Supporting Information

Enantio- and Diastereoselective Synthesis of Chromeno[4,3-*b*]pyrrole Derivatives bearing Tetra-substituted Chirality Centres through Carbene Catalyzed Cascade Reactions

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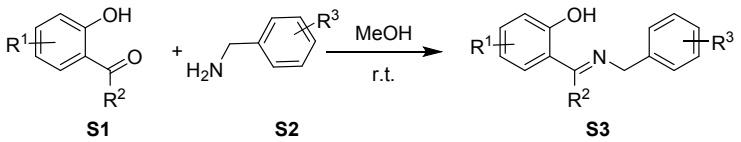
I. General information

Commercially available materials purchased from Energy Chemical and J&K were used as received. THF was distilled from Na and used directly. Unless otherwise specified, all reactions were carried out under an atmosphere of Air in 10 mL Schlenk tube. NMR spectra were measured either on a JEOL-ECX-500 (500 MHz) or on a Bruker ASCEND 400 (400 MHz) spectrometer. The chemical shift values were corrected to 7.26 ppm (^{1}H NMR) and 77.16 ppm (^{13}C NMR) for $CHCl_3$. 1H NMR splitting patterns are designated as singlet (s), double (d), triplet (t), quartet (q), doublet of doublets (dd), multiplets (m), and etc. All first-order splitting patterns were assigned on the base of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). High resolution mass spectrometer analysis (HRMS) was performed on Thermo Fisher Q Exactive mass spectrometer. HPLC analyses were measured on Waters systems with Empower 3 system controller, Alliance column heater, and 2998 Diode Array Waters 2489 UV/Vis detector. Chiralcel brand chiral columns from Daicel Chemical Industries were used with models IA in 4.6 x 250 mm size. UPLC analyses were measured on Waters systems with Empower3 system controller, Waters UPLC H-Class, and Waters ACQUITY UPLC PDA detector. Chiralcel brand chiral columns from Daicel Chemical Industries were used with models IA-U, IB-U, IC-U or OD-3 in 3.0 x 100 mm size. The racemic products used to determine the er values were synthesized using racemic catalyst. Optical rotations were measured on a Insmark IP-digi Polarimeter in a 1 dm cuvette. The concentration (c) is given in g/100 mL. Melting Point (MP): Melting points were measured on a Beijing Tech Instrument X-4 digital display micro melting point apparatus and are uncorrected. Analytical thin-layer chromatography (TLC) was carried out on pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

II. Preparation of substrates



S1 **S2** **S3**

The mixture of **S1** (1.0 equiv) and **S2** (1.1 equiv) was dissolved with MeOH stirred overnight at room temperature and a precipitation formed. After stirring, the product was filtered, washed with petroleum ether and vacuum dried to obtained **S3**.[1]

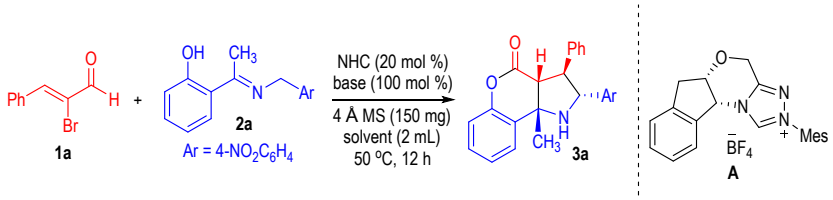
α-Bromoenals were prepared according to reported procedures.[2]

References:

(1) Qaisi, F. A.; Genjang, N.; Nieger, M.; Repo, T. *Inorganica. Chimica. Acta.* **2016**, *442*, 81.

(2) Liu, Y.; Chen, J.; Zhang, Z.; Qin, J.; Zhao, M.; Zhang, W. *Org. Biomol. Chem.* **2016**, *14*, 7099.

III. Experimental section: condition optimization for the synthesis of 3a[a]

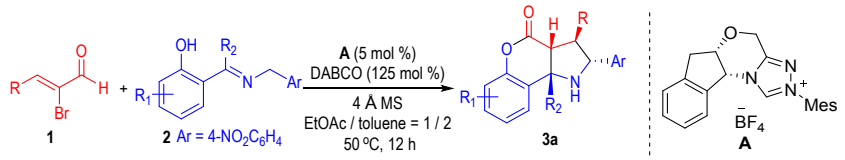


entry	NHC	base	solvent	T/°C	yield[b]	e.r.[c]	dr[d]
1	B	DABCO	THF	50	71	96:4	10:1
2	A	DABCO(1.0eq.)	THF(1ml)	50	75	95:5	-
3	A	DABCO(1.25eq.)	THF(1ml)	50	83	96:4	11:1
4	A	DABCO(1.5eq.)	THF(1ml)	50	82	96:4	12:1
5	A (20%)	DABCO	THF(1ml)	50	76	96:4	11:1
6	A (10%)	DABCO	THF(1ml)	50	81	97:3	11:1
7	A (5%)	DABCO	THF(1ml)	50	82	98:2	11:1
8	A (5%)	DABCO(1.25eq.)	THF(1ml)	50	76		
9	A (5%)	DABCO(1.25eq.)	THF(1ml)	40	72		
10	A (5%)	DABCO(1.25eq.)	THF(1ml)	25	<5		
11	A (5%)	DABCO(1.25eq.)	THF/DCM(1/1)	50	42	96:4	10:1
12	A (5%)	DABCO(1.25eq.)	THF/Tol(1/1)	50	70	98:2	11:1
13	A (5%)	DABCO(1.25eq.)	EA/DCM(1/1)	50	82	97:3	7:1
14	A (5%)	DABCO(1.25eq.)	EA/Tol(1/1)	50	84	98:2	10:1
15	A (5%)	DABCO(1.25eq.)	EA/Tol(2/1)	50	83	98:2	14:1
16	A (5%)	DABCO(1.25eq.)	EA/Tol(3/1)	50	84	98:2	11:1
17	A (5%)	DABCO(1.25eq.)	EA/Tol(1/2)	50	79	98:2	16:1
`18	A (5%)	DABCO(1.25eq.)	EA/Tol(1/3)	50	77	98:2	12:1
19	A (5%)	DABCO(1.25eq.)	EA(1ml)	50	84	98:2	13:1
20	A (5%)	DABCO(1.25eq.)	Tol(1ml)	50	77	99:1	>20:1
21[e]	A (5%)	DABCO(1.25eq.)	EA/Tol(1/2)	50	82	98:2	19:1
22[f]	A	DABCO	EA	50	75	96:4	8:1

[a]General conditions (unless otherwise specified): **1a** (0.10 mmol), **2a** (0.15 mmol), NHC (0.02 mmol), base (0.10 mmol), 4 Å MS (150 mg), solvent (2.0 mL), 50 °C, 12 h. [b]Isolated yield of **3a**. [c]Er was determined via HPLC on chiral stationary phase. [d]Dr was determined by ^{1}H NMR on the crude reaction mixture. [e]**1a** (0.10 mmol), **2a** (0.15 mmol), **A** (0.005 mmol), base (0.125 mmol), 4 Å MS (150 mg), solvent mixture (EtOAc / toluene = 1 / 2, 1.0 mL), 50 °C, 12 h. [f]1.0 eq. of **2a** was used. THF = Tetrahydrofuran. EA = Ethyl acetate, Tol = toluene, DABCO = 1,4-Diazabicyclo[2.2.2]octane;triethylenediamine

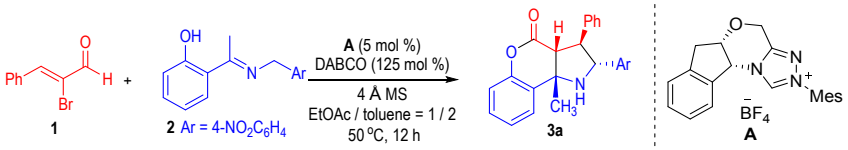
IV. General procedure for the catalytic reactions

General procedure for the catalytic reactions of 2-Bromoenals **1** and substrates **2** to synthesize product **3** or **4**:



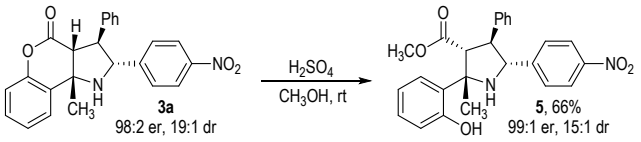
To a 10 mL flame-dry Schlenk reaction tube equipped with a magnetic stir bar, was added chiral NHC pre-catalyst A (0.005 mmol, 5 mol %, 2.1 mg), DABCO (0.125 mmol, 125 mol %, 14 mg), 4 Å molecular sieves (150 mg), 2-bromoenals **1** (0.1 mmol) and substrates 2 (0.15 mmol). Freshly distilled anhydrous EtOAc/toluene (1/2, v/v, 1 mL) was added via syringe. The reaction mixture was allowed to stir for 12 hours at 50 °C. After completion of the reaction, monitored by TLC plate, The mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel (7:1 hexanes/EtOAc) to afford the desired product **3** or **4**.

Procedure for synthesis of **3a** with gram scale:

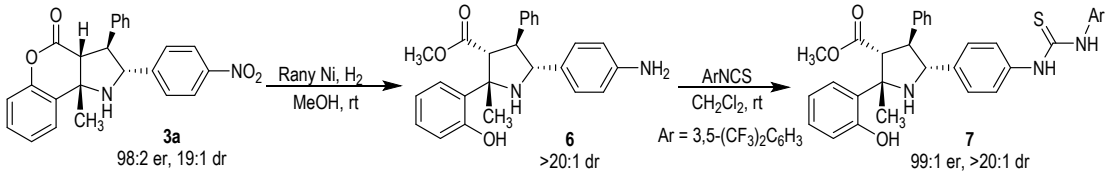


To a 100 mL flame-dry Schlenk reaction tube equipped with a magnetic stir bar, was added chiral NHC pre-catalyst A (0.25 mmol, 105 mg), DABCO (6.25 mmol, 701 mg), 4 Å molecular sieves (7.5 g), 2-bromoenals **1a** (5 mmol, 1.06 g) and aldimines **2a** (7.5 mmol, 2.03 g). Freshly distilled anhydrous EtOAc/toluene (1/2, v/v, 50 mL) was added via syringe. The reaction mixture was allowed to stir for 12 hours at 50 °C. After completion of the reaction, monitored by TLC plate, the mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel (7:1 hexanes/EtOAc) to afford the desired product **3a** (65% yield, 96% ee value, 15:1 dr).

Synthetic transformations and catalytic applications of chiral products **3a**:



To a 10 mL round bottom bottle was added compound **3a** (50 mg) and sulfuric acid (12 mg) in methanol (1 mL) at room temperature, the mixture was stirred for 6 h. Then solvent was removed by a vacuum pump and was purified by chromatography with petroleum ether/EtOAc (2:1) to give **5** (white solid, 66 % yield, 98% ee, 15:1 dr).



To a 25 mL flame-dry Schlenk reaction tube equipped with a magnetic stir bar was added compound **3a** (280 mg) and excess Ni, the Schlenk tube was sealed with a septum, evacuated and refilled with H_2 (3 cycles). Solvent (MeOH, 5.0 mL) was then added via syringe. The reaction mixture was allowed to stir for 10 min at room temperature. After completion of the reaction (monitored by TLC), the mixture was concentrated under reduced pressure. The resulting crude residue was purified via column chromatography on silica gel (5:1 to 2:1 petroleum ether /EtOAc) to afford the desired product **6** (white solid, 96% yield, >20:1 dr).

To a mixture of CH_2Cl_2 (10 mL) and **6** (100 mg) was added isothiocyanate (5.0 mmol), and the resulting mixture was stirred at room temperature until TLC indicated the reaction was complete. The reaction mixture was evaporated in vacuum. The pure products **7** were obtained by recrystallization from petroleum ether and ether (white solid, 72% yield, 99:1 er, >20:1 dr).

V. Studies on the relative acidities of the substrates.

We have examined the H-D exchanging rates of the nucleophilic C(sp3)-H bonds on the substrates bearing different imine groups (as shown in Figure S1).

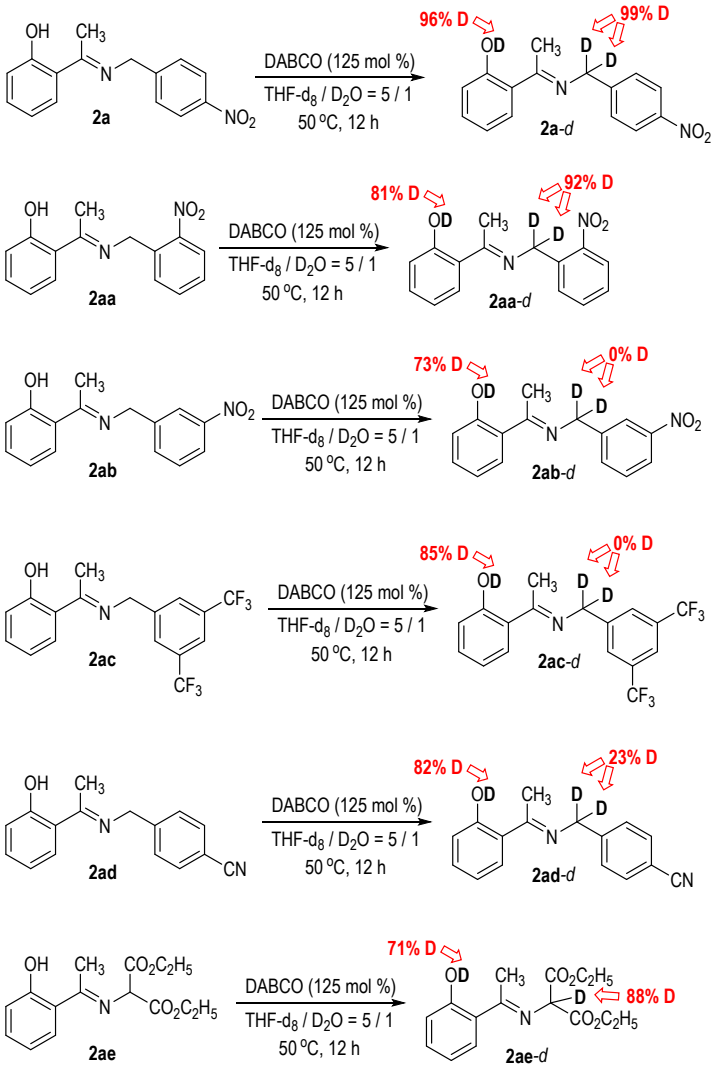


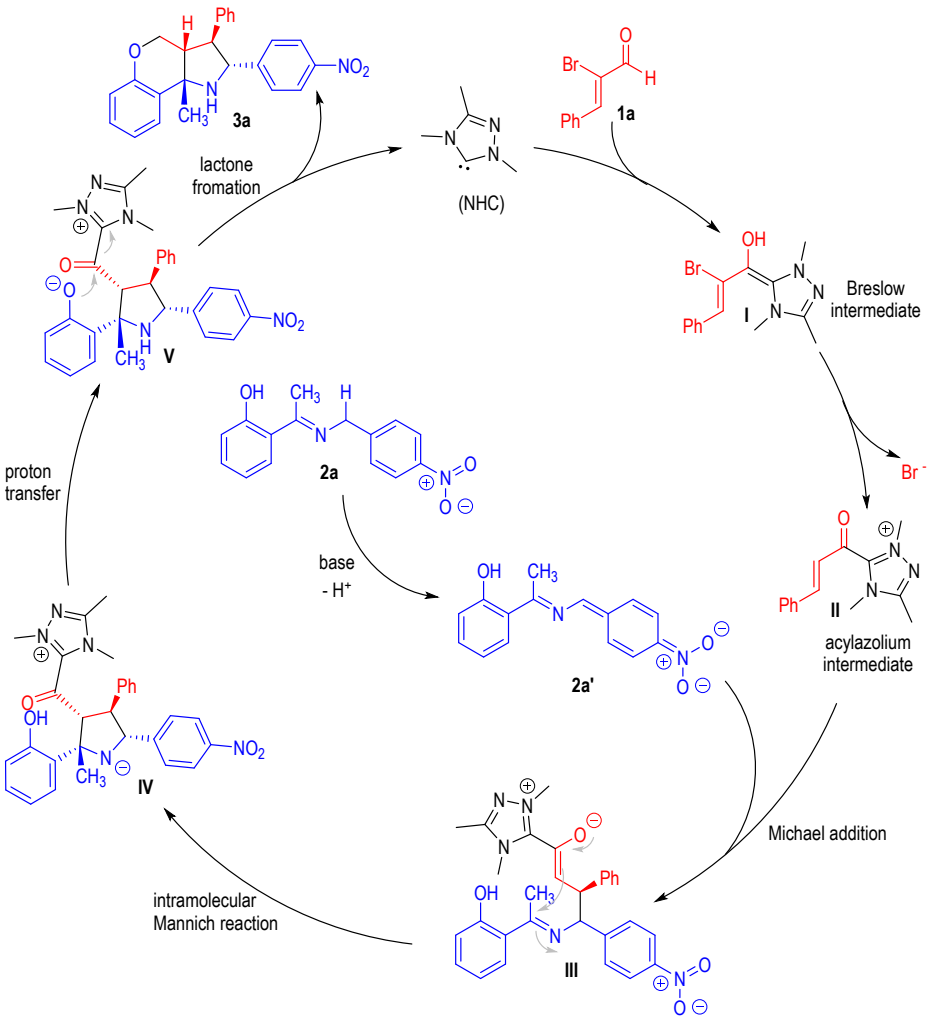
Figure S1. H-D exchanging studies

The phenol –OH groups of the substrates could be mostly deuterated by D2O under basic conditions in THF-d8. Meanwhile, the nucleophilic C(sp3)-H bonds of substrates **2a**, **2aa** could be fully deuterated, the nucleophilic C(sp3)-H bonds of substrates **2ad**, **2ae** could be partially deuterated, and the nucleophilic C(sp3)-H bonds of substrates **2ab**, **2ac** could not be deuterated. This indicates that the substrates **2a**, **2aa** could be actvie enough to be deprotonated and react with electrophiles, while the other substrates (**2ab**, **2ac**, **2ad**, **2ae**) may not be reactive enough.

Moreover, steric hindrance may also play significant roles in this catalytic cascade reaction. The nucleophilic additions of the substrates **2ab** and **2ae** are much more steric hindered than that of **2a**.

Therefore, the cascade reactions using substrates **2aa, 2ab**, **2ac, 2ad** and **2ae** could not happen under the current catalytic conditions.

VI. Proposed reaction mechanism.



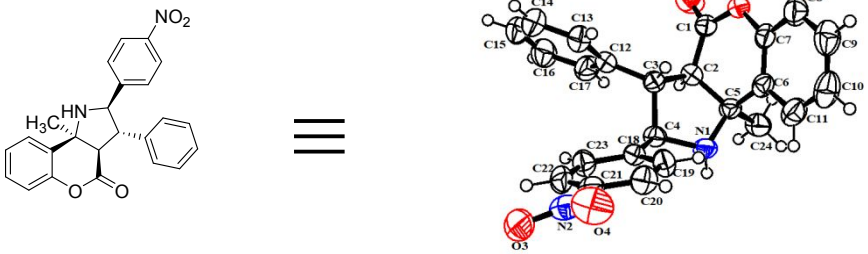
The NHC catalyst can react with the β-bromo-α,β-unsaturated enal **1a** and gives the Breslow interemediate **I**. The α,β-unsaturated acylazolium intermediate **II** can be effectively afforded from intermediate **I** on loosing of a Br^- anion.

The benzylic C(sp^3)-H of the 4-nitrobenyl group in **2a** can be deprotonated by base and generate **2a'** bearing a reactive nucleophilic benzylic carbon. **2a'** Can react with

the NHC-bound α,β−unsaturated acylazolium intermediate **II** through Michael addition and gives intermediate **III**. A sterically congested tetra-substituted chirality carbon center is formed in excellent diastereoselective fashion during the intramolecular Mannich reaction of the intermediate **III** and gives intermediate **IV** bearing a chiral substituted pyrrolidine structure. After a proton transfer process, the final product **3a** is readily formed through lactone formation from intermediate **V**, with the NHC catalyst released for additional catalytic cycles.

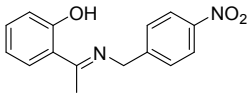
VII. X-ray crystallography of compound 3a.

Good quality crystal of **3a** (yellow block crystal) was obtained by vaporization of a CH_2Cl_2 / petroleum ether solution of compound **3a** (~100mg). CCDC 1960143 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/.



VIII. Characterization of substrates and products

(*E*)-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2a):



2a

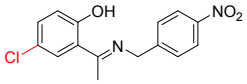
Light yellow solid, 91% yield, 5.6 g; m.p. 128-130 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 15.60 (s, 1H), 8.22 (d, *J* = 8.7 Hz, 2H), 7.62 – 7.49 (m, 3H), 7.37 – 7.29 (m, 1H), 6.95 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.90 – 6.79 (m, 1H), 4.89 (s, 2H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 162.7, 147.2, 146.2, 132.9, 128.3, 128.2, 124.0, 119.5, 118.4, 117.8, 53.2, 15.1.

HRMS (ESI, m/z) calcd. for $C_{15}H_{14}N_2O_3H^+$: 271.1077, found: 271.1068.

(*E*)-4-chloro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2b):



2b, 92%

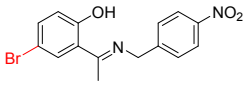
Light yellow solid, 92% yield, 1.81 g; m.p. 139-142 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.54 (s, 1H), 8.23 (d, *J* = 8.6 Hz, 2H), 7.58 – 7.49 (m, 3H), 7.27 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 4.89 (s, 2H), 2.43 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.4, 161.3, 147.3, 145.7, 132.7, 128.2, 127.7, 124.1, 122.4, 120.2, 119.9, 77.3, 77.0, 76.8, 53.3, 15.2.

HRMS (ESI, m/z) calcd. for $C_{15}H_{13}N_2O_3ClH^+$: 305.0687, found: 305.0697.

(*E*)-4-bromo-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2c):



2c, 93%

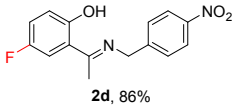
Light yellow solid, 93% yield, 1.97 g; m.p. 143-149 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.54 (s, 1H), 8.23 (d, *J* = 8.6 Hz, 2H), 7.58 – 7.49 (m, 3H), 7.27 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 4.89 (s, 2H), 2.43 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 161.8, 147.2, 145.7, 135.4, 130.7, 128.2, 124.0, 120.8, 120.4, 109.3, 77.4, 77.1, 76.7, 53.2, 15.3.

HRMS (ESI, m/z) calcd. for $C_{15}H_{13}N_2O_3BrH^+$: 349.0182, found: 349.0172.

(*E*)-4-fluoro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2d):



2d, 86%

Light yellow solid, 86% yield, 1.60 g; m.p. 124-138 °C;

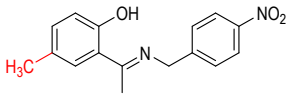
^{1}H NMR (600 MHz, $CDCl_3$) δ 15.54 (s, 1H), 8.23 (d, *J* = 8.6 Hz, 2H), 7.58 – 7.49 (m, 3H), 7.27 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.90 (d, *J* = 8.8 Hz, 1H), 4.89 (s, 2H), 2.43 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3 (d, *J* = 2.5 Hz), 158.6, 154.0, 147.3, 145.9, 128.3, 124.0, 119.9 (d, *J* = 23.4 Hz), 119.2 (d, *J* = 7.5 Hz), 113.8 (d, *J* = 24.2 Hz), 53.4, 15.3.

^{19}F NMR (565 MHz, $CDCl_3$) δ -125.76.

HRMS (ESI, m/z) calcd. for $C_{15}H_{13}N_2O_3FH^+$: 289.0983, found: 289.0980.

(*E*)-4-methyl-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2e):



2e, 93%

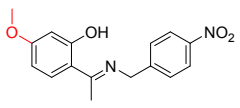
Light yellow solid, 86% yield, 1.75 g; m.p. 155-159 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 15.40 (s, 1H), 8.20 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 8.5 Hz, 2H), 7.37 (s, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 4.86 (s, 2H), 2.41 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 160.3, 147.1, 146.4, 133.7, 128.3, 128.2, 126.8, 123.9, 119.1, 118.0, 77.4, 77.1, 76.8, 53.2, 20.7, 15.1.

HRMS (ESI, m/z) calcd. for $C_{16}H_{16}N_2O_3H^+$: 285.1234, found: 285.1230.

(*E*)-5-methoxy-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2f):



2f, 72%

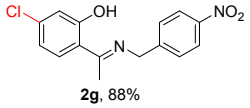
Light yellow solid, 72% yield, 1.70 g; m.p. 106-113 oC

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.7 Hz, 2H), 7.45 (d, J = 9.0 Hz, 1H), 6.43 (d, J = 2.5 Hz, 1H), 6.36 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.86 (s, 2H), 3.81 (s, 3H), 2.39 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 172.7, 167.9, 164.1, 147.3, 145.7, 129.7, 128.1, 124.0, 112.6, 106.2, 102.0, 77.3, 77.0, 76.8, 55.4, 51.7, 14.9.

HRMS (ESI, m/z) calcd. for $C_{16}H_{16}N_2O_4H^+$: 301.1183, found: 301.1183.

(*E*)-5-chloro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2g):



2g, 88%

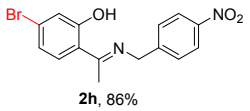
Light yellow solid, 88% yield, 1.88 g; m.p. 135-137 oC

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.48 (d, *J* = 8.6 Hz, 1H), 6.94 (d, *J* = 2.1 Hz, 1H), 6.79 (dd, *J* = 8.6, 2.1 Hz, 1H), 4.88 (s, 2H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 164.3, 147.2, 145.6, 138.4, 129.3, 128.2, 124.0, 118.6, 118.0, 117.7, 77.4, 77.1, 76.8, 52.7, 15.2.

HRMS (ESI, m/z) calcd. for $C_{15}H_{13}N_2O_3H^+$: 305.0687, found: 305.0683.

(*E*)-5-bromo-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2h):



2h, 86%

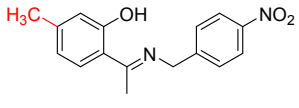
Light yellow solid, 86% yield, 1.96 g; m.p. 142-144 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.40 (d, *J* = 8.6 Hz, 1H), 7.11 (d, *J* = 2.0 Hz, 1H), 6.94 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.87 (s, 2H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 164.3, 147.2, 145.5, 129.4, 128.2, 126.9, 124.0, 121.7, 120.8, 118.0, 77.4, 77.1, 76.8, 52.8, 15.2.

HRMS (ESI, m/z) calcd. for $C_{15}H_{13}N_2O_3BrH^+$: 349.0182, found: 349.0179.

(*E*)-5-methyl-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2i):



2i, 68%

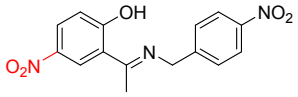
Light yellow solid, 68% yield, 1.29 g; m.p. 131-135 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.64 (s, 1H), 8.22 (d, *J* = 8.7 Hz, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 1H), 6.76 (s, 1H), 6.66 (dd, *J* = 8.1, 0.9 Hz, 1H), 4.87 (s, 2H), 2.40 (s, 3H), 2.32 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.0, 162.8, 147.2, 146.3, 143.8, 128.2, 128.1, 124.0, 119.0, 118.7, 117.1, 77.3, 77.0, 76.8, 53.0, 21.6, 15.0.

HRMS (ESI, m/z) calcd. for $C_{16}H_{16}N_2O_3H$+: 285.1234, found: 285.1231.

(*E*)-4-nitro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2j):



2j, 97%

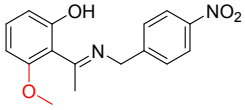
Light yellow solid, 97% yield, 1.85 g; m.p. 121-126 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (d, *J* = 2.7 Hz, 1H), 8.28 (d, *J* = 8.7 Hz, 2H), 8.21 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.57 (d, *J* = 8.7 Hz, 2H), 6.96 (d, *J* = 9.3 Hz, 1H), 4.98 (s, 2H), 2.60 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.8, 171.3, 147.6, 144.0, 137.8, 128.6, 128.3, 125.7, 124.3, 120.5, 116.9, 77.3, 77.1, 76.8, 52.3, 15.2.

HRMS (ESI, m/z) calcd. for $C_{15}H_{13}N_3O_5^+$: 315.0850, found: 315.0839.

(*E*)-3-methoxy-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2k):



2k, 46%

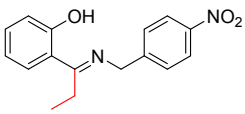
Light yellow solid, 46% yield, 1.07 g; m.p. 121-126 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.7 Hz, 2H), 7.20 (t, *J* = 8.3 Hz, 1H), 6.56 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.34 (d, *J* = 8.2 Hz, 1H), 4.82 (s, 2H), 3.84 (s, 3H), 2.50 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 174.6, 164.2, 160.1, 147.1, 146.2, 132.4, 128.3, 124.0, 111.4, 110.9, 100.4, 77.3, 77.1, 76.9, 55.4, 52.1, 20.7.

HRMS (ESI, m/z) calcd. for $C_{16}H_{16}N_2O_4H^+$: 301.1183, found: 301.1179.

(*E*)-2-(1-((4-nitrobenzyl)imino)propyl)phenol (2l):



2l, 55%

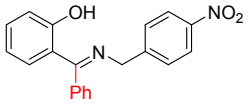
Light yellow solid, 55% yield, 1.35 g; m.p. 126-128 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.83 (s, 1H), 8.22 (d, *J* = 8.7 Hz, 2H), 7.59 – 7.51 (m, 3H), 7.36 – 7.30 (m, 1H), 6.96 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.89 – 6.82 (m, 1H), 4.92 (s, 2H), 2.88 (q, *J* = 7.8 Hz, 2H), 1.27 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 178.0, 163.5, 147.2, 146.2, 132.9, 128.2, 124.0, 118.7, 117.9, 117.8, 77.3, 77.1, 76.9, 52.2, 21.4, 11.9.

HRMS (ESI, m/z) calcd. for $C_{16}H_{16}N_2O_3H^+$: 285.1234, found: 285.1230.

(*E*)-2-(((4-nitrobenzyl)imino)(phenyl)methyl)phenol (2m):



2m, 25%

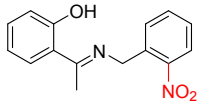
Light yellow solid, 25% yield, 617 mg; m.p. 152-155 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.05 (s, 1H), 8.18 (d, *J* = 8.7 Hz, 2H), 7.53 (dd, *J* = 5.0, 1.7 Hz, 3H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.35 – 7.28 (m, 1H), 7.20 (dd, *J* = 6.4, 3.0 Hz, 2H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.85 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.70 (t, *J* = 7.6 Hz, 1H), 4.64 (s, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 176.2, 162.6, 147.1, 146.5, 133.7, 132.9, 131.9, 129.4, 129.2, 129.0, 128.1, 127.1, 123.9, 119.8, 117.9, 117.9, 77.3, 77.1, 76.8, 55.1.

HRMS (ESI, m/z) calcd. for $C_{20}H_{16}N_2O_3H^+$: 333.1234, found: 333.1230.

(*E*)-2-(1-((2-nitrobenzyl)imino)ethyl)phenol (2aa)



2aa, 37%

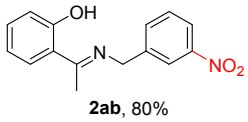
Light yellow solid, 37% yield, 810 mg; m.p. 91-92 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.59 (s, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 7.64 (d, *J* = 4.1 Hz, 2H), 7.59 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.47 (dp, *J* = 8.1, 4.0 Hz, 1H), 7.34 – 7.29 (m, 1H), 6.94 (d, *J* = 8.3 Hz, 1H), 6.84 (t, *J* = 7.6 Hz, 1H), 5.13 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.3, 162.7, 148.2, 134.3, 133.9, 132.7, 130.0, 128.3, 128.2, 125.2, 119.6, 118.4, 117.8, 50.9, 15.1.

HRMS (ESI, m/z) calcd. for $C_{15}H_{14}N_2O_3H^+$: 271.1077, found: 271.1077.

(*E*)-2-(1-((3-nitrobenzyl)imino)ethyl)phenol (2ab)



2ab, 80%

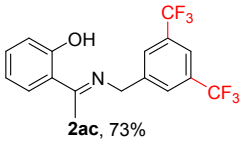
light yellow solid, 80% yield, 2.31 g; m.p. 114-115 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.57 (s, 1H), 8.21 (s, 1H), 8.15 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.59 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.35 – 7.29 (m, 1H), 6.94 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.87 – 6.82 (m, 1H), 4.87 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.12, 162.67, 148.45, 140.87, 133.67, 132.80, 129.83, 128.26, 122.56, 122.37, 119.55, 118.41, 117.81, 53.12, 15.14.

HRMS (ESI, m/z) calcd. for $C_{15}H_{14}N_2O_3H^+$: 271.1077, found: 271.1075.

(*E*)-2-(1-((3,5-bis(trifluoromethyl)benzyl)imino)ethyl)phenol (2ac)



2ac, 73%

light yellow solid, 73% yield, 2.92 g; m.p. 119-120 °C;

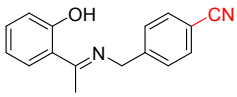
^{1}H NMR (600 MHz, $CDCl_3$) δ 15.23 (s, 1H), 7.83 (s, 3H), 7.59 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.35 – 7.30 (m, 1H), 6.96 (dd, *J* = 8.3, 1.0 Hz, 1H), 6.88 – 6.82 (m, 1H), 4.87 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.4, 162.5, 141.5, 132.9, 132.1 (q, *J* = 33.4 Hz), 128.3, 127.8 (d, *J* = 2.5 Hz), 123.3 (q, *J* = 272.6 Hz), 121.4 (dt, *J* = 7.5, 3.6 Hz), 119.6, 118.4, 118.0, 53.2, 15.3.

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.82.

HRMS (ESI, m/z) calcd. for $C_{17}H_{13}NOF_6H^+$: 362.0974, found: 362.0970.

(*E*)-4-(((1-(2-hydroxyphenyl)ethylidene)amino)methyl)benzonitrile (2ad)



2ad, 98%

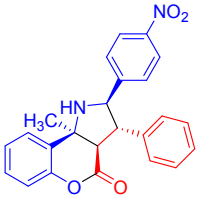
light yellow solid, 98% yield, 2.70 g; m.p. 144-145 °C;

^{1}H NMR (600 MHz, $CDCl_3$) δ 15.67 (s, 1H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.58 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.36 – 7.29 (m, 1H), 6.95 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.88 – 6.80 (m, 1H), 4.84 (s, 2H), 2.42 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 173.2, 162.8, 144.1, 132.8, 132.6, 128.2, 128.1, 119.5, 118.7, 118.4, 117.8, 111.2, 53.3, 15.1.

HRMS (ESI, m/z) calcd. for $C_{16}H_{14}N_2OH^+$: 251.1179, found: 251.1179.

(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3a)



3a, 82%
98:2 er, 19:1 dr

White solid, 82% yield, 33.9 mg; m.p. 194-196 °C;

[α]^{25}D = -20.7 (c = 1.0 in $CHCl_3$); 19:1 dr (reaction mixture);

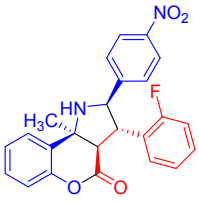
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.8 Hz, 2H), 7.87 (dd, *J* = 5.9, 3.5 Hz, 1H), 7.37 – 7.27 (m, 5H), 7.14 – 7.00 (m, 5H), 4.78 (d, *J* = 9.9 Hz, 1H), 3.52 (d, *J* = 12.4 Hz, 1H), 3.21 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.77 (s, 1H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 150.2, 148.0, 147.1, 135.7, 129.8, 129.2, 129.0, 128.3, 128.2, 128.0, 127.5, 125.3, 123.3, 117.0, 77.4, 77.3, 77.1, 76.8, 68.9, 62.4, 58.9, 58.8, 30.0.

HRMS (ESI) calcd. for $C_{24}H_{20}N_2O_4H^+$: 401.1501, found : 401.1500;

UPLC analysis: 98:2 er (OD-3 column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.4 min, Rt (major) = 3.1 min

(2*R*,3*S*,3*aR*,9*bS*)-3-(2-fluorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3b)



3b, 76%
98:2 er, >20:1 dr

White solid, 76% yield, 31.6 mg; m.p. 191-192 °C;

[α]^{25}D = -18.9 (c = 0.5 in $CHCl_3$); >20:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.90 (m, 2H), 7.90 – 7.81 (m, 1H), 7.40 – 7.27 (m, 3H), 7.18 – 6.99 (m, 6H), 4.93 (d, *J* = 9.8 Hz, 1H), 3.66 (d, *J* = 12.5 Hz, 1H), 3.44 (dd, *J* = 12.5, 9.9 Hz, 1H), 2.78 (s, 1H), 1.68 (s, 3H).

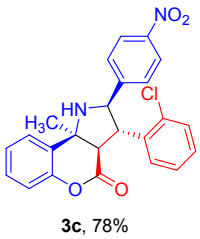
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 161.3 (d, *J* = 246.8 Hz), 150.2, 148.0, 147.2, 130.0 (dd, *J* = 6.6, 2.0 Hz), 129.4, 129.3, 128.2, 127.3, 125.3, 124.8 (d, *J* = 3.5 Hz), 123.4, 122.9, 122.8, 117.0, 116.3 (d, *J* = 22.4 Hz), 66.7, 62.5, 57.3, 57.2, 53.6, 30.1.

^{19}F NMR (377 MHz, $CDCl_3$) δ -116.26.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4FH^+$: 419.1402, found : 419.1402;

UPLC analysis: 98:2 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.5 min, Rt (major) = 3.2 min

(2*R*,3*S*,3*aR*,9*bS*)-3-(2-chlorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3c)



3c, 78%
99:1 er, >20:1 dr

White solid, 78% yield, 33.9 mg; m.p. 230-231 °C;

[α]^{25}D = -33.3 (c = 0.4 in $CHCl_3$); >20:1 dr (reaction mixture);

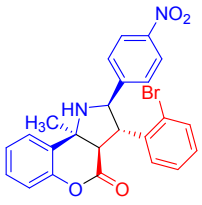
^{1}H NMR (40 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.89 – 7.81 (m, 1H), 7.52 (d, *J* = 7.4 Hz, 1H), 7.39 – 7.17 (m, 5H), 7.13 (d, *J* = 8.7 Hz, 2H), 7.09 – 7.02 (m, 1H), 4.91 (d, *J* = 9.9 Hz, 1H), 3.97 (dd, *J* = 12.3, 10.1 Hz, 1H), 3.52 (d, *J* = 12.5 Hz, 1H), 2.81 (s, 1H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 150.0, 148.0, 147.1, 134.8, 133.4, 130.3, 129.4, 129.3, 129.2, 128.6, 128.1, 127.6, 127.3, 125.3, 123.4, 116.9, 67.6, 62.6, 58.5, 54.0, 29.9.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4ClH^+$: 435.1106, found : 435.1102;

UPLC analysis: 99:1 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.6 min, Rt (major) = 3.8 min.

(2*R*,3*S*,3*aR*,9*bS*)-3-(2-bromophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3d)



3d, 61%
99.5:0.5 er, >20:1 dr

White solid, 61% yield, 29.2 mg; m.p. 215-216 °C;

[α]^{25}D = -30.7 (c = 1.0 in $CHCl_3$); >20:1 dr (reaction mixture);

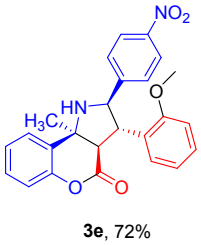
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.93 (m, 2H), 7.88 – 7.81 (m, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.49 – 7.29 (m, 4H), 7.18 – 7.04 (m, 4H), 4.87 (d, *J* = 9.8 Hz, 1H), 4.14 – 3.90 (m, 1H), 3.46 (d, *J* = 12.4 Hz, 1H), 2.80 (s, 1H), 1.68 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 149.8, 148.0, 147.2, 135.1, 133.5, 129.5, 129.4, 129.4, 128.4, 128.2, 128.1, 127.3, 125.8, 125.3, 123.4, 116.9, 68.1, 62.6, 59.0, 56.1, 29.8.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4BrH^+$:479.0601, found : 479.0600;

UPLC analysis: 99.5:0.5 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.6 min, Rt (major) = 4.0 min

(2*R*,3*S*,3*aR*,9*bS*)-3-(2-methoxyphenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3e)



3e, 72%
97:3 er, >20:1 dr

White solid, 72% yield, 31 mg; m.p. 205-206 °C;

[α]^{25}D = -26.8 (c = 1.0 in $CHCl_3$); >20:1 dr (reaction mixture);

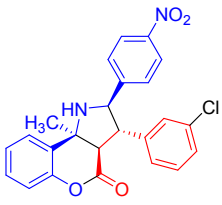
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.91 (m, 2H), 7.87 – 7.81 (m, 1H), 7.36 – 7.23 (m, 3H), 7.20 – 7.11 (m, 3H), 7.07 – 7.00 (m, 1H), 6.92 (td, *J* = 7.5, 0.9 Hz, 1H), 6.85 (d, *J* = 8.2 Hz, 1H), 5.02 (d, *J* = 9.3 Hz, 1H), 3.66 (s, 3H), 3.65 – 3.58 (m, 2H), 2.73 (s, 1H), 1.64 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.3, 157.7, 151.3, 148.3, 146.8, 129.6, 129.2, 129.1, 128.9, 128.2, 127.4, 125.0, 123.8, 123.2, 121.0, 116.8, 111.3, 65.3, 62.5, 57.3, 55.3, 53.6, 30.0.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_5H^+$: 431.1601, found : 431.1597;

UPLC analysis: 97:3 er (OD-3 column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 10.0 min, Rt (major) = 7.4 min

(2*R*,3*S*,3*aR*,9*bS*)-3-(3-chlorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-b]pyrrol-4(1*H*)-one (3f)



3f, 85%
98:2 er, 7:1 dr

White solid, 85% yield, 37 mg; m.p. 97-98 °C;

[α]^{25}D = -13.8 (c = 1.0 in $CHCl_3$); 7:1 dr (reaction mixture);

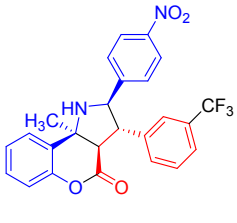
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.94 (m, 2H), 7.85 (dd, *J* = 6.1, 3.3 Hz, 1H), 7.34 (dd, *J* = 5.9, 3.5 Hz, 2H), 7.29 – 7.19 (m, 2H), 7.17 – 7.02 (m, 4H), 6.97 – 6.90 (m, 1H), 4.76 (d, *J* = 9.8 Hz, 1H), 3.48 (d, *J* = 12.4 Hz, 1H), 3.19 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.78 (s, 1H), 1.68 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 149.7, 147.9, 147.3, 138.0, 134.9, 130.3, 129.5, 129.3, 128.5, 128.2, 128.0, 127.5, 126.5, 125.4, 123.5, 117.0, 68.8, 62.5, 58.9, 58.3, 29.9.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4ClH^+$: 435.1106, found : 435.1104;

UPLC analysis: 98:2 er (IB-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 7.9 min, Rt (major) = 3.0 min.

(2*R*,3*S*,3*aR*,9b*S*)-9b-methyl-2-(4-nitrophenyl)-3-(3-(trifluoromethyl)phenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3g)



3g, 56%
97:3 er, 9:1 dr

White solid, 56% yield, 26 mg; m.p. 84-85 °C;

[α]^{25}D = 1.8 (c = 0.3 in $CHCl_3$); 9:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.93 (m, 2H), 7.90 – 7.83 (m, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.38 – 7.32 (m, 3H), 7.26 (t, *J* = 3.8 Hz, 1H), 7.12 – 7.03 (m, 3H), 4.77 (d, *J* = 9.8 Hz, 1H), 3.54 (d, *J* = 12.5 Hz, 1H), 3.29 (dd, *J* = 12.5, 9.9 Hz, 1H), 2.80 (s, 1H), 1.70 (s, 3H).

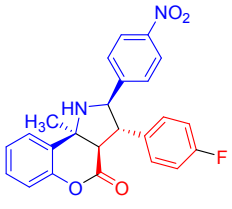
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 149.4, 147.9, 147.3, 136.9, 131.6, 129.6, 129.5, 129.4, 128.6, 128.1, 127.5, 125.5, 125.19 (q, *J* = 3.5 Hz), 124.62 (q, *J* = 3.6 Hz), 123.5, 122.8, 117.1, 69.0, 62.5, 58.6, 58.3, 30.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.61.

HRMS (ESI) calcd. for $C_{25}H_{19}N_2O_4F_3H^+$: 469.1370, found : 469.1366;

UPLC analysis: 97:3 er (IB-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 8.7 min, Rt (major) = 2.4 min.

(2*R*,3*S*,3*aR*,9*bS*)-3-(4-fluorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3h)



3h, 86%
97:3 er, 9:1 dr

White solid, 86% yield, 36.0 mg; m.p. 173-174 °C;

[α]^{25}D = -5.2 (c = 1.0 in $CHCl_3$); 9:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.91 (m, 2H), 7.90 – 7.81 (m, 1H), 7.38 – 7.29 (m, 2H), 7.13 – 6.92 (m, 7H), 4.72 (d, *J* = 9.9 Hz, 1H), 3.48 (d, *J* = 12.5 Hz, 1H), 3.20 (dd, *J* = 12.5, 9.9 Hz, 1H), 2.75 (s, 1H), 1.68 (s, 3H).

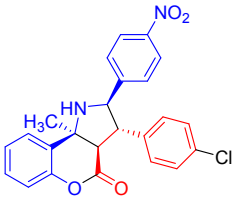
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 162.4 (d, *J* = 247.1 Hz), 149.9, 147.9, 147.2, 131.4 (d, *J* = 3.3 Hz), 129.7, 129.6 (d, *J* = 8.1 Hz), 129.3, 128.2, 127.5, 125.4, 123.4, 117.0, 116.0 (d, *J* = 21.4 Hz), 69.1, 62.3, 58.8, 58.0, 30.0.

^{19}F NMR (377 MHz, CDCl3) δ -113.60.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4FH^+$: 419.1402, found : 419.1399;

UPLC analysis: 97:3 er (AD-3 column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 5.3 min, Rt (major) = 6.9 min

(2*R*,3*S*,3*aR*,9*bS*)-3-(4-chlorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-b]pyrrol-4(1*H*)-one (3i)



3i, 80%
97:3 er, 8:1 dr

White solid, 80% yield, 34.9 mg; m.p. 171-172 °C;

[α]^{25}D = -11.2 (c = 1.0 in $CHCl_3$); 8:1 dr (reaction mixture);

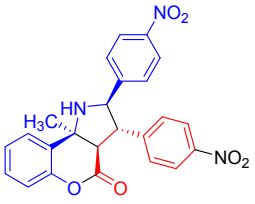
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.94 (m, 2H), 7.88 – 7.83 (m, 1H), 7.37 – 7.31 (m, 2H), 7.30 – 7.26 (m, 2H), 7.11 – 6.97 (m, 5H), 4.72 (d, *J* = 9.9 Hz, 1H), 3.48 (d, *J* = 12.5 Hz, 1H), 3.19 (dd, *J* = 12.5, 9.9 Hz, 1H), 2.75 (s, 1H), 1.68 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 149.7, 147.9, 147.2, 134.2, 134.1, 129.6, 129.3, 129.3, 128.1, 127.5, 125.4, 123.4, 117.0, 69.0, 62.3, 58.7, 58.1, 30.0.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4ClH^+$: 435.1106, found : 435.1104;

UPLC analysis: 97:3 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.4 min, Rt (major) = 3.4 min

(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-2,3-bis(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3j)



3j, 56%
93:7 er, 6:1 dr

Light yellow solid, 56% yield, 24.9 mg; m.p. 216-217 °C;

[α]^{25}D = -30.9 (c = 1.0 in $CHCl_3$); 6:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 – 8.15 (m, 2H), 8.03 – 7.96 (m, 2H), 7.86 (dd, *J* = 6.0, 3.4 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.30 – 7.26 (m, 3H), 7.11 – 7.05 (m, 3H), 4.78 (d, *J* = 9.8 Hz, 1H), 3.56 (d, *J* = 12.5 Hz, 1H), 3.35 (dd, *J* = 12.5, 9.9 Hz, 1H), 2.83 (s, 1H), 1.72 (s, 3H).

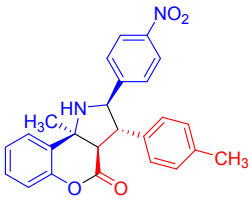
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 149.0, 147.8, 147.7, 147.4, 143.2, 129.5, 129.3, 129.0, 128.1, 127.5, 125.6, 124.2, 123.6, 117.1, 69.0, 62.5, 58.5, 58.2, 30.0.

HRMS (ESI) calcd. for $C_{24}H_{19}N_3O_6H^+$: 446.1347, found : 446.1338;

UPLC analysis: 93:7 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min,

λ = 254 nm), Rt (minor) = 4.5 min, Rt (major) = 8.5 min.

