Supporting Information

Synthesis of α-arylacetophenone derivatives by Grignard reactions and transformations of arynes via C–C bond cleavage

Yukitaka Hoshi, Shinya Tabata, and Suguru Yoshida*

Department of Biological Science and Technology, Faculty of Advanced Engineering, Tokyo University of Science, 6-3-1 Niijuku, Katsushika-ku Tokyo 125-8585
E-mail: s-yoshida@rs.tus.ac.jp

Contents

General Information **S1**
Structures of Substrates and Products **S2**
Experimental Procedures **S3**
Characterization Data of New Compounds **S6**
References for Supporting Information **S14**
^{1}H and ^{13}C NMR Spectra of New Compounds **S15**

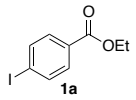
General Information

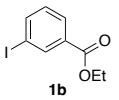
All reactions were performed with dry glassware under atmosphere of argon, unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed on precoated (0.25 mm) silica-gel plates (Merck Chemicals, Silica Gel 60 F254, Cat. No. 1.05715). Column chromatography was conducted using silica-gel (Kanto Chemical Co., Inc., Silica Gel 60N, spherical neutral, particle size 40–50 μm, Cat. No. 37562-85 or particle size 63–210 μm, Cat. No. 37565-85). Preparative TLC (PTLC) was performed on silica gel (Wako Pure Chemical Industries Ltd., Wakogel B-5F, Cat. No. 230-00043). Melting points (Mp) were measured on an OptiMelt MPA100 (Stanford Research Systems), and are uncorrected. ^{1}H NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 400 MHz. ^{13}C NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 101 MHz. ^{19}F NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 376 MHz. All NMR measurements were carried out at 25 ºC. $CDCl_3$, acetone-d_6, or DMSO-d_6 was used as a solvent for obtaining NMR spectra. Chemical shifts (δ) are given in parts per million (ppm) downfield from the solvent peak (δ 7.26 for ^{1}H NMR in $CDCl_3$, δ 77.0 for ^{13}C NMR in $CDCl_3$; δ 2.09 for ^{1}H NMR in acetone-d_6, δ 30.6 for ^{13}C NMR in acetone-d_6; δ 2.54 for ^{1}H NMR in DMSO-d_6, δ 40.5 for ^{13}C NMR in DMSO-d_6) as an internal reference with coupling constants (*J*) in hertz (Hz). The abbreviations s, d, t, q, and m signify singlet, doublet, triplet, quartet, and multiplet, respectively. IR spectra were measured on a Shimadzu IRSpirit spectrometer with the absorption band given in cm^{-1}. High-resolution mass spectra (HRMS) were measured on a JEOL JMS-T100CS "AccuTOF CS" mass spectrometer under positive electrospray ionization (ESI^{+}) conditions or negative electrospray ionization (ESI^{-}) conditions, or JMS-700 (JEOL, Tokyo, Japan) mass spectrometer under electron impact ionization (EI) conditions.

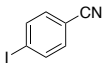
Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. 8-Oxobicyclo[4.2.0]octa-1(6),2,4-trien-2-yl trifluoromethanesulfonate (**2a**)[S1] and 2-iodo-5-methyl-1,3-phenylene bis(trifluoromethanesulfonate) (**16**)[S2] were prepared according to the reported methods.

Structures of Substrates and Products

Starting mterials shown in Figs 2–5

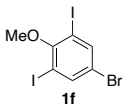

1a


1b

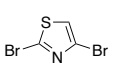

1c

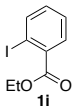

1d


1e

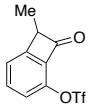

1f

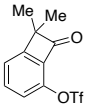

1g

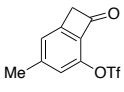

1h

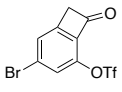

1i

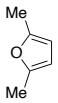

2a


2b


2c

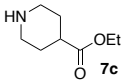

2d


2e


5

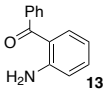

7a

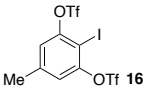

7b

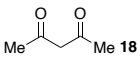

7c


9

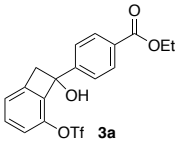

11

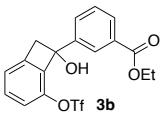

13

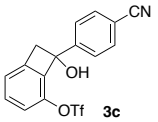

16

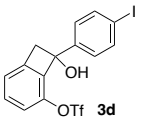

18

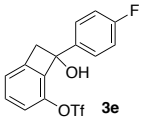
Products shown in Table 1 and Figs 2–5

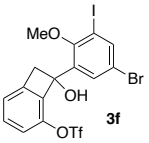

3a

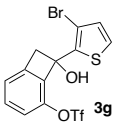

3b

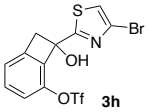

3c

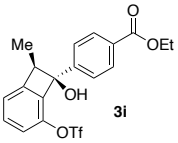

3d

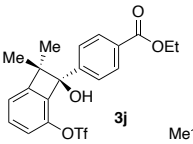

3e

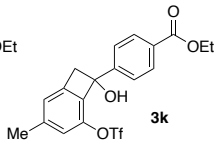

3f

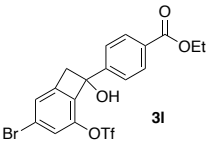

3g

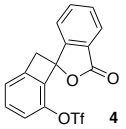

3h

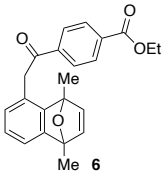

3i

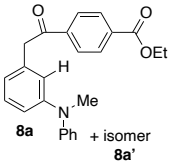

3j

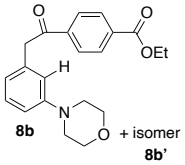

3k

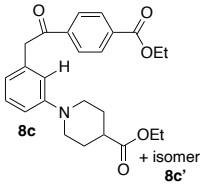

3l


4


6


8a + isomer **8a'**


8b + isomer **8b'**


8c + isomer **8c'**

8d + isomer **8d'**

10

12

14

15

3m

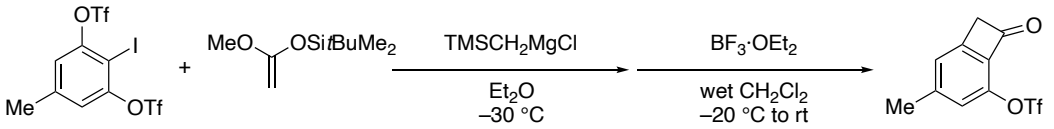
17

19

20

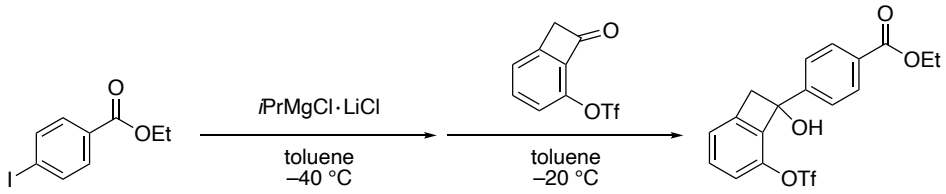
Experimental Procedures

Synthesis of 3-methyl-5-(triflyloxy)bicyclo[4.2.0]octa-1,3,5-trien-7-one



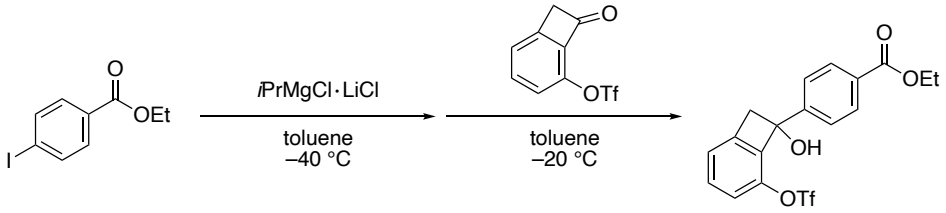
To a solution of 1,1′-(2-iodo-5-methyl-1,3-phenylene) bis(trifluoromethanesulfonate) (**16**) (514 mg, 1.00 mmol) and ketene *tert*-butyldimethylsilyl methyl acetal (**11**) (372 mg, 1.98 mmol, 2.0 equiv) dissolved in Et_2O (15 mL) was slowly added (trimethylsilyl)methylmagnesium chloride (2.0 M, Et_2O solution, 1.00 mL, 2.0 mmol, 2.0 equiv) at −30 °C. After stirring for 1 h at the same temperature, to the mixture was added an aqueous phosphate buffer solution (pH 7, 5.0 mL). The mixture was extracted with EtOAc (5 mL × 3). The combined organic extract was washed with brine (5 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. To the resulting mixture in CH_2Cl_2 (12 mL) and H_2O (12.0 μL) was slowly added boron trifluoride diethyl ether complex (0.788 mL, 6.32 mmol) at −20 °C. After gradually warming to room temperature, the mixture was stirred at room temperature for 2 h. To this was added an aqueous saturated solution of sodium bicarbonate (10 mL). The mixture was extracted with CH_2Cl_2 (5 mL × 3). The combined organic extract was washed with brine (5 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 5/1) to give 3-methyl-5-(triflyloxy)bicyclo[4.2.0]octa-1,3,5-trien-7-one (149 mg, 0.533 mmol, 53 %) as a colorless oil.

*A typical procedure for preparation of benzocyclobutenols **3***



To a solution of ethyl 4-iodobenzoate (**1a**) (99.0 μL, 0.595 mmol) in toluene (2.0 mL) was added *i*PrMgCl·LiCl (0.461 mL, 0.60 mmol, 1.3 M in THF) at –40 °C. The reaction mixture was stirred for 1 h at the same temperature. Then, the resulting solution was slowly added to a solution of 2-(triflyloxy)bicyclo[4.2.0]octa-1,3,5-triene-8-one (**2a**) (52.3 mg, 0.197 mmol) in toluene (1.0 mL) at –20 °C. After stirring for 20 min at the same temperature, to the mixture was added an aqueous phosphate buffer solution (pH 7, 10 mL). The mixture was extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 3/1) to give ethyl 4-(7-hydroxy-5-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1,3,5-trien-7-yl)benzoate (**3a**) (72.4 mg, 0.174 mmol, 87%) as a colorless oil.

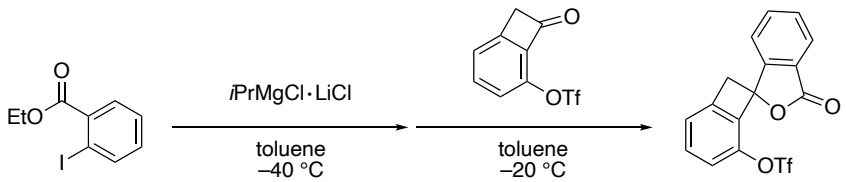
*Gram-scale synthesis of benzocyclobutenol **3a***



To a solution of ethyl 4-iodobenzoate (**1a**) (2.49 mL, 15.0 mmol) in toluene (15.0 mL) was added *i*PrMgCl·LiCl (11.5 mL, 15 mmol, 1.3 M in THF) at –40 °C. The reaction mixture was stirred for 1 h at the same temperature. Then, the resulting solution was slowly added to a solution of 2-(triflyloxy)bicyclo[4.2.0]octa-1,3,5-triene-8-one (**2a**) (1.30 g, 4.89 mmol) in toluene (5.0 mL) at –20 °C. After stirring for 20 min at the same temperature, to the mixture was added an aqueous phosphate buffer solution (pH 7, 10 mL). The mixture was extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with

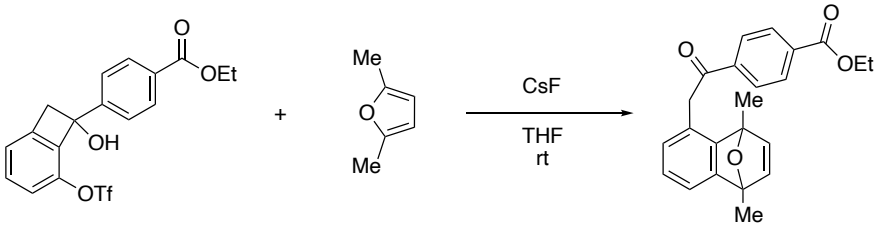
Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 3/1) to give ethyl 4-(7-hydroxy-5-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1,3,5-trien-7-yl)benzoate (**3a**) (2.00 g, 4.78 mmol, 98%) as a colorless oil.

*Preparation of lactone **4***



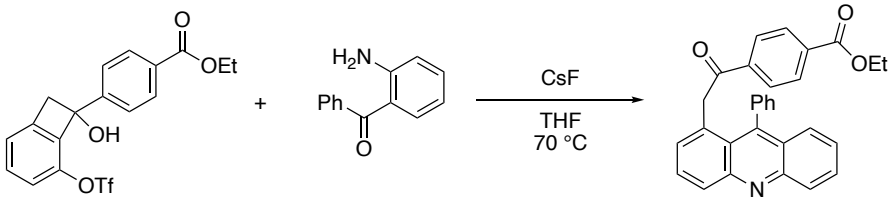
To a solution of ethyl 2-iodobenzoate (**1j**) (19.5 µL, 0.130 mmol) in toluene (1.0 mL) was added *i*PrMgCl·LiCl (0.100 mL, 0.13 mmol, 1.3 M in THF) at –40 °C. The reaction mixture was stirred for 1 h at the same temperature. Then, the resulting solution was slowly added to a solution of 2-(triflyloxy)bicyclo[4.2.0]octa-1,3,5-triene-8-one (**2a**) (28.3 mg, 0.106 mmol) in toluene (1.0 mL) at –20 °C. After stirring for 1 h at the same temperature, to the mixture was added an aqueous phosphate buffer solution (pH 7, 10 mL). The mixture was extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 3/1) to give 3'-oxo-3'*H*-spiro[bicyclo[4.2.0]octane-7,1'-isobenzofuran]-1(6),2,4-trien-5-yl trifluoromethanesulfonate (**4**) (28.3 mg, 76.5 µmol, 72%) as a colorless solid.

*A typical procedure for transformations of **3a** via aryne generation*



To a mixture of 8-hydroxy-8-(4-iodophenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3a**) (40.1 mg, 96.4 µmol) and 2,5-dimethylfuran (**5**) (48.0 mg, 0.499 mmol, 5.2 equiv) dissolved in THF (1.0 mL) was added cesium fluoride (60.4 mg, 0.398 mmol, 4.1 equiv) at room temperature. After stirring for 12 h at the same temperature, to the mixture was added an aqueous phosphate buffer solution (pH 7, 10 mL). The mixture was extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 3/1) to give ethyl 4-(2-(1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalen-5-yl)acetyl)benzoate (**6**) (31.9 mg, 88.1 µmol, 92%) as a yellow oil.

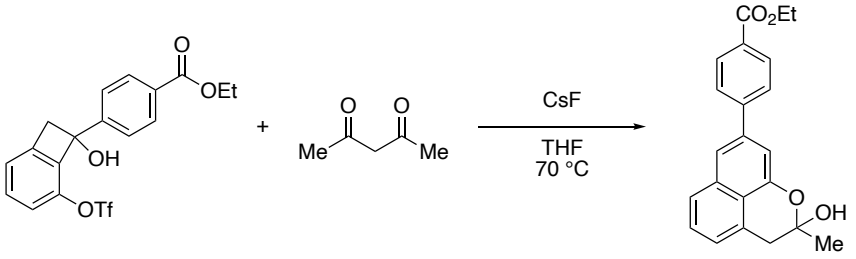
*Preparation of acridine **14***



To a mixture of 8-hydroxy-8-(4-iodophenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3a**) (39.5 mg, 95.0 µmol) and 2-aminobenzophenone (**13**) (98.6 mg, 0.499 mmol, 5.3 equiv) dissolved in THF (1.0 mL) was added cesium fluoride (60.4 mg, 0.398 mmol, 4.2 equiv) at room temperature. The mixture was stirred with heating at 70 °C (aluminum heating block) for 12 h. After cooling to room temperature, to the mixture

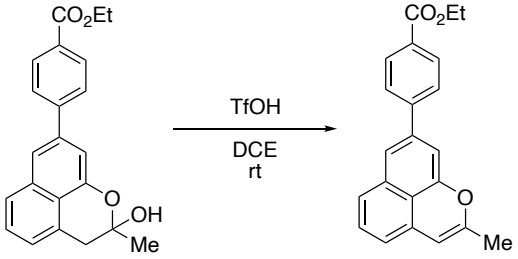
was added an aqueous phosphate buffer solution (pH 7, 10 mL). The mixture was extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 3/1) to give ethyl 4-(2-(1-benzyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzoate (**14**) (11.4 mg, 25.6 μmol, 27%) as a yellow oil.

*Preparation of benzochromene **19***



To a mixture of 8-hydroxy-8-(4-iodophenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3a**) (40.7 mg, 97.8 μmol) and acetylacetone (**18**) (50.0 mg, 0.499 mmol, 5.1 equiv) dissolved in THF (1.0 mL) was added cesium fluoride (90.6 mg, 0.596 mmol, 6.0 equiv) at room temperature. The mixture was stirred with heating at 70 °C (aluminum heating block) for 12 h. After cooling to room temperature, to the mixture was added an aqueous phosphate buffer solution (pH 7, 10 mL). The mixture was extracted with EtOAc (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 3/1) to give ethyl 4-(2-hydroxy-2-methyl-2,3-dihydrobenzo[*de*]chromen-8-yl)benzoate (**19**) (12.9 mg, 37.0 μmol, 38%) as a colorless oil.

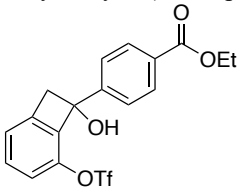
*Preparation of benzochromene **20***



To a solution of ethyl 4-(2-hydroxy-2-methyl-2,3-dihydrobenzo[*de*]chromen-8-yl)benzoate (**19**) (10.0 mg, 28.7 μmol) in 1,2-dichloroethane (DCE) (0.30 mL) was added trifluoromethanesulfonic acid (TfOH) (**6**) (1.27 μL, 14.4 μmol, 0.5 equiv) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with CH_2Cl_2 (10 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 3/1) to give ethyl 4-(2-methylbenzo[*de*]chromen-8-yl)benzoate (**20**) (7.1 mg, 22 μmol, 74%) as a green oil.

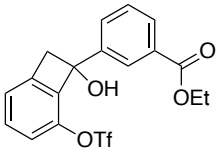
Characterization Data of New Compounds

8-Hydroxy-8-(4-iodophenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3a**)



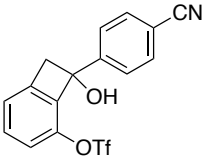
Yield: 98% (2.00 g, 4.81 mmol); Colorless oil; TLC R_f 0.54 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06–8.01 (AA'BB', 2H), 7.52–7.46 (m, 3H), 7.33 (d, 1H, *J* = 7.3 Hz), 7.15 (d, 1H, *J* = 8.5 Hz), 4.37 (q, 2H, *J* = 7.1 Hz), 3.69 (d, 1H, *J* = 14.5 Hz), 3.61–3.52 (m, 2H), 1.39 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.3, 147.1, 145.8, 141.0, 138.8, 132.2, 130.1, 129.9, 125.1, 124.8, 119.9, 118.5 (q, *J* = 321 Hz), 80.6, 61.0, 50.0, 14.3; ^{19}F{^{1}H} NMR ($CDCl_3$, 367 MHz): δ −72.7 (s); IR (NaCl, cm^{-1}) 900, 1022, 1140, 1213, 1311, 1418, 1462, 1510, 2909, 2983, 3451; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{15}F_3NaO_6S^+$ 439.0439; Found 439.0438.

Ethyl 3-(7-hydroxy-5-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)benzoate (**3b**)



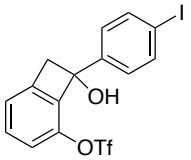
Yield: 86% (71.4 mg, 0.172 mmol); Colorless oil; TLC R_f 0.51 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14 (dd, 1H, *J* = 1.7, 1.7 Hz), 8.00 (ddd, 1H, *J* = 7.6, 1.7, 1.2 Hz), 7.63 (ddd, 1H, *J* = 7.6, 1.7, 1.2 Hz), 7.48 (dd, 1H, *J* = 8.4, 7.3 Hz), 7.43 (dd, 1H, *J* = 7.6, 7.6 Hz), 7.31 (d, 1H, *J* = 7.3 Hz), 7.15 (d, 1H, *J* = 8.4 Hz), 4.36 (q, 2H, *J* = 7.1 Hz), 3.70 (d, 1H, *J* = 7.3 Hz), 3.61 (d, 1H, *J* = 7.3 Hz), 3.61−3.52 (br, 1H, OH), 1.38 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.5, 145.8, 142.7, 141.1, 138.7, 132.2, 130.9, 129.6, 129.2, 128.7, 126.4, 124.8, 119.9, 118.2 (q, *J* = 321 Hz), 80.7, 61.2, 49.7, 14.3; ^{19}F{^{1}H} NMR ($CDCl_3$, 367 MHz): δ −72.7 (s); IR (NaCl, cm^{-1}) 841, 1022, 1115, 1212, 1371, 1404, 1590, 1704, 2984, 3507; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{15}F_3NaO_6S^+$ 439.0439; Found 439.0437.

8-(4-Cyanophenyl)bicyclo[4.2.0]octa-1(6),2,4-triene-2-yl trifluoromethanesulfonate (**3c**)



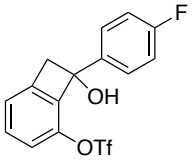
Yield: 67% (47.9 mg, 0.139 mmol); Colorless oil; TLC R_f 0.45 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.68–7.62 (AA'BB', 2H), 7.55–7.47 (m, 3H), 7.33 (d, 1H, *J* = 6.9 Hz), 7.15 (d, 1H, *J* = 8.5 Hz), 3.74–3.63 (m, 2H), 3.56 (d, 1H, *J* = 14.5 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 147.4, 145.6, 140.9, 138.3, 132.6, 132.5, 125.9, 124.9, 120.1, 118.8, 115.3 (q, *J* = 320 Hz), 111.8, 80.2, 50.2; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.7 (s); IR (NaCl, cm^{-1}) 826, 994, 1140, 1213, 1424, 1608, 2232, 3404; HRMS (ESI) m/z: $[M-H]^-$ Calcd for $C_{16}H_9F_3NO_4S^-$ 368.0210; Found 368.0207.

8-Hydroxy-8-(4-iodophenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3d**)



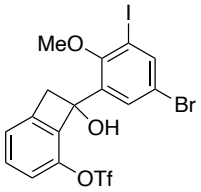
Yield: 80% (86.3 mg, 0.184 mmol); Colorless oil; TLC R_f 0.43 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72−7.65 (AA'BB', 2H), 7.47 (dd, 1H, *J* = 7.7, 7.7 Hz), 7.30 (d, 1H, *J* = 7.7 Hz), 7.20–7.11 (m, 3H), 3.66 (d, 1H, *J* = 14.4 Hz), 3.62–3.51 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 145.7, 142.0, 141.1, 138.6, 137.7, 132.2, 127.2, 124.8, 119.9, 119.0 (q, *J* = 321 Hz), 93.7, 80.6, 49.8; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.7 (s); IR (NaCl, cm^{-1}) 812, 844, 1103, 1249, 1397, 1485, 1590, 1605, 3564; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{10}F_3INaO_4S^+$ 492.9194; Found 492.9196.

8-(4-Fluorophenyl)-8-hydroxybicyclo[4.2.0]octa-1(6),2,4-trien-2-yl trifluoromethanesulfonate (**3e**)



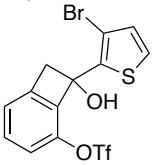
Yield: 60% (43.4 mg, 0.120 mmol); Colorless oil; TLC R_f 0.67 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.47 (dd, 1H, *J* = 8.5, 7.3 Hz), 7.44−7.37 (AA'BB', 2H), 7.30 (d, 1H, *J* = 7.3 Hz), 7.14 (d, 1H, *J* = 8.5 Hz), 7.08−7.00 (AA'BB', 2H), 3.67 (d, 1H, *J* = 14.4 Hz), 3.56 (d, 1H, *J* = 14.4 Hz), 3.49 (s, 1H, OH); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 162.4 (d, *J* = 247 Hz), 145.8, 141.1, 139.0, 138.1 (d, *J* = 3.0 Hz), 132.1, 127.0 (d, *J* = 8.1 Hz), 124.8, 119.8, 118.6 (q, *J* = 320 Hz), 115.4 (d, *J* = 21.1 Hz), 80.6, 49.8; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.8 (s, 3F), −114.4 (s, 1F); IR (NaCl, cm^{-1}) 830, 994, 1140, 1218, 1418, 1511, 1604, 3446; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{10}F_4NaO_4S^+$ 385.0134; Found 385.0134.

8-Hydroxy-8-(5-bromo-3-iodo-2-methoxyphenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3f**)



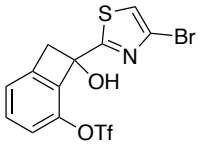
Yield: 60% (148 mg, 0.256 mmol); Colorless oil; TLC R_f 0.69 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.91 (d, 1H, *J* = 2.4 Hz), 7.52−7.43 (m, 2H), 7.28 (d, 1H, *J* = 7.2 Hz), 7.20 (d, 1H, *J* = 8.5 Hz), 3.97 (s, 1H, OH), 3.86 (s, 3H), 3.73 (d, 1H, *J* = 14.7 Hz), 3.68 (d, 1H, *J* = 14.7 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 157.7, 146.1, 142.0, 141.1, 137.8, 137.4, 132.4, 131.1, 124.9, 120.0, 118.6 (q, *J* = 332 Hz), 117.6, 93.4, 80.6, 62.3, 49.5; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.8 (s); IR (NaCl, cm^{-1}) 810, 993, 1142, 1223, 1404, 1468, 1591, 1607, 3573; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{16}H_{11}BrF_3INaO_5S^+$ 600.8405; Found 600.8408.

8-(3-Bromothiophen-2-yl)-8-hydroxybicyclo[4.2.0]octa-1,3,5-trien-2-yl trifluoromethanesulfonate (**3g**)



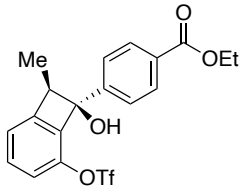
Yield: 82% (72.6 mg, 0.161 mmol); Colorless oil; TLC R_f 0.60 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.48 (dd, 1H, *J* = 8.4, 7.4 Hz), 7.28 (d, 1H, *J* = 7.4 Hz), 7.21 (d, 1H, *J* = 5.3 Hz), 7.13 (d, 1H, *J* = 8.4 Hz), 6.97 (d, 1H, *J* = 5.3 Hz), 3.99−3.92 (m, 2H), 3.75 (d, 1H, *J* = 14.5 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 146.3, 141.1, 139.4, 137.7, 132.5, 132.1, 124.73, 124.69, 119.6, 118.6 (q, *J* = 321 Hz), 107.1, 77.5, 48.8; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.6 (s); IR (NaCl, cm^{-1}) 804, 1021, 1196, 1244, 1370, 1425, 1513, 1606, 3544, 3564; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{13}H_8BrF_3NaO_4S_2^+$ 450.8897; Found 450.8893.

8-(3-Bromothiophen-2-yl)-8-hydroxybicyclo[4.2.0]octa-1,3,5-trien-2-yl trifluoromethanesulfonate (**3h**)



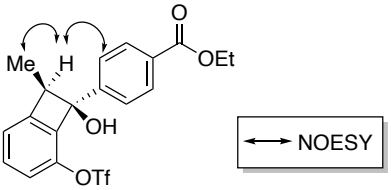
Yield: 78% (68.2 mg, 0.159 mmol); Colorless oil; TLC R_f 0.53 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59 (dd, 1H, *J* = 7.9, 7.9 Hz), 7.43 (d, 1H, *J* = 7.9 Hz), 7.37 (s, 1H), 7.21 (d, 1H, *J* = 7.9 Hz), 4.51–4.42 (br, 1H, OH), 4.15 (d, 1H, *J* = 14.4 Hz), 3.79 (d, 1H, *J* = 14.4 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 173.1, 145.6, 140.6, 137.8, 132.8, 124.3, 120.0, 118.6 (q, *J* = 321 Hz), 118.3, 116.8, 78.5, 49.2; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.6 (s); IR (NaCl, cm^{-1}) 886, 996, 1010, 1249, 1291, 1464, 1485, 1627, 1761, 3297; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_7BrF_3NNaO_4S_2^+$ 451.8850; Found 451.8853.

Ethyl 4-((7*S**,8*R**)-7-hydroxy-8-methyl-5-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)benzoate (**3i**)

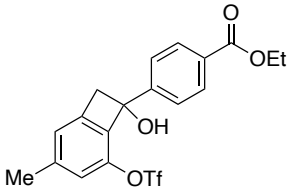


Yield: 58% (52.3 mg, 0.122 mmol); Colorless oil; TLC R_f 0.60 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05–7.97 (AA'BB', 2H), 7.52–7.40 (m, 3H), 7.29 (d, 1H, J = 7.3 Hz), 7.15 (d, 1H, J = 8.4 Hz), 4.36 (q, 2H, J = 7.1 Hz), 3.71 (q, 1H, J = 7.2 Hz), 3.49–3.40 (br, 1H, OH), 1.48 (d, 3H, J = 7.2 Hz), 1.38 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.4, 152.0, 147.9, 141.5, 137.8, 132.3, 129.8, 124.9, 123.5, 120.2, 118.6 (q, J = 321 Hz), 116.9, 81.3, 61.0, 54.4, 14.3, 14.1; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.9 (s); IR (NaCl, cm^{-1}) 833, 1020, 1049, 1085, 1216, 1362, 1651, 1723, 2982, 3480; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{17}F_3NaO_6S^+$ 453.0596; Found 453.0589.

