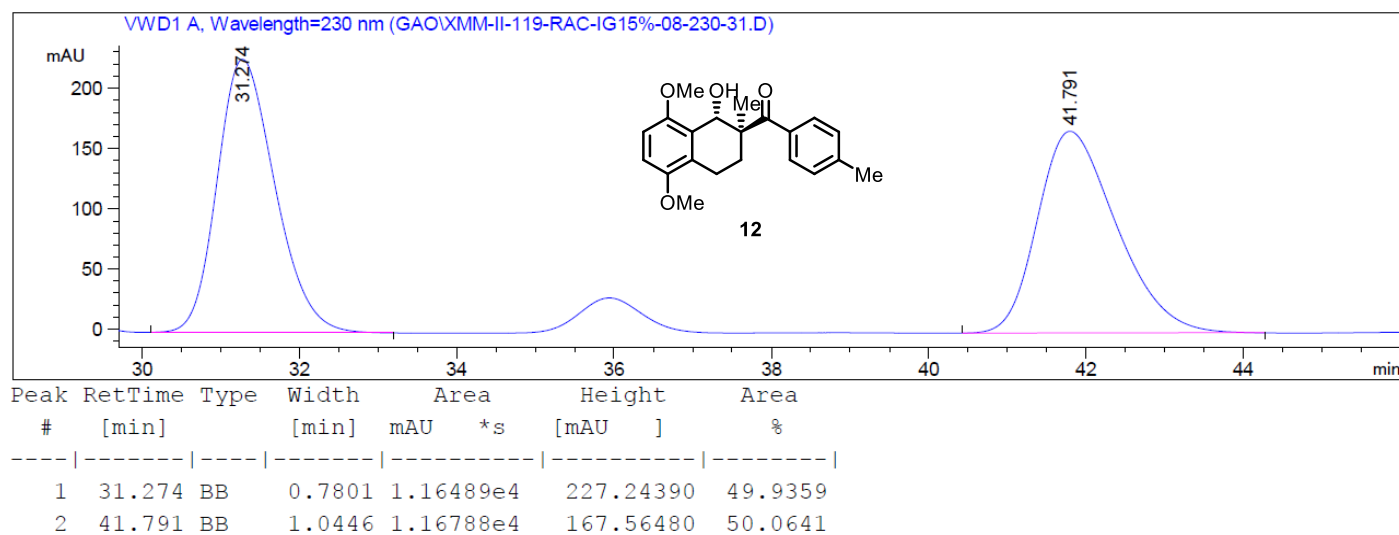
Enantiomeric excess: 97%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 13.027 min (major), t_R = 15.067 min (minor).



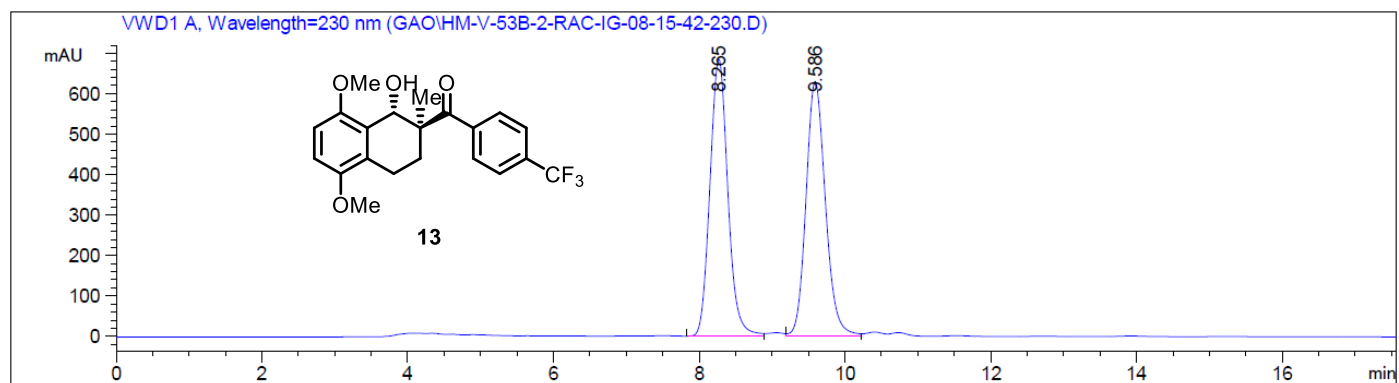
Enantiomeric excess: 79%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 13.843 min (major), t_R = 16.134 min (minor).



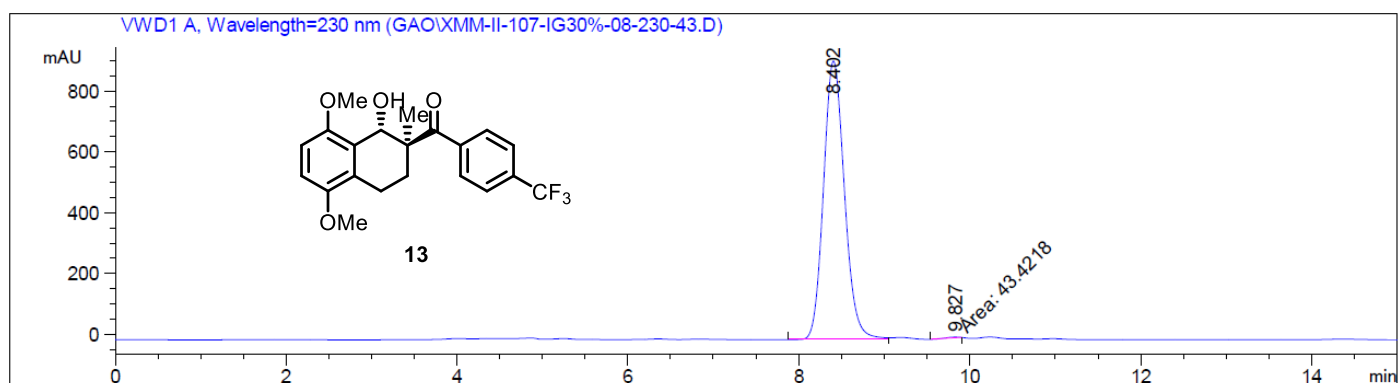
Enantiomeric excess: 82%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 26.115 min (major), t_R = 31.599 min (minor).



Enantiomeric excess: 85%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 33.565 min (major), t_R = 38.586 min (minor).