(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-2-(4-nitrophenyl)-3-(p-tolyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3k)



3k, 61%
99.5:0.5 er, 19:1 dr

White solid, 61% yield, 25.4 mg; m.p. 224-226 °C;

$[\alpha]^{25}D$ = -6.2 (c = 1.0 in $CHCl_3$); 19:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.89 – 7.82 (m, 1H), 7.36 – 7.28 (m, 2H), 7.10 (d, *J* = 8.6 Hz, 4H), 7.05 – 7.00 (m, 1H), 6.97 (d, *J* = 8.1 Hz, 2H), 4.76 (d, *J* = 9.9 Hz, 1H), 3.48 (d, *J* = 12.4 Hz, 1H), 3.18 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.76 (s, 1H), 2.31 (s, 3H), 1.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.9, 150.4, 148.0, 147.1, 137.9, 132.6, 129.8, 129.7, 129.2, 128.2, 127.8, 127.5, 125.3, 123.3, 116.9, 68.8, 62.4, 59.1, 58.6, 30.0, 21.2.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_4H^+$: 415.1652, found : 415.1653;

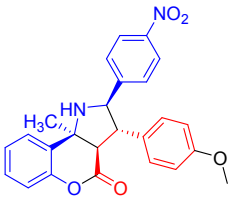
UPLC analysis: 99.5:0.5 er (IA-U column, 25 °C, hexane / iPrOH = 90 / 10, 0.5 mL / min, λ = 254 nm), Rt (minor) = 4.0 min, Rt (major) = 6.0 min.

(2*R*,3*S*,3*aR*,9*bS*)-3-(4-methoxyphenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3l)

White solid, 85% yield, 36.5 mg; m.p. 150-151 °C;

$[\alpha]^{25}D$ = -24.4 (c = 1.0 in $CHCl_3$); >20:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.91 (m, 2H), 7.90 – 7.83 (m, 1H), 7.37 – 7.29 (m, 2H), 7.10 (d, J = 8.7 Hz, 2H), 7.06 – 6.96 (m, 3H), 6.87 – 6.78 (m, 2H), 4.72 (d, *J* = 9.9 Hz, 1H), 3.77 (s, 3H), 3.46 (d, *J* = 12.4 Hz, 1H), 3.16 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.72 (s, 1H), 1.66 (s, 3H).



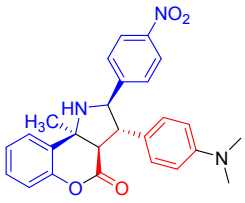
3l, 85%
99:1 er, >20:1 dr

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 159.3, 150.4, 148.0, 147.1, 129.9, 129.2, 129.0, 128.2, 127.5, 125.3, 123.3, 116.9, 114.4, 68.9, 62.3, 59.0, 58.2, 55.2, 30.0.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_5H^+$: 431.1601, found : 431.1595;

UPLC analysis: 99:1 er (IB-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 11.0 min, Rt (major) = 4.5 min.

(2*R*,3*S*,3*aR*,9*bS*)-3-(4-(dimethylamino)phenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3m)



3m, 89%
99:1 er, >20:1 dr

White solid, 89% yield, 39.3 mg; m.p. 195-196 °C;

[α]^{25}D = -48.2 (c = 1.0 in $CHCl_3$); >20:1 dr (reaction mixture);

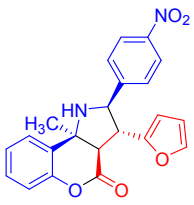
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.92 (m, 2H), 7.90 – 7.83 (m, 1H), 7.36 – 7.28 (m, 2H), 7.16 – 7.09 (m, 2H), 7.07 – 7.00 (m, 1H), 6.97 – 6.89 (m, 2H), 6.67 – 6.56 (m, 2H), 4.72 (d, *J* = 9.8 Hz, 1H), 3.44 (d, *J* = 12.4 Hz, 1H), 3.12 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.93 (s, 6H), 1.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 150.7, 150.1, 148.0, 147.0, 129.9, 129.0, 128.6, 128.2, 127.5, 125.1, 123.2, 122.6, 116.9, 112.6, 68.8, 62.2, 59.1, 58.3, 40.4, 30.0.

HRMS (ESI) calcd. for $C_{26}H_{25}N_3O_4H^+$: 444.1918, found : 444.1911;

UPLC analysis: 99:1 er (IA-U column, 25 °C, hexane / iPrOH = 90 / 10, 0.5 mL / min, λ = 254 nm), Rt (minor) = 6.9 min, Rt (major) = 10.0 min

(2*R*,3*R*,3*aR*,9*bS*)-3-(furan-2-yl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3n)



3n, 73%
98:2 er, 6:1 dr

White solid, 73% yield, 28.6 mg; m.p. 140-142 °C;

[α]^{25}D = -25.6 (c = 1.0 in $CHCl_3$); 6:1 dr (reaction mixture);

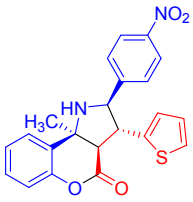
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 7.95 (m, 2H), 7.87 – 7.77 (m, 1H), 7.45 (d, *J* = 1.2 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.08 – 6.98 (m, 1H), 6.31 (dd, *J* = 3.2, 1.9 Hz, 1H), 6.04 (d, *J* = 2.9 Hz, 1H), 4.95 (d, *J* = 9.7 Hz, 1H), 3.54 (dd, *J* = 12.1, 6.4 Hz, 1H), 3.33 (dd, *J* = 12.0, 9.7 Hz, 1H), 2.70 (s, 1H), 1.66 (s, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 149.1, 148.1, 147.0, 146.1, 141.9, 128.3, 128.0, 127.1, 126.3, 124.3, 122.4, 115.9, 109.6, 108.2, 64.3, 61.4, 56.1, 50.9, 28.6.

HRMS (ESI) calcd. for $C_{22}H_{18}N_2O_5H^+$: 391.1288, found : 391.1287;

UPLC analysis: 98:2 er (IB-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 4.6 min, Rt (major) = 3.1 min.

(2*R*,3*R*,3*aR*,9*bS*)-9b-methyl-2-(4-nitrophenyl)-3-(thiophen-2-yl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3o)



3o, 60%
99:1 er, 7:1 dr

White solid, 60% yield, 24.5 mg; m.p. 169-171 °C;

[α]^{25}D = -5.3 (c = 1.0 in $CHCl_3$); 7:1 dr (reaction mixture);

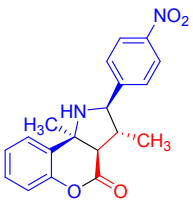
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.8 Hz, 2H), 7.86 – 7.80 (m, 1H), 7.36 – 7.29 (m, 2H), 7.27 (d, *J* = 5.3 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.09 – 7.02 (m, 1H), 6.90 (dd, *J* = 5.1, 3.5 Hz, 1H), 6.71 (d, *J* = 2.9 Hz, 1H), 4.79 (d, *J* = 9.6 Hz, 1H), 3.56 (dd, *J* = 12.1, 9.7 Hz, 1H), 3.43 (d, *J* = 12.1 Hz, 1H), 2.75 (s, 1H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 149.7, 147.9, 147.2, 139.3, 129.4, 129.3, 128.1, 127.6, 127.2, 126.8, 125.3, 125.3, 123.4, 117.0, 69.7, 62.5, 60.5, 54.0, 29.8.

HRMS (ESI) calcd. for $C_{22}H_{18}N_2O_4SH^+$: 407.1060, found : 407.1055;

UPLC analysis: 99:1 er (OD-3 column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 12.3 min, Rt (major) = 7.9 min

(2*R*,3*R*,3*aR*,9*bS*)-3,9b-dimethyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3p)



3p, 21%
97:3 er, 6:1 dr

Yellow solid, 21% yield, 7.2 mg; m.p. 129-131 °C;

[α]^{25}D = 0.4 (c = 0.5 in $CHCl_3$); 6:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.8 Hz, 2H), 7.82 – 7.71 (m, 1H), 7.34 – 7.27 (m, 4H), 7.03 (dt, *J* = 4.9, 3.0 Hz, 1H), 4.22 (d, *J* = 9.6 Hz, 1H), 2.86 (d, *J* = 12.1 Hz, 1H), 2.61 (s, 1H), 2.24 – 2.06 (m, 1H), 1.59 (s, 4H), 1.16 (d, *J* = 6.5 Hz, 3H).

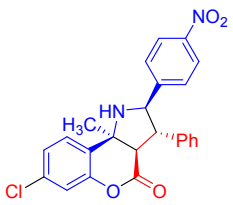
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 150.8, 147.8, 147.2, 130.1, 129.0, 128.0, 127.9, 125.3, 123.6, 116.8, 69.1, 61.8, 59.1, 47.7, 30.2, 29.7.

HRMS (ESI) calcd. for $C_{19}H_{18}N_2O_4H^+$: 339.1339, found : 339.1339;

UPLC analysis: 97:3 er (IA-U column, 25 °C, hexane / iPrOH = 85 / 15, 0.5 mL /

min, λ = 254 nm), Rt (minor) = 2.7 min, Rt (major) = 2.9 min

(2*R*,3*S*,3*aR*,9*bS*)-7-chloro-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4a)



4a, 65%
98:2 er, 18:1 dr

White solid, 65% yield, 28.3 mg; m.p. 222-223 °C;

[α]^{25}D = -14.7 (c = 0.5 in $CHCl_3$); 18:1 dr (reaction mixture);

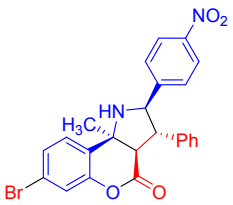
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.7 Hz, 2H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.32-7.30 (m, 4H), 7.09-7.05 (m, 5H), 4.78 (d, *J* = 9.9 Hz, 1H), 3.51 (d, *J* = 12.5 Hz, 1H), 3.18 (dd, *J* = 12.3, 10.0 Hz, 1H), 2.76 (s, 1H), 1.66 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 149.8, 148.3, 147.1, 135.3, 134.3, 129.4, 129.0, 128.5, 128.3, 127.9, 127.4, 125.6, 123.4, 117.2, 68.8, 62.1, 58.7, 58.6, 29.8.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4ClH^+$: 435.1106, found : 435.1104;

UPLC analysis: 98:2 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.4 min, Rt (major) = 2.9 min.

(2*R*,3*S*,3*aR*,9*bS*)-7-bromo-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4b)



4b, 55%
99:1 er, >20:1 dr

White solid, 55% yield, 26.4 mg; m.p. 201-202 °C;

[α]^{25}D = -14.0 (c = 1.0 in $CHCl_3$); >20:1 dr (reaction mixture);

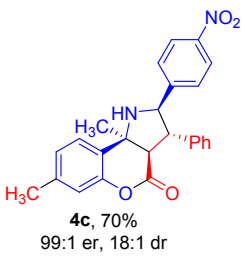
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.94 (m, 2H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.46 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.31-7.28 (m, 3H), 7.20 (d, *J* = 1.9 Hz, 1H), 7.12 – 7.04 (m, 4H), 4.78 (d, *J* = 9.9 Hz, 1H), 3.51 (d, *J* = 12.5 Hz, 1H), 3.17 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.71 (s, 1H), 1.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 149.8, 148.4, 147.1, 135.3, 129.7, 129.0, 128.5, 128.3, 127.9, 127.4, 123.4, 121.9, 120.1, 68.7, 62.2, 58.7, 58.6, 29.7.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4BrH^+$: 479.0601, found : 479.0600;

UPLC analysis: 99:1 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.5 min, Rt (major) = 3.1 min.

(2*R*,3*S*,3*aR*,9*bS*)-7,9b-dimethyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4c)



4c, 70%
99:1 er, 18:1 dr

White solid, 70% yield, 28.9 mg; m.p. 175-176 °C;

[α]^{25}D = -8.0 (c = 1.0 in $CHCl_3$); 18:1 dr (reaction mixture);

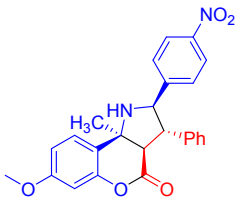
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.7 Hz, 2H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.15 – 7.07 (m, 5H), 6.84 (s, 1H), 4.76 (d, *J* = 9.8 Hz, 1H), 3.49 (d, *J* = 12.4 Hz, 1H), 3.21 (dd, *J* = 12.3, 9.9 Hz, 1H), 2.71 (s, 1H), 2.38 (s, 3H), 1.64 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 150.4, 147.8, 147.0, 139.5, 135.8, 129.0, 128.1, 128.0, 127.9, 127.5, 126.7, 126.1, 123.3, 117.2, 68.9, 62.3, 59.0, 58.8, 29.9, 21.1.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_4H^+$: 415.1652, found : 415.1651;

UPLC analysis: 99:1 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.4 min, Rt (major) = 3.2 min.

(2*R*,3*S*,3*aR*,9*bS*)-7-methoxy-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4d)



4d, 76%
99:1 er, 7:1 dr

Light yellow solid, 76% yield, 32.8 mg; m.p. 85-87 °C;

[α]^{25}D = -18.9 (c = 0.5 in $CHCl_3$); 7:1 dr (reaction mixture);

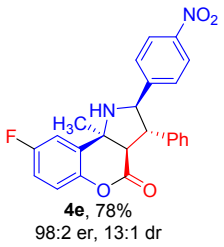
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.74 (d, *J* = 8.6 Hz, 1H), 7.30 – 7.27 (m, 3H), 7.11 – 7.07 (m, 4H), 6.89 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.56 (d, *J* = 2.5 Hz, 1H), 4.76 (d, *J* = 9.8 Hz, 1H), 3.82 (s, 3H), 3.48 (d, *J* = 12.4 Hz, 1H), 3.23 (dd, *J* = 12.3, 9.9 Hz, 1H), 2.42 (s, 1H), 1.64 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 160.2, 150.3, 148.7, 147.0, 135.8, 129.0, 128.9, 128.2, 128.0, 127.5, 123.3, 121.6, 111.8, 101.8, 68.9, 62.2, 59.1, 59.0, 55.6, 30.0.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_5H^+$: 431.1601, found : 431.1595;

UPLC analysis: 99:1 er (IA-U column, 25 °C, hexane / iPrOH = 90 / 10, 0.5 mL / min, λ = 254 nm), Rt (minor) = 5.7 min, Rt (major) = 8.0 min.

(2*R*,3*S*,3*aR*,9*bS*)-8-fluoro-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrah ydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4e)



4e, 78%
98:2 er, 13:1 dr

White solid, 78% yield, 32.6 mg; m.p. 101-103 °C;

[α]^{25}D = -7.9 (c = 1.0 in $CHCl_3$); 13:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.59 – 7.56 (m, 1H), 7.32 – 7.27 (m, 3H), 7.11 – 7.08 (m, 4H), 7.02 – 7.00 (m, 2H), 4.79 (d, *J* = 9.9 Hz, 1H), 3.52 (d, *J* = 12.5 Hz, 1H), 3.18 (dd, *J* = 12.5, 9.9 Hz, 1H), 2.82 (s, 1H), 1.65 (s, 3H).

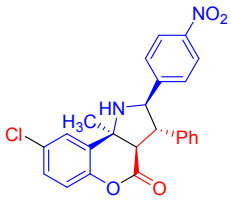
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 159.7 (d, *J* = 244.1 Hz), 149.9, 147.1, 143.8 (d, *J* = 2.2 Hz), 135.4, 132.0 (d, *J* = 6.6 Hz), 129.0, 128.3, 128.0, 127.4, 123.3, 118.5 (d, *J* = 8.2 Hz), 116.1 (d, *J* = 24.0 Hz), 114.4 (d, *J* = 24.5 Hz), 68.7, 62.4, 58.6, 58.4, 29.6.

^{19}F NMR (377 MHz, $CDCl_3$) δ -116.30.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4FH^+$: 419.1402, found : 419.1400;

UPLC analysis: 98:2 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.3 min, Rt (major) = 2.9 min.

(2*R*,3*S*,3*aR*,9*bS*)-8-chloro-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrah ydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4f)



4f, 71%
98:2 er, >20:1 dr

White solid, 71% yield, 30.9 mg; m.p. 89-91 °C;

[α]^{25}D = 82.2 (c = 1.0 in $CHCl_3$); >20:1 dr (reaction mixture);

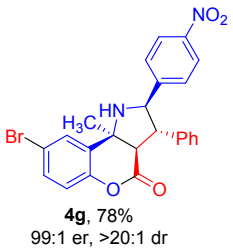
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.95 (m, 2H), 7.85 - 7.83 (m, 1H), 7.32 – 7.26 (m, 4H), 7.11 – 7.07 (m, 4H), 6.99 (d, *J* = 8.7 Hz, 1H), 4.78 (d, *J* = 9.9 Hz, 1H), 3.51 (d, *J* = 12.5 Hz, 1H), 3.17 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.76 (s, 1H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 149.7, 147.2, 146.5, 135.4, 131.7, 130.4, 129.3, 129.1, 128.4, 128.1, 128.0, 127.4, 123.4, 118.5, 68.8, 62.3, 58.7, 58.5, 29.7.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4ClH^+$: 435.1106, found : 435.1100;

UPLC analysis: 98:2 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.2 min, Rt (major) = 2.7 min.

(2*R*,3*S*,3*aR*,9*bS*)-8-bromo-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4g)



4g, 78%
99:1 er, >20:1 dr

White solid, 78% yield, 37.6 mg; m.p. 105-106 °C;

$[\alpha]^{25}D$ = 63.6 (c = 0.5 in $CHCl_3$); >20:1 dr (reaction mixture);

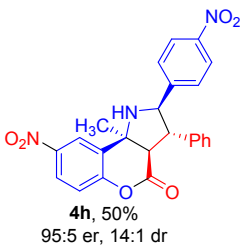
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 2.4 Hz, 1H), 7.99 – 7.96 (m, 2H), 7.43 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.32 – 7.28 (m, 3H), 7.11 – 7.05 (m, 4H), 6.93 (d, *J* = 8.6 Hz, 1H), 4.78 (d, *J* = 9.8 Hz, 1H), 3.50 (d, *J* = 12.5 Hz, 1H), 3.17 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.78 (s, 1H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 149.7, 147.2, 147.0, 135.4, 132.2, 132.0, 131.2, 129.1, 128.4, 127.9, 127.4, 123.4, 118.8, 117.8, 68.7, 62.3, 58.64 58.5, 29.6.

HRMS (ESI) calcd. for $C_{24}H_{19}N_2O_4BrH^+$: 479.0601, found : 479.0598;

UPLC analysis: 99:1 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.3 min, Rt (major) = 2.7 min.

(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-8-nitro-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4h)



4h, 50%
95:5 er, 14:1 dr

White solid, 50% yield, 22.3 mg; m.p. 124-125 °C;

[α]^{25}D = 33.5 (c = 0.3 in $CHCl_3$); 14:1 dr (reaction mixture);

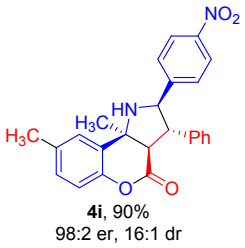
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, *J* = 2.7 Hz, 1H), 8.21 (dd, *J* = 8.9, 2.8 Hz, 1H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.34-7.32 (m, 3H), 7.19 (d, *J* = 8.9 Hz, 1H), 7.11 – 7.08 (m, 4H), 4.85 (d, *J* = 9.9 Hz, 1H), 3.60 (d, *J* = 12.5 Hz, 1H), 3.14 (dd, *J* = 12.4, 9.9 Hz, 1H), 2.90 (s, 1H), 1.75 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 152.2, 149.1, 147.3, 145.1, 134.9, 131.7, 129.2, 128.6, 128.0, 127.2, 124.9, 124.7, 123.5, 118.2, 68.5, 62.1, 58.7, 58.2, 29.7.

HRMS (ESI) calcd. for $C_{24}H_{19}N_3O_6H^+$: 446.1347, found : 446.1350;

UPLC analysis: 95:5 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 3.6 min, Rt (major) = 4.3 min.

(2*R*,3*S*,3*aR*,9*bS*)-8,9b-dimethyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4i)



4i, 90%
98:2 er, 16:1 dr

White solid, 90% yield, 37.4 mg; m.p. 88-90 °C;

[α]^{25}D = 34.2 (c = 0.5 in $CHCl_3$); 16:1 dr (reaction mixture);

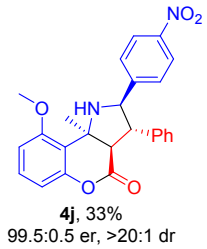
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.93 (m, 2H), 7.64 (d, *J* = 1.8 Hz, 1H), 7.32 – 7.26 (m, 3H), 7.13 – 7.07 (m, 5H), 6.92 (d, *J* = 8.2 Hz, 1H), 4.76 (d, *J* = 9.8 Hz, 1H), 3.48 (d, *J* = 12.4 Hz, 1H), 3.21 (dd, *J* = 12.4, 9.8 Hz, 1H), 2.45 (s, 3H), 1.65 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 150.3, 147.1, 145.9, 135.9, 134.9, 129.8, 129.3, 129.0, 128.3, 128.2, 128.0, 127.6, 123.3, 116.7, 68.9, 62.5, 59.0, 58.8, 29.9, 21.1.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_4H^+$: 415.1652, found : 415.1651;

UPLC analysis: 98:2 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.1 min, Rt (major) = 2.6 min.

(2*R*,3*S*,3*aR*,9*bS*)-9-methoxy-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4j)



4j, 33%
99.5:0.5 er, >20:1 dr

White solid, 73% yield, 14.1 mg; m.p. 95-97 °C;

[α]^{25}D = -11.4 (c = 0.4 in $CHCl_3$); >20:1 dr (reaction mixture);

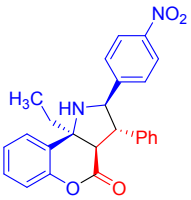
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.96 (m, 2H), 7.34 (t, *J* = 8.3 Hz, 1H), 7.29-7.25 (m, 3H), 7.11-7.09 (m, 2H), 6.99 – 6.94 (m, 2H), 6.85 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.79 (dd, *J* = 8.3, 1.0 Hz, 1H), 4.60 (d, *J* = 9.3 Hz, 1H), 3.92 (s, 3H), 3.71 (s, 1H), 3.53 (d, *J* = 12.3 Hz, 1H), 3.38 (dd, *J* = 12.2, 9.3 Hz, 1H), 1.72 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 158.0, 150.3, 148.9, 147.3, 136.0, 129.4, 128.9, 128.1, 127.8, 127.5, 123.8, 117.2, 110.4, 107.6, 69.1, 62.7, 58.5, 57.9, 56.0, 28.2.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_5H^+$: 431.1601, found : 431.1602;

UPLC analysis: 99.5:0.5 er (IA-U column, 25 °C, hexane / iPrOH = 90 / 10, 0.5 mL / min, λ = 254 nm), Rt (minor) = 3.5 min, Rt (major) = 4.0 min.

(2*R*,3*S*,3*aR*,9*bS*)-9b-ethyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4k)



4k, 75%
99:1 er, >20:1 dr

White solid, 75% yield, 31.1 mg; m.p. 72-74 °C;

[α]^{25}D = -2.2 (c = 0.5 in $CHCl_3$); >20:1 dr (reaction mixture);

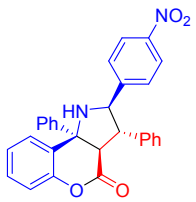
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.91 (m, 2H), 7.81 – 7.79 (m, 1H), 7.36 – 7.32 (m, 2H), 7.31 – 7.26 (m, 3H), 7.09 – 7.02 (m, 5H), 4.74 (d, *J* = 9.9 Hz, 1H), 3.49 (d, *J* = 12.4 Hz, 1H), 3.18 (dd, *J* = 12.4, 10.0 Hz, 1H), 2.75 (s, 1H), 2.06 – 1.88 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 150.2, 149.1, 147.1, 135.6, 129.2, 129.0, 128.7, 128.2, 128.2, 128.1, 127.5, 125.2, 123.3, 116.7, 68.7, 66.1, 58.8, 56.8, 36.6, 8.8.

HRMS (ESI) calcd. for $C_{25}H_{22}N_2O_4H^+$: 415.1652, found : 415.1650;

UPLC analysis: 99:1 er (IA-U column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 2.2 min, Rt (major) = 2.9 min.

(2*R*,3*S*,3*aR*,9*bR*)-2-(4-nitrophenyl)-3,9b-diphenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4l)



4l, 80%
99:1 er, >20:1 dr

White solid, 80% yield, 36.9 mg; m.p. 108-109 °C;

[α]^{25}D = 42.8 (c = 0.5 in $CHCl_3$); >20:1 dr (reaction mixture);

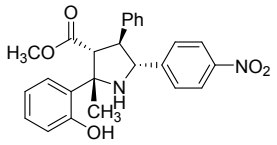
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.97 (m, 2H), 7.84 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.40 – 7.34 (m, 6H), 7.32-7.27 (m, 4H), 7.18-7.16 (m, 2H), 7.12 – 7.08 (m, 3H), 4.93 (d, *J* = 9.9 Hz, 1H), 3.95 (d, *J* = 12.1 Hz, 1H), 3.37 (dd, *J* = 12.1, 9.9 Hz, 1H), 3.25 (s, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 149.6, 148.7, 147.2, 144.5, 135.4, 129.6, 129.4, 129.3, 129.0, 128.6, 128.3, 128.2, 128.0, 127.6, 125.5, 125.4, 123.4, 117.1, 69.4, 67.8, 59.6, 58.8.

HRMS (ESI) calcd. for $C_{29}H_{22}N_2O_4H^+$: 463.1652, found : 463.1653;

UPLC analysis: 99:1 er (IA-U column, 25 oC, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 6.9 min, Rt (major) = 9.0 min.

methyl(2*S*,3*R*,4*S*,5*R*)-2-(2-hydroxyphenyl)-2-methyl-5-(4-nitrophenyl)-4-phenylpyrrolidine-3-carboxylate (5)



5, 66%
99:1 er, 15:1 dr

White solid, 66% yield, 36.9 mg; m.p. 166-168 °C;

[α]^{25}D = -21.4 (c = 0.5in $CHCl_3$); 15:1 dr (reaction mixture);

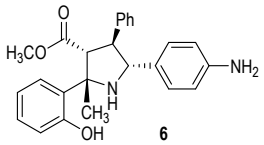
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.12 (m, 2H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.26 – 7.11 (m, 7H), 6.86 – 6.77 (m, 2H), 4.70 (d, *J* = 11.0 Hz, 1H), 4.05 (t, *J* = 10.9 Hz, 1H), 3.36 (d, *J* = 10.7 Hz, 1H), 3.13 (s, 3H), 2.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 158.6, 147.9, 145.7, 137.0, 129.8, 129.0, 128.2, 127.8, 127.7, 124.7, 124.0, 118.5, 117.7, 67.2, 66.2, 65.3, 56.1, 51.7, 30.6.

HRMS (ESI) calcd. for $C_{25}H_{25}N_2O_5H^+$: 433.1758, found : 433.1754;

HPLC analysis: 99:1 er (IA column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 24.0 min, Rt (major) = 20.1 min.

(2*R*,3*S*,3a*R*,9b*S*)-2-(4-aminophenyl)-9b-methyl-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-b]pyrrol-4(1H)-one (6)



6
>20:1 dr

White solid, 96% yield, 200 mg; m.p. 94-96 °C;

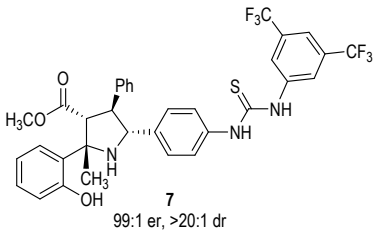
[α]^{25}D = -74.9 (c = 0.5 in $CHCl_3$); >20:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.11 (m, 9H), 6.82 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.78 – 6.72 (m, 1H), 6.61 – 6.55 (m, 2H), 4.47 (d, *J* = 11.1 Hz, 1H), 4.04 (t, *J* = 11.0 Hz, 1H), 3.29 (d, *J* = 10.9 Hz, 1H), 3.11 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 159.1, 146.4, 138.2, 129.4, 128.6, 128.5, 127.9, 127.6, 127.6, 127.1, 125.2, 118.1, 117.5, 115.3, 66.3, 66.2, 65.4, 55.1, 51.5, 30.5.

HRMS (ESI) calcd. for $C_{25}H_{26}N_2O_3H^+$: 403.2016, found : 403.2014;

1-(3,5-bis(trifluoromethyl)phenyl)-3-(4-((2*R*,3*S*,3a*R*,9b*S*)-9b-methyl-4-oxo-3-phenyl-1,2,3,3a,4,9b-hexahydrochromeno[4,3-b]pyrrol-2-yl)phenyl)thiourea (7)



7
99:1 er, >20:1 dr

White solid, 72% yield, 61.5 mg; m.p. 135-136 °C; **[α]^{25}D** = -81.4 (c = 0.5 in $CHCl_3$); >20:1 dr (reaction mixture);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.34 (s, 1H), 7.96 (s, 2H), 7.59 (s, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.17 (dd, *J* = 17.4, 7.9 Hz, 4H), 7.05 (dt, *J* = 20.3, 7.6 Hz, 3H), 6.89 (d, *J* = 7.4 Hz, 2H), 6.78 (dd, *J* = 7.3, 4.8 Hz, 2H), 4.60 (d, *J* = 11.1 Hz, 1H), 3.82 (t, *J* = 11.1 Hz, 1H), 3.36 (d, *J* = 11.1 Hz, 1H), 3.11 (s, 3H), 2.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 180.3, 172.2, 158.5, 140.3, 137.7, 136.8, 131.5 (q, *J* = 33.5 Hz), 129.9, 129.0, 127.9, 127.7, 127.4, 125.6, 125.5, 124.5, 123.5 (d, *J* = 2.6 Hz), 121.8, 119.1, 118.2 (d, *J* = 3.7 Hz), 117.6, 66.1, 65.7, 65.3, 55.9, 51.8, 29.9.

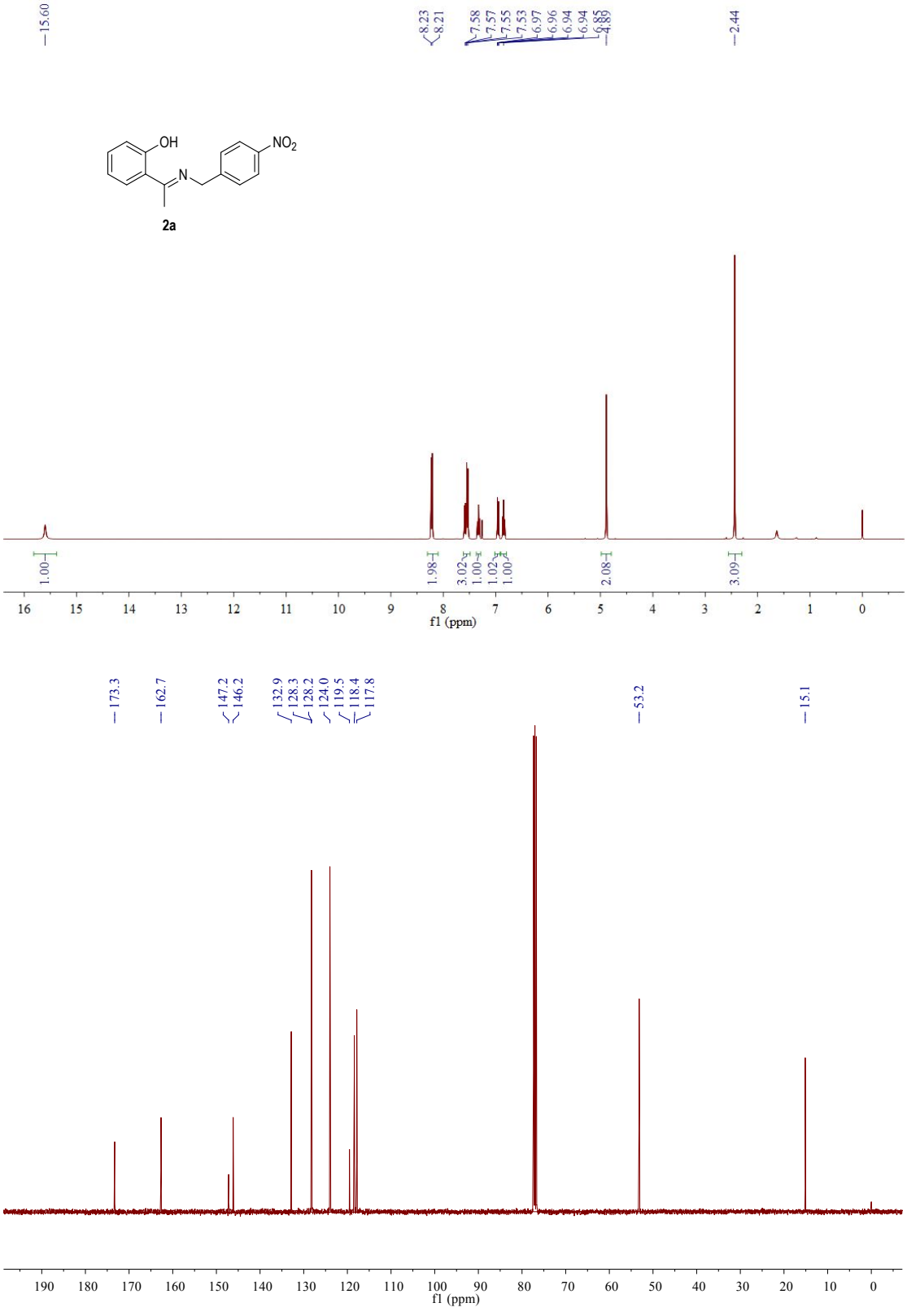
^{19}F NMR (377 MHz, $CDCl_3$) δ -62.87.

HRMS (ESI) calcd. for $C_{34}H_{29}N_3O_3F_6SH^+$: 674.1907, found : 674.1902;

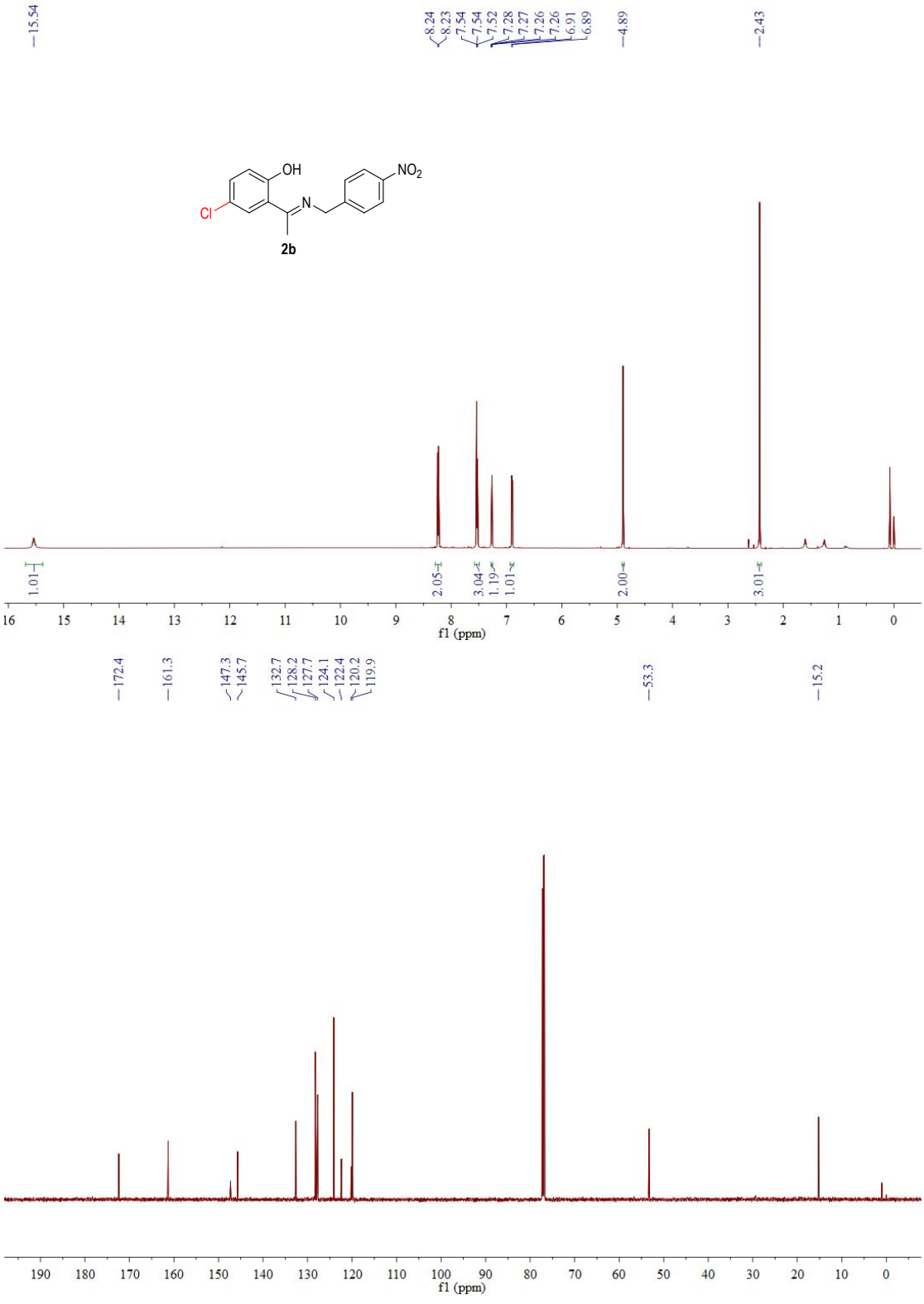
HPLC analysis: 99:1 er (IA column, 25 °C, hexane / iPrOH = 80 / 20, 0.5 mL / min, λ = 254 nm), Rt (minor) = 12.8 min, Rt (major) = 35.1 min.

IX. ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HPLC spectra

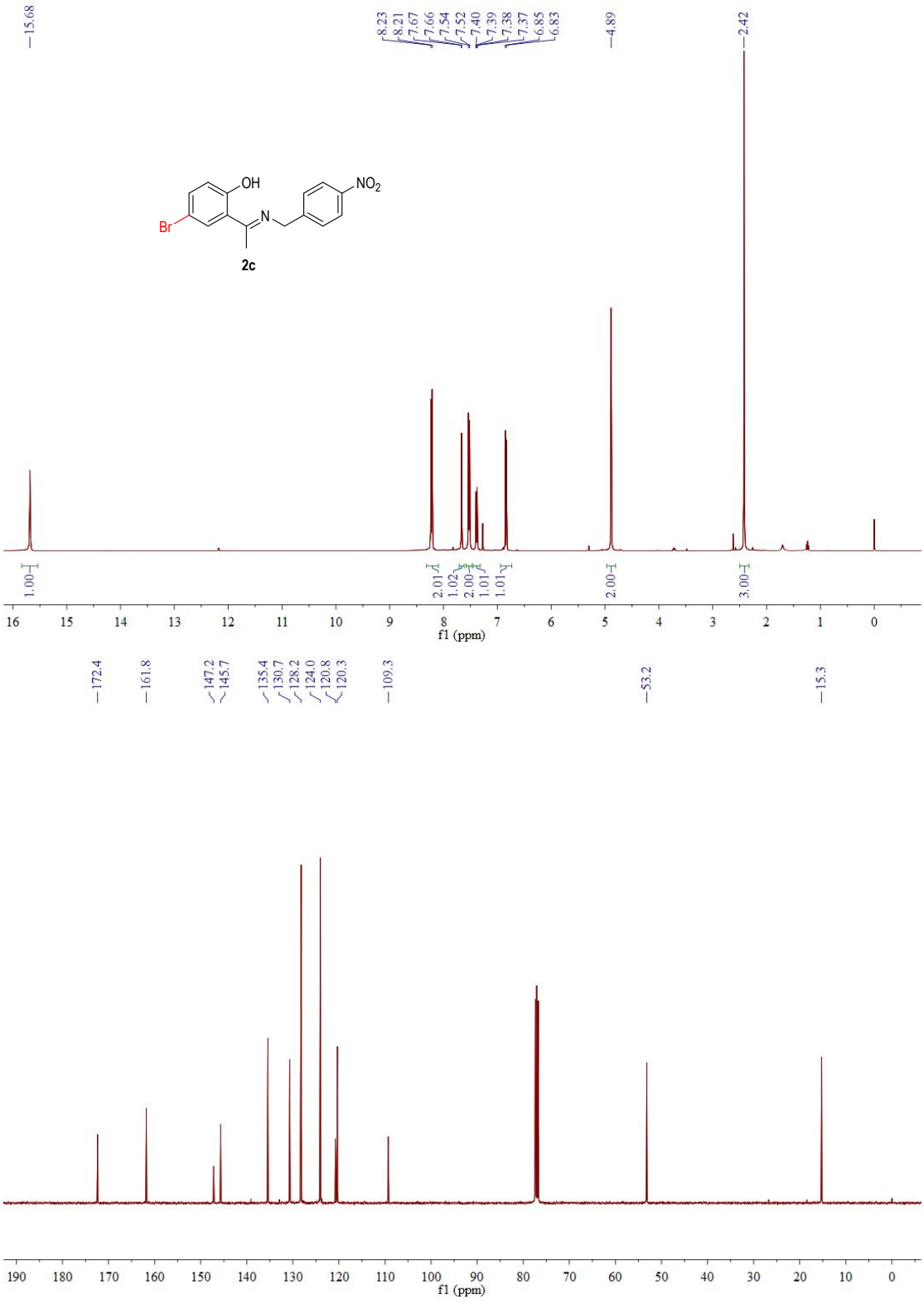
(*E*)-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2a):



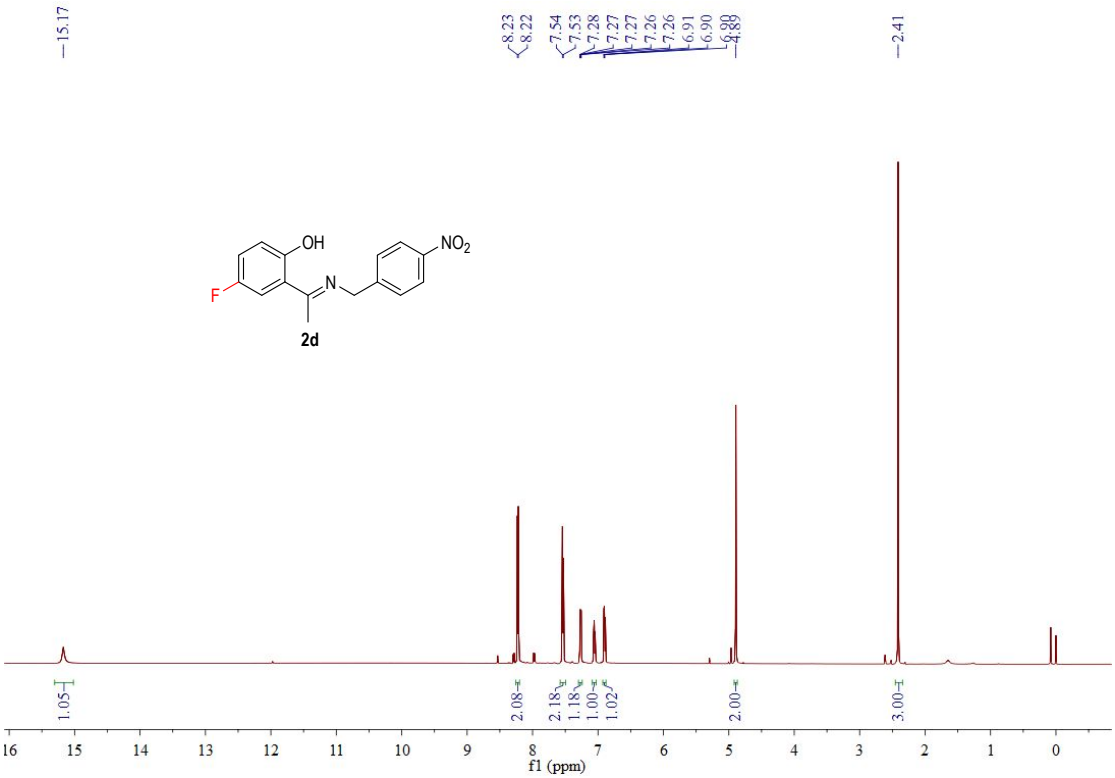
(*E*)-4-chloro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2b):

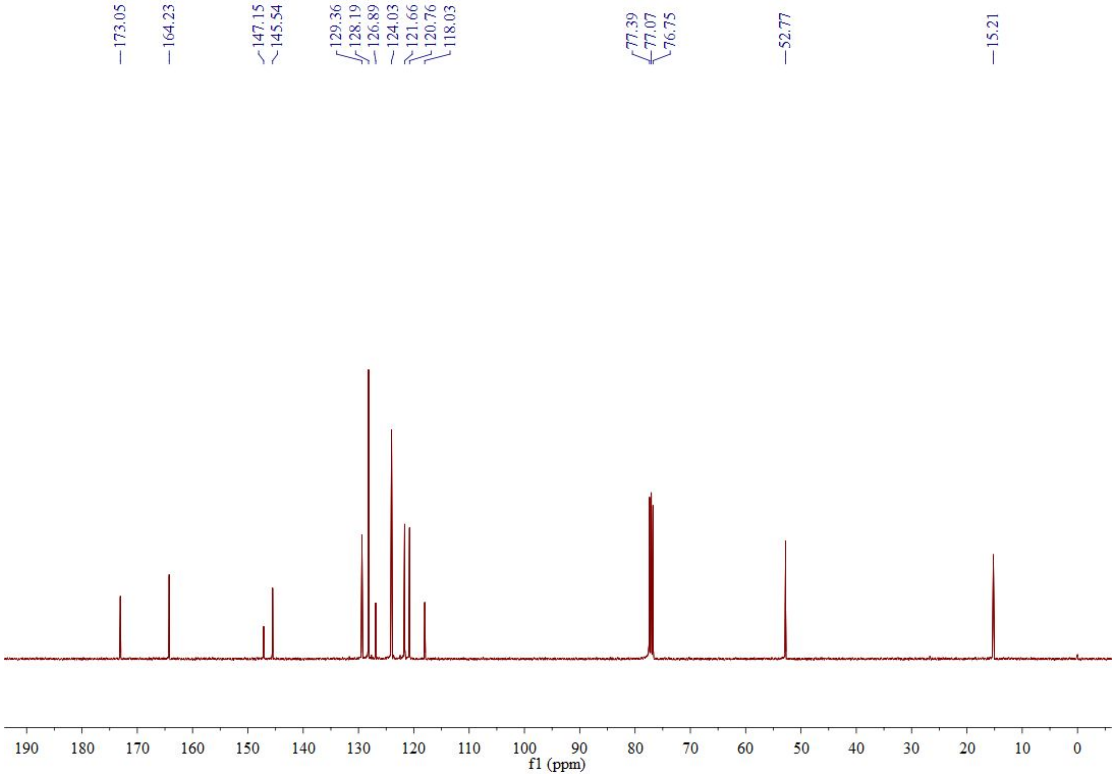


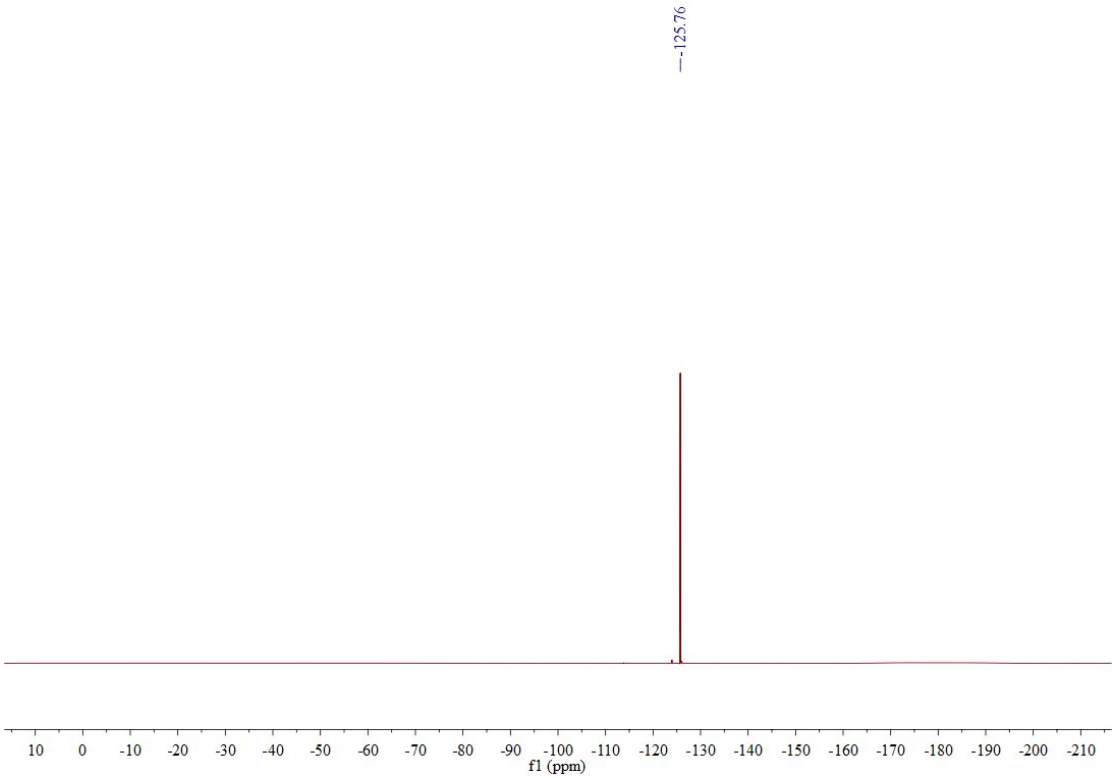
(*E*)-4-bromo-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2c):