The regiochemistry of **3i** was determined by the NOESY experiment.

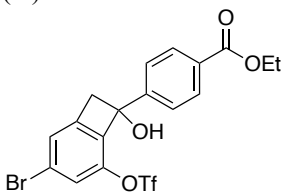


Ethyl 4-(7-hydroxy-3-methyl-5-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1,3,5-trien-7-yl)benzoate (**3k**)



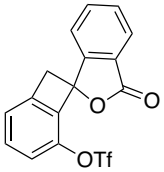
Yield: 77% (70.0 mg, 0.154 mmol); Colorless oil; TLC R_f 0.35 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.05−7.98 (AA'BB', 2H), 7.50–7.45 (AA'BB', 2H), 7.12 (s, 1H), 6.94 (s, 1H), 4.37 (q, 2H, J = 7.1 Hz), 3.64 (d, 1H, J = 14.4 Hz), 3.58–3.48 (m, 2H), 2.44 (s, 3H), 1.38 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.3, 147.4, 145.4, 143.4, 140.7, 135.4, 130.0, 129.9, 125.4, 125.1, 120.3, 118.5 (q, J = 321 Hz), 80.1, 61.0, 49.7, 21.9, 14.3; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.8 (s); IR (NaCl, cm^{-1}) 828, 852, 1104, 1236, 1419, 1452, 1614, 1715, 2930; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{17}F_3NaO_6S^+$ 453.0596; Found 453.0595.

Ethyl 4-(3-bromo-7-hydroxy-5-(((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)benzoate (**3l**)



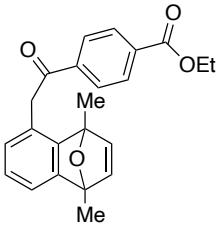
Yield: 67% (66.4 mg, 0.134 mmol); Colorless oil; TLC R_f 0.44 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06–8.01 (AA'BB', 2H), 7.50–7.43 (m, 3H), 7.34 (s, 1H), 4.37 (q, 2H, J = 7.1 Hz), 3.69 (d, 1H, J = 14.7 Hz), 3.61–3.53 (m, 2H), 1.39 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.2, 146.9, 146.4, 141.1, 137.5, 130.4, 130.0, 128.3, 125.0, 124.7, 123.5, 118.5 (q, J = 324 Hz), 80.4, 61.1, 49.8, 14.3; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.6 (s); IR (NaCl, cm^{-1}) 836, 1009, 1110, 1250, 1418, 1597, 1721, 3473; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{14}BrF_3NaO_6S^+$ 516.9544; Found 516.9536.

3'-Oxo-3'*H*-spiro[bicyclo[4.2.0]octane-7,1'-isobenzofuran]-1,3,5-trien-5-yl trifluoromethanesulfonate (**4**)



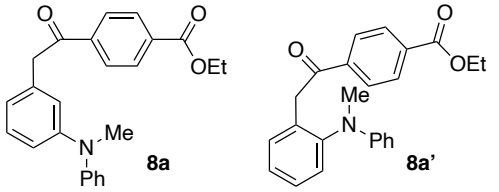
Yield: 72% (380 mg, 1.03 mmol); White solid; Mp 83–85 ºC; TLC R_f 0.41 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.97 (dd, 1H, *J* = 7.6, 1.0 Hz), 7.68 (ddd, 1H, *J* = 7.6, 7.6, 1.0 Hz), 7.61 (ddd, 1H, *J* = 7.6, 7.6, 0.9 Hz), 7.57 (dd, 1H, *J* = 8.4, 7.4 Hz), 7.38 (d, 1H, *J* = 7.4 Hz), 7.30 (dd, 1H, *J* = 7.6, 0.9 Hz), 7.21 (d, 1H, *J* = 8.4 Hz), 4.04 (d, 1H, *J* = 14.6 Hz), 3.81 (d, 1H, *J* = 14.6 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 168.9, 148.2, 144.6, 141.4, 134.7, 134.5, 133.6, 130.1, 125.7, 125.6, 123.0, 121.4, 121.0, 118.3 (q, *J* = 321 Hz), 85.3, 46.1; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −73.7 (s); IR (NaCl, cm^{-1}) 804, 1021, 1196, 1244, 1370, 1425, 1513, 1606, 3544, 3564; HRMS (ESI) m/z: [M+Na]$^+$ Calcd for $C_{16}H_9F_3NaO_5S^+$ 393.0021; Found 393.0020.

Ethyl 4-(2-(1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalen-5-yl)acetyl)benzoate (**6**)



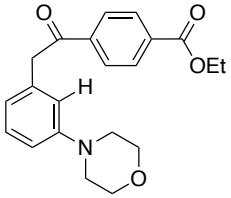
Yield: 92% (31.9 mg, 88.1 μmol); Yellow oil; TLC R_f 0.41 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.19–8.13 (AA'BB', 2H), 8.09–8.04 (AA'BB', 2H), 7.07 (d, 1H, *J* = 7.2 Hz), 6.98–6.91 (m, 2H), 6.78 (d, 1H, *J* = 5.2 Hz), 6.70 (d, 1H, *J* = 7.2 Hz), 4.53 (d, 1H, *J* = 17.4 Hz), 4.42 (q, 2H, *J* = 7.1 Hz), 4.35 (d, 1H, *J* = 17.4 Hz), 1.90 (s, 3H), 1.85 (s, 3H), 1.42 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 196.9, 165.7, 153.6. 151.4, 146.9, 146.3, 139.7, 134.6, 130.0, 128.2, 127.7, 126.0, 125.4, 117.5, 89.9, 88.1, 61.6, 42.7, 17.1, 15.3, 14.3; IR (NaCl, cm^{-1}) 840, 994, 1103, 1252, 1334, 1468, 1594, 1607; HRMS (ESI) m/z: [M+Na]$^+$ Calcd for $C_{23}H_{22}NaO_4^+$ 385.1416; Found 385.1418.

Ethyl 4-(2-(3-(methyl(phenyl)amino)phenyl)acetyl)benzoate (**8a**)
Ethyl 4-(2-(2-(methyl(phenyl)amino)phenyl)acetyl)benzoate (**8a'**)



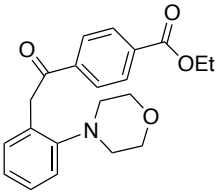
An inseparable mixture of **8a** and **8a'** (80:20) was obtained. Yield: 65% (24.2 mg, 64.9 μmol); Yellow oil; TLC R_f 0.45 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz) for **8a**: δ 8.16–8.10 (AA'BB', 2H), 8.08–8.02 (AA'BB', 2H), 7.33–7.26 (m, 2H), 7.22 (dd, 1H, *J* = 8.8, 7.6 Hz), 7.08–6.97 (m, 3H), 6.93–6.87 (m, 2H), 6.83 (d, 1H, *J* = 7.4 Hz), 4.43 (q, 2H, *J* = 8.8 Hz), 4.25 (s, 2H), 3.32 (s, 3H), 1.44 (t, 3H, *J* = 8.8 Hz); for **8a'**: δ 8.04–7.99 (AA'BB', 2H), 7.84–7.79 (AA'BB', 2H), 7.42–7.33 (m, 3H), 7.19–7.11 (m, 3H), 6.78–6.72 (AA'BB'C, 1H), 6.48–6.43 (AA'BB'C, 2H), 4.41 (q, 2H, *J* = 8.8 Hz), 4.19 (s, 2H), 3.07 (s, 3H), 1.43 (t, 3H, *J* = 8.8 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz) for **8a**: δ 197.3, 165.8, 149.3, 148.8, 139.7, 134.9, 134.2, 129.8, 129.5, 129.3, 128.5, 121.9, 121.7, 121.4, 120.5, 118.2, 61.5, 46.1, 14.3; for **8a'**: δ 197.4, 165.8, 147.0, 140.0, 134.5, 134.0, 131.6, 130.0, 129.6, 129.0, 128.2, 128.1, 126.8, 123.9, 117.8, 113.5, 61.5, 41.7, 39.5, 29.7; IR (NaCl, cm^{-1}) 1016, 1106, 1275, 1495, 1684, 1718, 2928; HRMS (ESI) *m/z*: [M+Na]$^+$ Calcd for $C_{24}H_{23}NNaO_3^+$ 396.1576; Found 396.1571.

Ethyl 4-(2-(3-morpholinophenyl)acetyl)benzoate (**8b**)



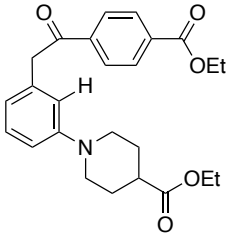
Yield: 65% (21.4 mg, 60.6 μmol); Yellow oil; TLC R_f 0.42 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15–8.08 (AA'BB', 2H), 8.08–8.01 (AA'BB', 2H), 7.26–7.20 (m, 1H), 6.83–6.75 (m, 3H), 4.40 (q, 2H, *J* = 7.1 Hz), 4.26 (s, 2H), 3.89–3.80 (m, 4H), 3.18–3.10 (m, 4H), 1.40 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 197.3, 165.7, 151.6, 139.7, 135.0, 134.2, 129.8, 129.6, 128.5, 121.0, 116.5, 114.3, 66.9, 61.5, 49.2, 46.2, 14. R (NaCl, cm^{-1}) 856, 1016, 1122, 1275, 1368, 1495, 1601, 1683, 1704; HRMS (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{24}NO_4^+$ 354.1700; Found 354.1699.

Ethyl 4-(2-(2-morpholinophenyl)acetyl)benzoate (**8b'**)



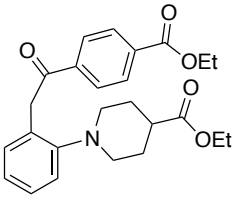
Yield: 19% (6.3 mg, 17 μmol); Yellow oil; TLC R_f 0.58 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.08−8.03 (AA'BB', 2H), 8.03−7.98 (AA'BB', 2H), 7.31−7.24 (m, 2H), 7.17−7.10 (m, 2H), 4.39 (q, 2H, *J* = 7.1 Hz), 4.30 (s, 2H), 3.70−3.61 (m, 4H), 2.81−2.72 (m, 4H), 1.40 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 197.7, 165.8, 150.7, 140.0, 133.9, 132.0, 130.9, 129.6, 128.5, 128.2, 125.2, 121.4, 66.9, 61.5, 52.6, 42.6, 14.3; IR (NaCl, cm^{-1}) 936, 1017, 1115, 1271, 1368, 1454, 1683, 1716, 1721; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{21}H_{23}NNaO_4^+$ 376.1519; Found 376.1519.

Ethyl 1-(3-(2-(4-(ethoxycarbonyl)phenyl)-2-oxoethyl)phenyl)piperidine-4-carboxylate (**8c**)



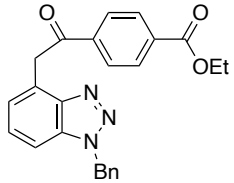
Yield: 48% (53.7 mg, 0.127 mmol); Yellow oil; TLC R_f 0.41 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14–8.07 (AA'BB', 2H), 8.07–8.00 (AA'BB', 2H), 7.19 (dd, 1H, *J* = 7.6, 7.6 Hz), 6.86–6.76 (m, 2H), 6.73 (d, 1H, *J* = 7.5 Hz), 4.39 (q, 2H, *J* = 7.1 Hz), 4.24 (s, 2H), 4.15 (q, 2H, *J* = 7.1 Hz), 3.68–3.56 (m, 2H), 2.83–2.70 (m, 2H), 2.47–2.36 (m, 1H), 2.08–1.94 (m, 2H), 1.91–1.77 (m, 2H), 1.40 (t, 3H, *J* = 7.1 Hz), 1.26 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 197.4, 174.9, 165.7, 151.9, 139.8, 134.8, 134.2, 129.8, 129.5, 128.5, 120.6, 117.5, 115.2, 61.5, 60.5, 49.1, 46.3, 41.0, 28.1, 14.29, 14.25; IR (NaCl, cm^{-1}) 857, 1017, 1106, 1206, 1271, 1368, 1385, 1646, 1737; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{29}NNaO_5^+$ 446.1943; Found 446.1942.

Ethyl 1-(2-(2-(4-(ethoxycarbonyl)phenyl)-2-oxoethyl)phenyl)piperidine-4-carboxylate (**8c'**)



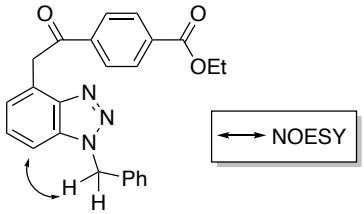
Yield: 20% (22.4 mg, 52.9 μmol); Yellow oil; TLC R_f 0.53 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.07–7.98 (m, 4H), 7.28–7.19 (m, 2H), 7.18–7.10 (m, 2H), 4.38 (q, 2H, *J* = 7.1 Hz), 4.30 (s, 2H), 4.14 (q, 2H, *J* = 7.1 Hz), 2.99–2.88 (m, 2H), 2.72–2.60 (m, 2H), 2.41–2.30 (m, 1H), 1.98–1.88 (m, 2H), 1.83–1.70 (m, 2H), 1.39 (t, 3H, *J* = 7.1 Hz), 1.25 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 197.9, 174.9, 165.9, 151.5, 139.9, 133.8, 131.5, 130.6, 129.6, 128.32, 128.25, 124.7, 121.1, 61.4, 60.4, 52.4, 42.2, 40.8, 28.5, 14.3, 14.2; IR (NaCl, cm^{-1}) 859, 1017, 1107, 1271, 1368, 1627, 1733, 3061; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{25}H_{29}NNaO_5^+$ 446.1943; Found 446.1932.

Ethyl 4-(2-(1-benzyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzoate (**10**)

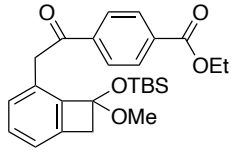


Yield: 48% (19.2 mg, 48.1 μmol); Yellow oil; TLC R_f 0.38 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24–8.19 (AA'BB', 2H), 8.17–8.11 (AA'BB', 2H), 7.41–7.24 (m, 8H), 5.87 (s, 2H), 4.93 (s, 2H), 4.42 (q, 2H, J = 7.1 Hz), 1.43 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 196.4, 165.8, 145.9, 139.6, 134.7, 134.4, 133.0, 129.8, 129.0, 128.6, 128.5, 127.7, 127.6, 126.7, 124.7, 108.7, 61.5, 52.5, 40.5, 14.3; IR (NaCl, cm^{-1})1019, 1106, 1276, 1312, 1368, 1408, 1457, 1683, 1721; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{24}H_{21}NaO_3^+$ 422.1475; Found 422.1471.

The regiochemistry of **10** was determined by the NOESY experiment.

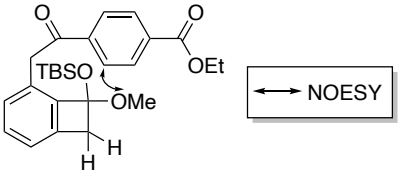


Ethyl 4-(2-(8-((*tert*-butyldimethylsilyl)oxy)-8-methoxybicyclo[4.2.0]octa-1(6),2,4-trien-2-yl)acetyl)benzoate (**12**)

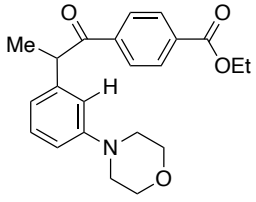


Yield: 46% (27.9 mg, 61.5 μmol); Colorless oil; TLC R_f 0.74 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.10–8.05 (m, 4H), 7.23 (dd, 1H, J = 7.6, 7.6 Hz), 7.08 (d, 1H, J = 7.6 Hz), 7.03 (d, 1H, J = 7.6 Hz), 4.43–4.26 (m, 4H), 3.54 (d, 1H, J = 13.7 Hz), 3.40 (s, 3H), 3.36 (d, 1H, J = 13.7 Hz), 1.40 (t, 3H, J = 7.1 Hz), 0.91 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 196.7, 165.8, 146.4, 141.4, 139.5, 134.2, 130.2, 129.8, 128.7, 128.0, 127.8, 122.3, 103.6, 61.4, 52.2, 47.2, 42.1, 25.7, 18.0, 14.3, −3.4, −3.8; IR (NaCl, cm^{-1}) 837, 1017, 1106, 1138, 1275, 1698, 1723, 2903; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{34}NaO_5Si^+$ 477.2073; Found 477.2079.

The regiochemistry of **12** was determined by the NOESY experiment.



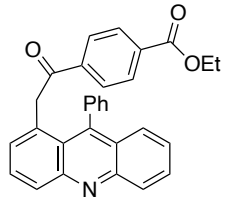
Ethyl 4-(2-(3-morpholinophenyl)propanoyl)benzoate (**8d**)



Yield: 56% (19.3 mg, 52.6 μmol); Yellow oil; TLC R_f 0.46 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.06–8.00 (AA'BB', 2H), 8.00–7.94 (AA'BB', 2H), 7.19 (dd, 1H, J = 7.7, 7.7 Hz), 6.82–6.71 (m, 3H), 4.61 (q, 1H, J = 6.8 Hz), 4.36 (q, 2H, J = 7.1 Hz), 3.88–3.78 (m, 4H), 3.16–3.06 (m, 4H), 1.53 (d, 3H, J = 6.8 Hz), 1.38 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 199.9, 165.8, 151.8, 142.0, 139.8, 133.8, 129.9, 129.6,

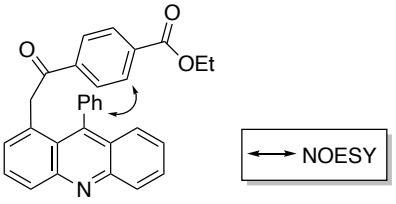
128.6, 119.5, 114.7, 114.1, 66.9, 61.4, 49.1, 48.8, 19.4, 14.3; IR (NaCl, cm^{-1}) 967, 1122, 1213, 1275, 1448, 1600, 1687, 1721, 2973; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{25}NNaO_4^+$ 390.1681; Found 390.1682.

Ethyl 4-(2-(1-benzyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzoate (**14**)

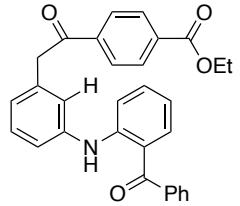


Yield: 30% (13.4 mg, 30.1 μmol); Yellow oil; TLC R_f 0.31 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.32 (d, 1H, *J* = 8.7 Hz), 8.26 (d, 1H, *J* = 8.7 Hz), 8.08–7.99 (AA'BB', 2H), 7.78–7.69 (AA'BB'C, 2H), 7.68–7.62 (AA'BB', 2H), 7.37–7.00 (m, 8H), 4.43 (q, 2H, *J* = 7.1 Hz), 4.25 (s, 2H), 1.44 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 196.7, 165.8, 149.9, 147.8, 139.5, 139.0, 134.1, 131.8, 131.2, 130.7, 130.00, 129.95, 129.4, 129.3, 129.2, 128.5 (two signals overlapped), 128.1, 127.8, 126.8, 126.5, 125.8, 124.3, 61.5, 47.0, 14.3; IR (NaCl, cm^{-1}) 856, 984, 1106, 1206, 1278, 1366, 1404, 1694, 1721; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{24}NO_3^+$ 446.1756; Found 446.1759.

The regiochemistry of **14** was determined by the NOESY experiment.

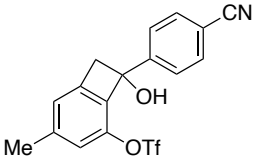


Ethyl 4-(2-(1-benzyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzoate (**15**)



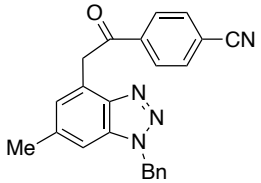
Yield: 12% (5.2 mg, 12 μmol); Yellow oil; TLC R_f 0.56 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.08 (s, 1H), 8.17–8.11 (AA'BB', 2H), 8.09–8.03 (AA'BB', 2H), 7.73–7.66 (AA'BB'C, 2H), 7.59–7.44 (m, 4H), 7.36–7.27 (m, 3H), 7.21–7.15 (m, 2H), 6.97 (d, 1H, *J* = 7.6 Hz), 6.74–6.68 (m, 1H), 4.40 (q, 2H, *J* = 7.1 Hz), 4.30 (s, 2H), 1.41 (t, 3H, *J* = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 199.2, 197.0, 165.7, 147.6, 141.1, 139.7, 139.6, 135.3, 135.0, 134.3, 134.2, 131.5, 129.9, 129.8, 129.5, 128.5, 128.2, 124.4, 122.8, 120.6, 120.1, 116.9, 114.8, 61.5, 45.9, 14.3; IR (NaCl, cm^{-1}) 1106, 1275, 1447, 1511, 1574, 1683, 1721, 2362; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{26}NO_4^+$ 464.1856; Found 464.1864.

8-(4-Cyanophenyl)bicyclo[4.2.0]octa-1(6),2,4-triene-2,8-diyl bis(trifluoromethanesulfonate) (**3m**)



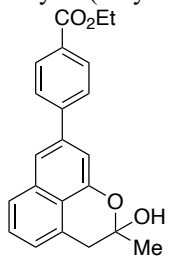
Yield: 56% (32.4 mg, 84.6 mmol); Colorless oil; TLC R_f 0.48 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.66–7.61 (AA'BB', 2H), 7.54–7.48 (AA'BB', 2H), 7.14 (s, 1H), 6.95 (s, 1H), 3.68–3.57 (m, 2H), 3.49 (d, 1H, *J* = 14.5 Hz), 2.45 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 147.8, 145.2, 143.8, 140.7, 135.0, 132.4, 125.9, 125.5, 122.4 (q, *J* = 333 Hz), 120.5, 118.7, 111.7, 79.7, 50.0, 22.0; ^{19}F{^{1}H} NMR ($CDCl_3$, 377 MHz): δ −72.7 (s); IR (NaCl, cm^{-1}) 824, 850, 1016, 1140, 1213, 1242, 1422, 1611, 2232, 3418; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{12}F_3NNaO_4S^+$ 406.0337; Found 406.0328.

4-(2-(1-Benzyl-6-methyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzonitrile (**17**)



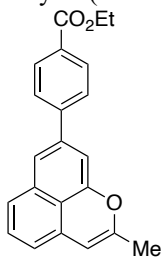
Yield: 39% (9.2 mg, 25 μmol); Pale yellow oil; TLC R_f 0.30 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.30–8.24 (AA'BB', 2H), 7.80–7.75 (AA'BB', 2H), 7.40–7.26 (m, 5H), 7.08 (s, 1H), 7.07 (s, 1H), 5.81 (s, 2H), 4.84 (s, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 195.8, 139.3, 138.4, 134.7, 133.5, 132.8, 132.6, 129.2, 129.0, 128.5, 127.6, 126.9, 125.3, 118.0, 116.5, 108.1, 52.2, 40.3, 22.0; IR (NaCl, cm^{-1}) 828, 997, 1095, 1211, 1329, 1404, 1730, 2231, 2952; HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{23}H_{18}N_4NaO^+$ 389.1378; Found 389.1375.

Ethyl 4-(2-hydroxy-2-methyl-2,3-dihydrobenzo[*de*]chromen-8-yl)benzoate (**19**)



Yield: 38% (12.9 mg, 37.0 μmol); Colorless oil; TLC R_f 0.39 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.16–8.08 (AA'BB', 2H), 7.81–7.67 (m, 4H), 7.47 (dd, 1H, J = 7.6, 7.6 Hz), 7.27–7.19 (m, 2H), 4.41 (q, 2H, J = 7.1 Hz), 3.41 (d, 1H, J = 16.0 Hz), 3.32 (d, 1H, J = 16.0 Hz), 3.14–3.05 (br, 1H, OH), 1.81 (s, 3H), 1.42 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.6, 151.0, 145.4, 138.8, 133.9, 130.1, 129.3, 128.1, 127.2, 127.1, 126.6, 124.4, 120.2, 119.1, 110.4, 97.4, 61.0, 39.8, 28.1, 14.4; IR (NaCl, cm^{-1}) 801, 906, 1085, 1106, 1276, 1387, 1605, 1714, 2923; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}O_4^+$ 349.1434; Found 349.1439.

Ethyl 4-(2-methylbenzo[*de*]chromen-8-yl)benzoate (**20**)



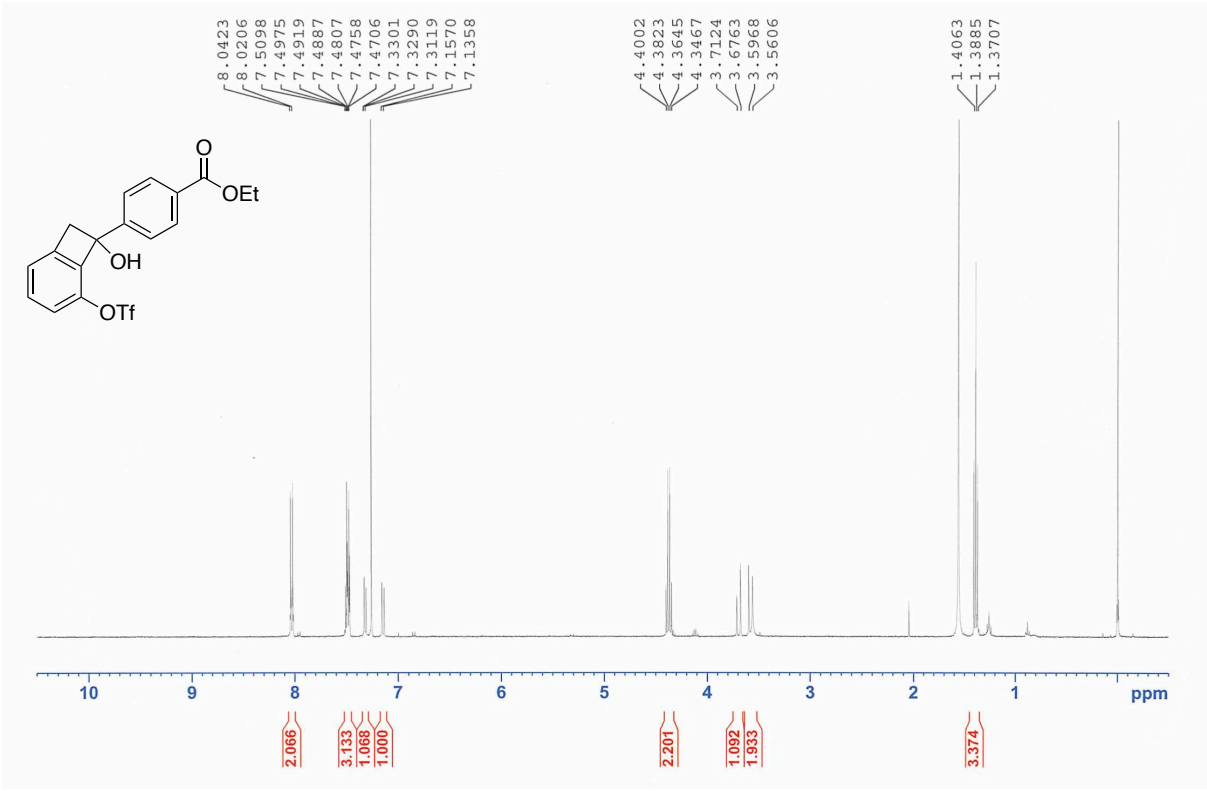
Yield: 74% (7.1 mg, 22 μmol); Green oil; TLC R_f 0.81 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.15–8.08 (AA'BB', 2H), 7.74–7.67 (AA'BB', 2H), 7.44 (d, 1H, J = 1.6 Hz), 7.35 (d, 1H, J = 8.3 Hz), 7.22 (dd, 1H, J = 8.3, 7.0 Hz), 6.99 (d, 1H, J = 1.6 Hz), 6.64 (d, 1H, J = 7.0 Hz), 5.81 (s, 1H), 4.41 (q, 2H, J = 7.1 Hz), 2.08 (s, 3H), 1.42 (t, 3H, J = 7.1 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$, 101 MHz): δ 166.5, 153.8, 153.1, 145.4, 139.2, 134.9, 130.2, 130.1, 129.4, 128.5, 127.1, 123.1, 122.4, 118.0, 114.8, 106.1, 103.7, 61.0, 19.6, 14.4; IR (NaCl, cm^{-1}) 820, 943, 1020, 1105, 1275, 1314, 1594, 1610, 1714, 2922; HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{19}O_3^+$ 331.1329; Found 331.1329.