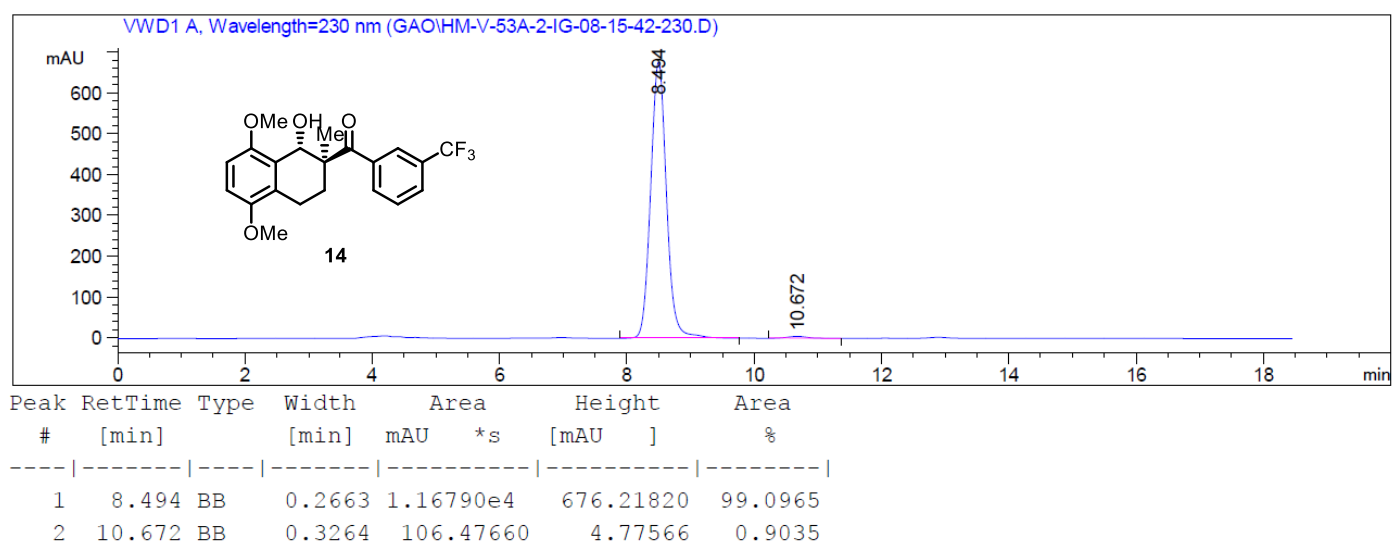
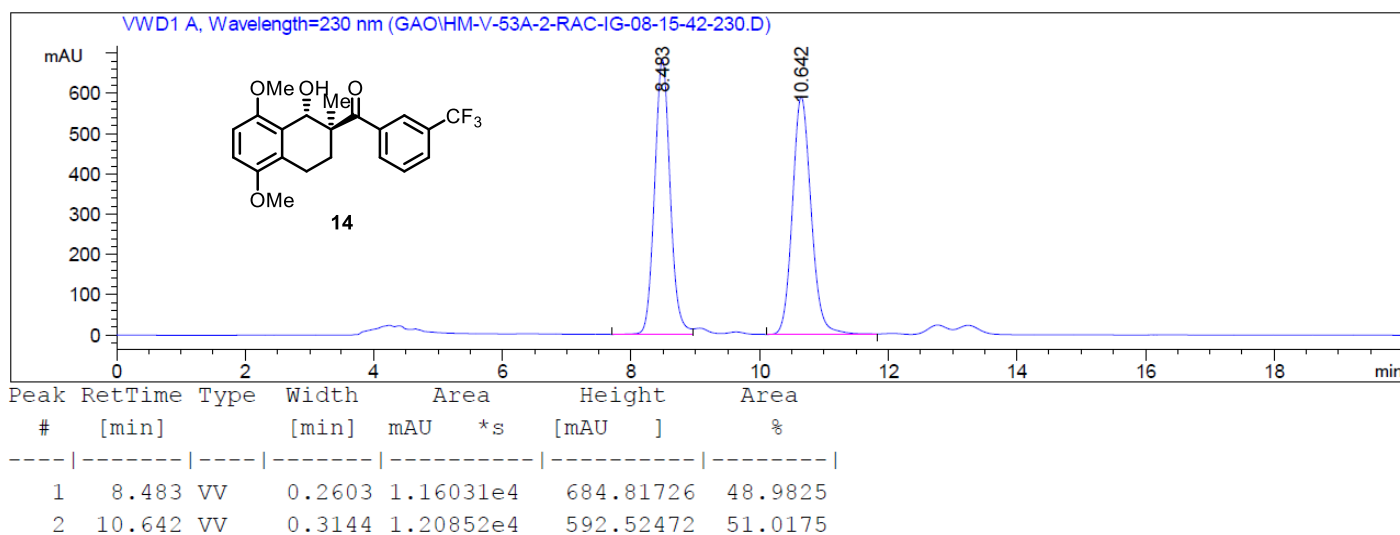


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	8.265	VV	0.2655	1.17005e4		685.04230	50.0496
2	9.586	VV	0.2861	1.16773e4		630.03430	49.9504

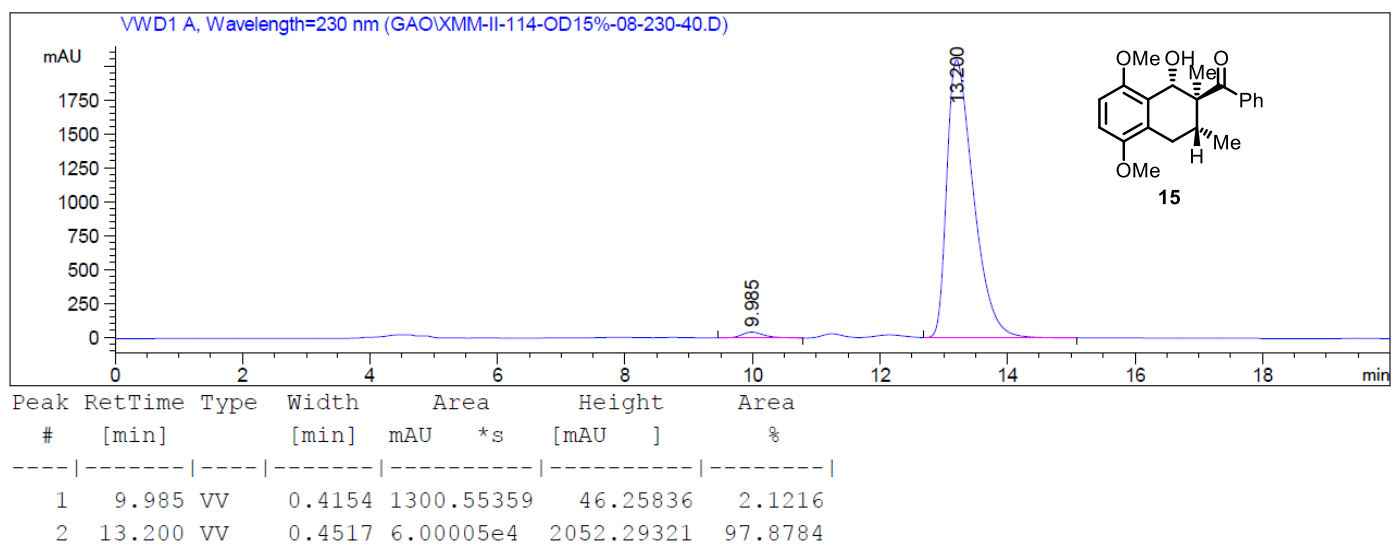
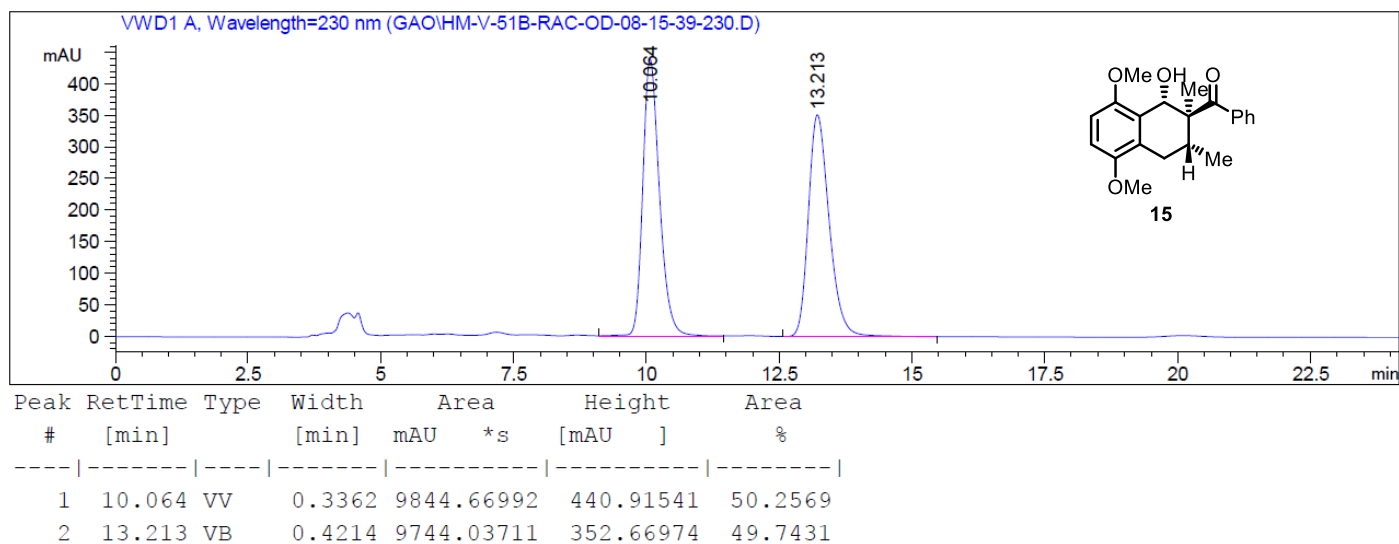