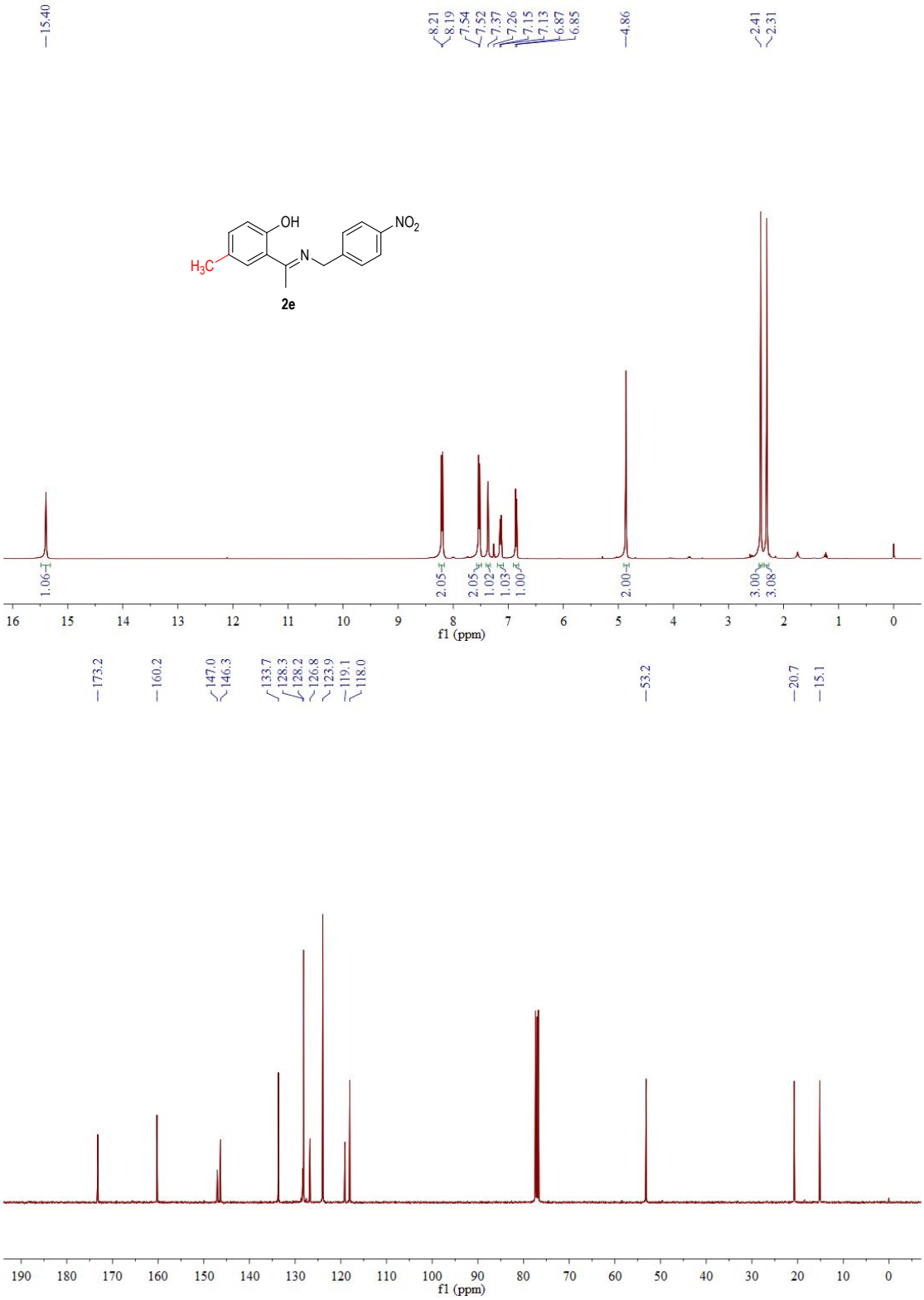
(*E*)-4-fluoro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2d):



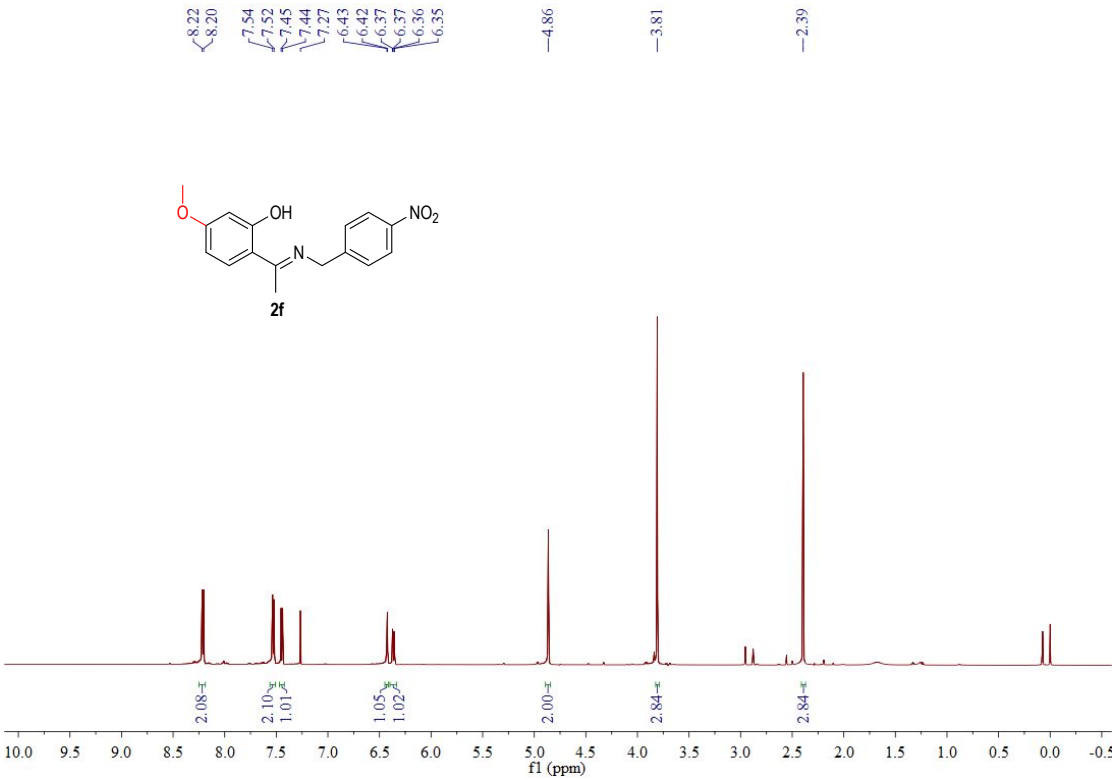


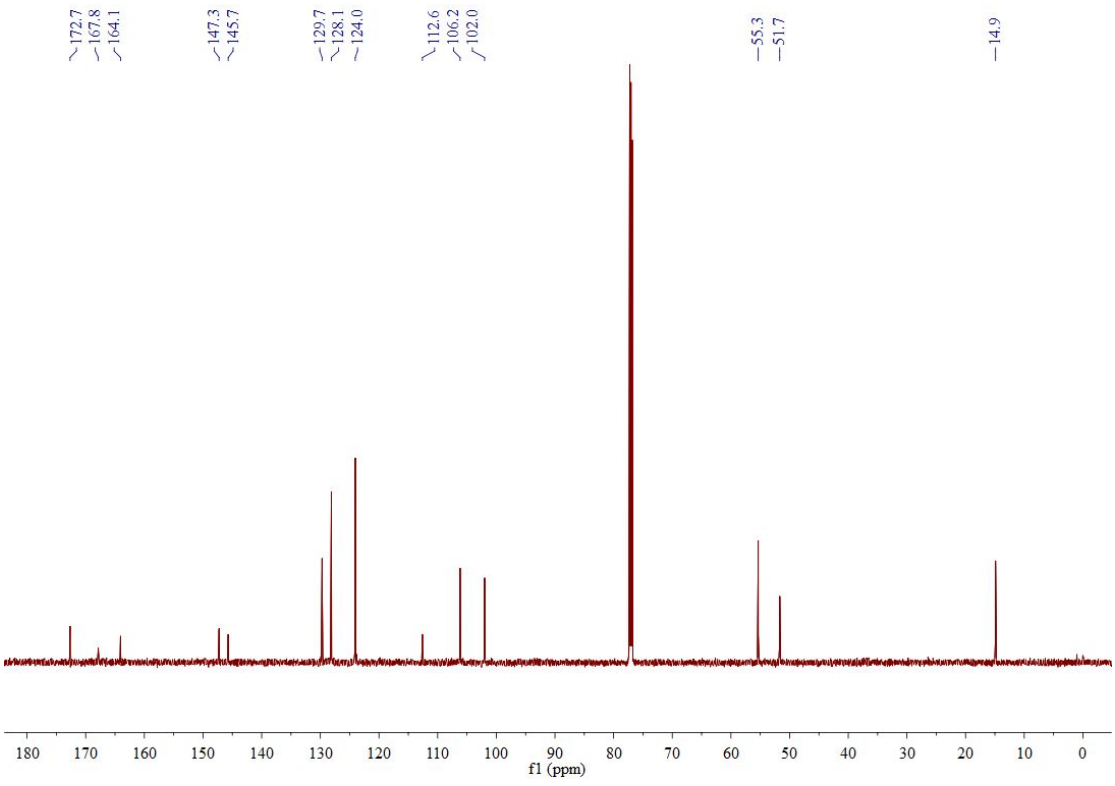

-125.76
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

(*E*)-4-methyl-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2e):

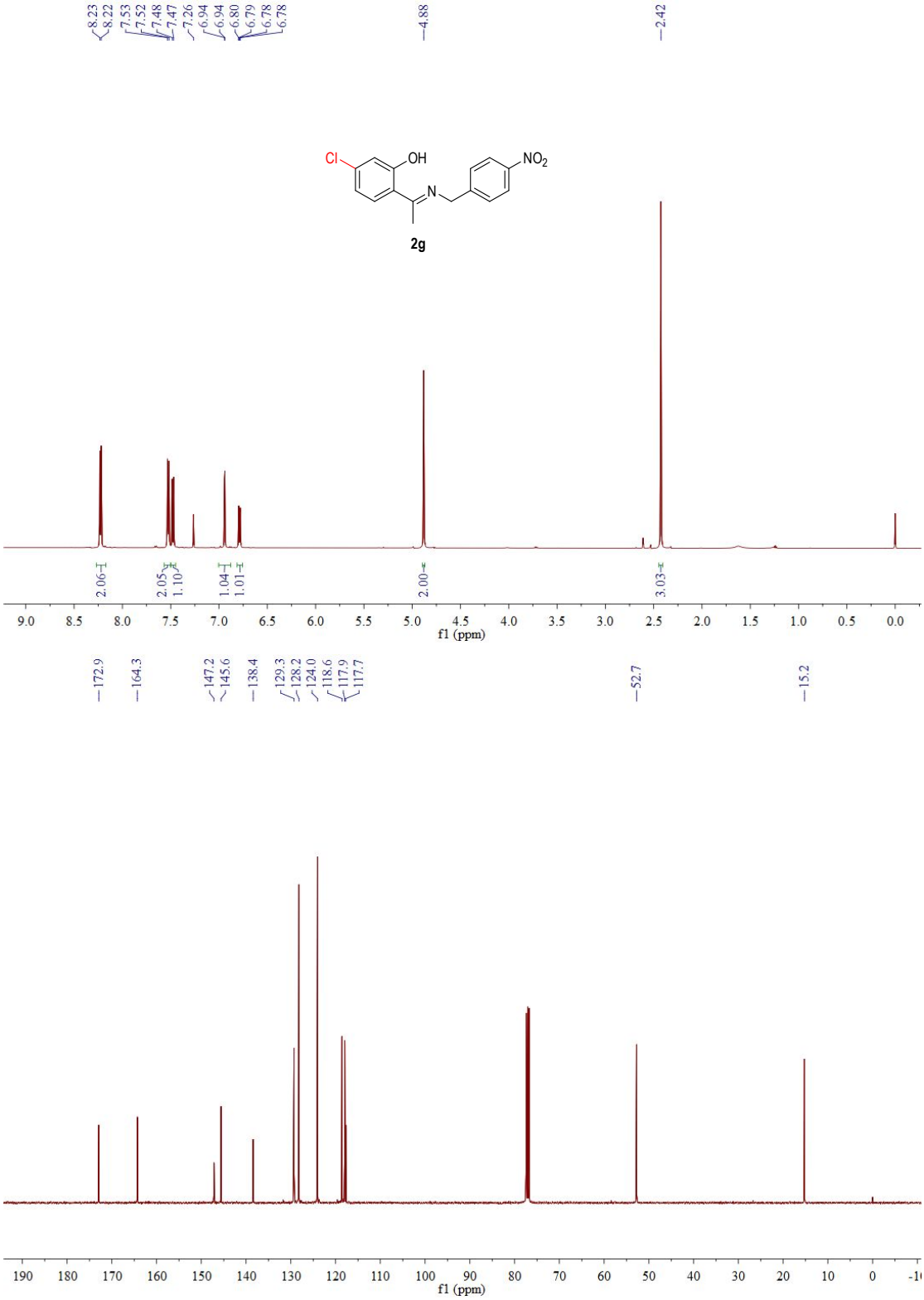


(*E*)-5-methoxy-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2f):

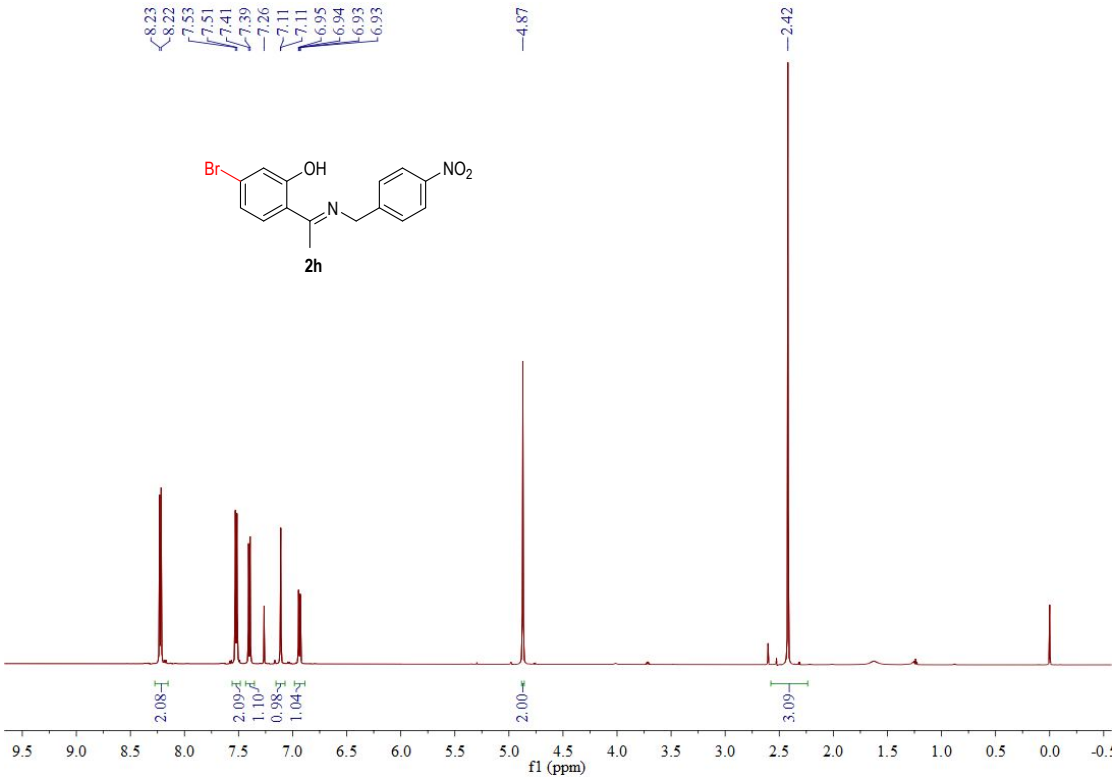


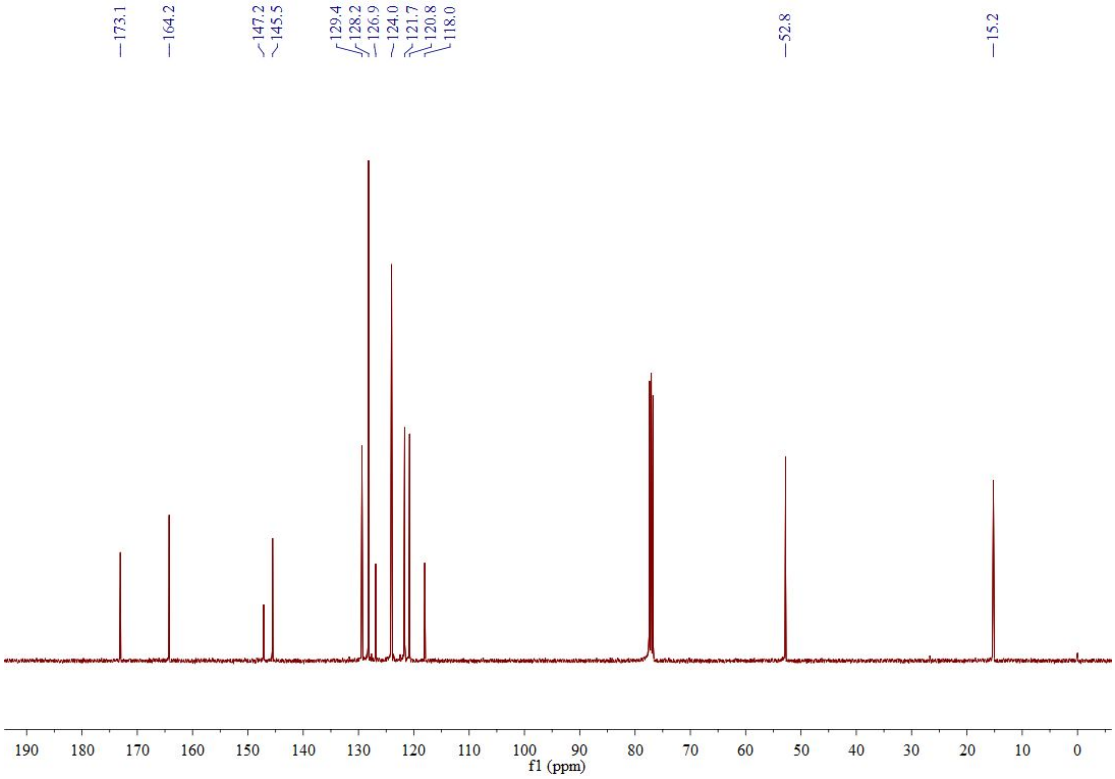


(*E*)-5-chloro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2g):

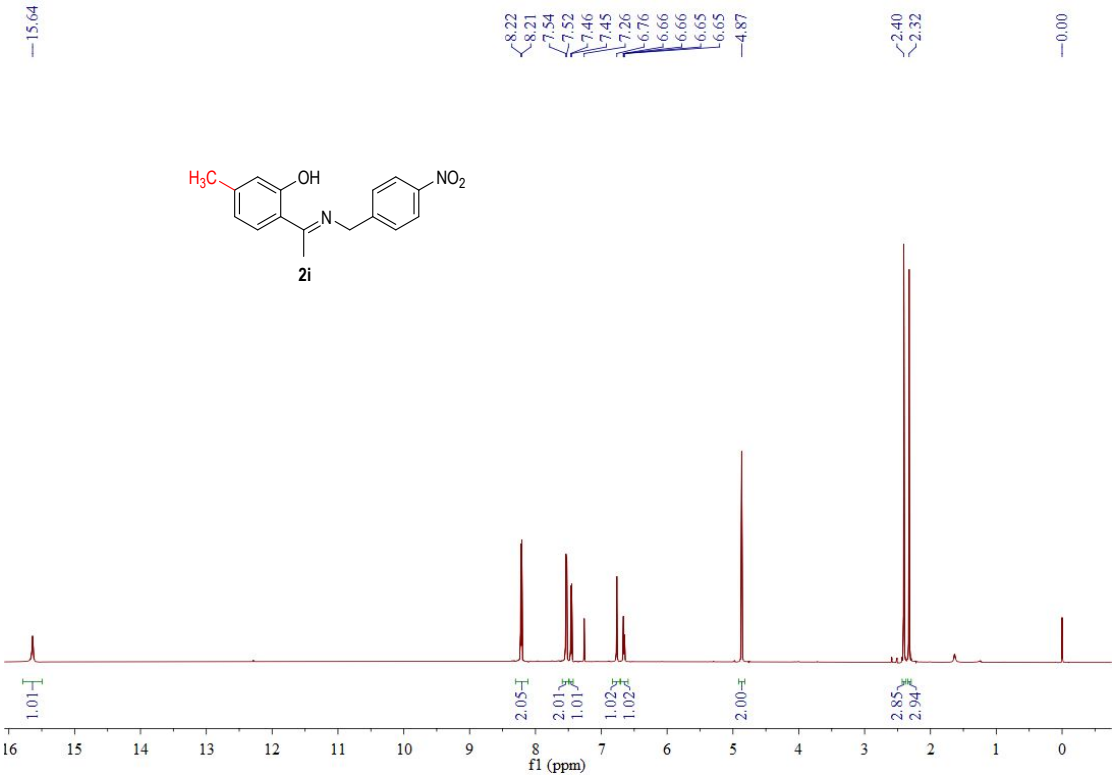


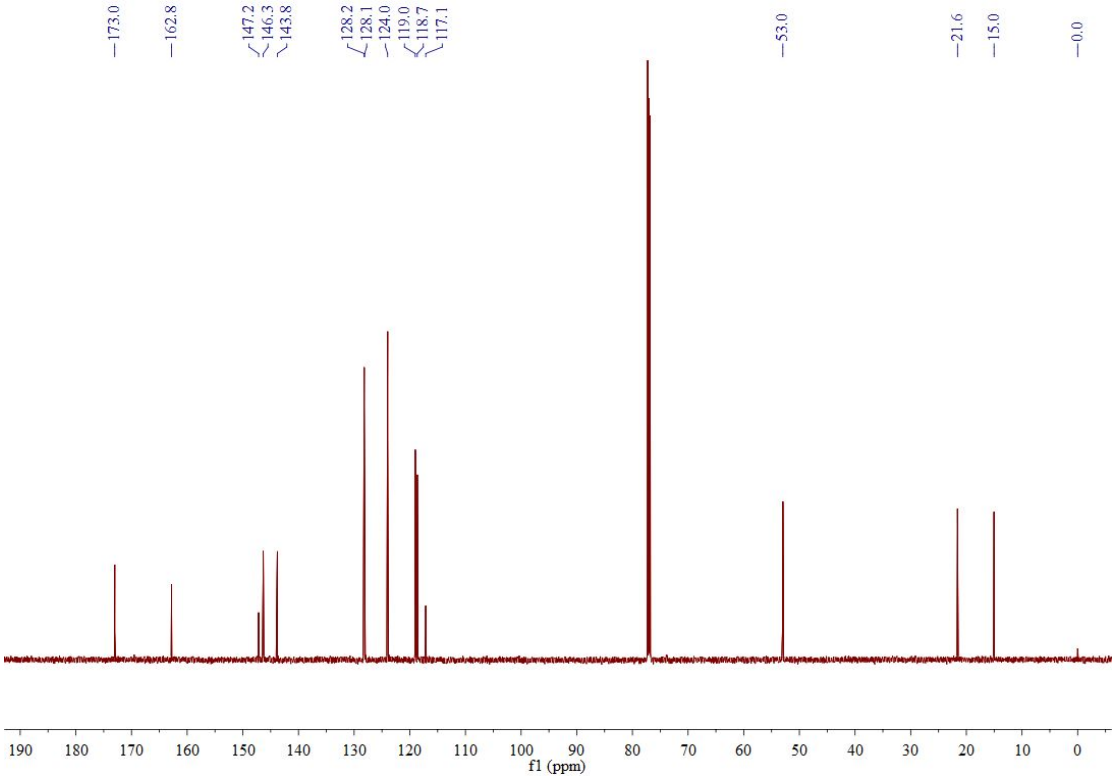
(*E*)-5-bromo-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2h):



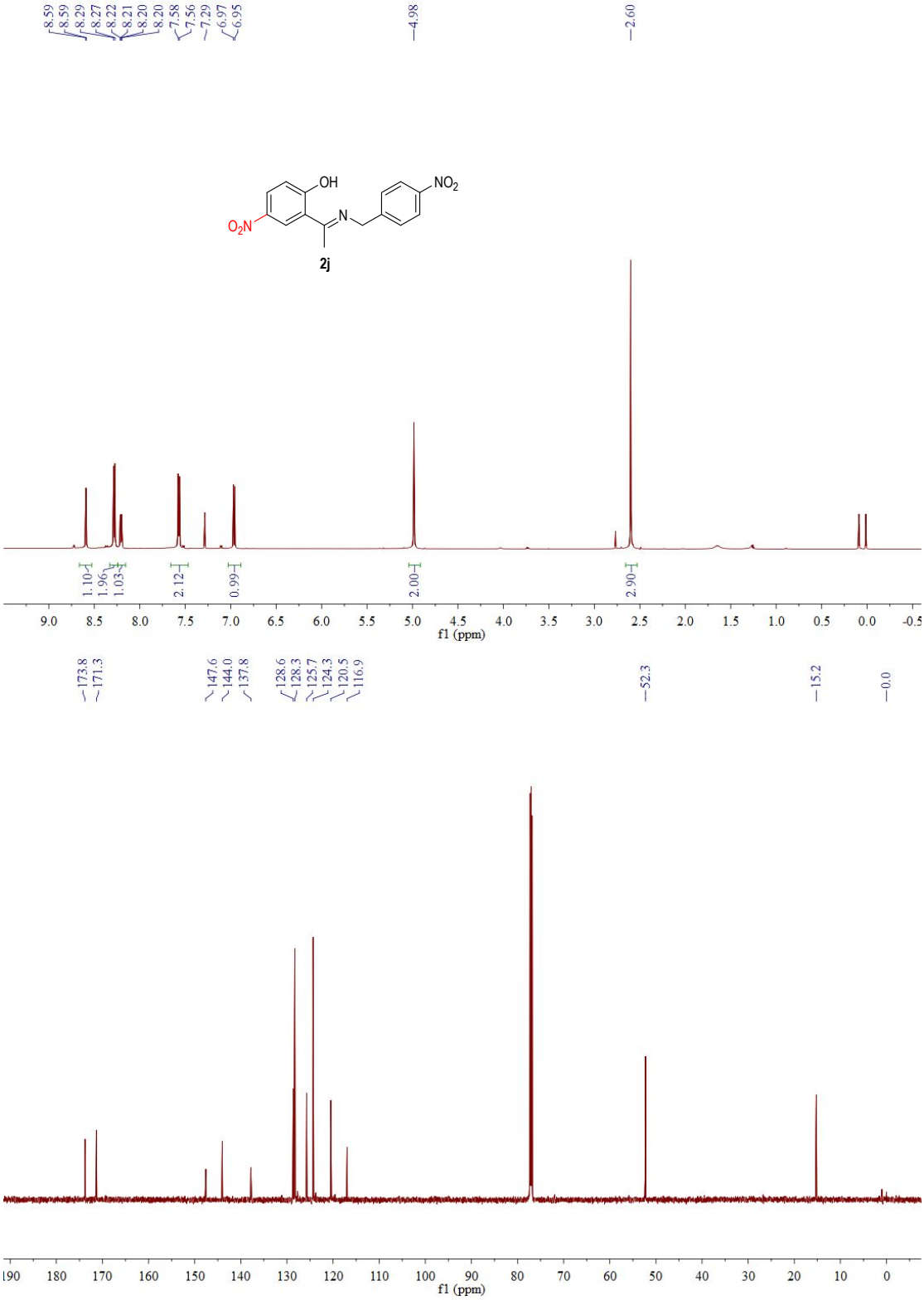


(*E*)-5-methyl-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2i):

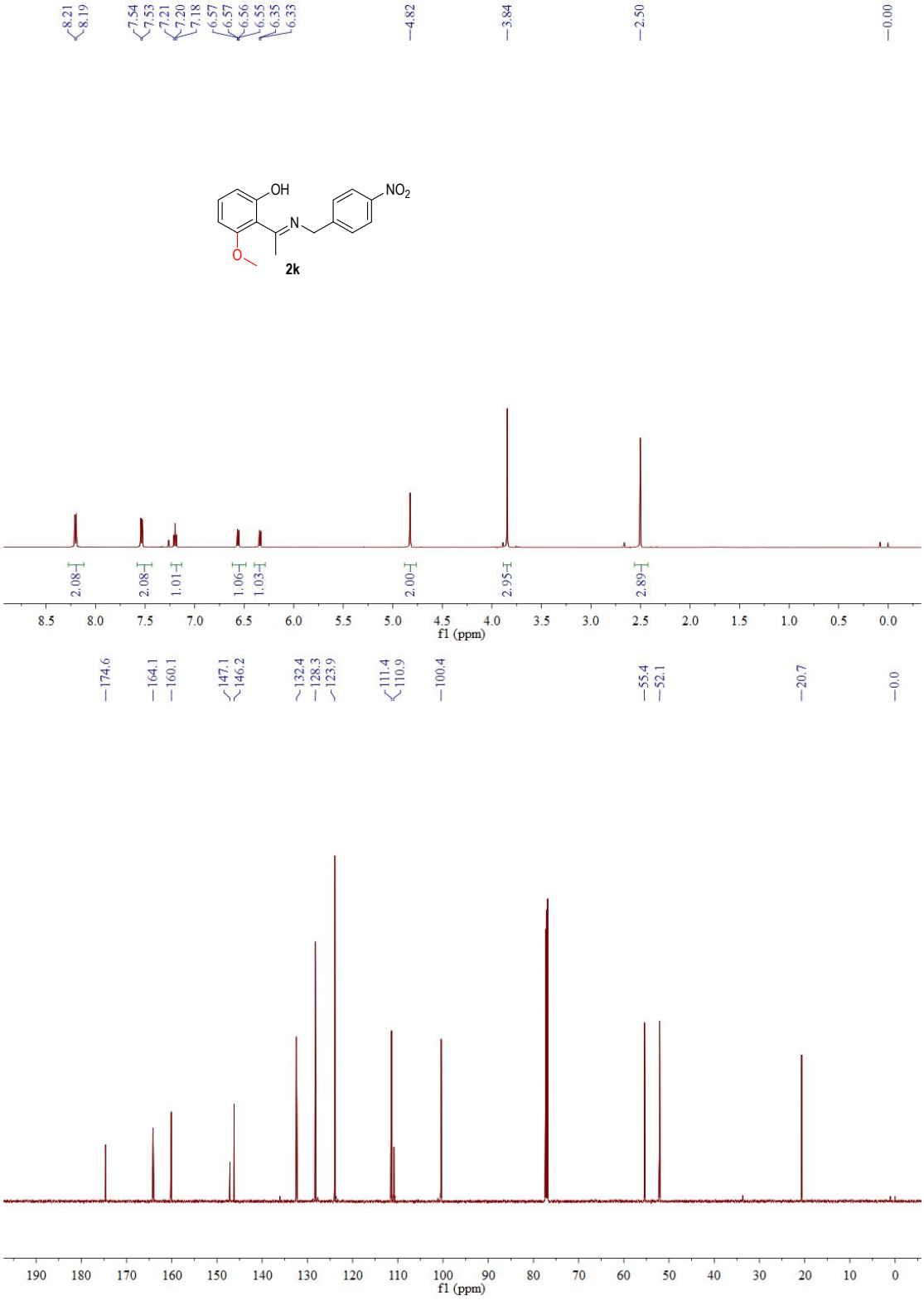




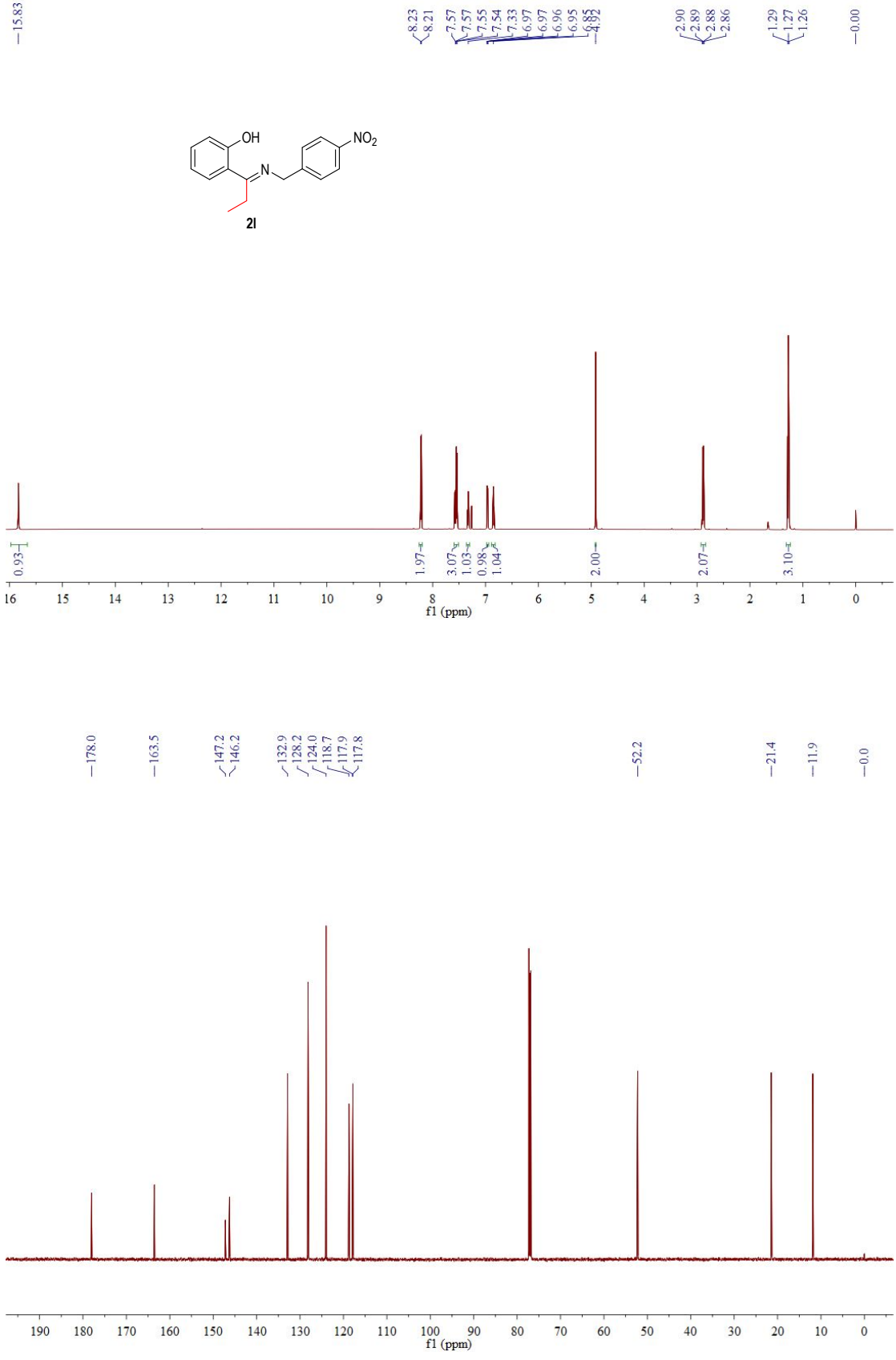
(*E*)-4-nitro-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2j):



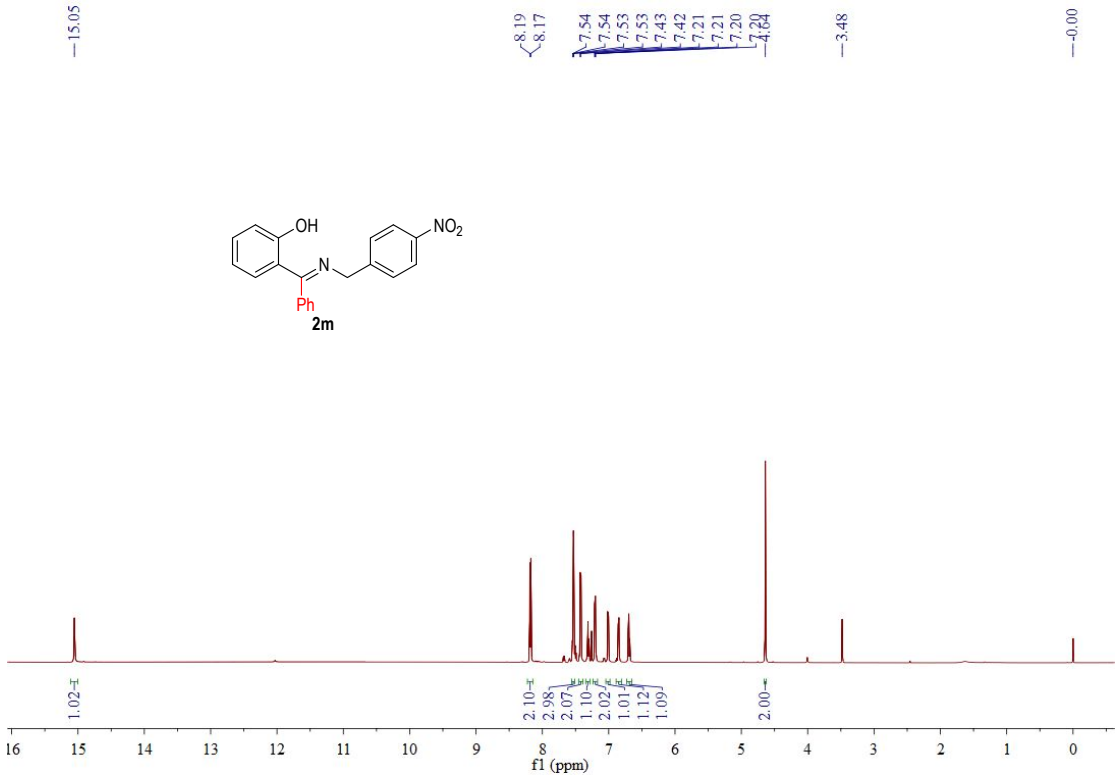
(*E*)-3-methoxy-2-(1-((4-nitrobenzyl)imino)ethyl)phenol (2k):

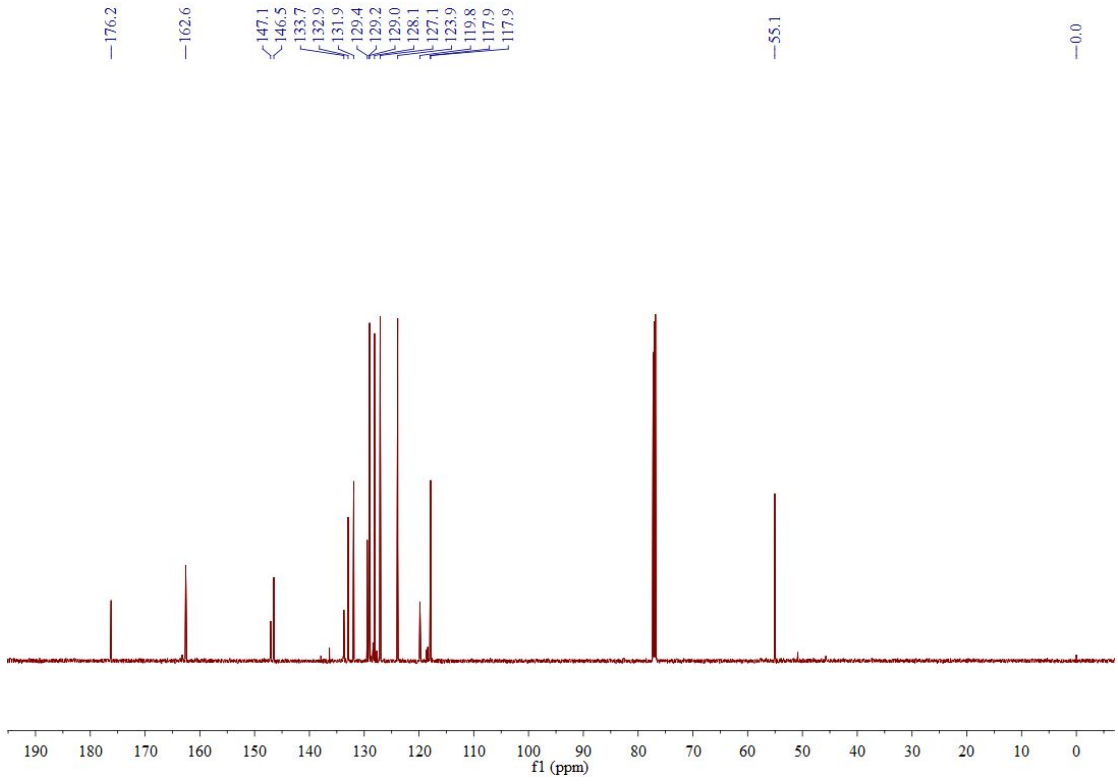


(*E*)-2-(1-((4-nitrobenzyl)imino)propyl)phenol (2l):

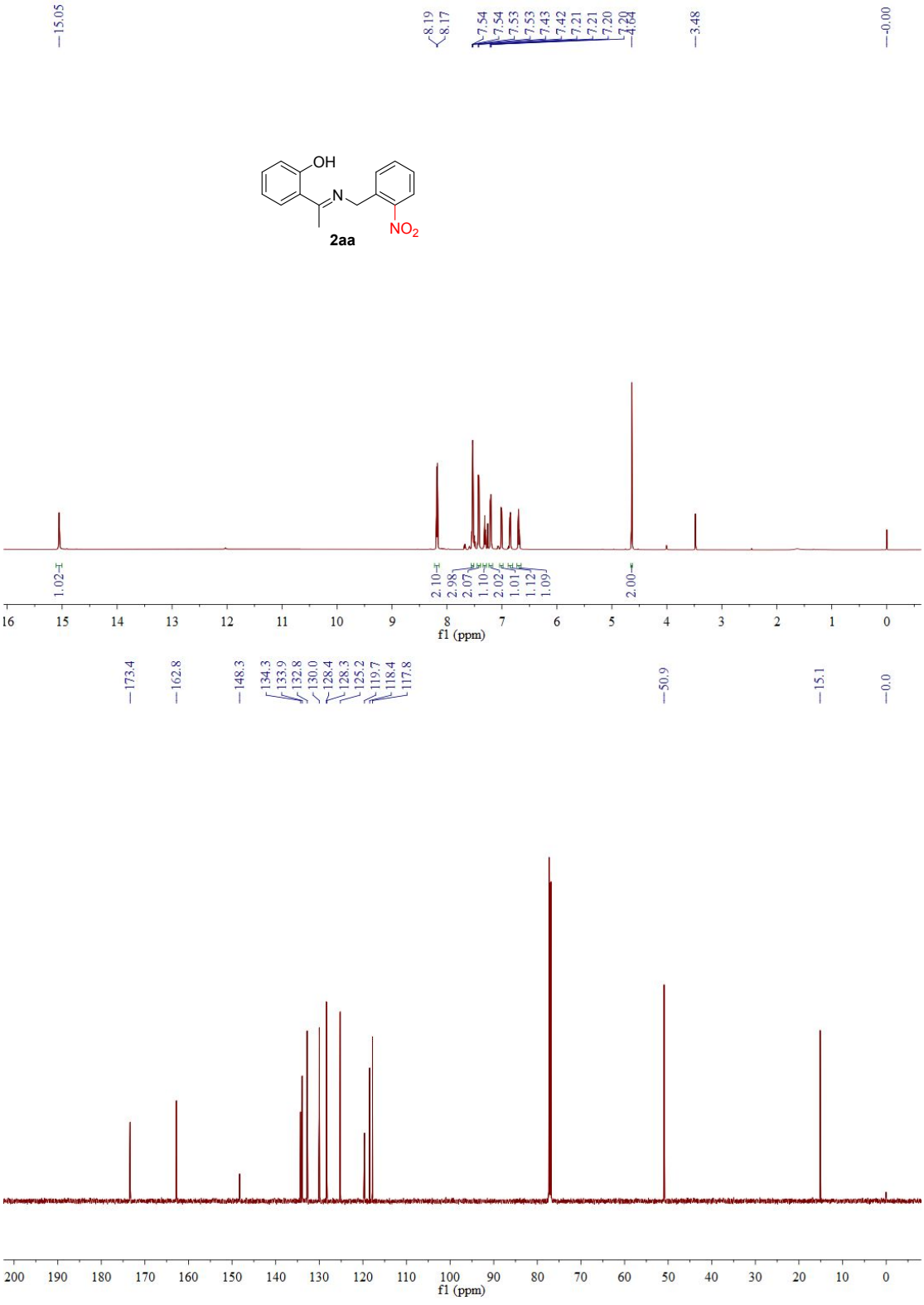


(*E*)-2-(((4-nitrobenzyl)imino)(phenyl)methyl)phenol (2m):

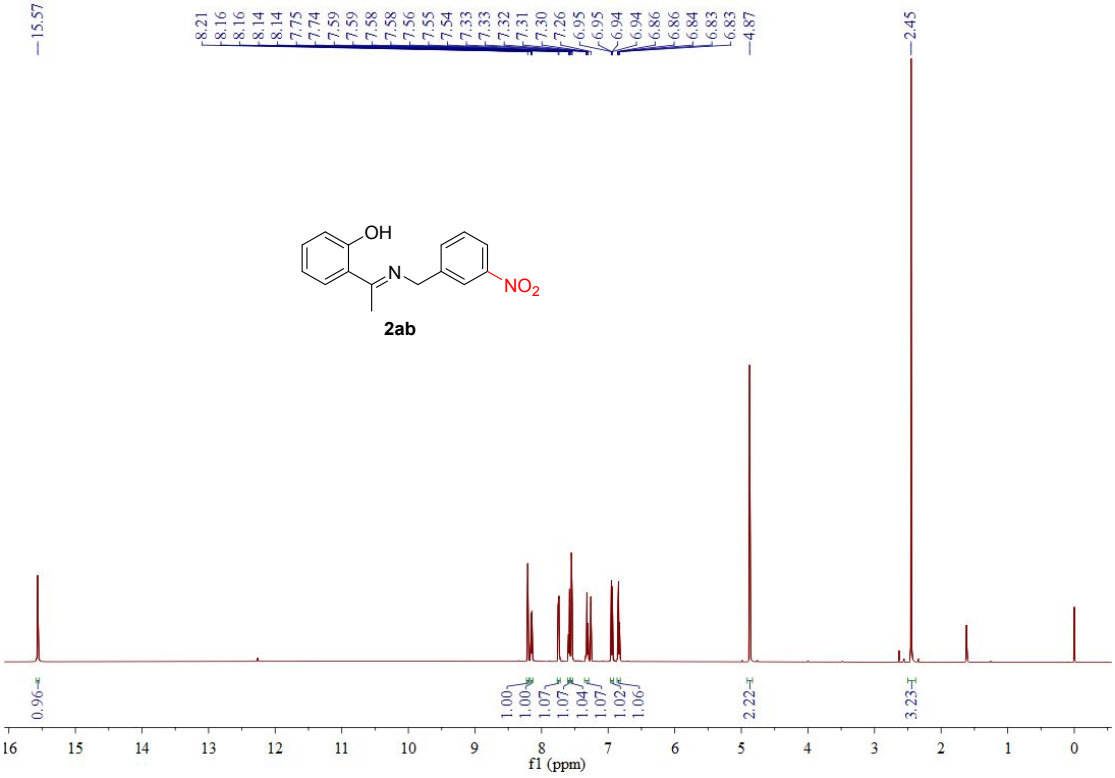


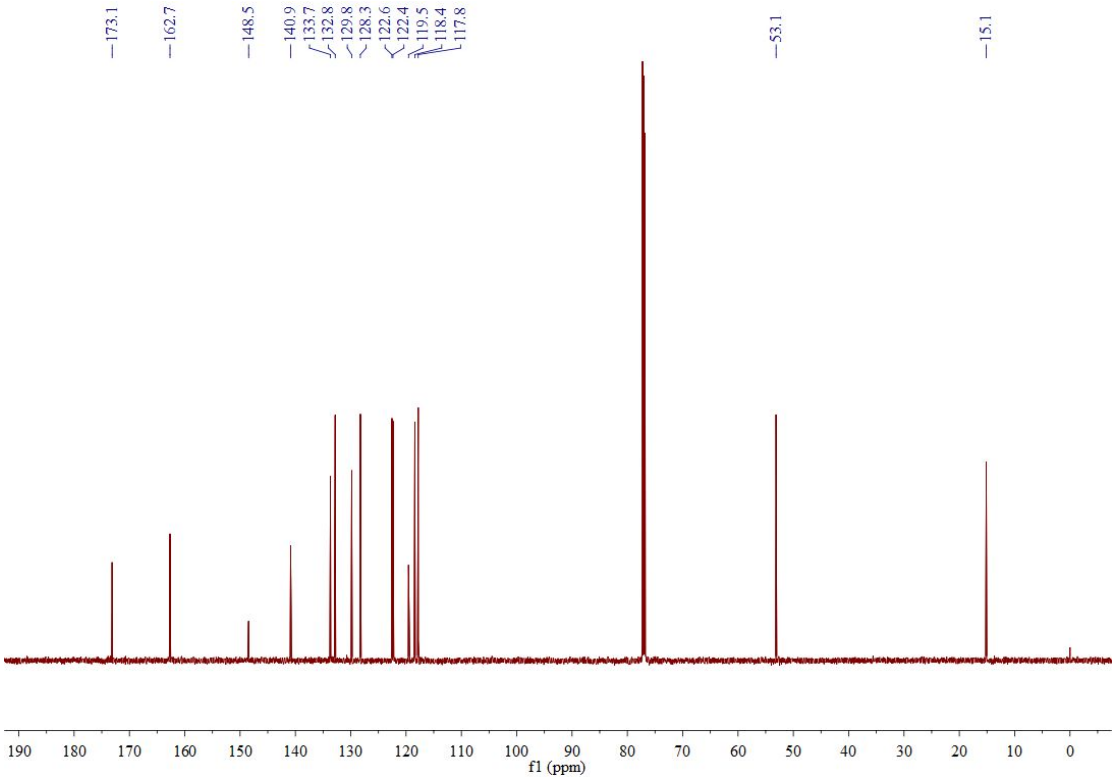


(*E*)-2-(1-((2-nitrobenzyl)imino)ethyl)phenol (2aa):