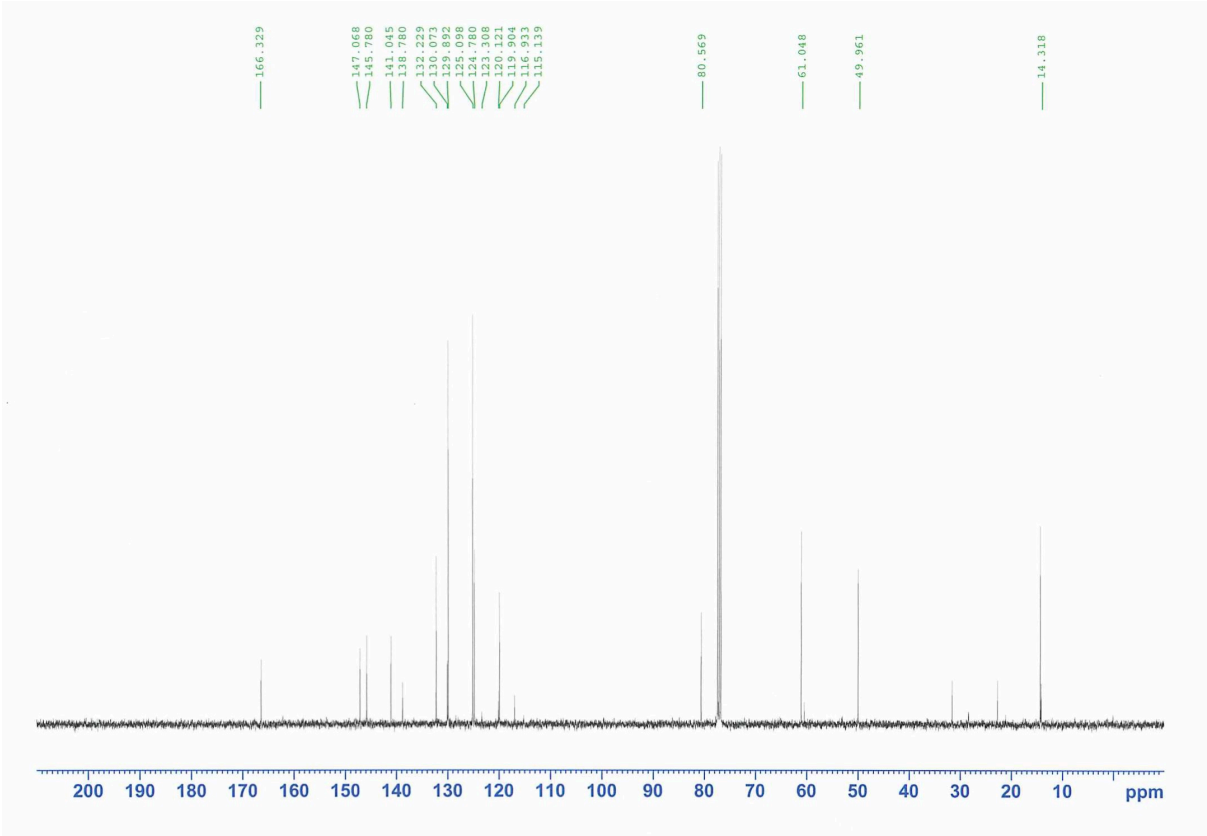
References for Supporting Information

S1 S. Yoshida, K. Uchida, K. Igawa, K. Tomooka, T. Hosoya, *Chem. Commun.* **2014**, *50*, 15059.
S2 K. Uchida, S. Yoshida, T. Hosoya, *Synthesis* **2016**, *48*, 4099.

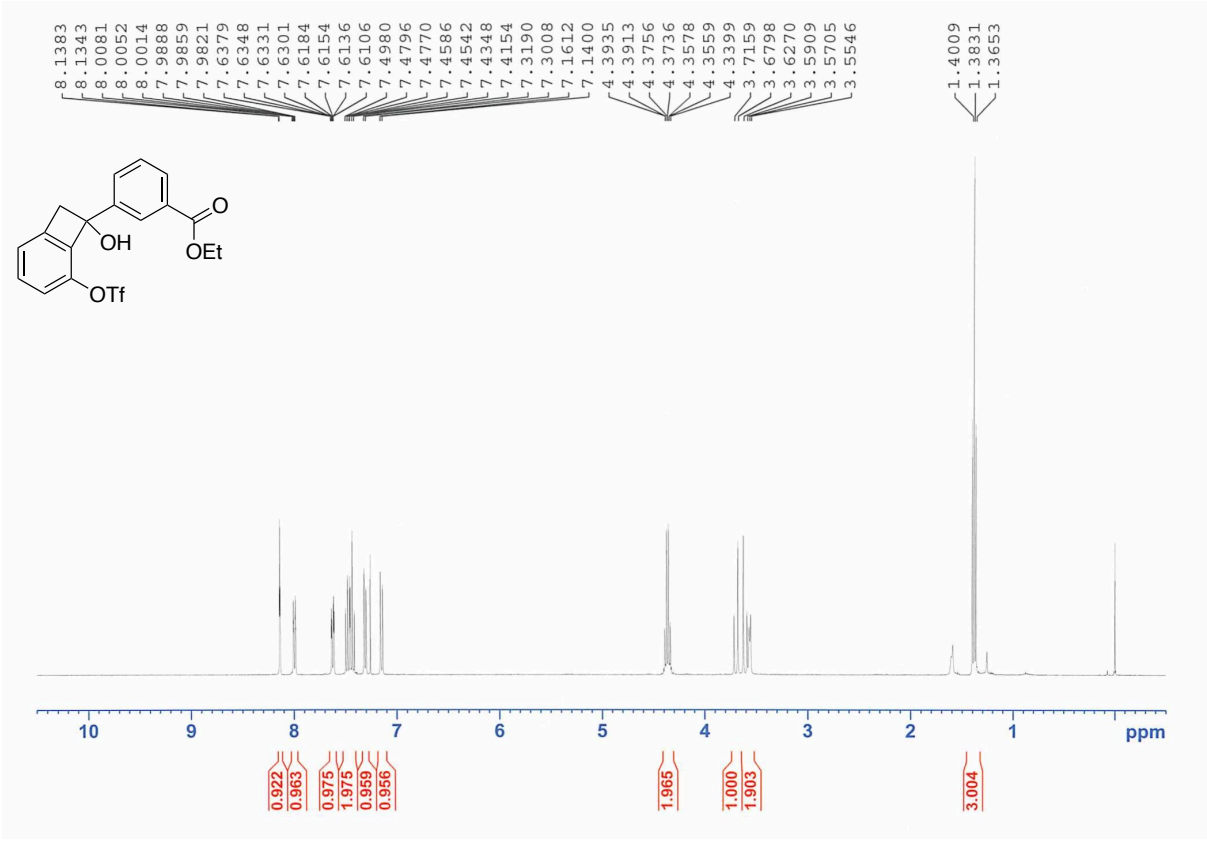
^{1}H and ^{13}C NMR Spectra of New Compounds

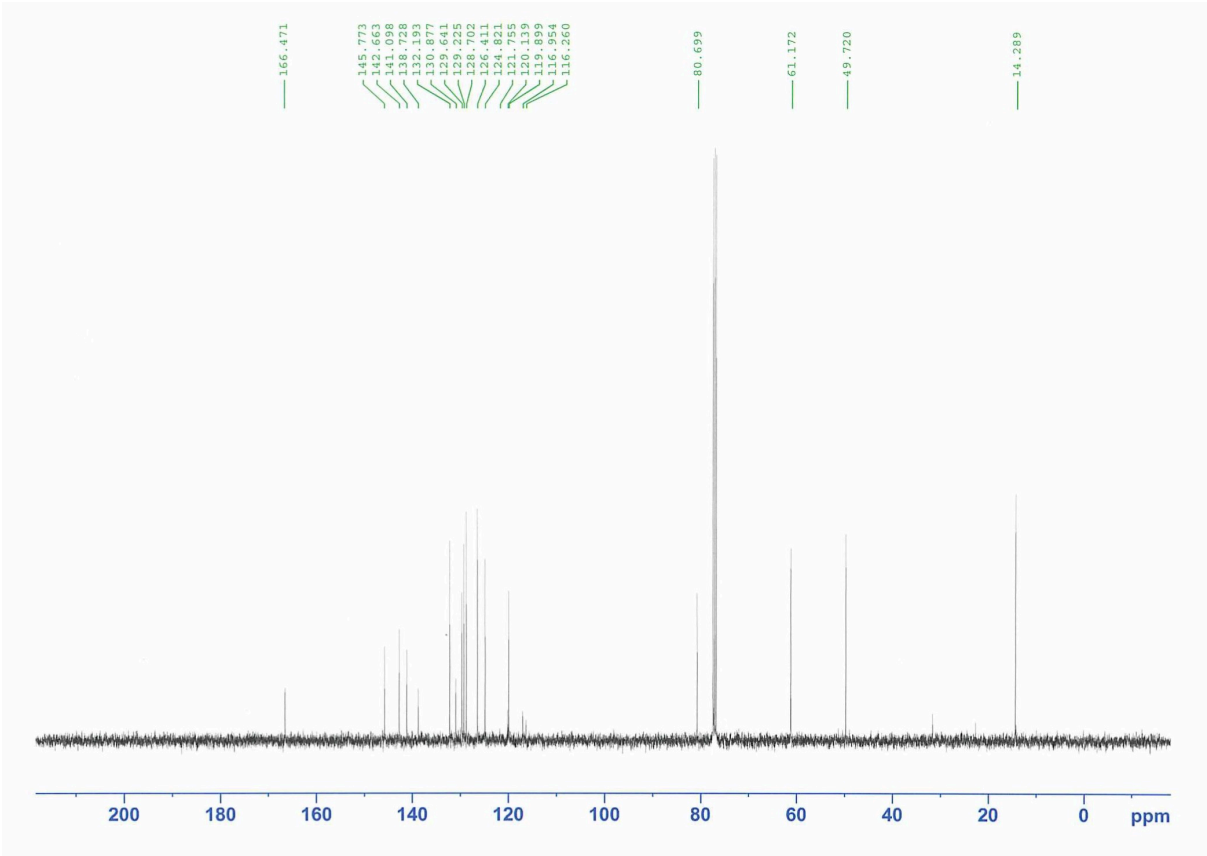
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-hydroxy-8-(4-iodophenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3a**) ($CDCl_3$)



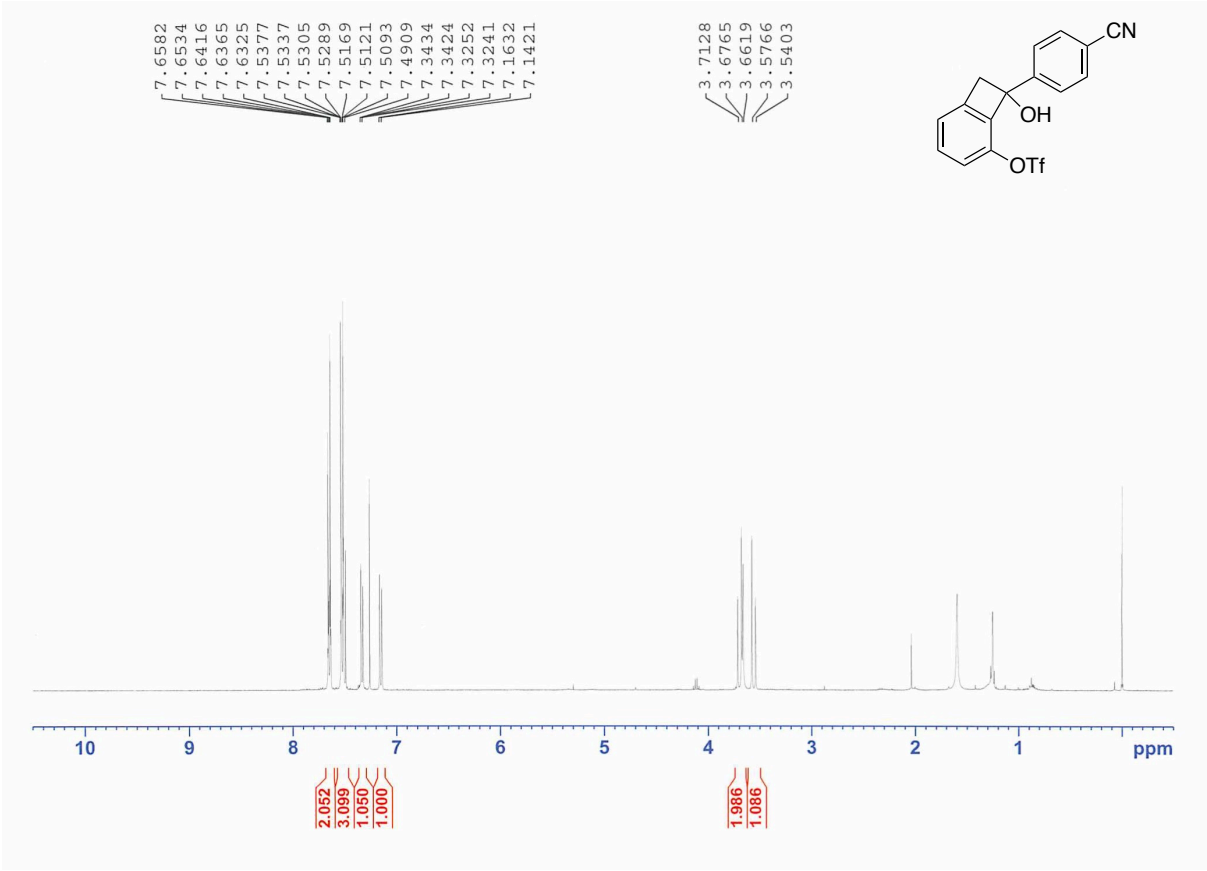


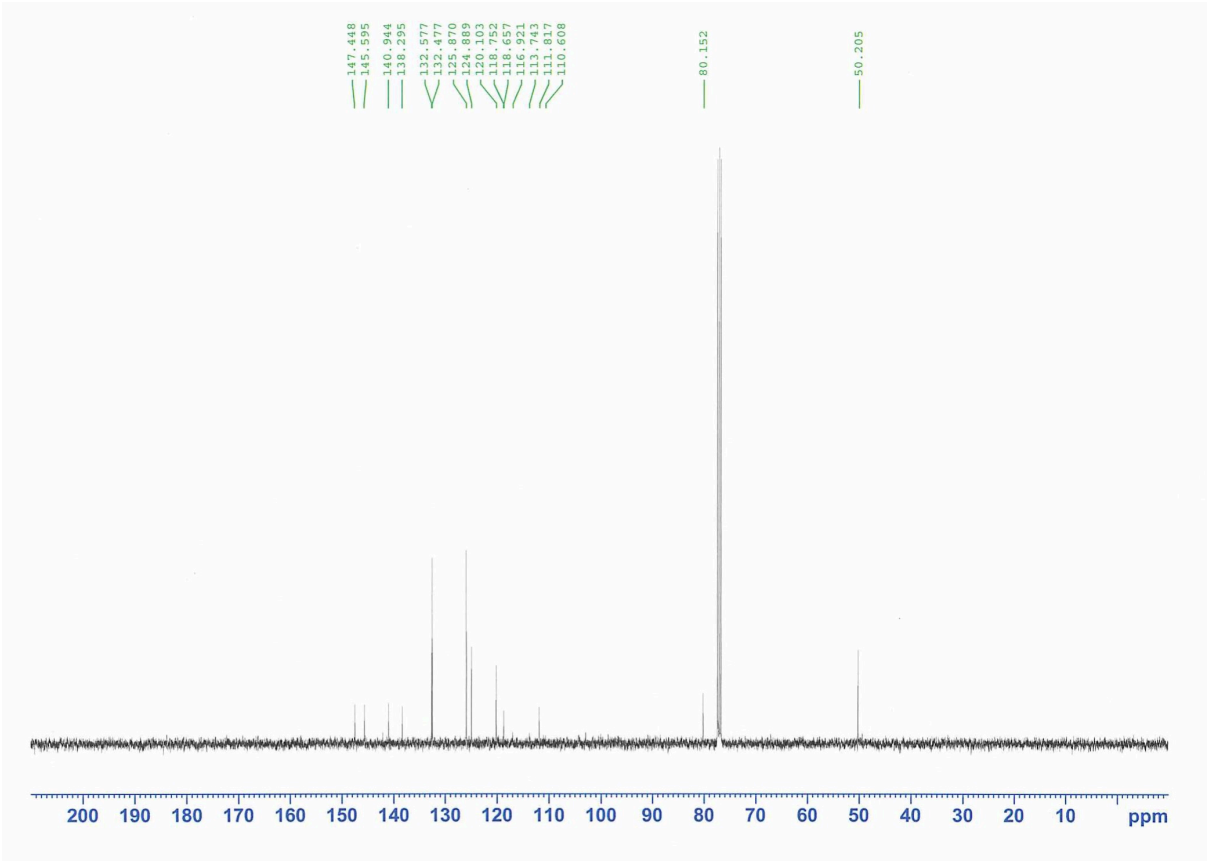
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 3-(7-hydroxy-5-((((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)benzoate (**3b**) ($CDCl_3$)



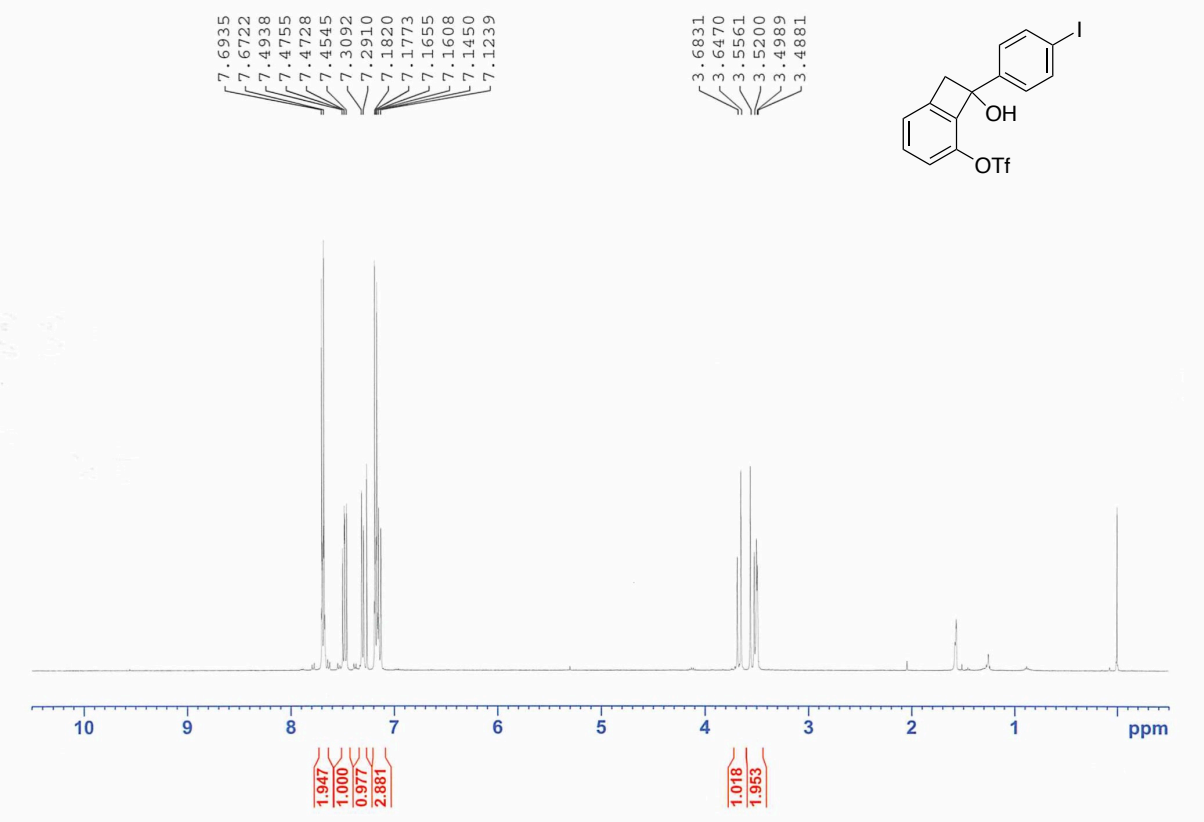


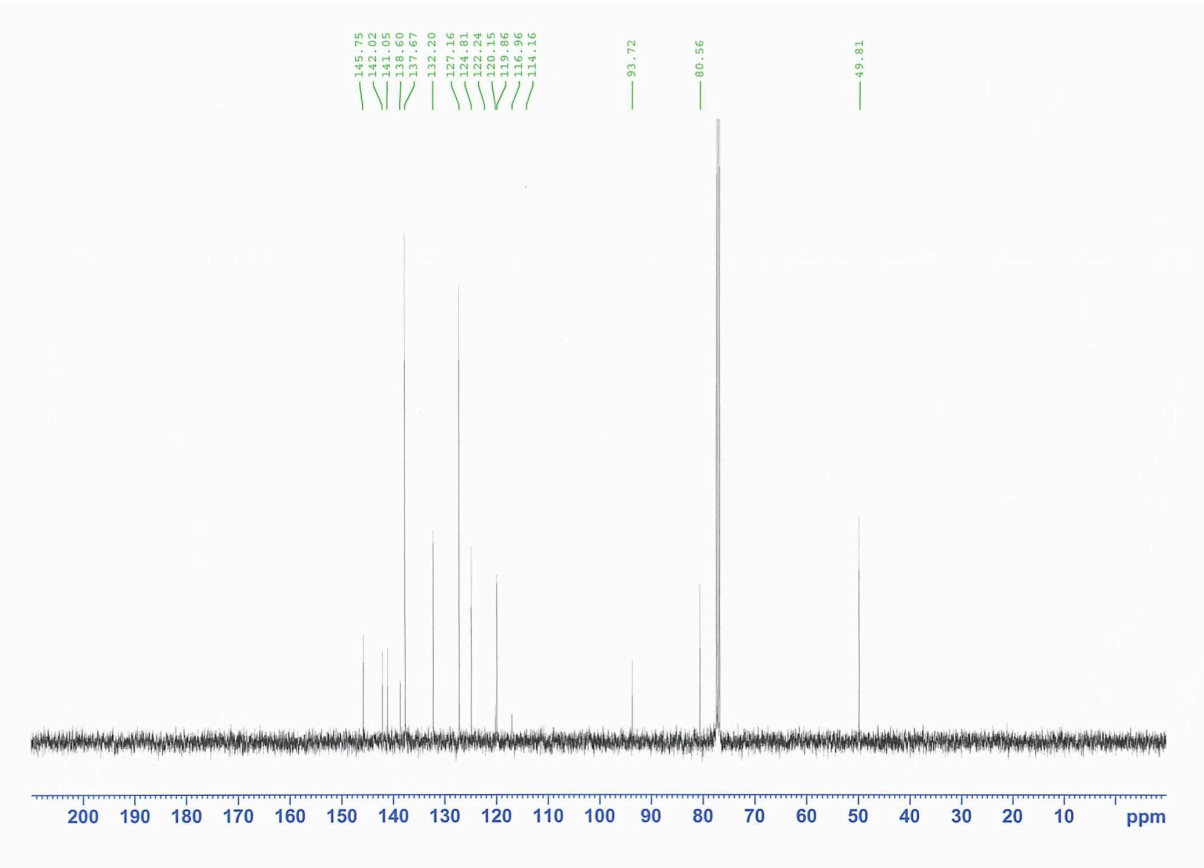
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-(4-cyanophenyl)bicyclo[4.2.0]octa-1(6),2,4-triene-2-yl trifluoromethanesulfonate (**3c**) ($CDCl_3$)



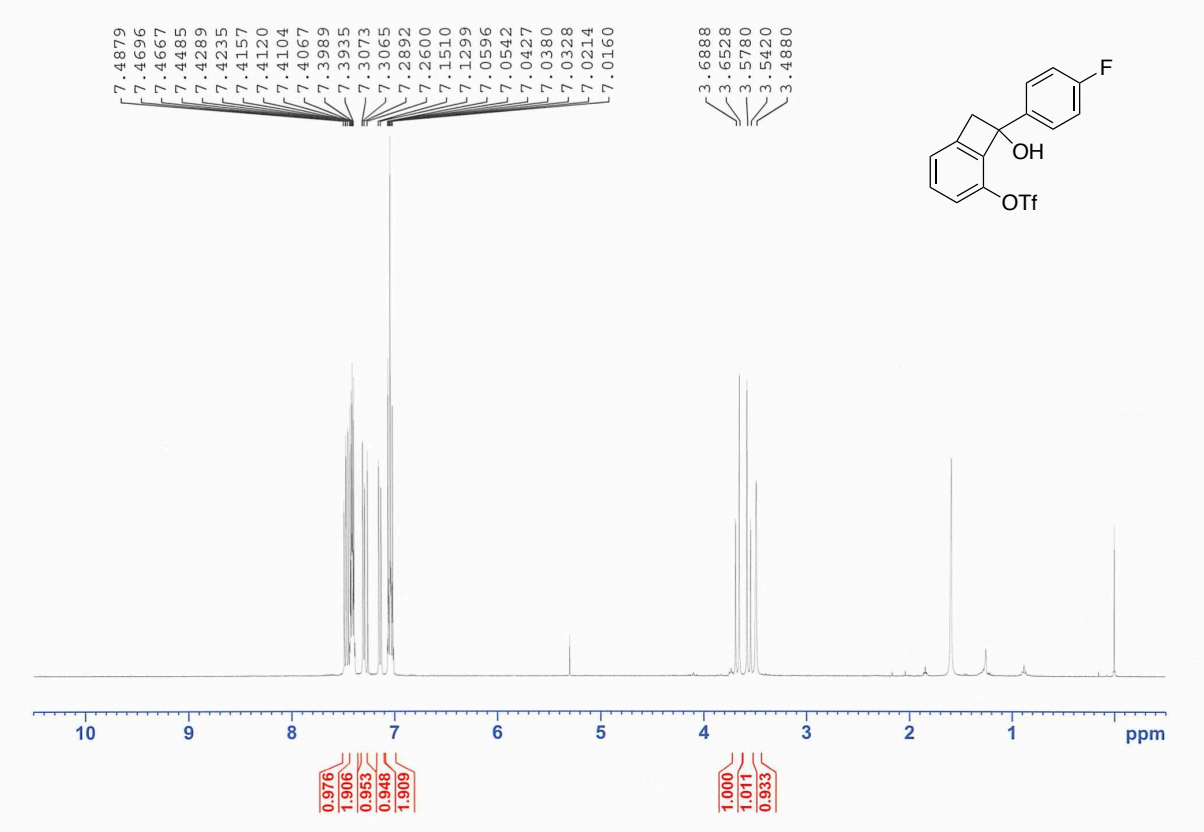


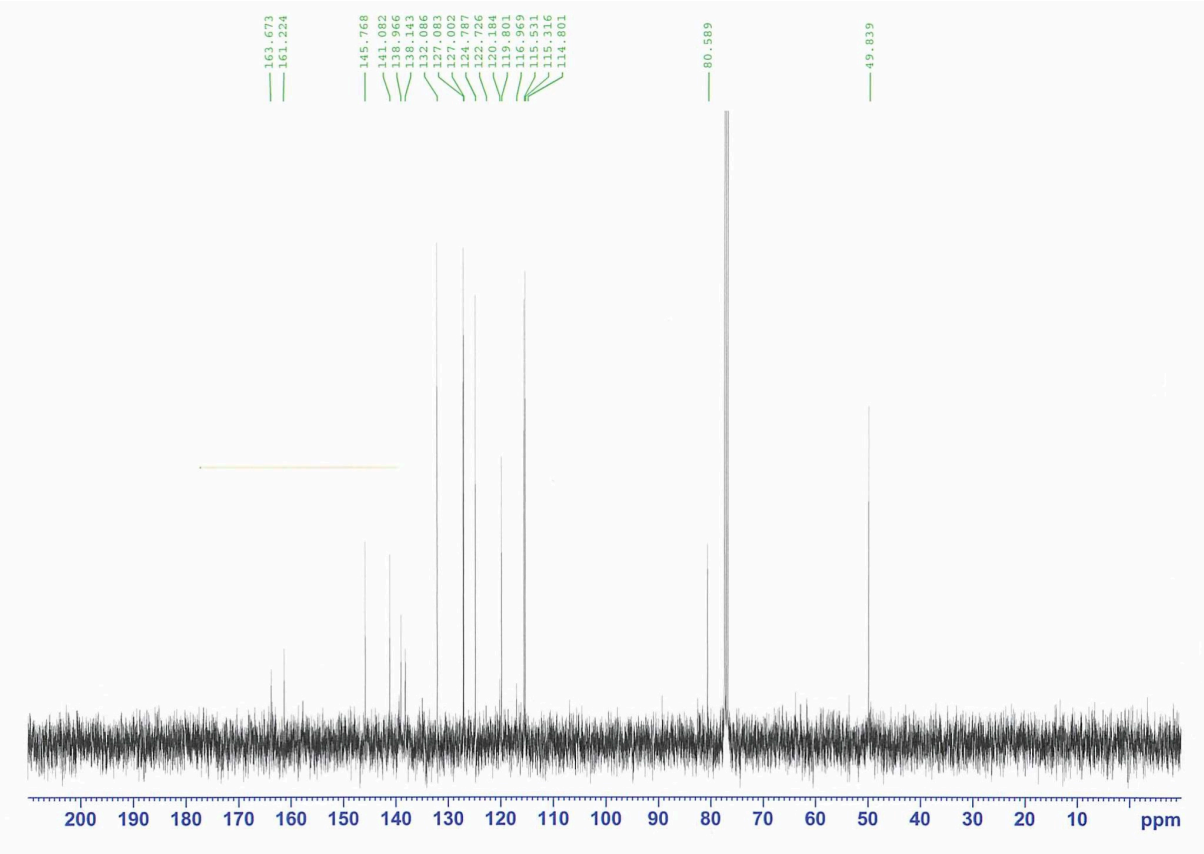
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-hydroxy-8-(4-iodophenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3d**) ($CDCl_3$)