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	8.402	BV	0.2642	1.56176e4		917.16034	99.7227
2	9.827	MM	0.2092	43.42182		3.45883	0.2773

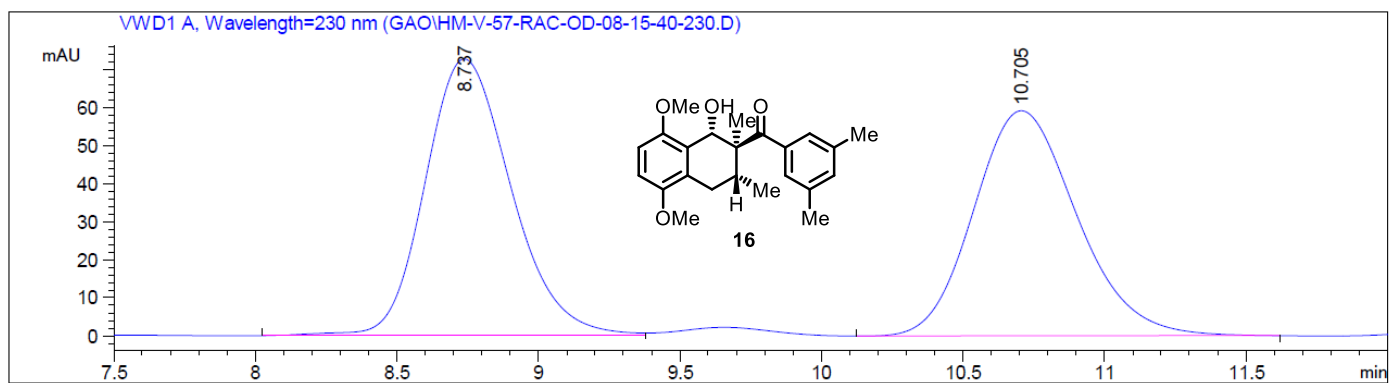
Enantiomeric excess: 99.5%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 8.402 min (major), t_R = 9.827 min (minor).



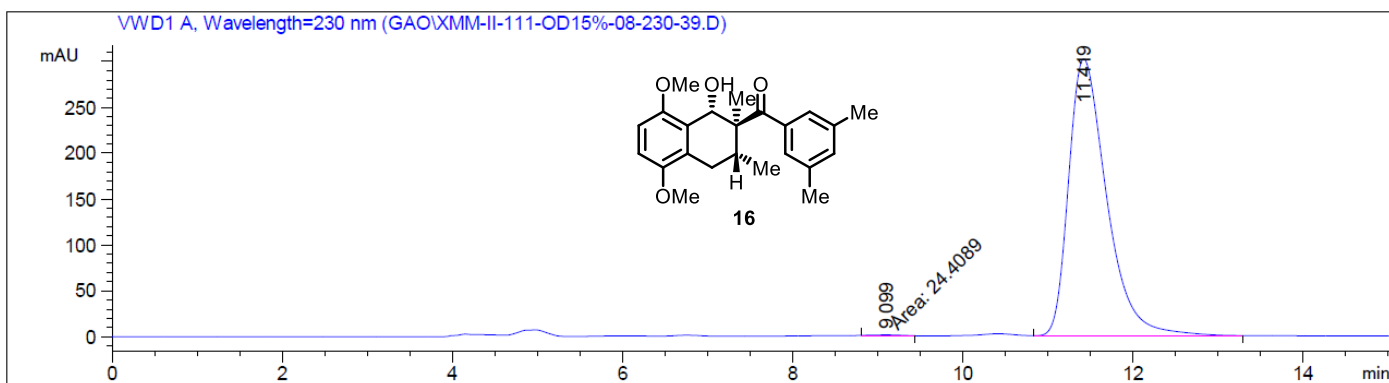
Enantiomeric excess: 98%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 8.494 min (major), t_R = 10.672 min (minor).



Enantiomeric excess: 96%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.985 min (minor), t_R = 13.200 min (major).

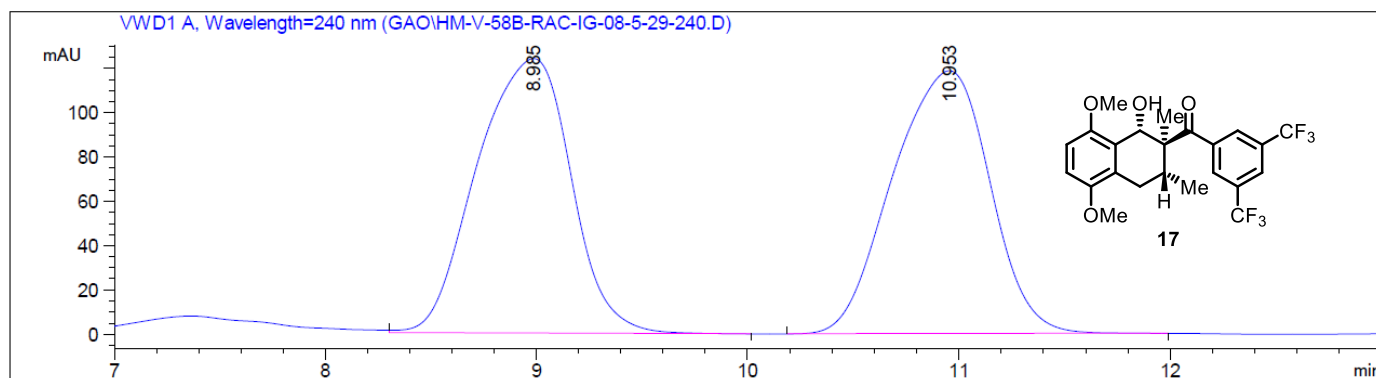


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	8.737	BV	0.3313	1544.34644		72.78861	50.6657
2	10.705	VB	0.3952	1503.76575		59.22474	49.3343