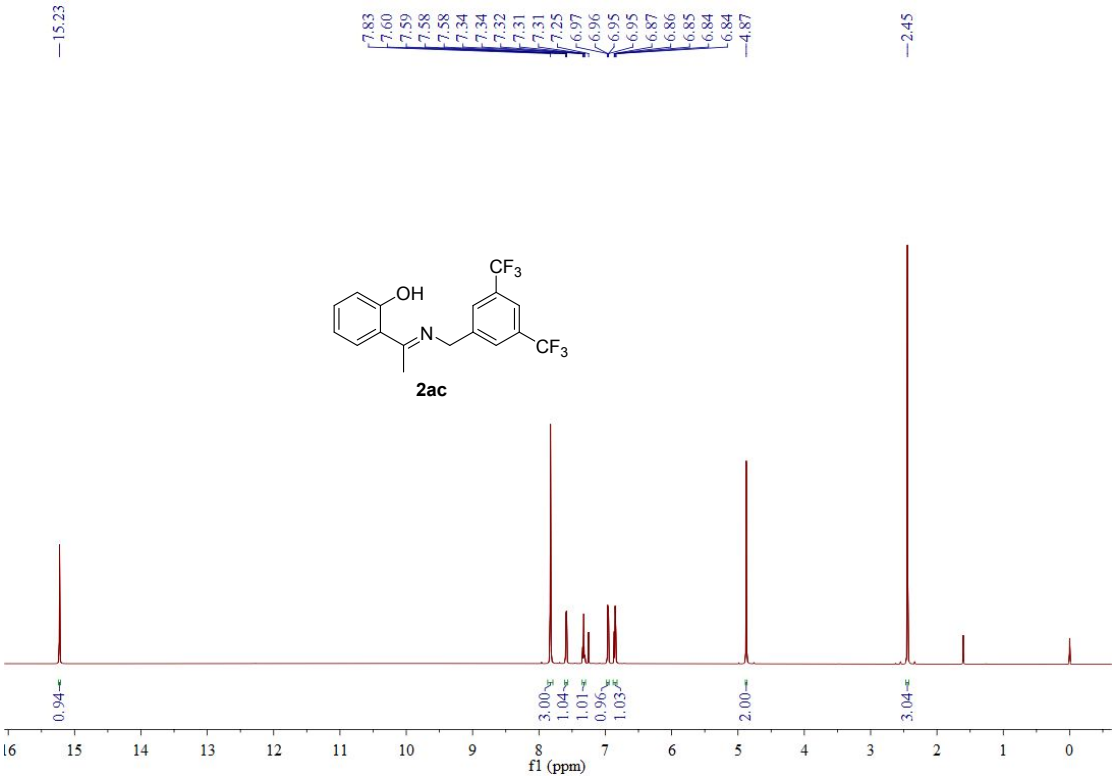


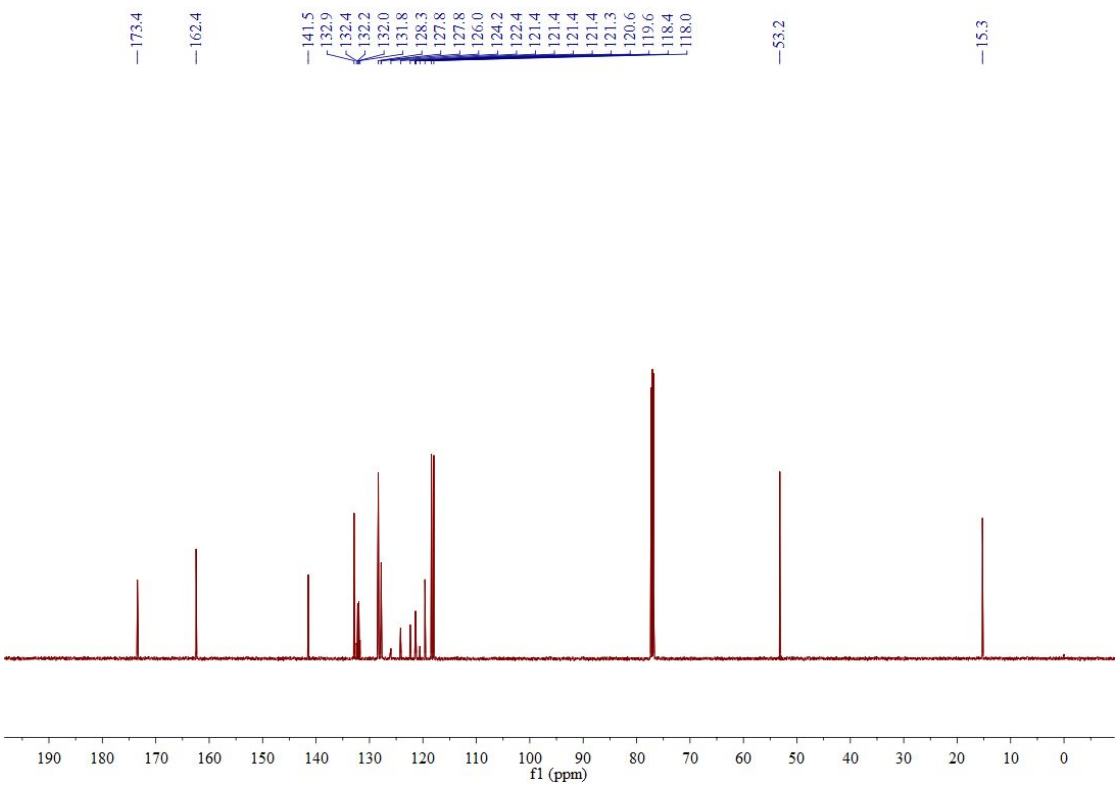
(*E*)-2-(1-((3-nitrobenzyl)imino)ethyl)phenol (2ab):

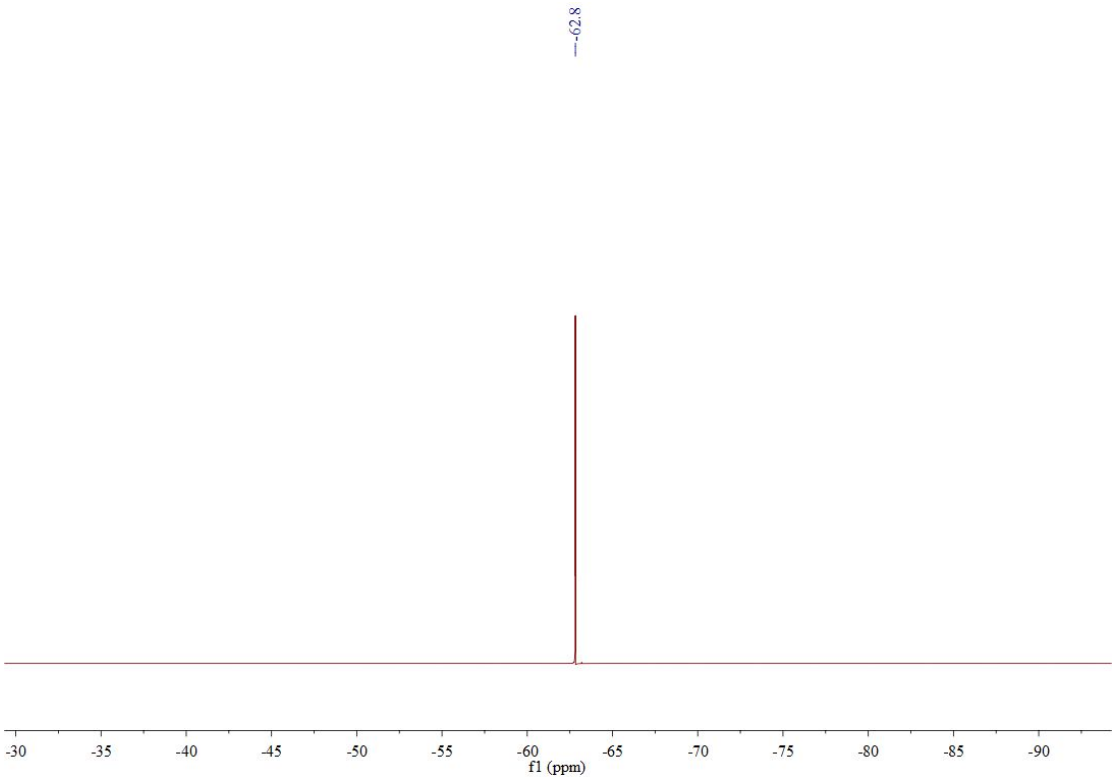




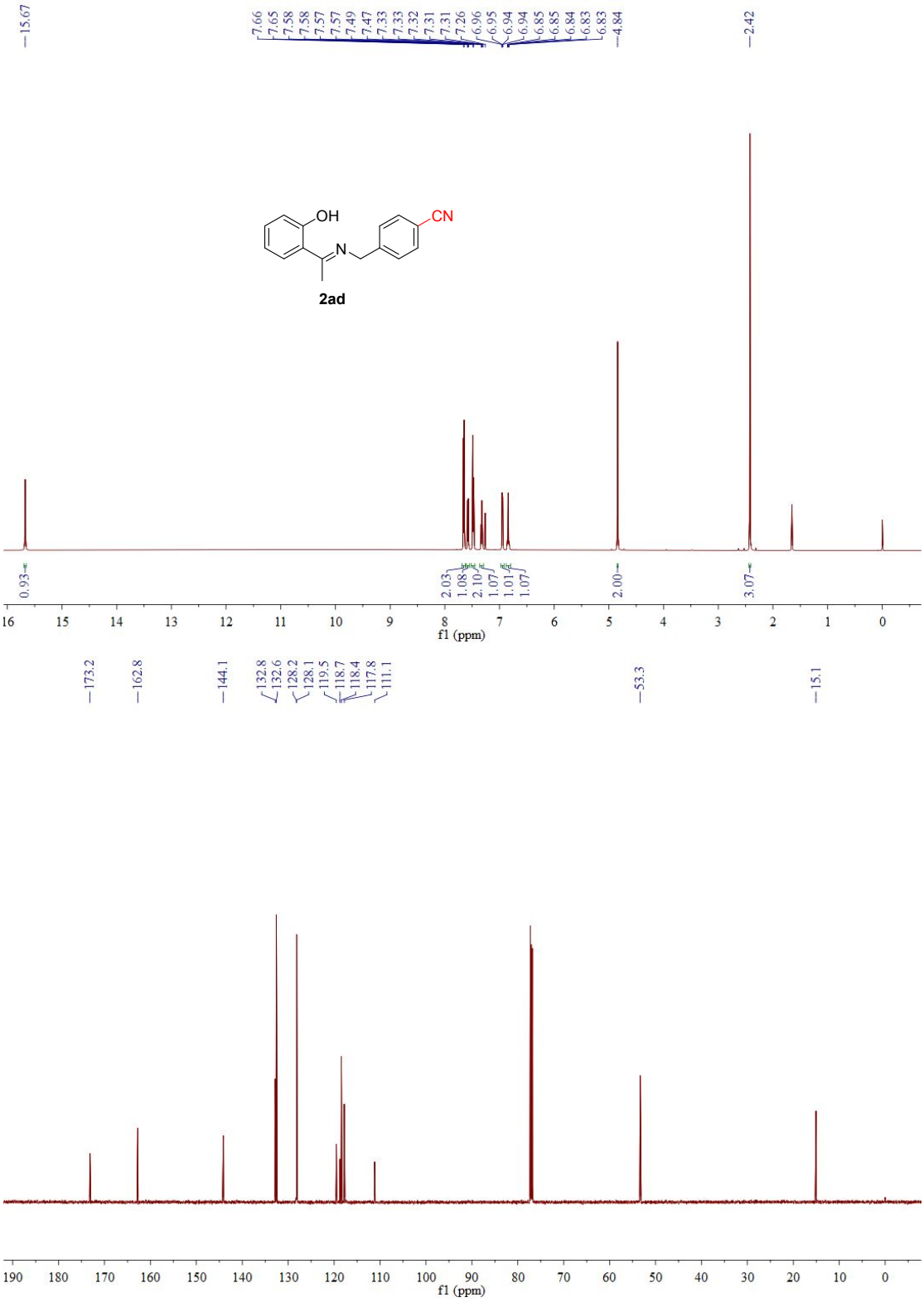
(*E*)-2-(1-((3,5-bis(trifluoromethyl)benzyl)imino)ethyl)phenol (2ac):



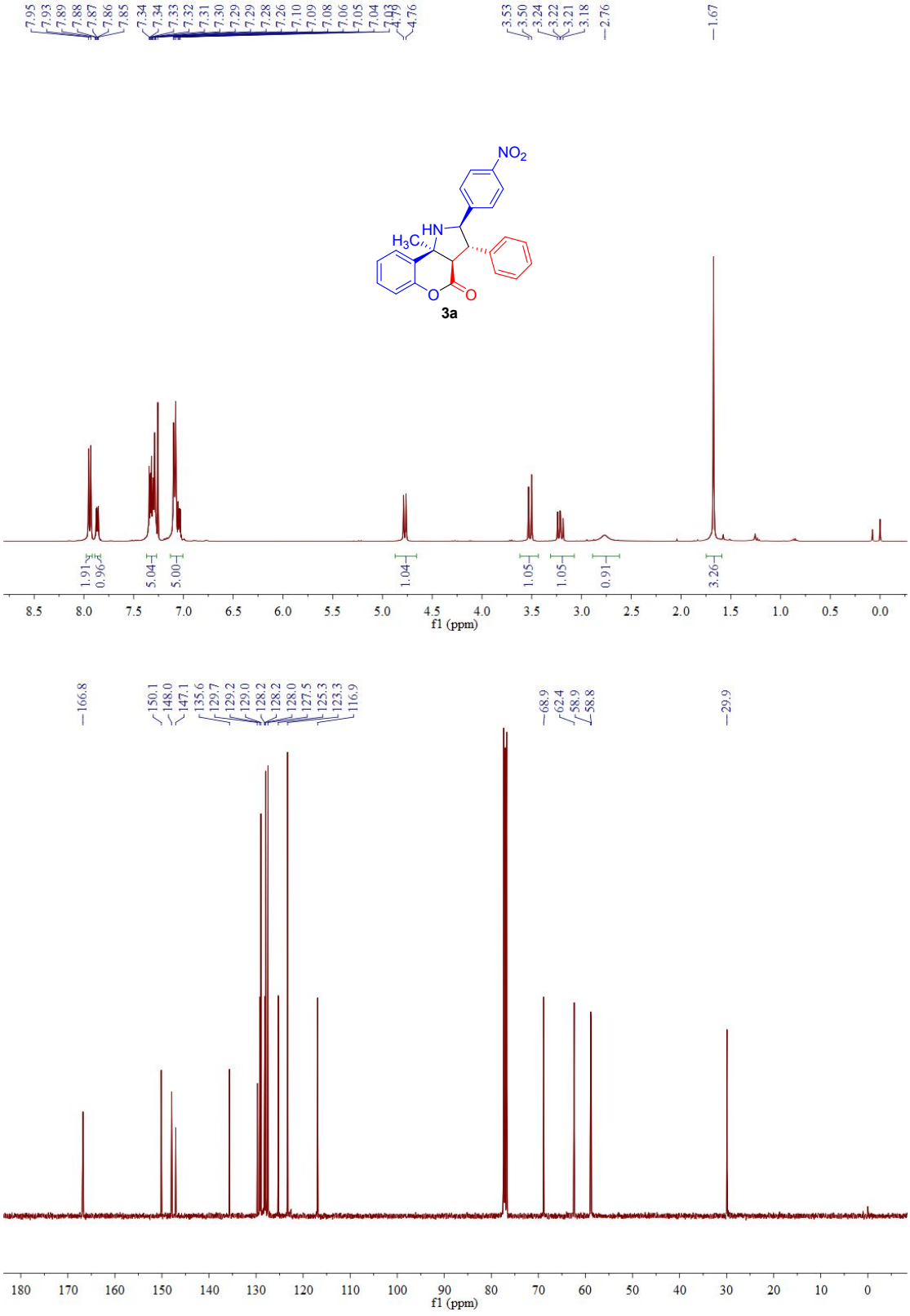


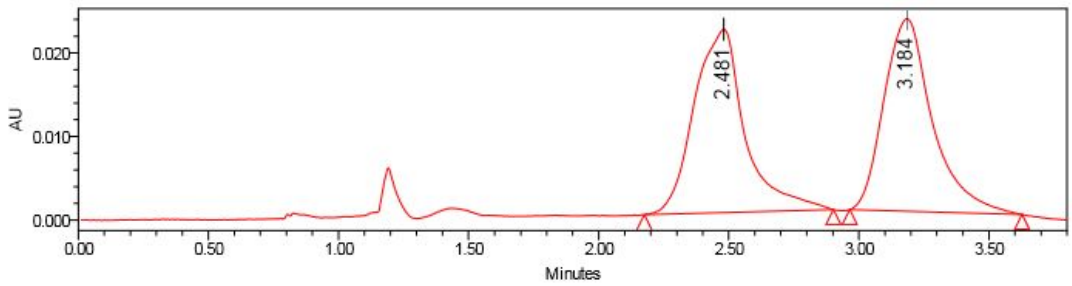

-62.8
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
f1 (ppm)

(*E*)-4-(((1-(2-hydroxyphenyl)ethylidene)amino)methyl)benzonitrile (2ad):



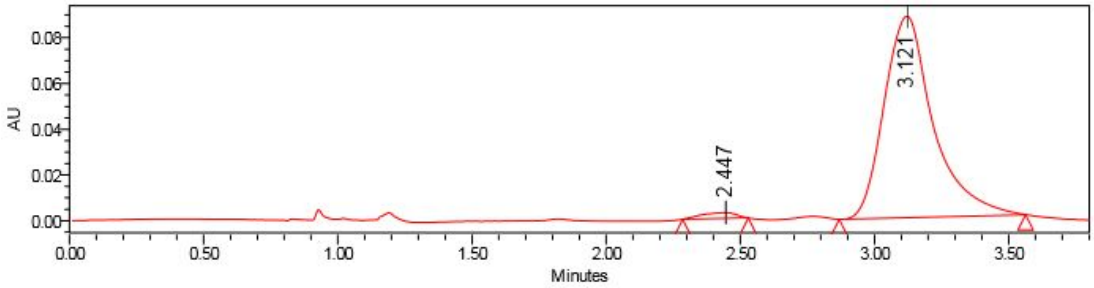
(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-b]pyrrol-4(1*H*)-one (3a):





Peak Results

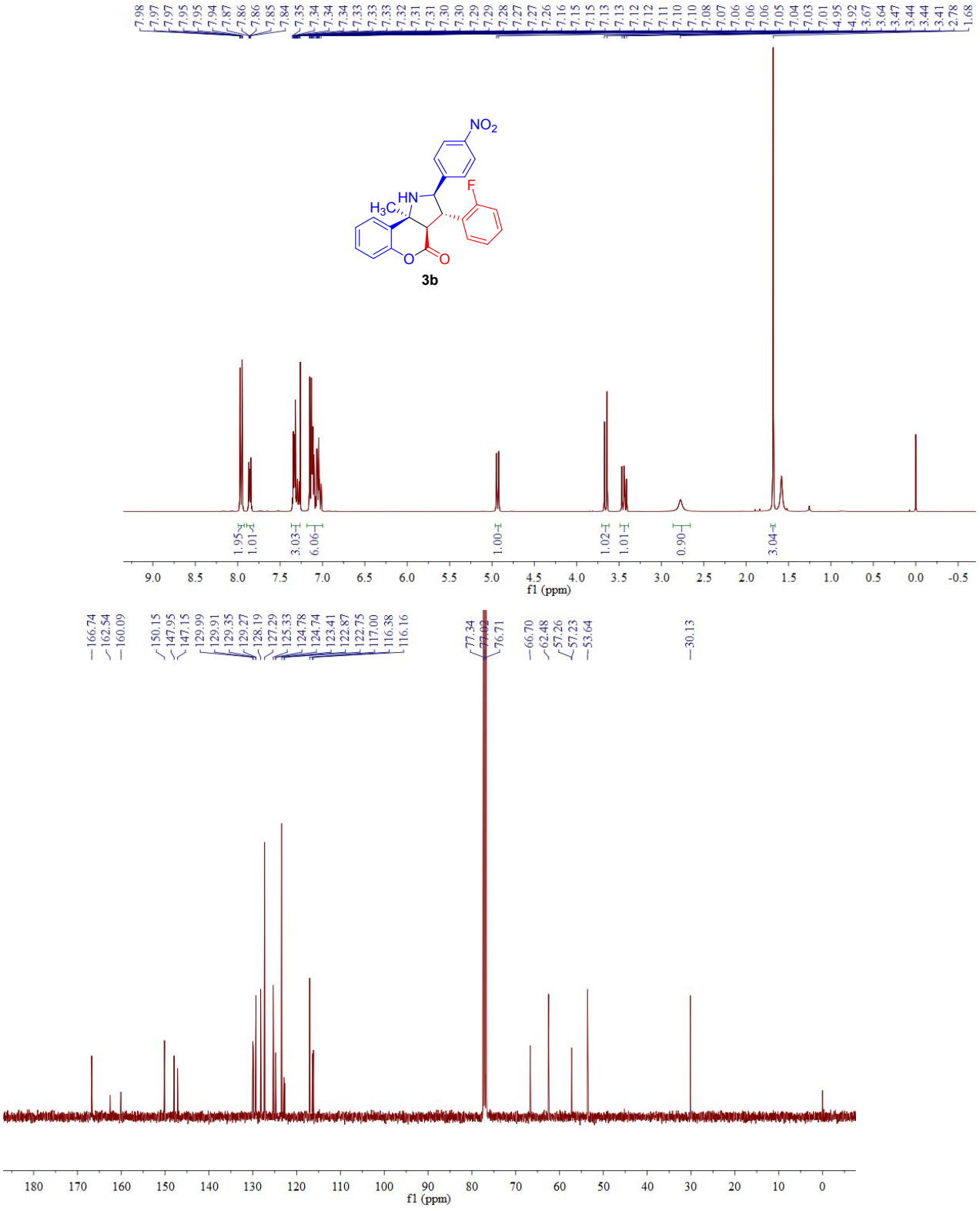
	RT	Area	Height	% Area
1	2.481	298062	21931	49.96
2	3.184	298500	23010	50.04

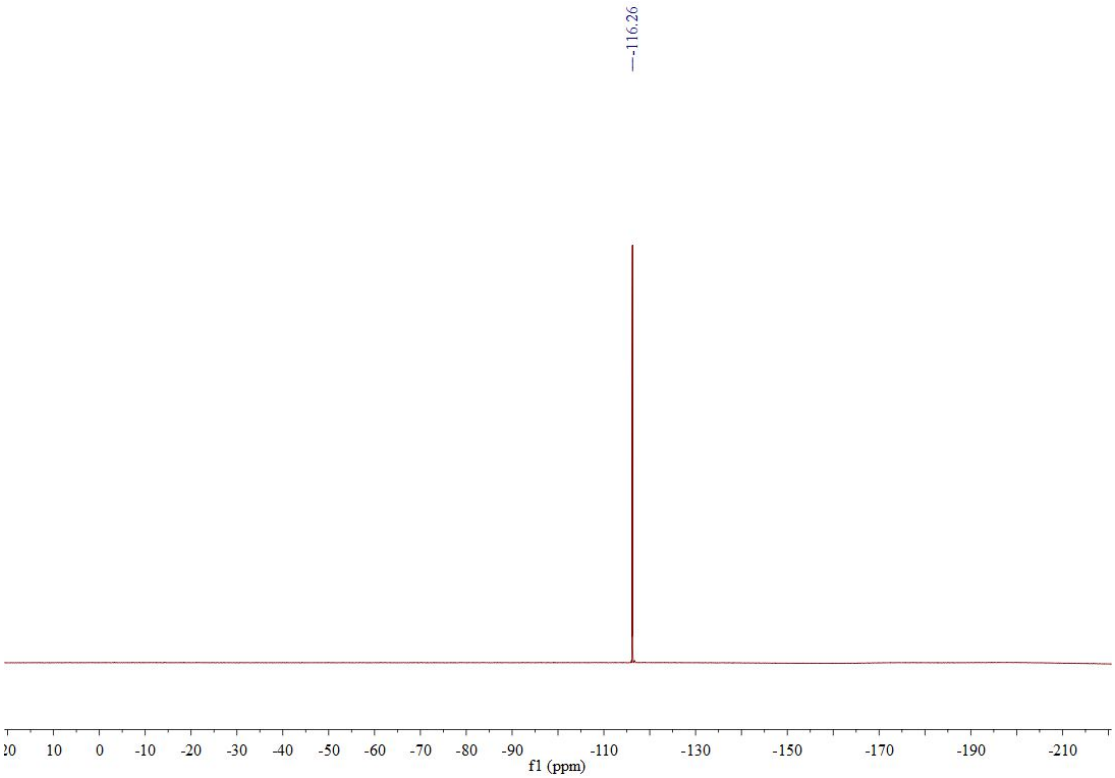


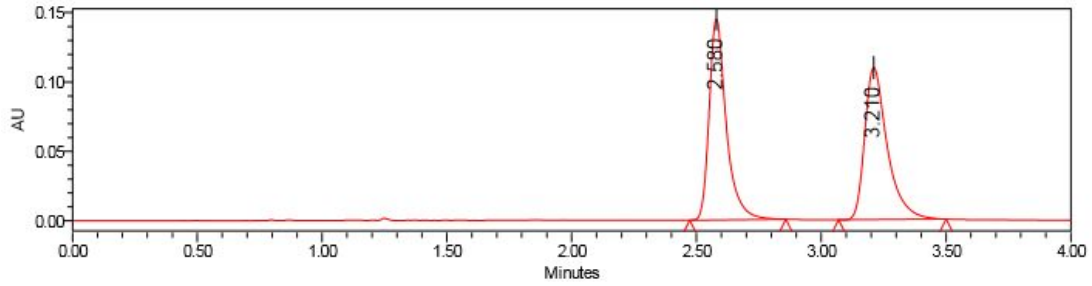
Peak Results

	RT	Area	Height	% Area
1	2.447	22586	2527	1.97
2	3.121	1123209	88132	98.03

(2*R*,3*S*,3*aR*,9*bS*)-3-(2-fluorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3b):

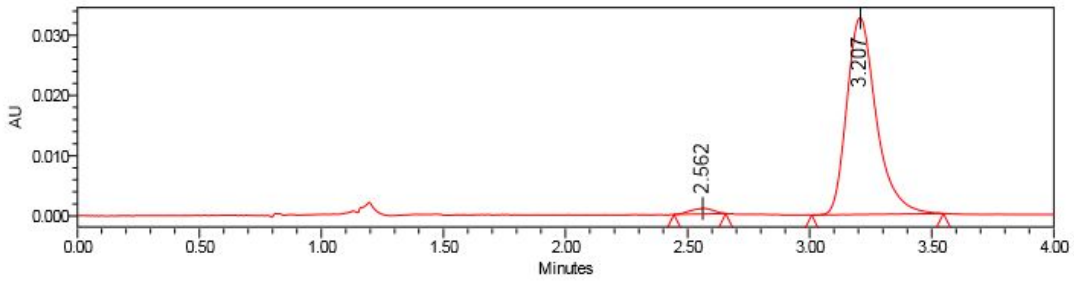






Peak Results

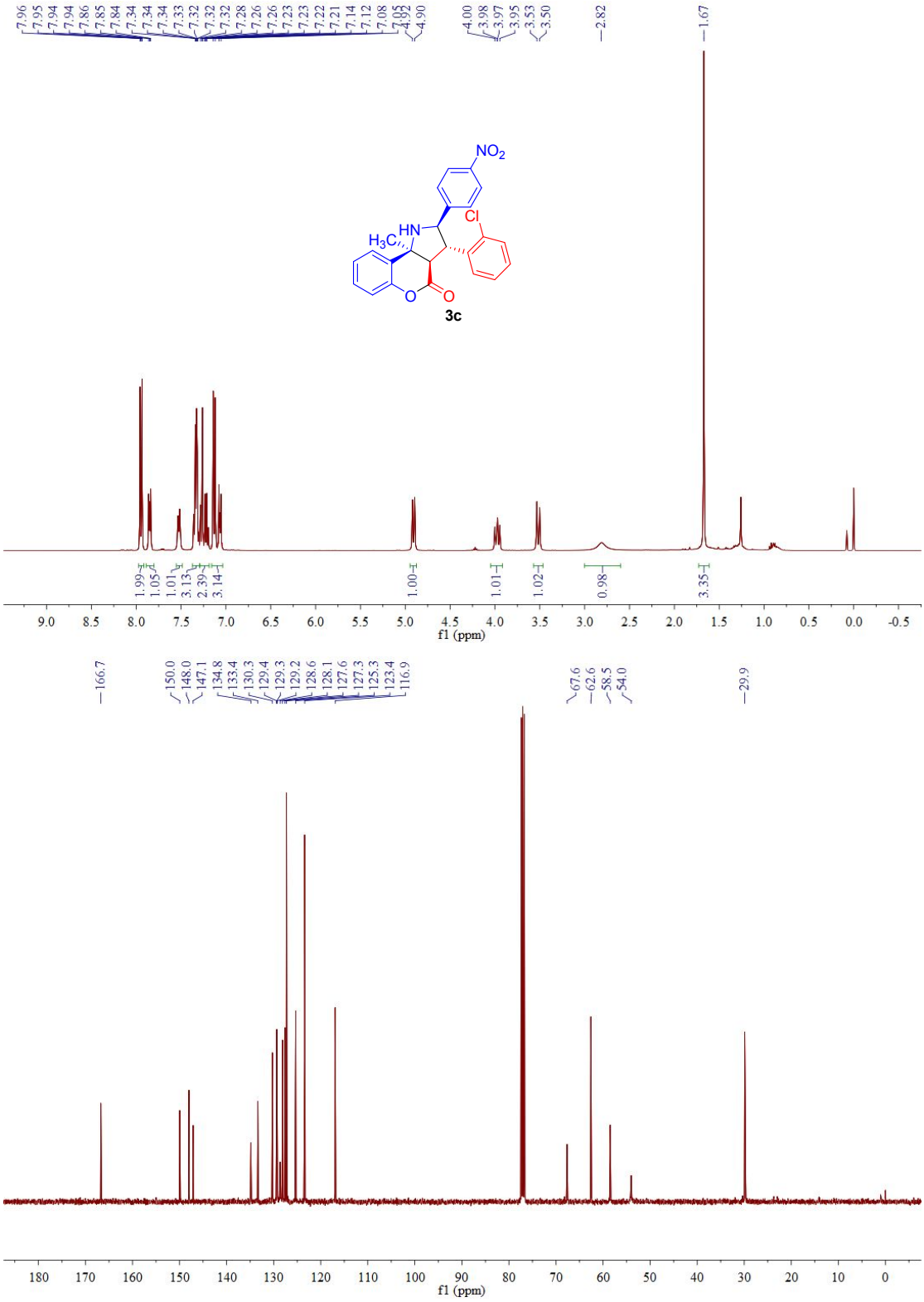
	RT	Area	Height	% Area
1	2.580	690185	144824	50.03
2	3.210	689243	109553	49.97

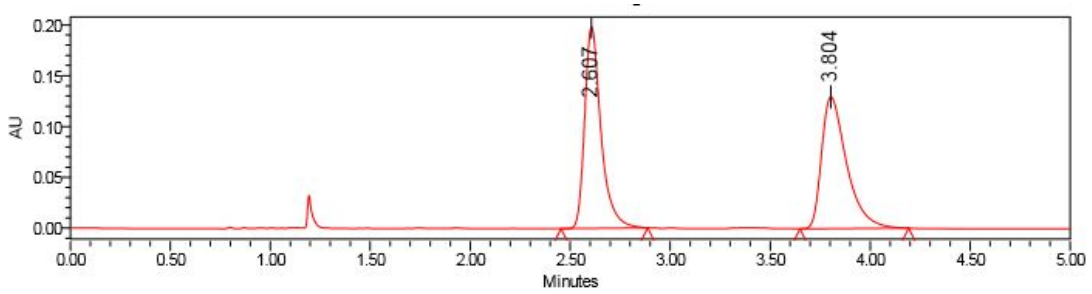


Peak Results

	RT	Area	Height	% Area
1	2.562	6013	914	2.14
2	3.207	274595	32685	97.86

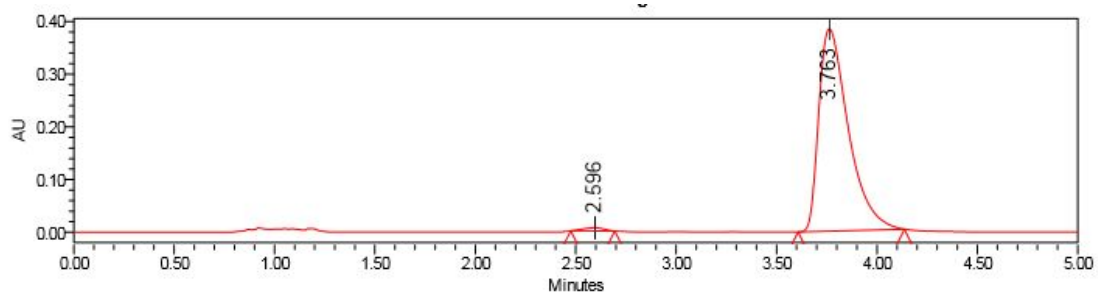
(2*R*,3*S*,3*aR*,9*bS*)-3-(2-chlorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3c):





Peak Results

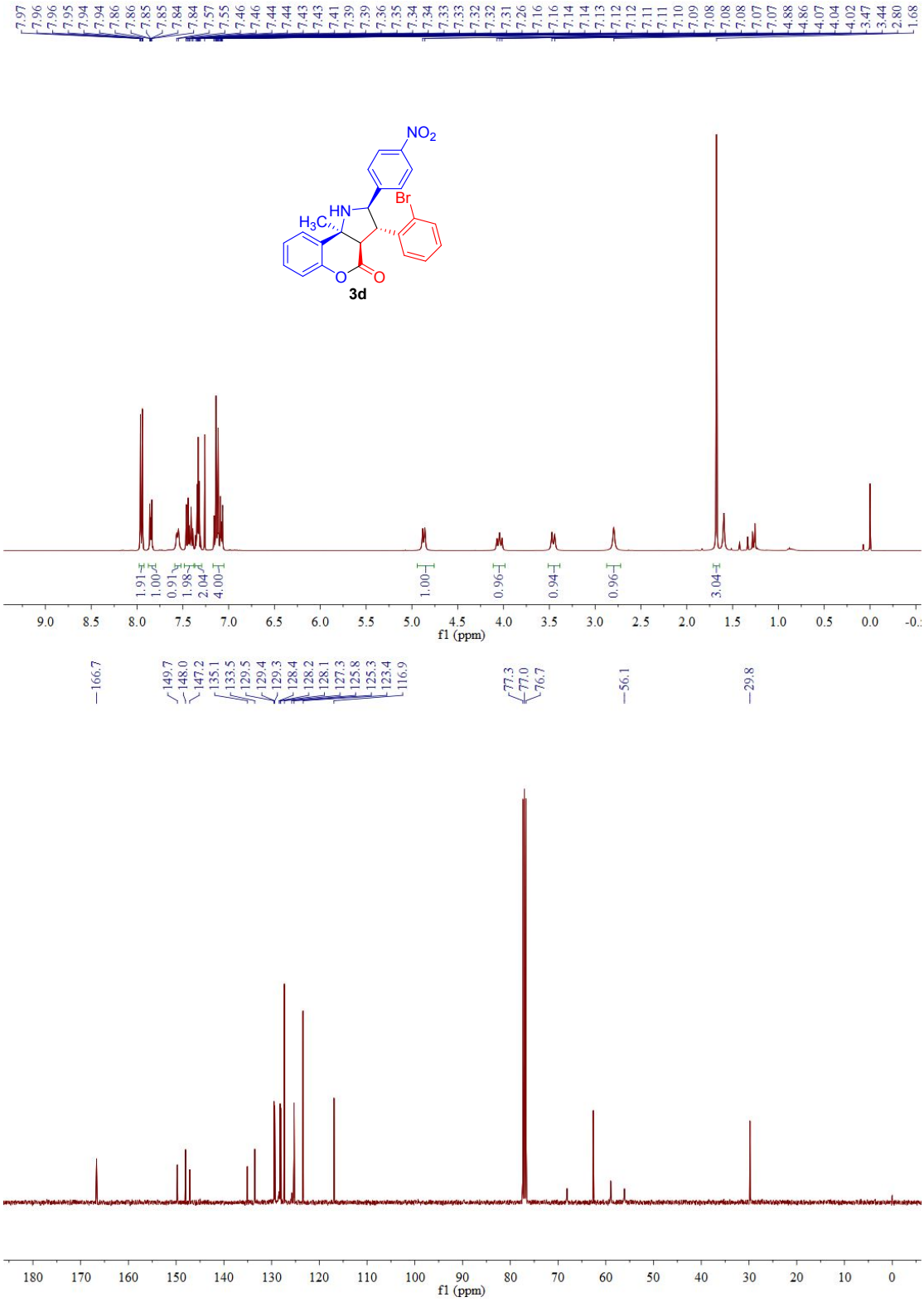
	RT	Area	Height	% Area
1	2.607	1124946	198198	49.96
2	3.804	1126851	129639	50.04

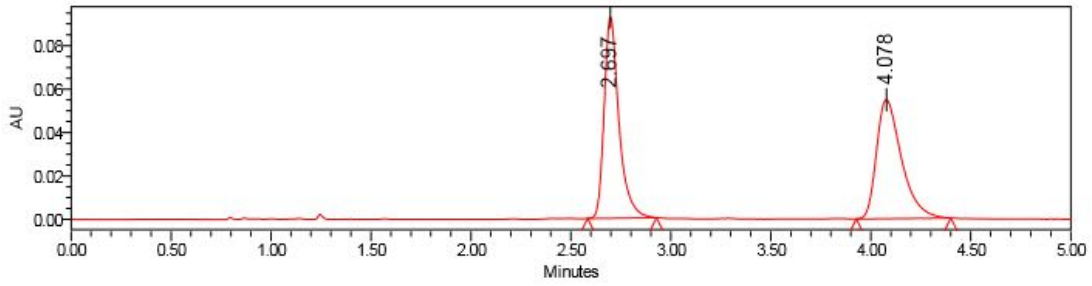


Peak Results

	RT	Area	Height	% Area
1	2.596	43958	6058	1.11
2	3.763	3921478	384159	98.89

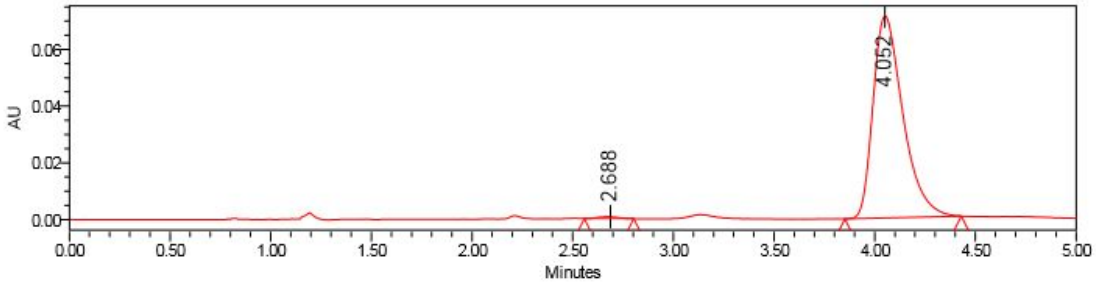
(2*R*,3*S*,3*aR*,9*bS*)-3-(2-bromophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetra hydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3d):





Peak Results

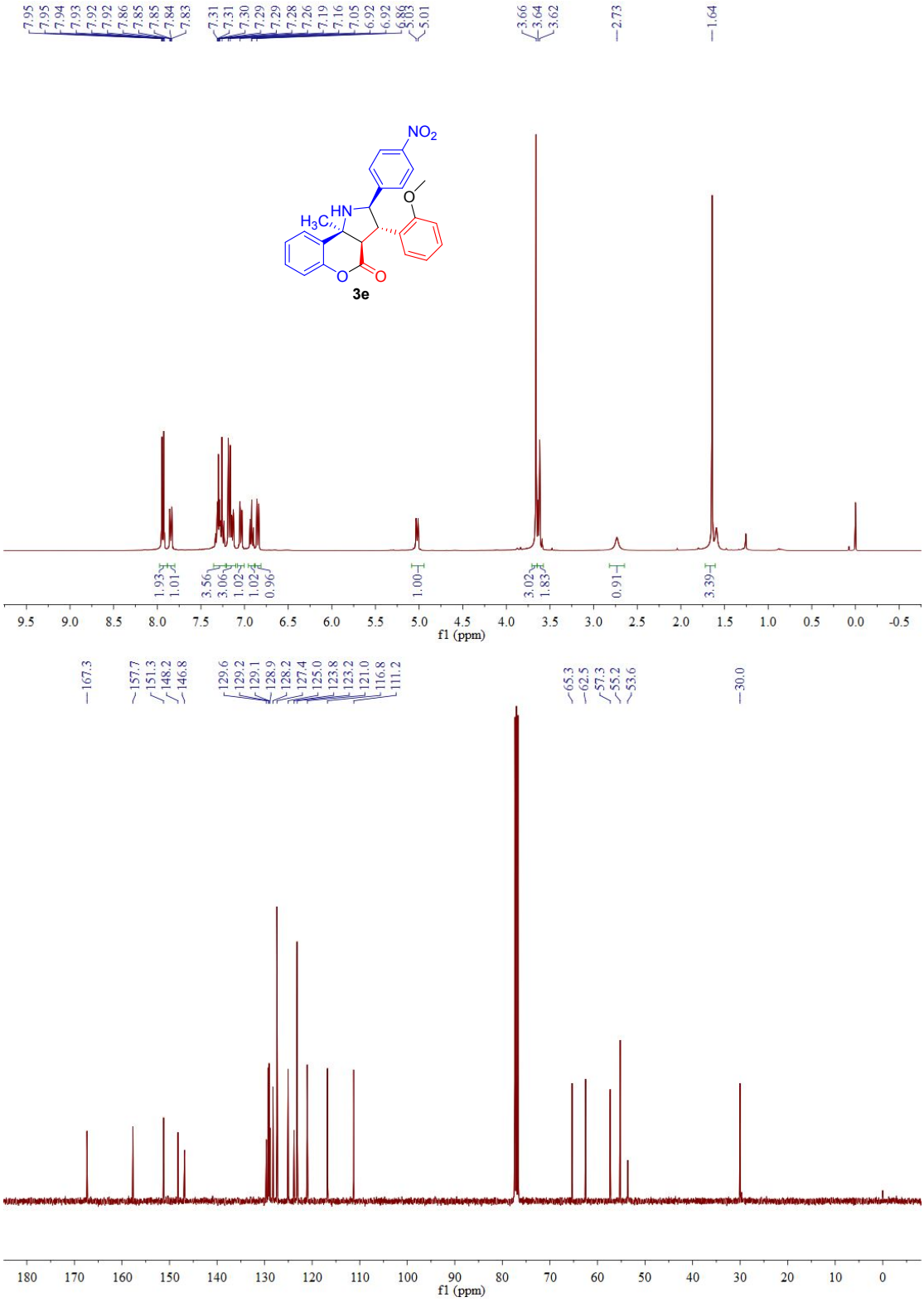
	RT	Area	Height	% Area
1	2.697	476144	92760	50.06
2	4.078	474964	54786	49.94

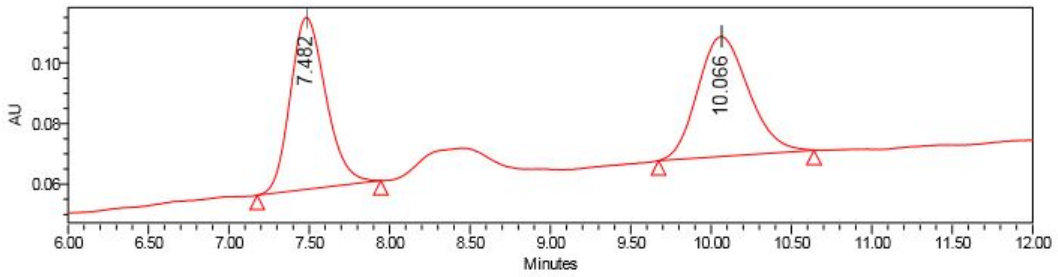


Peak Results

	RT	Area	Height	% Area
1	2.688	4435	678	0.60
2	4.052	733803	71171	99.40

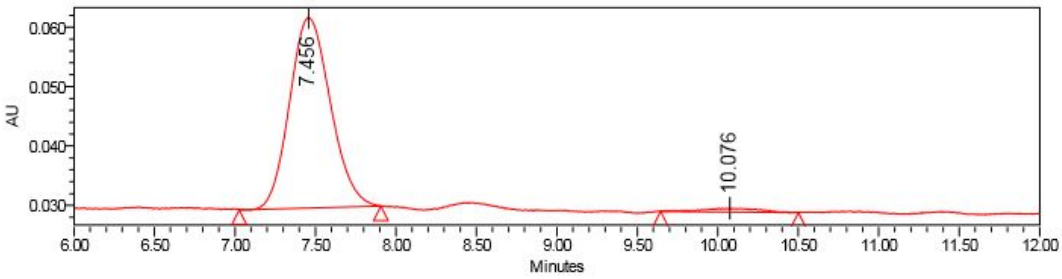
(2*R*,3*S*,3*aR*,9*bS*)-3-(2-methoxyphenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1H)-one (3e):





Peak Results

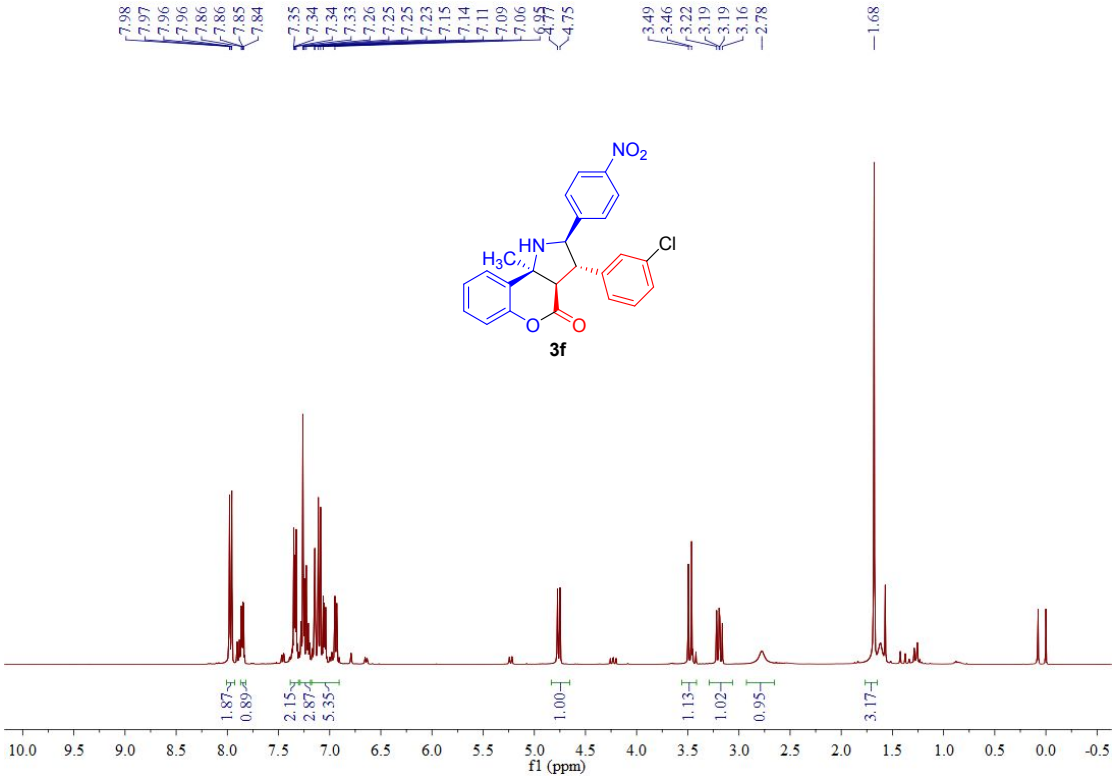
	RT	Area	Height	% Area
1	7.482	872554	56768	50.04
2	10.066	871040	39629	49.96

