Supporting Information

Enantioselective Transannular Reactions by Palladium-Catalysed Conjugate Addition of Aryl Boronic Acids

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1. General information

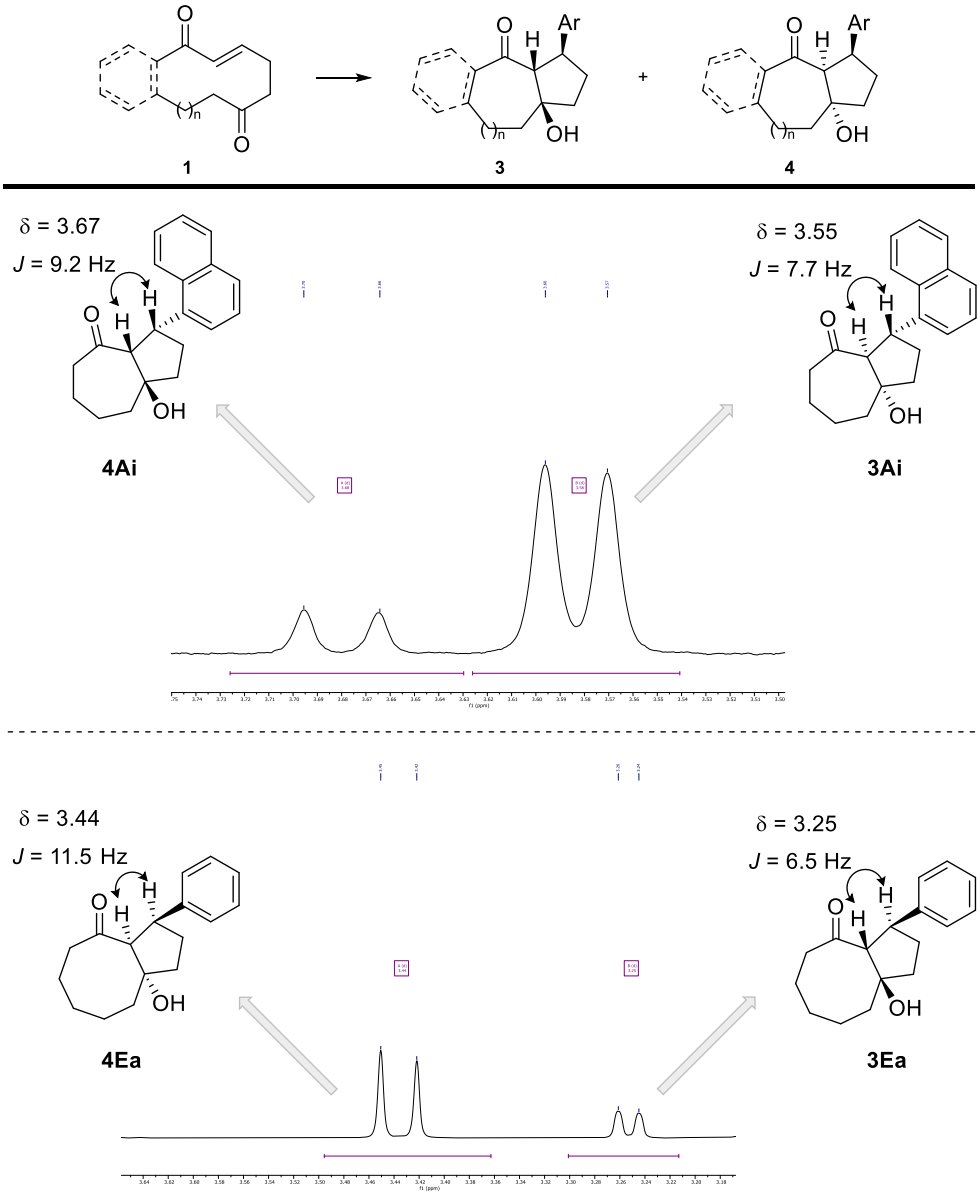
Analytical grade solvents and *commercially available reagents* were used without further purification. *Anhydrous solvents* were purified and dried with activated molecular sieves prior to use.[1] For reactions carried out under inert conditions, the argon was previously dried through a column of $CaCl_2$. All the glassware was dried for 12 hours prior to use in an oven at 140ºC, and allowed to cool under a dehumidified atmosphere. Reactions were monitored using analytical thin layer chromatography (TLC), in pre-coated TLC plates with fluorescent indicator (Merck Kiesegel 60 F_{254}). *Flash chromatography* was performed on standard silica gel (Silicycle 40-63, 230-400 mesh) and fractions visualized in TLC plates using standard visualizing agents: UV (254 and 366 nm), potassium permanganate/Δ and phosphomolybdic acid stains (PMA)/Δ. For the removal of the solvents under reduced pressure Büchi R-200 series rotatory evaporators were used. For precision weighting Sartorius Analytical Balance was used (±0.1 mg). *NMR spectra* were recorded at 25ºC on a Bruker spectrometer (400 or 300 MHz for ^{1}H and 100 or 75.5 MHz for ^{13}C). ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR chemical shifts (δ) are reported in ppm with the solvent (or TMS) resonance as the internal standard ($CHCl_3$: 7.26 ppm (^{1}H)) and ($CDCl_3$: 77.16 ppm (^{13}C). Data are reported as follows: chemical shift, multiplicity (d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz) and integration. *High resolution mass spectra (HRMS)* were recorded using an Aquity UPLC coupled to a QTOF mass spectrometer (SYNAPT G2 HDMS) using electrospray ionization (ESI^+ or ESI^-) or an Dionex, Ultimate 3000 UHPLC coupled to a Orbitrap mass spectrometer (Thermo Scientific, Orbitrap ELITE) using heated electrospray ionization (H-ESI). *Melting points (M.p.)* were measured in a Stuart apparatus in open capillary tubes and are uncorrected. The *enantiomeric excess (e.e.)* of the products was determined by High Performance Liquid Chromatography (HPLC) on a chiral stationary phase in a Waters chromatograph coupled to a photodiode array detector. Daicel Chiralpak ID-3 column (0.46 × 25 cm) and IC-3 column (0.46 × 25 cm) were used; specific conditions are indicated for each case. *Specific optical rotations* ($[\alpha]_D^{20}$) were measured at 20ºC on a Jasco polarimeter with sodium lamp at 589 nm and a path of length of 1 dm. Solvent and concentration are specified in each case.

[1] (a) Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 7th ed.; Elsevier: Oxford, 2012. (b) Williams, D. B. G.; Lawton, M. *J. Org. Chem*. **2010**, *75*, 8351.

2. Experimental procedures and characterizations

Assignation of minor stereoisomers

The configuration of compound **4Ea** has been assigned by comparison of its ^{1}H NMR spectra with those of compounds **3Ai** and **4Ai**. Compound **3Ai** has a doublet at 3.55 ppm for Hα with a coupling constant value (*J* = 7.7 Hz), which, as determined by the X-ray structure, corresponds to this proton being *trans* to the adjacent proton. A very similar coupling constant is also observed for adduct **3Ea** (*J* = 6.5 Hz) and for the other adducts **3Aa-j** (see ESI). The compound **4Ea**, on the contrary, shows a doublet for Hα at 3.44 ppm with a higher constant value (*J* = 11.5 Hz, 1H). Analogous values are also observed for the other diastereomers **4Aa-j** in the crude reaction mixtures.



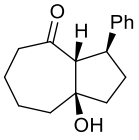
Scheme ESI-1. Analysis of crude reaction mixtures for the reaction of **1Ai** and **1Ea**

General Procedure **for the enantioselective transannular conjugate addition/aldol reaction**

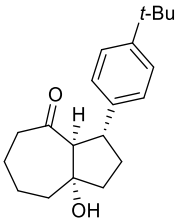
The reaction was performed using a literature procedure as follows.[2] In a flame dried tube equipped with a septum and stirring bar, Pd(O_2CCF_3) (0.01 mmol, 3.32 mg), and QuinoxP (0.011 mmol, 4.0 mg) were dissolved in THF (2 mL) and stirring under argon atmosphere at room temperature for 10 min. Boronic acid (**2**) (0.60 mmol) was added followed by the addition of the corresponding enone (**1**) (0.20 mmol). After the addition of H_2O (0.2 mL) the mixture

[2] Gini, F.; Hessen, B.; Minnaard, A. J. *Org. Lett.* **2005**, *7*, 5309-5312.

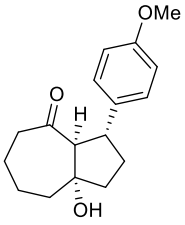
was purged, the septum substituted by a glass stopper and refluxed to 70 ºC for 18-72 h. The crude was cooled down to room temperature and a saturated aqueous solution of $NaHCO_3$ (10 mL) was added. The organic phase was separated and the resulting aqueous layer extracted with CH_2Cl_2 (3 × 7 mL). The combined organic phases were dried, the solvent removed under reduced pressure, the diastereoisomer ratio measured analysing the crude NMR and the residue purified onto silica-gel column. Racemic standars were prepared using *rac*-BINAP (0.011 mmol, 6.84 mg) as ligand



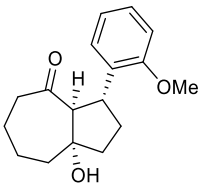
(3*S*,3a*R*,8a*R*)-8a-hydroxy-3-phenyloctahydroazulen-4(1H)-one (**3Aa**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **3Aa** (40 mg, 0.16 mmol) was isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc gradient 3:1) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2a** (73 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 82% (d.r. 7:1; e.e. 96%). White solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35 – 7.27 (m, 4H), 7.22 – 7.17 (m, 1H), 3.88 – 3.78 (m, 1H), 3.25 (d, *J* = 8.4 Hz, 1H), 2.56 – 2.39 (m, 2H), 2.22 – 1.90 (m, 5H), 1.80 (dd, *J* = 13.0, 5.5 Hz, 1H), 1.72 – 1.57 (m, 4H), 1.50 – 1.40 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.9, 144.8, 128.5, 127.8, 126.3, 82.2, 70.8, 45.4, 43.8, 43.5, 38.2, 32.3, 23.4, 22.1. HRMS (H-ESI/ Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{16}H_{20}NaO_2$ 267.1356; Found 267.1358. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{minor} = 11.2 min, t_{major} = 13.4 min (96% e.e.). $[\alpha]_D^{20}$: +20.8 (*c* 1.00, $CHCl_3$).



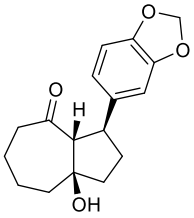
(3*R*,3a*S*,8a*S*)-3-(4-(*tert*-butyl)phenyl)-8a-hydroxyoctahydroazulen-4(1*H*)-one (**3Ab**). Following the *General Procedure* using (*R*,*R*)-QuinoxP, **3Ab** (37 mg, 0.12 mmol) was isolated after 48 h at 70 ºC by flash chromatography (petroleum ether/EtOAc gradient from 8:2 to 1:1) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2b** (106 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 62% (d.r. 4:1; e.e. 93%). Yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.30 (d, *J* = 8.4 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 3.79 (dt, *J* = 11.5, 8.0 Hz, 1H), 3.22 (d, *J* = 8.3 Hz, 1H), 2.55 – 2.35 (m, 2H), 2.20 – 1.86 (m, 5H), 1.77 (dd, *J* = 12.9, 5.3 Hz, 1H), 1.71 – 1.52 (m, 4H), 1.42 (ddd, *J* = 15.9, 12.9, 3.3 Hz, 1H), 1.30 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 210.9, 149.0, 141.7, 127.4, 125.4, 82.2, 70.8, 44.9, 43.8, 43.5, 38.2, 34.5, 32.3, 31.5, 23.4, 22.1. HRMS (UPLC/ESI/Q-TOF) m/z: $[M + Na]^+$ Calcd. for $C_{20}H_{28}NaO_2$ 323.1982; Found 323.1987. The e.e. was determined by HPLC using a Chiralpak ID-3 column [*n*-hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; t_{major} = 6.3 min, t_{minor} = 5.0 min (93% e.e.). $[\alpha]_D^{20}$: -16.7 (*c* 1.00, CH_2Cl_2). M.p. (petroleum ether/EtOAc 1:1): 153-155 ºC



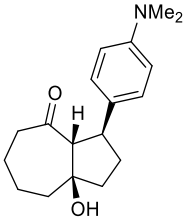
(3*R*,3a*S*,8a*S*)-8a-hydroxy-3-(4-methoxyphenyl)octahydroazulen-4(1*H*)-one (**3Ac**). Following the *General Procedure* using (*R*,*R*)-QuinoxP, **3Ac** (43 mg, 0.15 mmol) was isolated after 18 h at 70 ºC by flash chromatography (petroleum ether/EtOAc gradient from 8:2 to 1:1) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2c** (91 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 78% (d.r. 4:1; e.e. 91%). Yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) ($^+$ indicates partially overlapped signals): δ 7.31 – 7.11 (m, 2H), 6.85 – 6.76 (m, 2H), 4.03 – 3.65$^+$ (m, 1H), 3.77$^+$ (s, 3H), 3.16 (d, *J* = 8.4 Hz, 1H), 2.56 – 2.34 (m, 2H), 2.18 – 1.85 (m, 5H), 1.80 – 1.50 (m, 5H), 1.47 – 1.33 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 210.9, 158.1, 136.8, 128.7, 113.9, 82.1, 71.1, 55.4, 44.6, 43.8, 43.6, 38.3, 32.4, 23.5, 22.2. HRMS (UPLC/ESI/Q-TOF) m/z: $[M + Na]^+$ Calcd. for $C_{17}H_{22}NaO_3$ 297.1461; Found 297.1467. The e.e. was determined by HPLC using a Chiralpak ID-3 column [*n*-hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; t_{major} = 18.0 min, t_{minor} = 10.8 min (91% e.e.). $[\alpha]_D^{20}$: -11.9 (*c* 1.00, CH_2Cl_2).



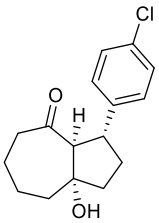
(3*R*,3a*S*,8a*S*)-8a-hydroxy-3-(2-methoxyphenyl)octahydroazulen-4(1*H*)-one (**3Ad**). Following the *General Procedure* using (*R*,*R*)-QuinoxP, **3Ad** (36 mg, 0.13 mmol) was isolated after 48 h at 70 ºC by flash chromatography (petroleum ether/EtOAc gradient from 8:2 to 1:1) starting from **1Aa** (34 mg, 0.2 mmol), boronic acid **2d** (91 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 65% (d.r. 4:1; e.e. 98%). Yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.21 – 7.06 (m, 2H), 6.82 (t, *z* = 7.4 Hz, 2H), 3.88 (dt, *J* = 11.5, 7.4 Hz, 1H), 3.80 (s, 3H), 3.34 (d, *J* = 7.0 Hz, 1H), 3.05 (bs, 1H), 2.37 (t, *J* = 6.3 Hz, 2H), 2.16 (ddt, *J* = 17.9, 11.9, 5.9 Hz, 1H), 2.05 – 1.82 (m, 4H), 1.68 (dd, *J* = 12.9, 6.0 Hz, 1H), 1.62 – 1.37 (m, 3H), 1.25 (t, *J* = 12.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 210.6, 130.4, 127.8, 121.2, 111.2, 83.0, 67.8, 55.4, 43.4, 42.4, 42.2, 36.9, 29.6, 23.4, 22.0. HRMS (UPLC/ESI/Q-TOF) m/z: $[M + Na]^+$ Calcd. for $C_{17}H_{22}NaO_3$ 297.1461; Found 297.1472. The e.e. was determined by HPLC using a Chiralpak ID-3 column [*n*-hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; t_{major} = 31.7 min, t_{minor} = 41.1 min (98% e.e.). $[\alpha]_D^{20}$: -23.5 (*c* 1.00, CH_2Cl_2).



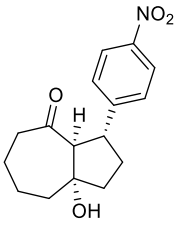
(3*S*,3a*R*,8a*R*)-3-(benzo[d][1,3]dioxol-5-yl)-8a-hydroxyoctahydroazulen-4(1H)-one (**3Ae**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **3Ae** (34 mg, 0.12 mmol) was isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc 1:3) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2e** (100 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 59% (d.r. 4:1; e.e. 90%). Yellow amorphous solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.84 (d, *J* = 1.6 Hz, 1H), 6.77 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 5.92 (s, 2H), 3.75 (dt, *J* = 11.2, 8.0 Hz, 1H), 3.17 (d, *J* = 8.3 Hz, 1H), 2.55 – 2.40 (m, 2H), 2.13 – 2.01 (m, 3H), 2-00 -1.90 (m, 2H), 1.76 (dd, *J* = 12.8, 5.0 Hz, 1H), 1.71 – 1.55 (m, 4H), 1.43 (ddd, *J* = 15.9, 12.8, 3.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.6, 147.6, 145.8, 138.6, 120.5, 108.1, 108.0, 100.8, 82.0, 70.9, 45.1, 43.6, 43.4, 38.1, 32.4, 23.3, 22.0. HRMS (H-ESI/ Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{17}H_{20}NaO_4$ 311.1254; Found 311.1255. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{minor} = 25.2 min, t_{major} = 30.0 min (90% e.e.). $[\alpha]_D^{20}$: +22 (*c* 1.00, $CHCl_3$).



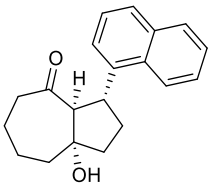
(3*S*,3a*R*,8a*R*)-3-(4-(dimethylamino)phenyl)-8a-hydroxyoctahydroazulen-4(1H)-one (**3Af**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **3Af** (31 mg, 0.11 mmol) was isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc gradient from 1:3) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2f** (99 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 55% (d.r. 5:1; e.e. 92%). Yellow amorphous solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.20 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 8.7 Hz, 2H), 3.74 (dt, *J* = 11.8, 7.7 Hz, 1H), 3.19 (d, *J* = 8.4 Hz, 1H), 2.92 (s, 6H), 2.52 – 2.38 (m, 2H), 2.17 – 1.87 (m, 6H), 1.77 (dd, *J* = 13.1, 5.4 Hz, 1H), 1.71 -1.56 (m, 3H), 1.43 (ddd, *J* = 16.1, 13.0, 3.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.9, 149.3, 132.7, 128.2, 112.9, 82.0, 71.0, 44.4, 43.7, 43.5, 40.9, 38.1, 32.3, 23.4, 22.1. HRMS (H-ESI/ Orbitrap) m/z: $[M + H]^+$ Calcd. for $C_{18}H_{26}NO_2$ 288.1958; Found 288.1958. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{major} = 36.7 min, t_{minor} = 46.0 min (92% e.e.). $[\alpha]_D^{20}$: +24 (*c* 1.00, $CHCl_3$).



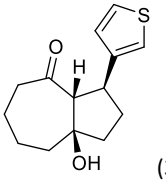
(3*R*,3a*S*,8a*S*)-3-(4-chlorophenyl)-8a-hydroxyoctahydroazulen-4(1*H*)-one (**3Ag**). Following the *General Procedure* using (*R*,*R*)-QuinoxP, **3Ag** (27 mg, 0.09 mmol) was isolated after 48 h at 70 ºC by flash chromatography (petroleum ether/EtOAc gradient from 8:2 to 1:1) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2g** (94 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 47% (d.r. 4:1; e.e. 89%). Yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.22 (s, 4H), 3.75 (dt, *J* = 11.0, 8.1 Hz, 1H), 3.15 (d, *J* = 8.4 Hz, 1H), 2.61 – 2.26 (m, 2H), 2.18 – 1.85 (m, 5H), 1.77 (dd, *J* = 12.6, 5.3 Hz, 1H), 1.72 – 1.51 (m, 4H), 1.41 (ddd, J = 16.1, 13.0, 3.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 210.7, 143.2, 132.0, 129.2, 128.6, 82.1, 70.9, 44.8, 43.8, 43.4, 38.2, 32.2, 23.4, 22.1. HRMS (UPLC/ESI/Q-TOF) m/z: $[M - H_2O + H]^+$ Calcd. for $C_{16}H_{18}ClO$ 261.1041; Found 261.1042. The e.e. was determined by HPLC using a Chiralpak ID-3 column [*n*-hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; t_{major} = 8.3 min, t_{minor} = 5.9 min (89% e.e.). $[\alpha]_D^{20}$: -13.3 (*c* 0.50, $CHCl_3$). M.p. (petroleum ether/EtOAc 1:1): 76-78 ºC



(3*R*,3a*S*,8a*S*)-8a-hydroxy-3-(4-nitrophenyl)octahydroazulen-4(1*H*)-one (**3Ah**). Following the *General Procedure* using (*R*,*R*)-QuinoxP, **3Ah** (3 mg, 0.01 mmol) was isolated after 72 h at 70 ºC by flash chromatography (petroleum ether/EtOAc gradient from 7:3 to 1:1) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2h** (100 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: <5% (d.r. 4:1; e.e. not determined). Yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.12 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 3.89 (dt, *J* = 11.4, 8.0 Hz, 1H), 3.19 (d, *J* = 8.4 Hz, 1H), 2.57 – 2.36 (m, 2H), 2.24 – 1.87 (m, 5H), 1.81 (dd, *J* = 12.6, 5.3 Hz, 1H), 1.75 – 1.52 (m, 4H), 1.52 – 1.37 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.1, 152. 7, 146.6, 128.7, 123.8, 82.2, 70.6, 45.3, 43.9, 43.3, 38.2, 32.2, 23.3, 22.0. HRMS (UPLC/ESI/Q-TOF) m/z: $[M - H_2O + H]^+$ Calcd. for $C_{16}H_{18}NO_3$ 272.1281; Found 272.1289.