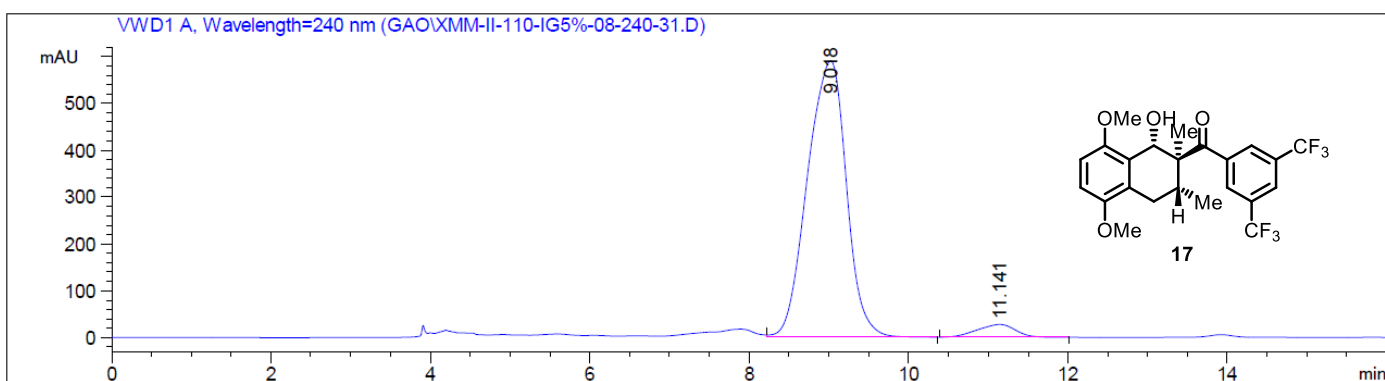


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	9.099	MM	0.4481	24.40888		9.07885e-1	0.2597
2	11.419	VB	0.4750	9374.61816		301.95764	99.7403

Enantiomeric excess: 99%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.099 min (major), t_R = 11.419 min (minor).

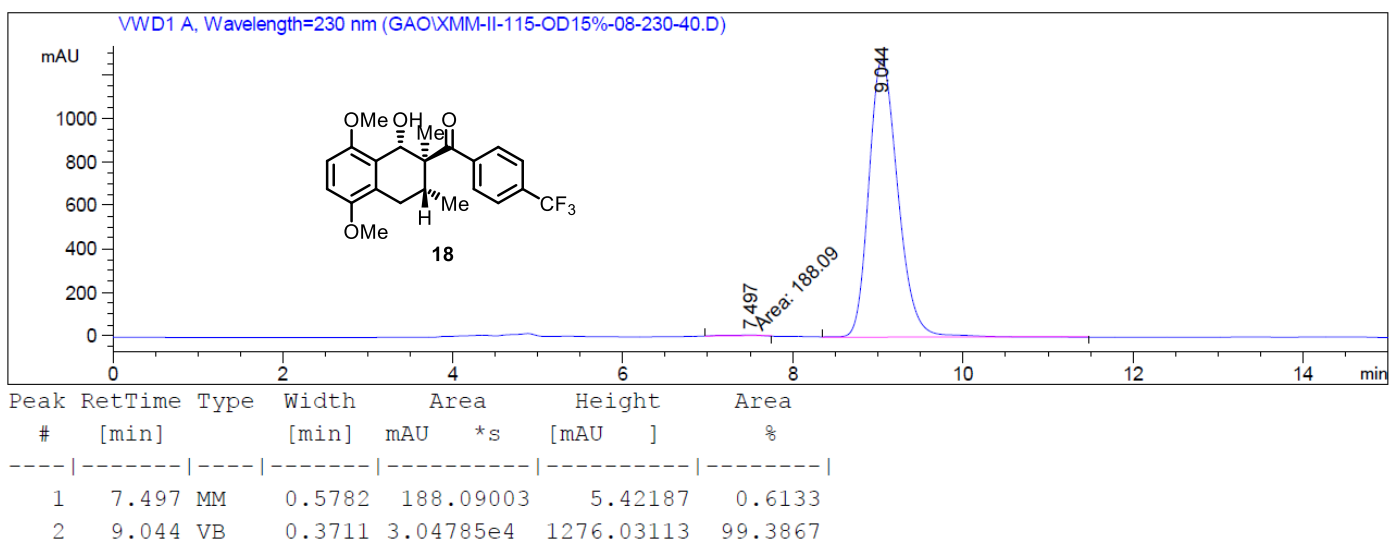
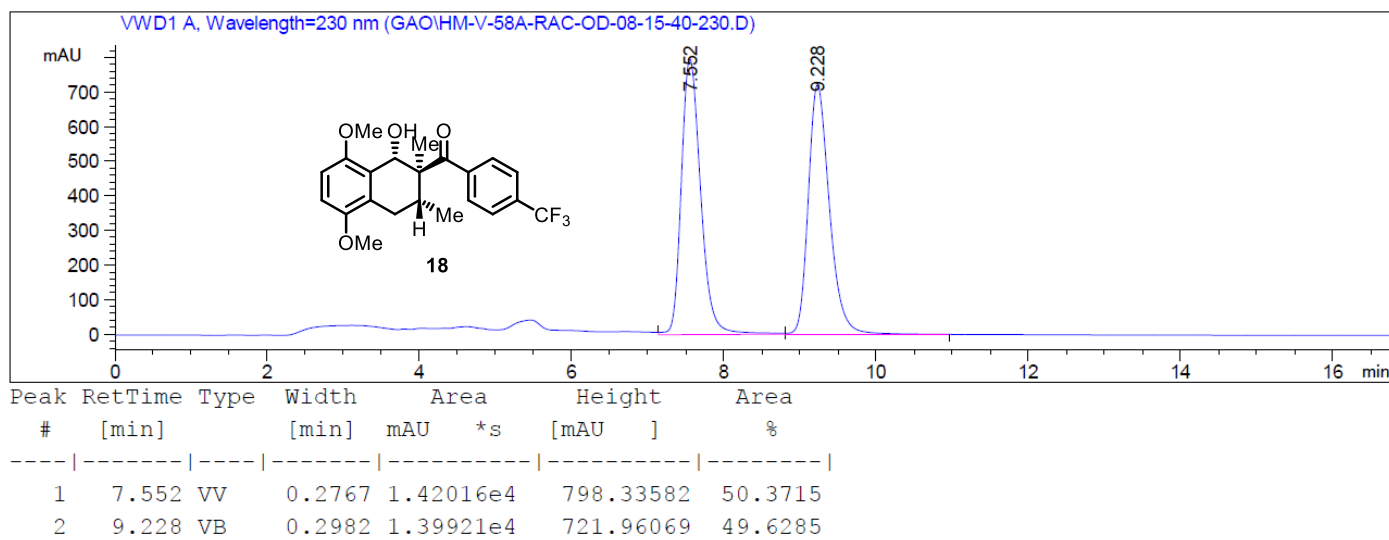


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.985	VB	0.5154	3850.94165	123.94193	50.2663
2	10.953	BB	0.5303	3810.13647	118.68534	49.7337