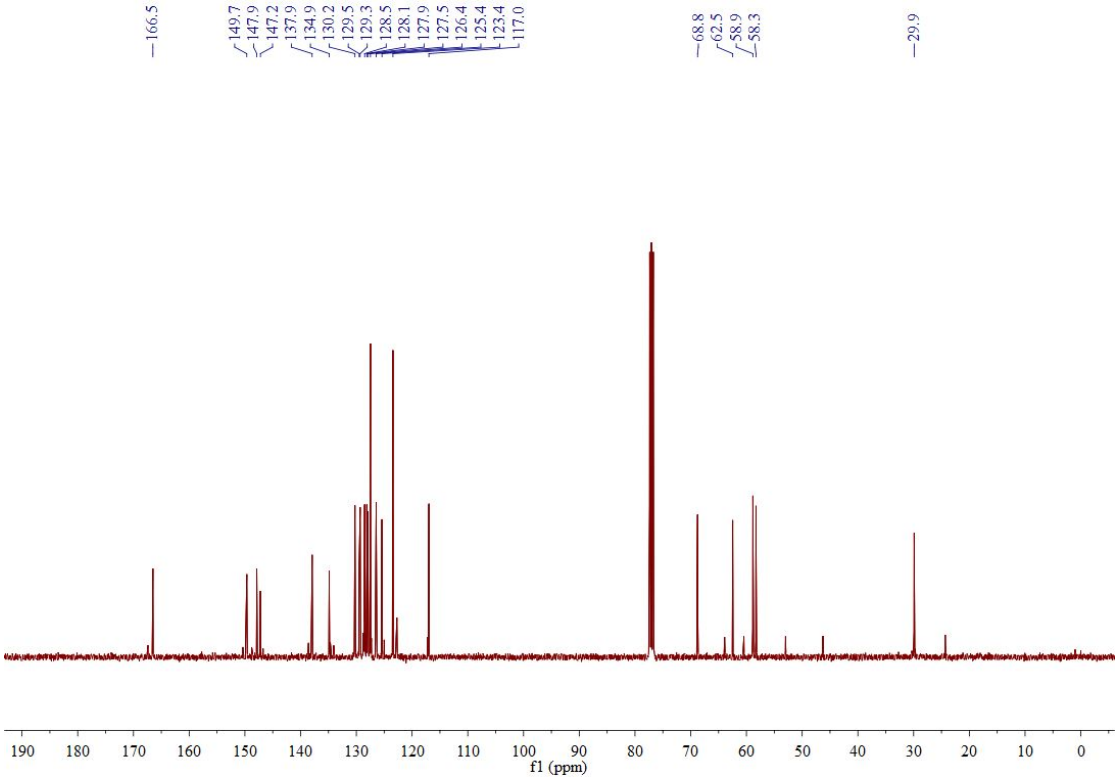


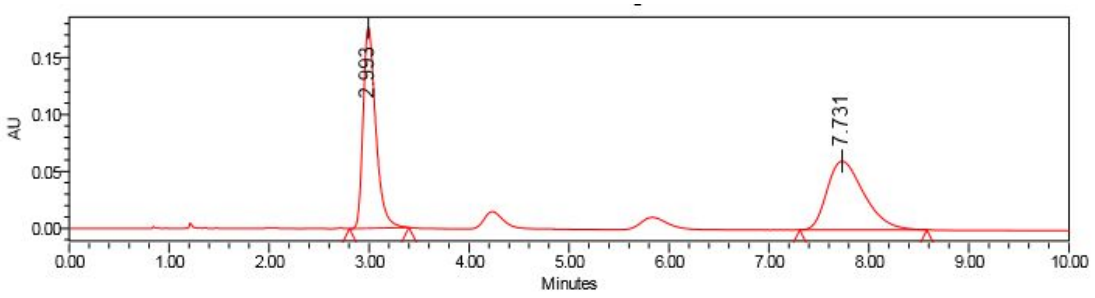
Peak Results

	RT	Area	Height	% Area
1	7.456	566369	32074	97.43
2	10.076	14927	644	2.57

(2*R*,3*S*,3*aR*,9*bS*)-3-(3-chlorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1H)-one (3f):

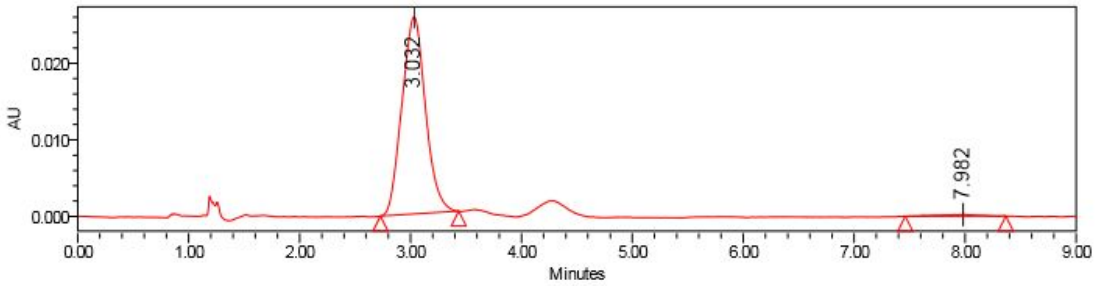






Peak Results

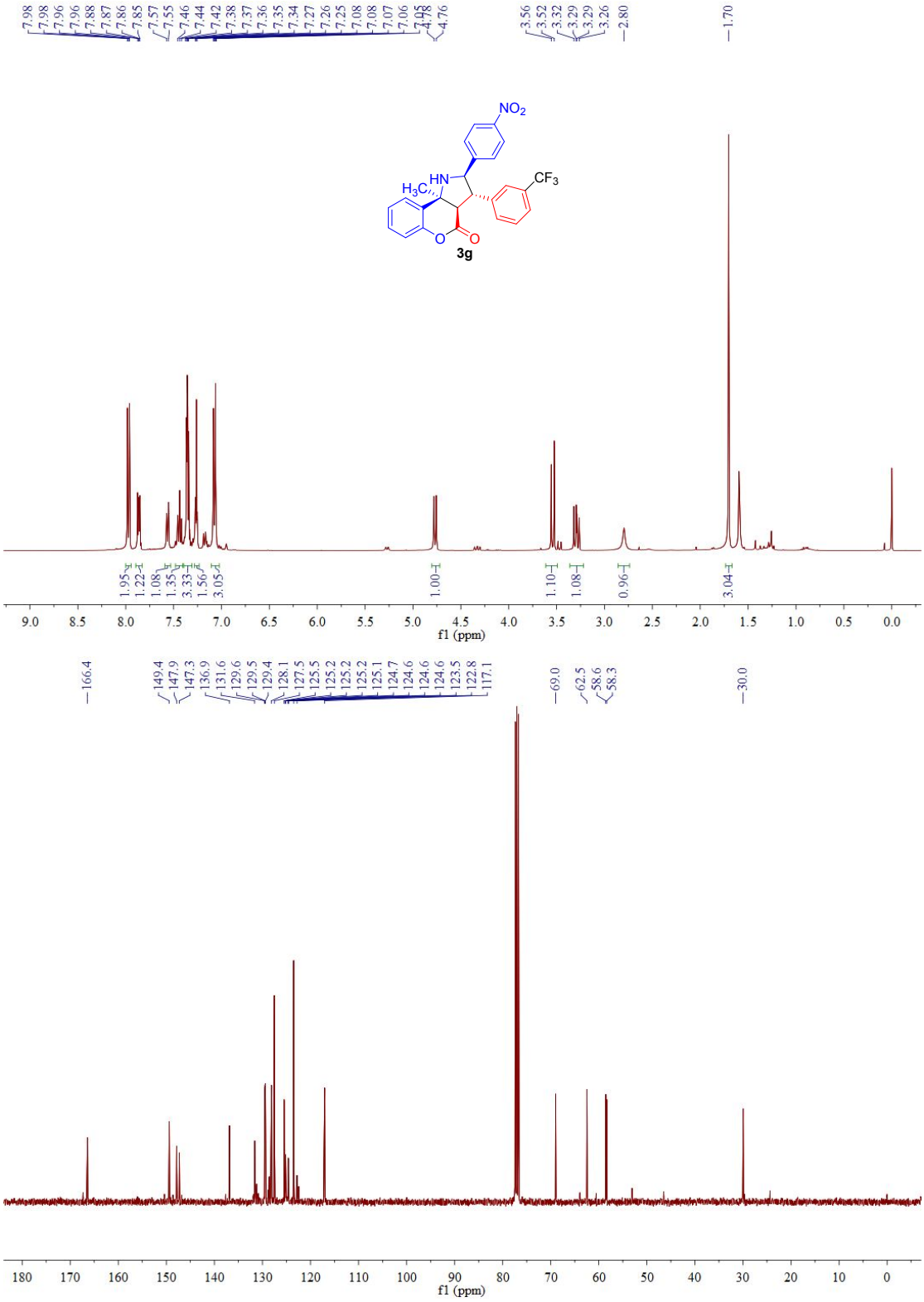
	RT	Area	Height	% Area
1	2.993	1556497	176841	50.07
2	7.731	1552148	60484	49.93

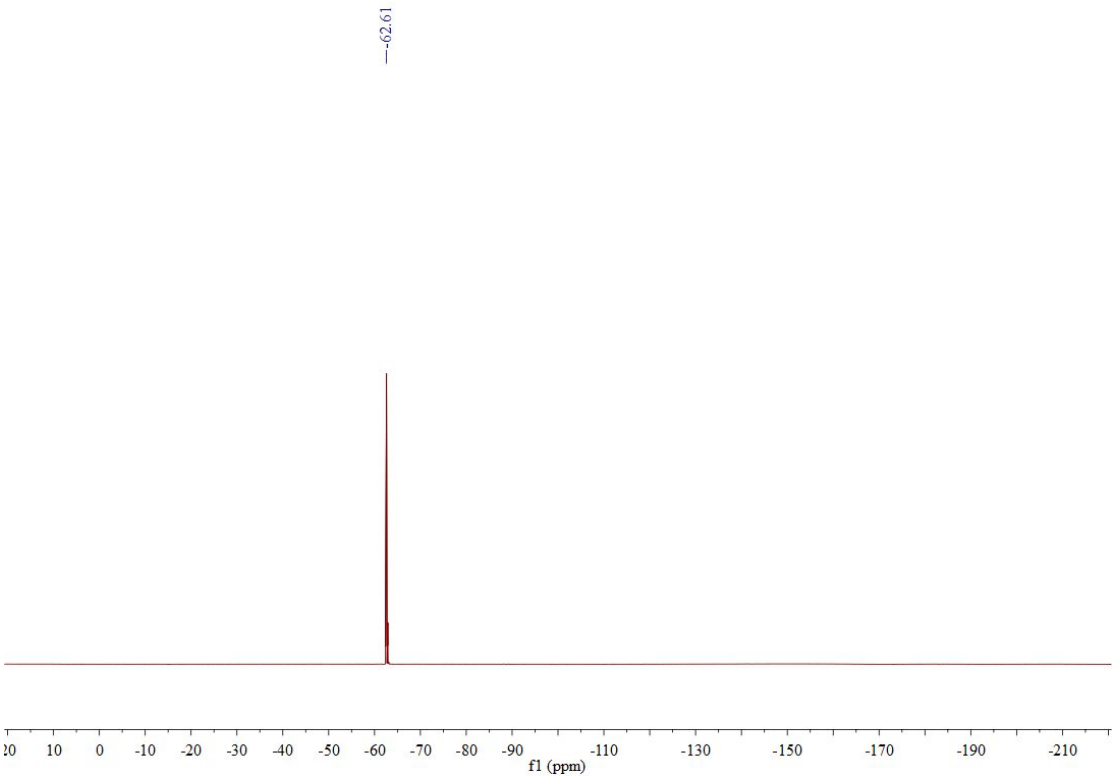


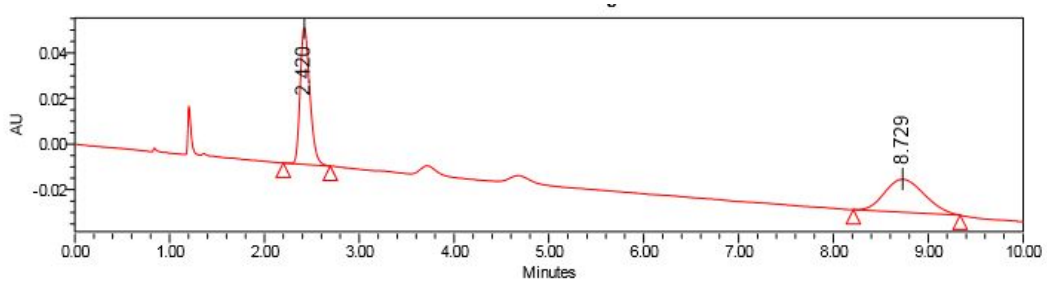
Peak Results

	RT	Area	Height	% Area
1	3.032	380074	25721	98.48
2	7.982	5877	231	1.52

(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-2-(4-nitrophenyl)-3-(3-(trifluoromethyl)phenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1H)-one (3g):

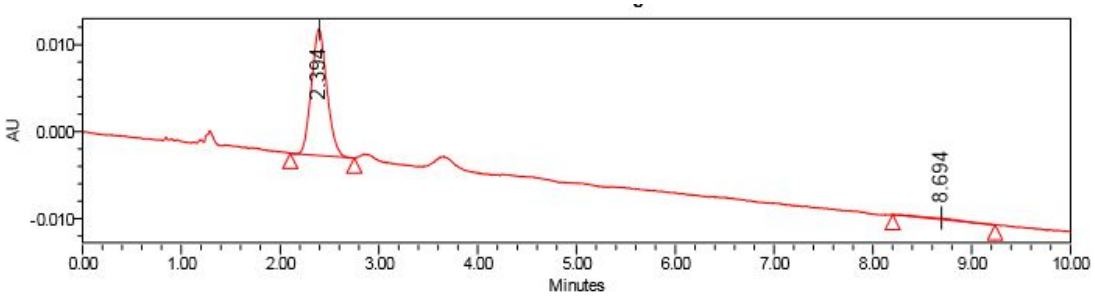






Peak Results

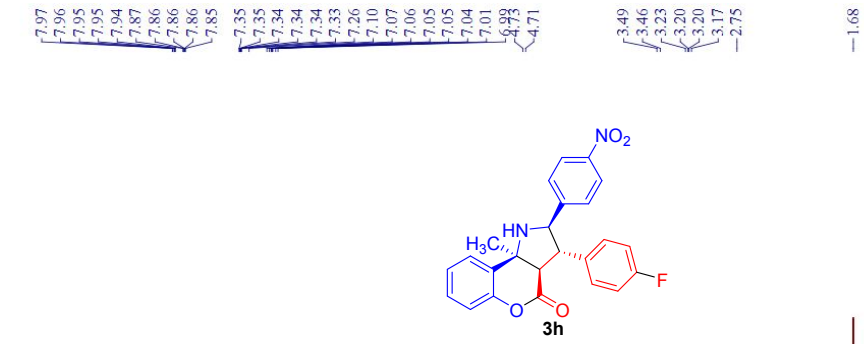
	RT	Area	Height	% Area
1	2.420	424386	59914	50.15
2	8.729	421835	14544	49.85

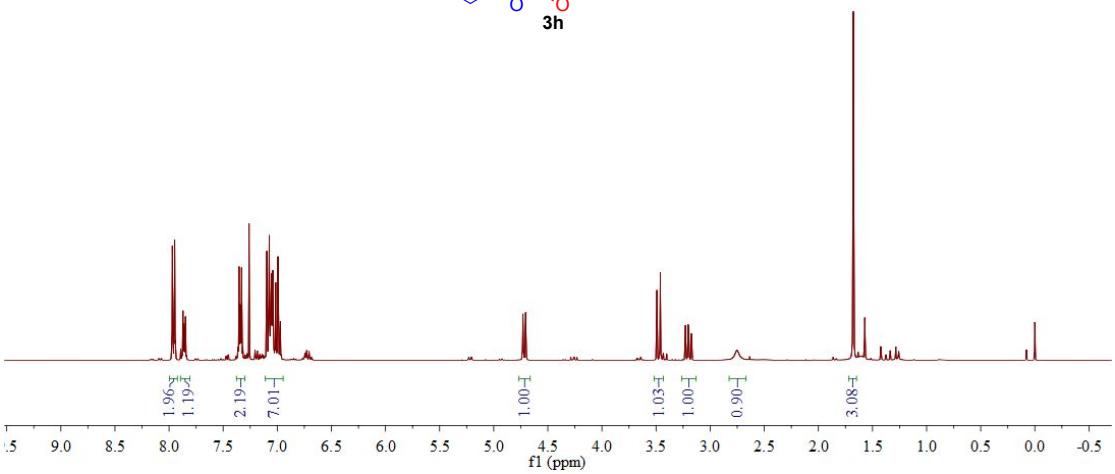


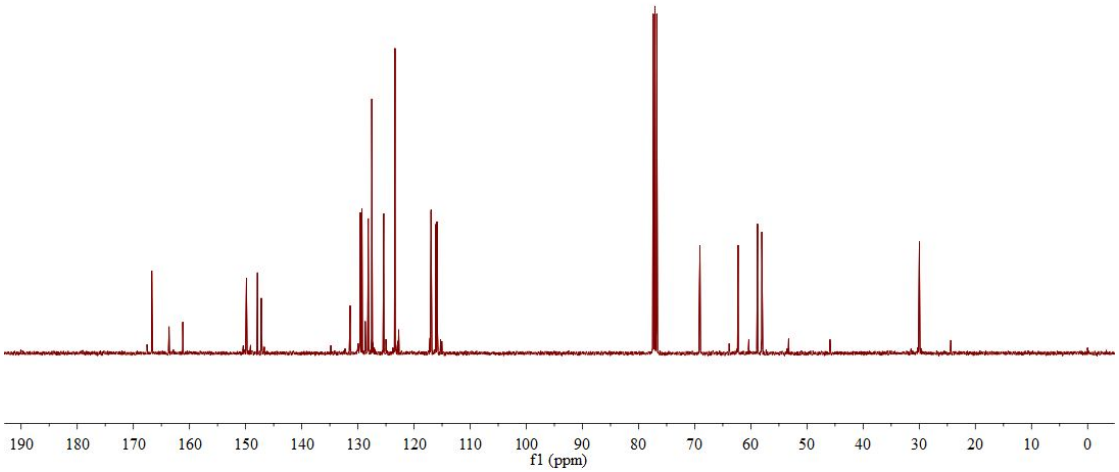
Peak Results

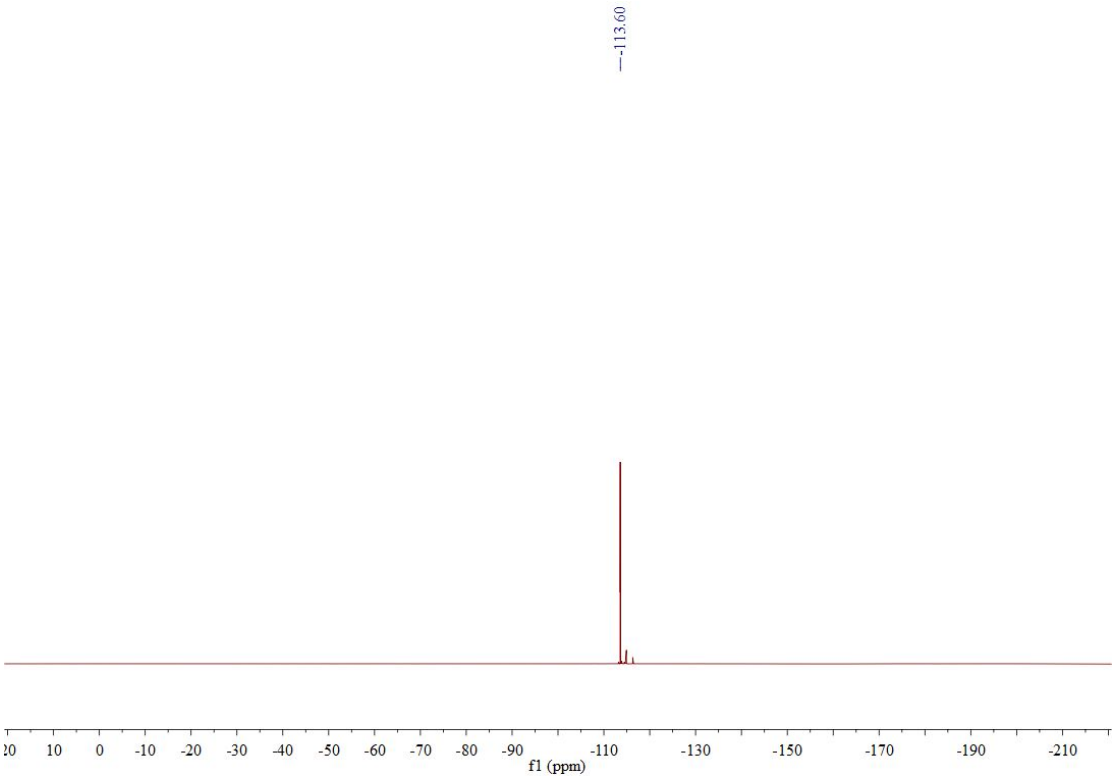
	RT	Area	Height	% Area
1	2.394	157934	14560	97.11
2	8.694	4707	212	2.89

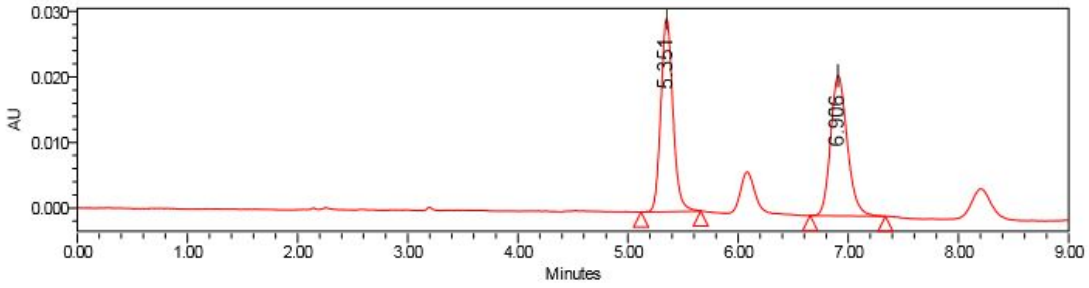
(2*R*,3*S*,3*aR*,9*bS*)-3-(4-fluorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3h):





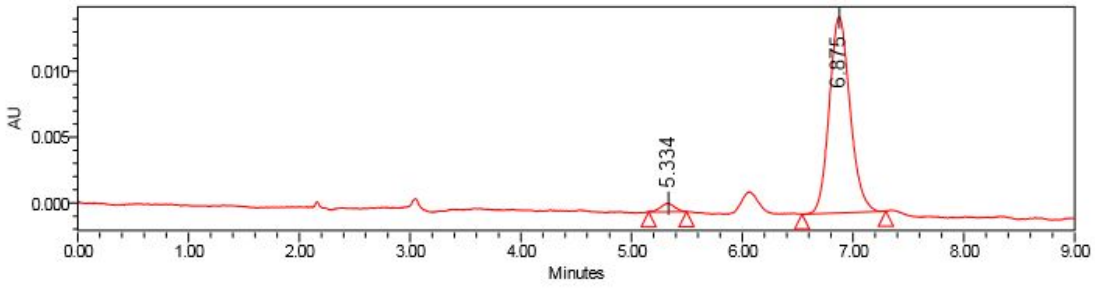






Peak Results

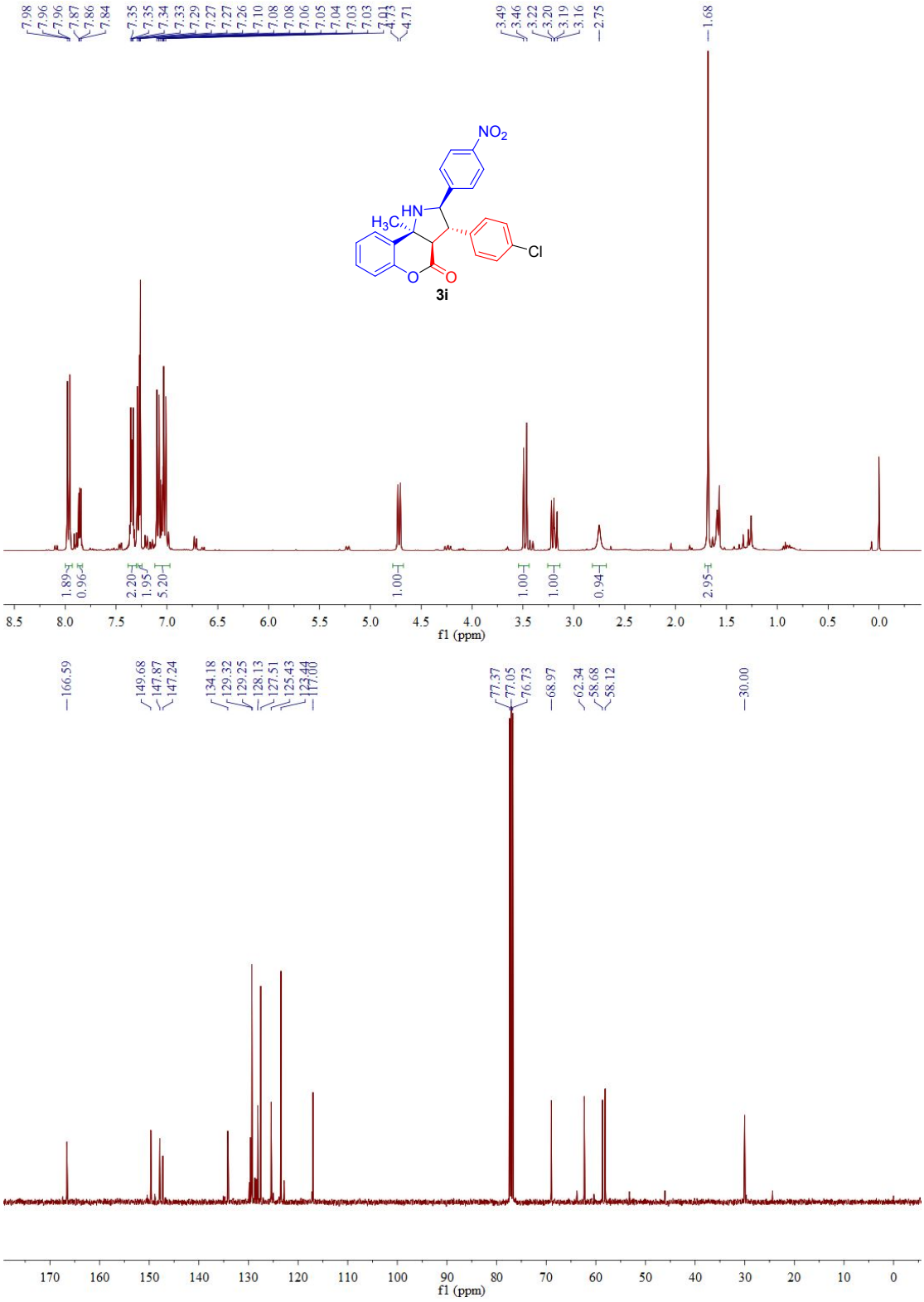
	RT	Area	Height	% Area
1	5.351	225355	29466	50.06
2	6.906	224783	21375	49.94

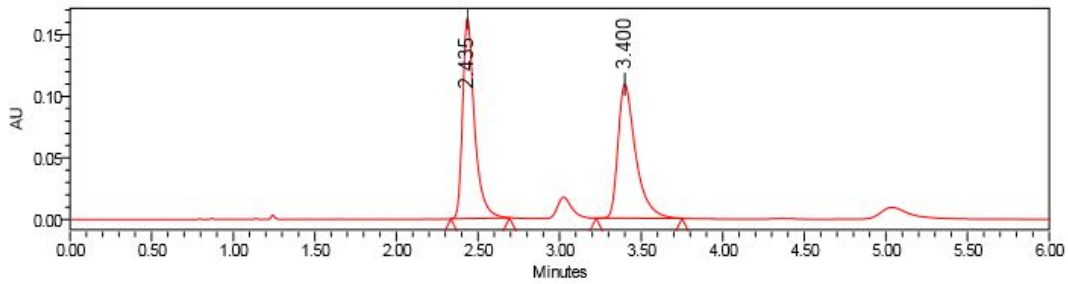


Peak Results

	RT	Area	Height	% Area
1	5.334	5765	656	2.88
2	6.875	194283	14907	97.12

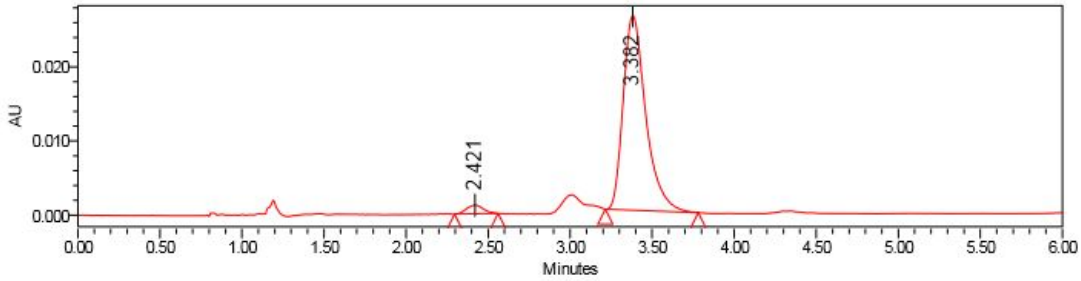
(2*R*,3*S*,3*aR*,9*bS*)-3-(4-chlorophenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3i):





Peak Results

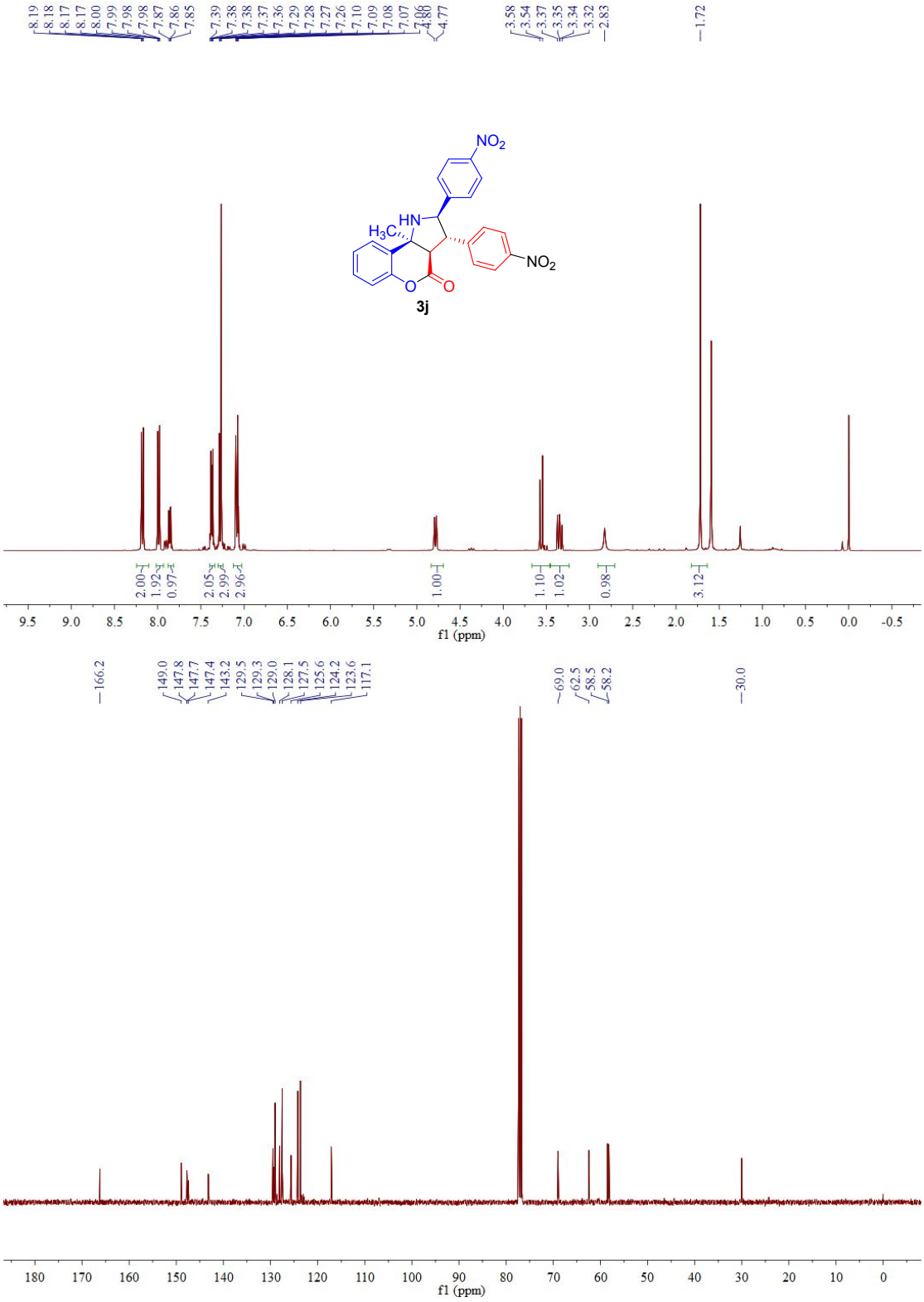
	RT	Area	Height	% Area
1	2.435	822341	162531	50.11
2	3.400	818716	108703	49.89

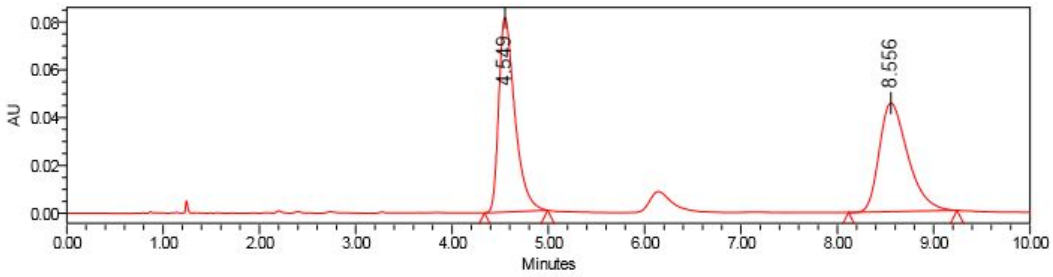


Peak Results

	RT	Area	Height	% Area
1	2.421	8230	1162	3.17
2	3.382	251387	26274	96.83

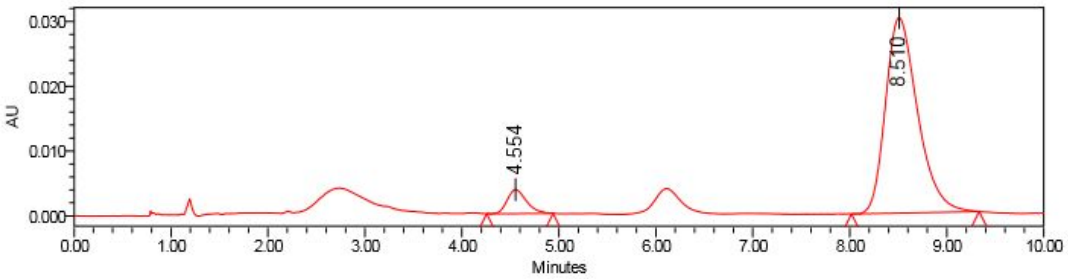
(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-2,3-bis(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno [4,3-*b*]pyrrol-4(1*H*)-one (3j):





Peak Results

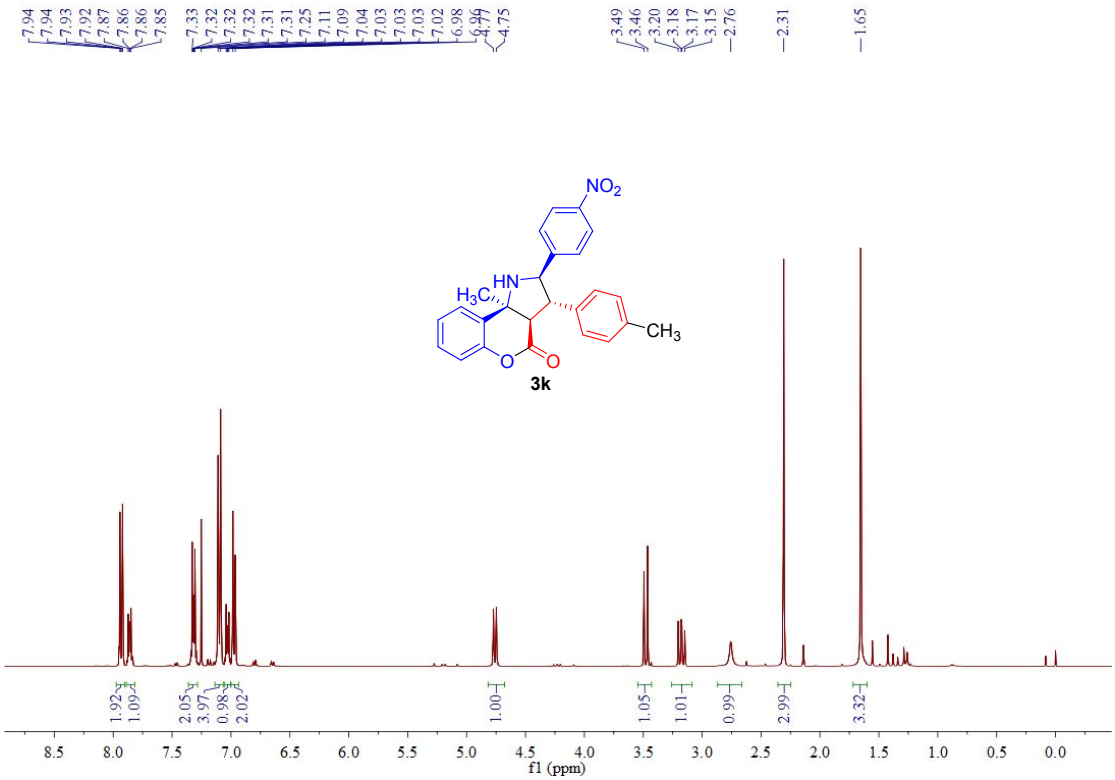
	RT	Area	Height	% Area
1	4.549	947174	81418	50.21
2	8.556	939254	45476	49.79

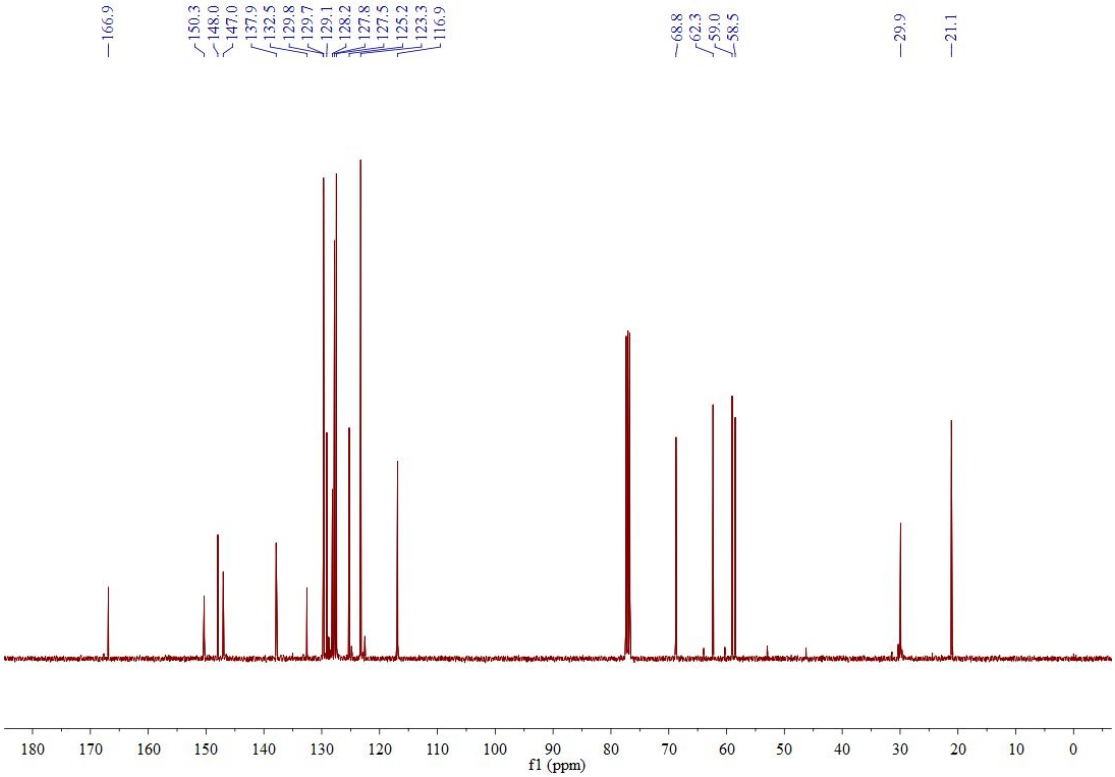


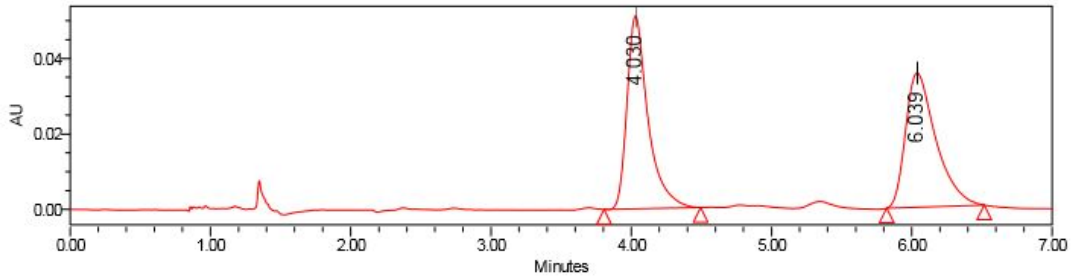
Peak Results

	RT	Area	Height	% Area
1	4.554	50864	3703	6.82
2	8.510	695450	30190	93.18

(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-2-(4-nitrophenyl)-3-(p-tolyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3k):

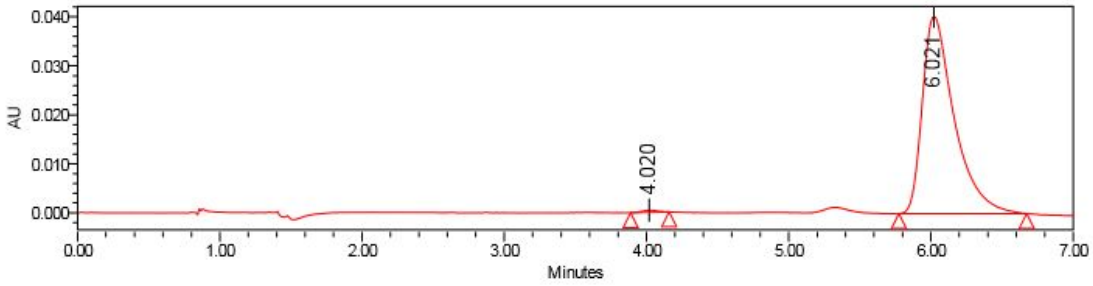






Peak Results

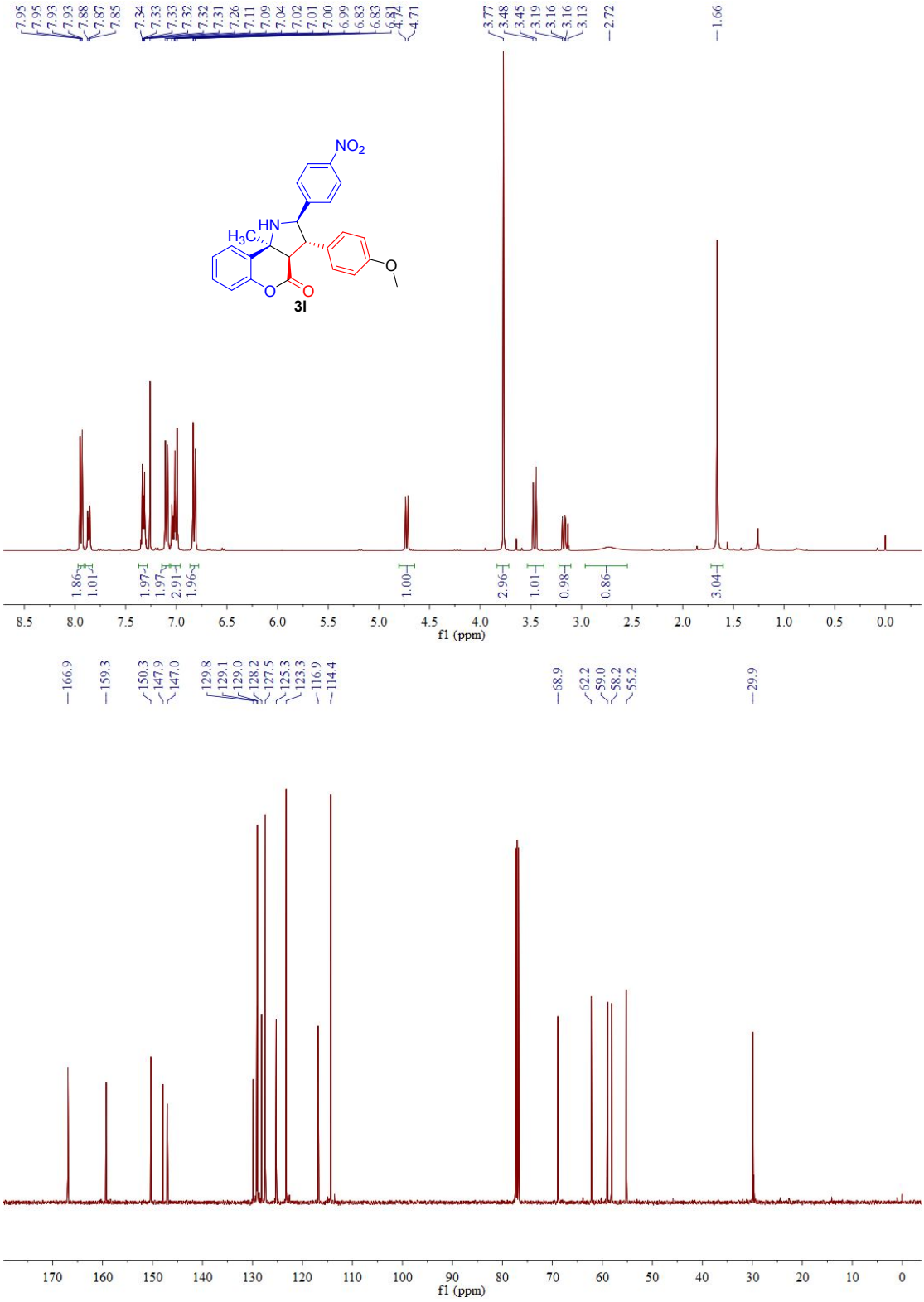
	RT	Area	Height	% Area
1	4.030	531553	51095	49.90
2	6.039	533640	35578	50.10

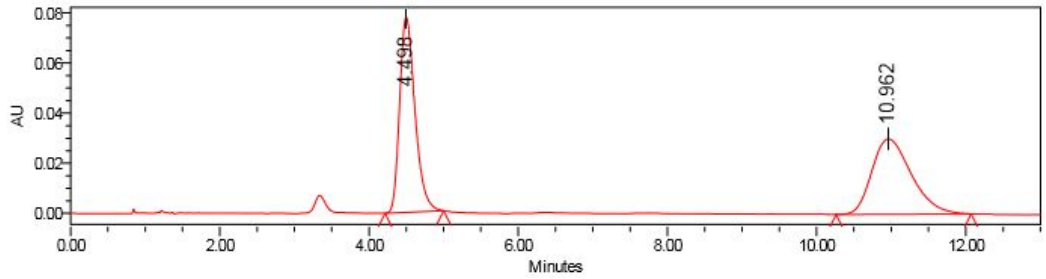


Peak Results

	RT	Area	Height	% Area
1	4.020	3214	445	0.51
2	6.021	626747	40262	99.49

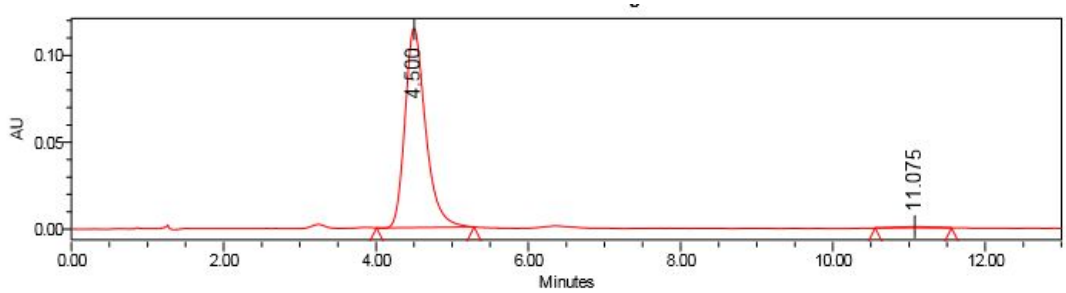
(2*R*,3*S*,3*aR*,9*bS*)-3-(4-methoxyphenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3l):





Peak Results

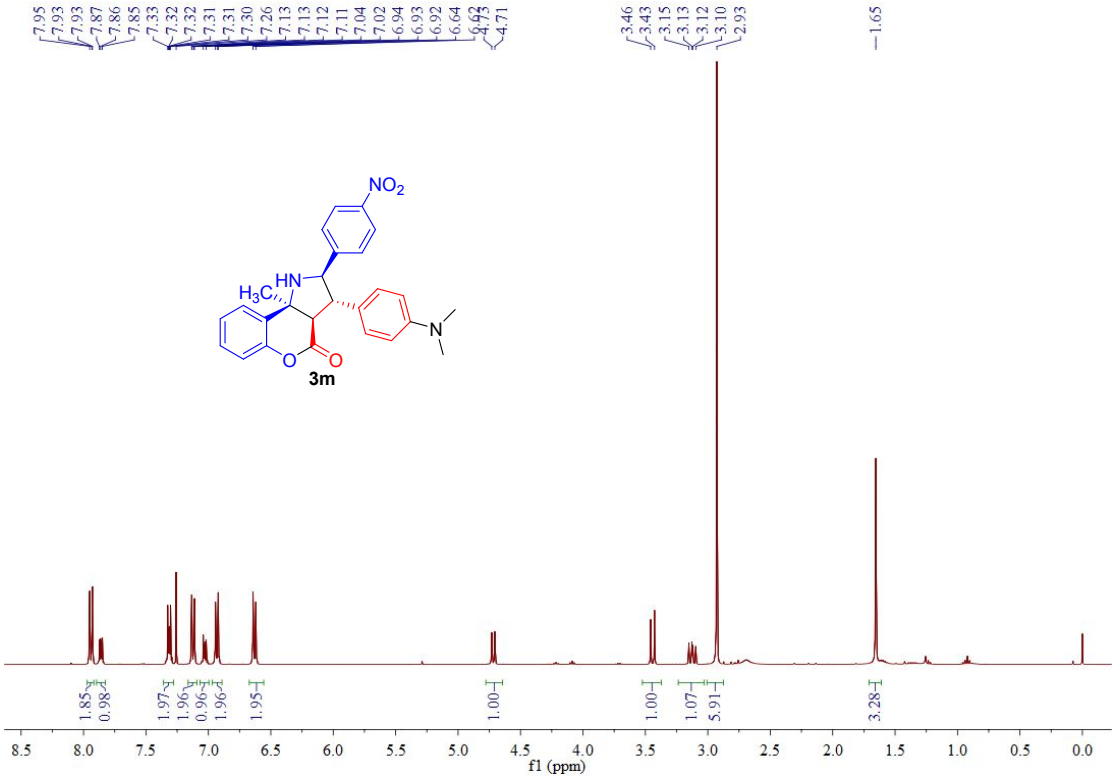
	RT	Area	Height	% Area
1	4.498	1109329	77799	50.06
2	10.962	1106815	30059	49.94