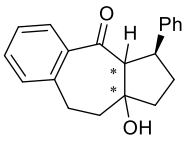


(3*R*,3a*S*,8a*S*)-8a-hydroxy-3-(naphthalen-1-yl)octahydroazulen-4(1*H*)-one (**3Ai**). Following the *General Procedure* using (*R*,*R*)-QuinoxP, **3Ai** (30 mg, 0.10 mmol) was isolated after 24 h at 70 ºC by flash chromatography (petroleum ether/EtOAc gradient from 8:2 to 1:1) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2i** (103 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 51% (d.r. 4:1; e.e. 79%). Yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.43 (d, *J* = 8.4 Hz, 1H), 7.83 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.61 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.56 – 7.40 (m, 3H), 4.71 (dt, *J* = 11.3, 7.6 Hz, 1H), 3.55 (d, *J* = 7.7 Hz, 1H), 2.42 (td, *J* = 5.7, 1.2 Hz, 2H), 2.32 – 2.15 (m, 2H), 2.12 – 1.90 (m, 3H), 1.89 – 1.43 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 211.1, 141.4, 134.0, 132.1, 128.8, 126.8, 126.0, 125.7, 125.6, 124.6, 124.1, 82.6, 70.0, 43.8, 43.4, 40.5, 38.2, 33.4, 23.3, 22.0. HRMS (UPLC/ESI/Q-TOF) m/z: $[M + Na]^+$ Calcd. for $C_{20}H_{22}NaO_2$ 317.1512; Found 317.1520. The e.e. was determined by HPLC using a Chiralpak ID-3 column [*n*-hexane/*i*-PrOH (90:10)]; flow rate 1.0 mL/min; t_{major} = 11.0 min, t_{minor} = 7.5 min (79% e.e.). $[\alpha]_D^{20}$: +53.2 (*c* 1.00, $CHCl_3$). M.p. (petroleum ether/EtOAc 1:1): 138-140 ºC

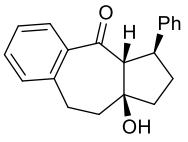


(3*S*,3a*R*,8a*R*)-8a-hydroxy-3-(thiophen-3-yl)octahydroazulen-4(1*H*)-one (**3Aj**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **3Aj** (32 mg, 0.13 mmol) was isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc 1:3) starting from **1A** (34 mg, 0.2 mmol), boronic acid **2j** (81 mg, 0.6 mmol), $Pd(O_2CCF_3)_2$ (3.32 mg, 0.01 mmol), (*S,S*)-QuinoxP (3.68 mg, 0.011 mmol) and THF/H_2O 10:1 (2.2 mL). Yield: 64% (d.r. 4:1; e.e. 92%).

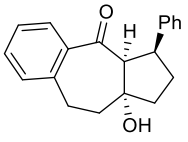
White amorphous solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.25 (dd, *J* = 4.7, 3.2 Hz, 1H), 7.02 – 6.99 (dm, 2H), 3.92 – 3.85 (m, 1H), 3.18 (d, *J* = 8.5 Hz, 1H), 2.59 – 2.44 (m, 2H), 2.16 – 2.02 (m, 3H), 2.01 – 1.91 (m, 2H), 1.81-1.75 (m, 1H), 1.71-1.58 (s, 4H), 1.42 (t, *J* = 14.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.8, 145.5, 125.4, 119.8, 81.9, 70.4, 43.6, 43.4, 40.5, 38.1, 31.4, 23.4, 22.1. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{14}H_{18}NaO_2S$ 273.0920; Found 273.0922. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{minor} = 11.7 min, t_{major} = 12.2 min (92% e.e.). $[\alpha]_D^{20}$: +23 (*c* 1.00, $CHCl_3$).



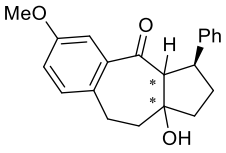
10a-Hydroxy-6-methoxy-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**3Ba** + **4Ba**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **3Ba** + **4Ba** (25 mg, 0.086 mmol) were isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc 1:3) starting from **1b** (21 mg, 0.1 mmol), boronic acid **2a** (37 mg, 0.3 mmol), $Pd(O_2CCF_3)_2$ (1.66 mg, 0.005 mmol), (*S,S*)-QuinoxP (1.84 mg, 0.0055 mmol) and THF/H_2O 10:1 (1.1 mL). Yield: 77% (d.r. 1:2).



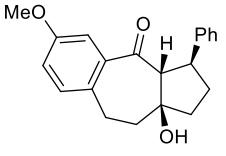
(3*S*,3a*R*,10a*S*)-10a-hydroxy-6-methoxy-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**3Ba**) (minor diastereomer, 8.2 mg, e.e. 97%). Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.30 – 7.22 (m, 4H), 7.19 – 7.15 (m, 1H), 4.26 (ddd, *J* = 10.3, 8.4, 5.4 Hz, 1H), 3.66 (dd, *J* = 17.8, 11.1 Hz, 1H), 3.40 (dd, *J* = 5.4, 1.4 Hz, 2H), 3.00 (dd, *J* = 17.7, 6.6 Hz, 1H), 2.40 – 2.31 (m, 1H), 2.28 – 2.16 (m, 2H), 1.93 – 1.79 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.9, 145.70, 141.4, 139.6, 130.7, 129.8, 128.9, 128.5, 127.8, 126.1, 83.8, 70.5, 44.5, 41.1, 38.5, 33.5, 29.6. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{20}H_{20}NaO_2$ 315.1356; Found 315.1354. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{minor} = 11.9 min, t_{major} = 15.2 min (97% e.e.). $[\alpha]_D^{20}$: +17 (*c* 1.00, $CHCl_3$).



(3*S*,3a*S*,10a*R*)-10a-hydroxy-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1H)-one (**4Ba**). (major diastereomer, 14.3 mg, e.e. >99%). Yellow amorphous solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39 – 7.33 (m, 2H), 7.30 – 7.15 (m, 7H), 3.98 – 3.88 (m, 2H), 3.54 (dd, *J* = 17.4, 11.6 Hz, 1H), 3.01 (dd, *J* = 17.4, 7.0 Hz, 1H), 2.82 – 2.72 (m, 1H), 2.44 (ddd, *J* = 13.2, 6.3, 3.4 Hz, 1H), 2.34 (dd, *J* = 15.0, 7.0 Hz, 1H), 2.18 – 2.04 (m, 2H), 1.88 (dd, *J* = 15.0, 11.9 Hz, 1H), 1.79 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.7, 142.3, 142.3, 140.4, 130.7, 129.8, 128.0, 127.4, 126.3, 125.4, 84.4, 66.2, 45.0, 40.4, 39.2, 30.8, 27.8. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{20}H_{20}NaO_2$ 315.1356; Found 315.1356. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{major} = 15.0 min, t_{minor} = 17.2 min (99% e.e.). $[\alpha]_D^{20}$: -7 (*c* 1.00, $CHCl_3$).

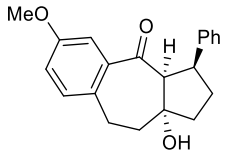


10a-hydroxy-6-methoxy-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**3Ca** + **4Ca**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **3Ca** + **4Ca** (25 mg, 0.08 mmol) was isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc 1:3) starting from **1C** (24 mg, 0.1 mmol), boronic acid **2a** (37 mg, 0.3 mmol), $Pd(O_2CCF_3)_2$ (1.66 mg, 0.005 mmol), (*S,S*)-QuinoxP (1.84 mg, 0.0055 mmol) and THF/H_2O 10:1 (1.1 mL). Yield: 77% (d.r. 1:3).

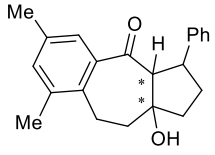


(3*S*,3a*R*,10a*S*)-10a-hydroxy-6-methoxy-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**3Ca**) (minor diastereomer, 7 mg, e.e. 95%). Yellow amorphous solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39 – 7.35 (m, 2H), 7.30 – 7.26 (m, 2H), 7.20 – 7.15 (m, 2H), 7.00 (d, *J* = 2.8 Hz, 1H), 6.93 (dd, *J* = 8.4, 2.9 Hz, 1H), 4.25 (ddd, *J* = 10.3, 8.4, 5.5 Hz, 1H), 3.80 (s, 3H), 3.57 (dd, *J* = 17.6, 11.8 Hz, 1H), 3.39 (d, *J* = 6.7 Hz, 1H), 2.94 (dd, *J* = 17.3, 6.6 Hz, 1H), 2.35 (dt, *J* = 12.4, 7.1 Hz, 1H), 2.27 – 2.16 (m, 2H), 1.95 – 1.77 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.7, 157.7, 145.7, 140.3, 133.6, 131.1, 128.5, 127.8, 127.8, 126.1, 118.1, 112.2, 83.9, 70.6, 55.5, 44.6, 41.1, 38.7, 33.5, 28.8. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{21}H_{22}NaO_3$ 345.1461; Found 345.1458. The e.e. was determined by HPLC

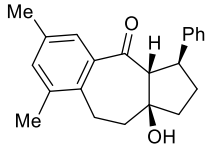
using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{minor} = 16.2 min, t_{major} = 35.9 min (95% e.e.). $[\alpha]_D^{20}$: +59 (*c* 1.00, $CHCl_3$).



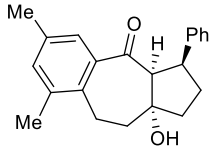
(3*S*,3a*S*,10a*R*)-10a-hydroxy-6-methoxy-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**4Ca**) (major diastereomer, 18 mg, e.e. 97%). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36 – 7.11 (m, 6H), 6.93 (dd, *J* = 8.4, 2.9 Hz, 1H), 6.86 (d, *J* = 2.9 Hz, 1H), 3.98 – 3.86 (m, 2H), 3.75 (s, 3H), 3.45 (dd, *J* = 17.2, 11.6 Hz, 1H), 2.95 (dd, *J* = 17.2, 6.9 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.48 – 2.39 (m, 1H), 2.33 (ddd, *J* = 14.9, 7.1, 1.0 Hz, 1H), 2.12 – 2.06 (m, 2H), 1.87 – 1.80 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 201.5, 157.9, 142.4, 141.2, 134.7, 131.2, 128.0, 127.3, 125.4, 117.8, 111.5, 84.4, 66.2, 55.5, 45.0, 40.7, 39.2, 30.0, 27.7. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{21}H_{22}NaO_3$ 345.1461; Found 345.1458. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{minor} = 18.0 min, t_{major} = 21.9 min (97% e.e.). $[\alpha]_D^{20}$: +39 (*c* 1.00, $CHCl_3$). M.p. (petroleum ether/EtOAc 1:1): 149-151 ºC.



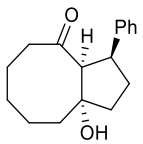
(3a*S*,10a*R*)-10a-hydroxy-6-methoxy-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**3Da** + **4Da**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **3Da** + **4Da** (15.8 mg, 0.05 mmol) were isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc 1:3) starting from **1D** (24 mg, 0.1 mmol), boronic acid **2a** (37 mg, 0.3 mmol), $Pd(O_2CCF_3)_2$ (1.66 mg, 0.005 mmol), (*S,S*)-QuinoxP (1.84 mg, 0.0055 mmol) and THF/H_2O 10:1 (1.1 mL). Yield: 49% (d.r. 1:2).



(3*S*,3a*R*,10a*S*)-10a-hydroxy-6,8-dimethyl-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**3Da**) (minor diastereomer, 5 mg, e.e. 95%). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35 – 7.32 (m, 2H), 7.29 – 7.24 (m, 3H), 7.18 – 7.14 (m, 1H), 7.09 – 7.06 (m, 2H), 4.21 (ddd, *J* = 10.6, 8.0, 5.7 Hz, 1H), 3.36 (dd, *J* = 5.6, 1.2 Hz, 1H), 3.30 (dd, *J* = 18.3, 12.1 Hz, 1H), 2.90 (dd, *J* = 18.3, 6.4 Hz, 1H), 2.39 – 2.14 (m, 3H), 2.30 (s, 3H), 2.28 (s, 3H), 1.94 – 1.81 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 203.9, 145.6, 140.56, 136.9, 135.9, 135.4, 133.1, 128.4, 127.7, 126.7, 126.0, 83.9, 70.8, 44.8, 41.4, 37.8, 33.4, 26.1, 20.6, 20.3. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{22}H_{24}NaO_2$ 343.1669; Found 343.1668. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{minor} = 10.4 min, t_{major} = 13.7 min (95% e.e.). $[\alpha]_D^{20}$: +10 (*c* 1.00, $CHCl_3$). M.p. (petroleum ether/EtOAc 1:1): 143-146 ºC



(3*S*,3a*S*,10a*R*)-10a-hydroxy-6,8-dimethyl-3-phenyl-2,3,3a,9,10,10a-hexahydrobenzo[f]azulen-4(1*H*)-one (**4Da**) (major diastereomer, 10.8 mg, e.e. >99%). Yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31 – 7.15 (m, 5H), 7.08 (dd, *J* = 1.3, 0.7 Hz, 1H), 6.93 (d, *J* = 2.0 Hz, 1H), 3.94 – 3.81 (m, 2H), 3.17 (dd, *J* = 18.0, 11.7 Hz, 1H), 3.00 (dd, *J* = 17.4, 6.5 Hz, 1H), 2.76 (dtd, *J* = 12.7, 11.4, 10.9, 6.0 Hz, 1H), 2.49 – 2.29 (m, 3H), 2.33 (s, 3H), 2.26 (s, 3H), 2.24 – 2.02 (m, 2H), 1.92 (ddd, *J* = 15.0, 11.6, 1.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.7, 142.2, 141.2, 137.1, 136.7, 135.6, 133.2, 128.0, 127.5, 126.0, 125.4, 84.5, 66.7, 45.4, 39.9, 39.6, 28.0, 26.6, 20.6, 20.4. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{22}H_{24}NaO_2$ 343.1669; Found 343.1665. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (95:5)]; flow rate 1.0 mL/min; t_{major} = 16.7 min, t_{minor} = 19.7 min (>99% e.e.). $[\alpha]_D^{20}$: +69 (*c* 1.00, $CHCl_3$). M.p. (petroleum ether/EtOAc 1:1): 194-196 ºC



(3*S*,3a*S*,9a*S*)-9a-hydroxy-3-phenyldecahydro-4*H*-cyclopenta[8]annulen-4-one (**4Ea**). Following the *General Procedure* using (*S*,*S*)-QuinoxP, **4Ea** (19 mg, 0.07 mmol) was isolated after 18 h at 70 ºC by flash chromatography (Cyclohexane/EtOAc gradient from 1:3) starting from **1E** (18 mg, 0.1 mmol), boronic acid **2a** (37 mg,

0.3 mmol), $Pd(O_2CCF_3)_2$ (1.66 mg, 0.005 mmol), (*S,S*)-QuinoxP (1.84 mg, 0.0055 mmol) and THF/H_2O 10:1 (1.1 mL). Yield: 74% (d.r. 1:3; e.e. 93%). White solid. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30 – 7.23 (m, 3H), 7.21 – 7.14 (m, 2H), 3.88 (td, *J* = 10.5, 7.8 Hz, 1H), 3.44 (d, *J* = 11.5 Hz, 1H), 3.14 (s, 1H), 2.50 – 2.40 (m, 1H), 2.32 – 2.24 (m, 1H), 2.20 – 1. 75 (m, 7H), 1.71 – 1.54 (m, 3H), 1.53 – 1.47 (m, 1H), 1.31 – 1.15 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 217.7, 143.9, 128.6, 126.9, 126.4, 84.7, 63.5, 47.6, 45.6, 41.3, 36.6, 30.6, 28.4, 22.4, 19.3. HRMS (H-ESI/Orbitrap) m/z: $[M + Na]^+$ Calcd. for $C_{17}H_{22}NaO_2$ 281.1512; Found 281.1514. The e.e. was determined by HPLC using a Chiralpak IC-3 column [*n*-hexane/*i*-PrOH (98:2)]; flow rate 1.0 mL/min; t_{major} = 37.7 min, t_{minor} = 39.3 min (93% e.e.). $[\alpha]_D^{20}$: +24 (*c* 1.00, $CHCl_3$).

3. NMR spectra

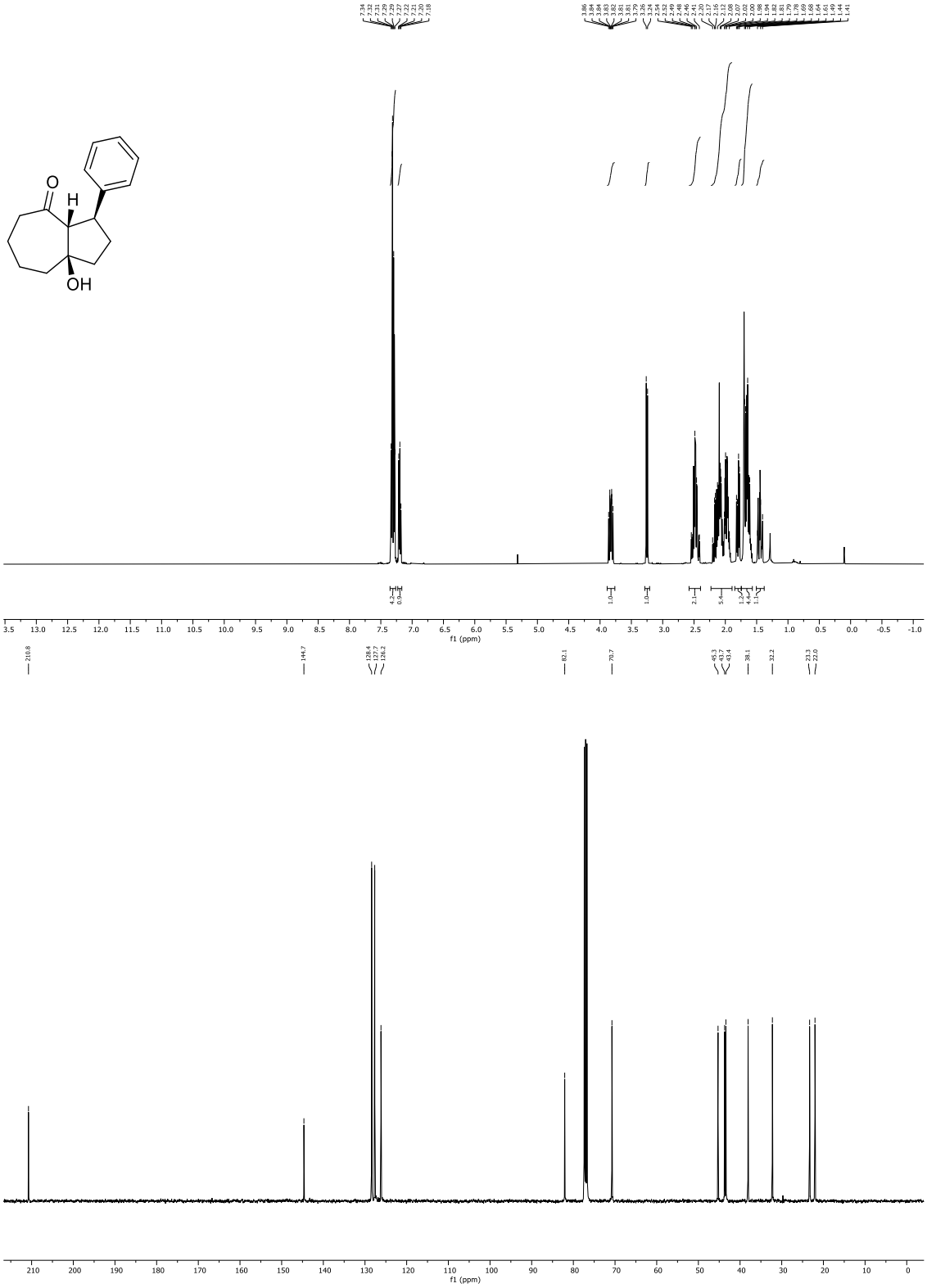


Figure ESI-1. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Aa**.

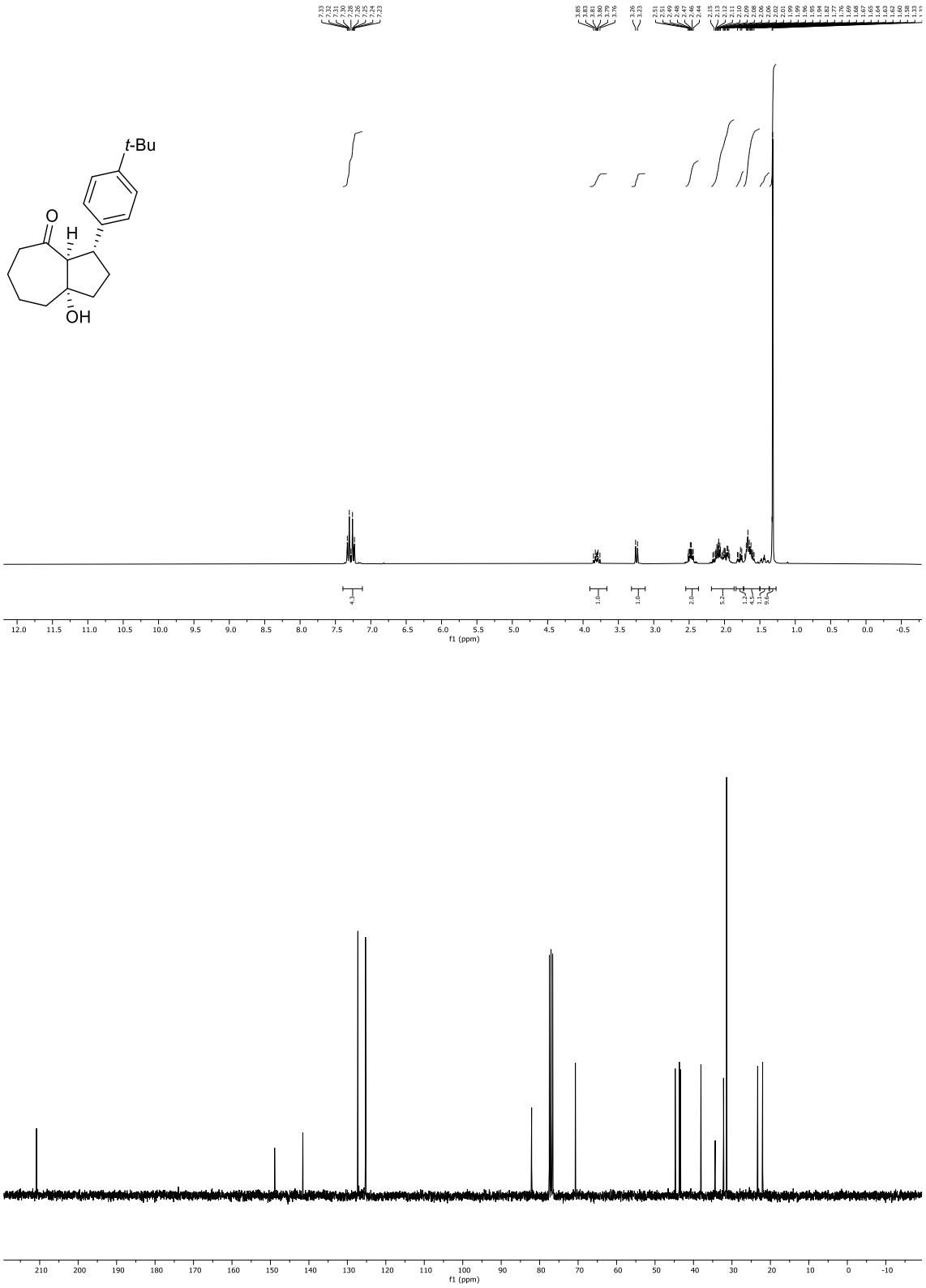


Figure ESI-2. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ab**.