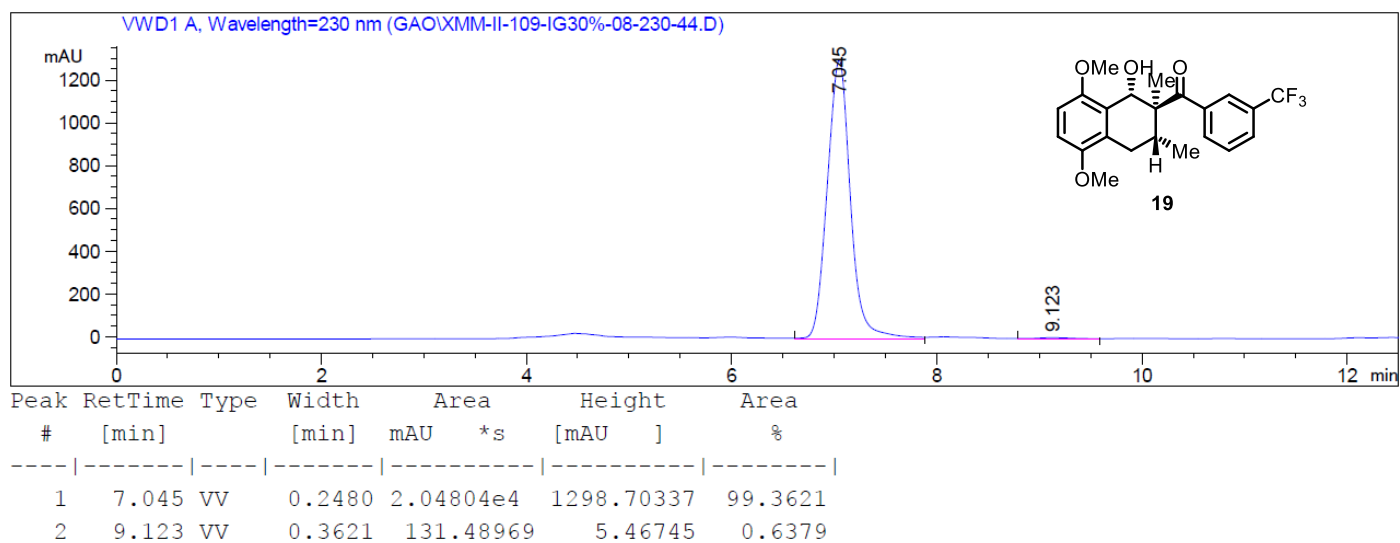
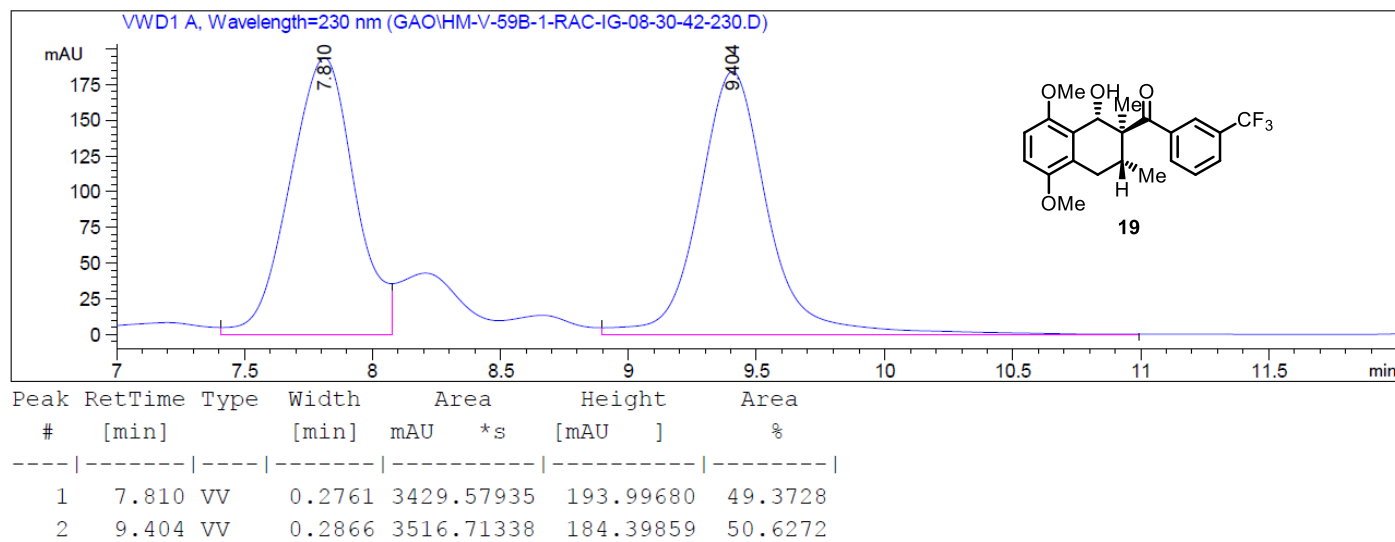


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.018	VB	0.5491	2.00868e4	590.39948	95.5540
2	11.141	BB	0.4889	934.61066	27.55549	4.4460

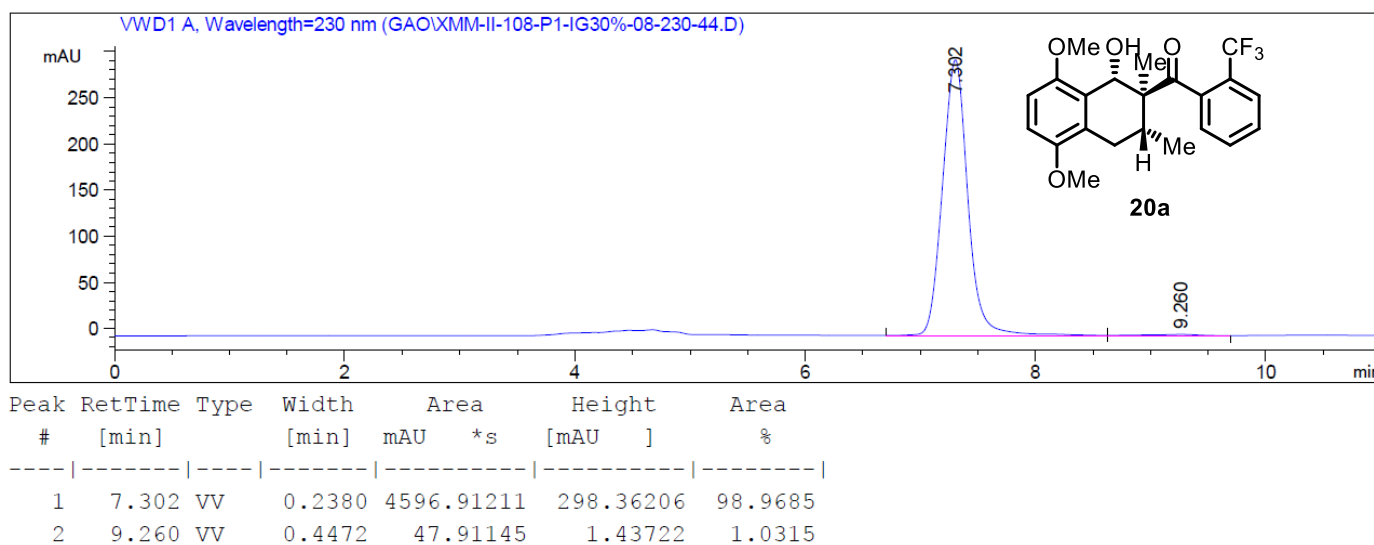
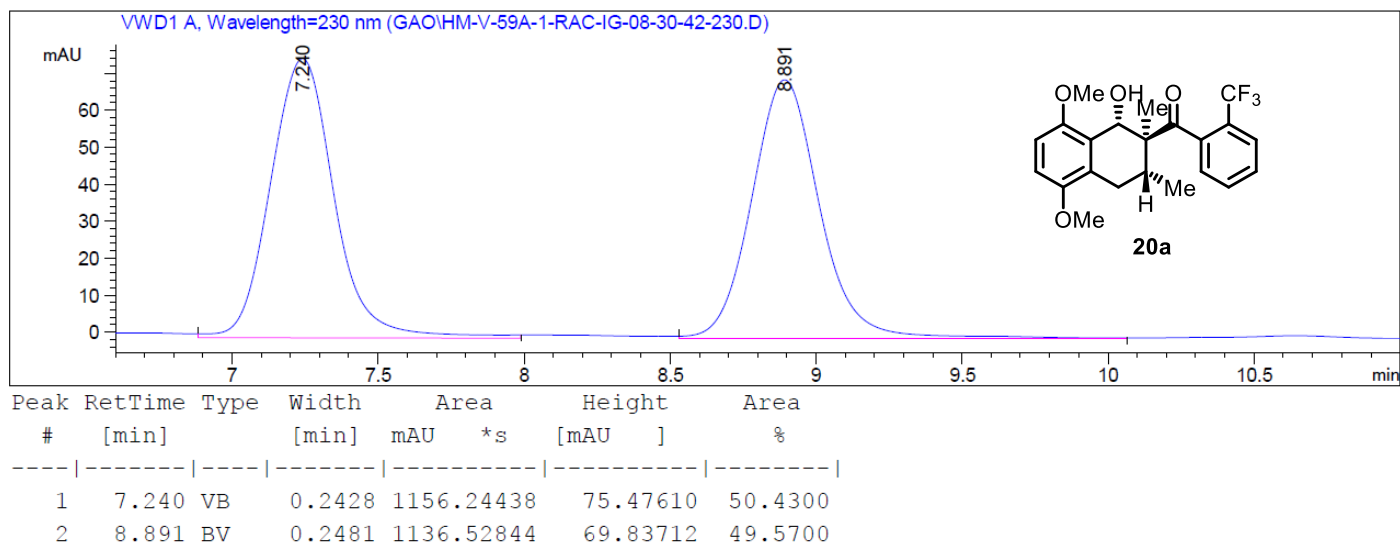
Enantiomeric excess: 91%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 95/5, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 9.018 min (major), t_R = 11.141 min (minor).