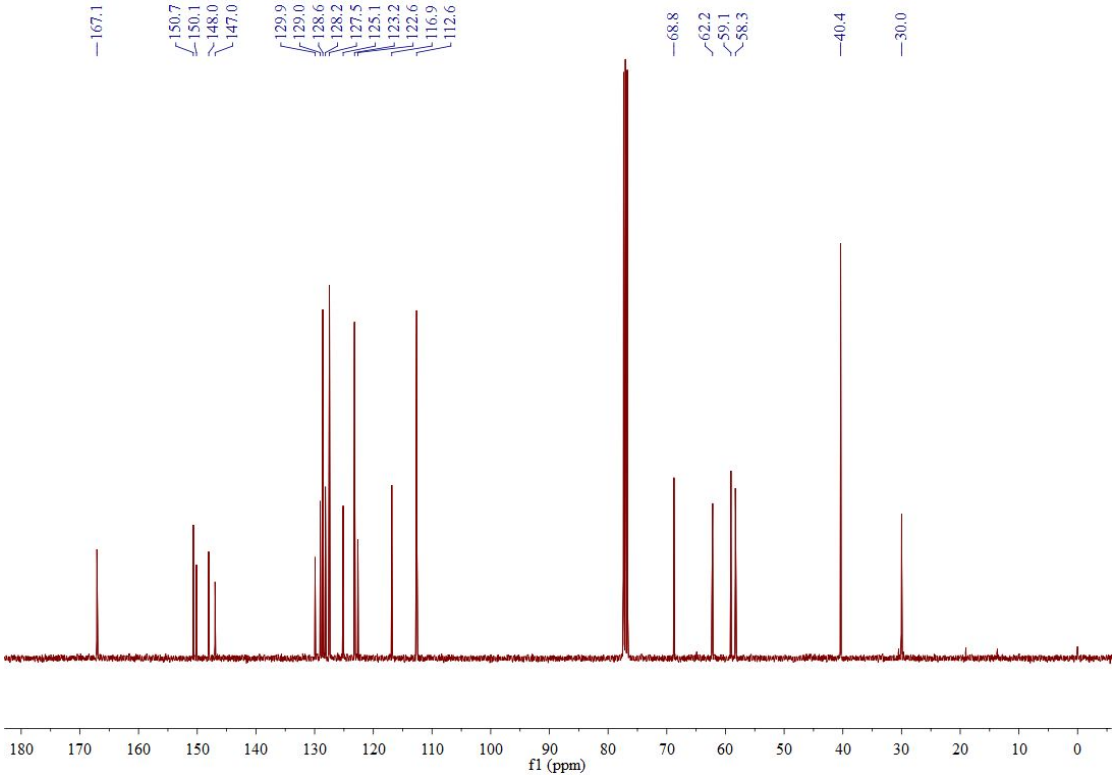


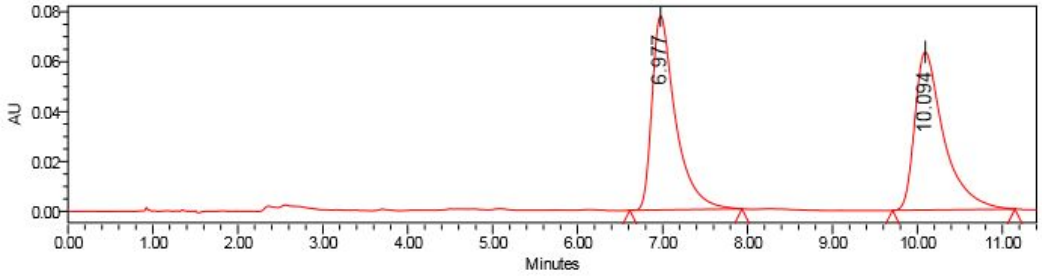
Peak Results

	RT	Area	Height	% Area
1	4.500	2146381	114526	98.91
2	11.075	23570	696	1.09

(2*R*,3*S*,3*aR*,9*bS*)-3-(4-(dimethylamino)phenyl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3m):

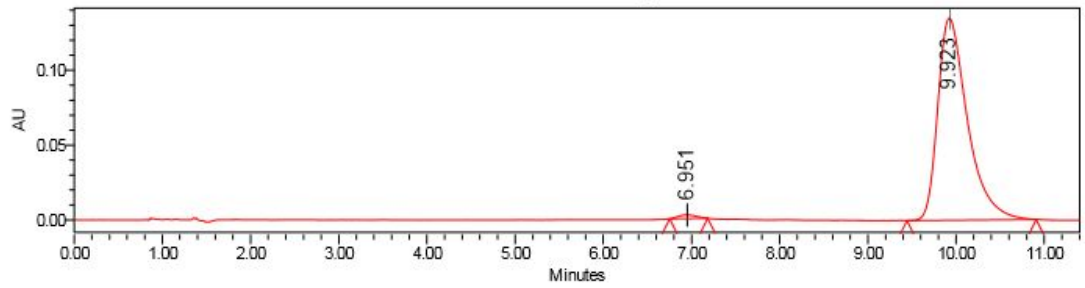






Peak Results

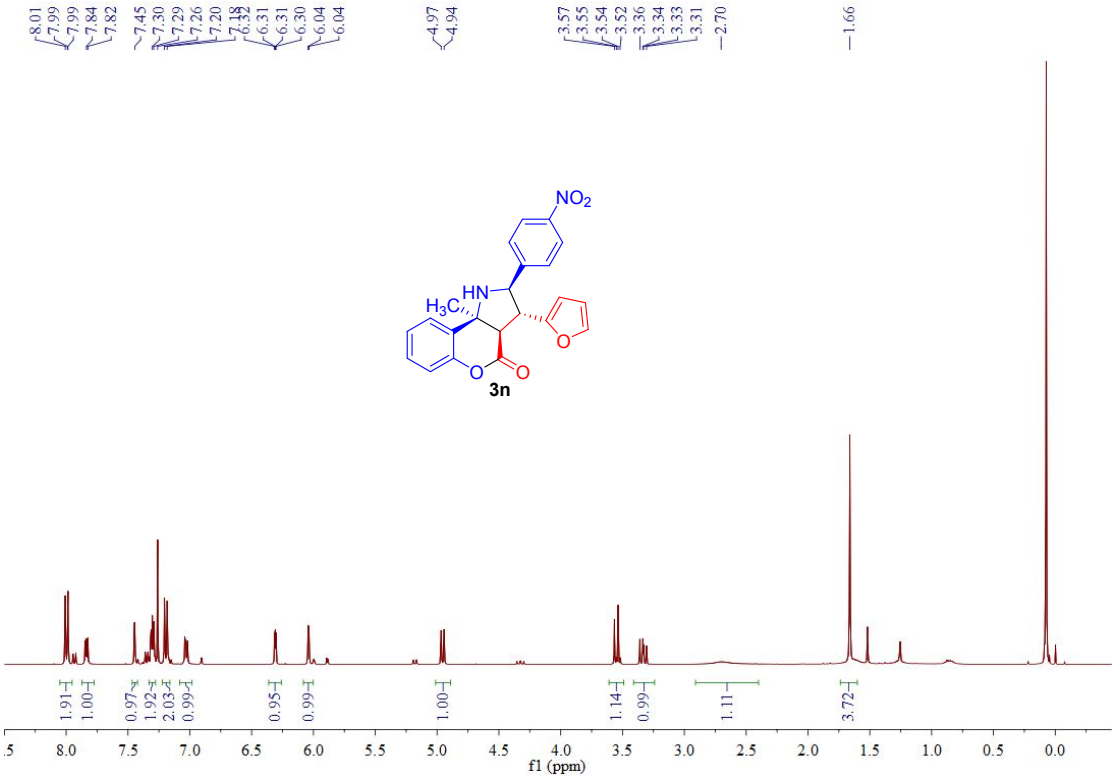
	RT	Area	Height	% Area
1	6.977	1496187	77800	49.88
2	10.094	1505256	63366	50.12

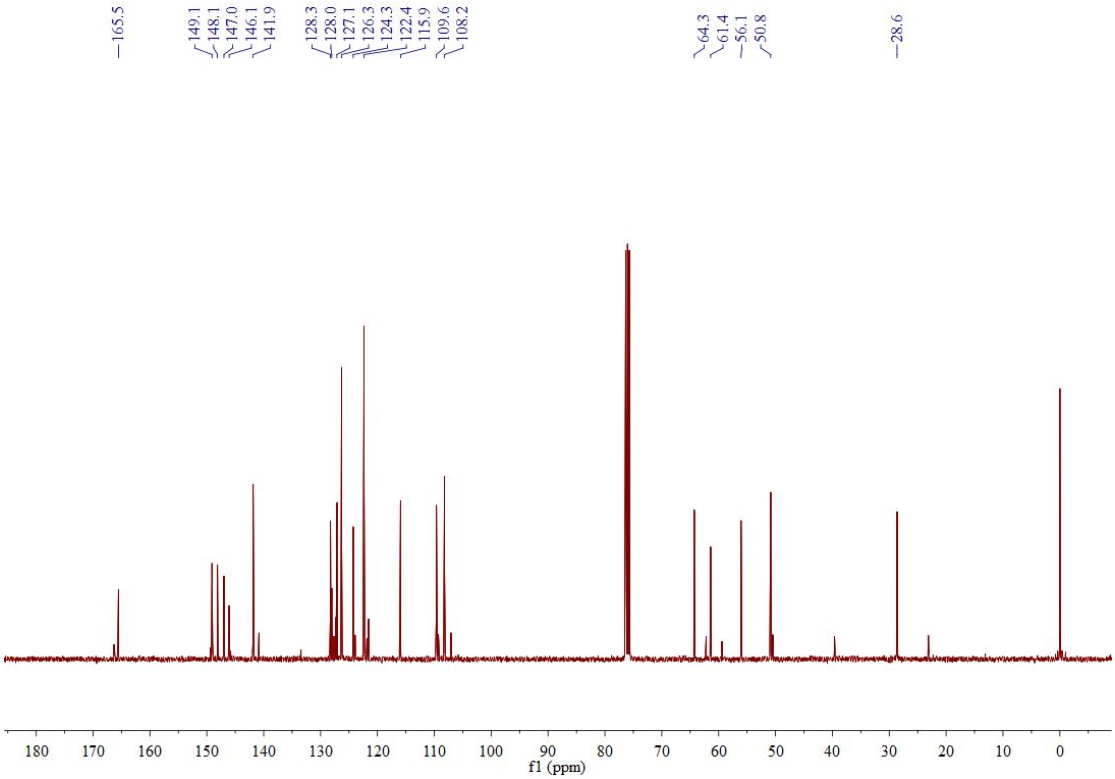


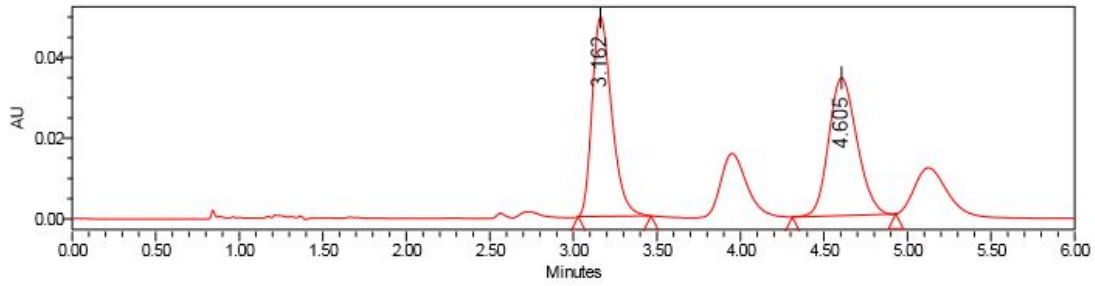
Peak Results

	RT	Area	Height	% Area
1	6.951	33804	2423	1.06
2	9.923	3143468	134681	98.94

(2*R*,3*R*,3*aR*,9*bS*)-3-(furan-2-yl)-9b-methyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3n):

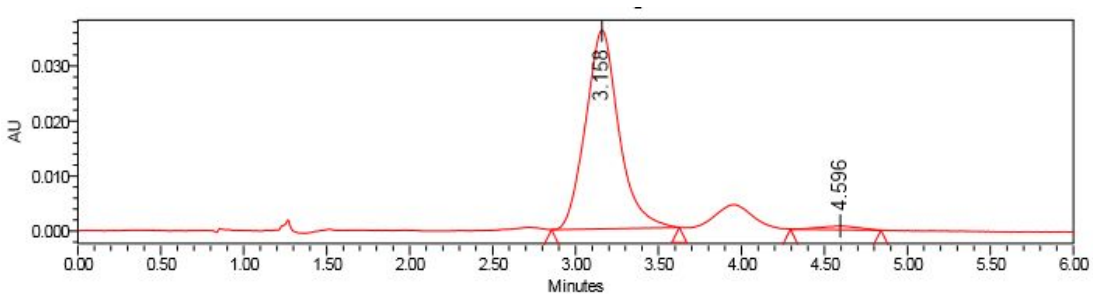






Peak Results

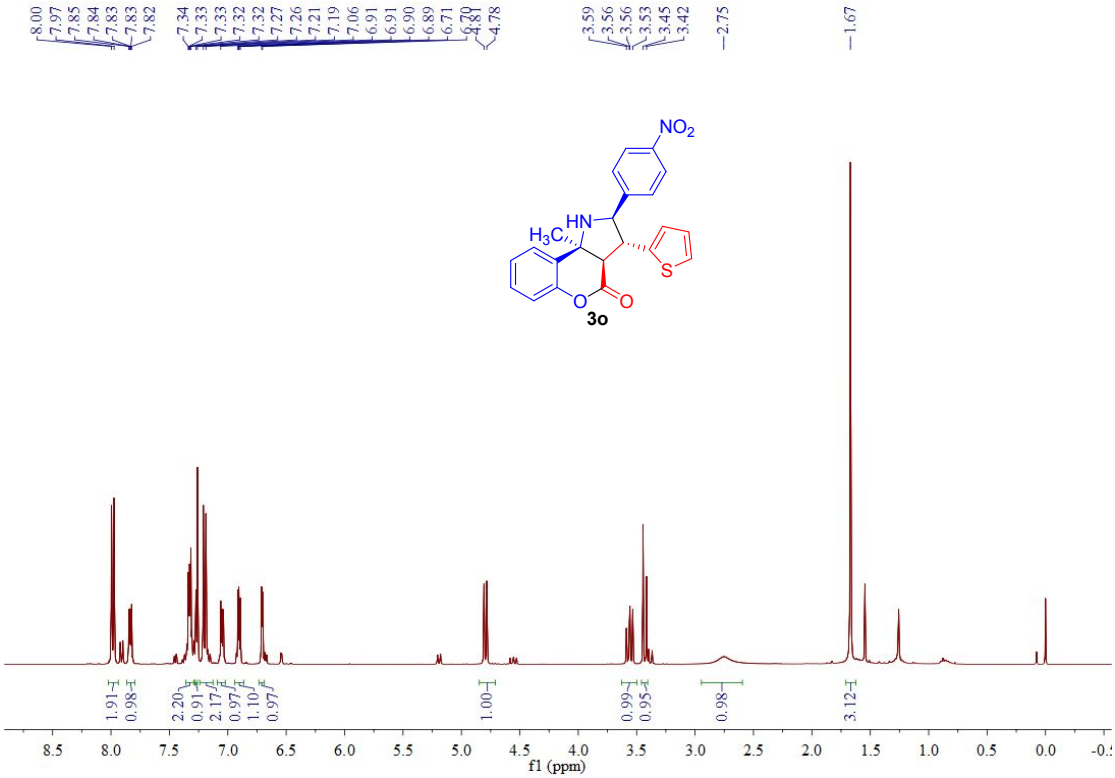
	RT	Area	Height	% Area
1	3.162	403869	49483	50.15
2	4.605	401375	34145	49.85

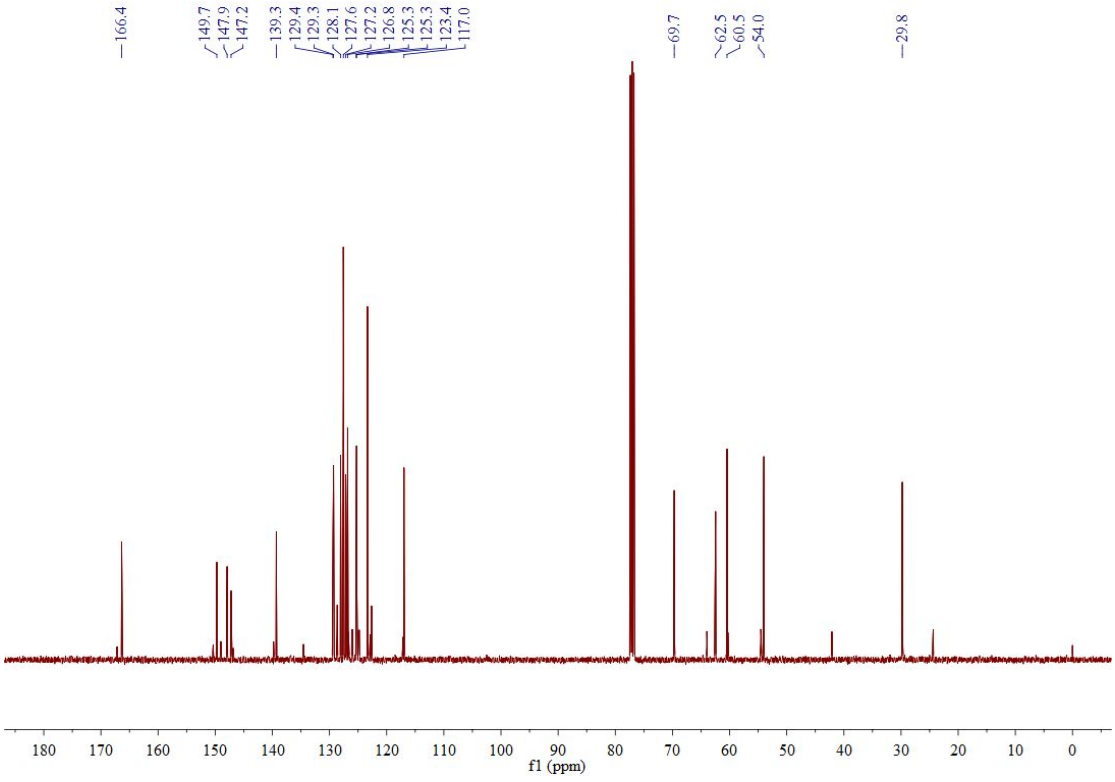


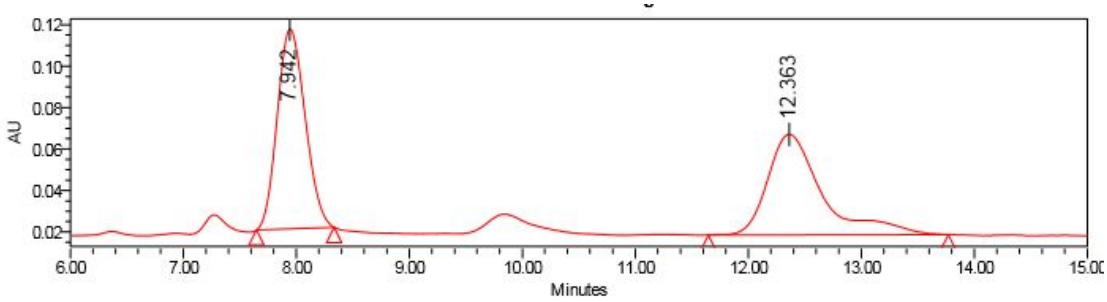
Peak Results

	RT	Area	Height	% Area
1	3.158	503555	36116	97.95
2	4.596	10535	669	2.05

(2*R*,3*R*,3*aR*,9*bS*)-9b-methyl-2-(4-nitrophenyl)-3-(thiophen-2-yl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3o):

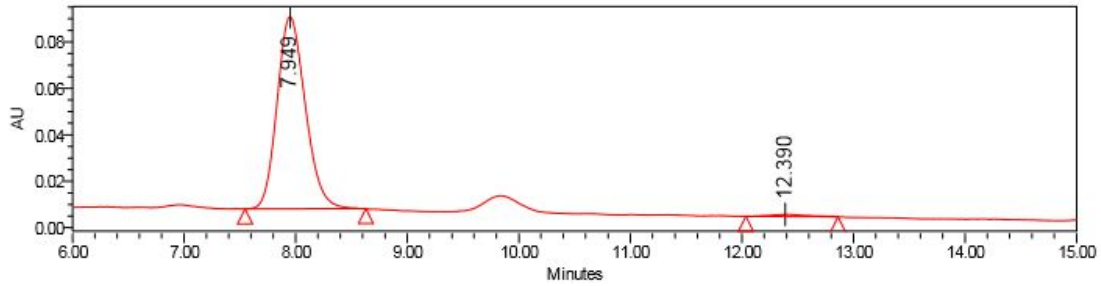






Peak Results

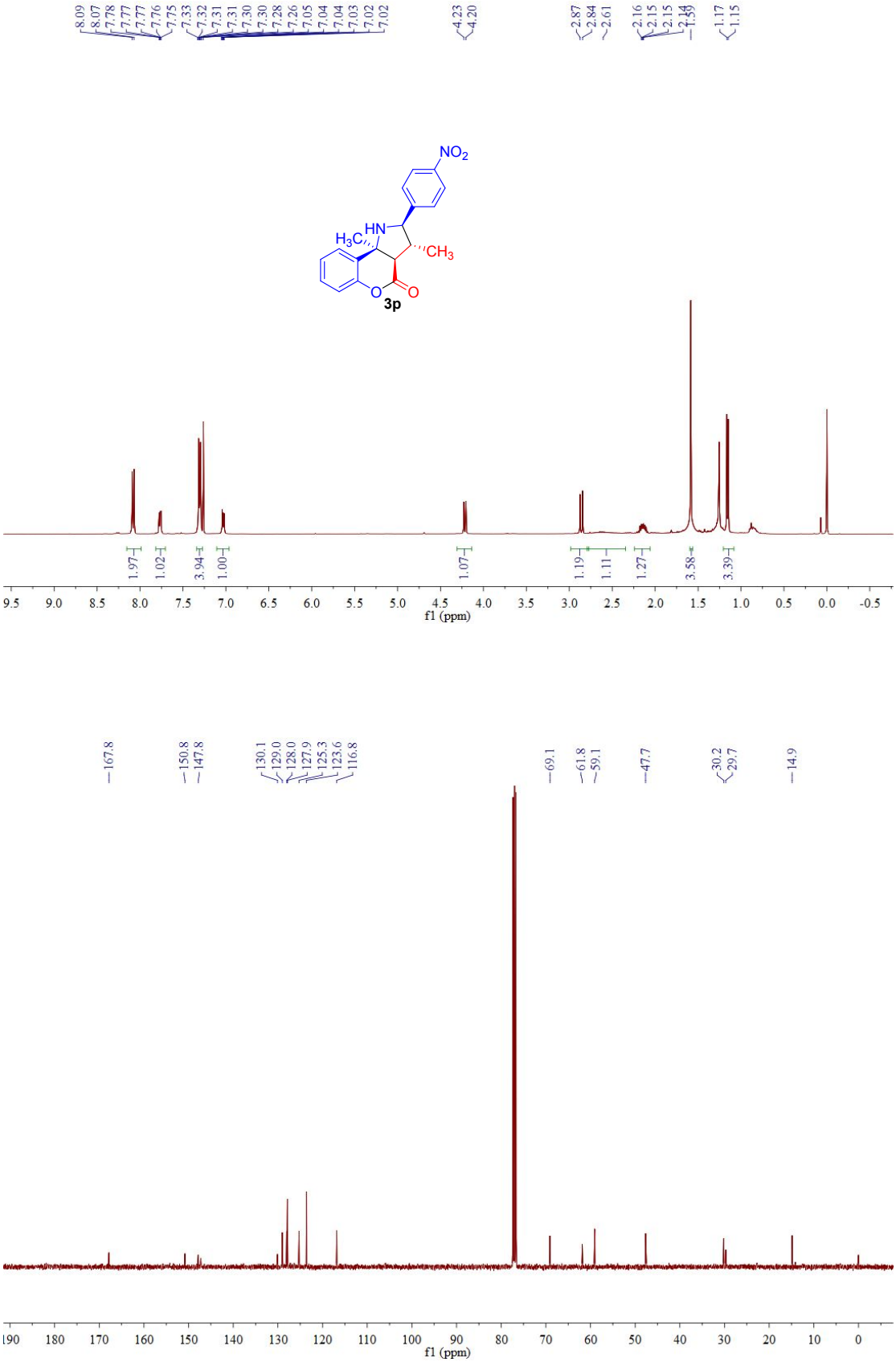
	RT	Area	Height	% Area
1	7.942	1652233	96386	50.33
2	12.363	1630792	48568	49.67

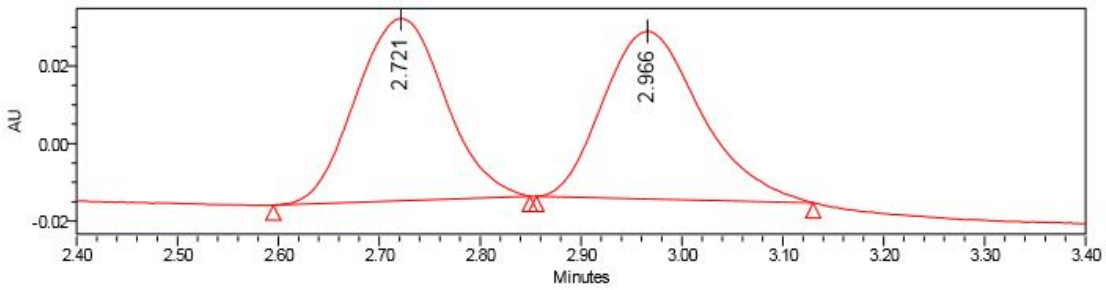


Peak Results

	RT	Area	Height	% Area
1	7.949	1454794	82722	98.54
2	12.390	21547	986	1.46

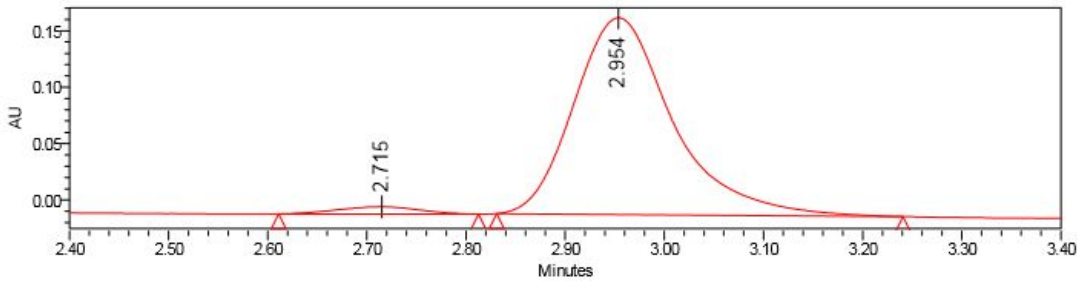
(2*R*,3*R*,3*aR*,9*bS*)-3,9b-dimethyl-2-(4-nitrophenyl)-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (3p):





Peak Results

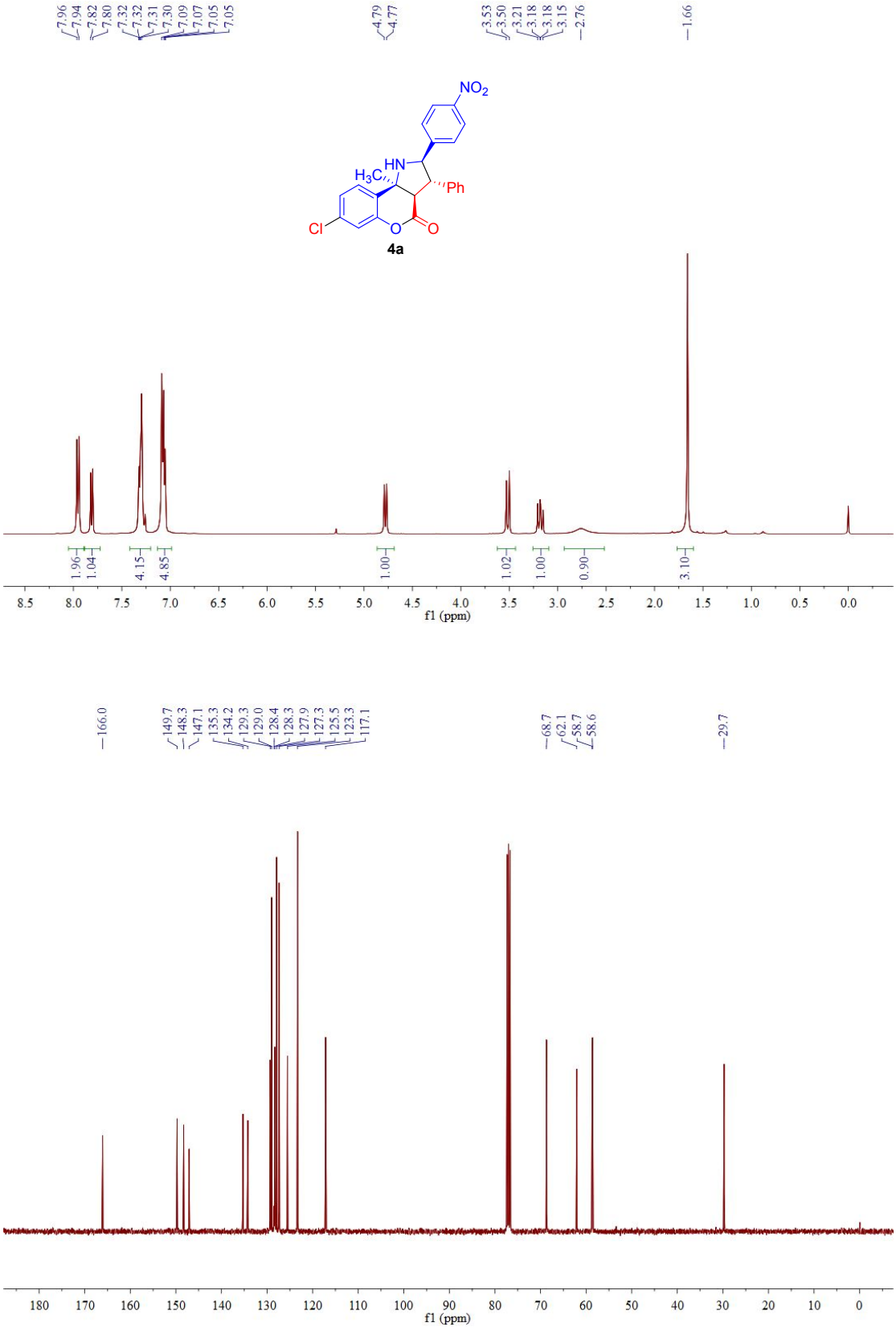
	RT	Area	Height	% Area
1	2.721	289376	46978	49.78
2	2.966	291913	43297	50.22

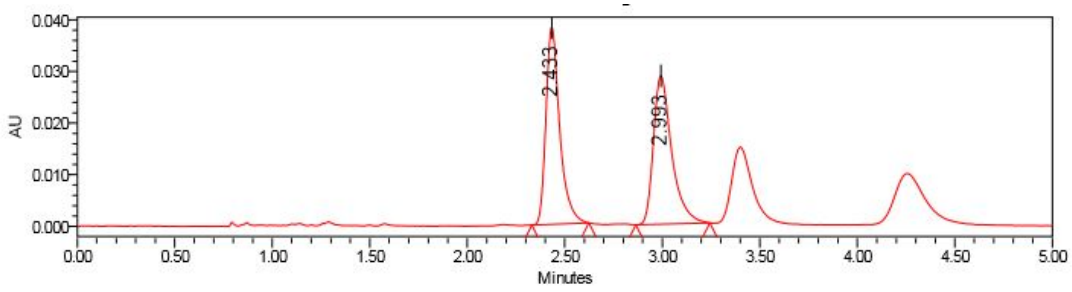


Peak Results

	RT	Area	Height	% Area
1	2.715	36657	6450	2.94
2	2.954	1209623	174407	97.06

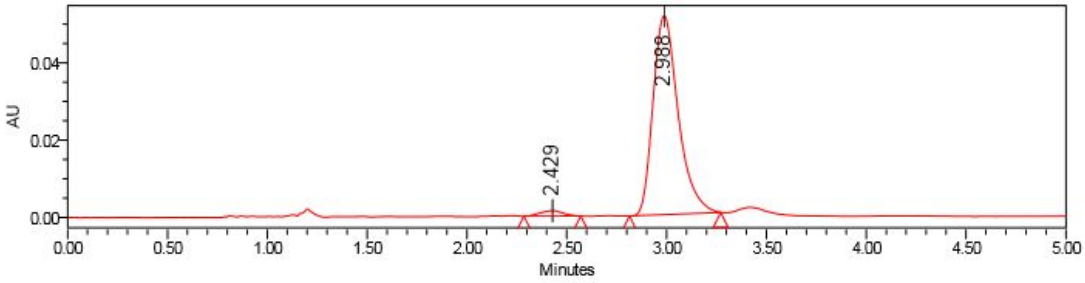
(2*R*,3*S*,3*aR*,9*bS*)-7-chloro-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4a):





Peak Results

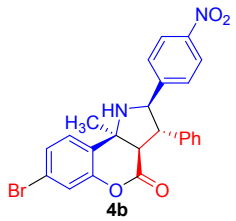
	RT	Area	Height	% Area
1	2.433	187036	38167	50.00
2	2.993	187015	28710	50.00

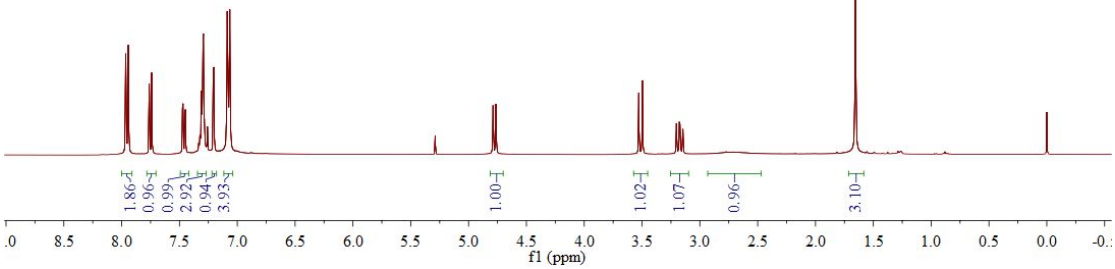


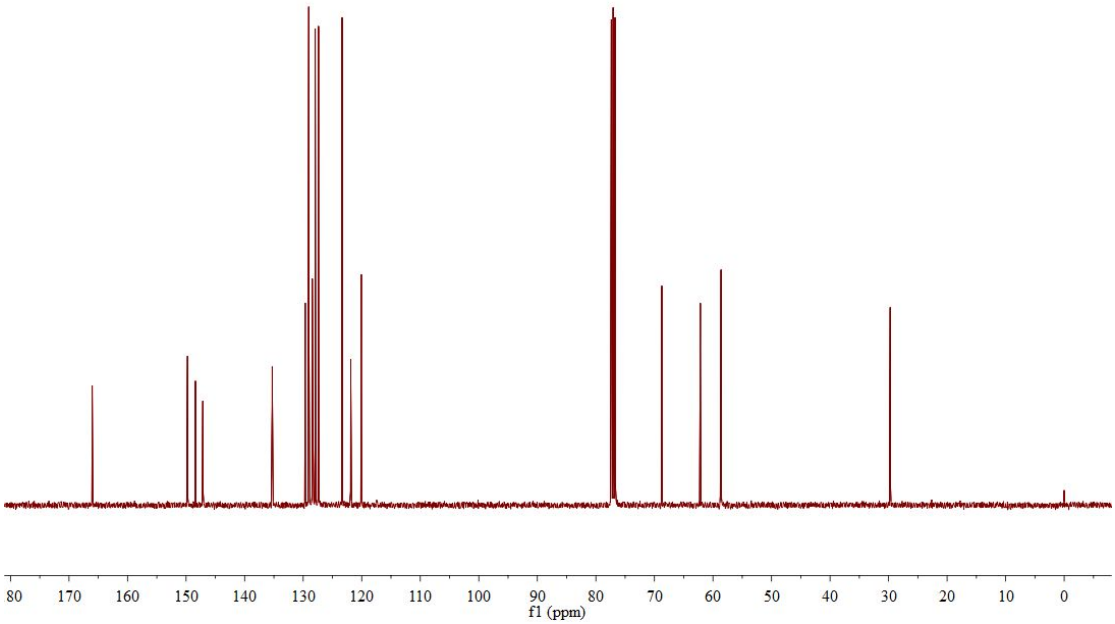
Peak Results

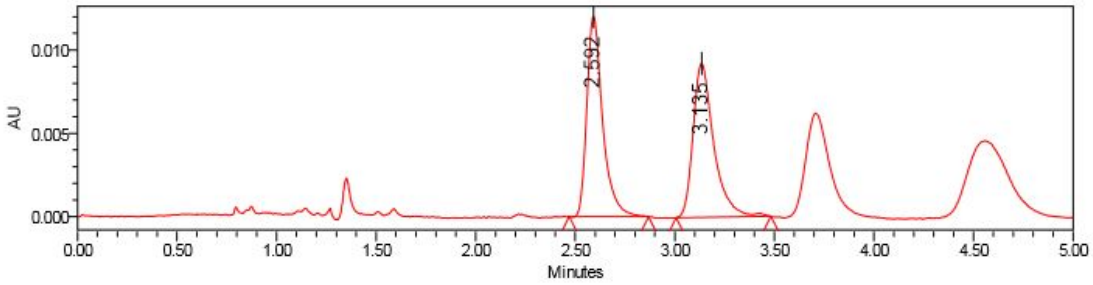
	RT	Area	Height	% Area
1	2.429	10922	1407	2.37
2	2.988	450848	51429	97.63

(2*R*,3*S*,3*aR*,9*bS*)-7-bromo-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4b):



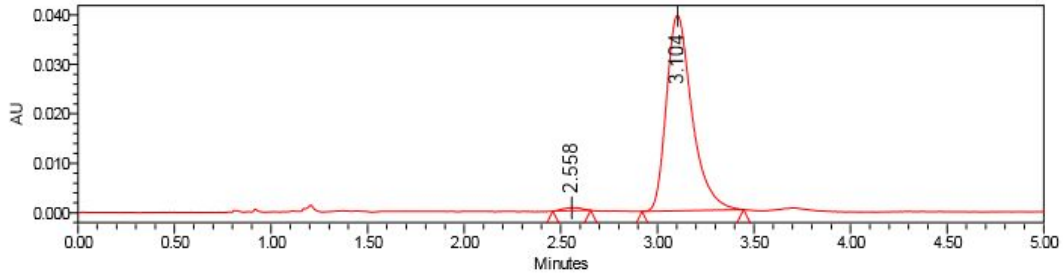






Peak Results

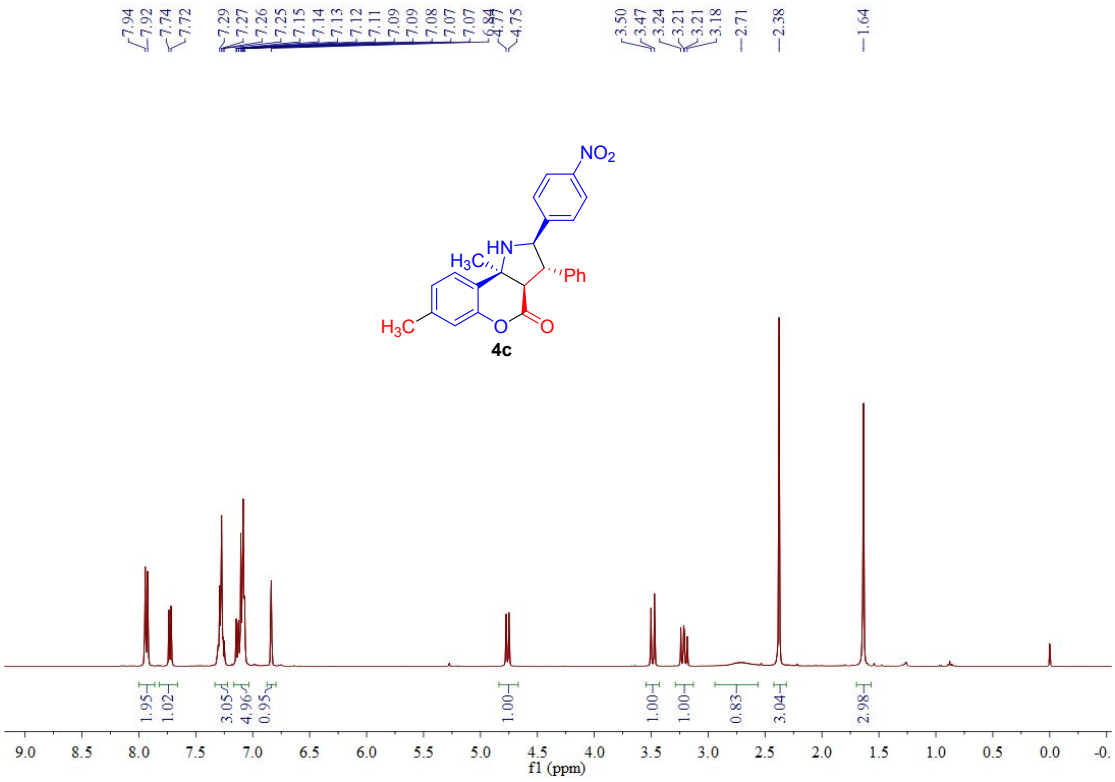
	RT	Area	Height	% Area
1	2.592	66372	12006	49.87
2	3.135	66718	9231	50.13

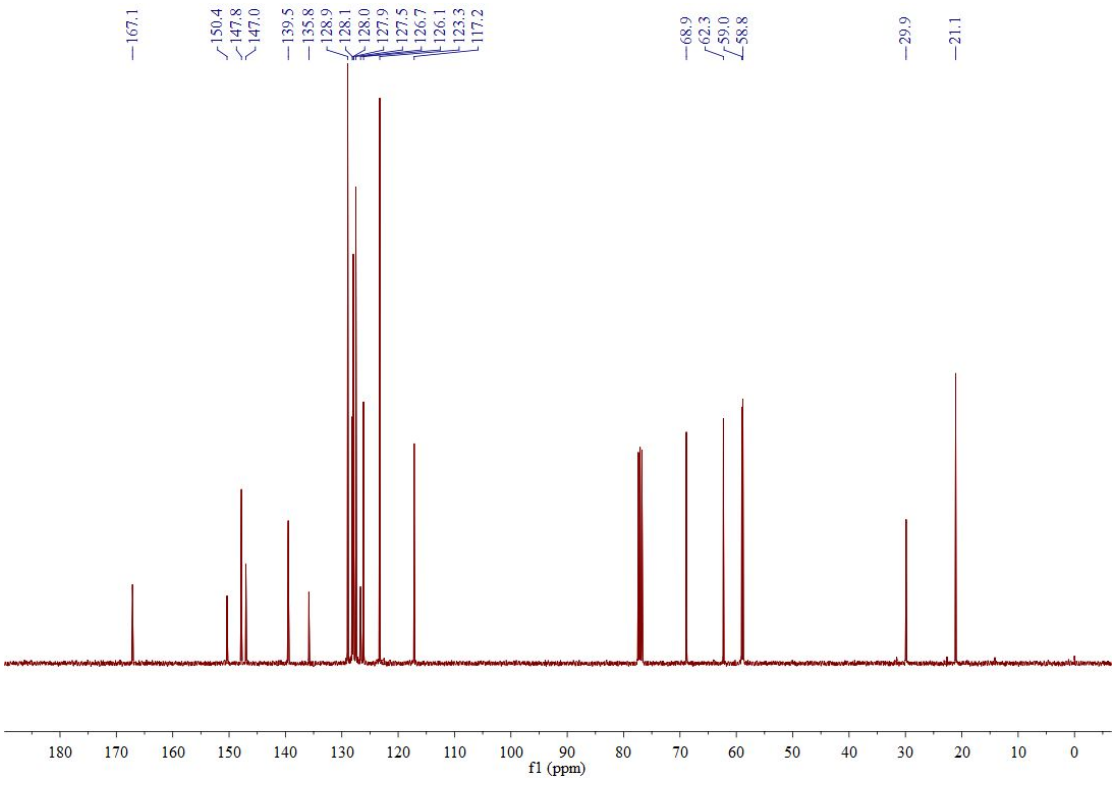


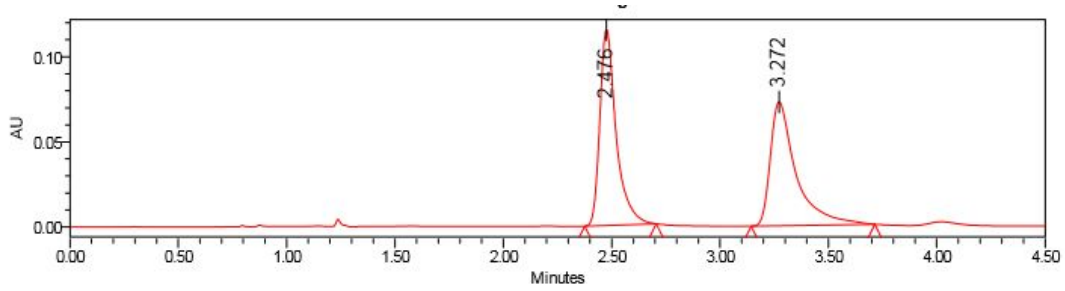
Peak Results

	RT	Area	Height	% Area
1	2.558	3913	599	1.06
2	3.104	364261	39486	98.94

(2R,3S,3aR,9bS)-7,9b-dimethyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-b]pyrrol-4(1*H*)-one (4c):

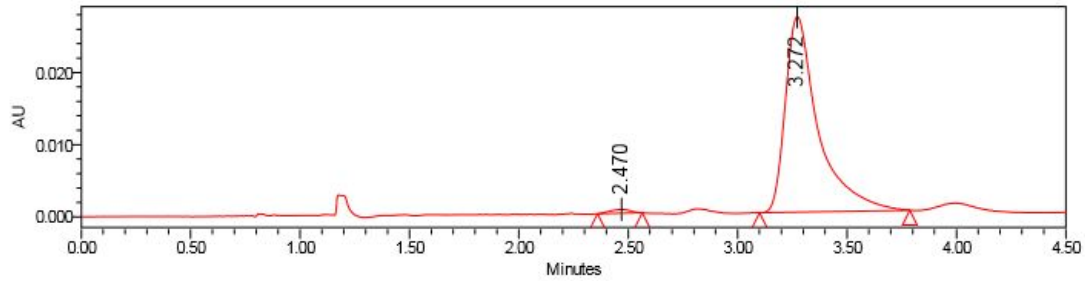






Peak Results

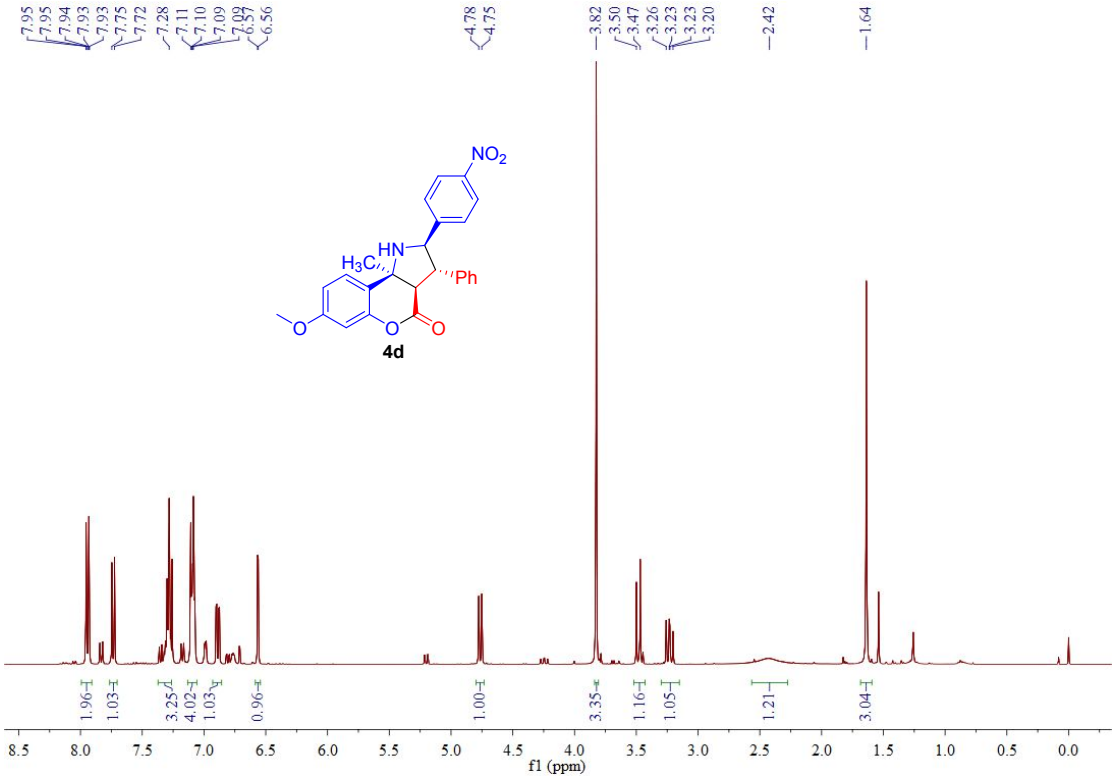
	RT	Area	Height	% Area
1	2.476	602956	115148	50.08
2	3.272	601047	72791	49.92