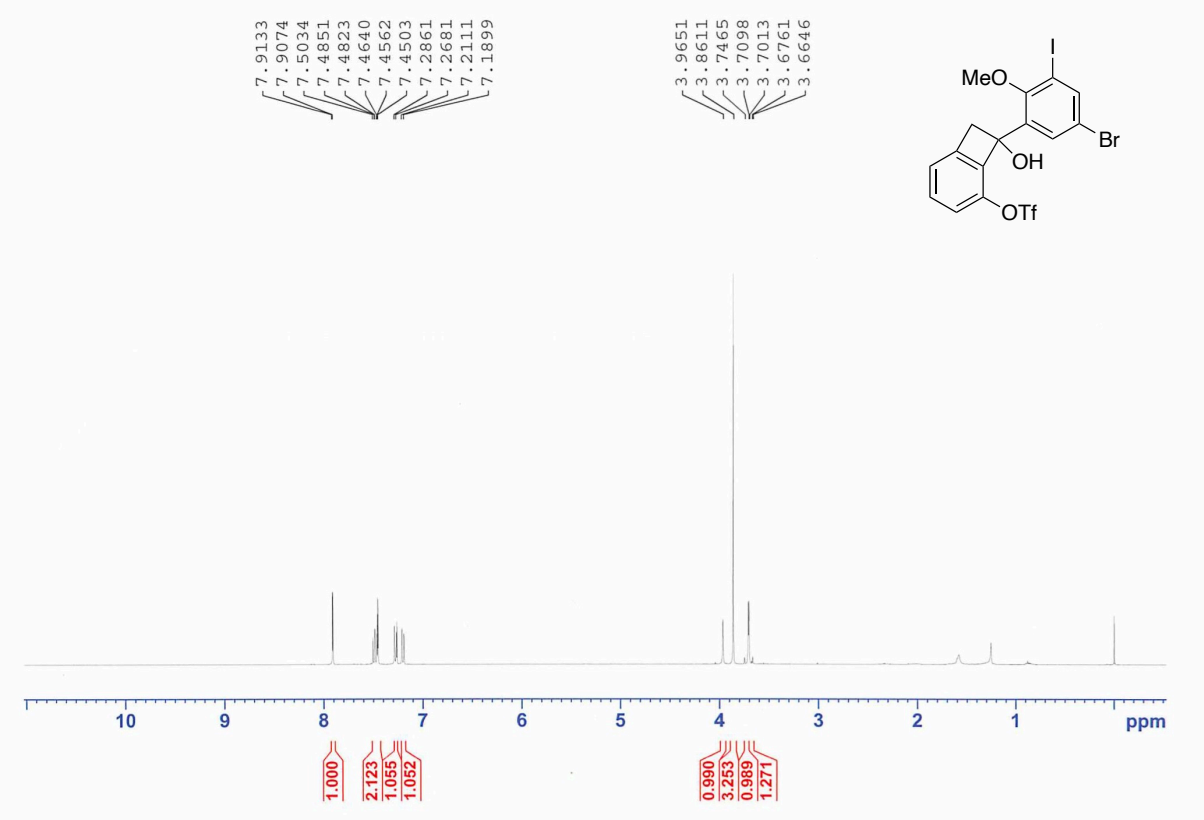


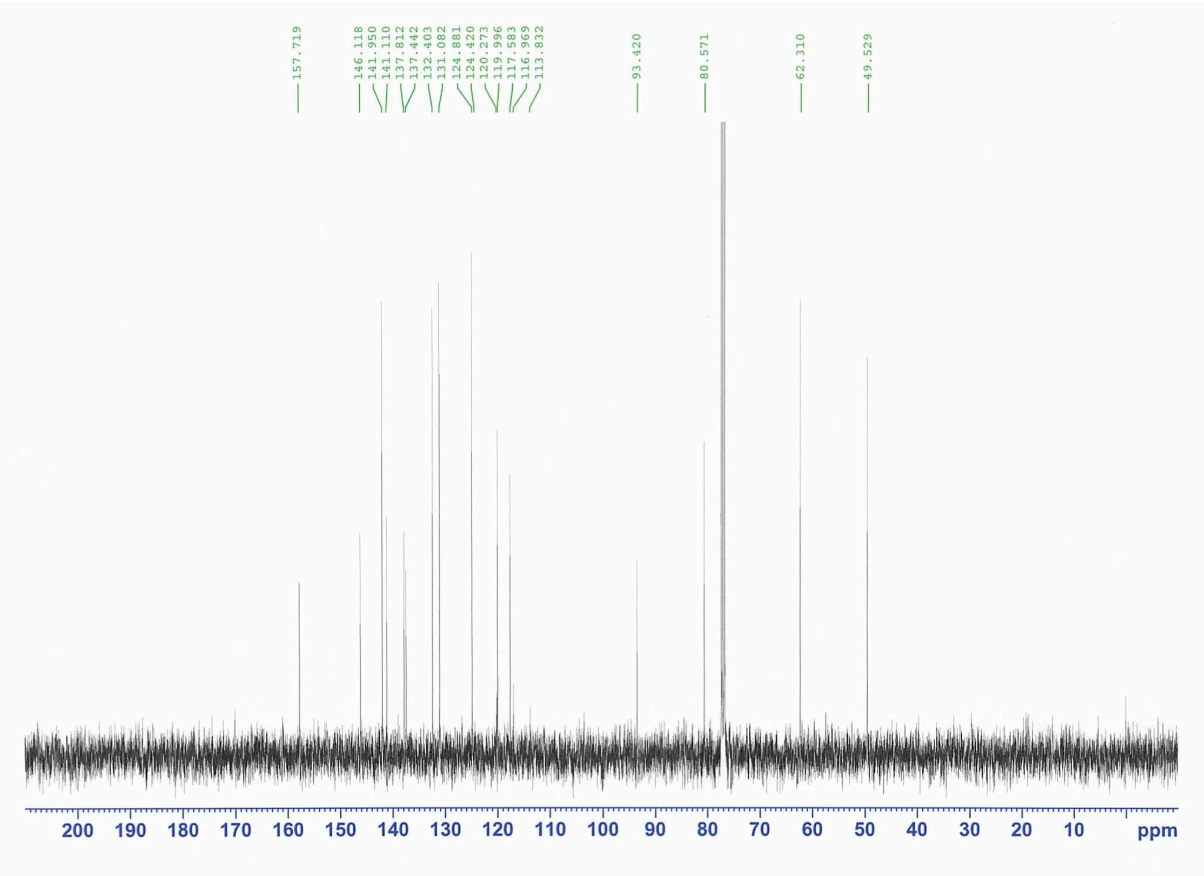
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-(4-fluorophenyl)-8-hydroxybicyclo[4.2.0]octa-1(6),2,4-trien-2-yl trifluoromethanesulfonate (**3e**) ($CDCl_3$)



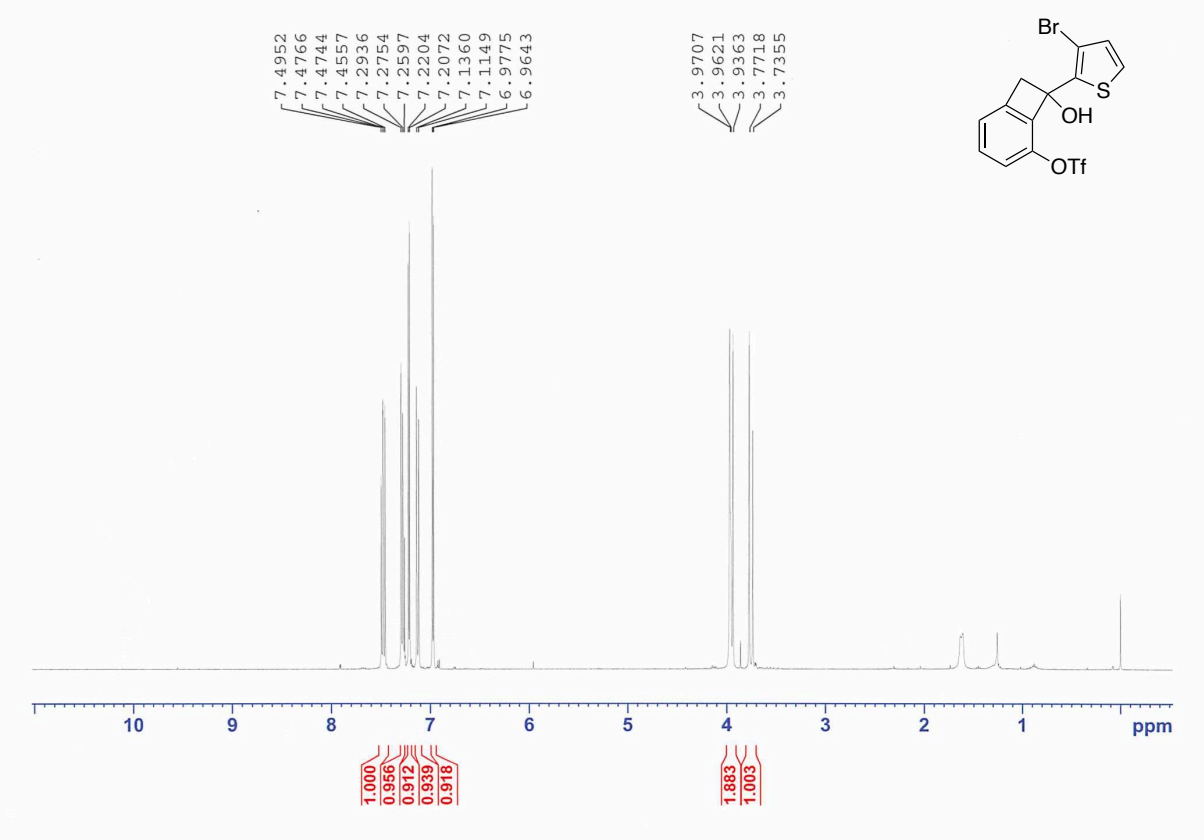


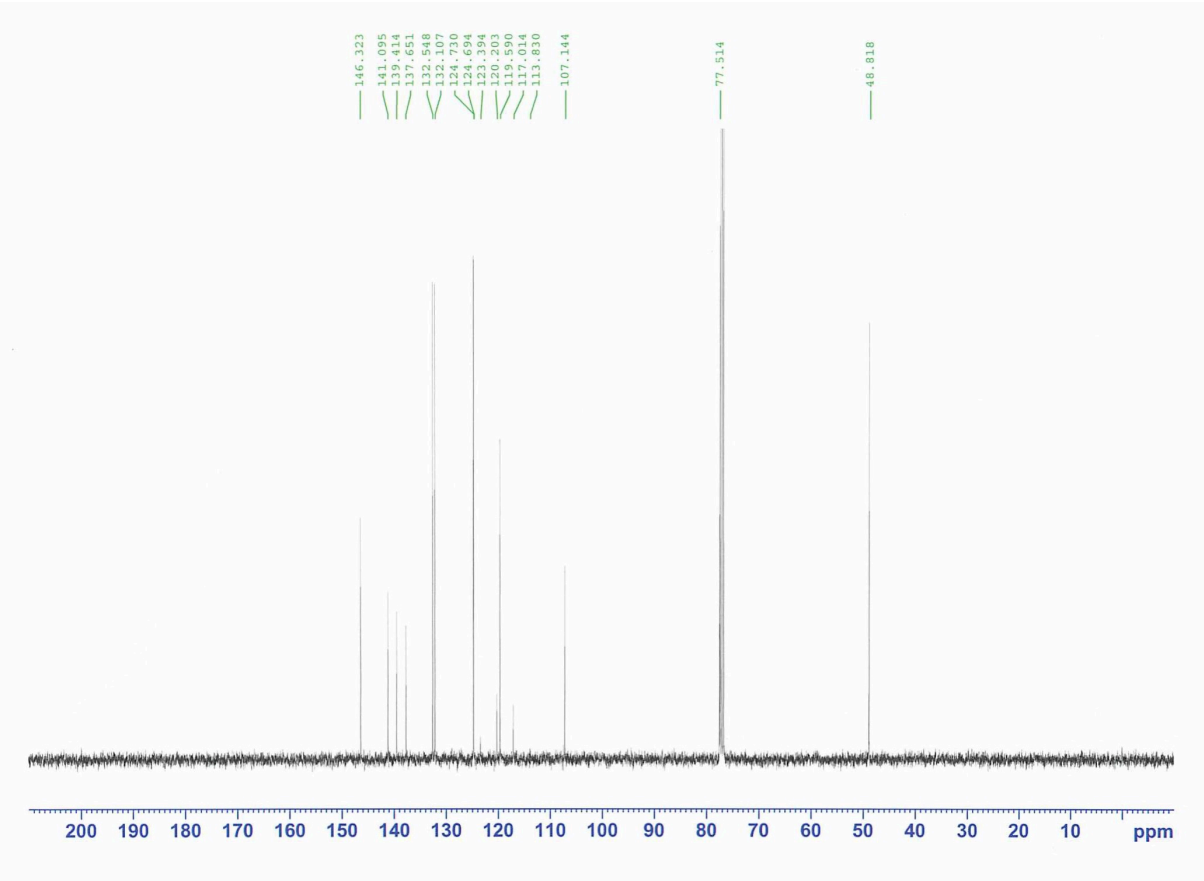
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-hydroxy-8-(5-bromo-3-iodo-2-methoxyphenyl)bicyclo[4.2.0]octa-1,2,4-trien-2-yl trifluoromethanesulfonate (**3f**) ($CDCl_3$)



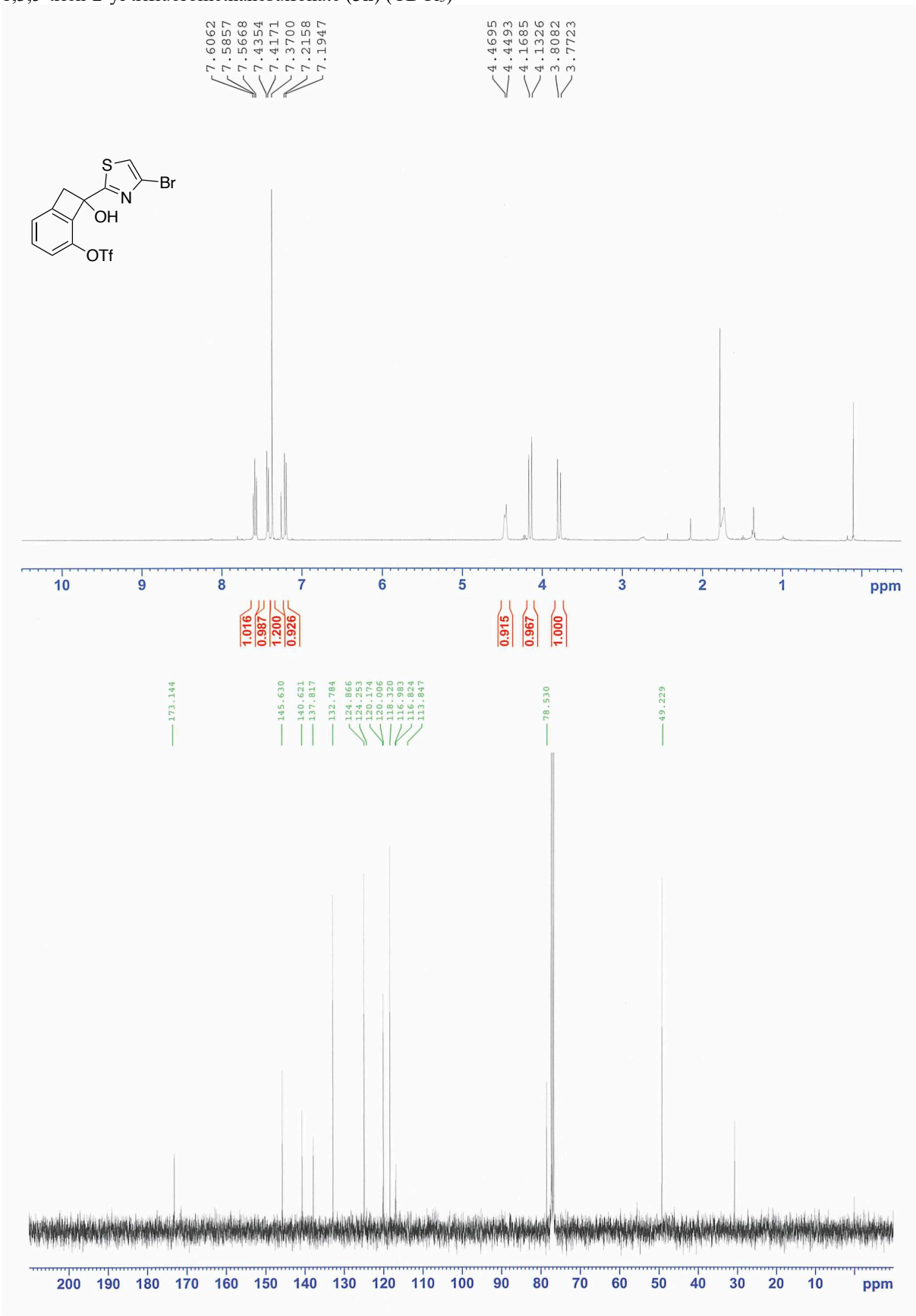


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-(3-bromothiophen-2-yl)-8-hydroxybicyclo[4.2.0]octa-1,3,5-trien-2-yl trifluoromethanesulfonate (**3g**) ($CDCl_3$)

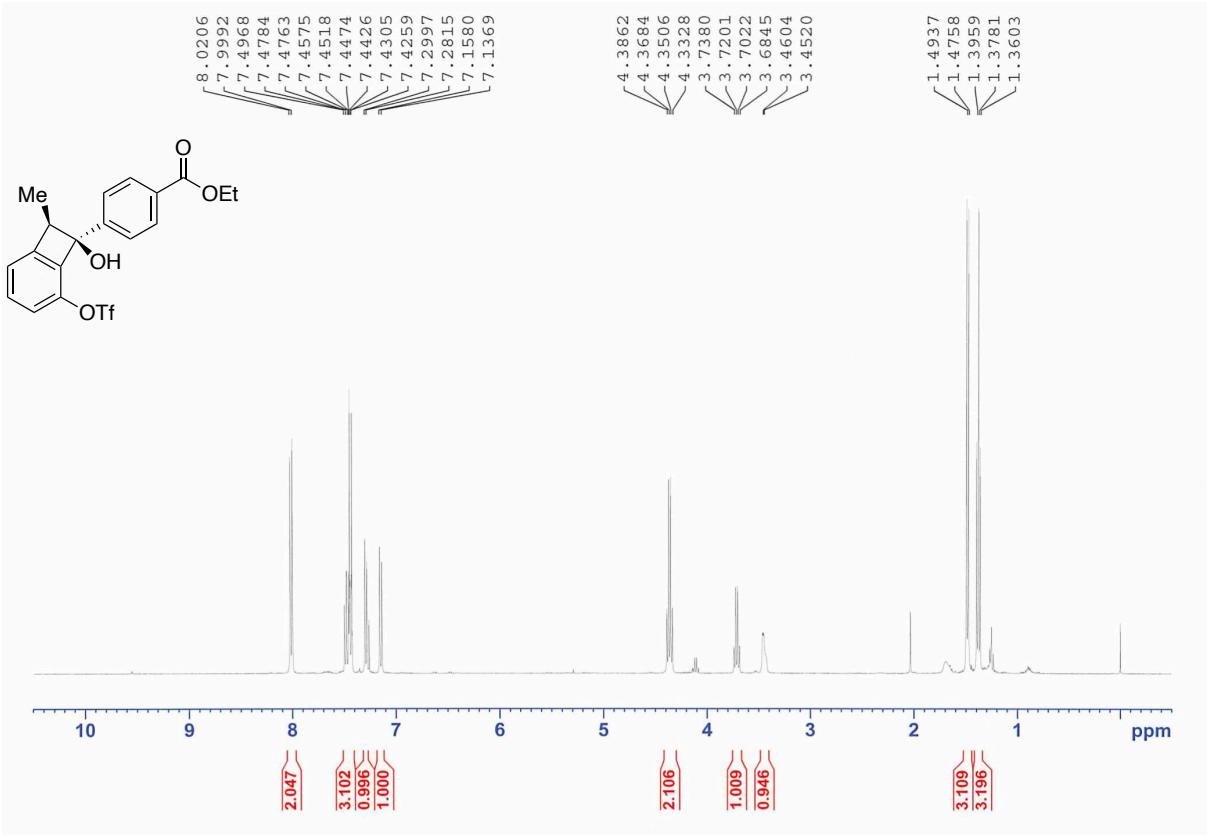


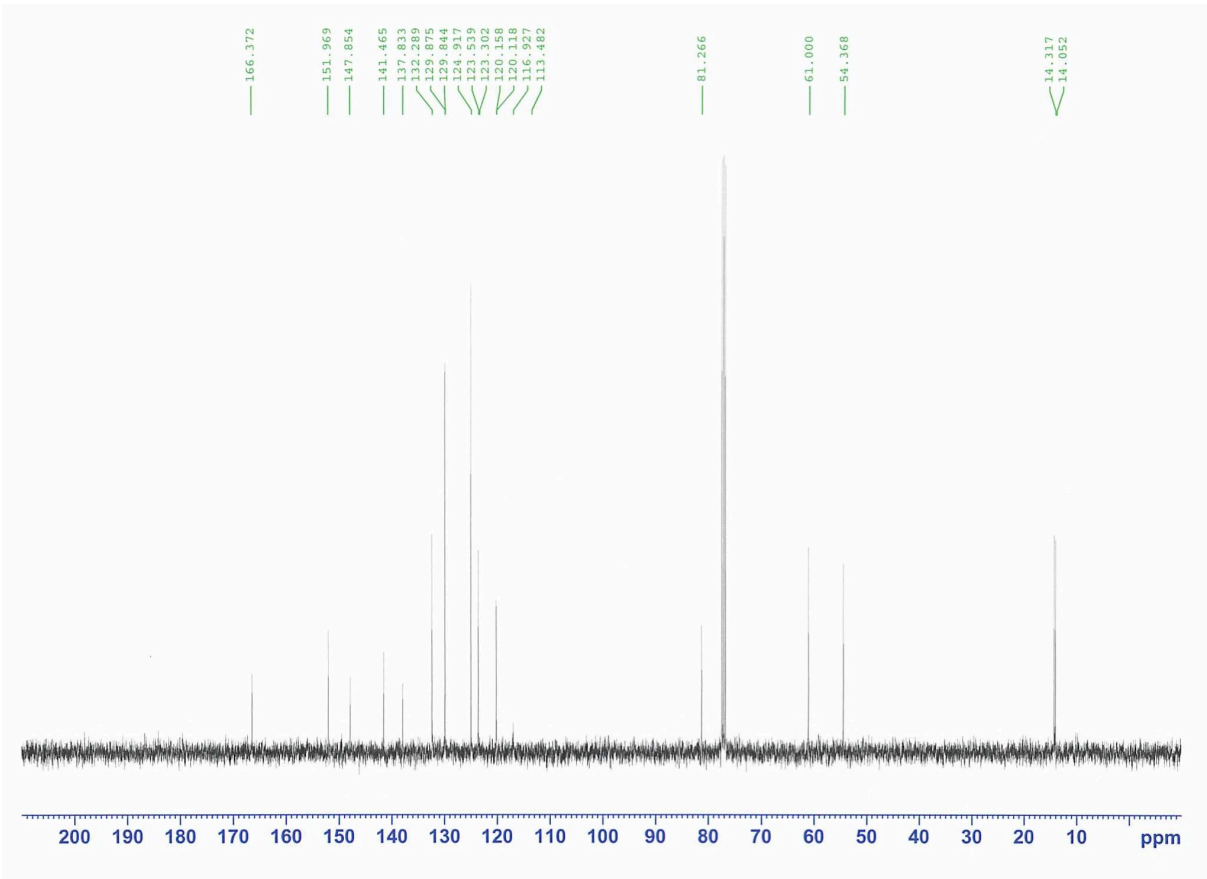


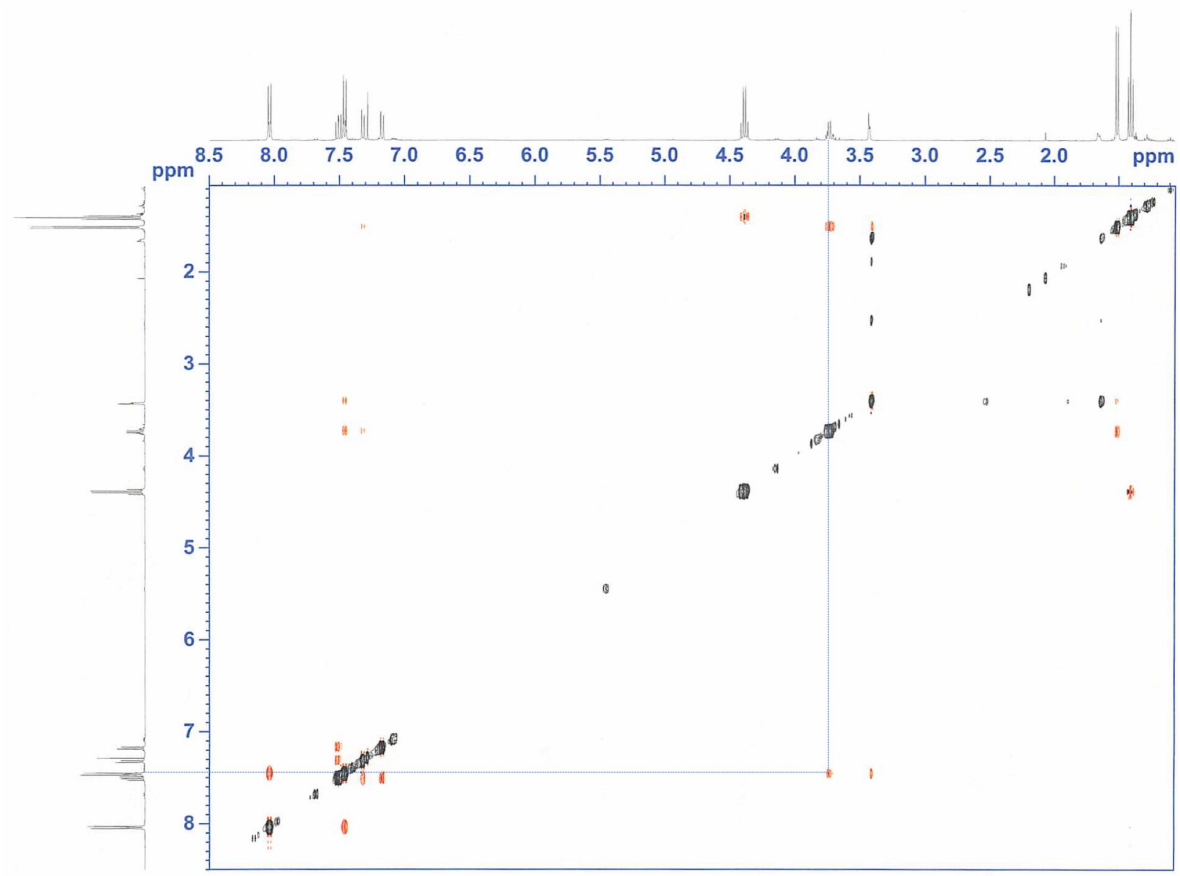
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-(3-bromothiophen-2-yl)-8-hydroxybicyclo[4.2.0]octa-1,3,5-trien-2-yl trifluoromethanesulfonate (**3h**) ($CDCl_3$)



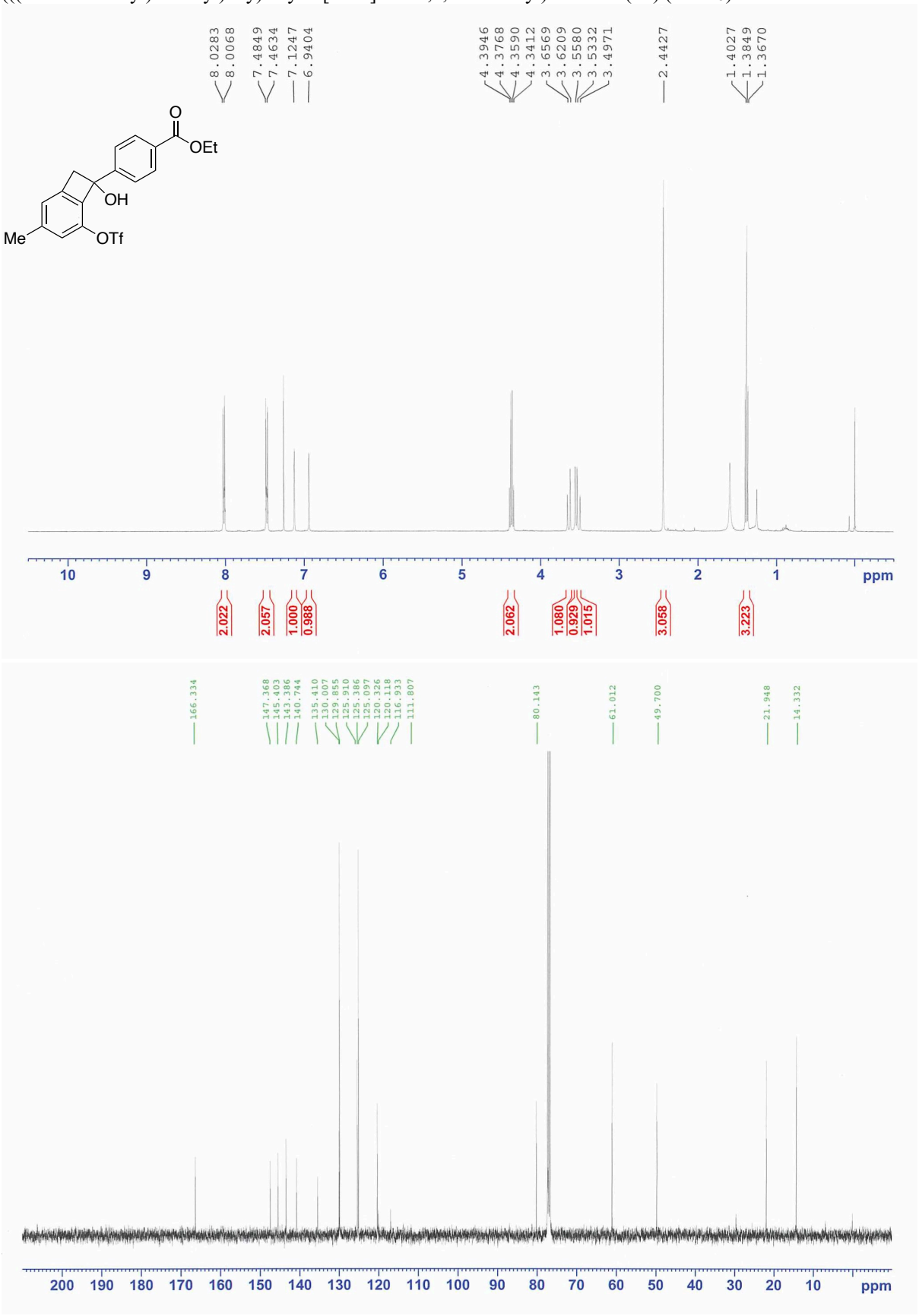
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and NOESY spectra of ethyl 4-((7*S**,8*R**)-7-hydroxy-8-methyl-5-((((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)benzoate (**3i**) ($CDCl_3$)