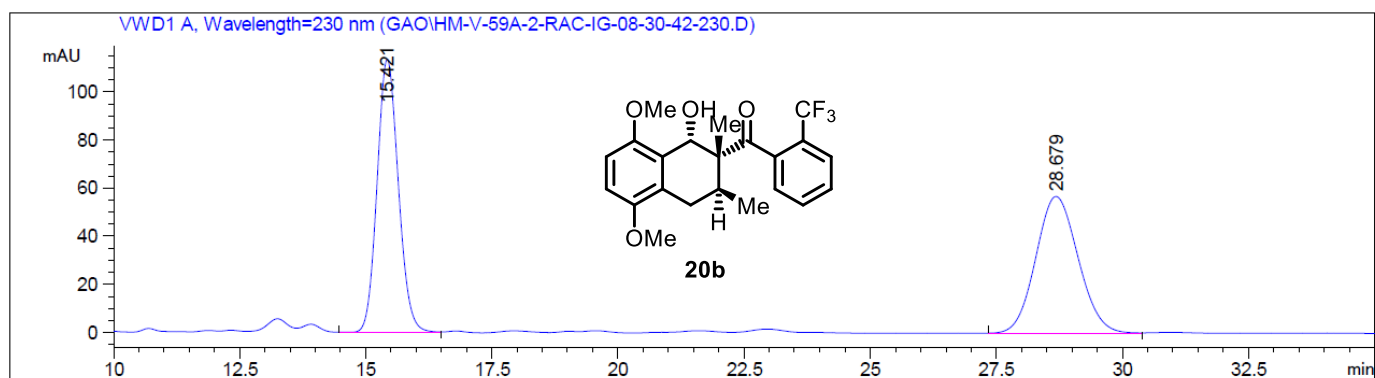
Enantiomeric excess: 99%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 7.497 min (minor), t_R = 9.044 min (major).



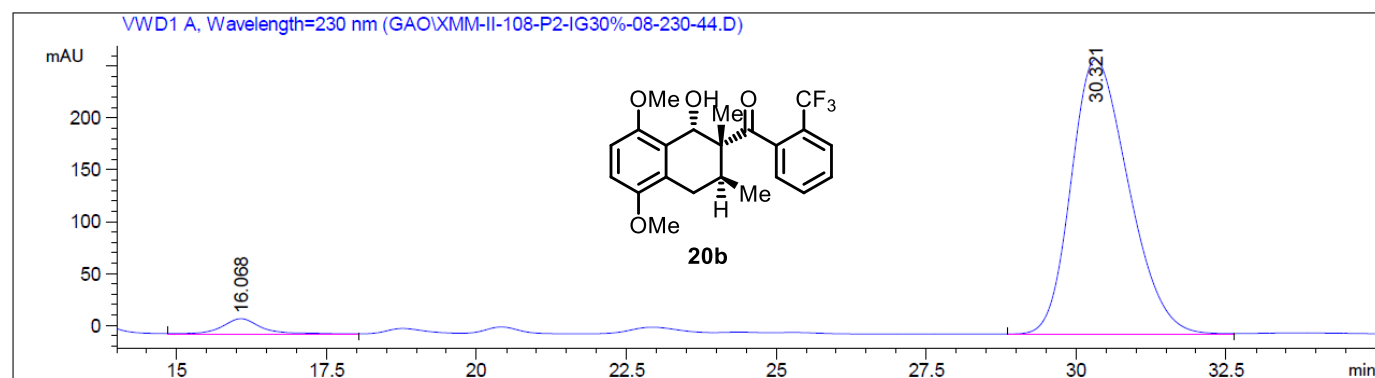
Enantiomeric excess: 99%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 7.045 min (major), t_R = 9.123 min (minor).



Enantiomeric excess: 98%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 7.302 min (major), t_R = 9.260 min (minor).