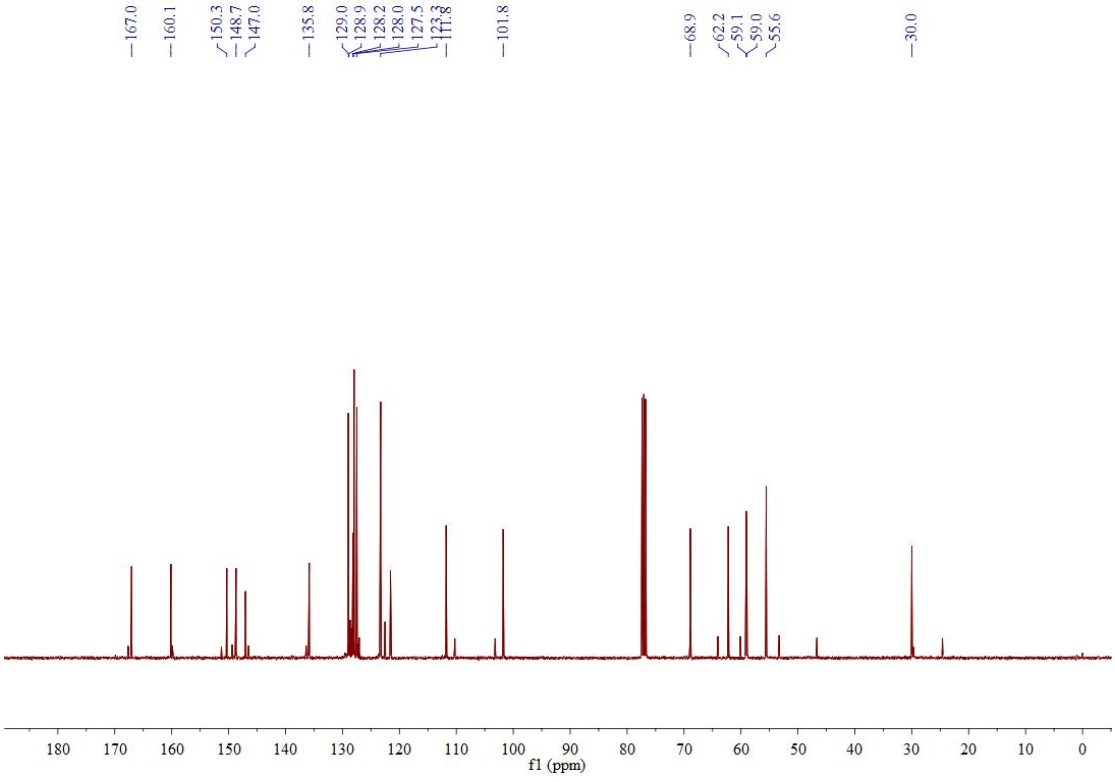


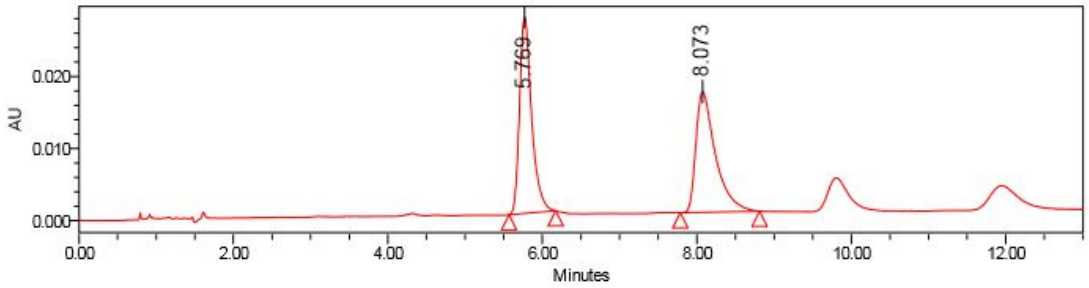
Peak Results

	RT	Area	Height	% Area
1	2.470	3511	554	1.22
2	3.272	284154	27107	98.78

(2*R*,3*S*,3*aR*,9*bS*)-7-methoxy-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4d):

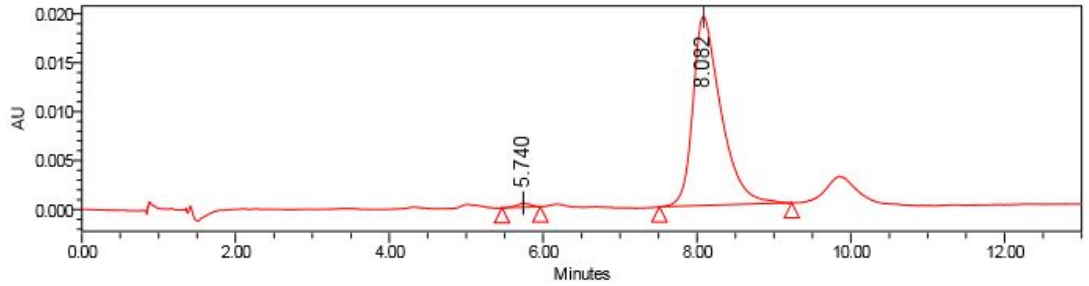






Peak Results

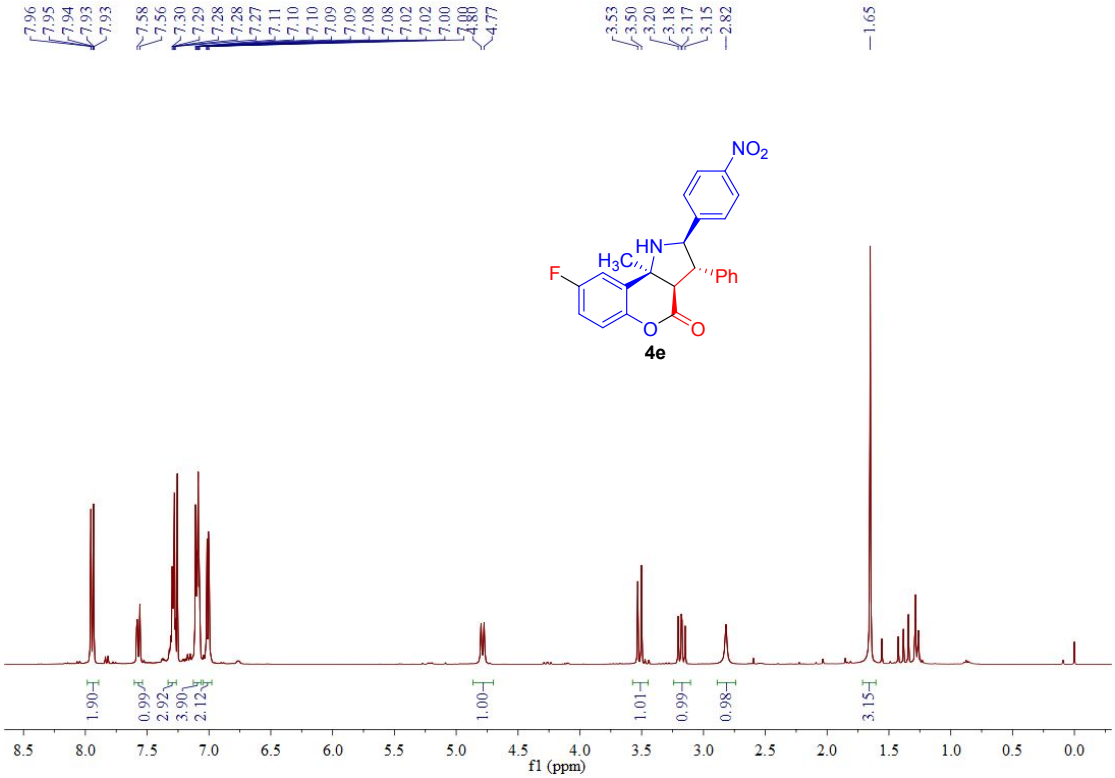
	RT	Area	Height	% Area
1	5.769	295002	27263	50.07
2	8.073	294204	16715	49.93

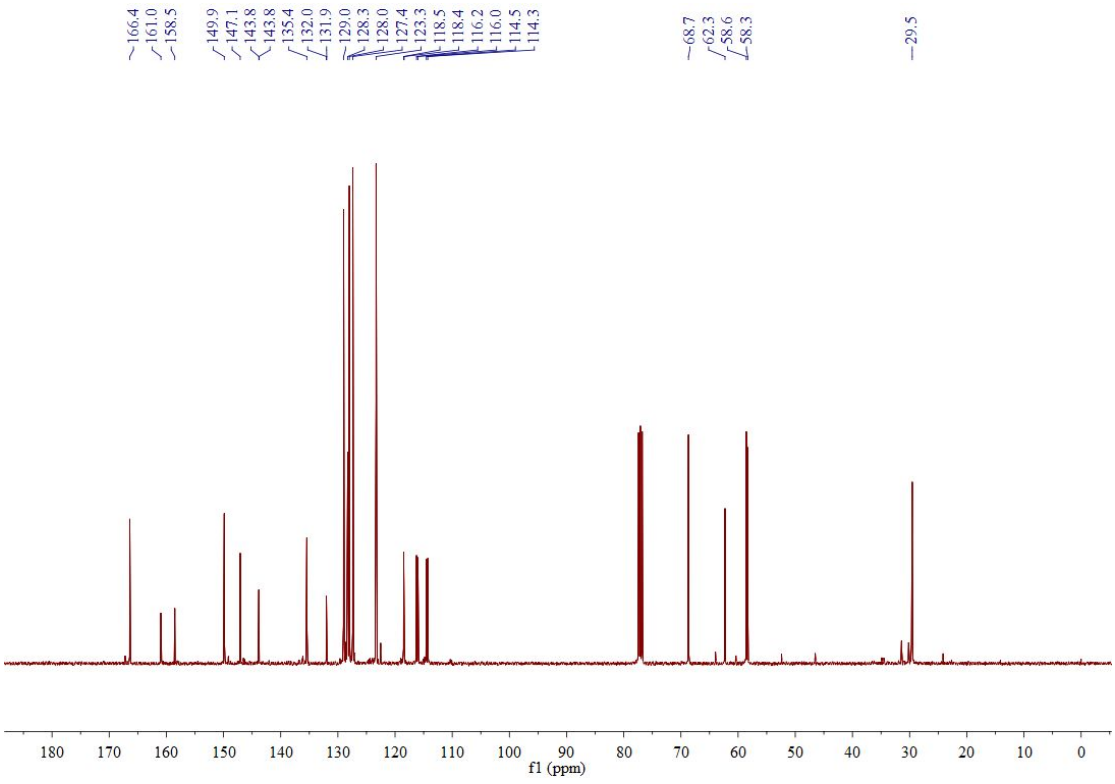


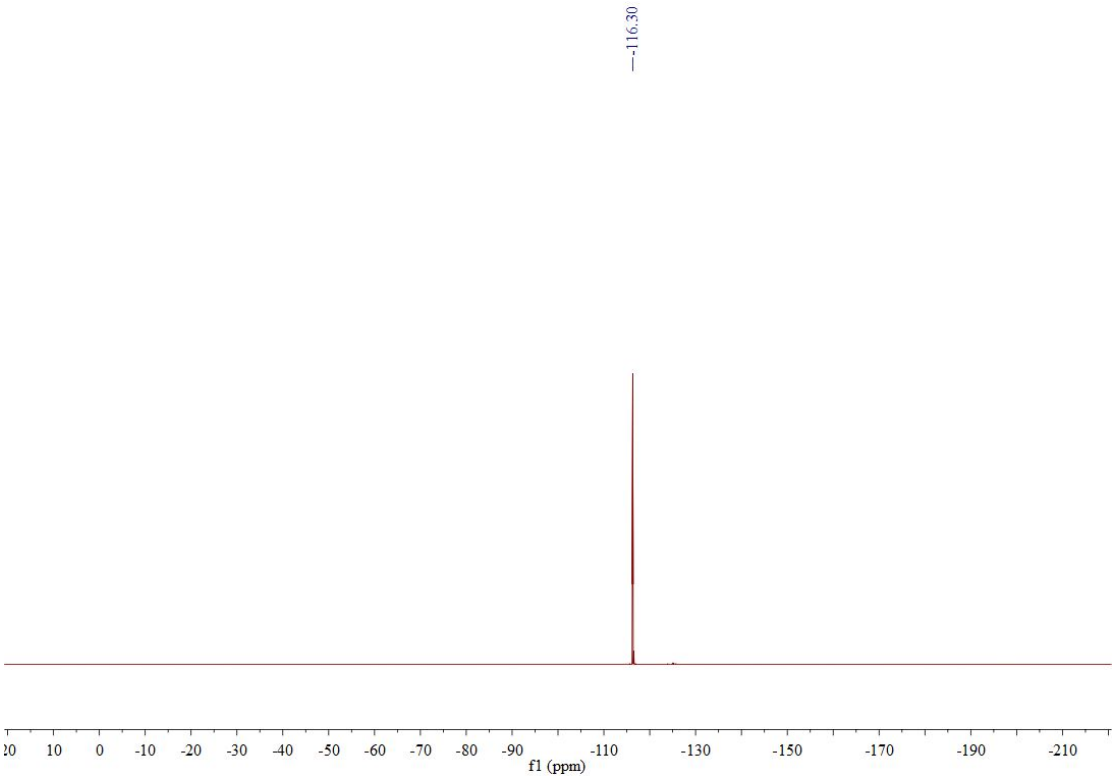
Peak Results

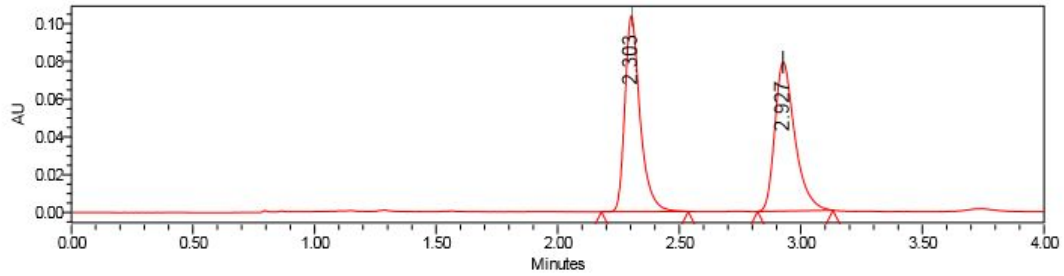
	RT	Area	Height	% Area
1	5.740	5138	433	1.03
2	8.082	493710	19339	98.97

(2*R*,3*S*,3*aR*,9*bS*)-8-fluoro-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4e):



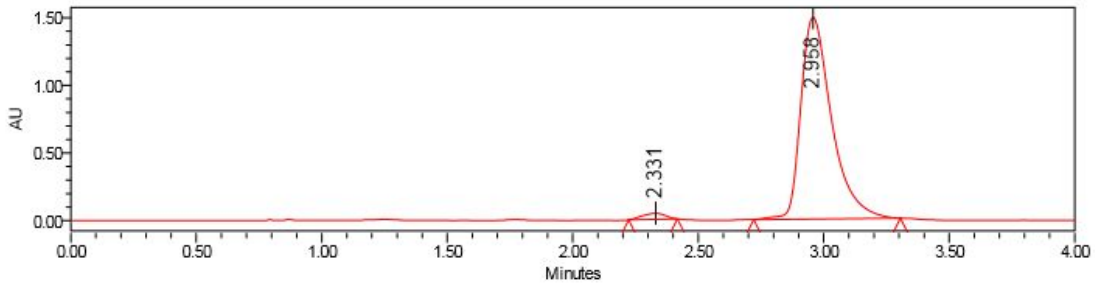






Peak Results

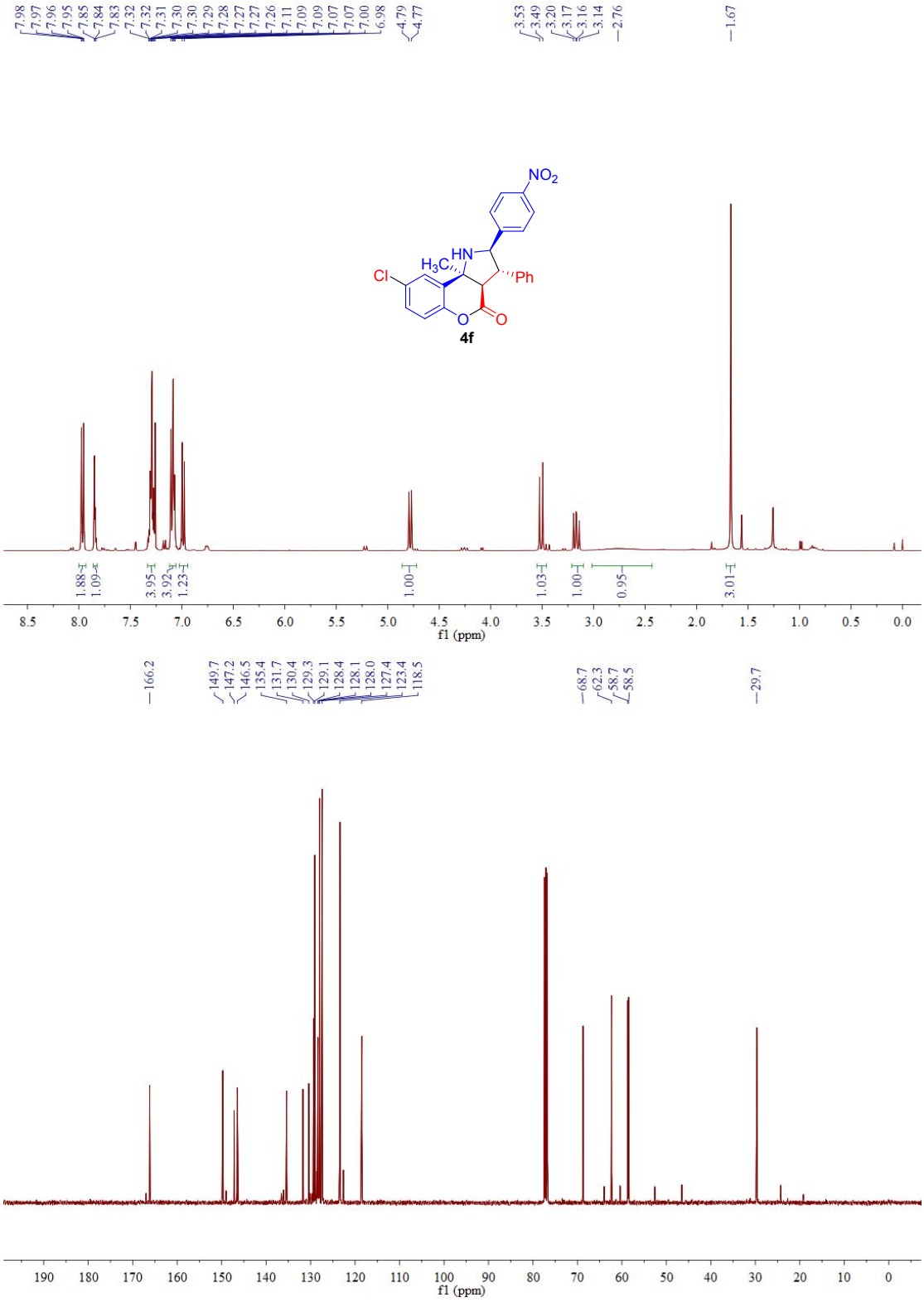
	RT	Area	Height	% Area
1	2.303	452080	103763	49.91
2	2.927	453637	78894	50.09

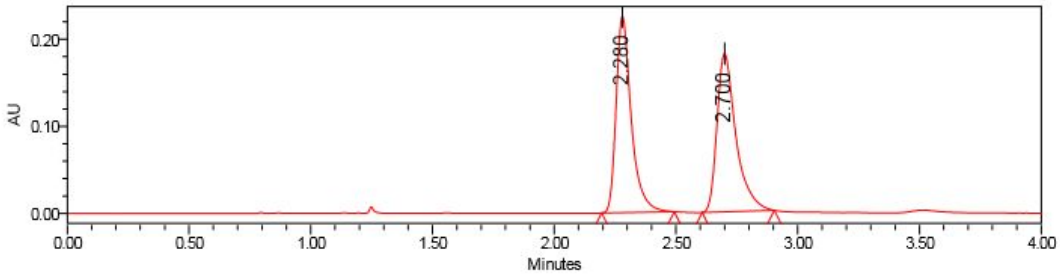


Peak Results

	RT	Area	Height	% Area
1	2.331	285743	44792	2.19
2	2.958	12748621	1490201	97.81

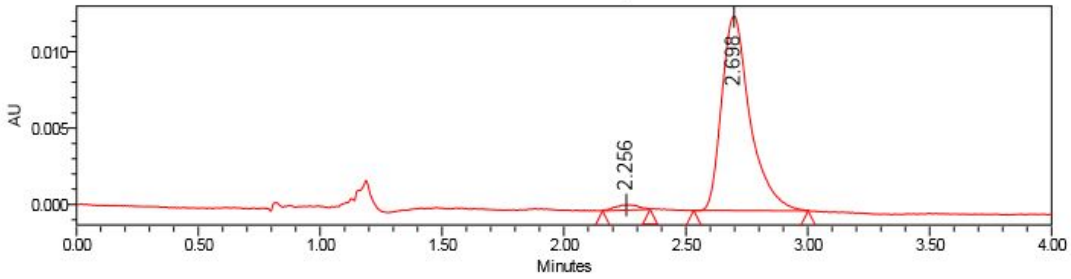
(2*R*,3*S*,3*aR*,9*bS*)-8-chloro-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4f):





Peak Results

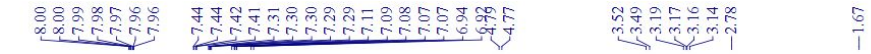
	RT	Area	Height	% Area
1	2.280	976713	225384	49.81
2	2.700	984318	181632	50.19

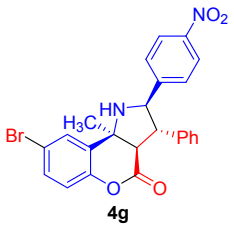


Peak Results

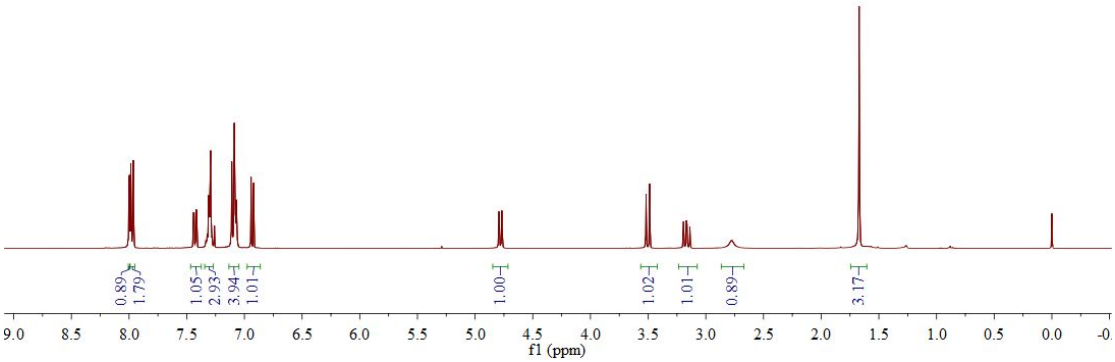
	RT	Area	Height	% Area
1	2.256	2227	338	2.11
2	2.698	103127	12732	97.89

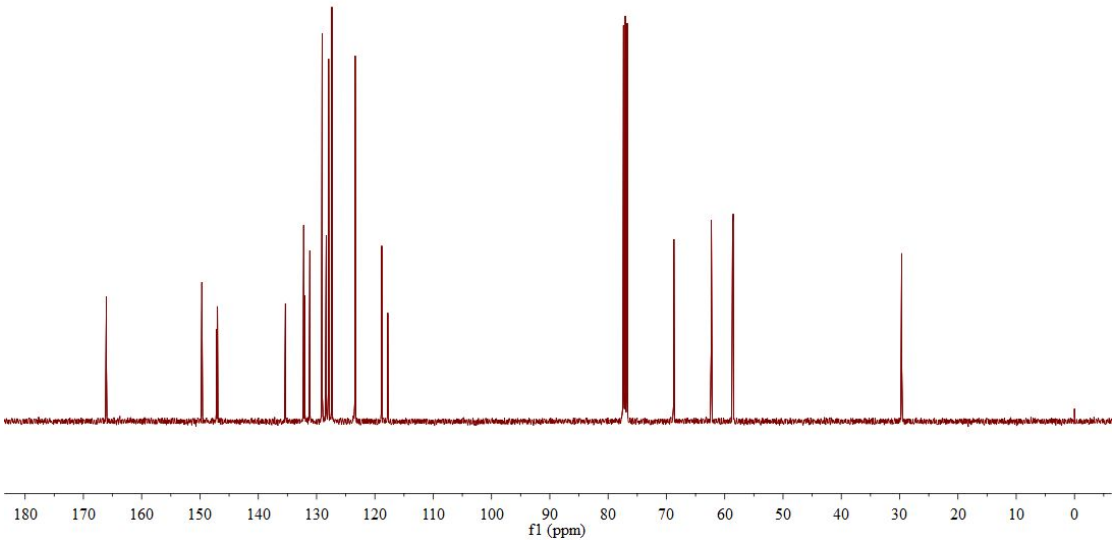
(2*R*,3*S*,3*aR*,9*bS*)-8-bromo-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4g):

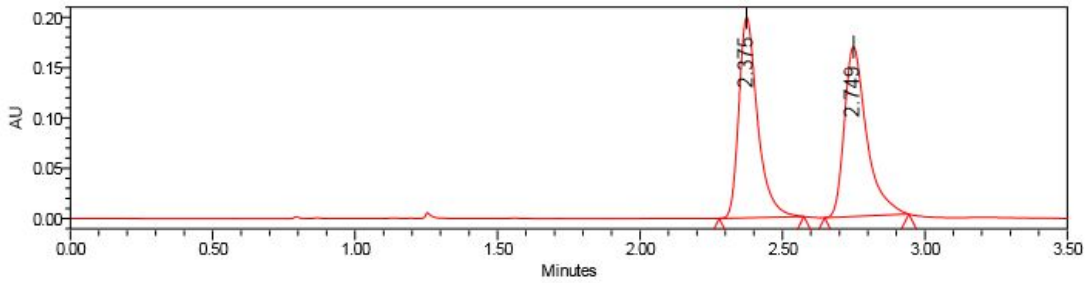




4g

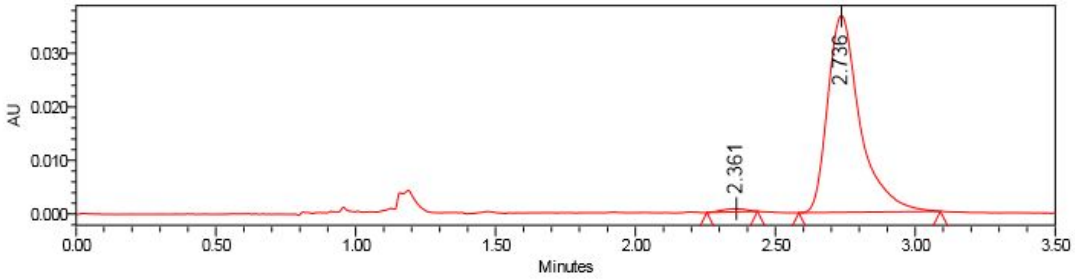






Peak Results

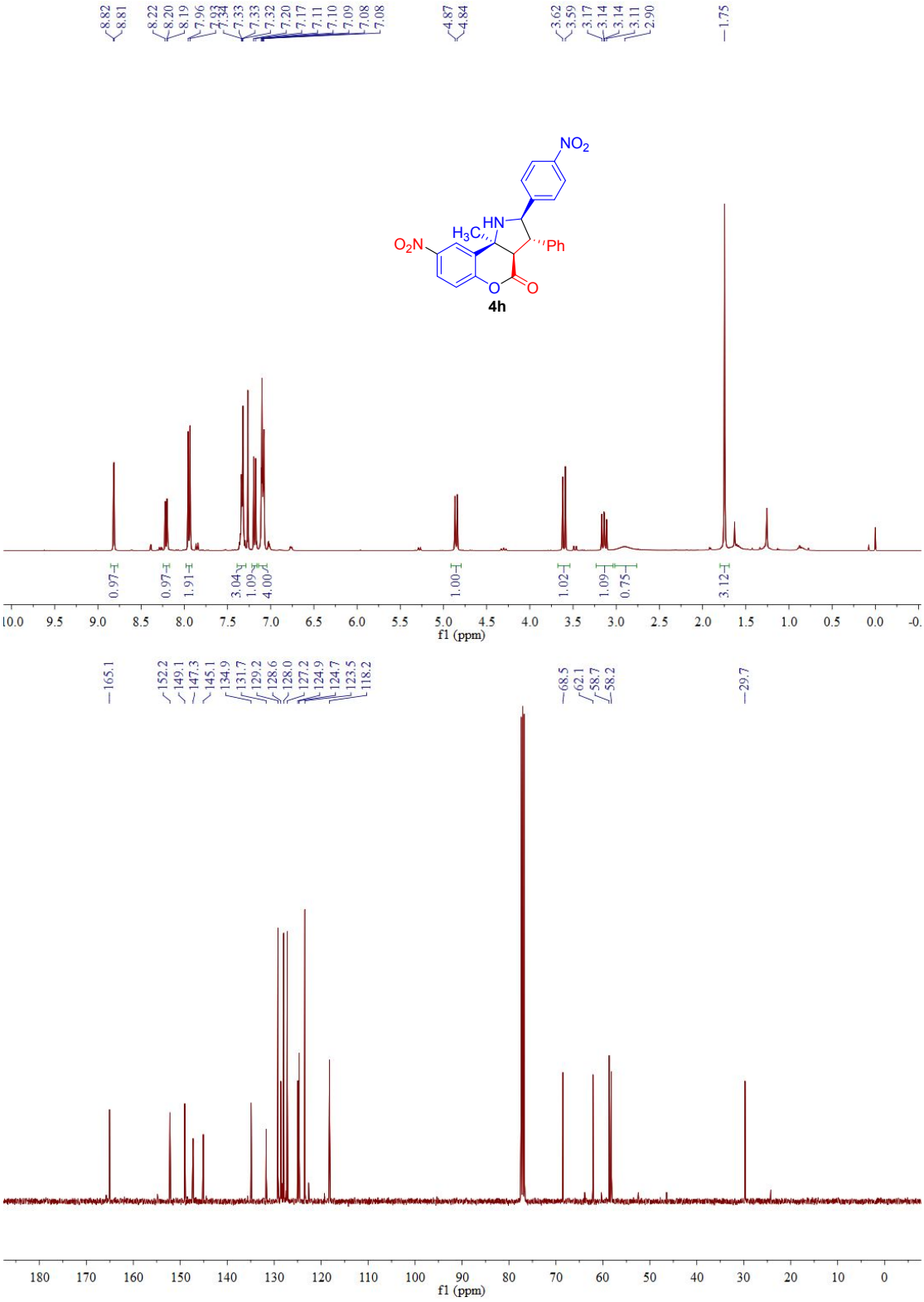
	RT	Area	Height	% Area
1	2.375	914581	199231	49.87
2	2.749	919259	168532	50.13

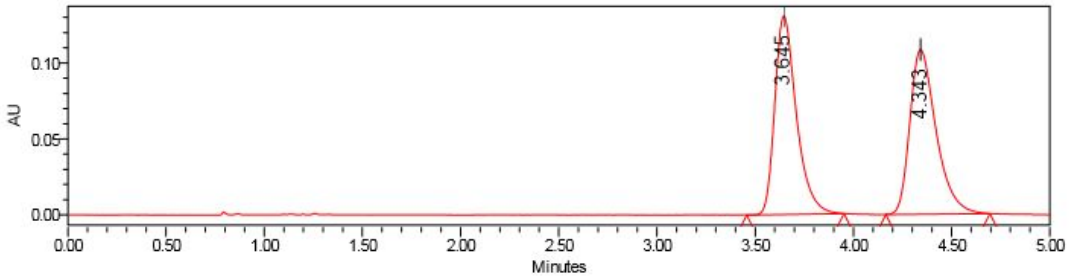


Peak Results

	RT	Area	Height	% Area
1	2.361	3440	598	1.15
2	2.736	295787	36748	98.85

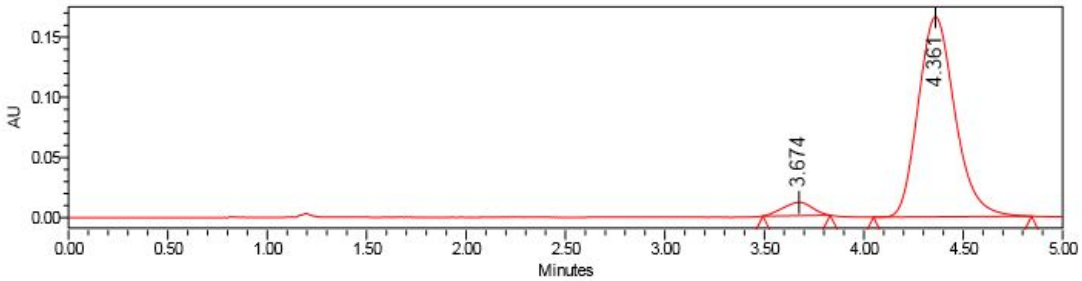
(2*R*,3*S*,3*aR*,9*bS*)-9b-methyl-8-nitro-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4h):





Peak Results

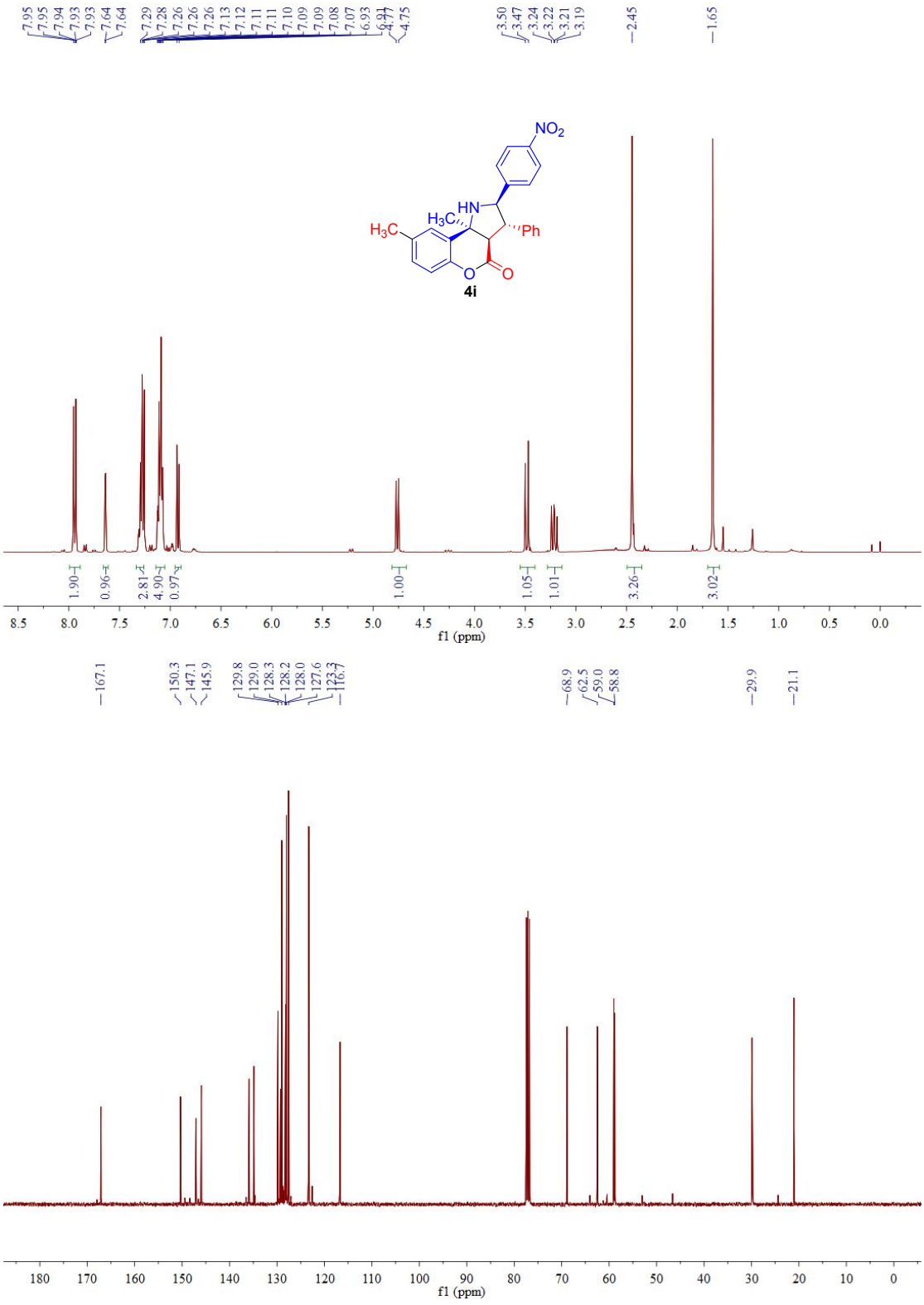
	RT	Area	Height	% Area
1	3.645	1001037	130691	49.86
2	4.343	1006640	108432	50.14

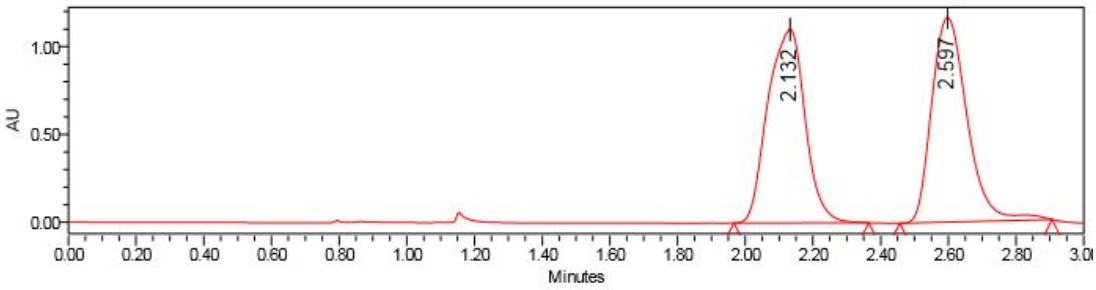


Peak Results

	RT	Area	Height	% Area
1	3.674	112329	11046	5.00
2	4.361	2133771	166200	95.00

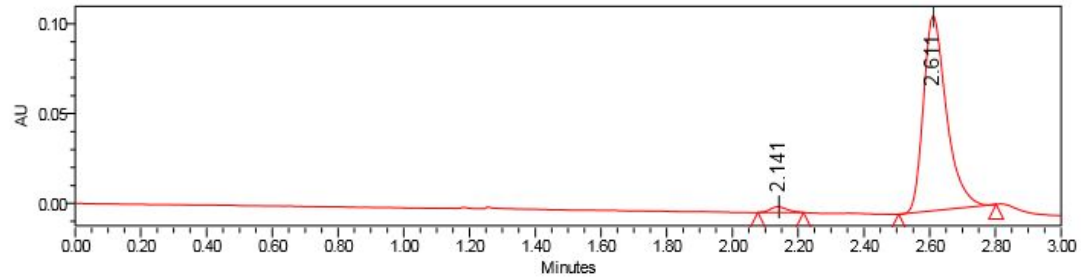
(2*R*,3*S*,3*aR*,9*bS*)-8,9b-dimethyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4i):





Peak Results

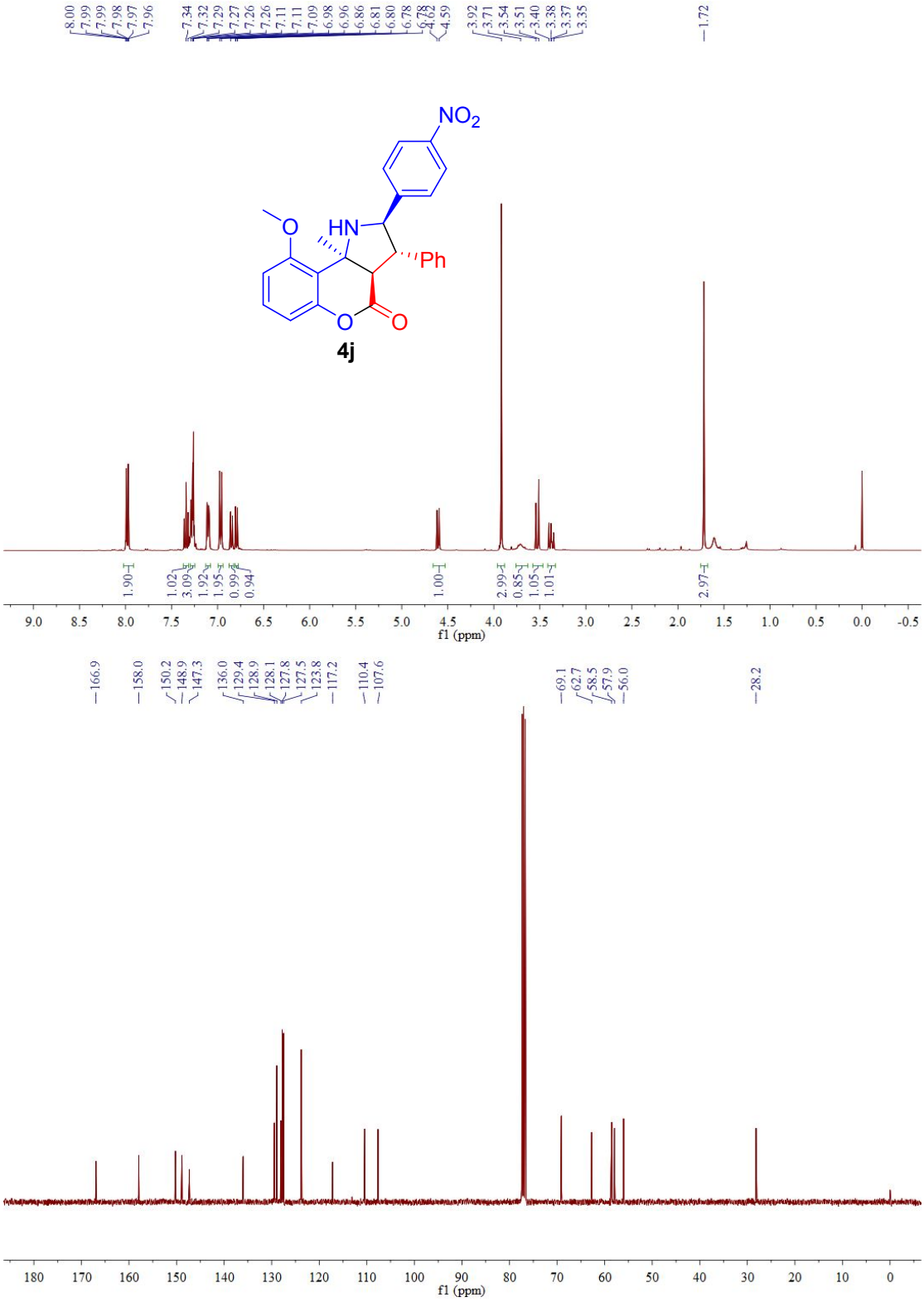
	RT	Area	Height	% Area
1	2.132	8429765	1101046	49.89
2	2.597	8467458	1164739	50.11

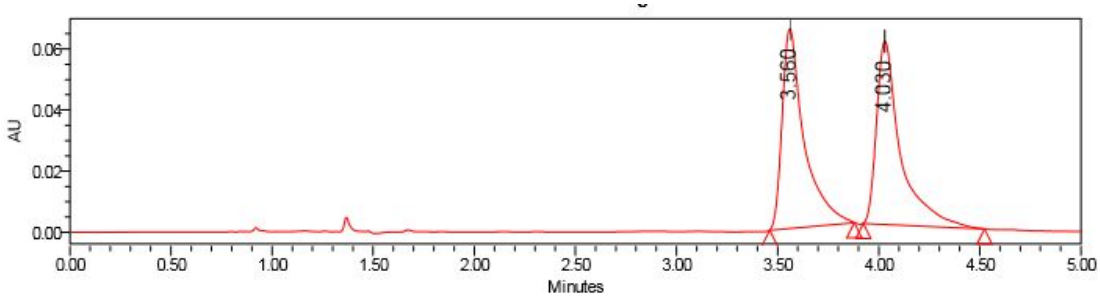


Peak Results

	RT	Area	Height	% Area
1	2.141	11535	3192	2.13
2	2.611	530089	108450	97.87

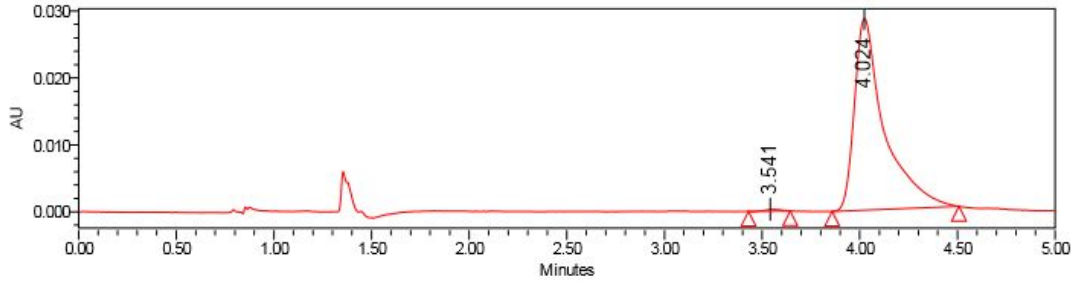
(2*R*,3*S*,3*aR*,9*bS*)-9-methoxy-9b-methyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4j):





Peak Results

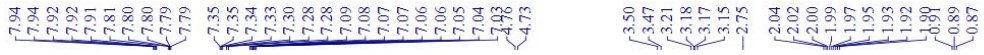
	RT	Area	Height	% Area
1	3.560	494881	65317	50.00
2	4.030	494871	60014	50.00