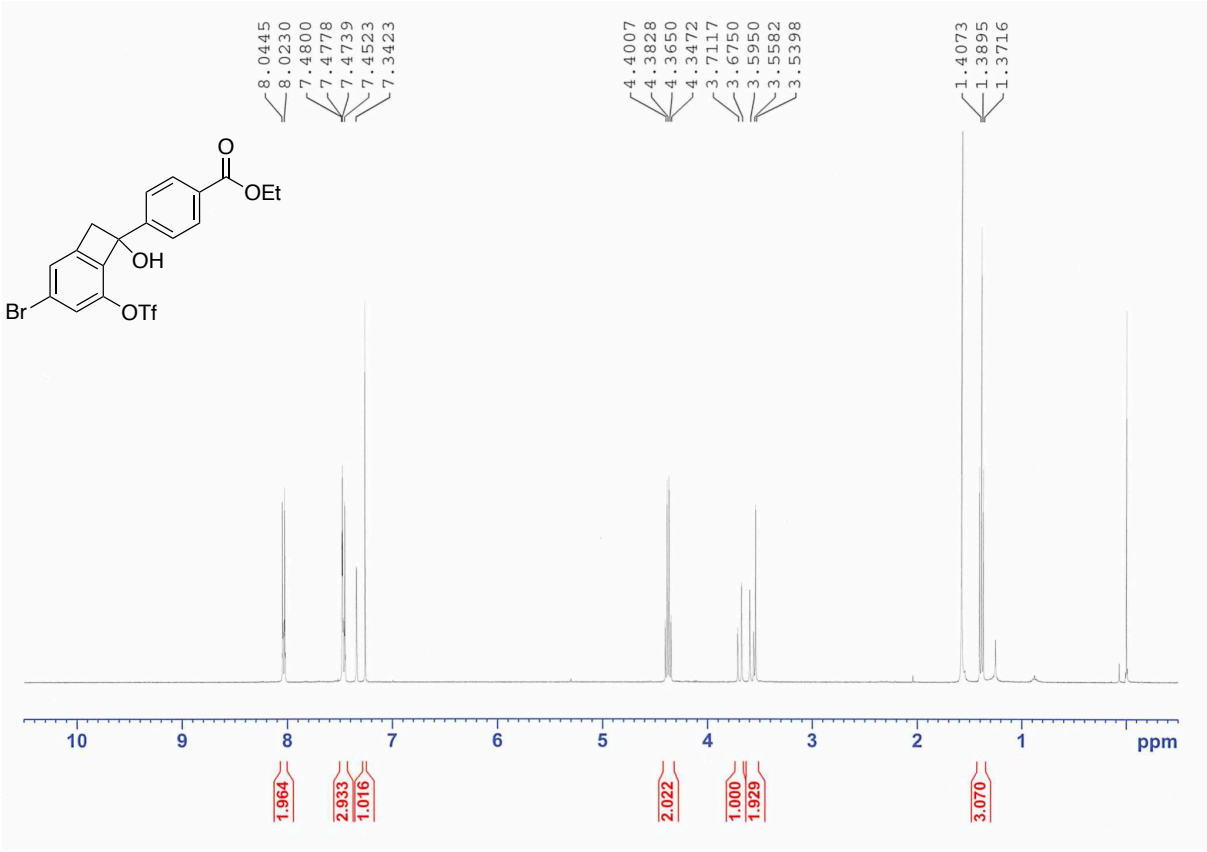


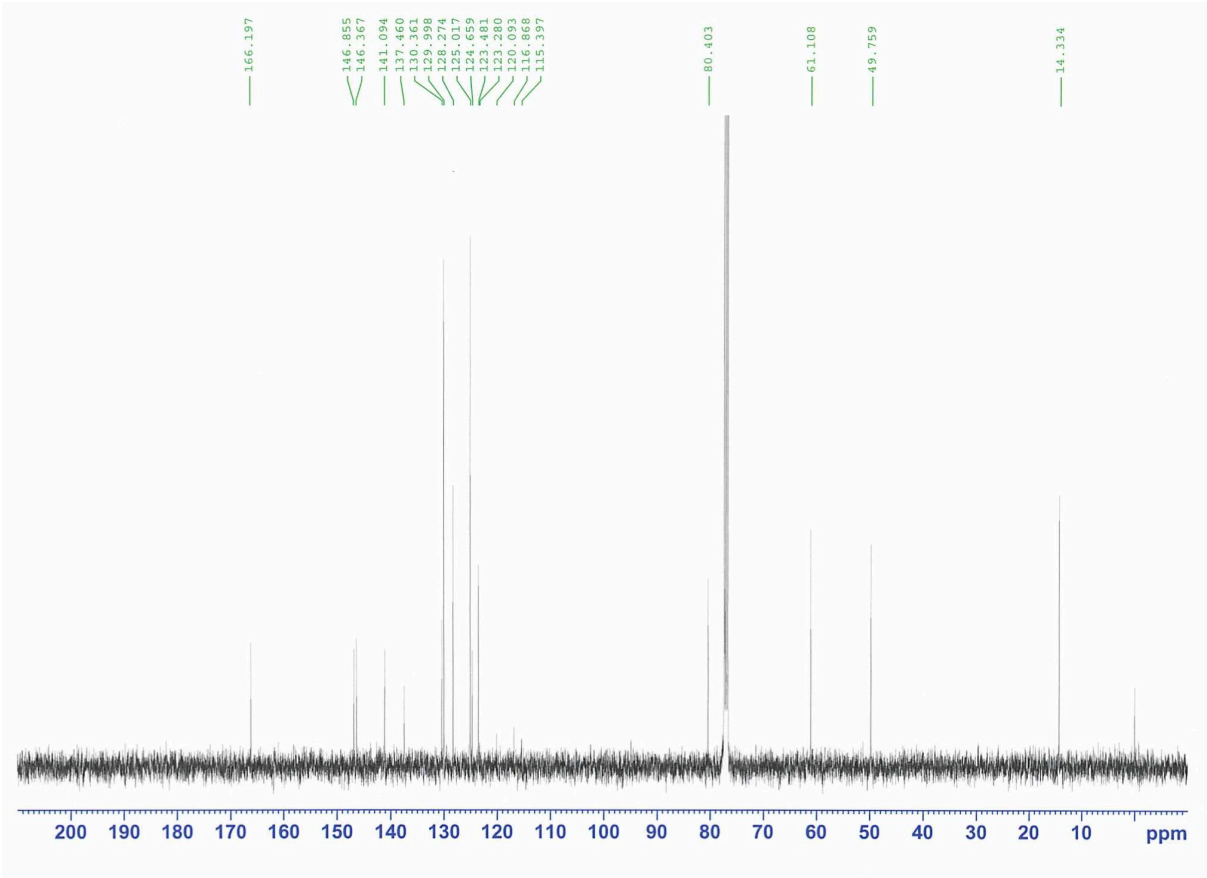

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
ppm
2
3
4
5
6
7
8

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(7-hydroxy-3-methyl-5-((((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1,3,5-trien-7-yl)benzoate (**3k**) ($CDCl_3$)

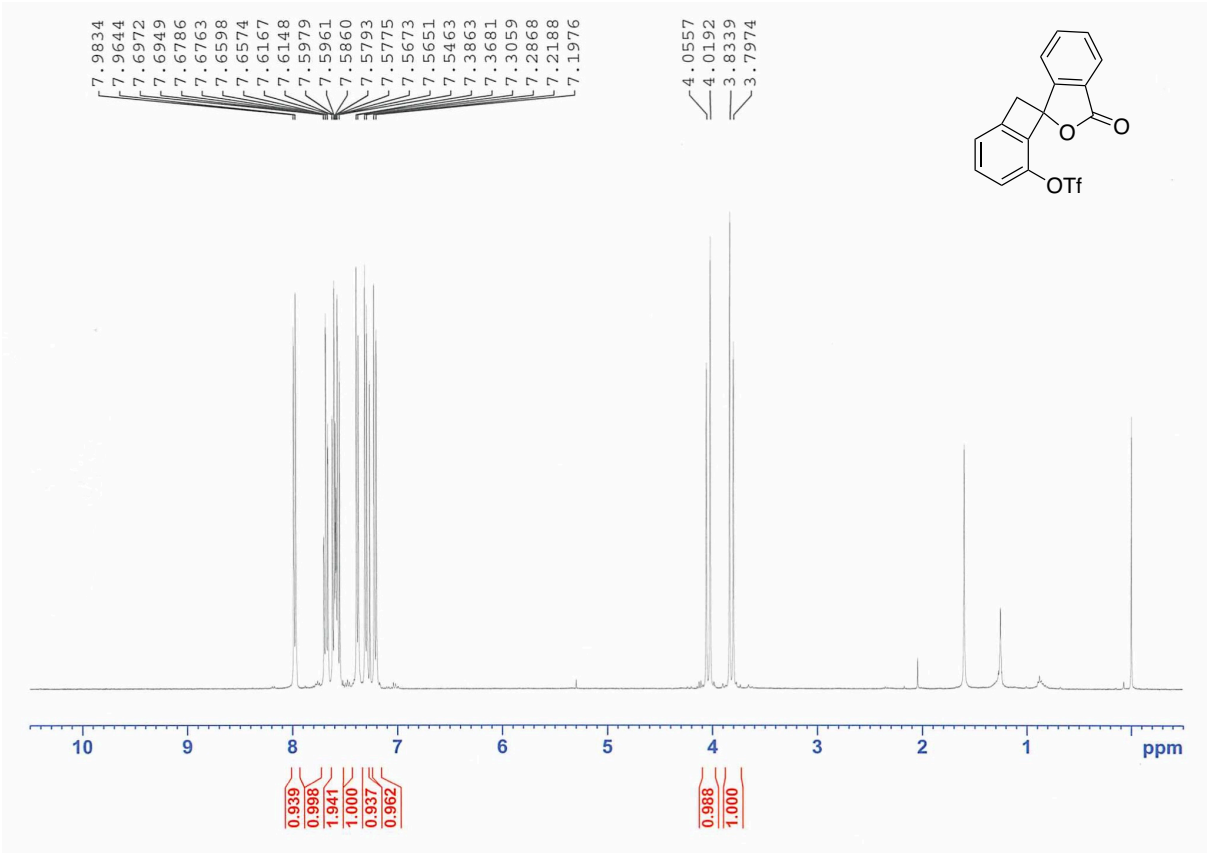


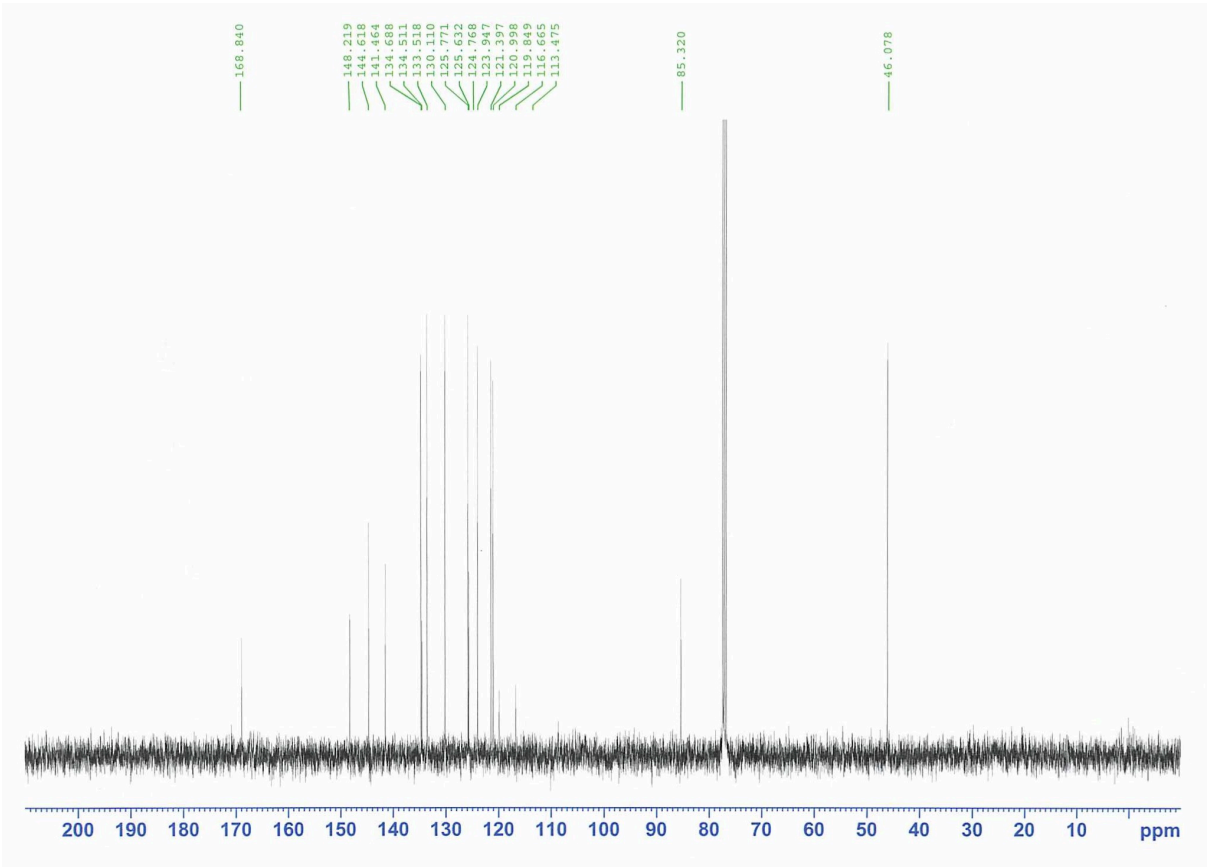
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(3-bromo-7-hydroxy-5-((((trifluoromethyl)sulfonyl)oxy)bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)benzoate (**3l**) ($CDCl_3$)



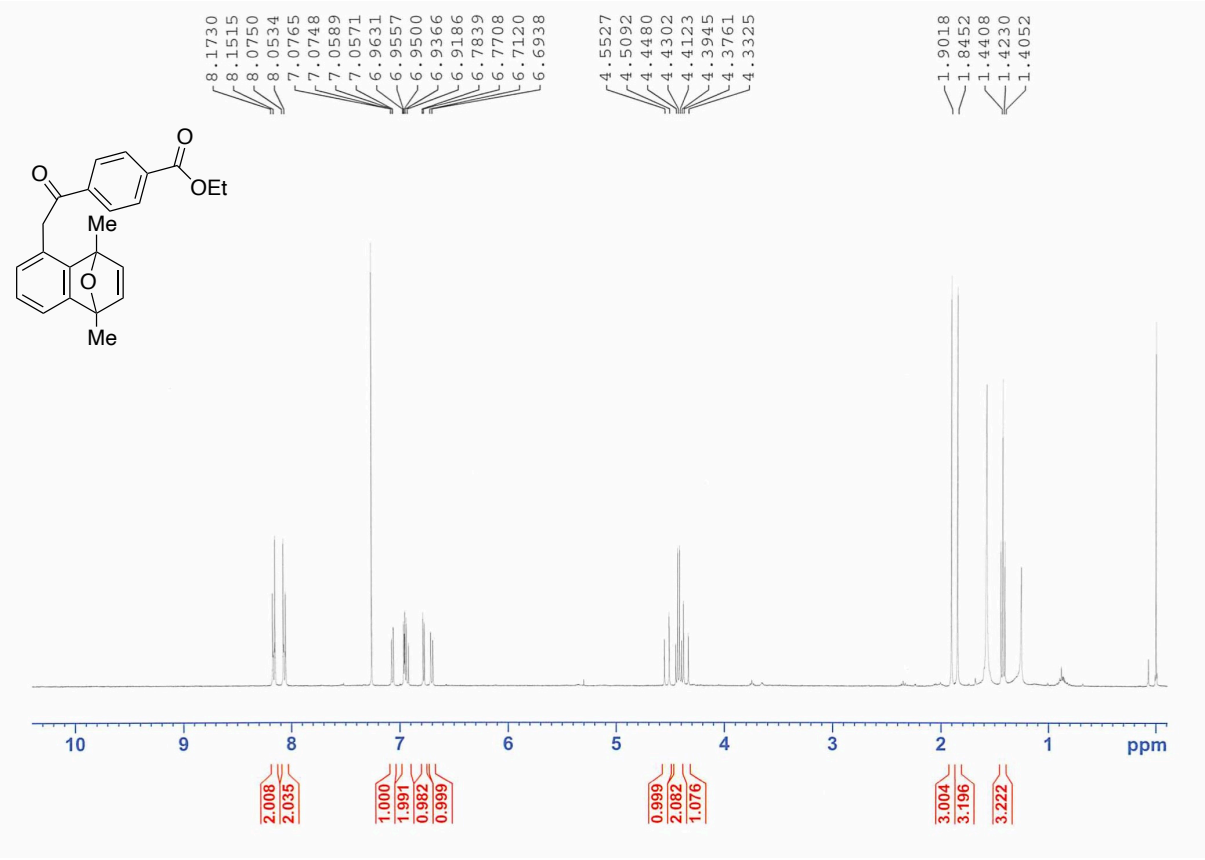


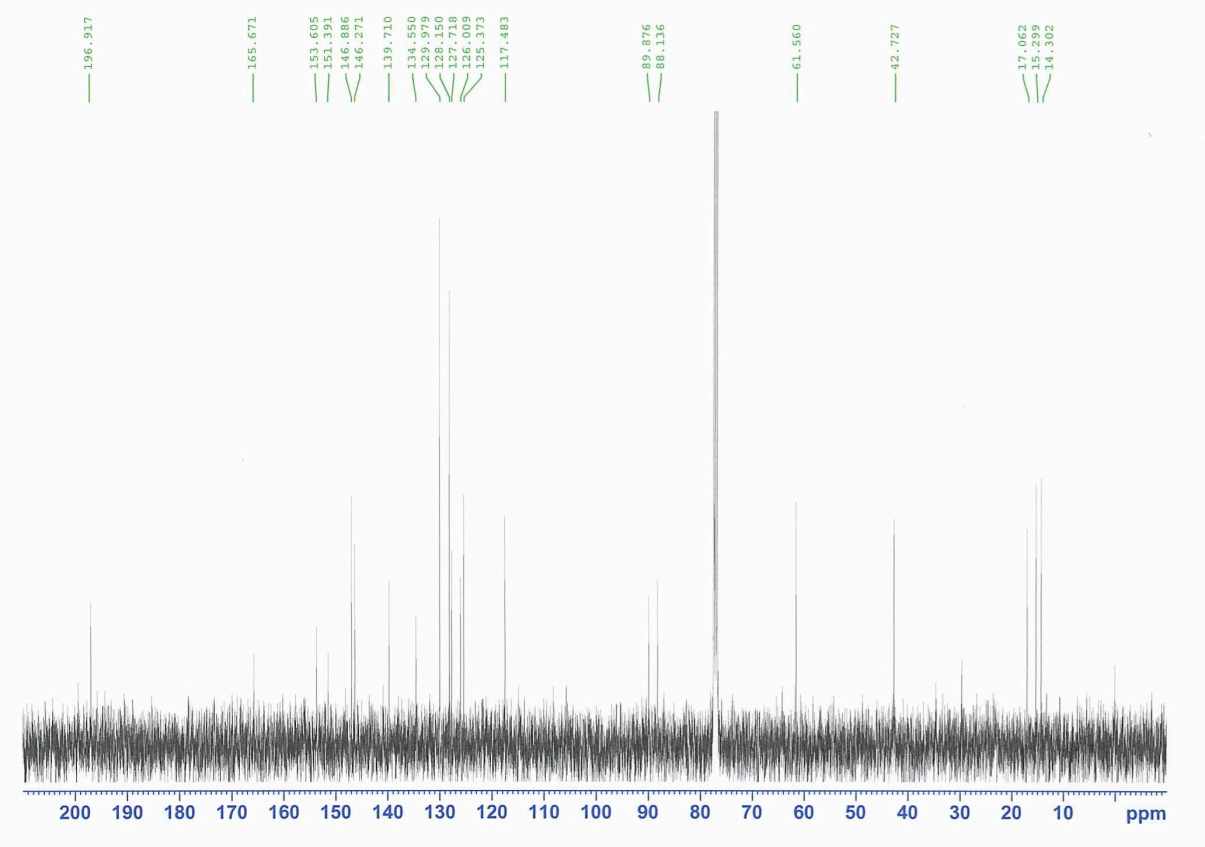
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3'-oxo-3'*H*-spiro[bicyclo[4.2.0]octane-7,1'-isobenzofuran]-1,3,5-trien-5-yl trifluoromethanesulfonate (**4**) ($CDCl_3$)



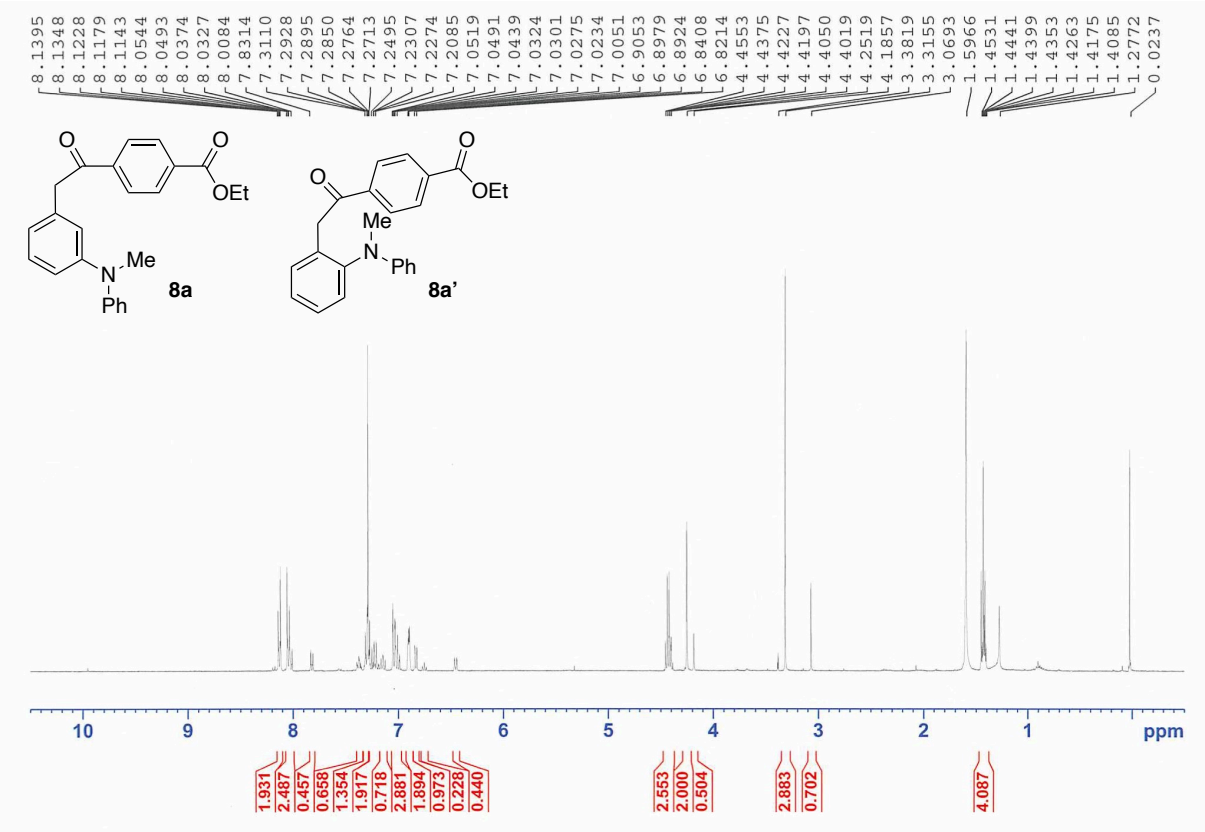


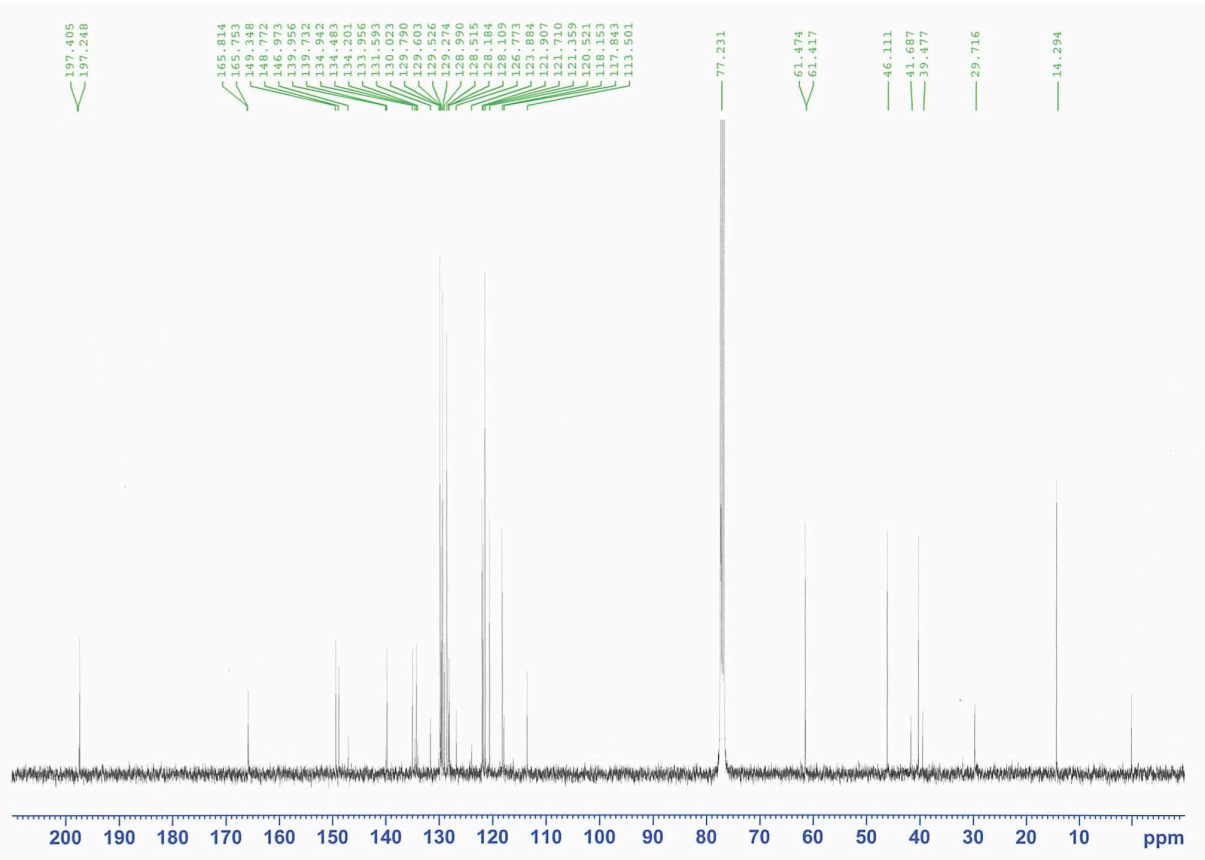
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-(1,4-dimethyl-1,4-dihydro-1,4-epoxynaphthalen-5-yl)acetyl)benzoate (**6**) ($CDCl_3$)