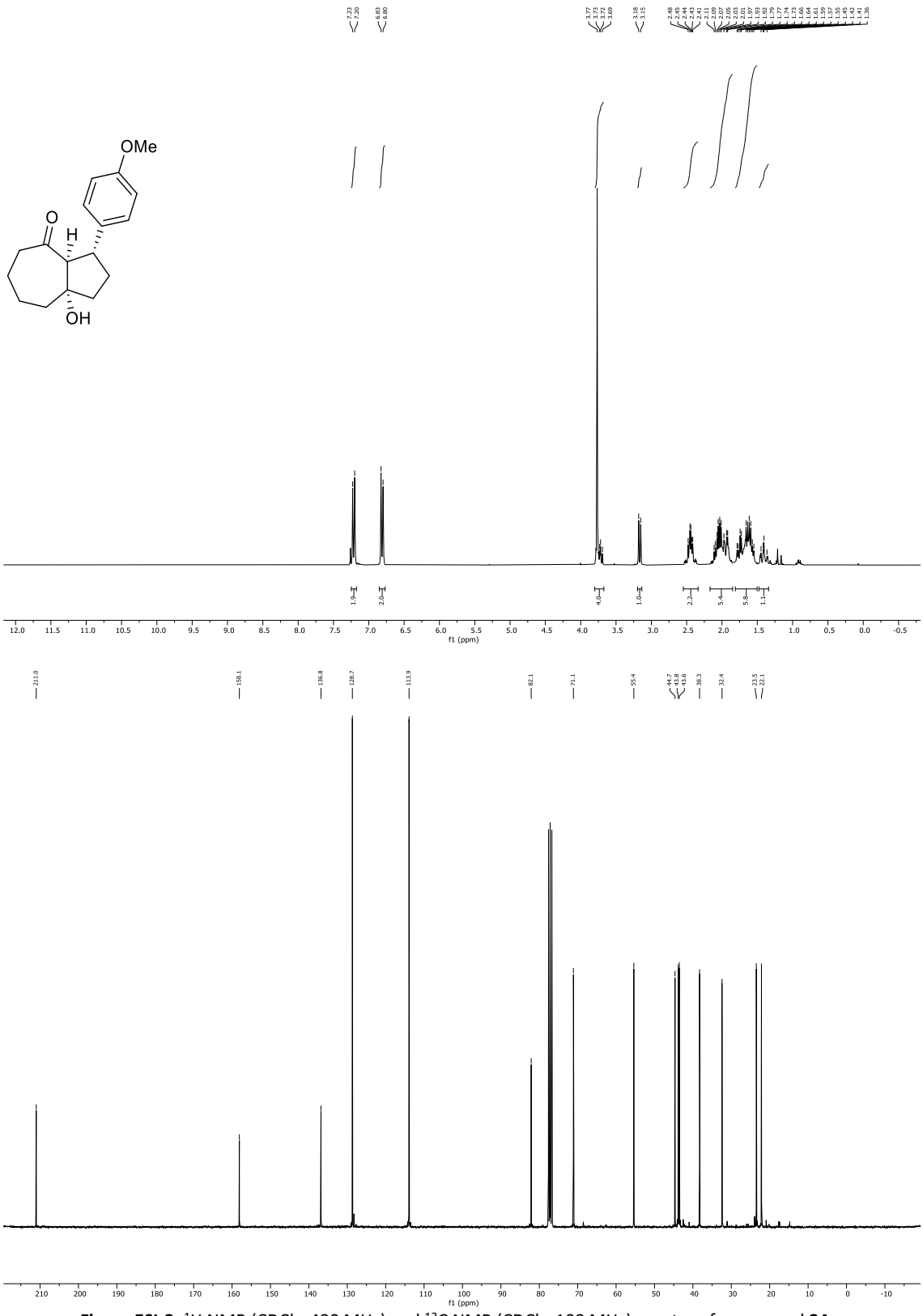


Figure ESI-3. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ac**.

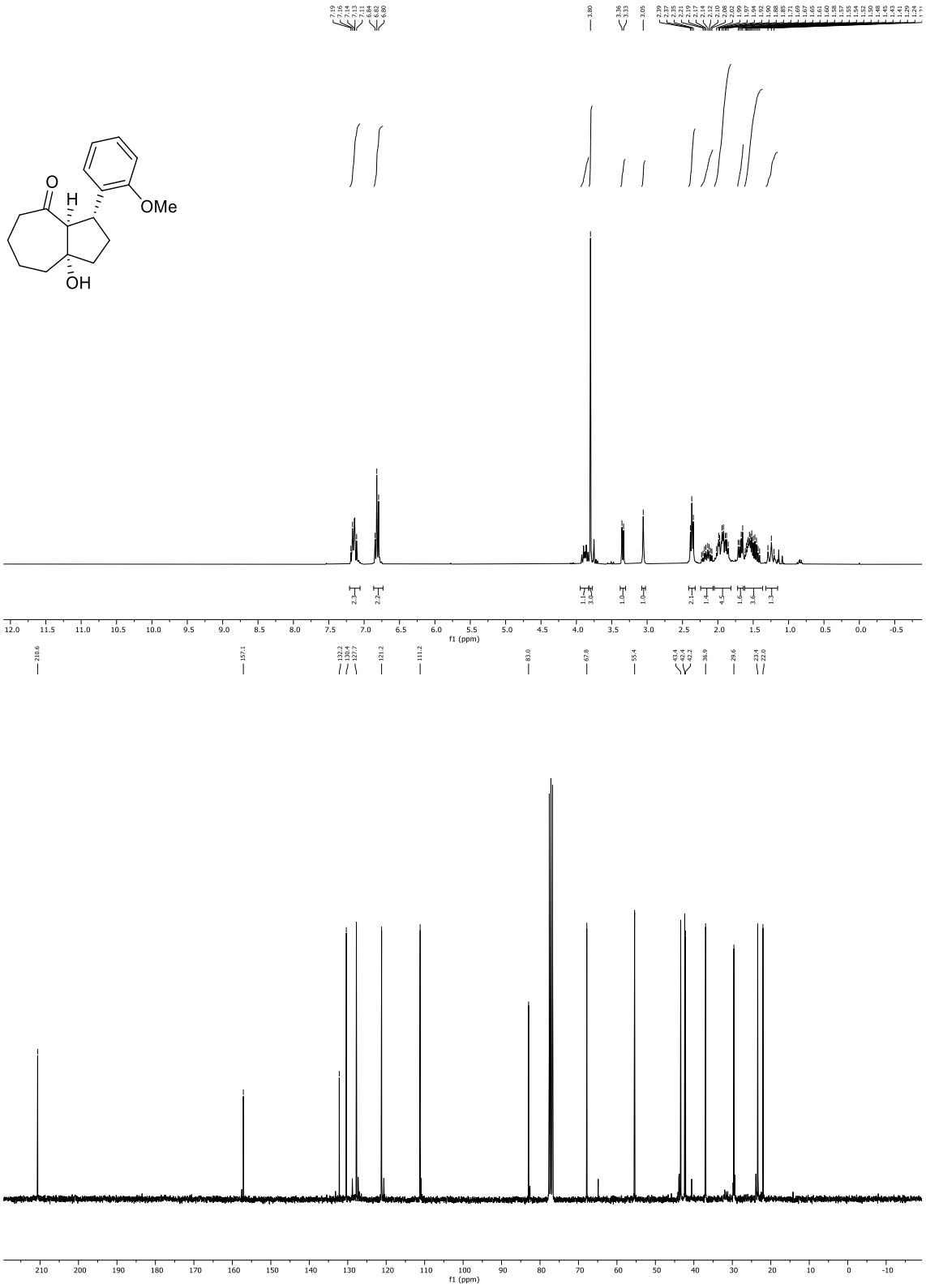


Figure ESI-4. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ad**.

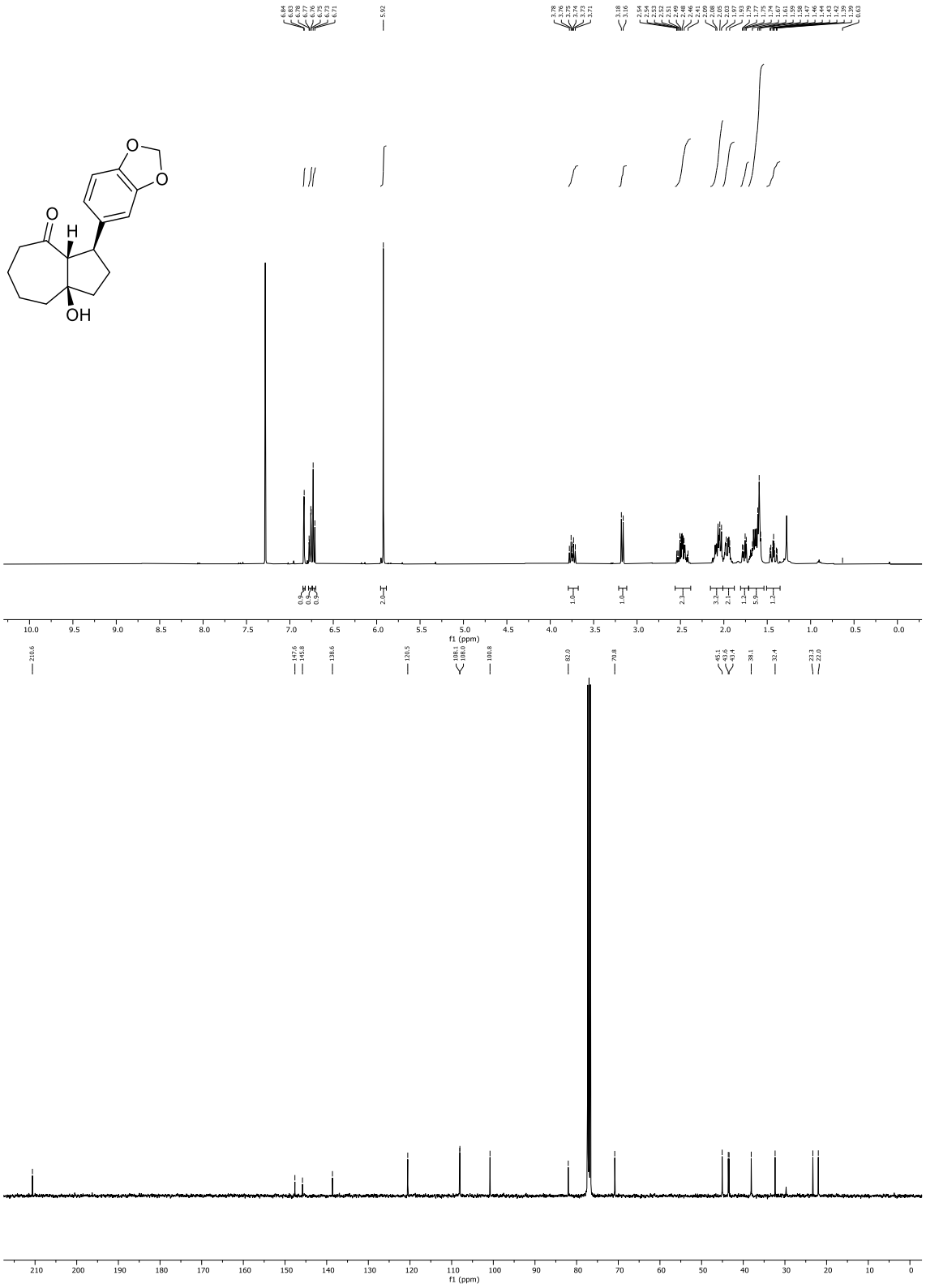


Figure ESI-5. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ae**.

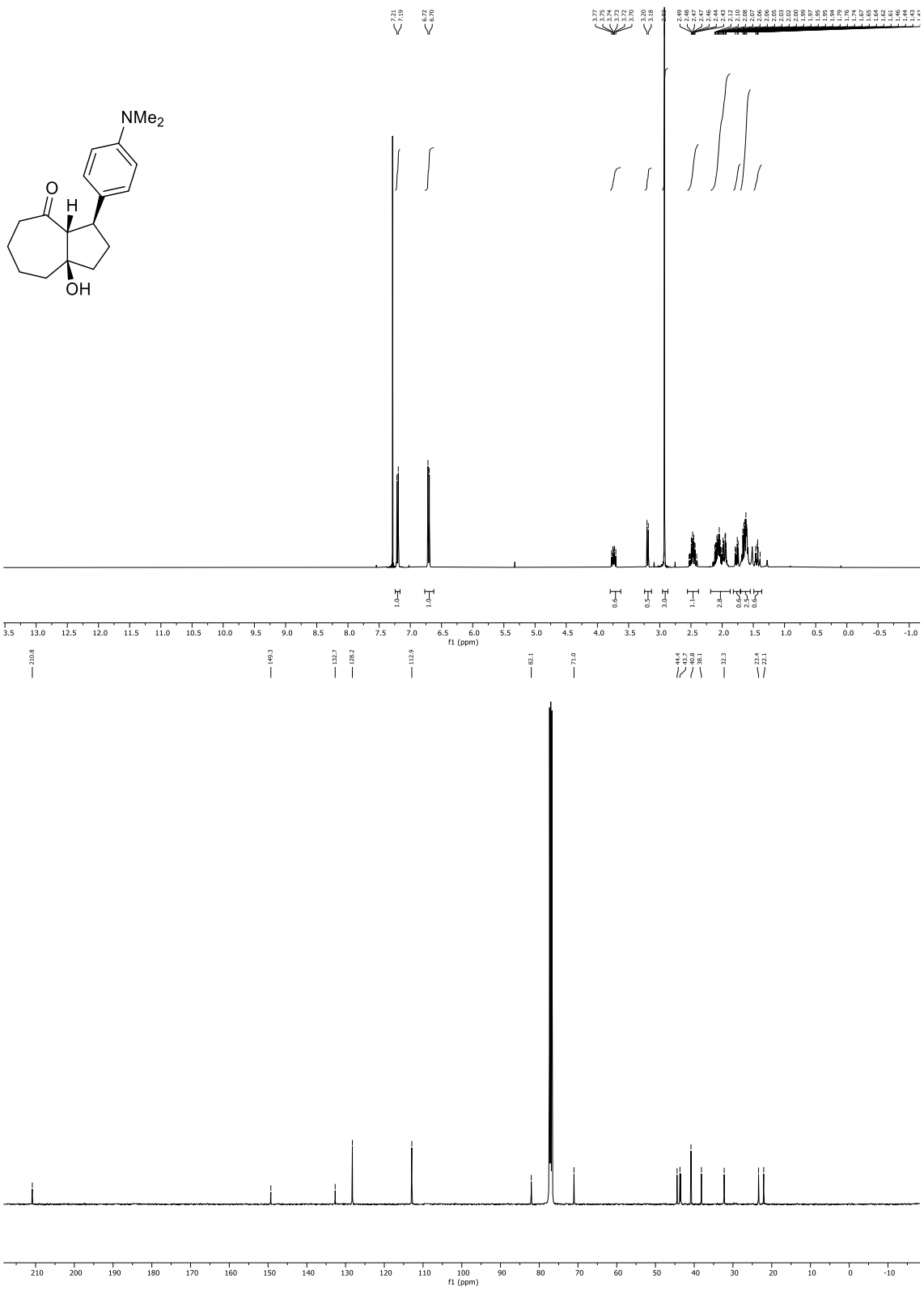


Figure ESI-6. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Af**.

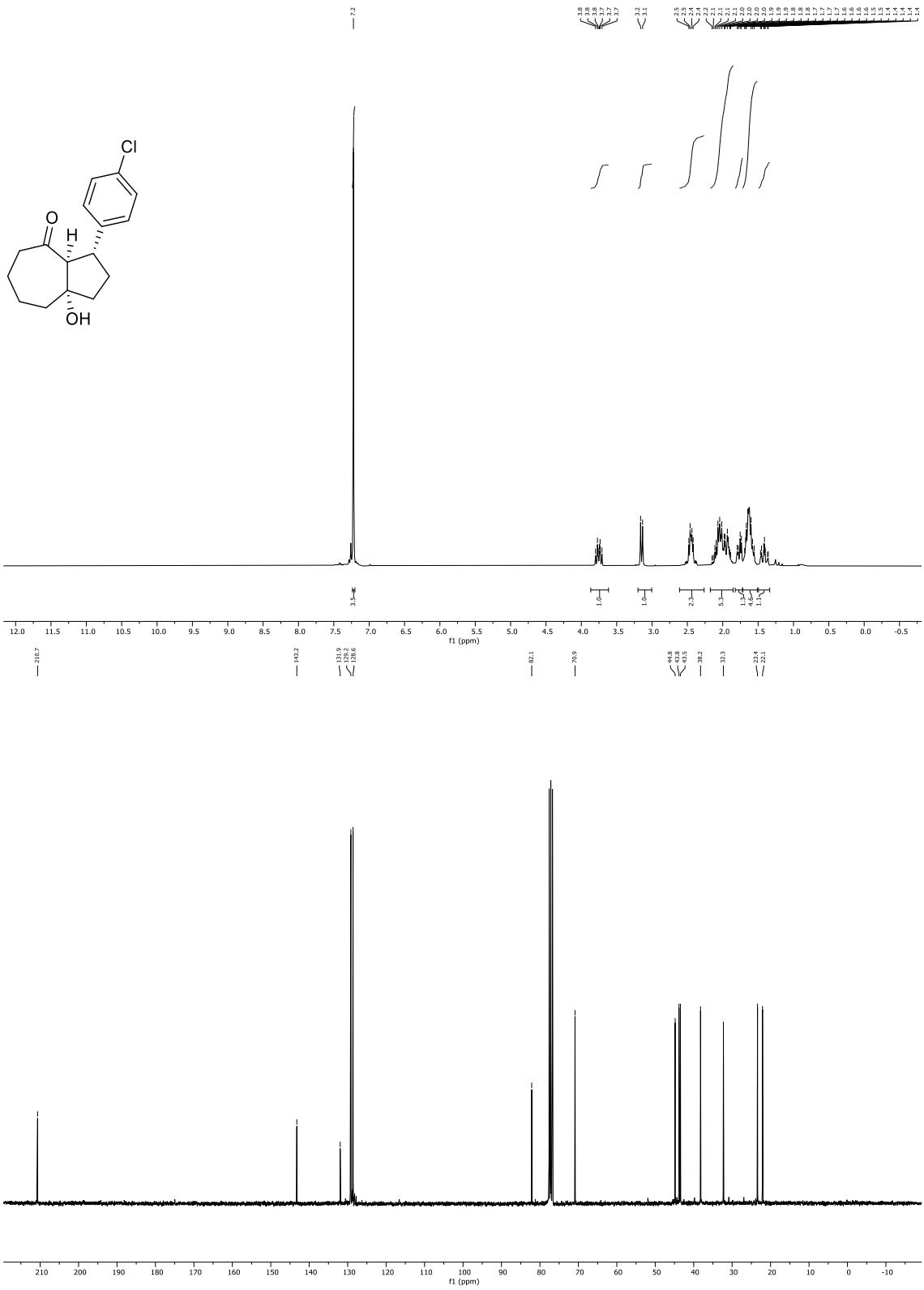


Figure ESI-7. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ag**.

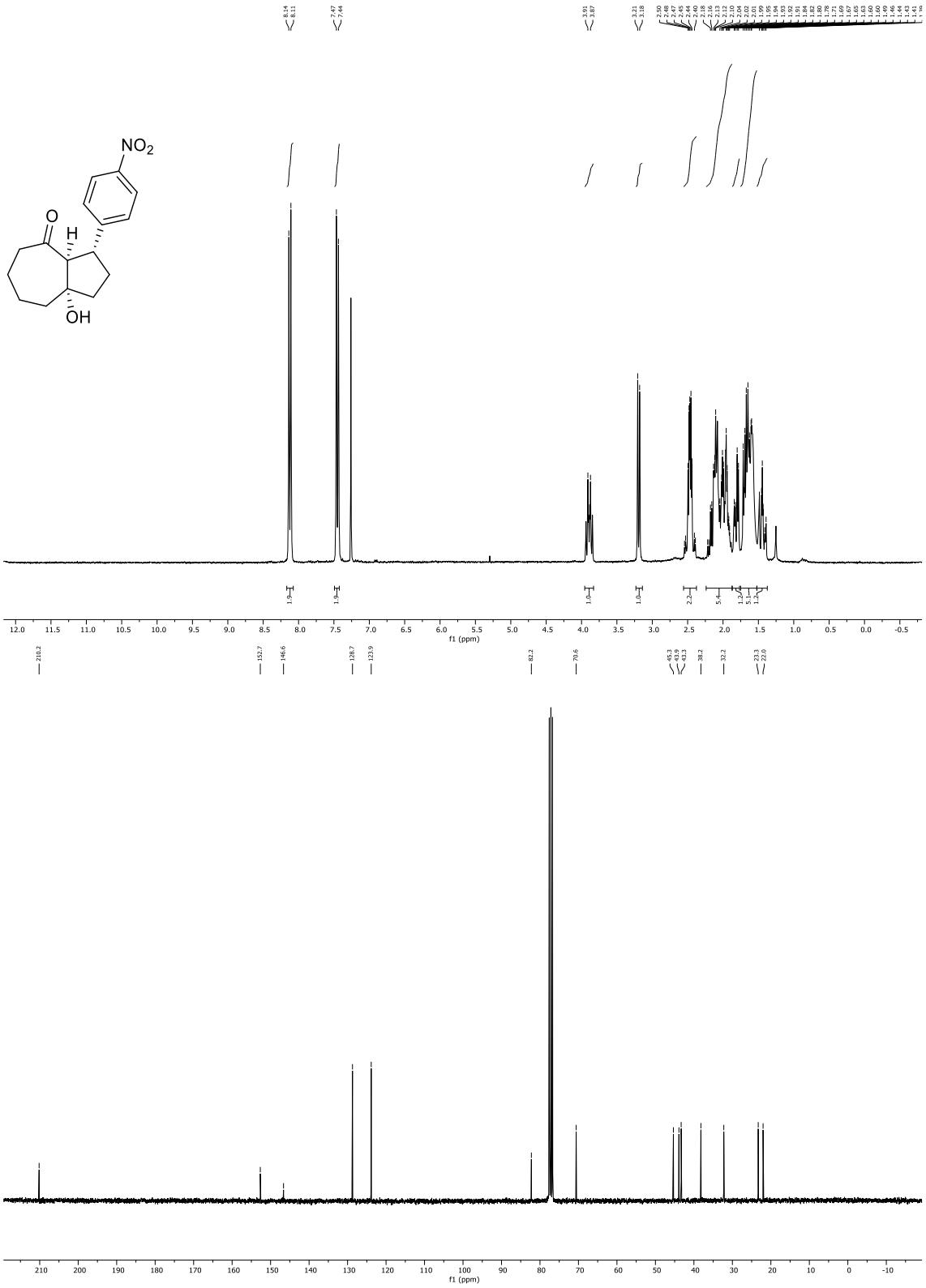


Figure ESI-8. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ah**.