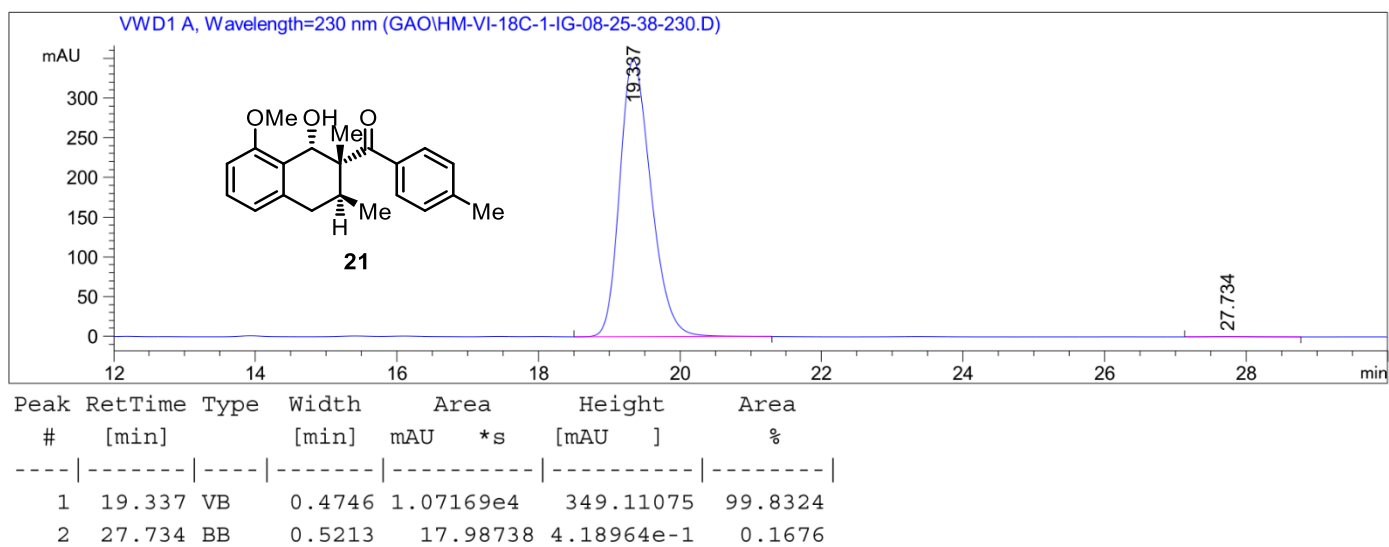
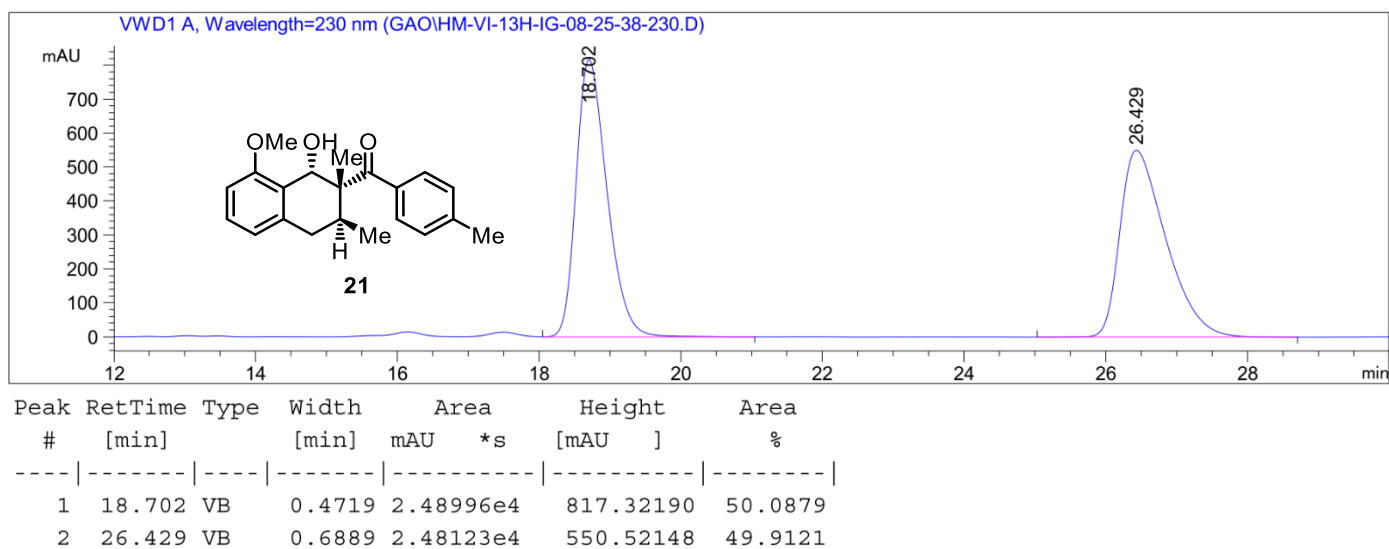


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	15.421	VV	0.4557	3364.09351		113.73121	50.3260
2	28.679	BV	0.9085	3320.50854		56.85246	49.6740

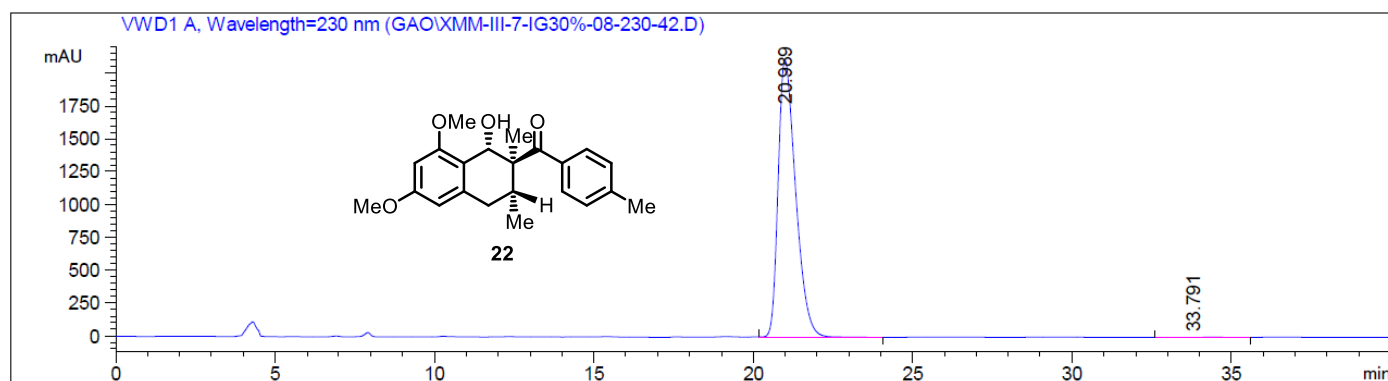
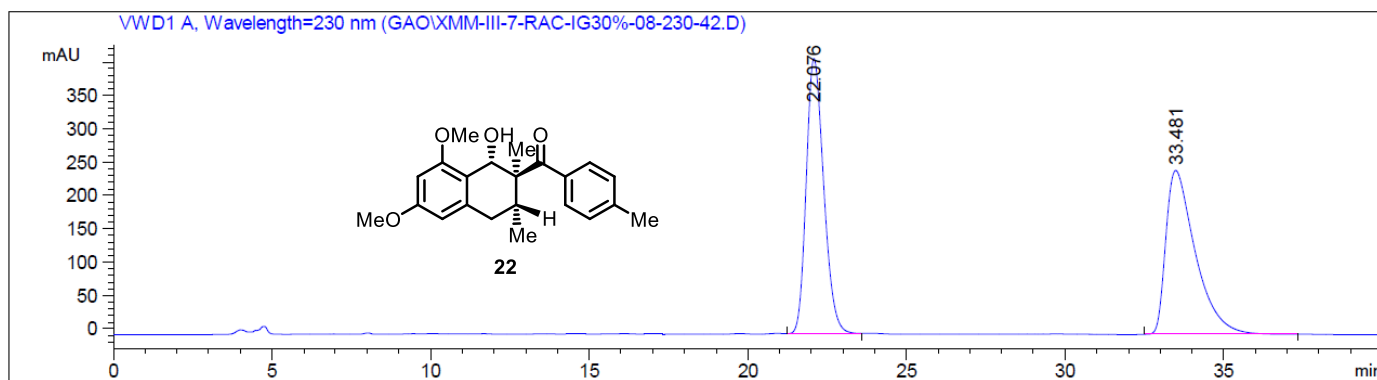


Peak #	RetTime [min]	Type	Width [min]	Area mAU	Area *s	Height [mAU]	Area %
1	16.068	VV	0.6835	699.70795		14.85572	3.8303
2	30.321	BV	1.0309	1.75678e4		264.57599	96.1697

Enantiomeric excess: 92%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 16.068 min (minor), t_R = 30.321 min (major).