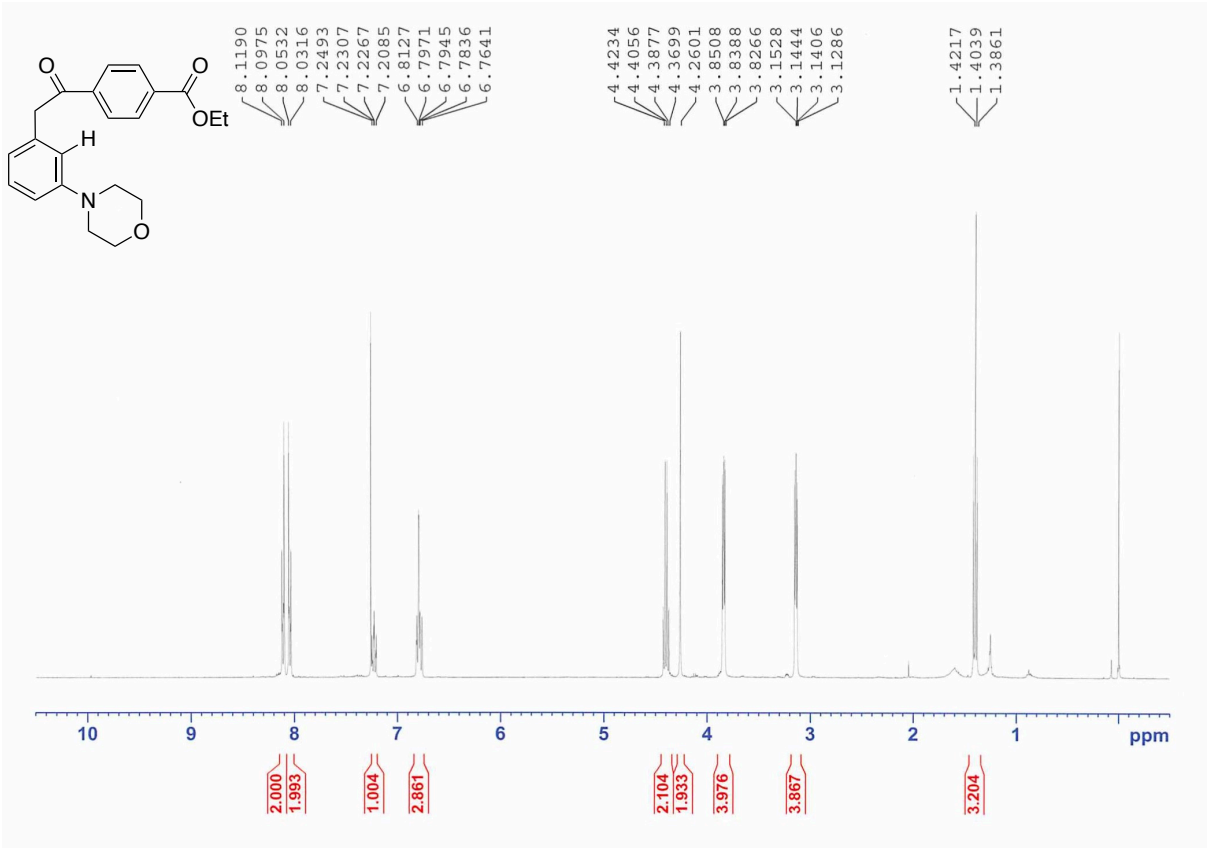


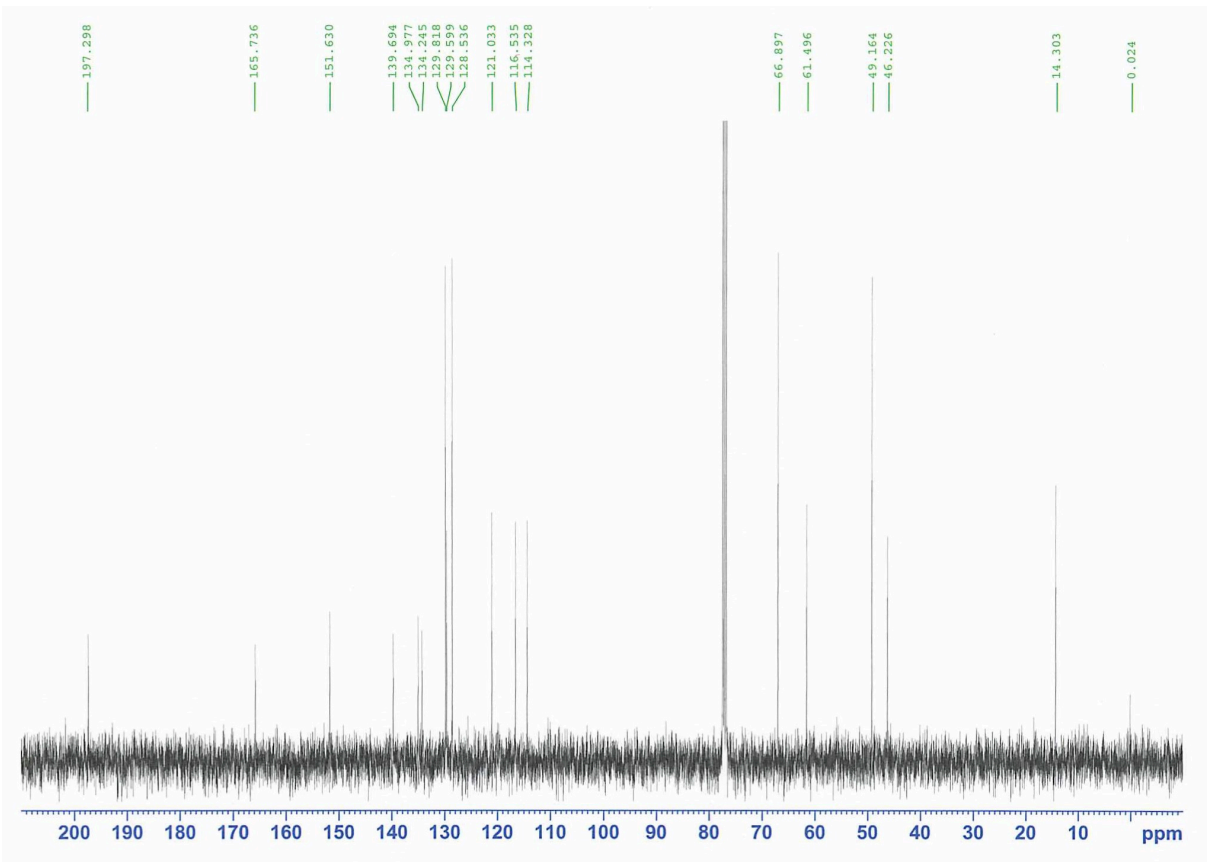
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-(3-(methyl(phenyl)amino)phenyl)acetyl)-benzoate (**8a**) and ethyl 4-(2-(2-(methyl(phenyl)amino)phenyl)acetyl)benzoate (**8a'**) ($CDCl_3$)



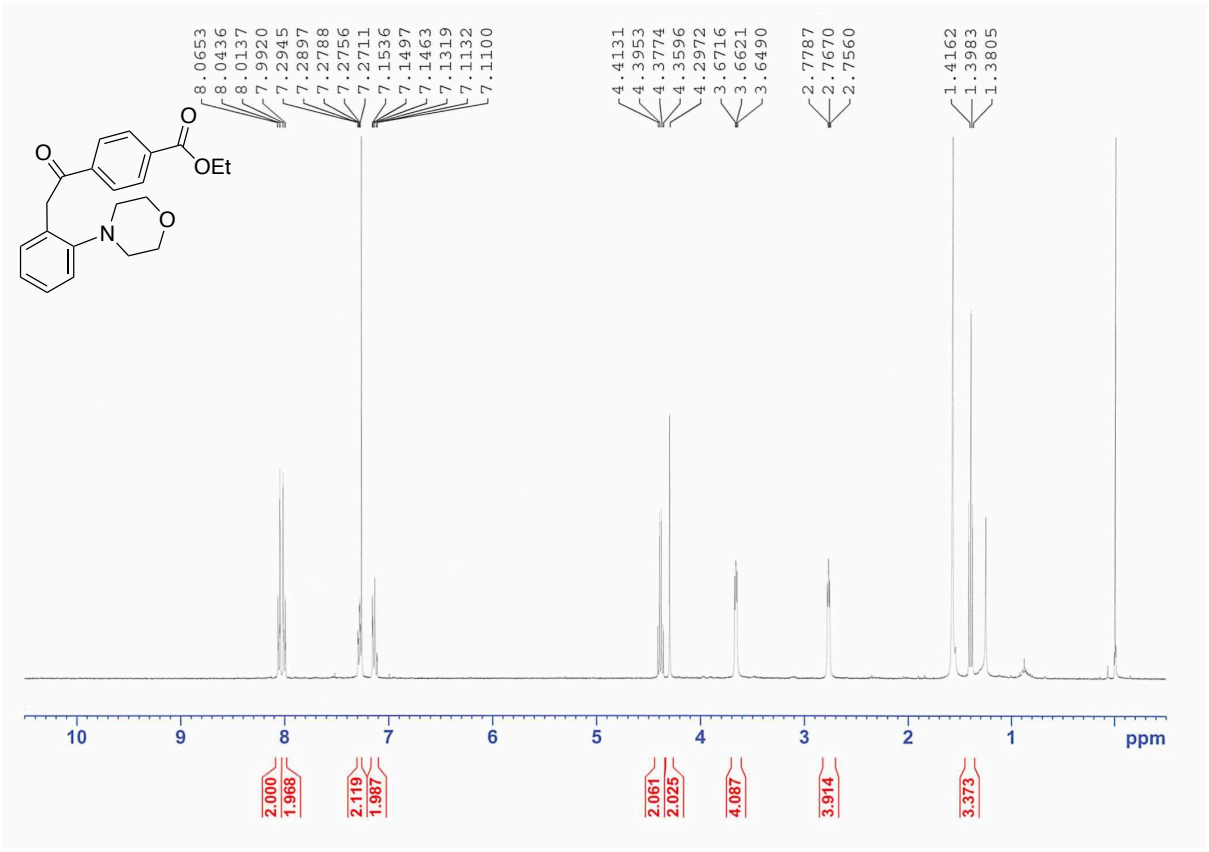


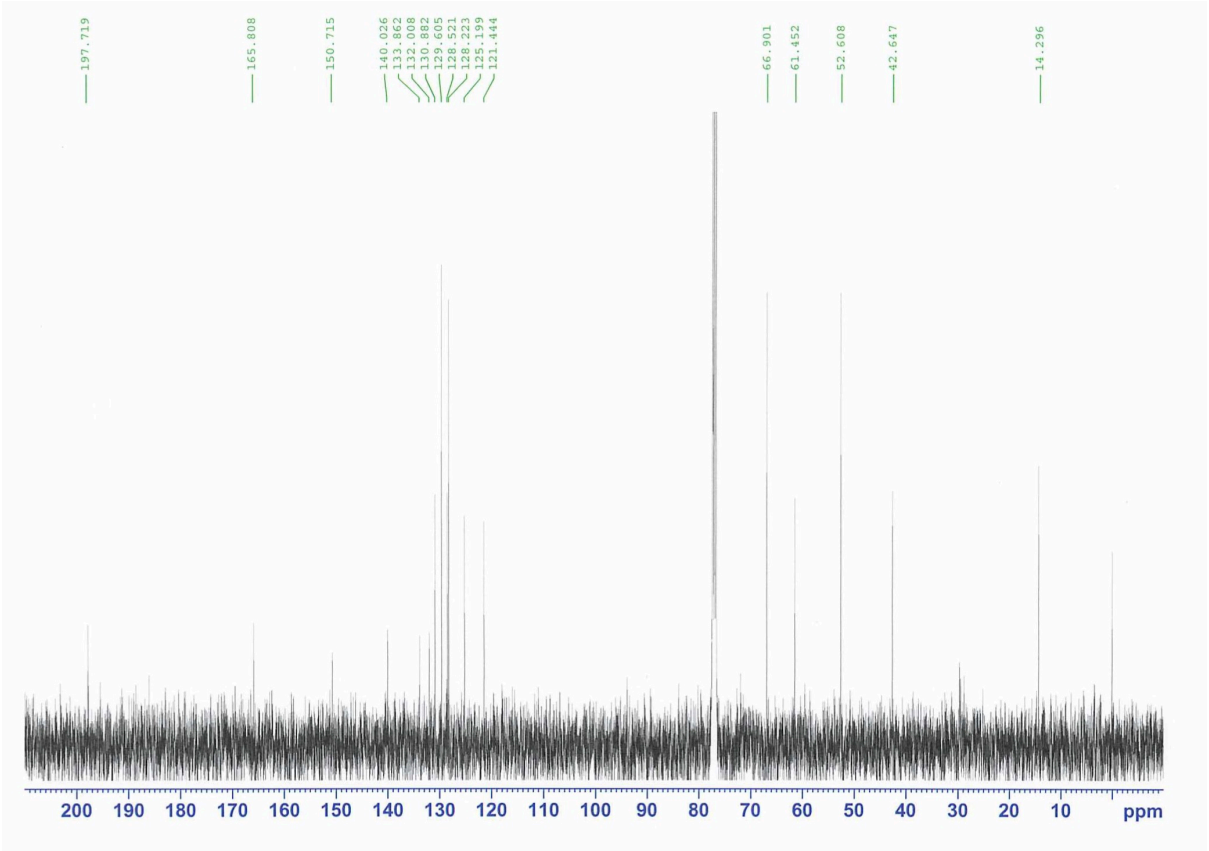
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-(3-morpholinophenyl)acetyl)benzoate (**8b**) ($CDCl_3$)



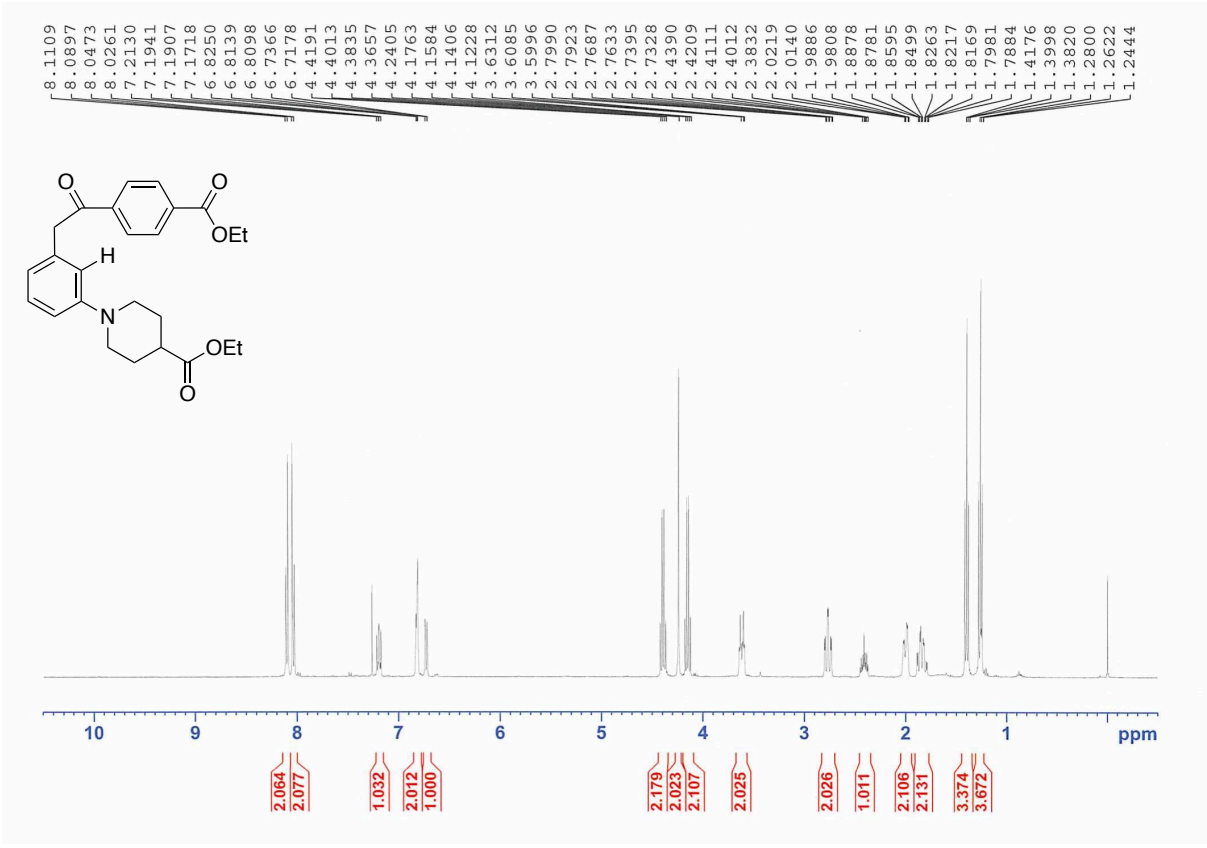


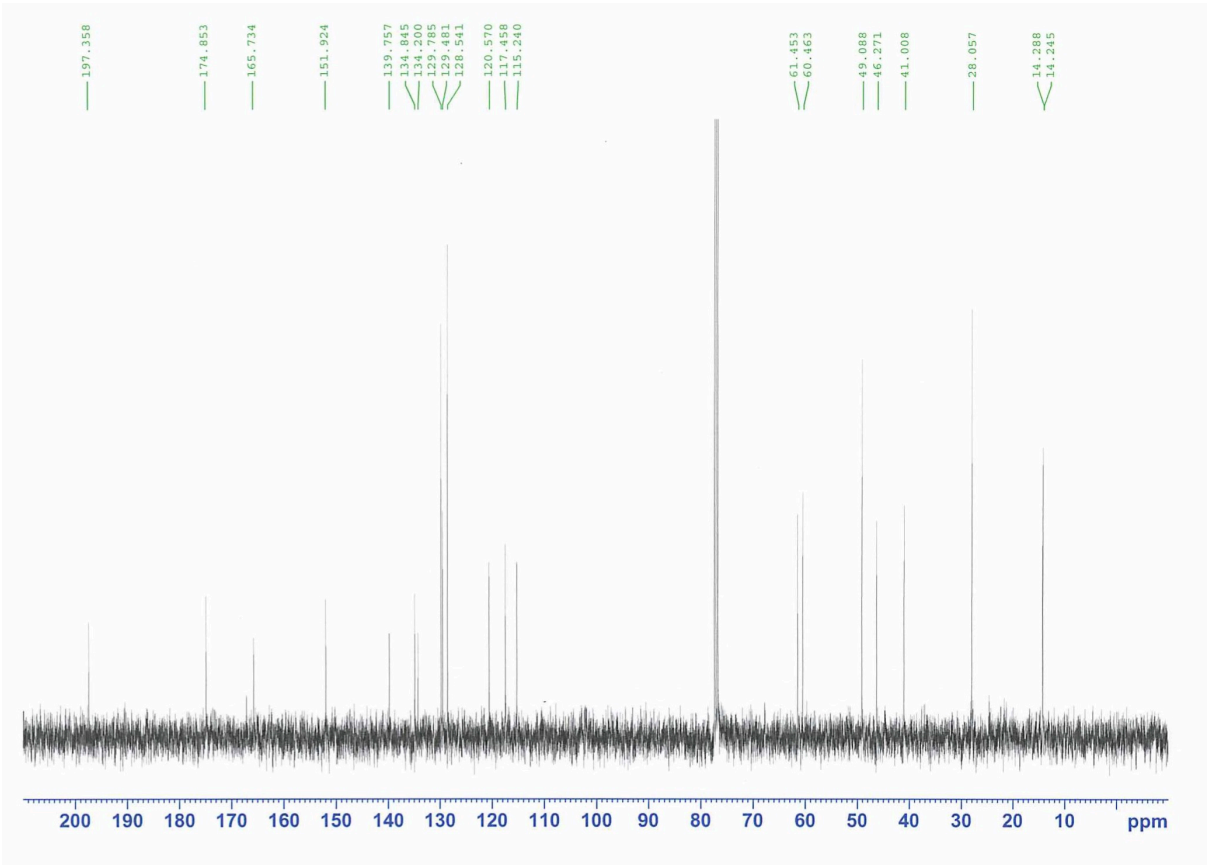
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-(2-morpholinophenyl)acetyl)benzoate (**8b'**) ($CDCl_3$)



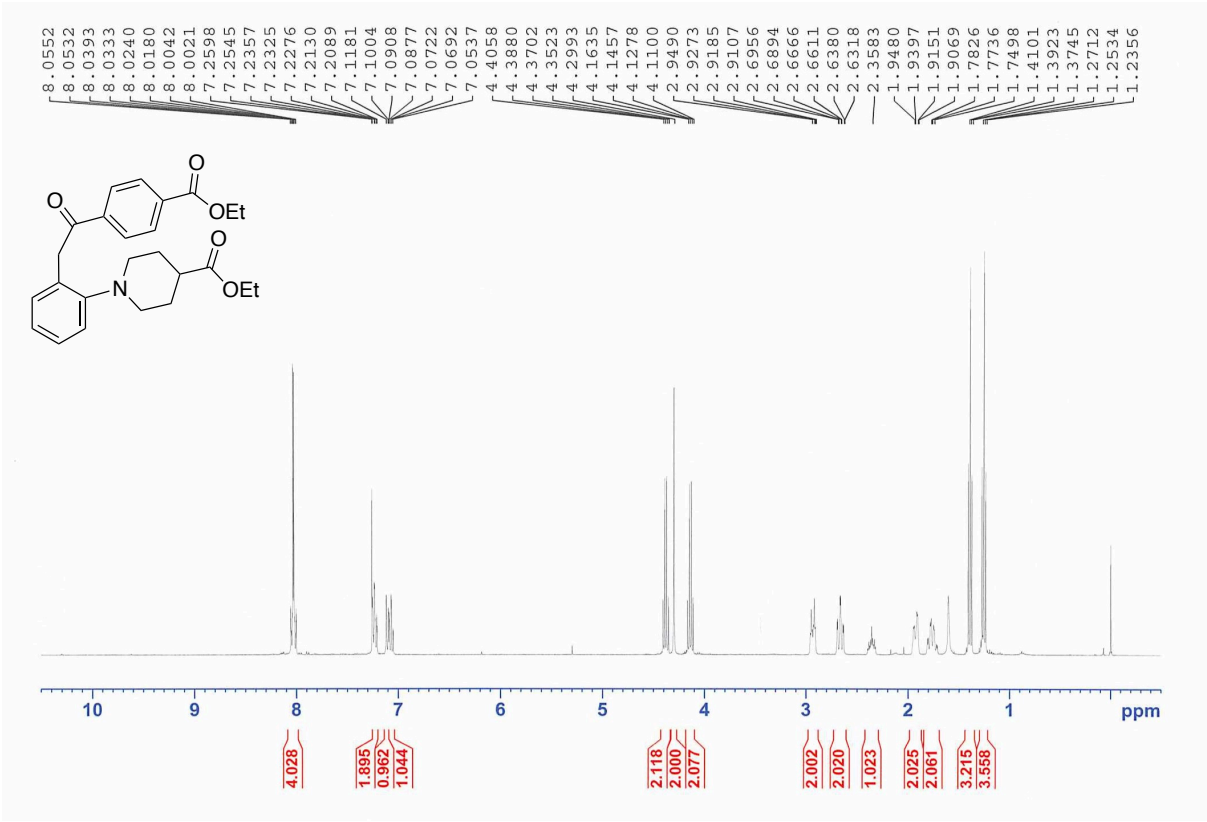


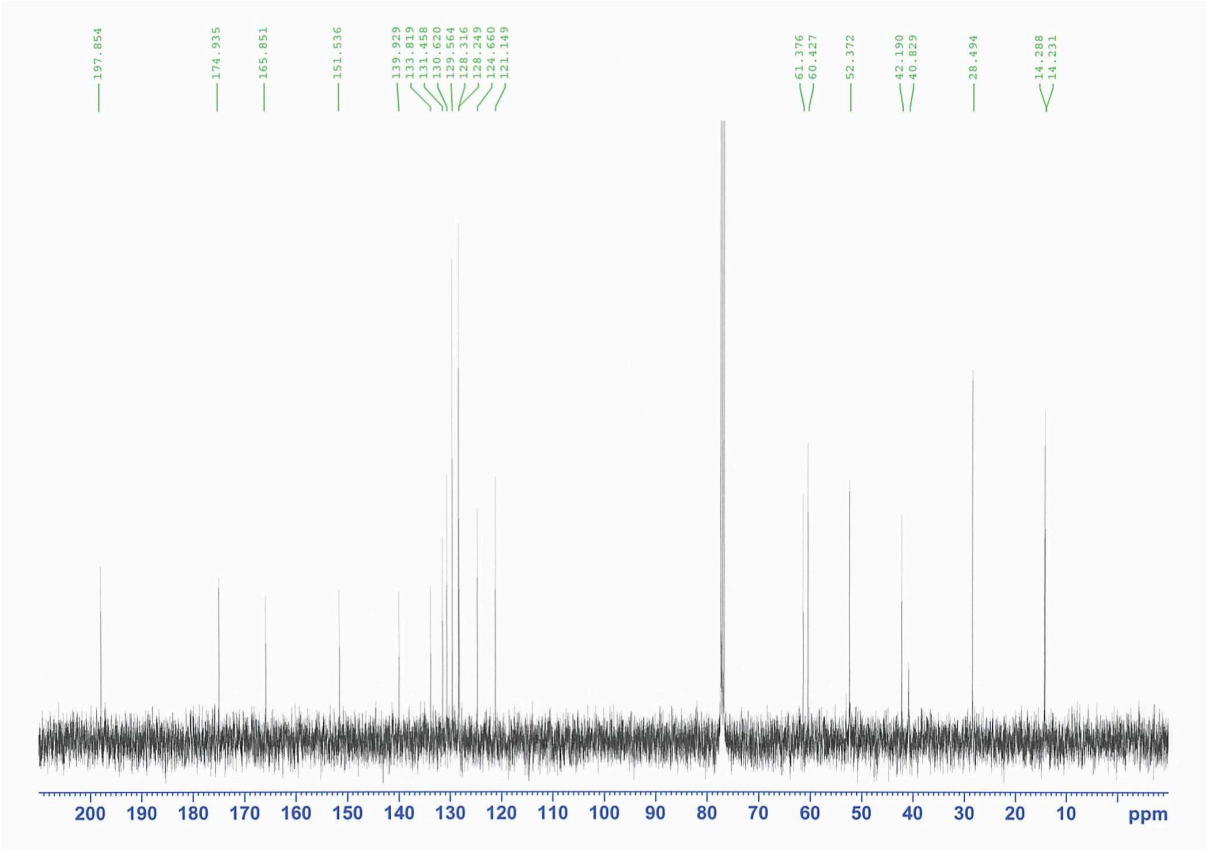
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 1-(3-(2-(4-(ethoxycarbonyl)phenyl)-2-oxoethyl)phenyl)piperidine-4-carboxylate (**8c**) ($CDCl_3$)



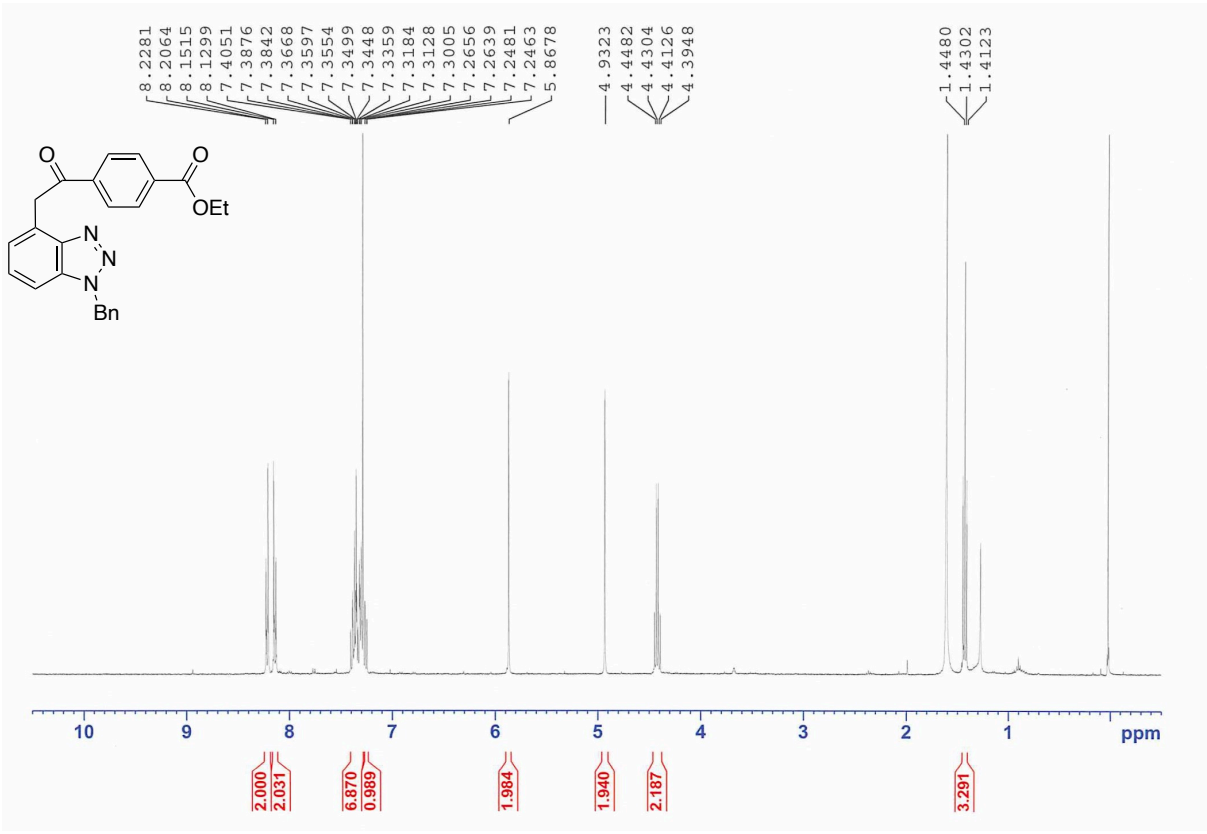


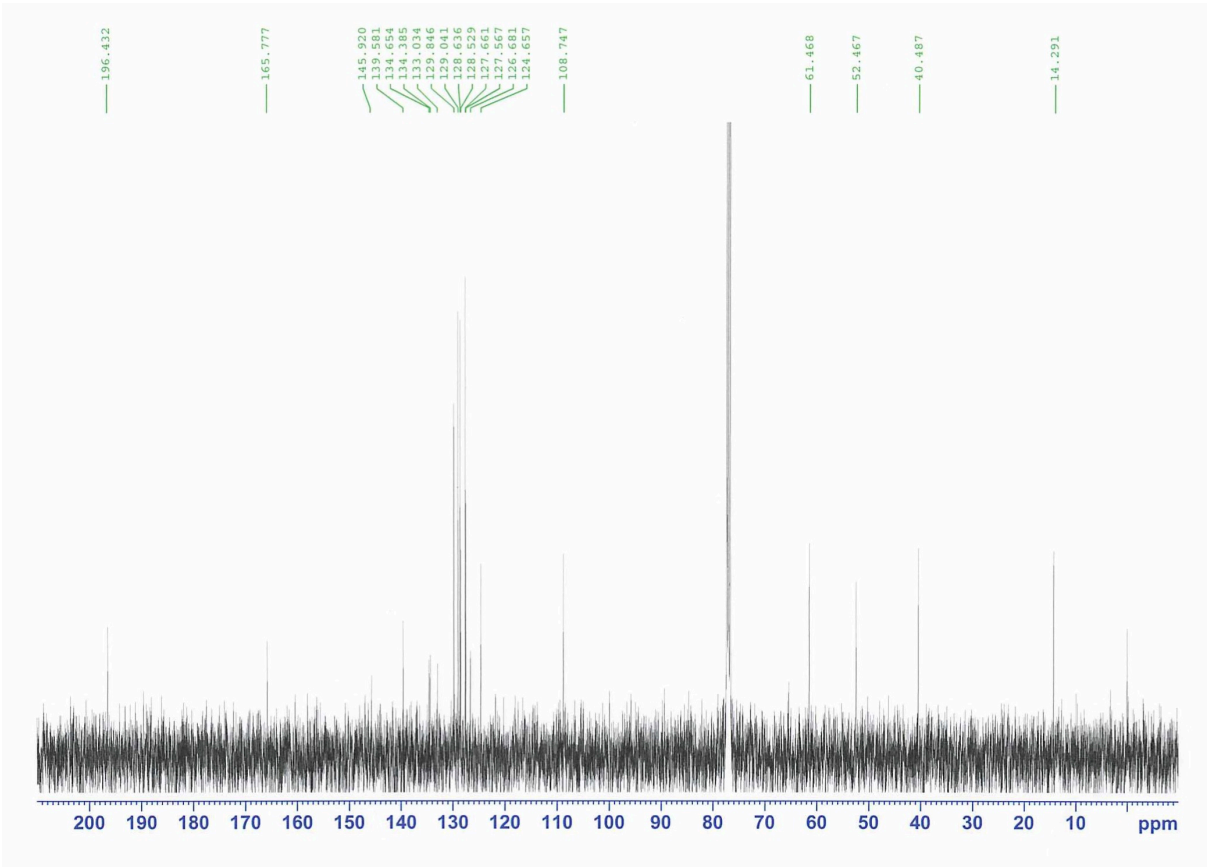
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 1-(2-(2-(4-(ethoxycarbonyl)phenyl)-2-oxoethyl)phenyl)piperidine-4-carboxylate (**8c'**) ($CDCl_3$)