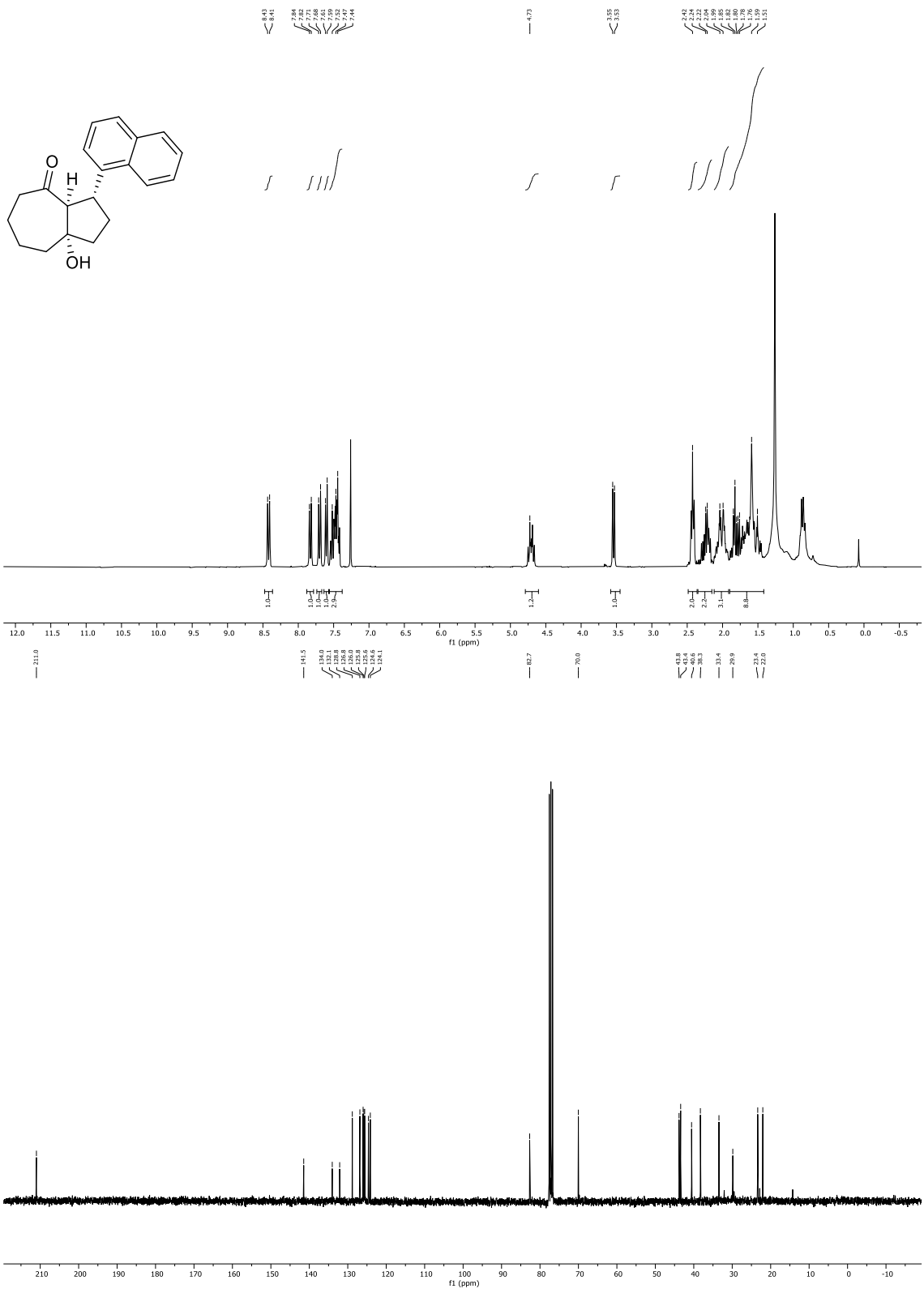


Figure ESI-9. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ai**.

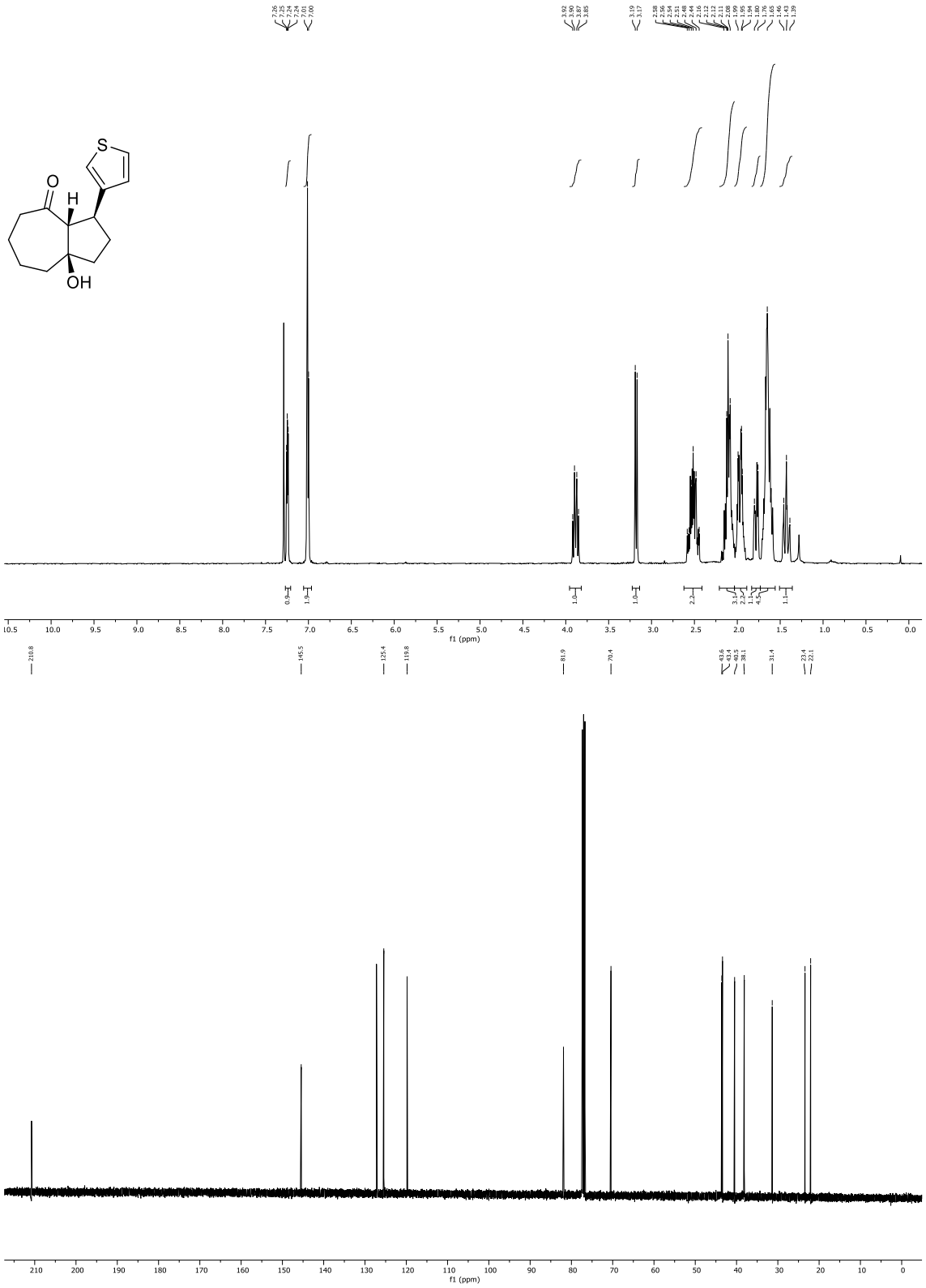


Figure ESI-10. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Aj**.

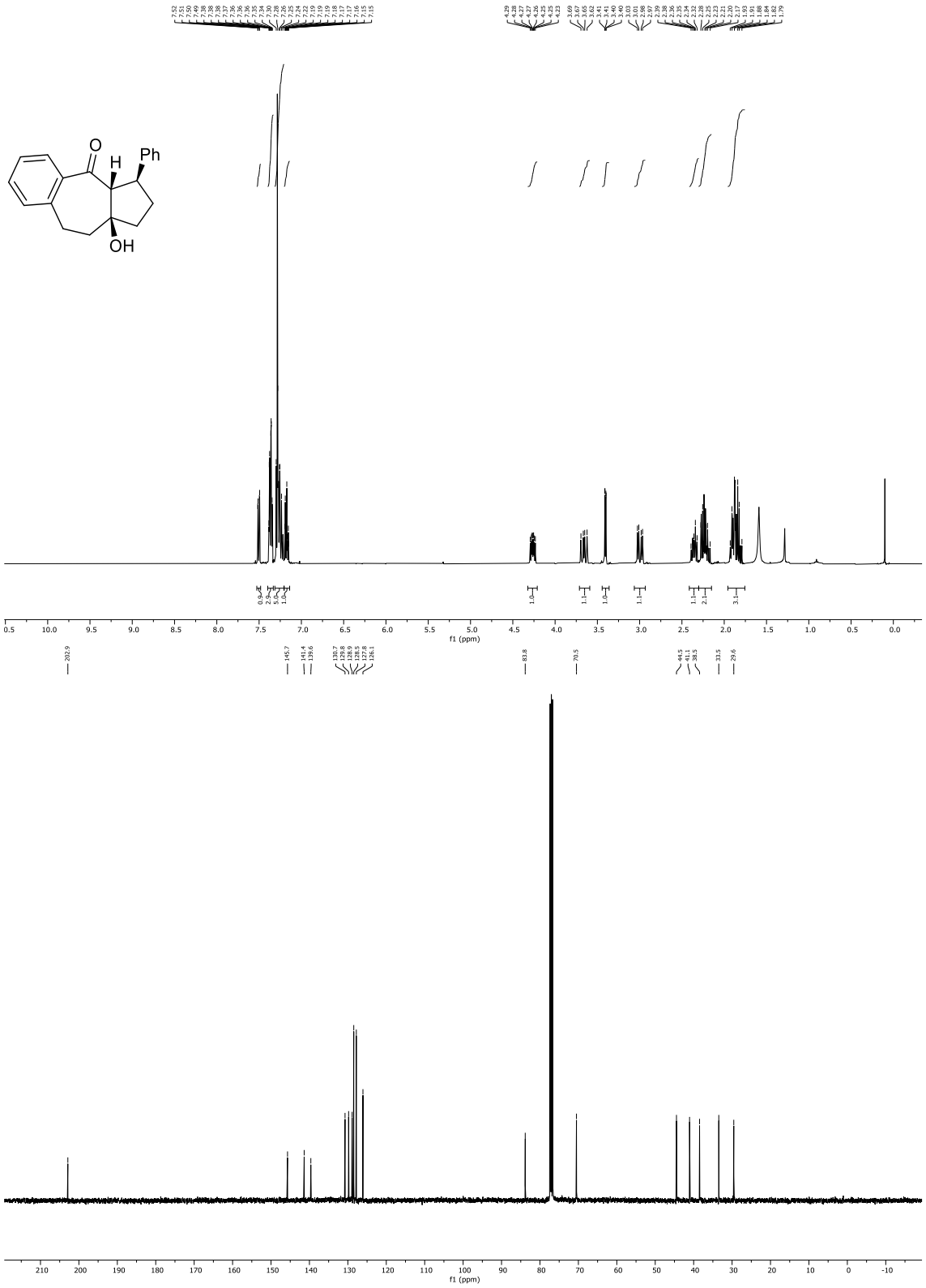


Figure ESI-11. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ba**.

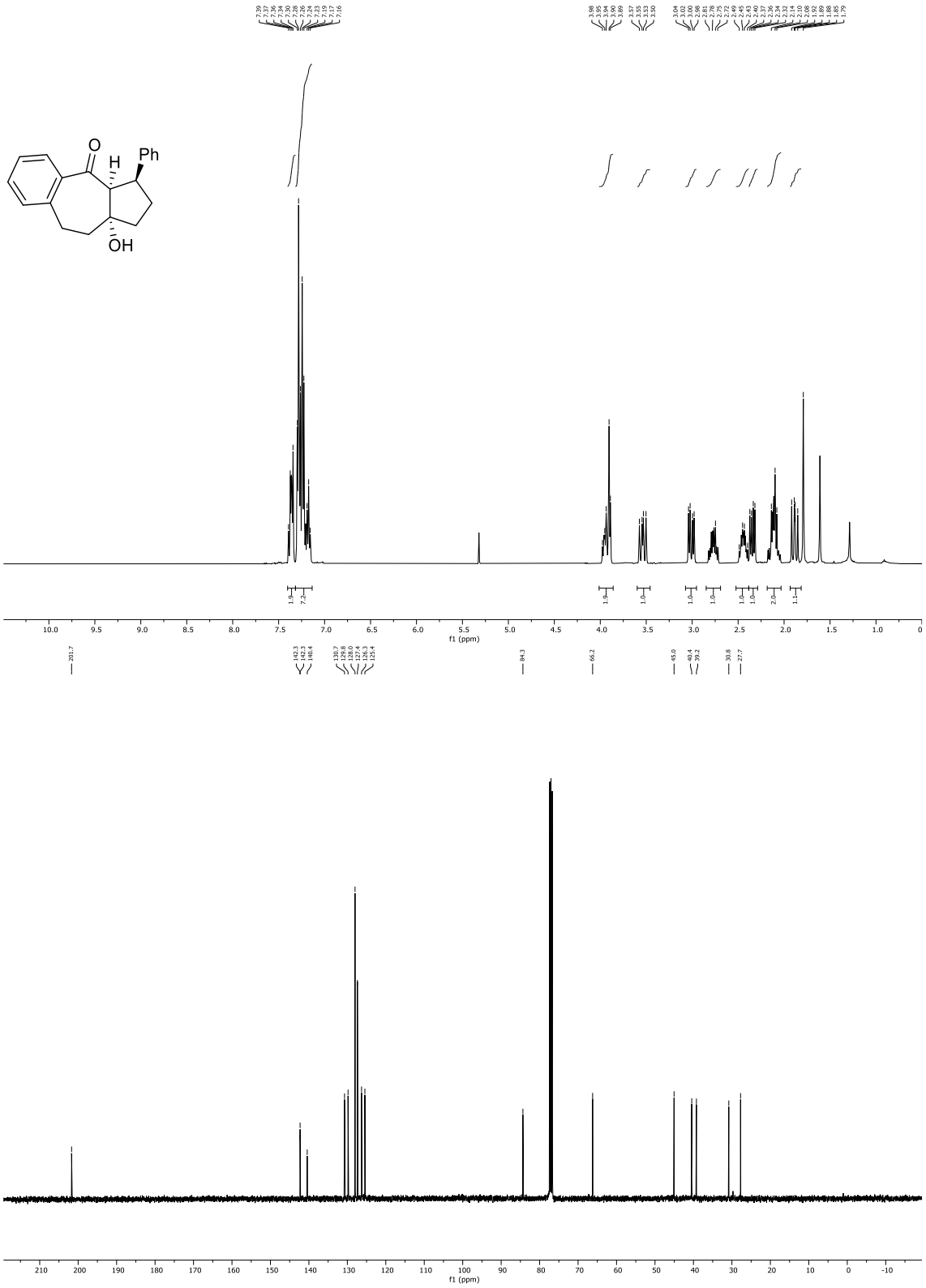


Figure ESI-12. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **4Ba**.

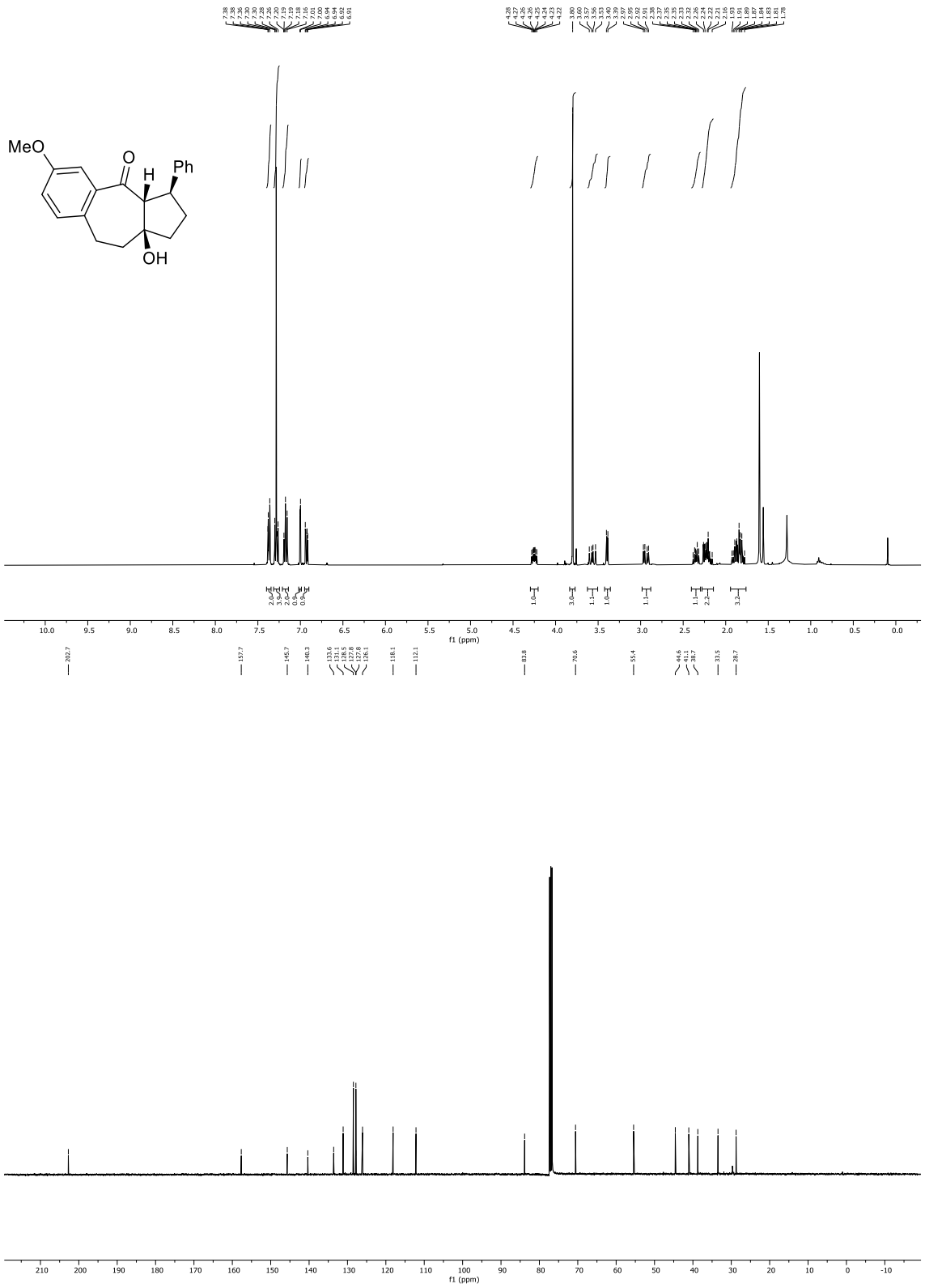


Figure ESI-13. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Ca**.