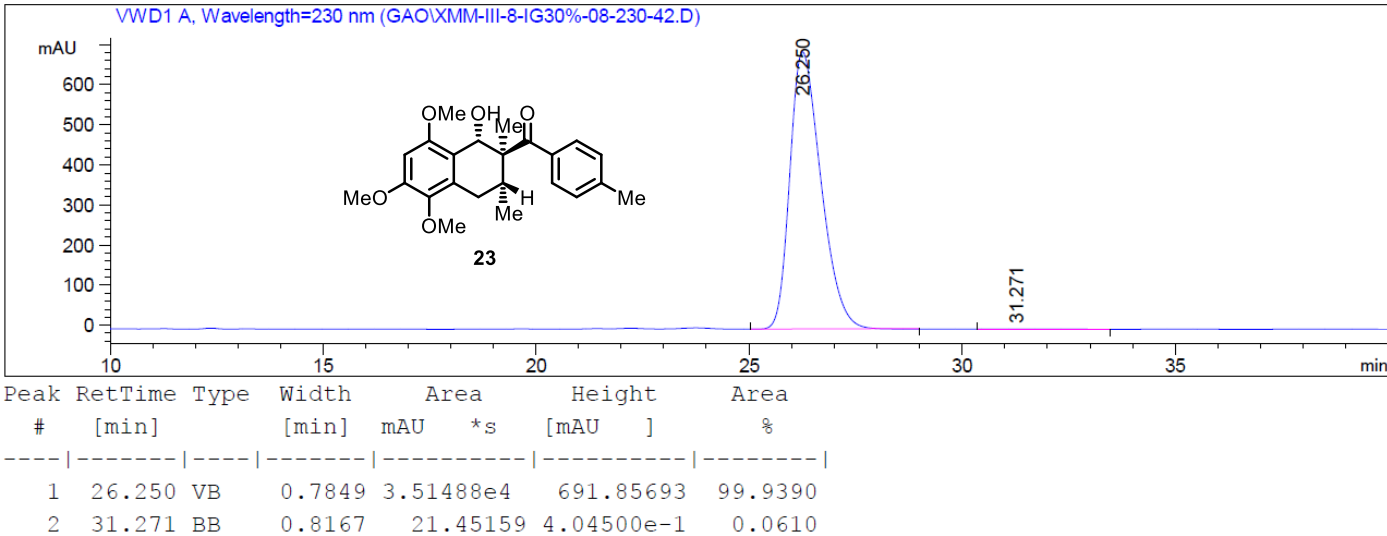


Enantiomeric excess: 99.7%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 75/ 25, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 19.337min (major), t_R = 27.734 min (minor).

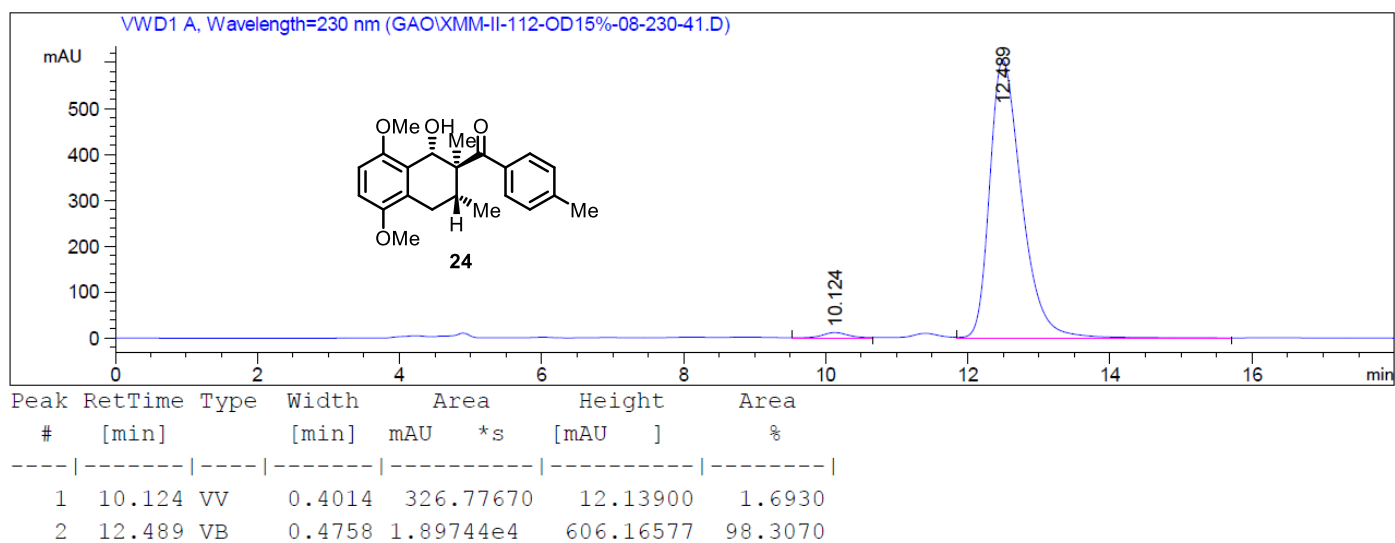
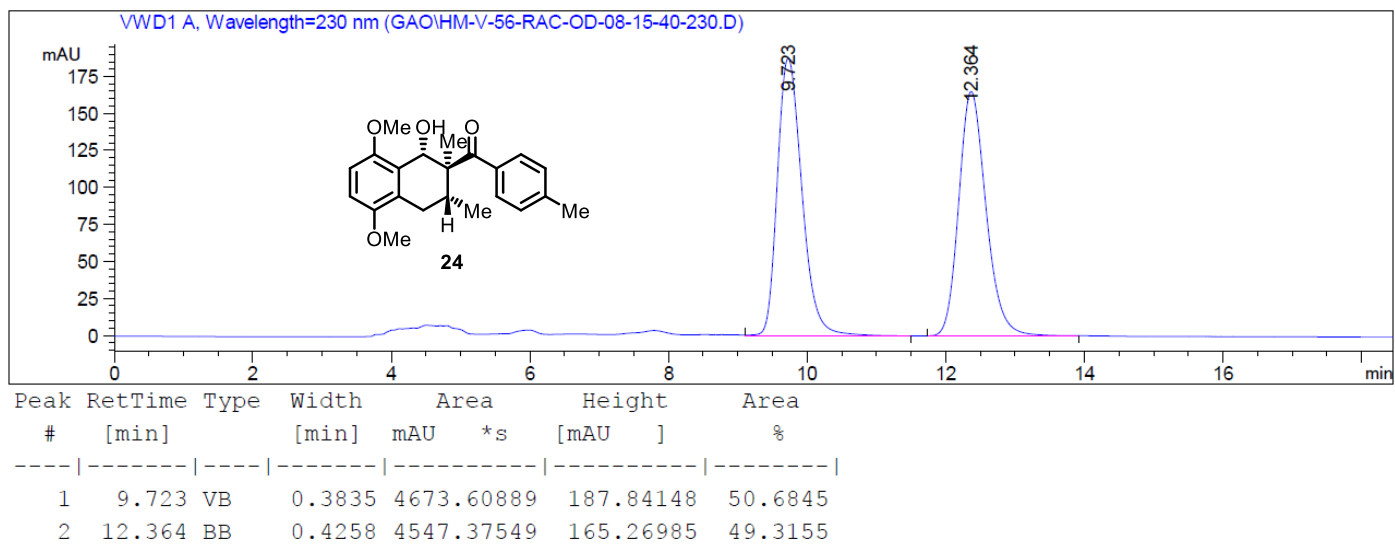


Peak #	RetTime [min]	Type	Width [min]	Area mAU	*s	Height [mAU]	Area %
1	20.989	VB	0.5846	8.04561e4		2110.25391	99.9483
2	33.791	BB	0.8272	41.60938		5.99532e-1	0.0517

Enantiomeric excess: 99.9%, determined by HPLC (Daicel Chiralpak IG, hexane/isopropanol = 70/30, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 20.989 min (major), t_R = 33.791 min (minor).



S60



Enantiomeric excess: 97%, determined by HPLC (Daicel Chiralpak OD-H, hexane/isopropanol = 85/15, flow rate 0.8 mL/min, T = 25 °C, 230 nm): t_R = 10.124 min (minor), t_R = 12.489 min (major).