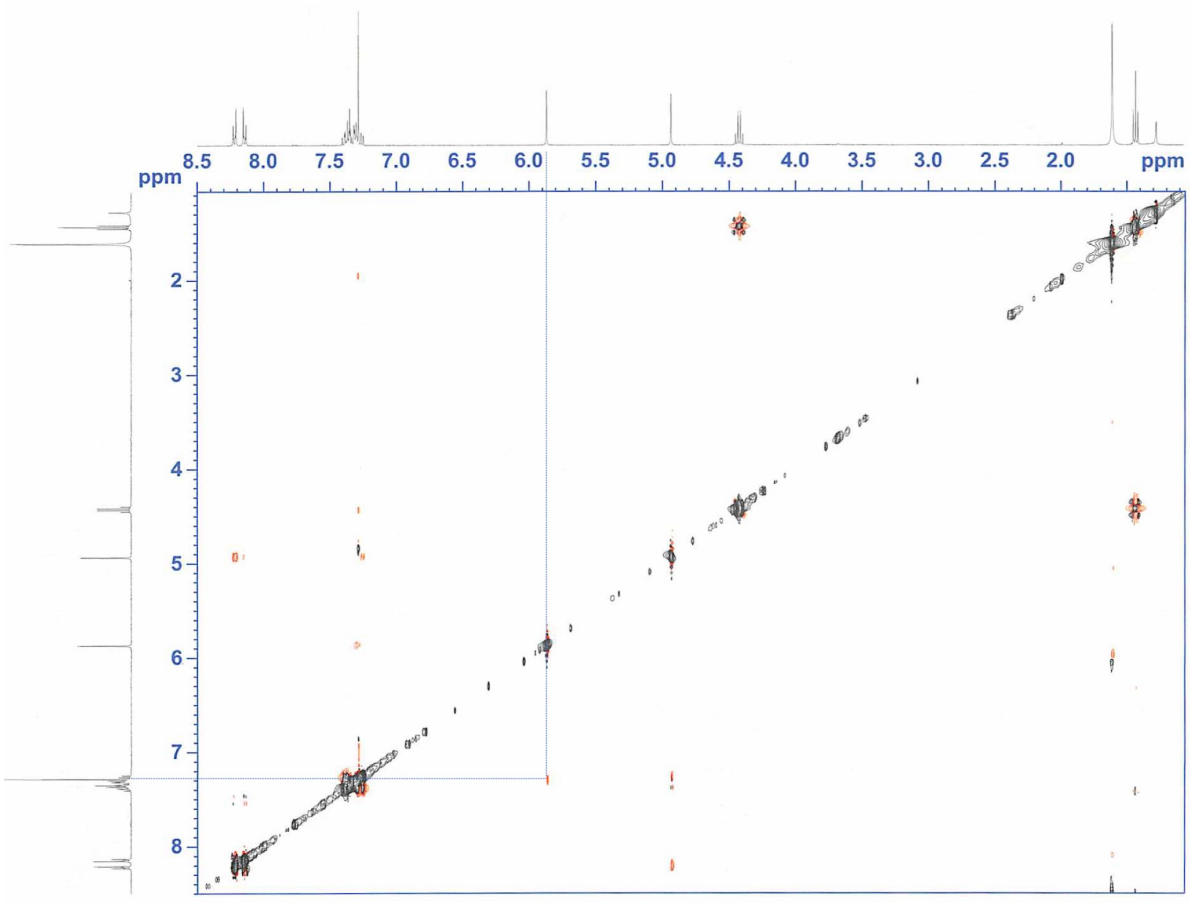




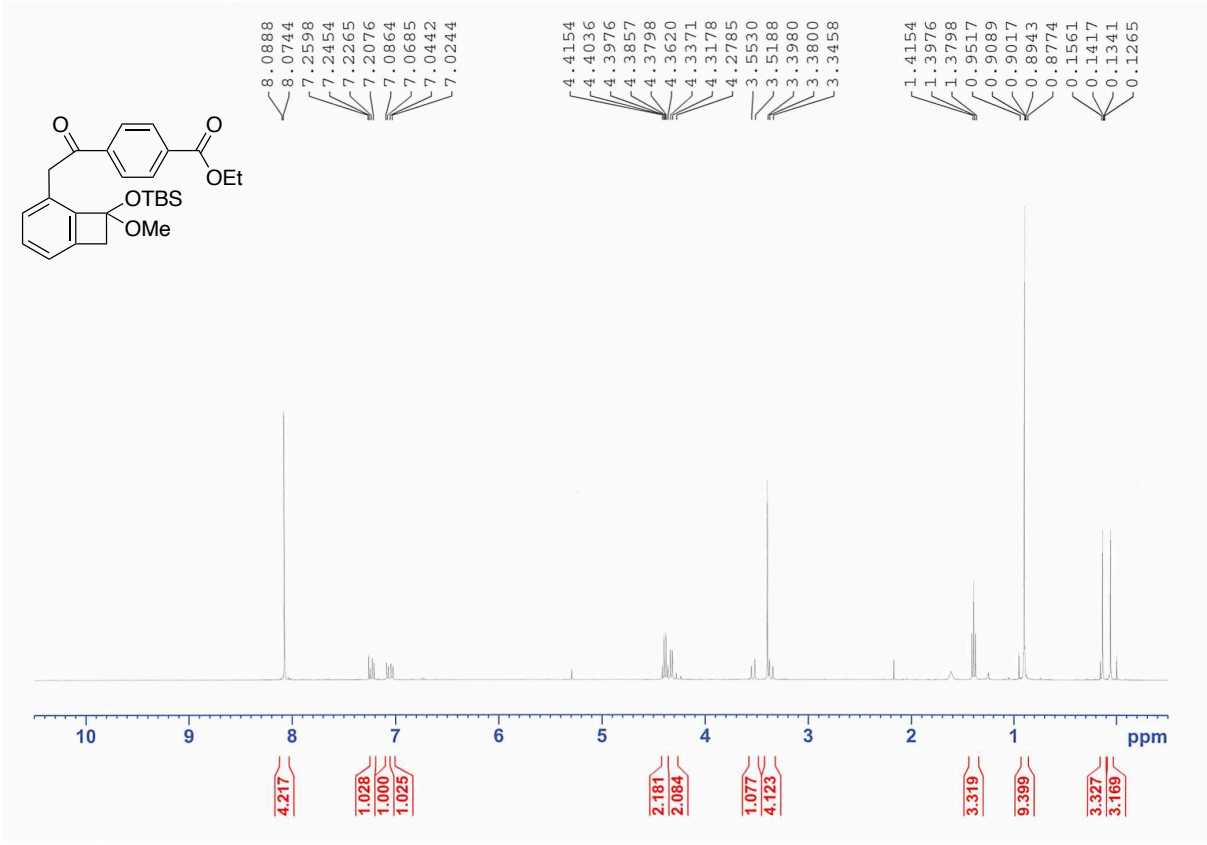
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and NOESY spectra of ethyl 4-(2-(1-benzyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzoate (**10**) ($CDCl_3$)

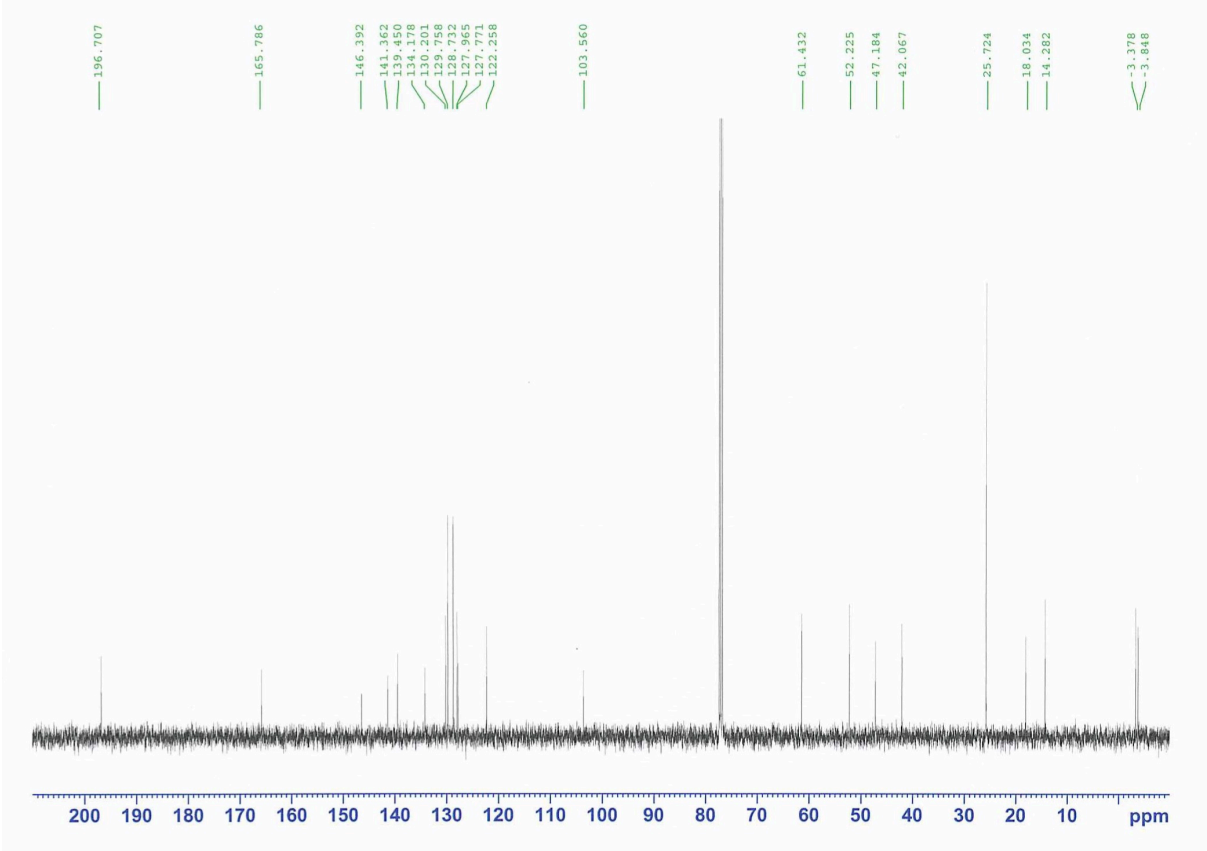


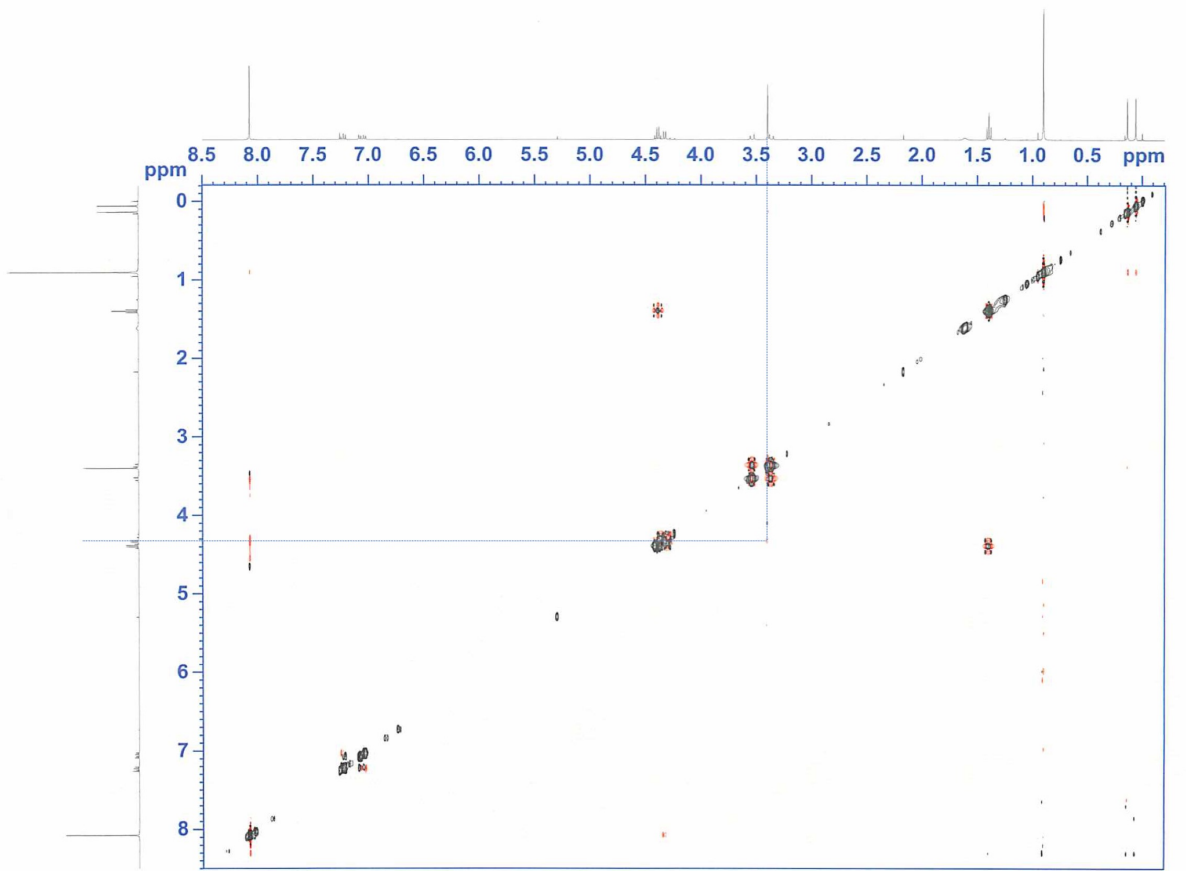



8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
ppm
2
3
4
5
6
7
8

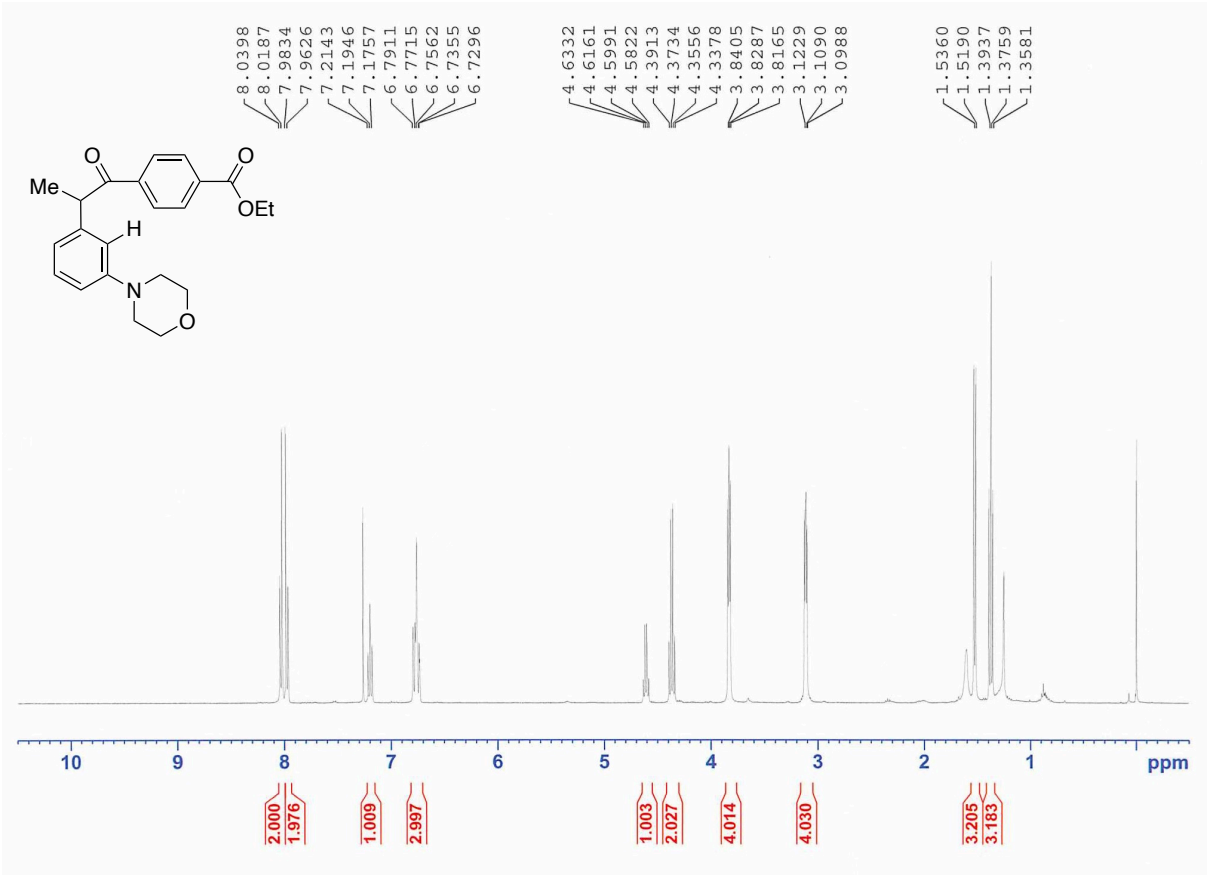
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and NOESY spectra of ethyl 4-(2-(8-((*tert*-butyldimethylsilyl)oxy)-8-methoxybicyclo[4.2.0]octa-1(6),2,4-trien-2-yl)acetyl)benzoate (**12**) ($CDCl_3$)

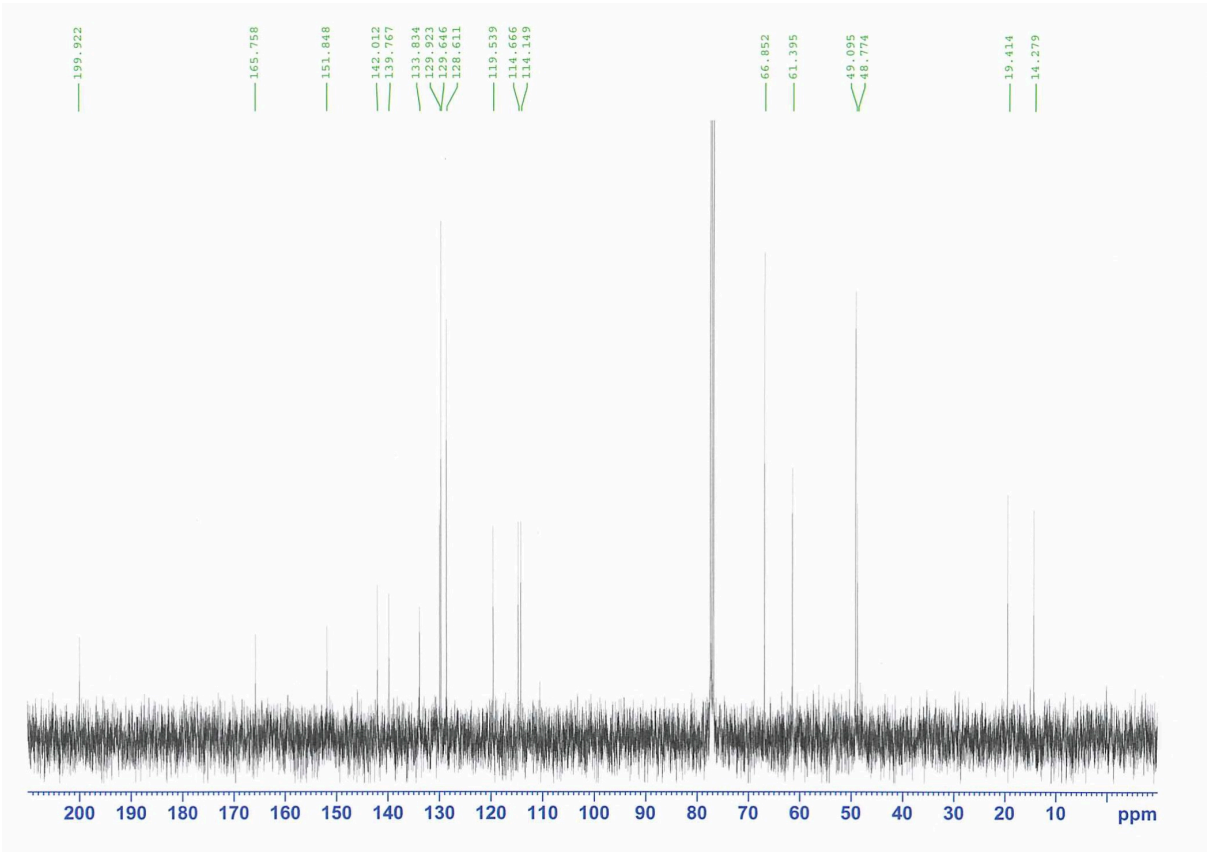




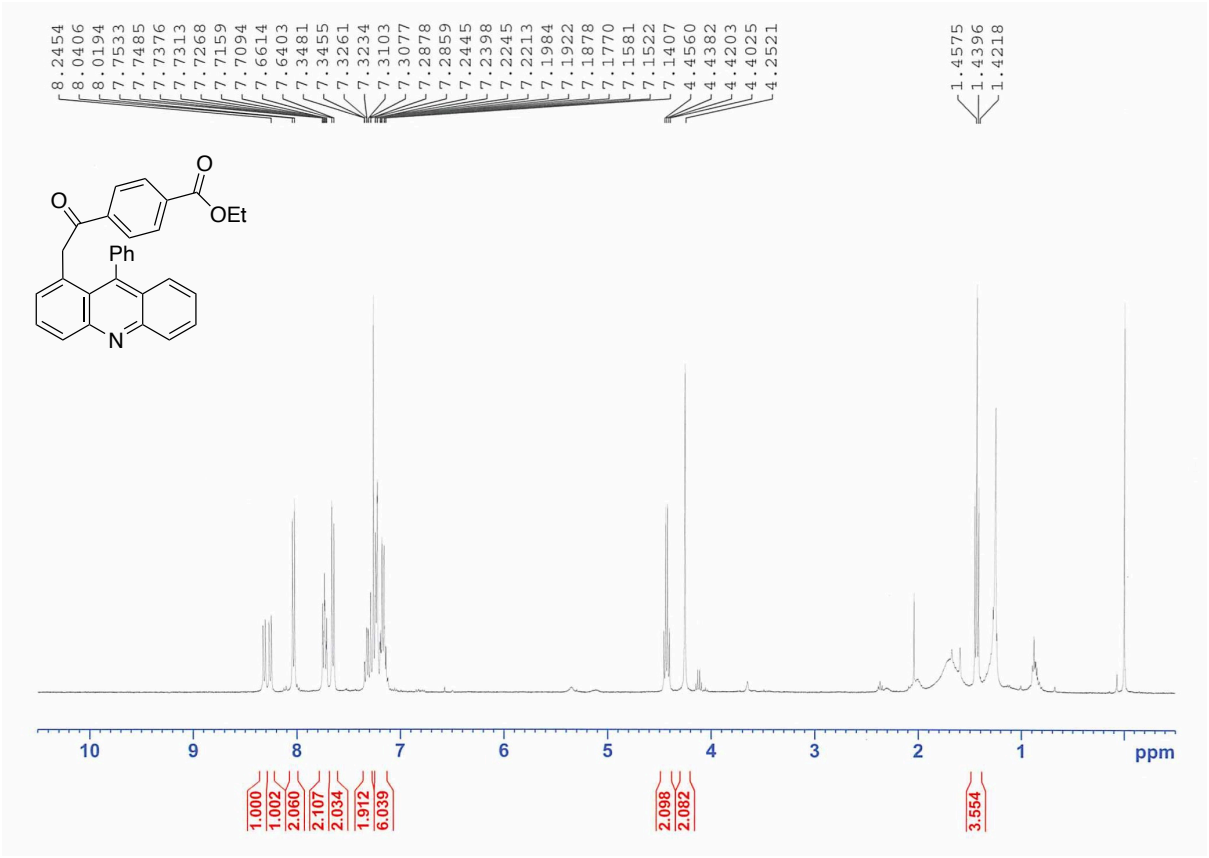

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
ppm
0
1
2
3
4
5
6
7
8

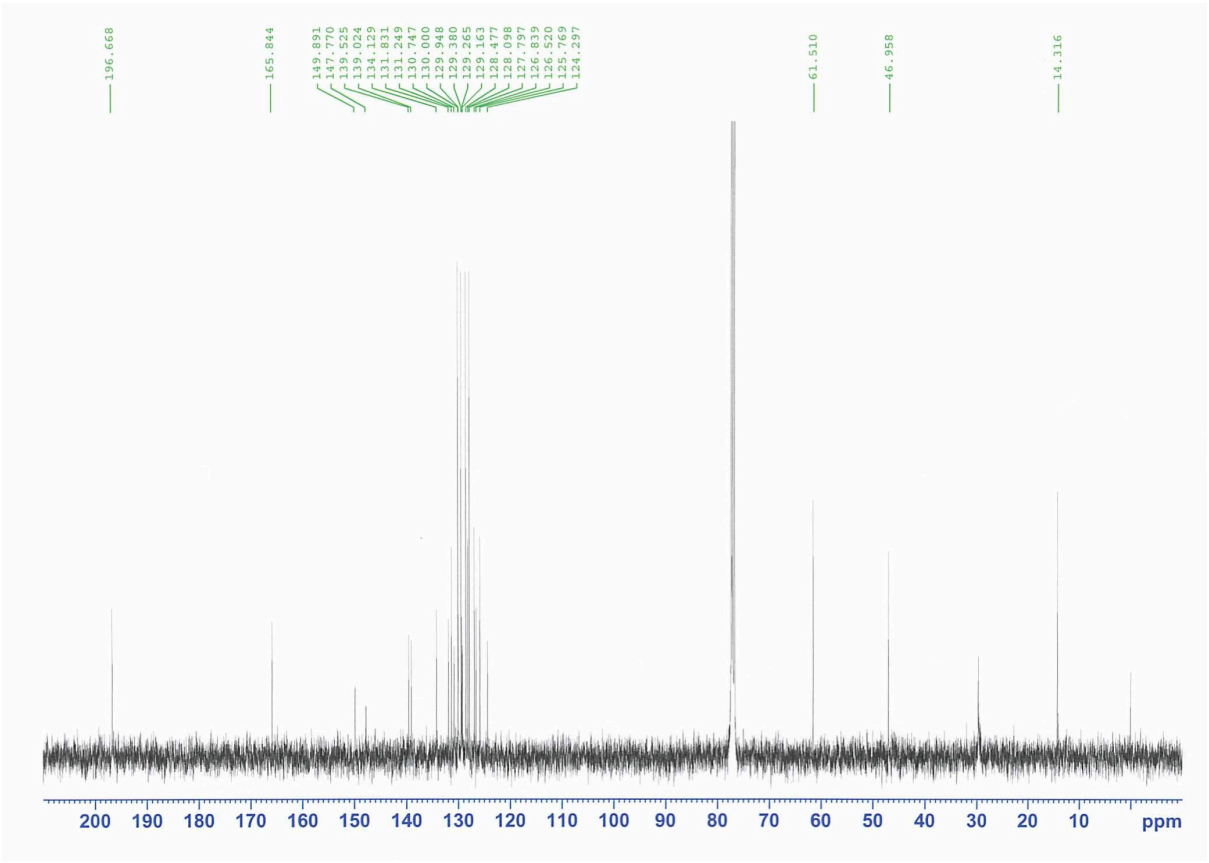
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-(3-morpholinophenyl)propanoyl)benzoate (**8d**) ($CDCl_3$)