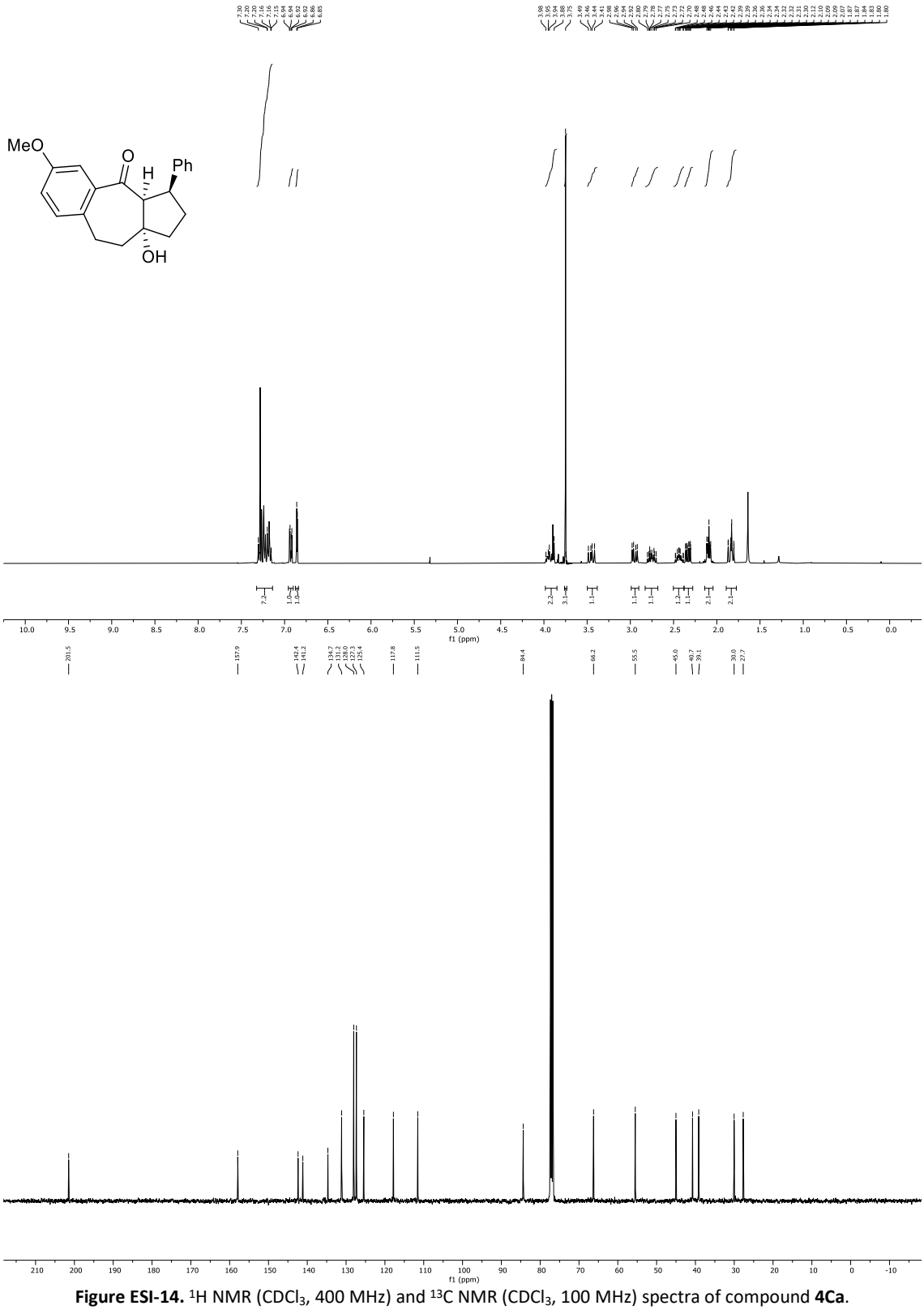


Figure ESI-14. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **4Ca**.

.

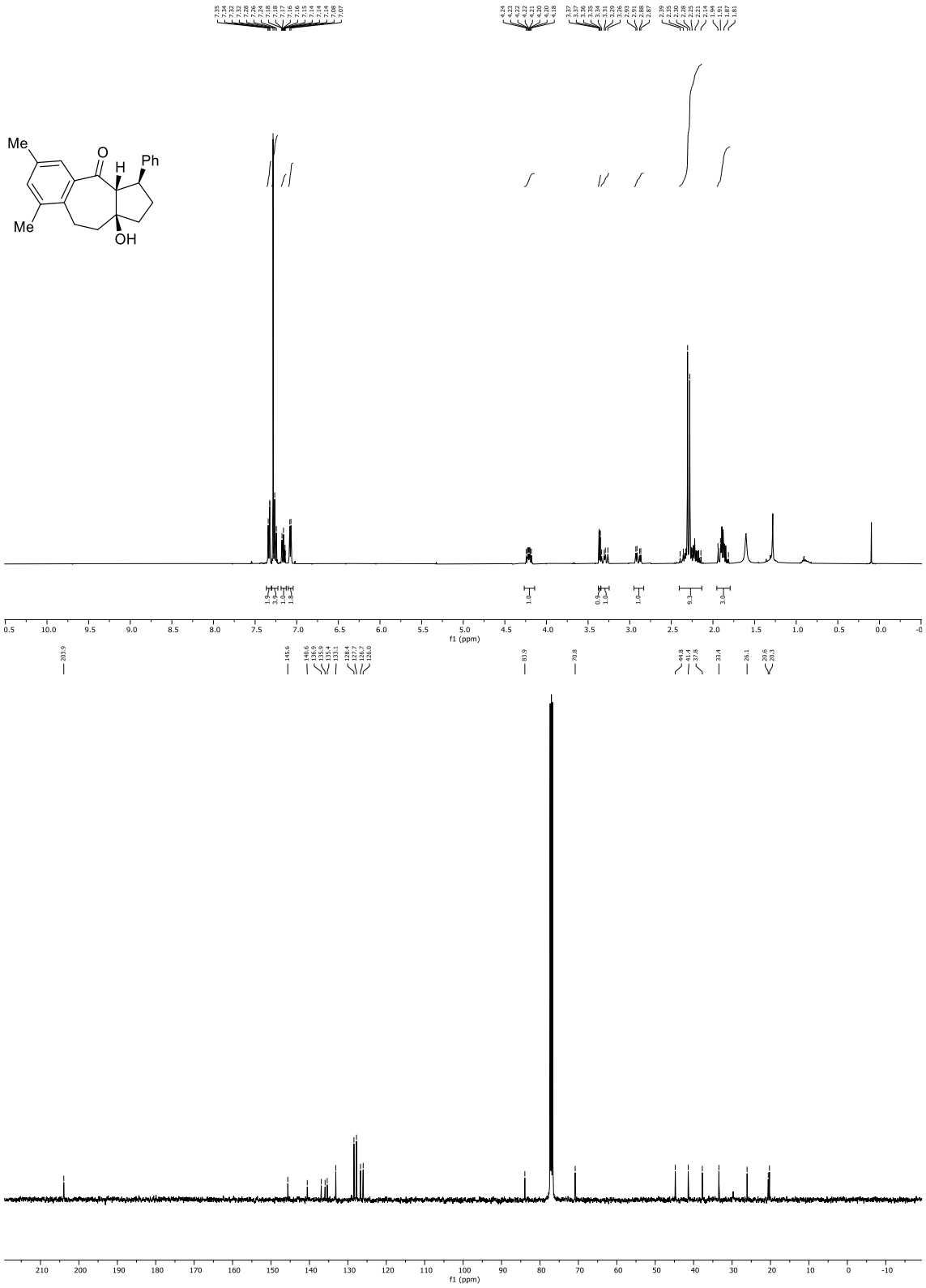


Figure ESI-15. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **3Da**.

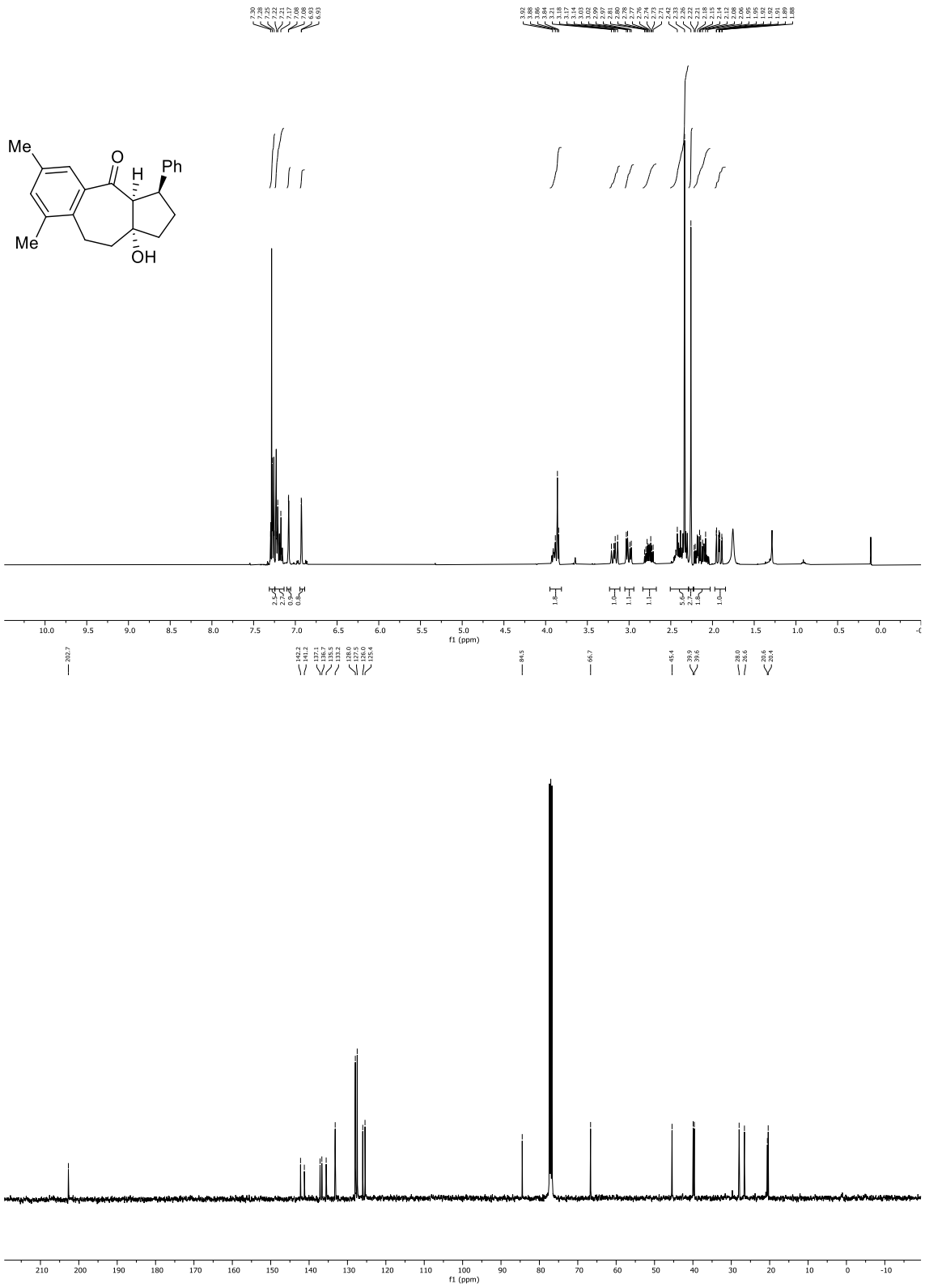


Figure ESI-16. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **4Da**.

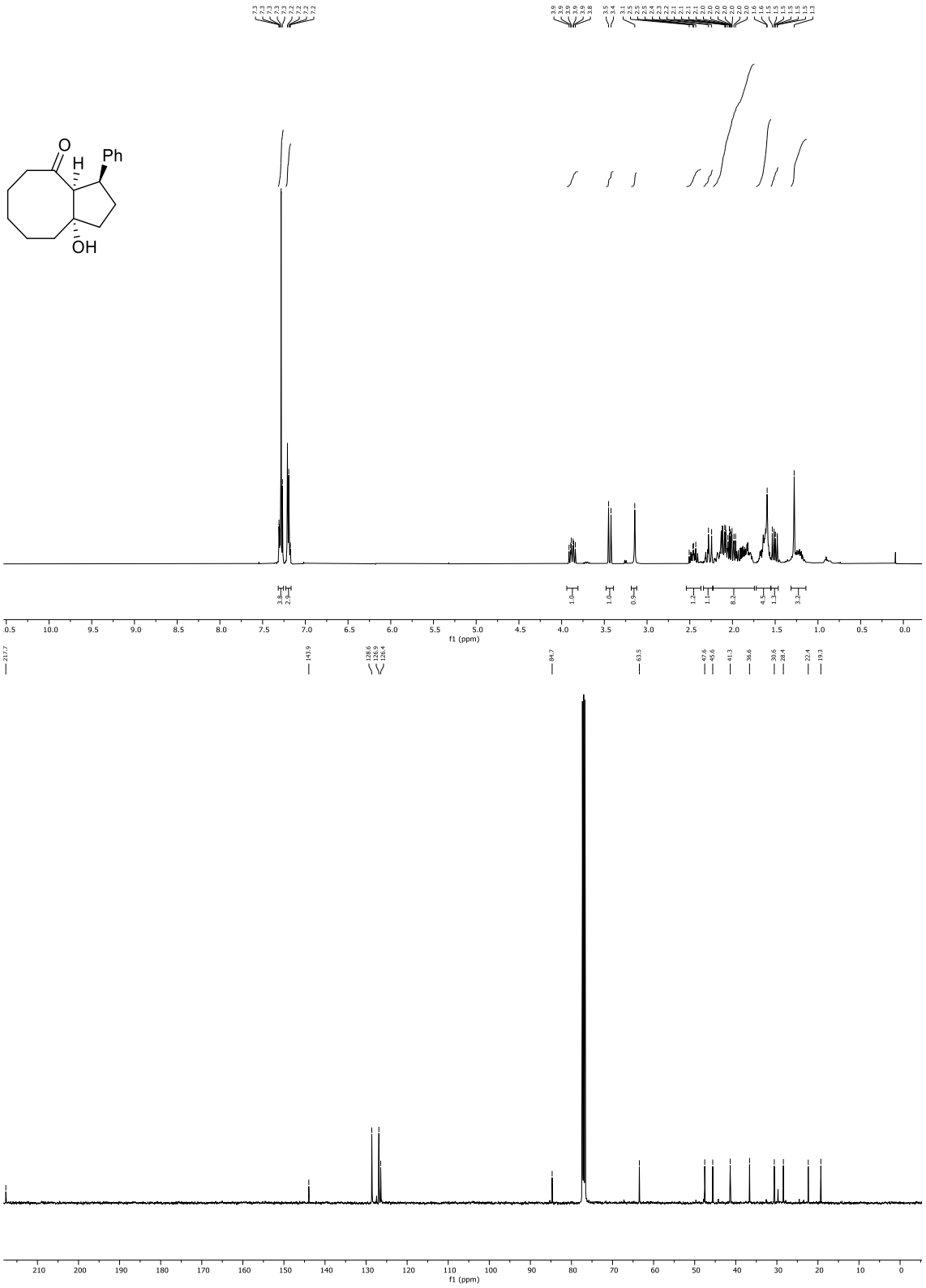
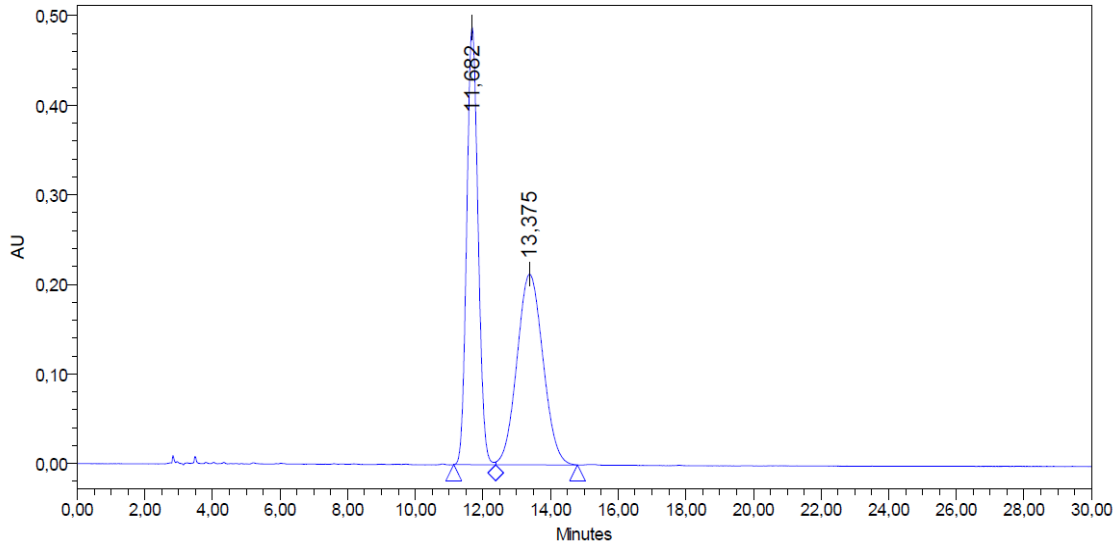
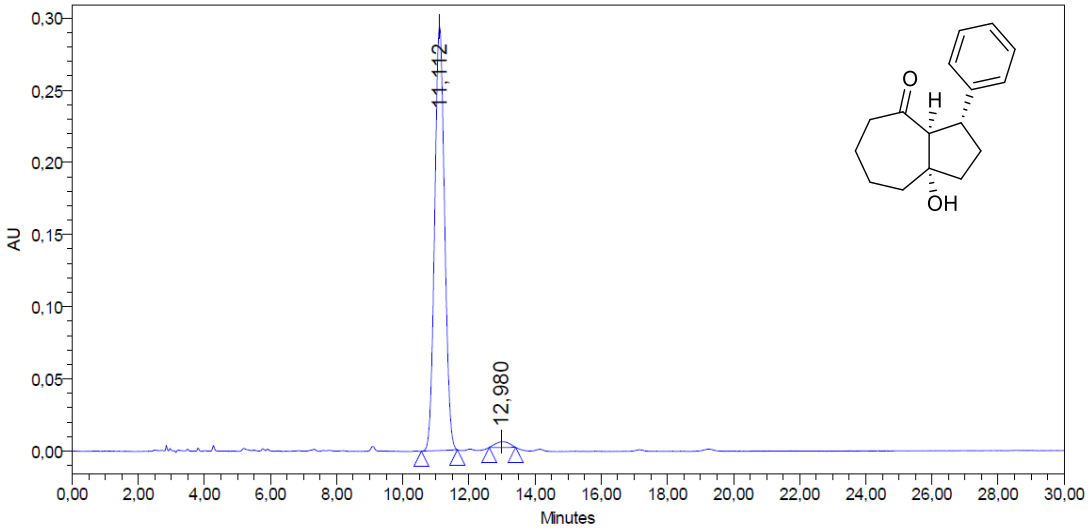


Figure ESI-17. ^{1}H NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz) spectra of compound **4Ea**.

4. HPLC traces





Peak Results

	RT	Area	Height	% Area
1	11,112	6118788	293941	98,12
2	12,980	117240	3961	1,88

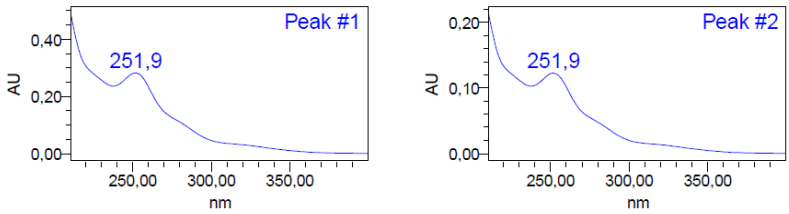
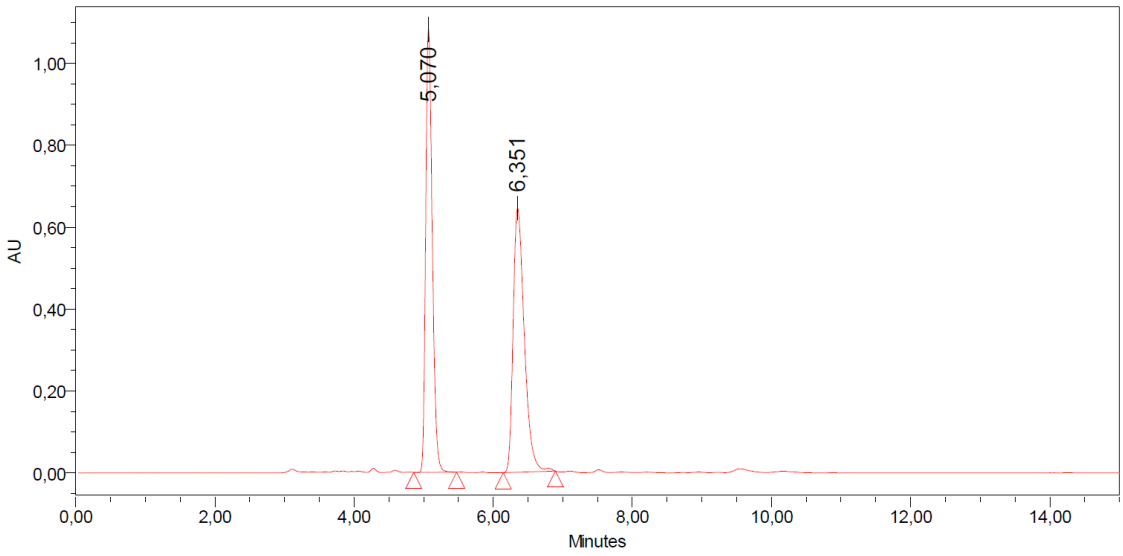
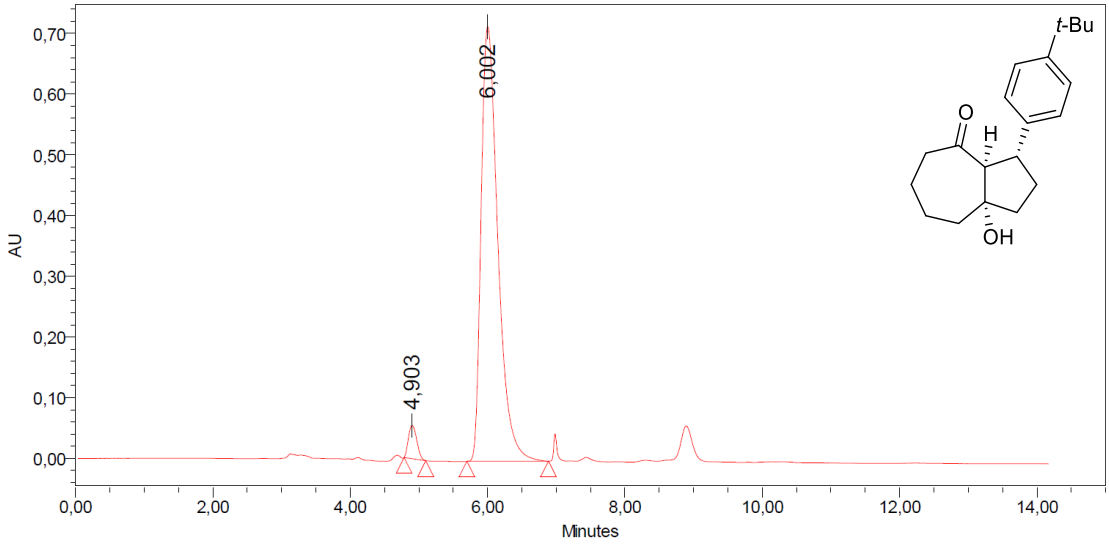


Figure ESI-18. HPLC traces for racemic and chiral compound **3Aa**.