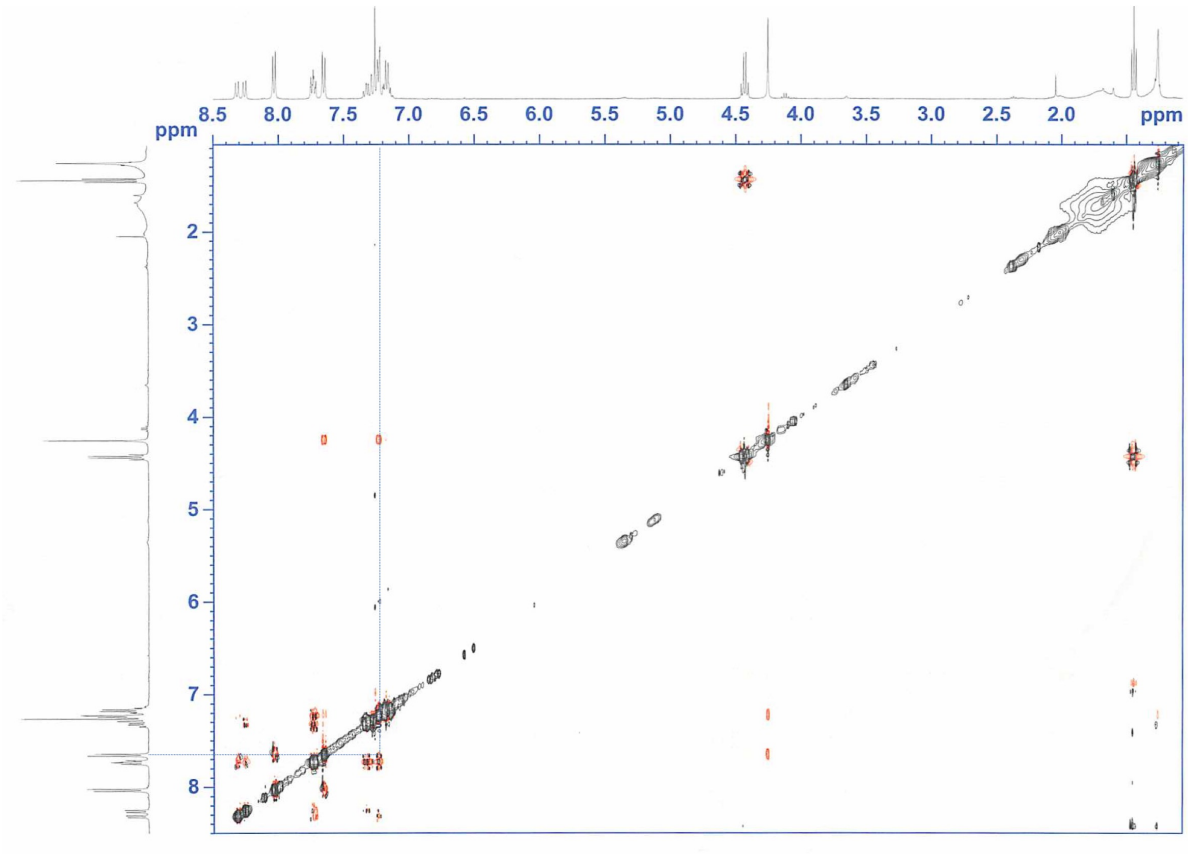




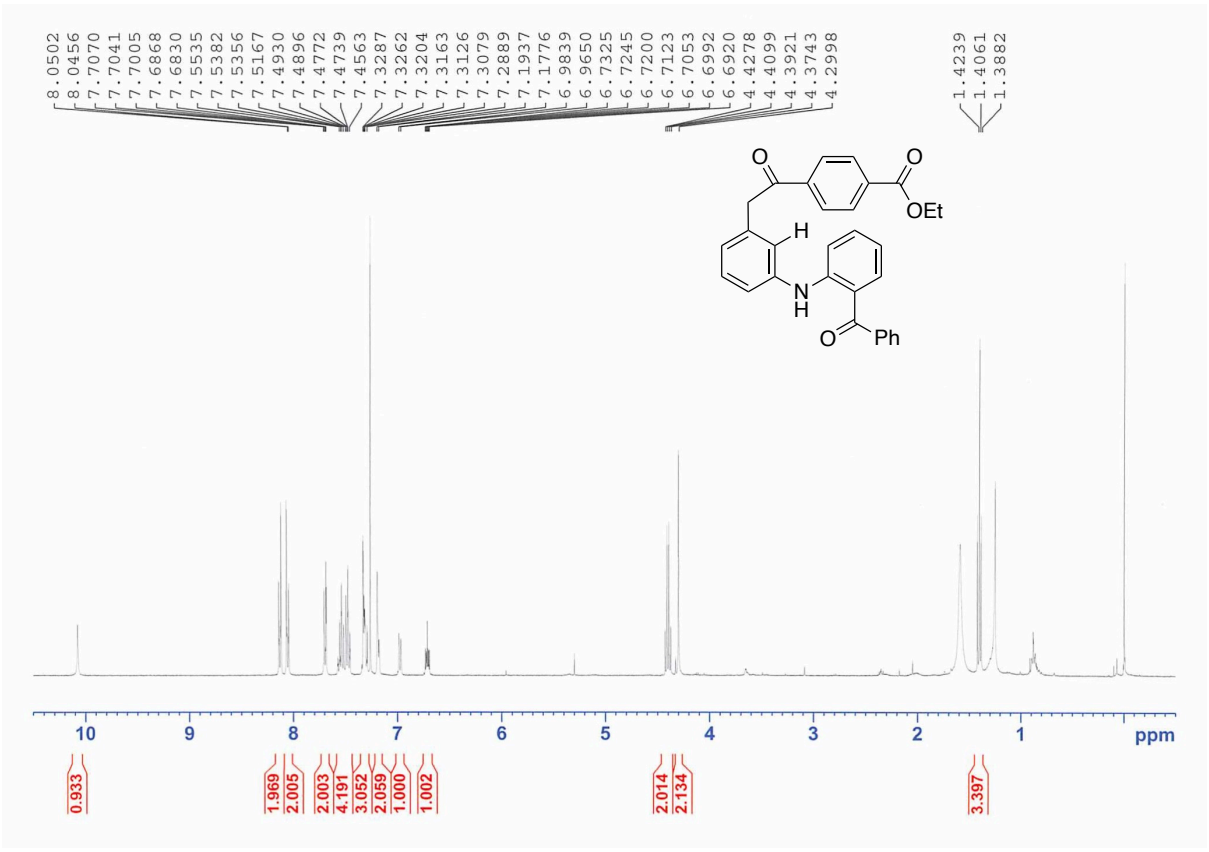
^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz), and NOESY spectra of ethyl 4-(2-(1-benzyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzoate (**14**) ($CDCl_3$)

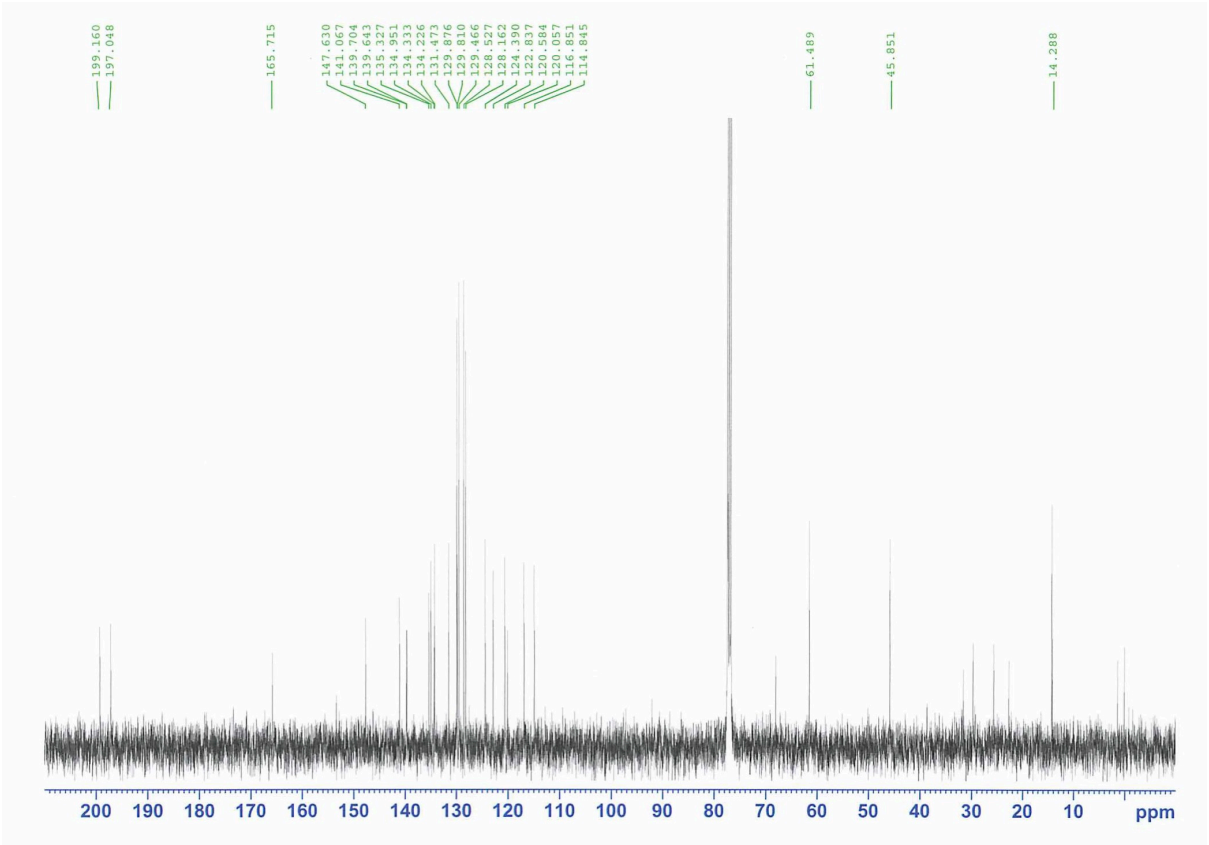




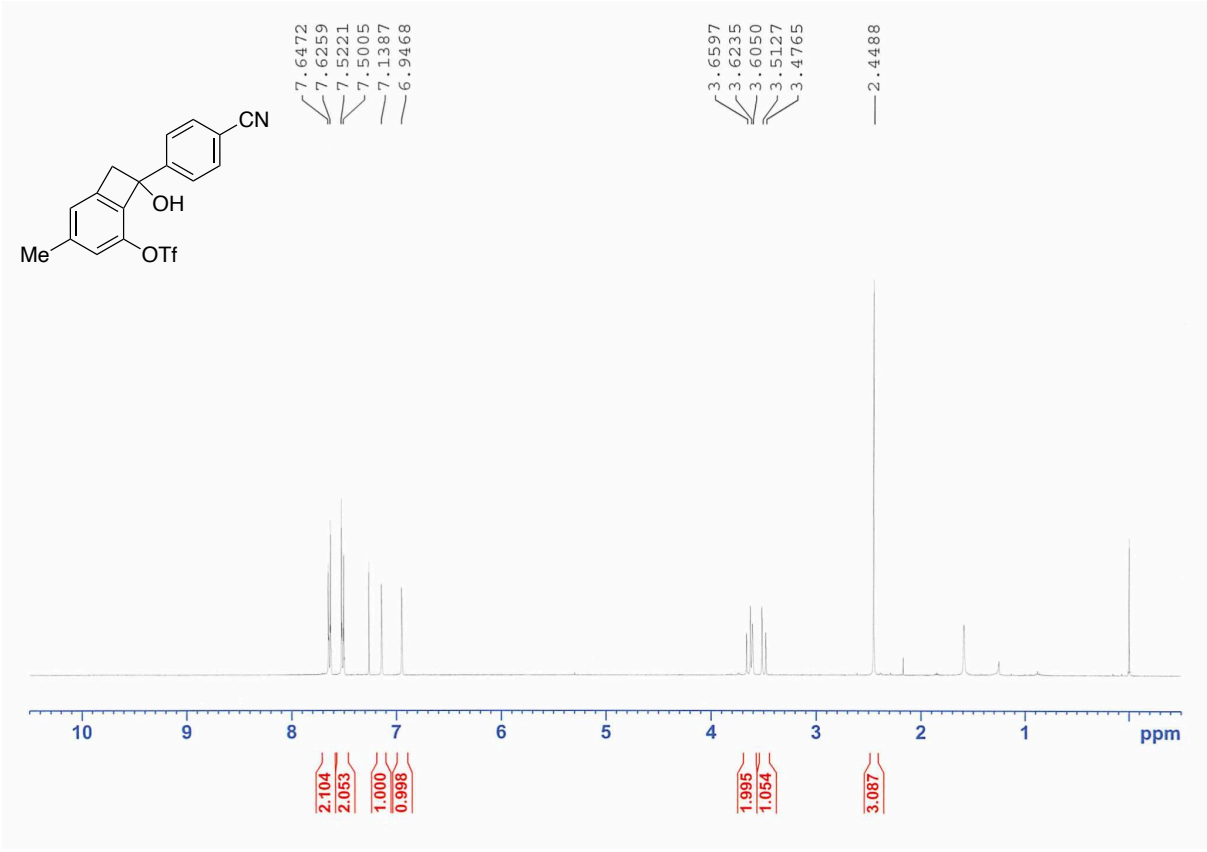

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
ppm
2
3
4
5
6
7
8

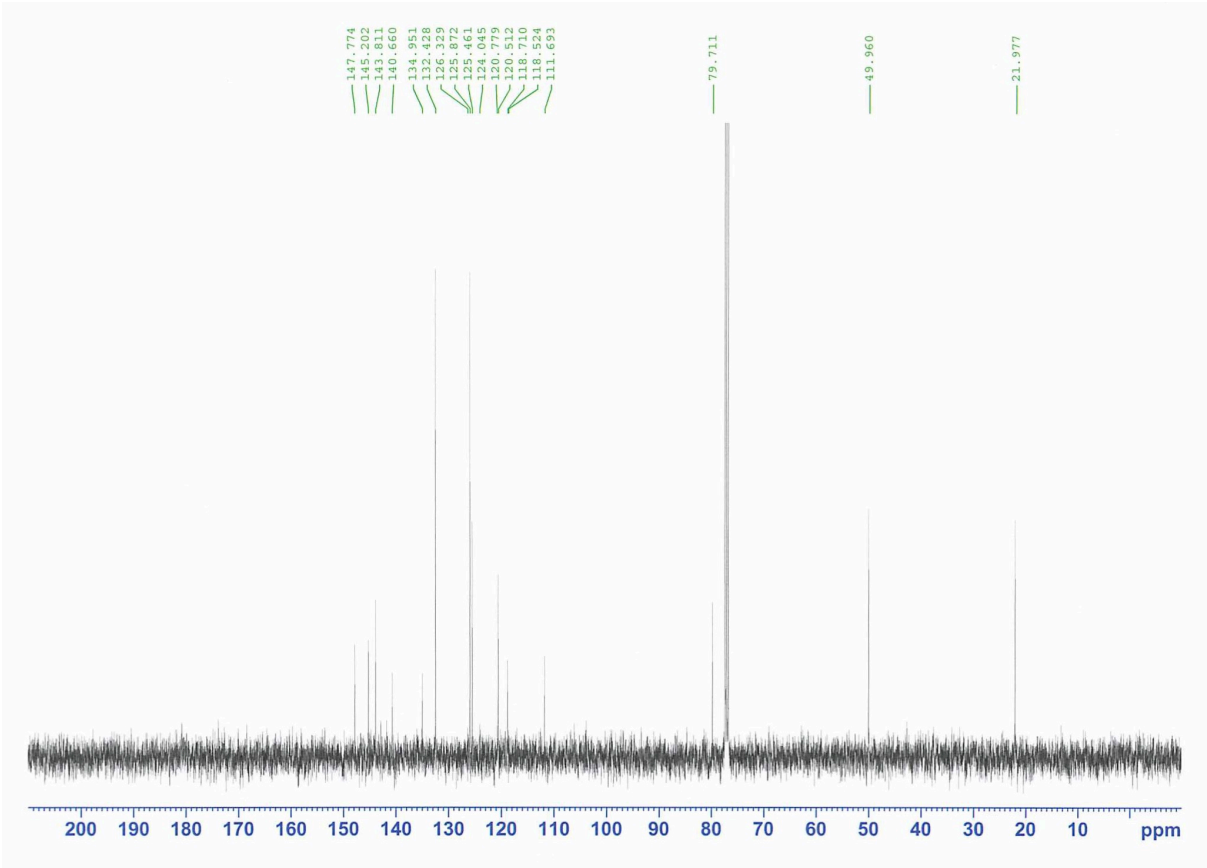
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-(1-benzyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzoate (**15**) ($CDCl_3$)



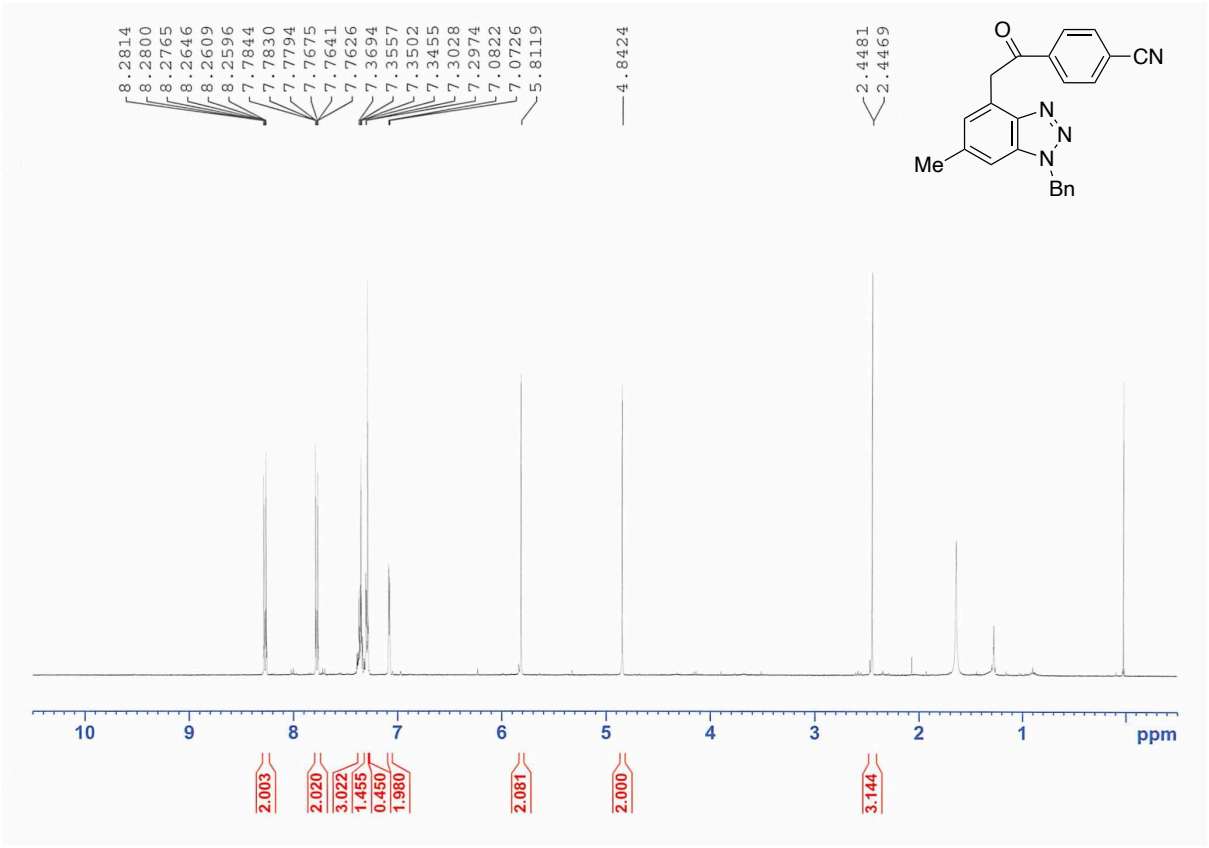


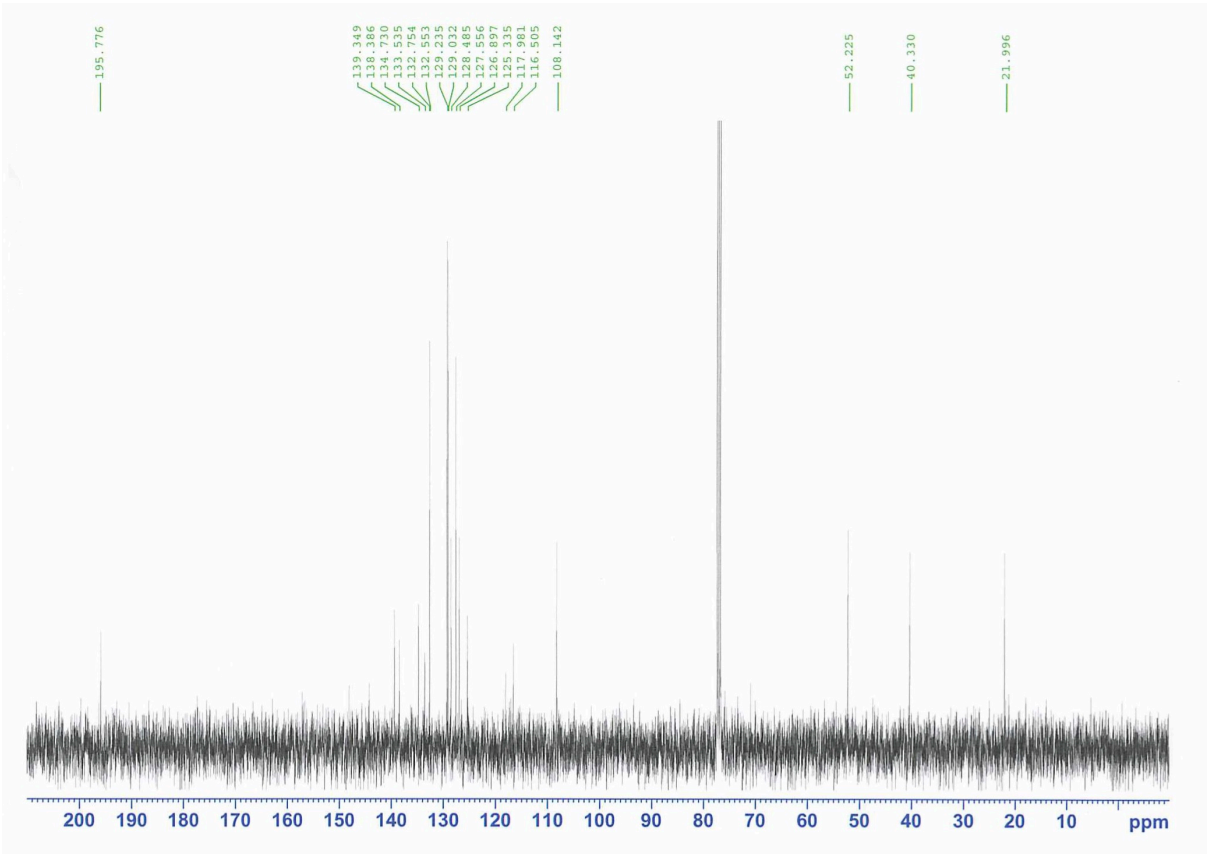
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 8-(4-cyanophenyl)bicyclo[4.2.0]octa-1(6),2,4-triene-2,8-diyl bis(trifluoromethanesulfonate) (**3m**) ($CDCl_3$)



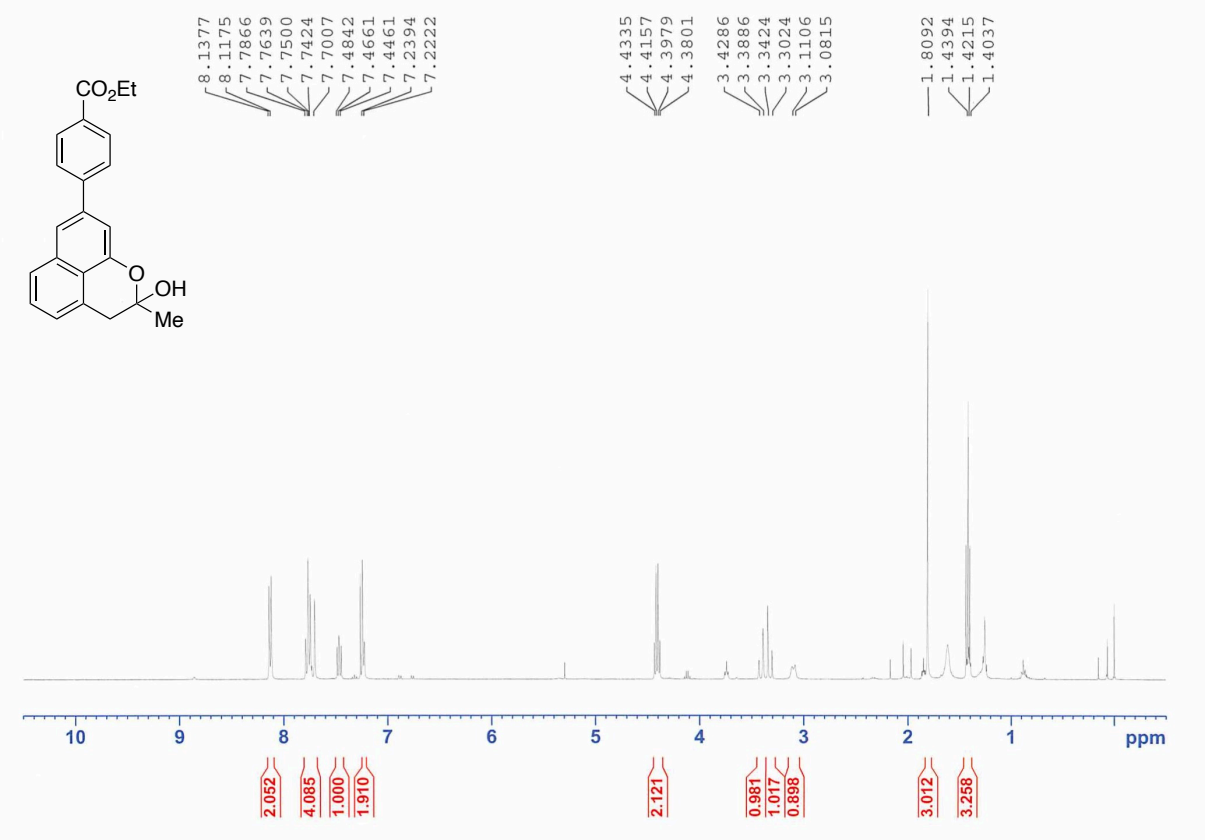


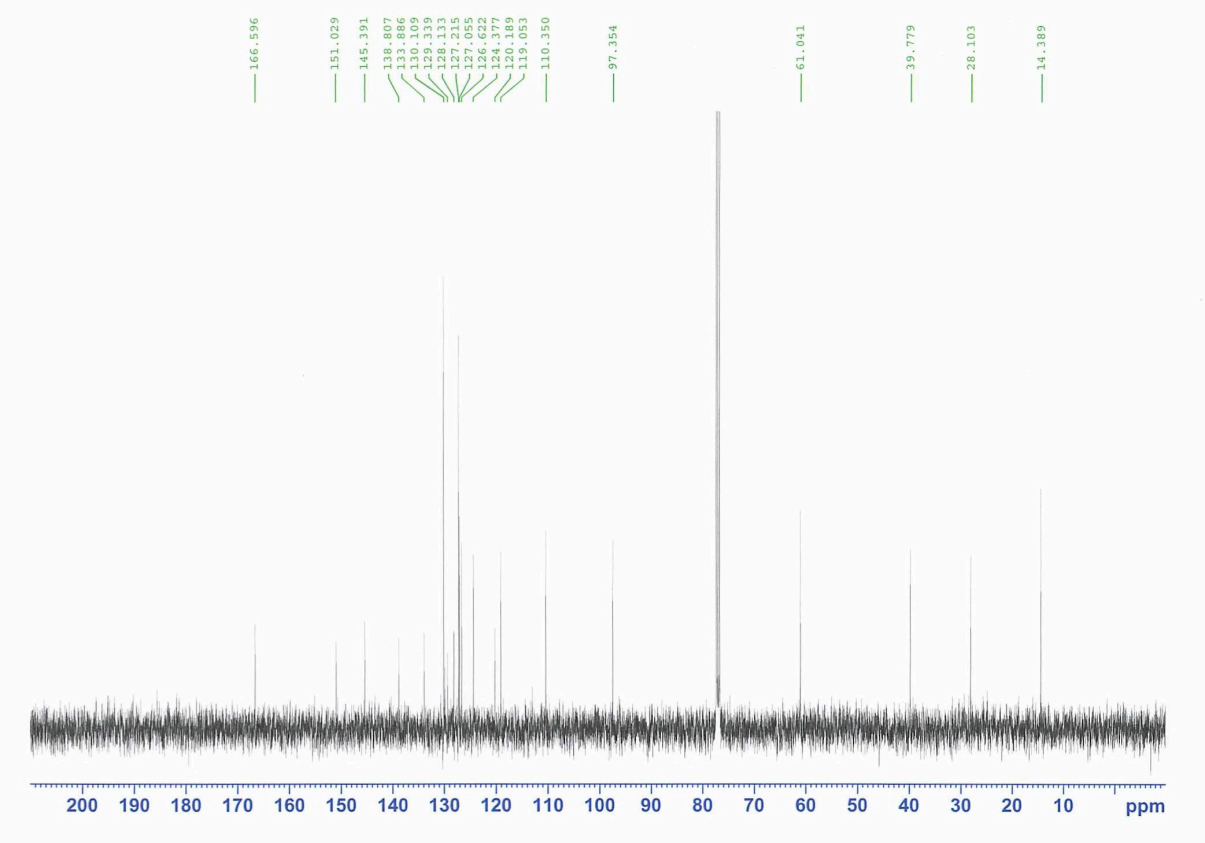
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(2-(1-benzyl-6-methyl-1*H*-benzo[*d*][1,2,3]triazol-4-yl)acetyl)benzonitrile (**17**) ($CDCl_3$)





^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-hydroxy-2-methyl-2,3-dihydrobenzo[*de*]chromen-8-yl)benzoate (**19**) ($CDCl_3$)





^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of ethyl 4-(2-methylbenzo[*de*]chromen-8-yl)benzoate (**20**) ($CDCl_3$)