Peak Results

	RT	Area	Height	% Area
1	4,903	463916	54938	3,69
2	6,002	12114408	715877	96,31

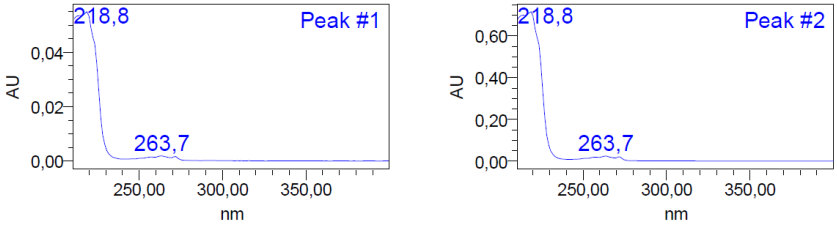
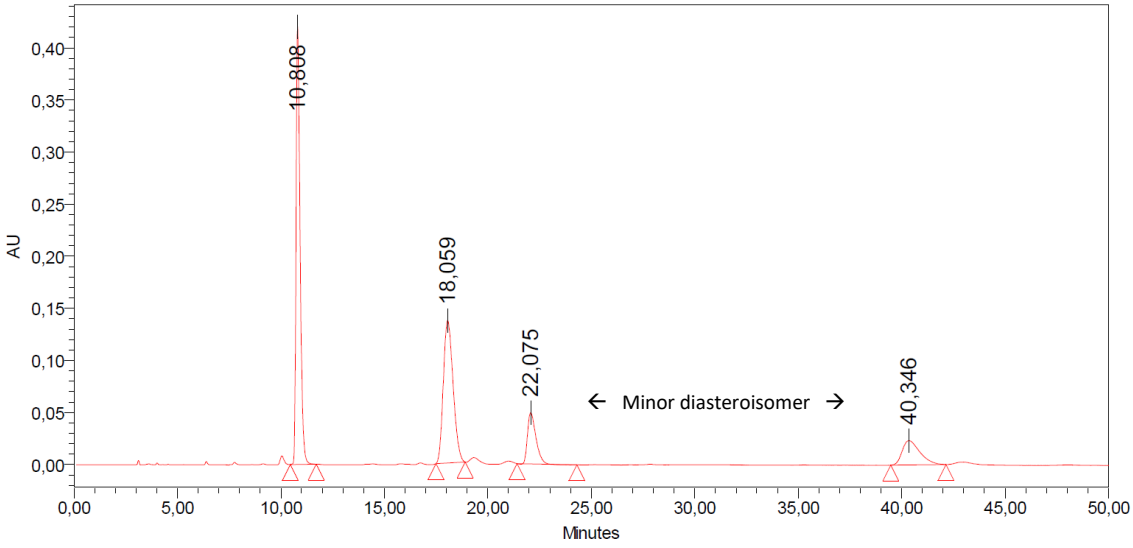
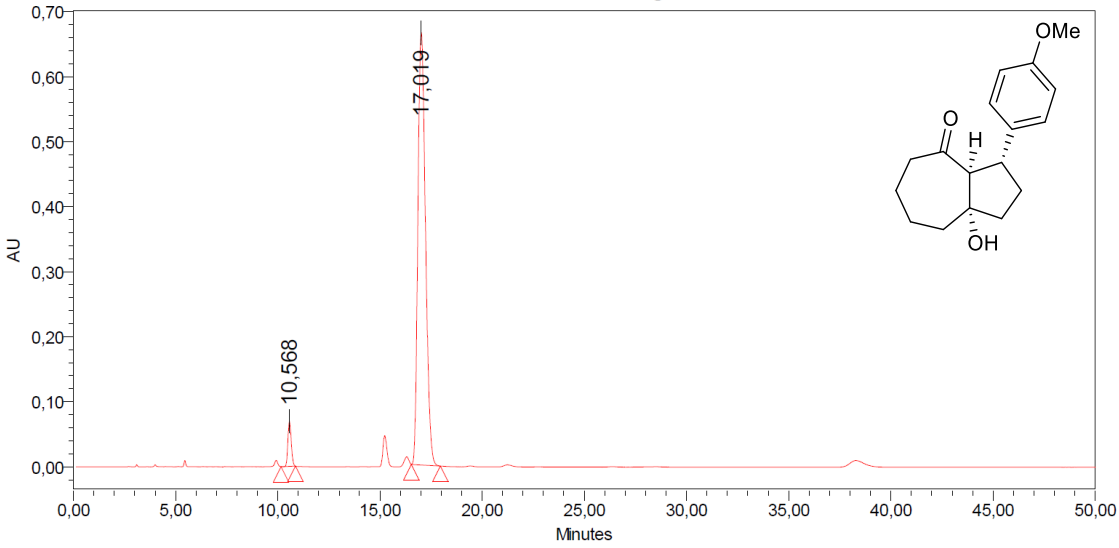


Figure ESI-19. HPLC traces for racemic and chiral compound **3Ab**.





Peak Results

	RT	Area	Height	% Area
1	10,568	789086	69365	4,40
2	17,019	17127349	664773	95,60

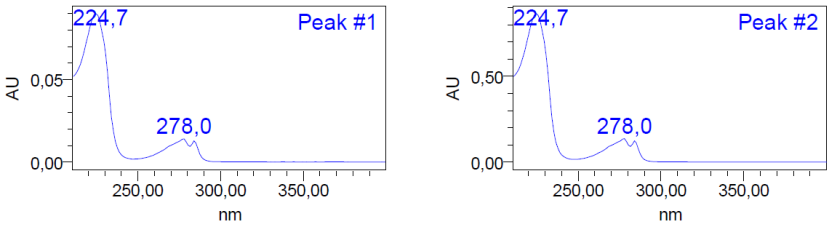
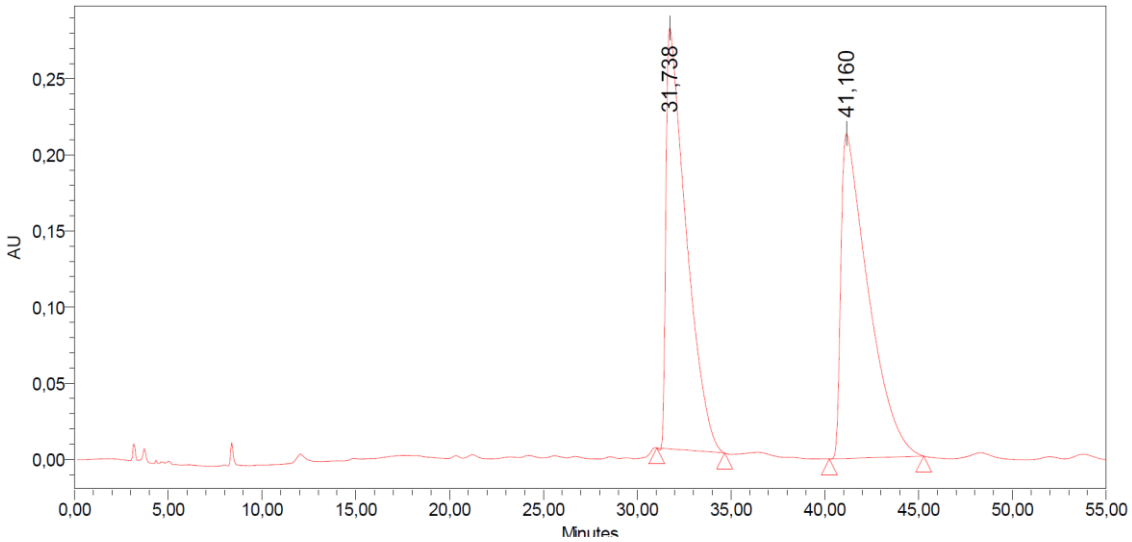
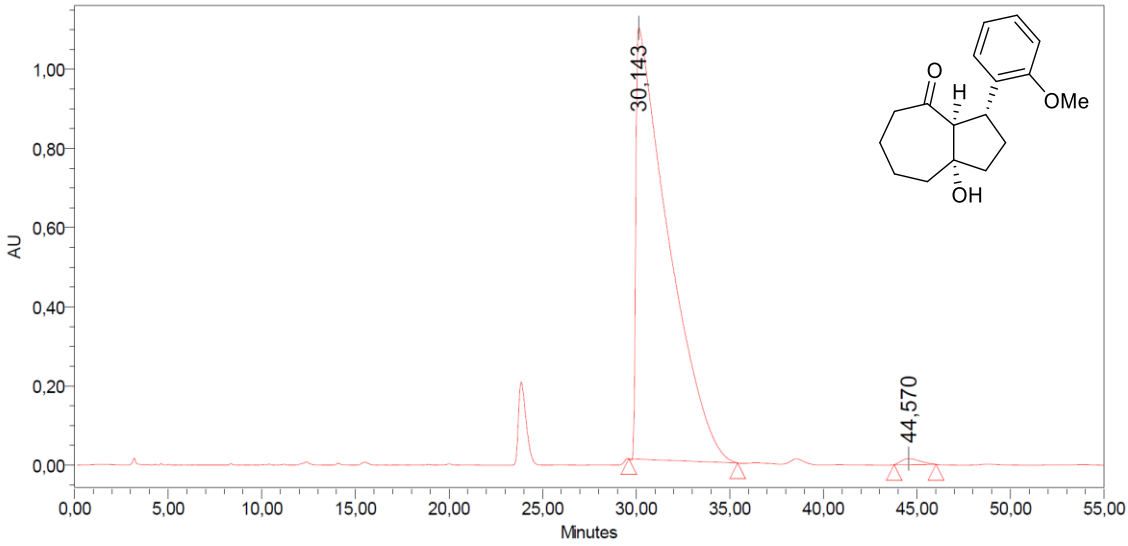


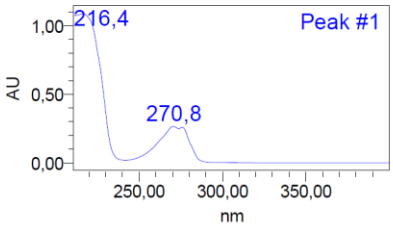
Figure ESI-20. HPLC traces for racemic and chiral compound **3Ac**.





Peak Results

	RT	Area	Height	% Area
1	30,143	131443293	1090164	99,22
2	44,570	1028950	14750	0,78



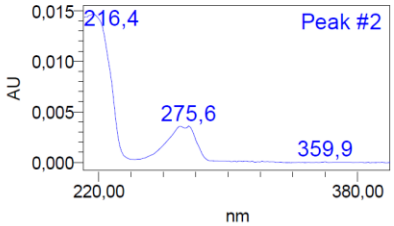
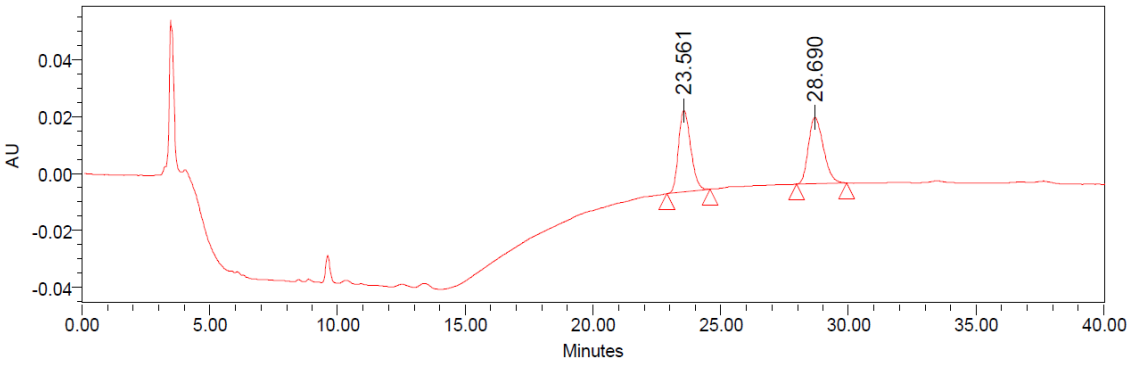
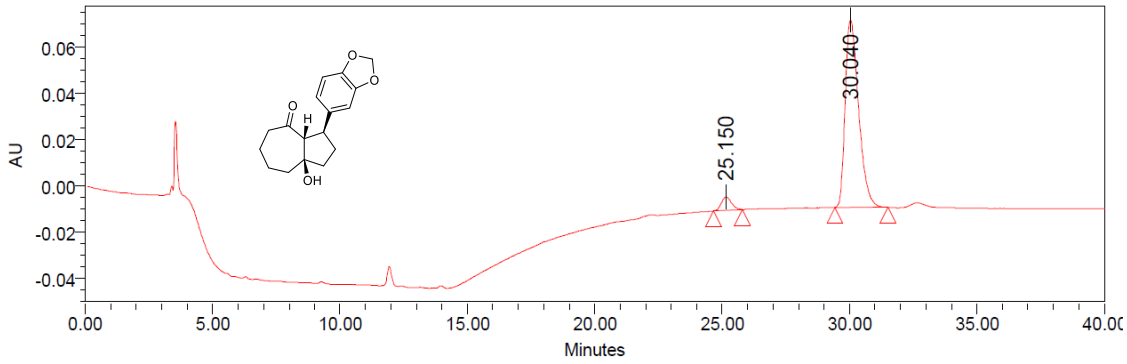


Figure ESI-21. HPLC traces for racemic and chiral compound **3Ad**.





Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	25.150	159381	5.13	5738
2	PDA 220.0 nm	30.040	2949273	94.87	80997

Spectrum Index Plot

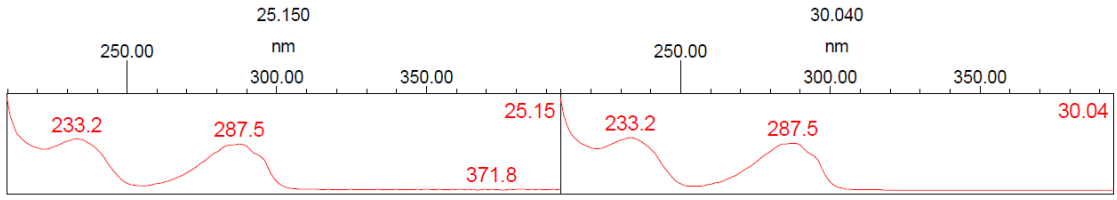
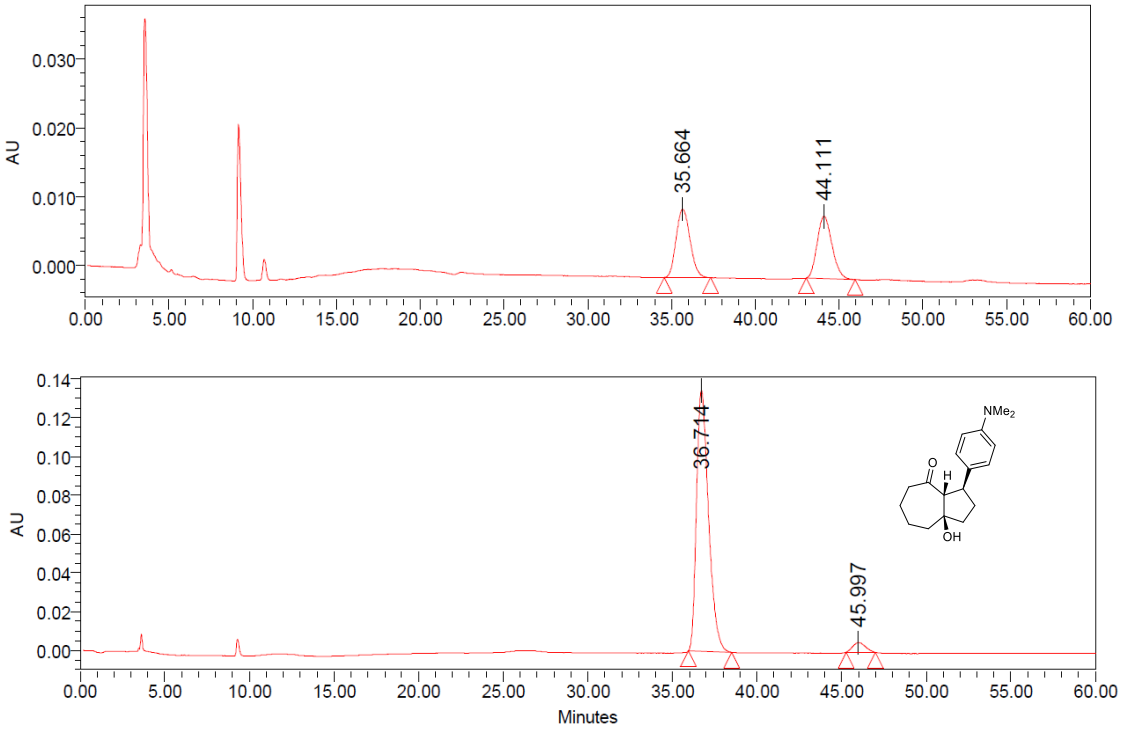


Figure ESI-22. HPLC traces for racemic and chiral compound **3Ae**.



Processed Channel: PDA 253.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 253.0 nm	36.714	6639236	96.23	134590
2	PDA 253.0 nm	45.997	260157	3.77	4993

Spectrum Index Plot

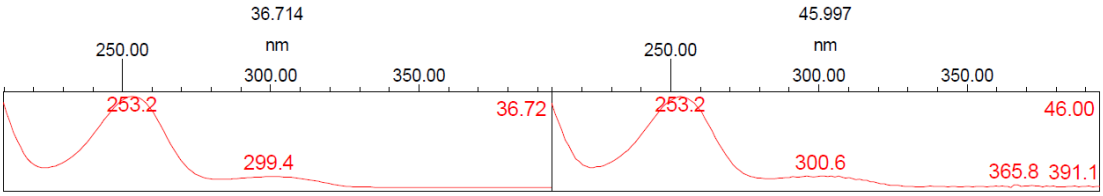
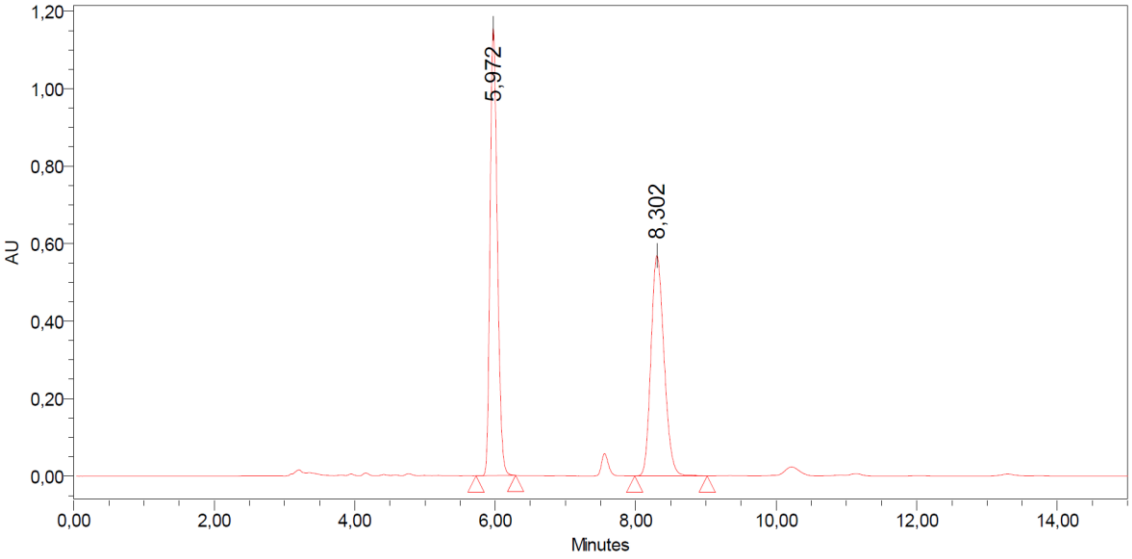
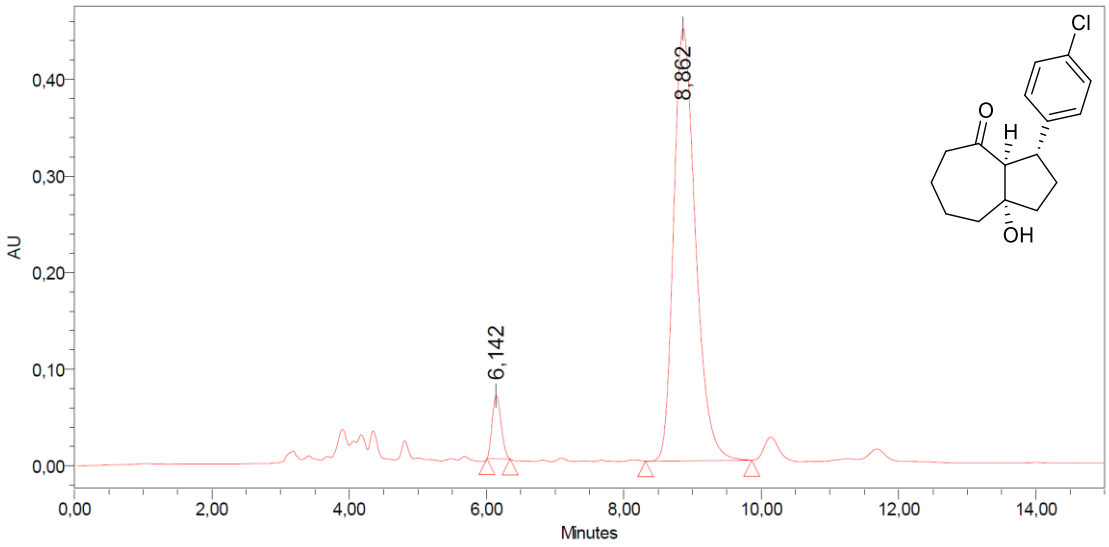


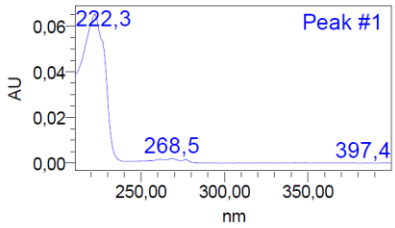
Figure ESI-23. HPLC traces for racemic and chiral compound **3Af**.





Peak Results

	RT	Area	Height	% Area
1	6,142	591475	65420	5,65
2	8,862	9870890	447387	94,35



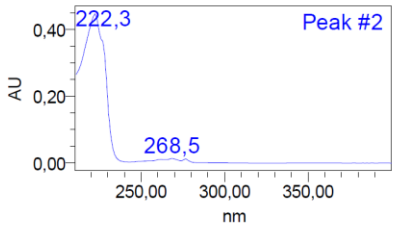
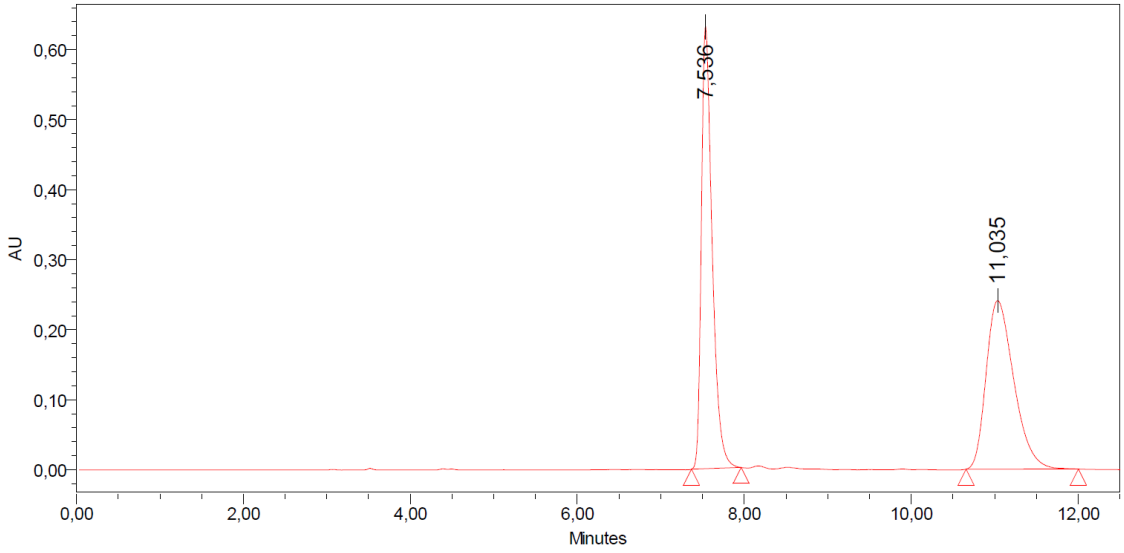
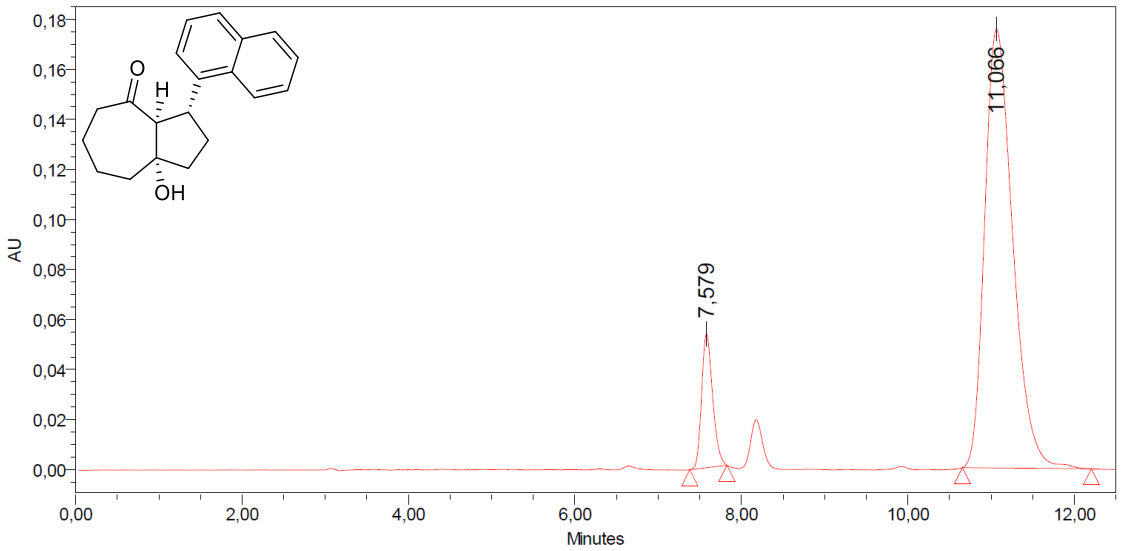


Figure ESI-24. HPLC traces for racemic and chiral compound **3Ag**.





Peak Results

	RT	Area	Height	% Area
1	7,579	492235	53506	10,68
2	11,066	4116710	175623	89,32

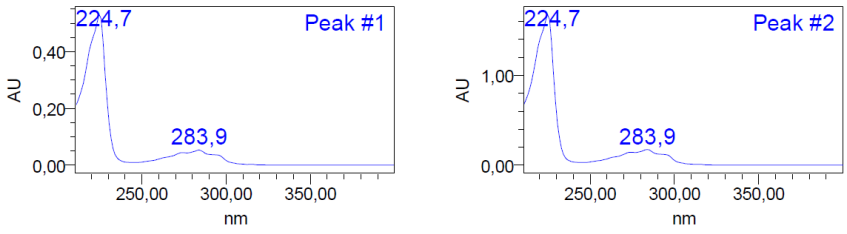
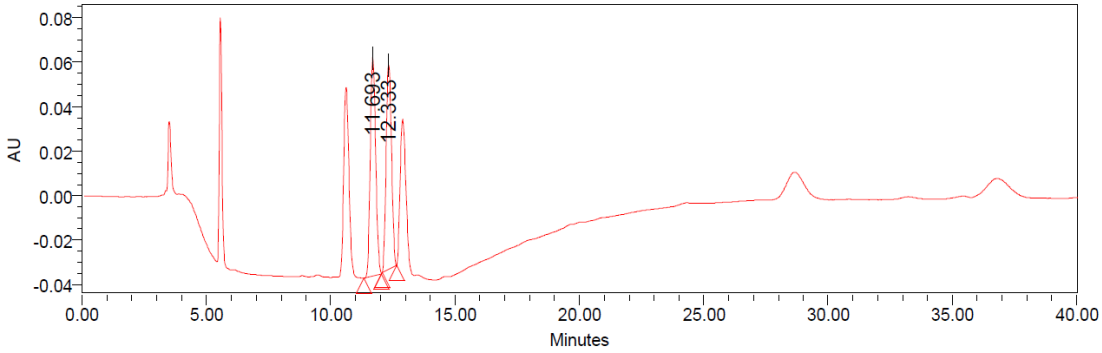
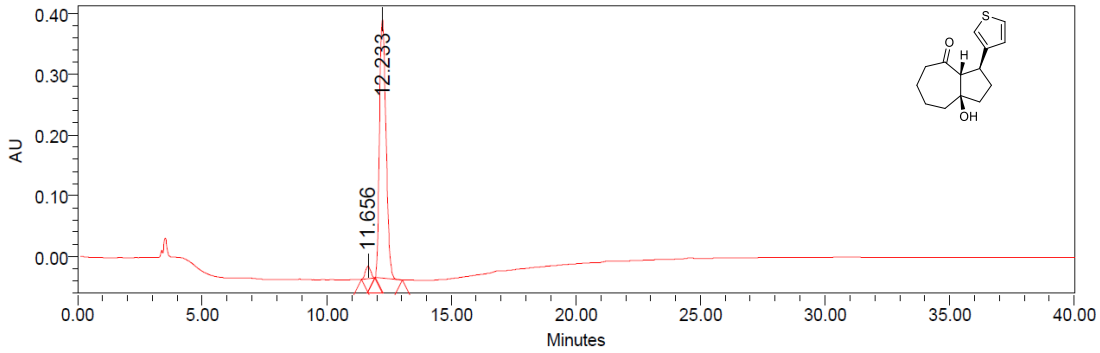


Figure ESI-25. HPLC traces for racemic and chiral compound **3Ai**.





Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	11.656	306638	3.82	21091
2	PDA 220.0 nm	12.233	7712292	96.18	426678

Spectrum Index Plot

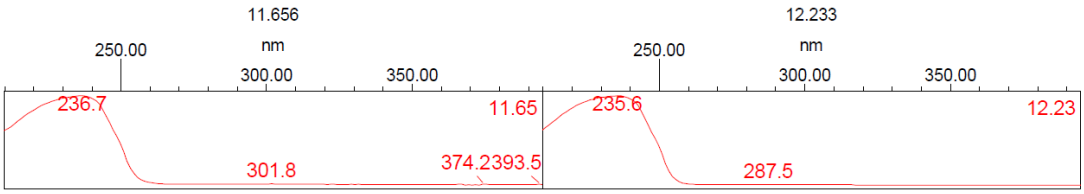
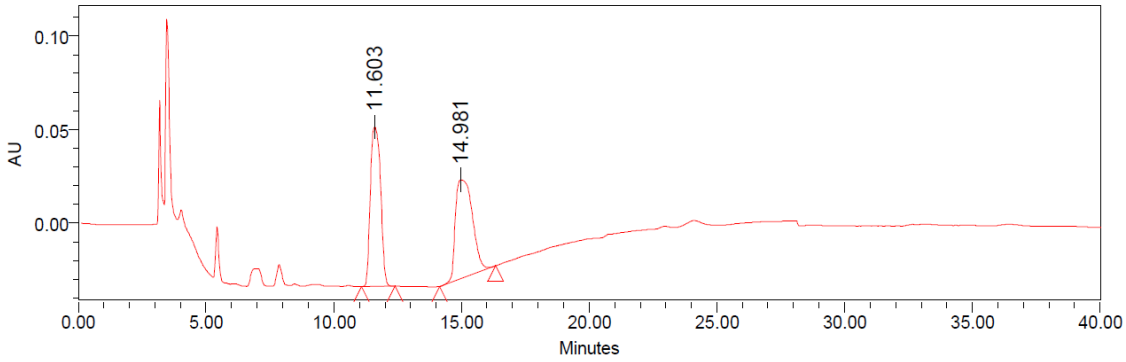
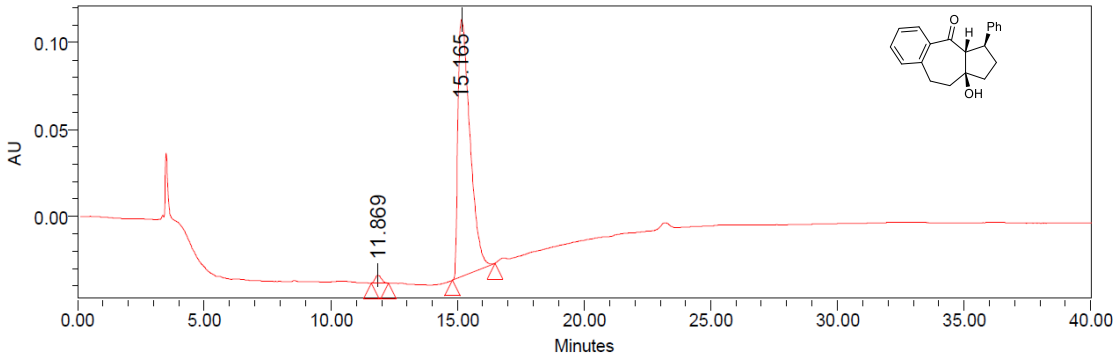


Figure ESI-26. HPLC traces for racemic and chiral compound **3Aj**.





Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	11.869	77630	1.56	4544
2	PDA 220.0 nm	15.165	4884540	98.44	148007

Spectrum Index Plot

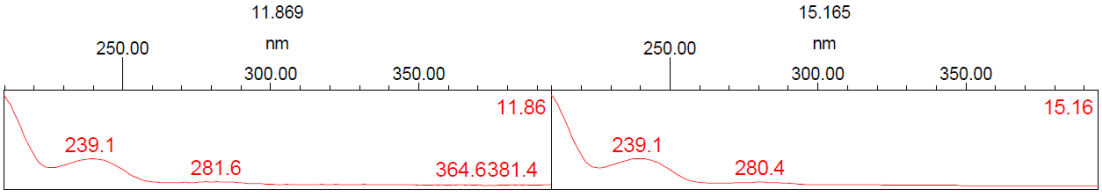
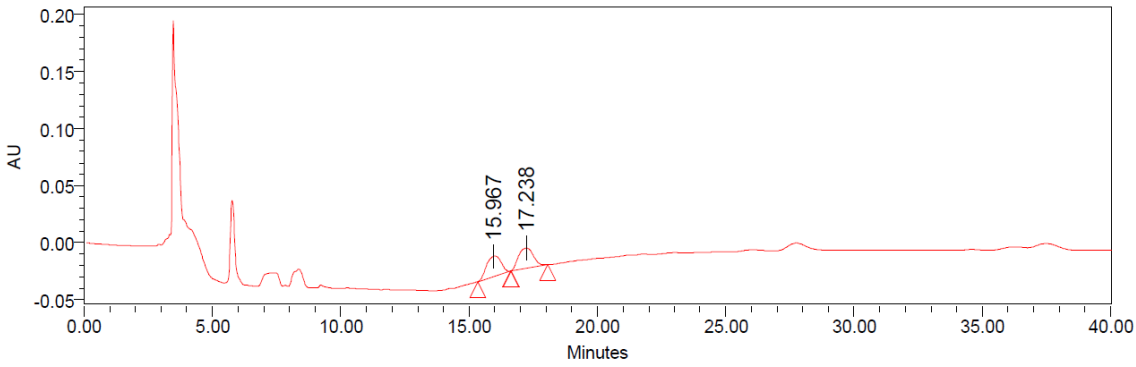
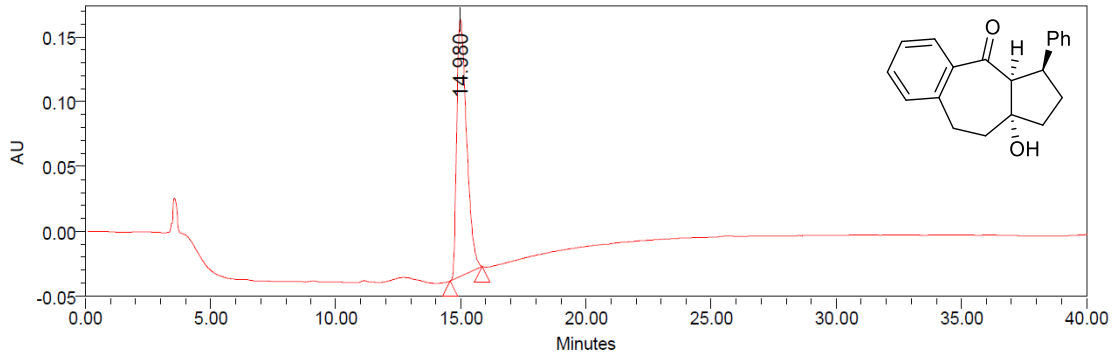


Figure ESI-27. HPLC traces for racemic and chiral compound **3Ba**.





Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	14.980	5456404	100.00	198530

Spectrum Index Plot

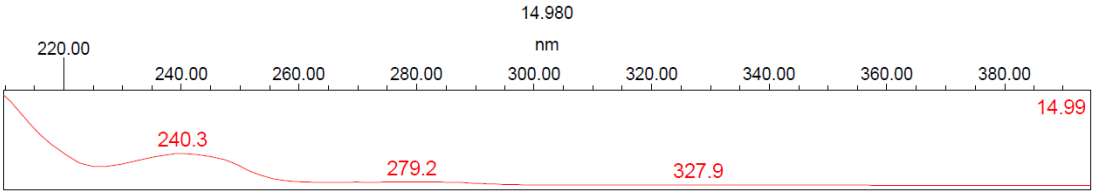
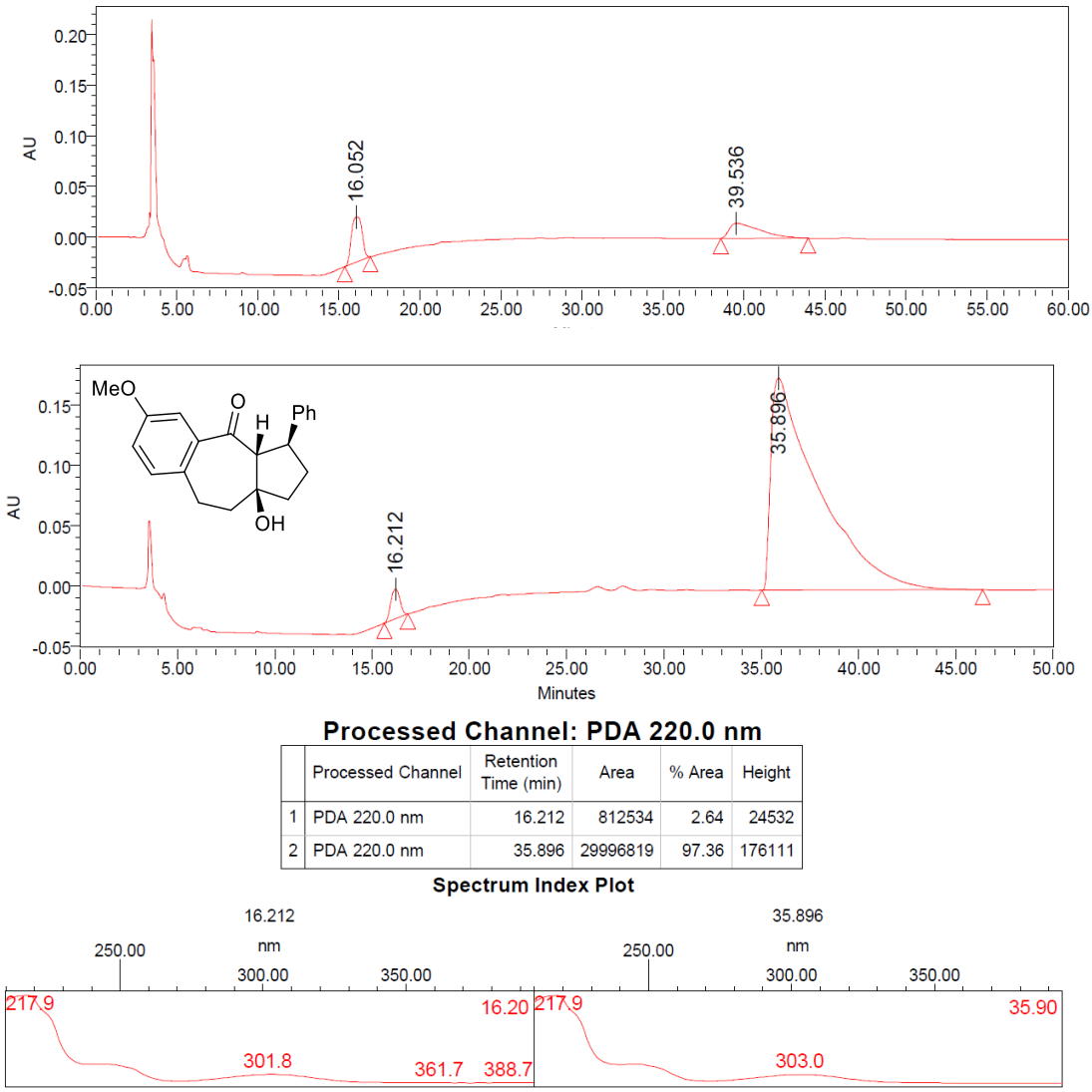


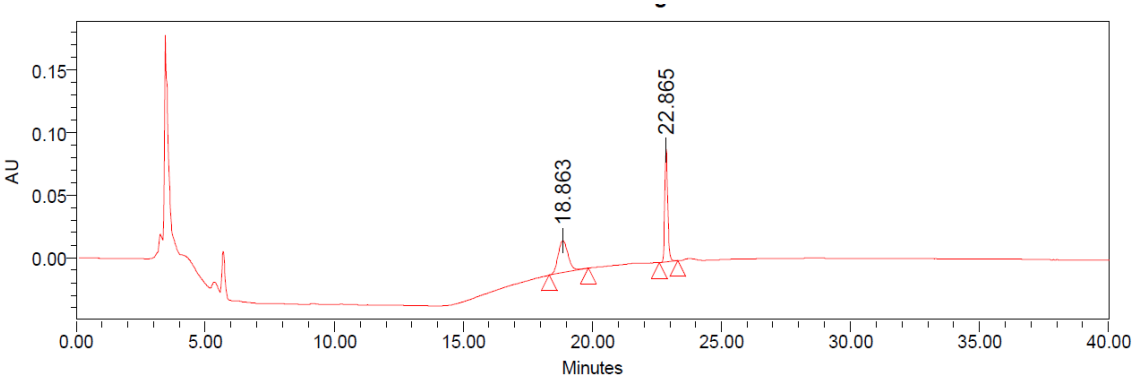
Figure ESI-28. HPLC traces for racemic and chiral compound **4Ba**.

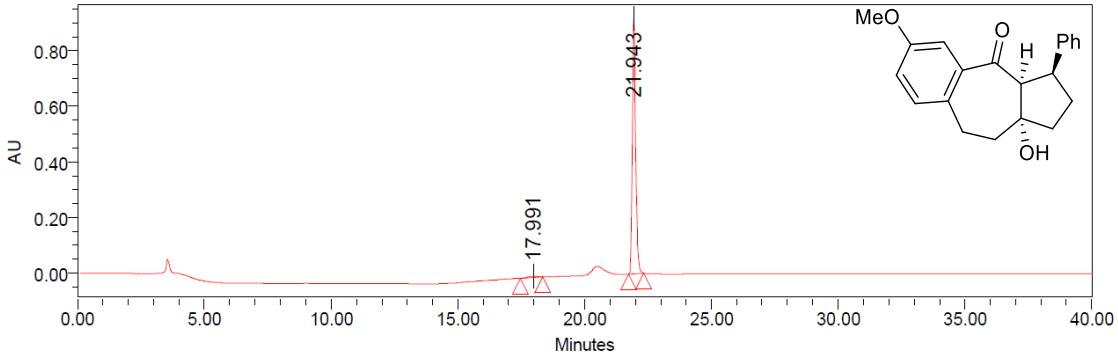


Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	16.212	812534	2.64	24532
2	PDA 220.0 nm	35.896	29996819	97.36	176111

Figure ESI-29. HPLC traces for racemic and chiral compound **3Ca**.





Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	17.991	120663	1.41	4818
2	PDA 220.0 nm	21.943	8442427	98.59	918947

Spectrum Index Plot

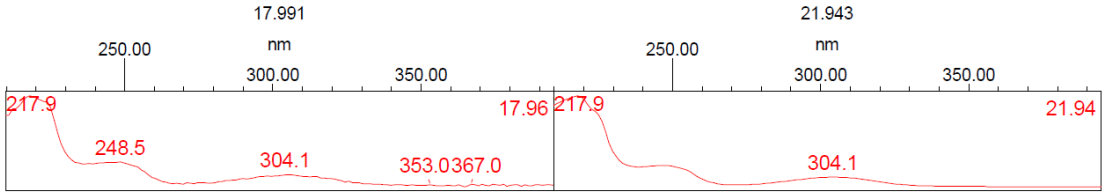
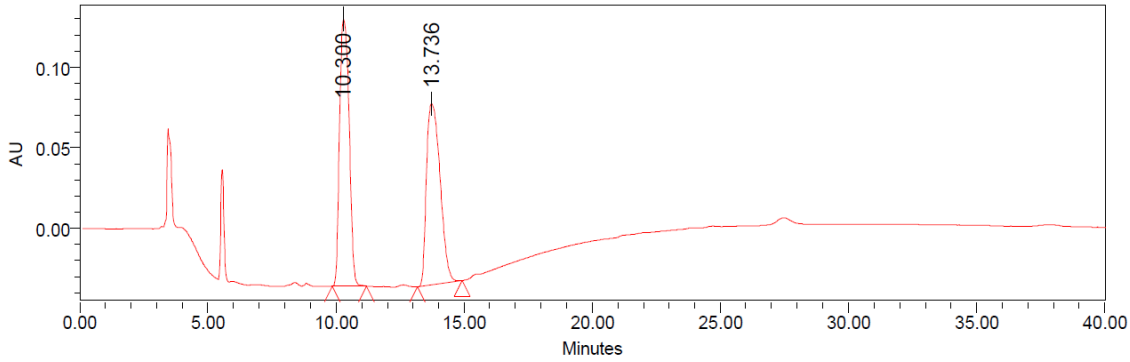
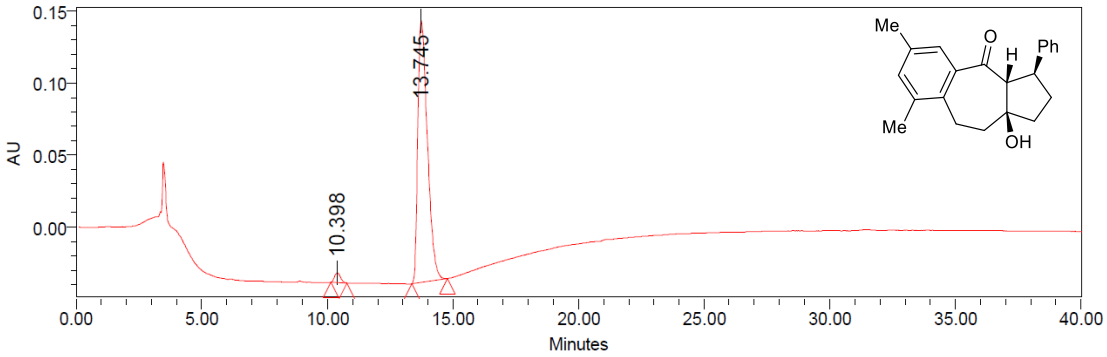


Figure ESI-30. HPLC traces for racemic and chiral compound **4Ca**.





Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	10.398	111527	2.26	6815
2	PDA 220.0 nm	13.745	4815452	97.74	181510

Spectrum Index Plot

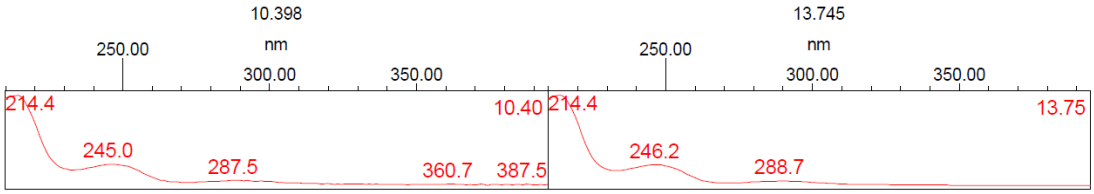
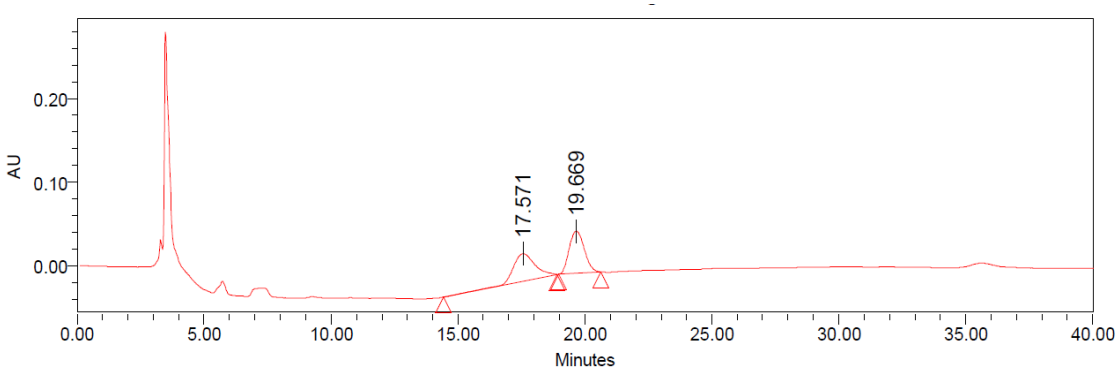
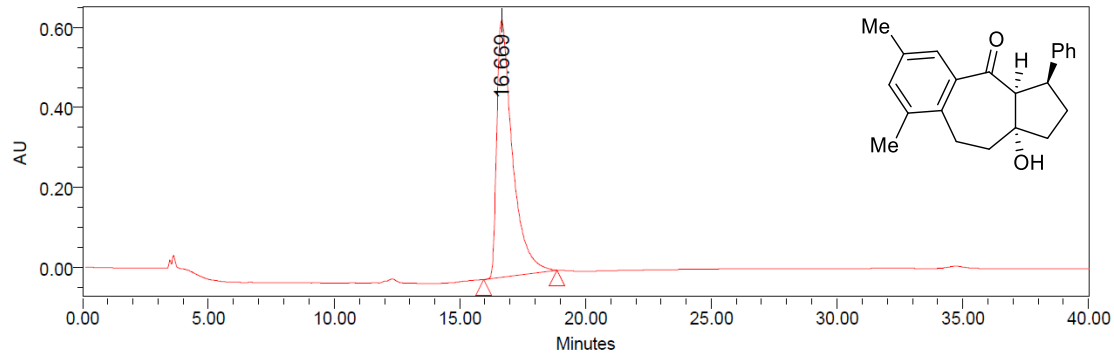


Figure ESI-31. HPLC traces for racemic and chiral compound **3Da**.





Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	16.669	27847101	100.00	643819

Spectrum Index Plot

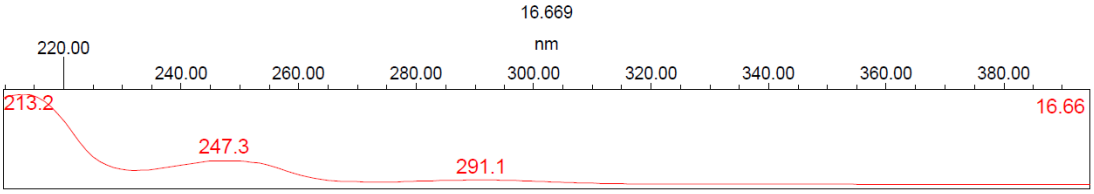
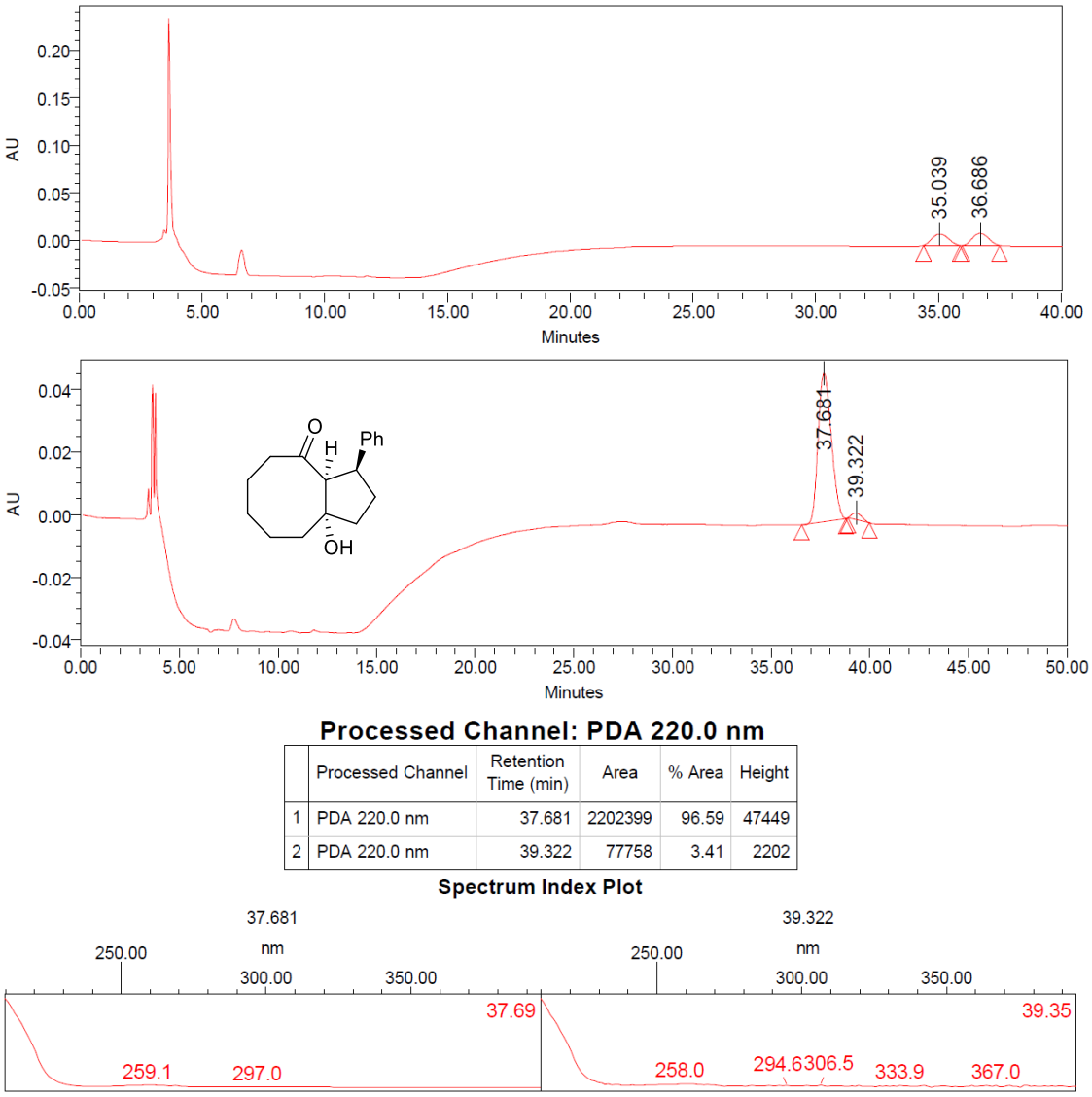


Figure ESI-32. HPLC traces for racemic and chiral compound **4Da**.



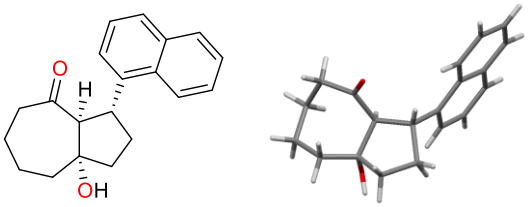
Processed Channel: PDA 220.0 nm

	Processed Channel	Retention Time (min)	Area	% Area	Height
1	PDA 220.0 nm	37.681	2202399	96.59	47449
2	PDA 220.0 nm	39.322	77758	3.41	2202

Figure ESI-33. HPLC traces for racemic and chiral compound **4Ea**.

5. X-ray details

Crystal Data for **3Ai** (CCDC 2145251) $C_{20}H_{22}O_2$ (M =294.38 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 7.0597(2) Å, b = 9.4699(2) Å, c = 11.8919(3) Å, β = 100.096(3)°, V = 782.72(3) Å^3, Z = 2, T = 150.3(3) K, μ(CuKα) = 0.618 mm^{-1}, *Dcalc* = 1.249 g/cm^3, 8452 reflections measured (7.56° ≤ 2Θ ≤ 137.94°), 2909 unique (R_{int} = 0.0333, R_{sigma} = 0.0409) which were used in all calculations. The final R_1 was 0.0452 (>2sigma(I)) and wR2 was 0.1121 (all data).



3Ai

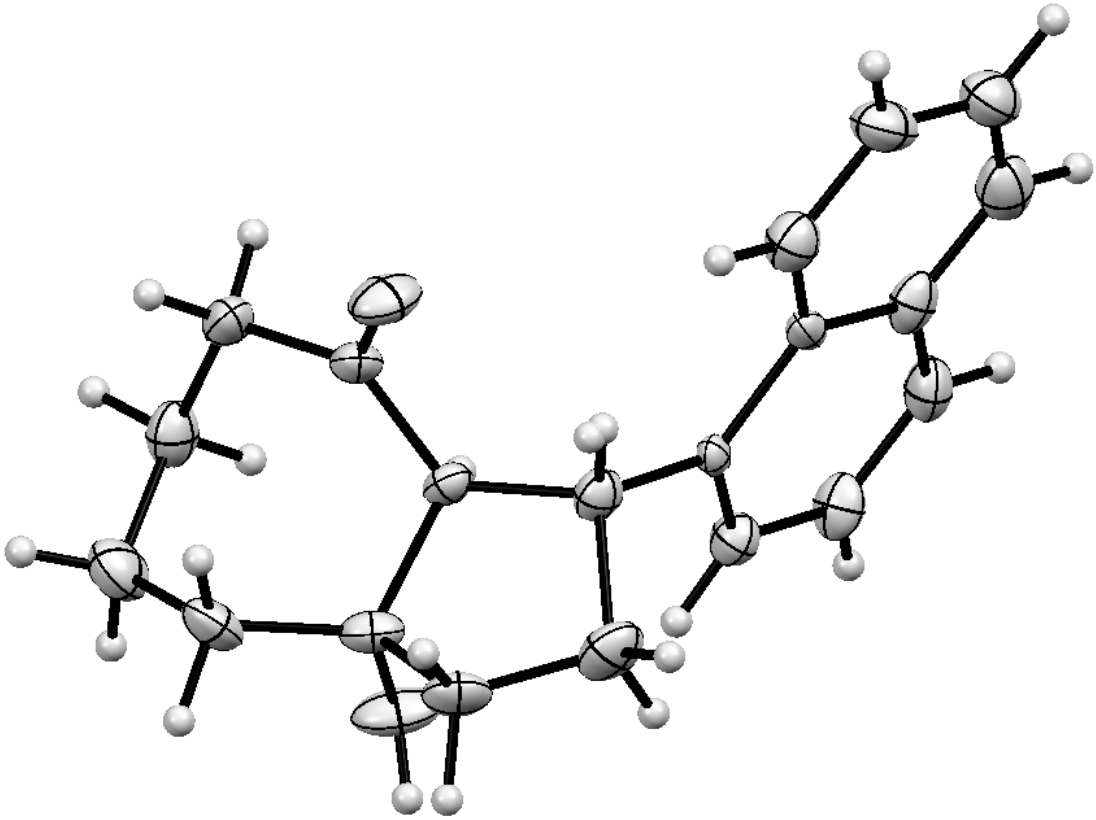
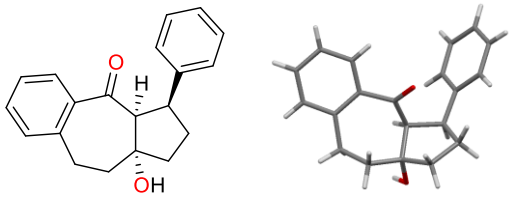


Figure ESI-34. X-Ray structure and ORTEP diagram (50% probability) for **3Ai** (disorder omitted for clarity)

Table ESI-2. Crystal data and structure refinement for 3Ai.

Identification code	a20210296_e487f1
Empirical formula	$C_{20}H_{22}O_2$
Formula weight	294.38
Temperature/K	150.3(3)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	7.0597(2)
b/Å	9.4699(2)
c/Å	11.8919(3)
α/°	90.00
β/°	100.096(3)
γ/°	90.00
Volume/Å^3	782.72(3)
Z	2
ρ_{calc}g/cm^3	1.249
μ/mm^{-1}	0.618
F(000)	316.0
Crystal size/mm^3	? × ? × ?
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.56 to 137.94
Index ranges	-8 ≤ h ≤ 8, -11 ≤ k ≤ 11, -14 ≤ l ≤ 14
Reflections collected	8452
Independent reflections	2909 [R_{int} = 0.0333, R_{sigma} = 0.0409]
Data/restraints/parameters	2909/121/267
Goodness-of-fit on F^2	1.064
Final R indexes [I>=2σ (I)]	R_1 = 0.0452, wR_2 = 0.1074
Final R indexes [all data]	R_1 = 0.0506, wR_2 = 0.1121
Largest diff. peak/hole / e Å^{-3}	0.19/-0.16
Flack parameter	-0.2(3)

Crystal Data for **4Ba** (CCDC 2145250) $C_{20}H_{20}O_2$ (*M* =292.36 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 5.82822(4) Å, *b* = 13.81370(9) Å, *c* = 18.94391(13) Å, *V* = 1525.159(19) Å^3, *Z* = 4, *T* = 150.99(13) K, μ(CuKα) = 0.635 mm^{-1}, *Dcalc* = 1.273 g/cm^3, 27285 reflections measured (7.922° ≤ 2Θ ≤ 137.992°), 2818 unique (R_{int} = 0.0417, R_{sigma} = 0.0238) which were used in all calculations. The final R_1 was 0.0358 (I > 2σ(I)) and wR_2 was 0.0956 (all data).



4Ba

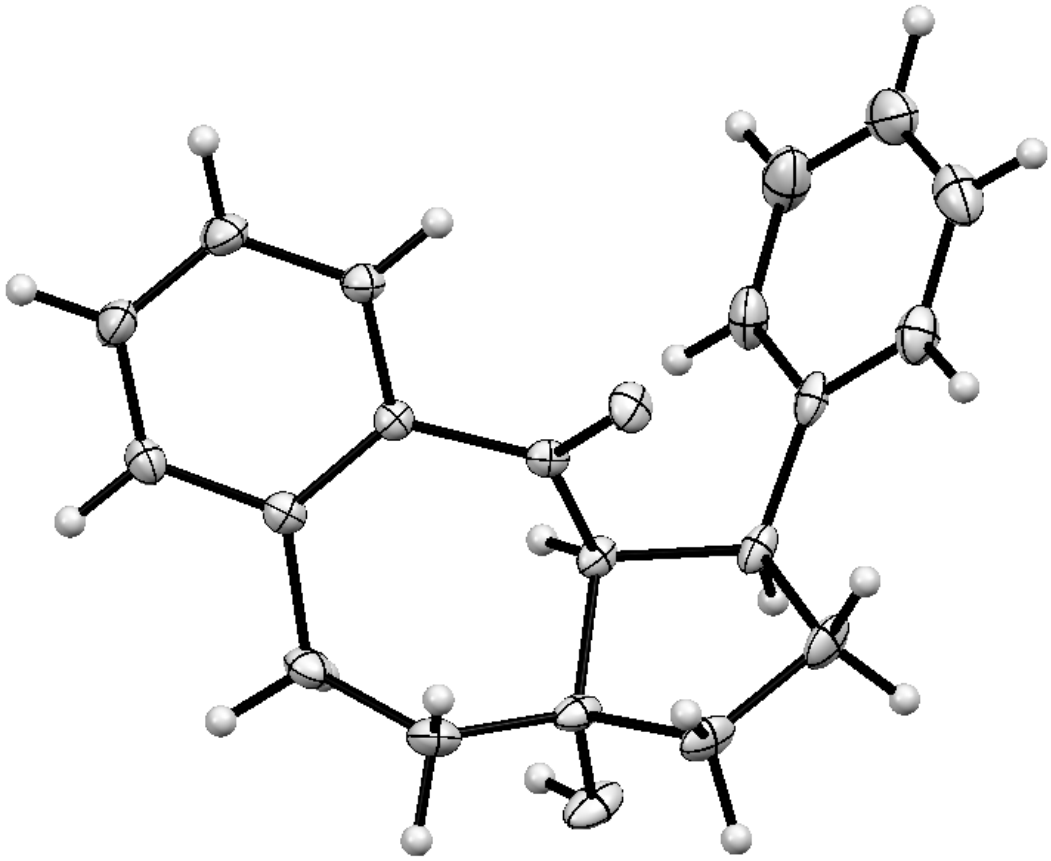


Figure ESI-35. X-Ray structure and ORTEP diagram (50% probability) for **4Ba**

Table ESI-3 Crystal data and structure refinement for 4Ba.

Identification code	a20210346_IIQ
Empirical formula	$C_{20}H_{20}O_2$
Formula weight	292.36
Temperature/K	150.99(13)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	5.82822(4)
b/Å	13.81370(9)
c/Å	18.94391(13)
α/°	90.0
β/°	90.0
γ/°	90.0
Volume/Å^3	1525.159(19)
Z	4
ρ_{calc}g/cm^3	1.273
μ/mm^{-1}	0.635
F(000)	624.0
Crystal size/mm^3	0.244 × 0.079 × 0.062
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.922 to 137.992
Index ranges	-7 ≤ h ≤ 5, -16 ≤ k ≤ 16, -22 ≤ l ≤ 22
Reflections collected	27285
Independent reflections	2818 [R_{int} = 0.0417, R_{sigma} = 0.0238]
Data/restraints/parameters	2818/0/200
Goodness-of-fit on F^2	1.059
Final R indexes [I>=2σ (I)]	R_1 = 0.0358, wR_2 = 0.0934
Final R indexes [all data]	R_1 = 0.0380, wR_2 = 0.0956
Largest diff. peak/hole / e Å^{-3}	0.15/-0.19
Flack parameter	0.10(10)