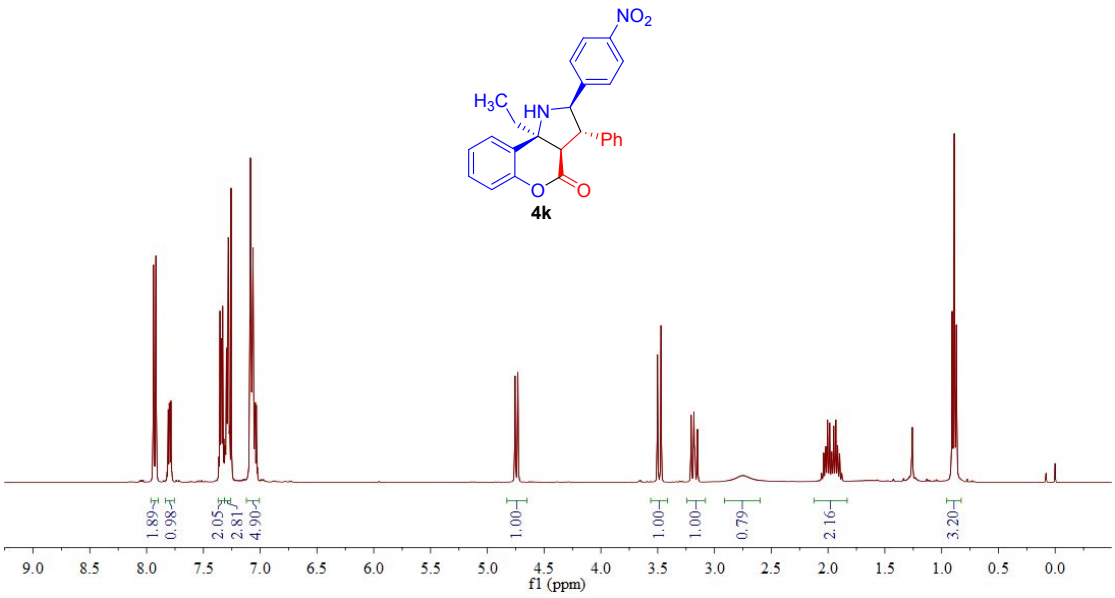


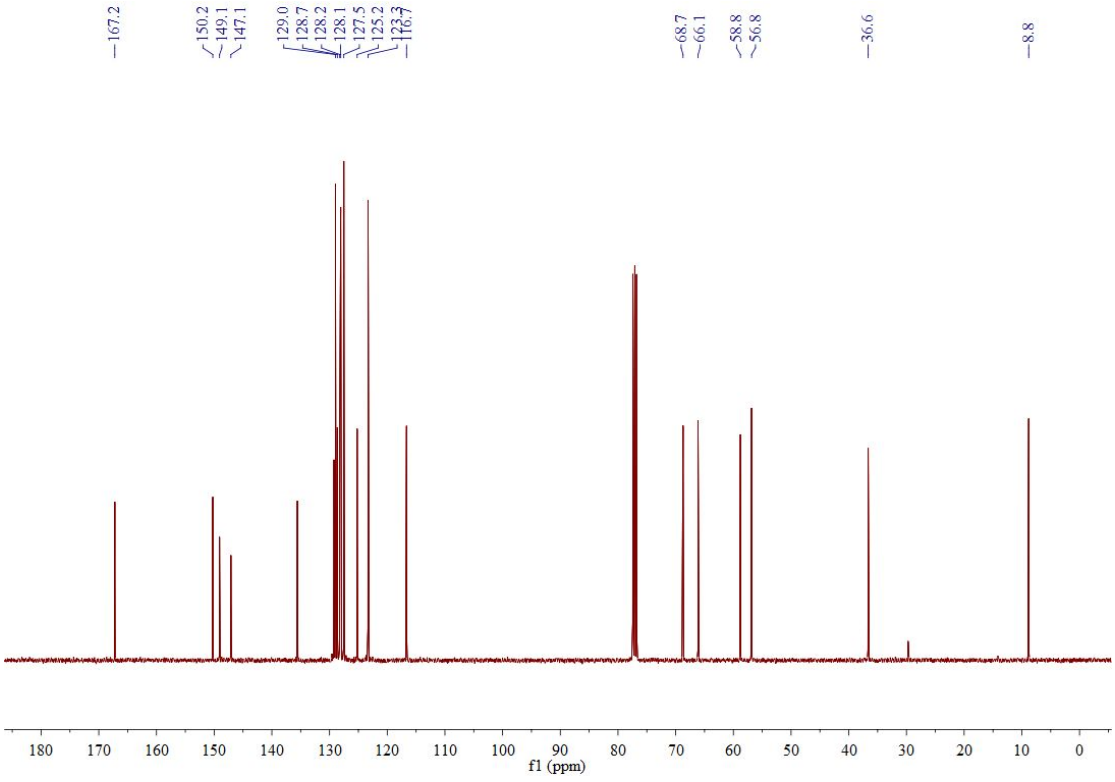
Peak Results

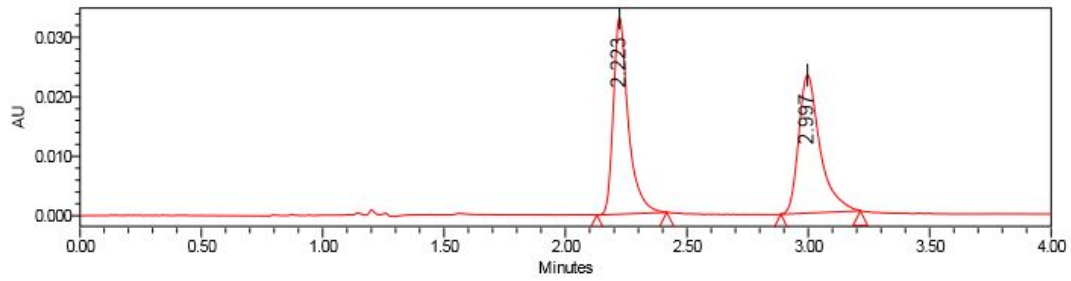
	RT	Area	Height	% Area
1	3.541	1488	270	0.49
2	4.024	304333	28608	99.51

(2*R*,3*S*,3*aR*,9*bS*)-9b-ethyl-2-(4-nitrophenyl)-3-phenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4k):



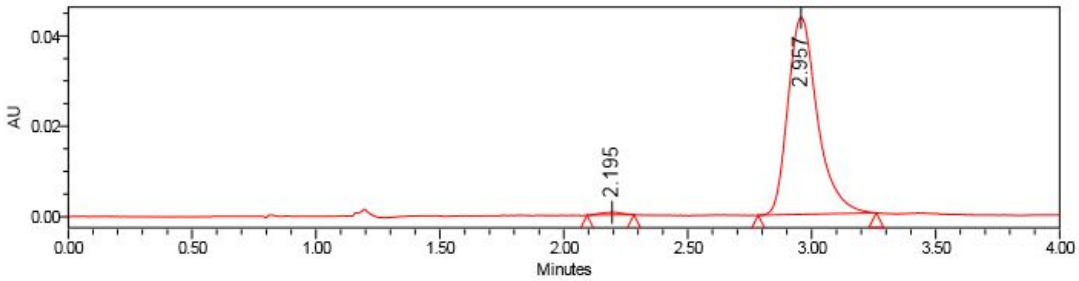






Peak Results

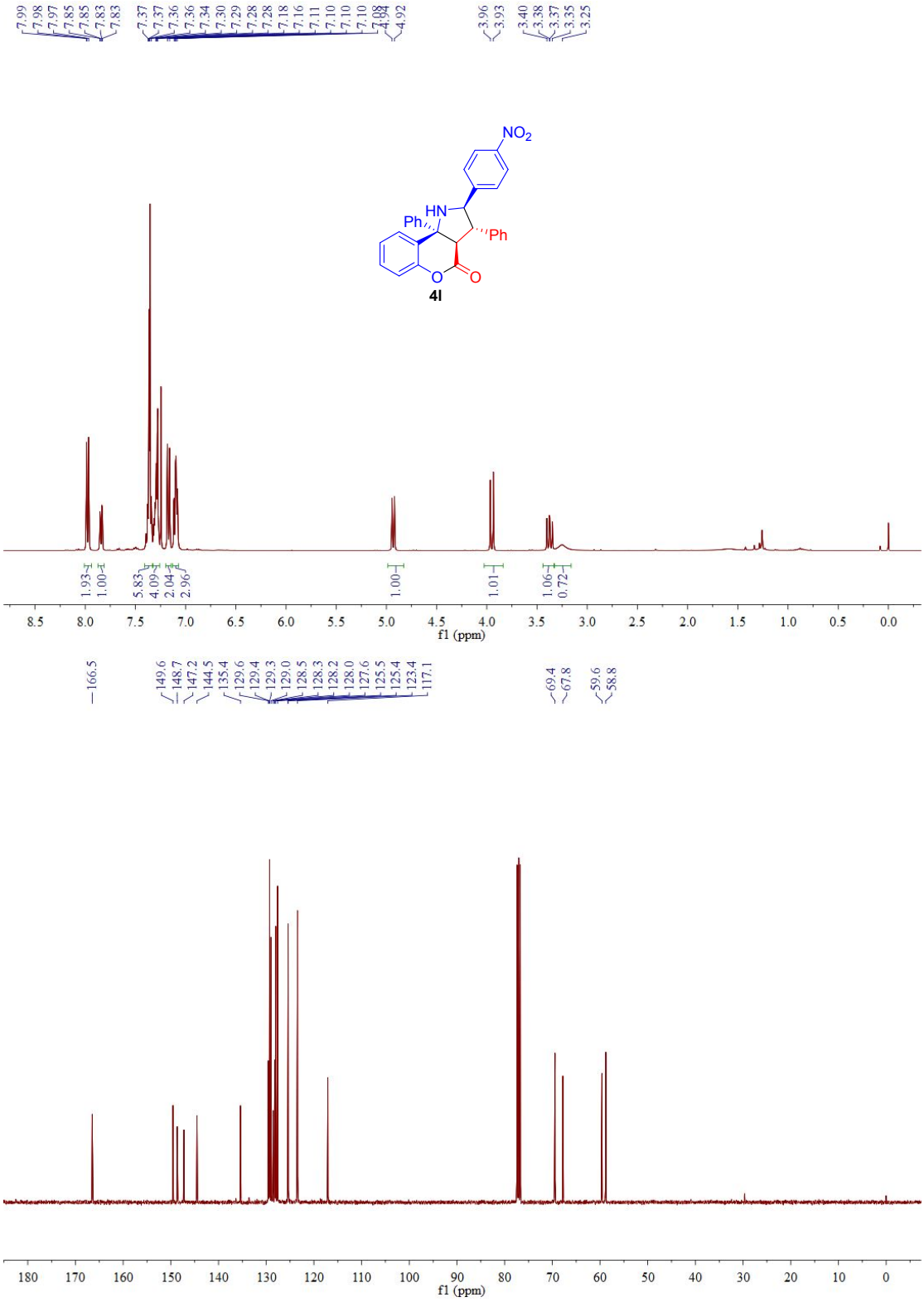
	RT	Area	Height	% Area
1	2.223	141774	32961	49.92
2	2.997	142218	23227	50.08

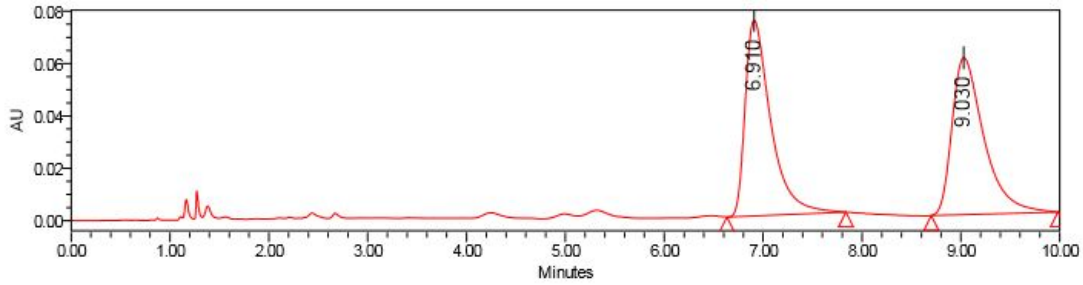


Peak Results

	RT	Area	Height	% Area
1	2.195	3795	630	1.04
2	2.957	361655	43645	98.96

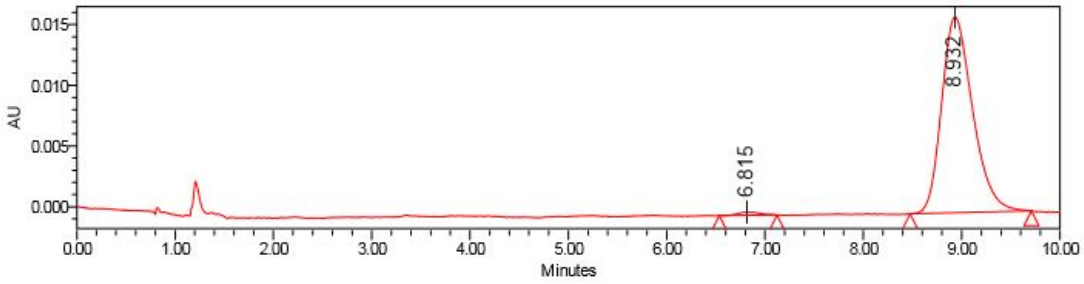
(2*R*,3*S*,3*aR*,9*bR*)-2-(4-nitrophenyl)-3,9b-diphenyl-2,3,3a,9b-tetrahydrochromeno[4,3-*b*]pyrrol-4(1*H*)-one (4l):





Peak Results

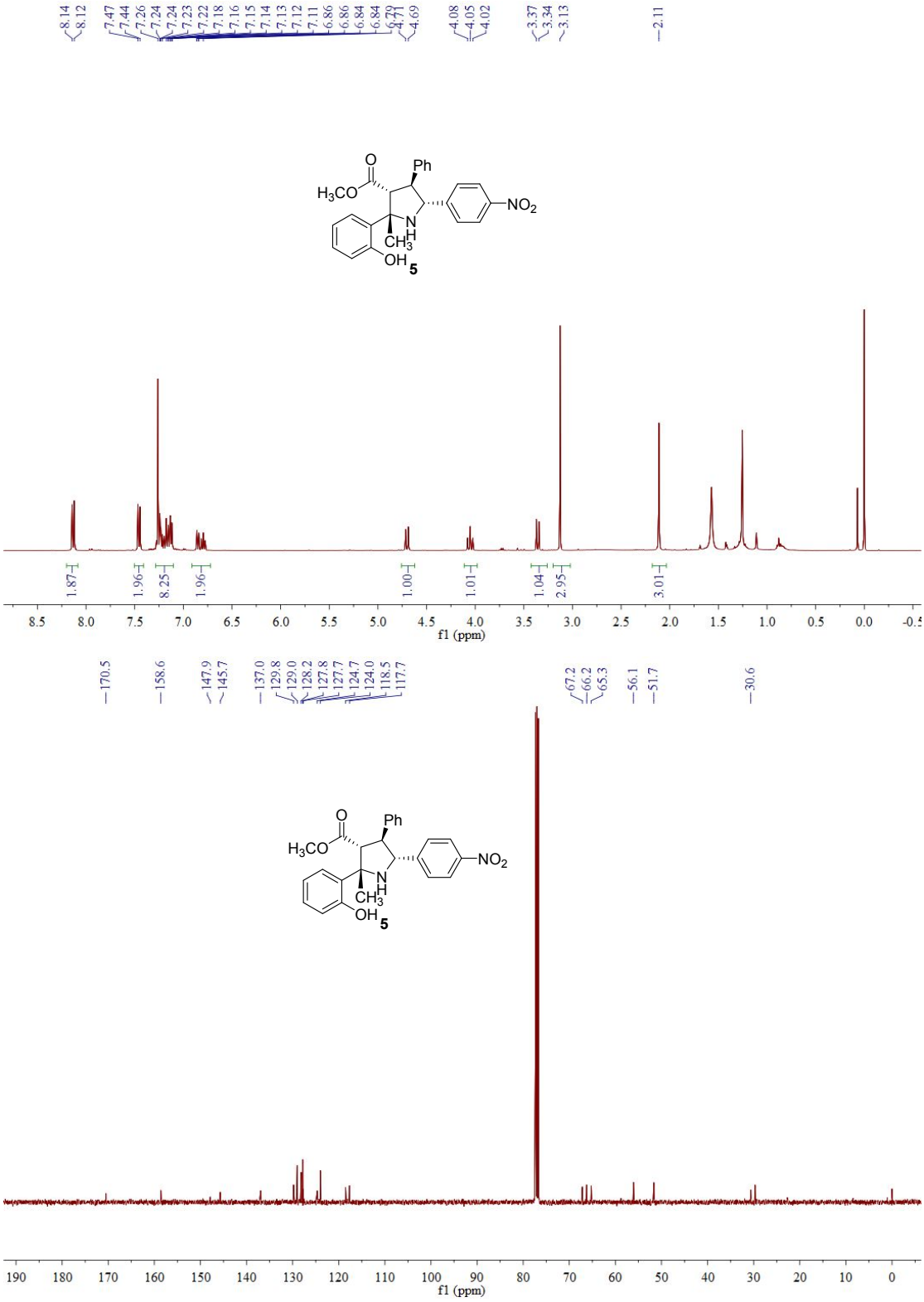
	RT	Area	Height	% Area
1	6.910	1342460	74686	49.96
2	9.030	1344733	59906	50.04

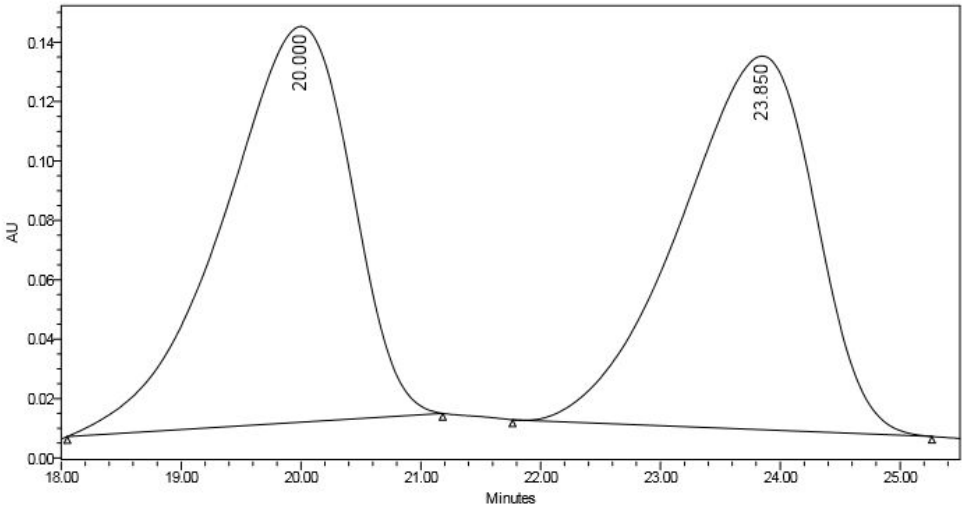


Peak Results

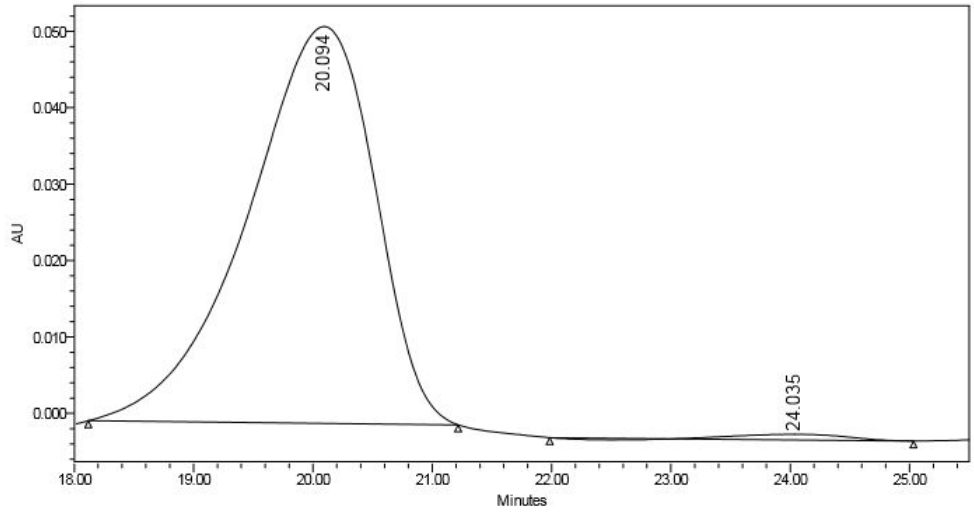
	RT	Area	Height	% Area
1	6.815	4117	273	1.15
2	8.932	354406	16146	98.85

methyl(2*S*,3*R*,4*S*,5*R*)-2-(2-hydroxyphenyl)-2-methyl-5-(4-nitrophenyl)-4-phenylpyrrolidine-3-carboxylate (5):



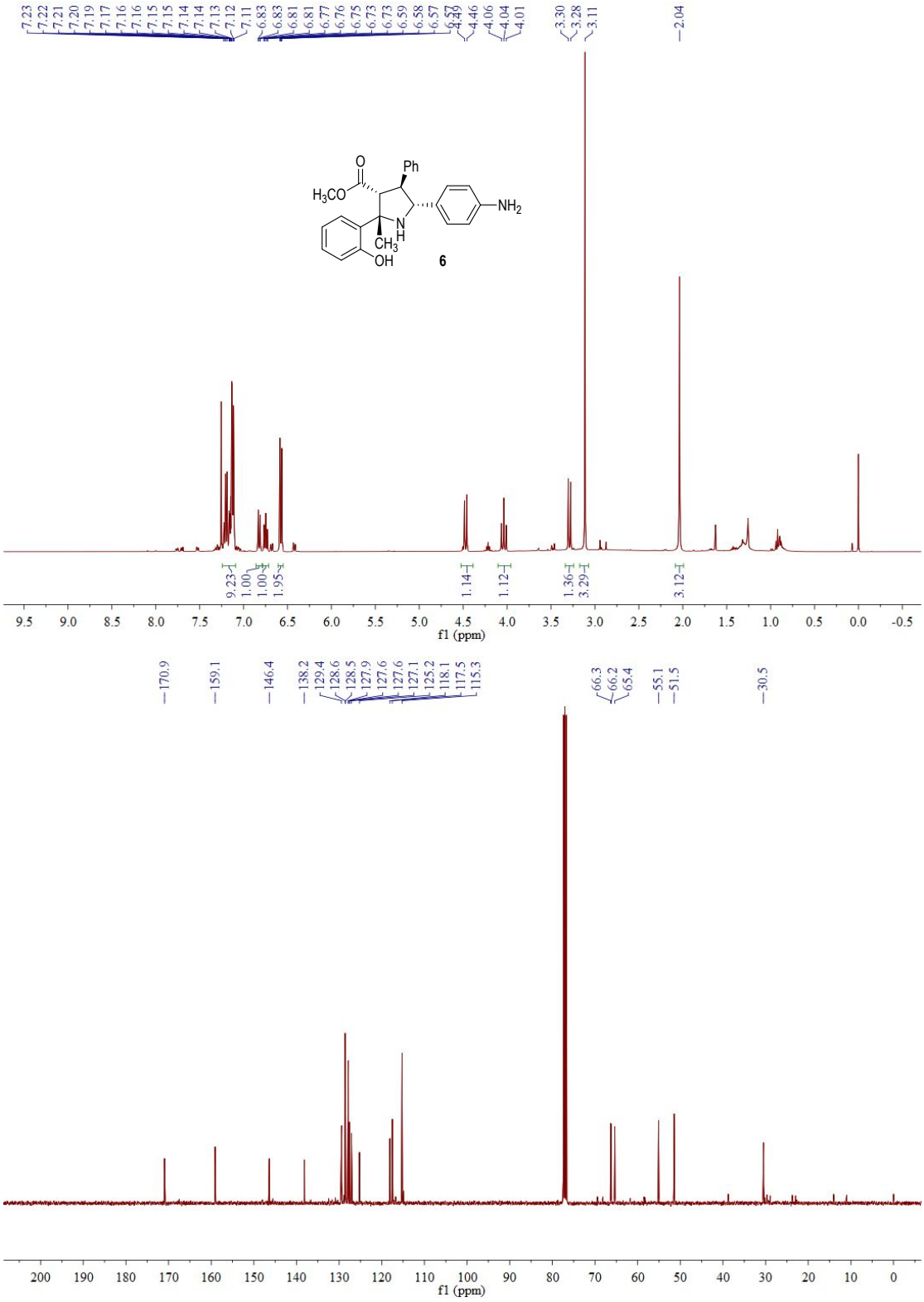


	RT	Area	% Area	Height
1	20.000	9938986	50.09	133237
2	23.850	9903492	49.91	125791

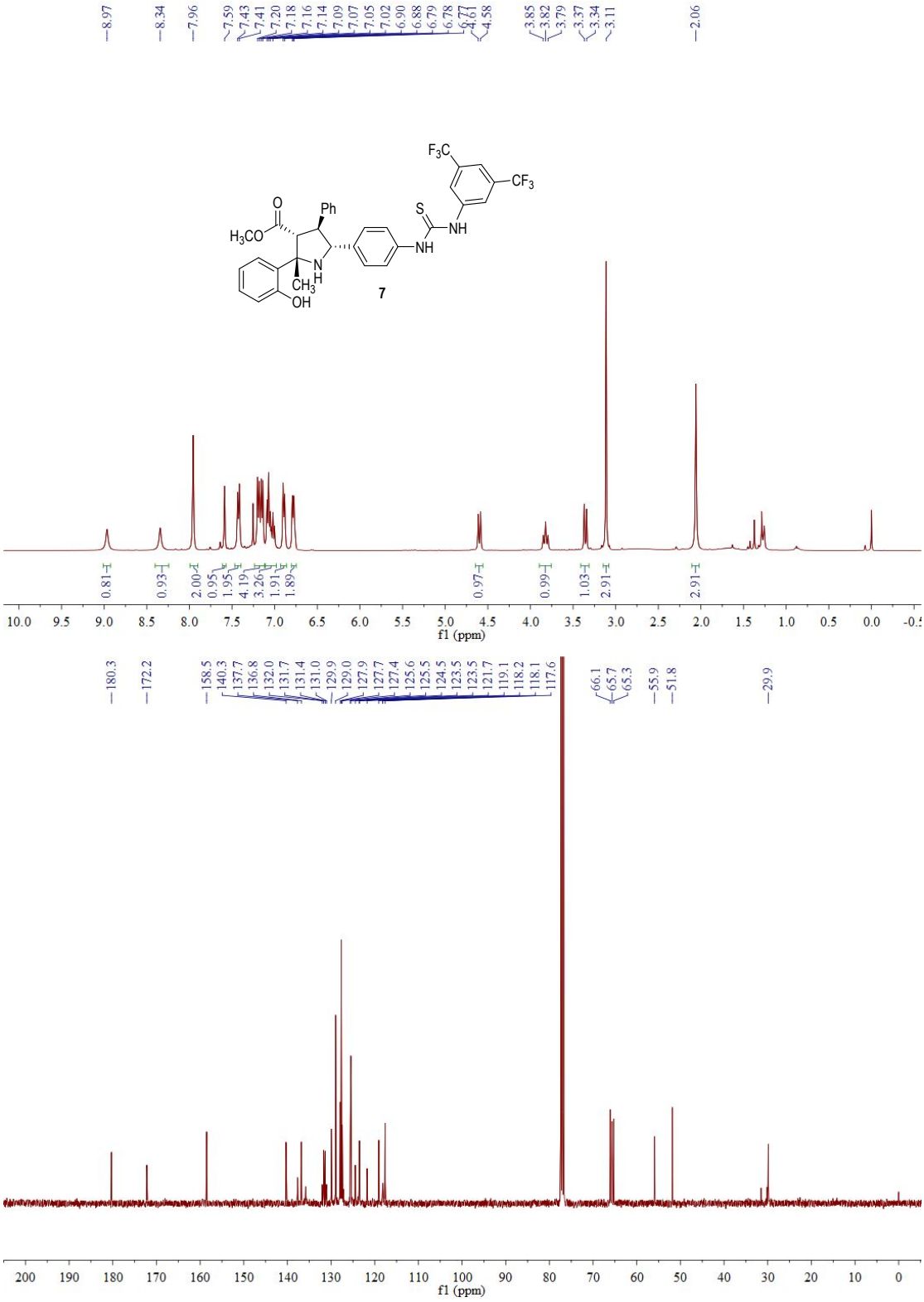


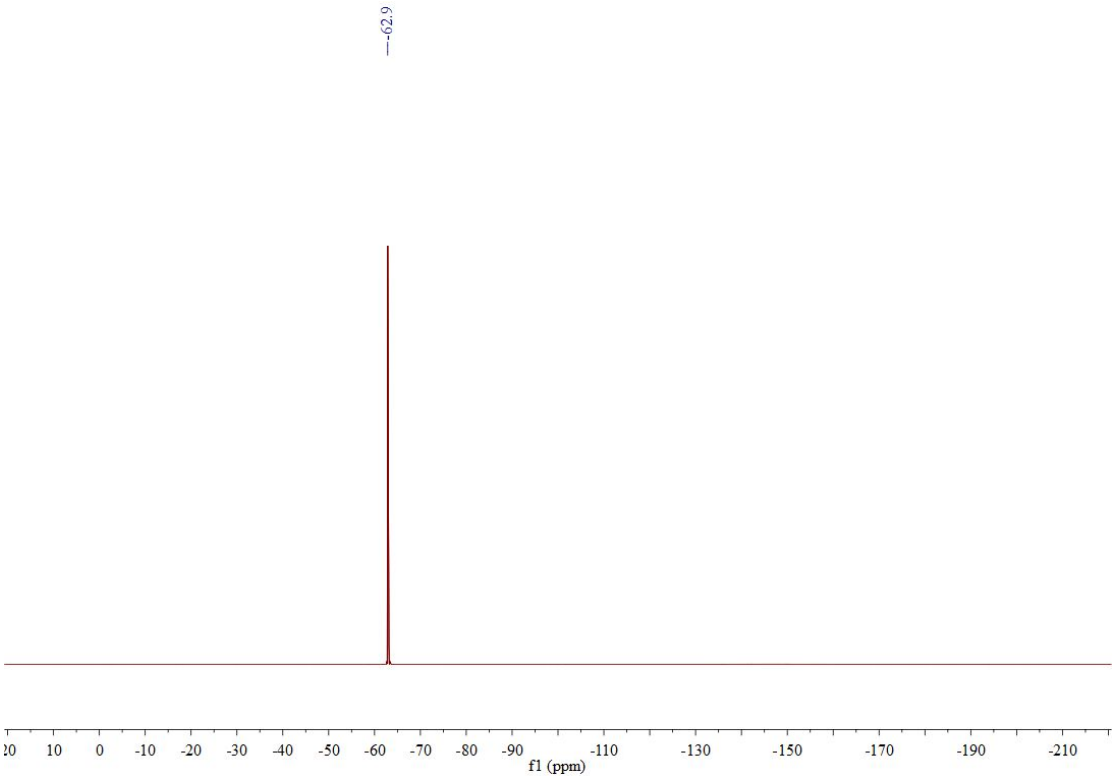
	RT	Area	% Area	Height
1	20.094	3854469	98.58	51924
2	24.035	55678	1.42	722

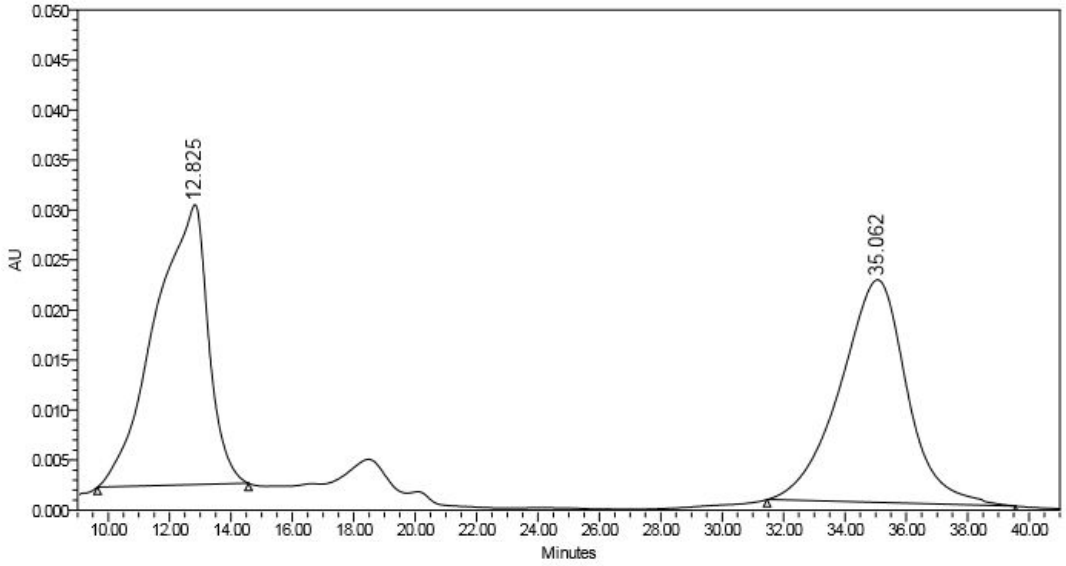
methyl(2S,3R,4S,5R)-5-(4-aminophenyl)-2-(2-hydroxyphenyl)-2-methyl-4-phenyl pyrrolidine-3-carboxylate (6)



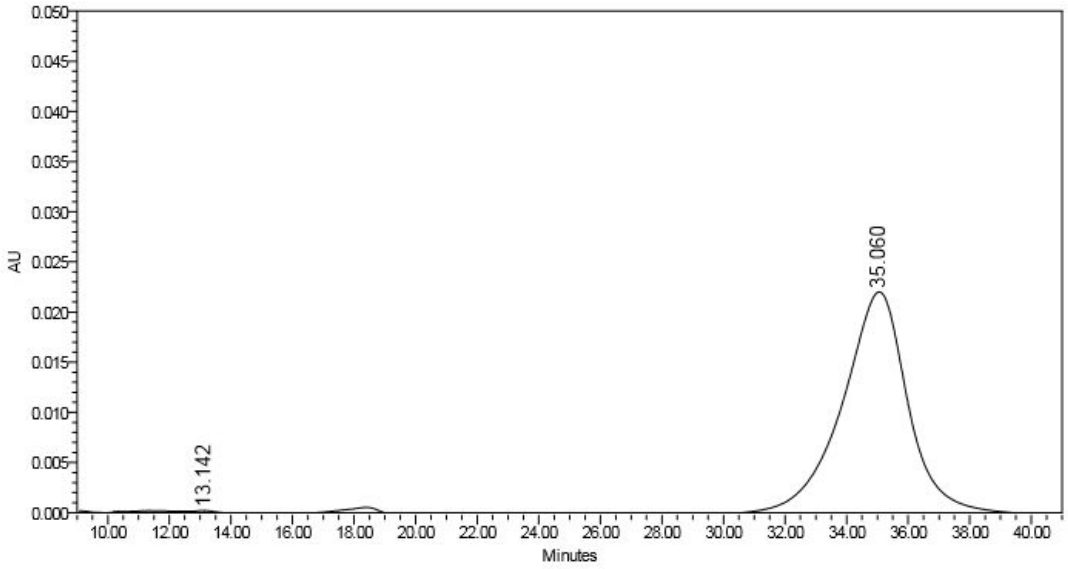
methyl(2*S*,3*R*,4*S*,5*R*)-5-(4-(3-(3,5-bis(trifluoromethyl)phenyl)thioureido)phenyl)-2-(2-hydroxyphenyl)-2-methyl-4-phenylpyrrolidine-3-carboxylate(7)





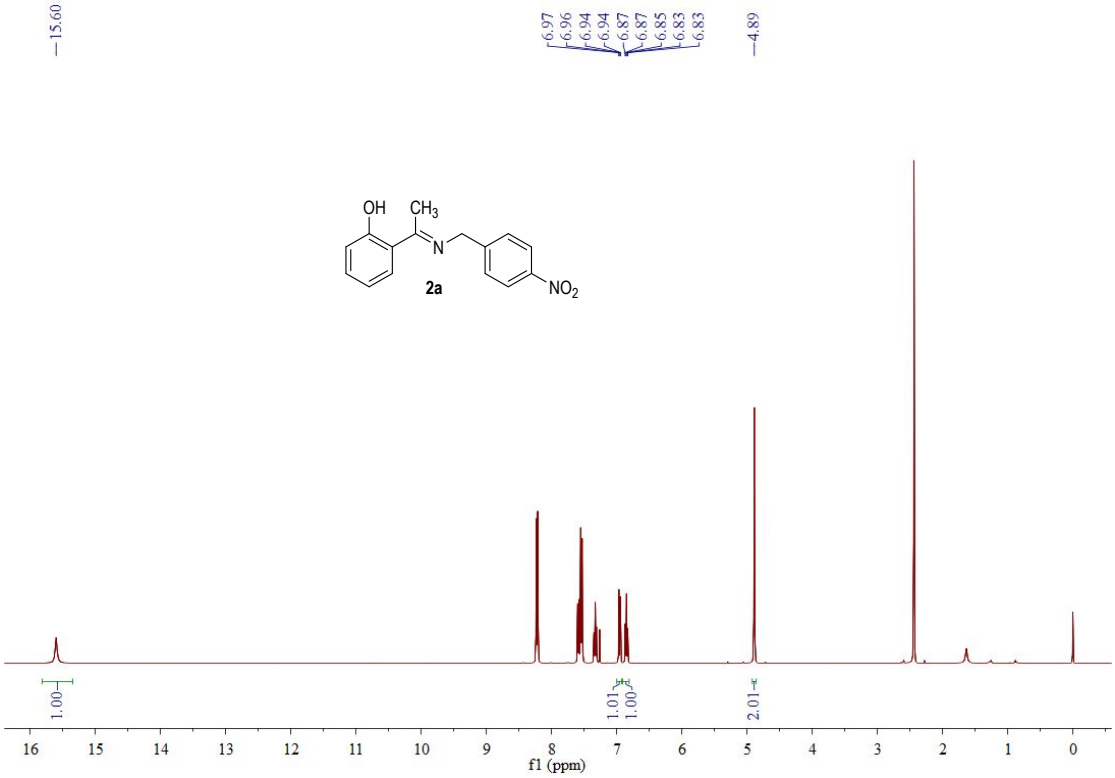


	RT	Area	% Area	Height
1	12.825	3386477	50.13	27974
2	35.062	3369337	49.87	22253

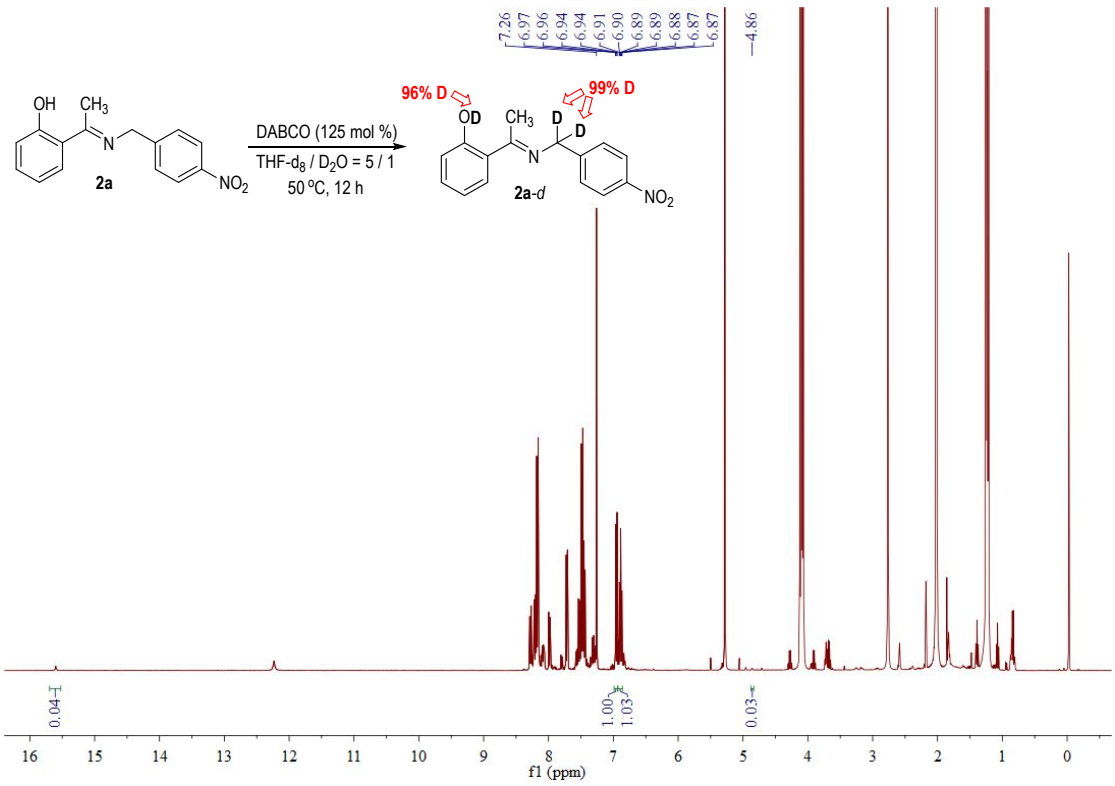


	RT	Area	% Area	Height
1	13.142	35801	1.09	281
2	35.060	3257049	98.91	22073

^{1}H NMR of H-D exchanging studies

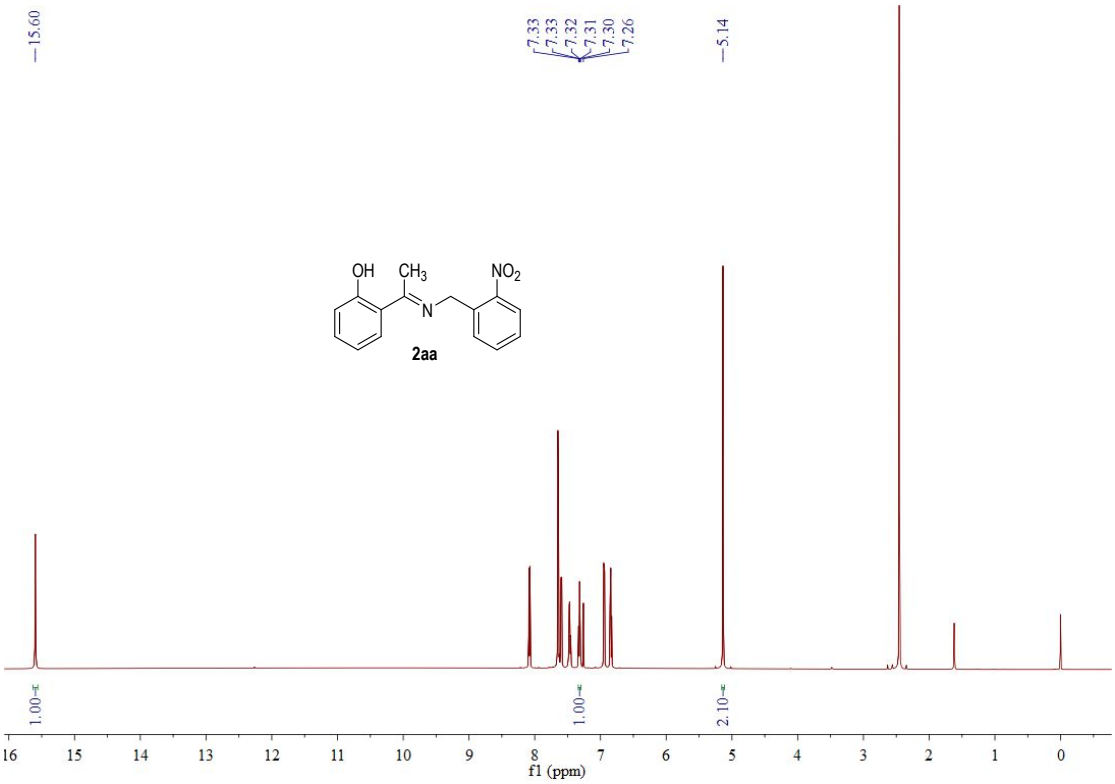


^{1}H NMR of compound **2a**

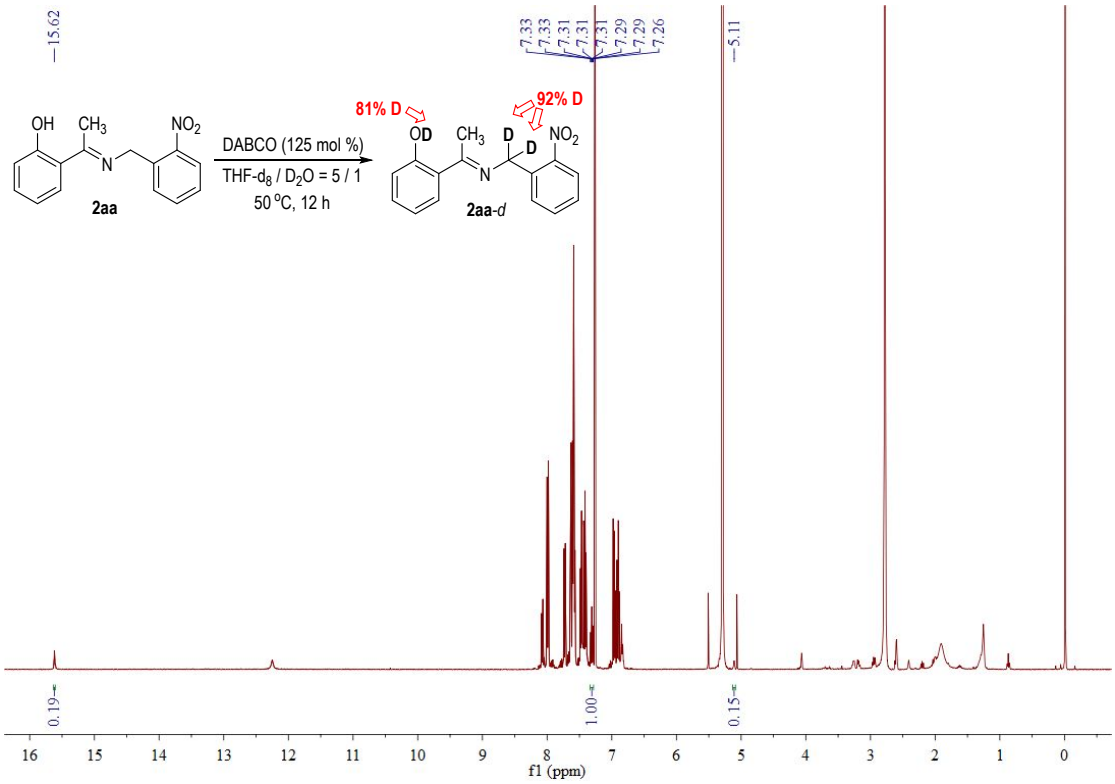


^{1}H NMR of the reaction mixture

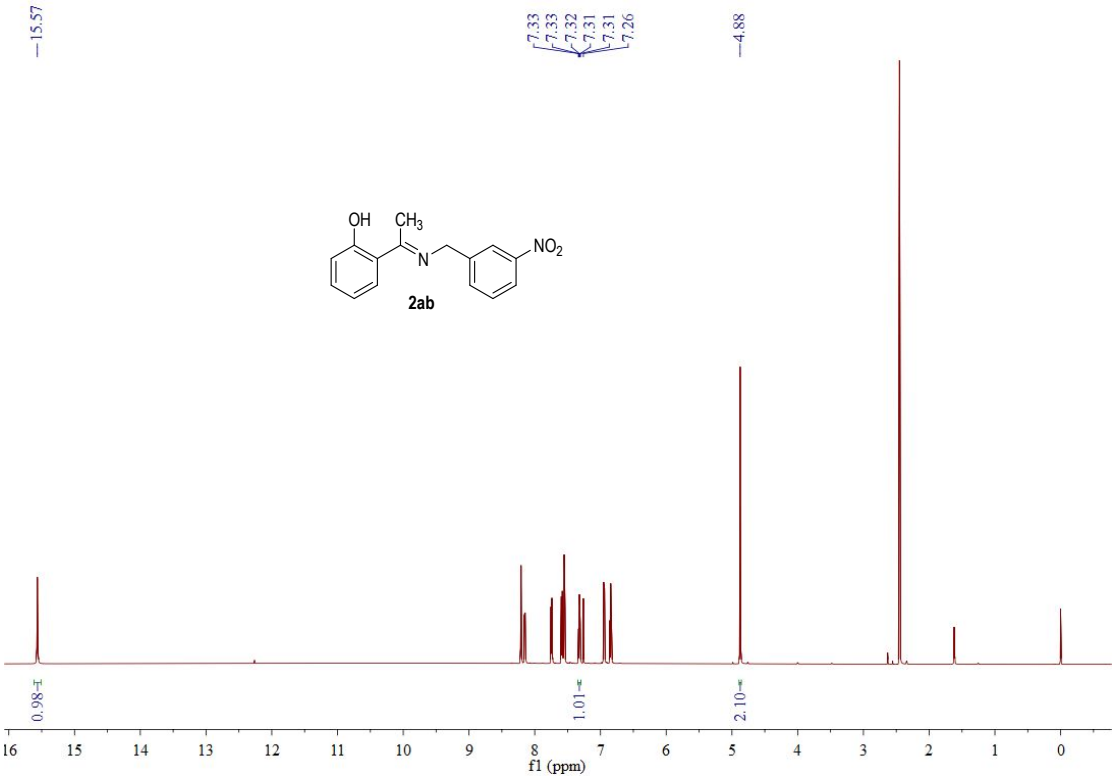
^{1}H NMR of compound **2aa** in $CDCl_3$



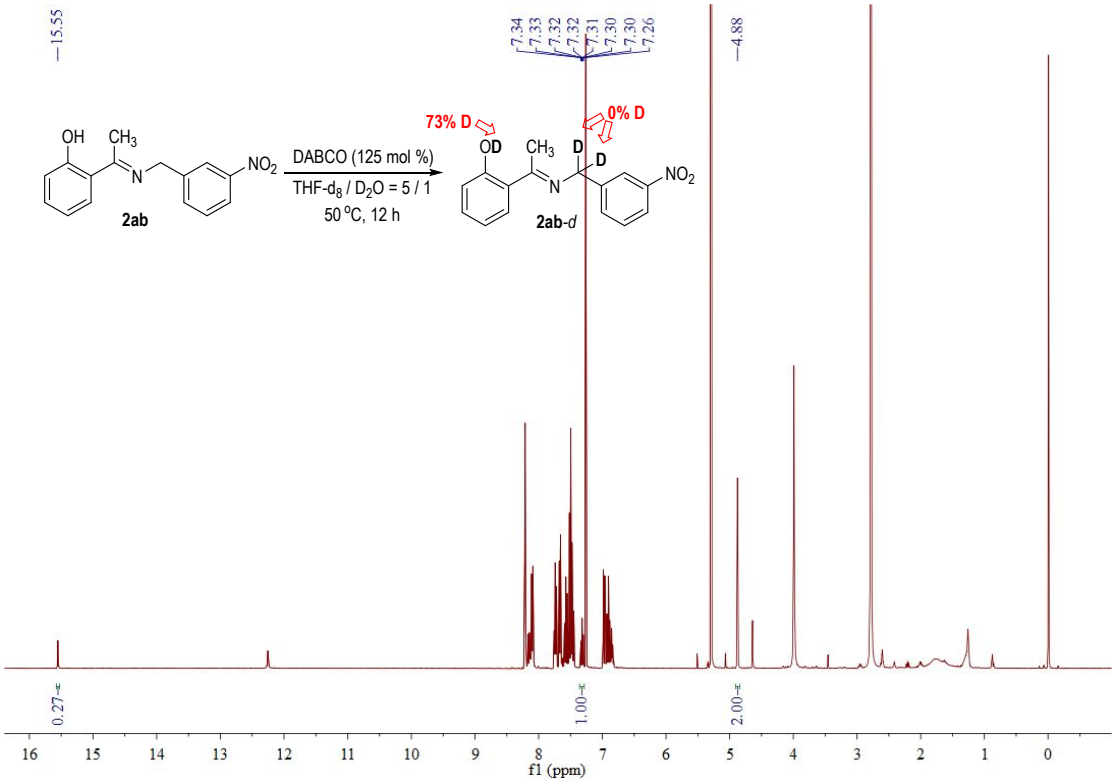
^{1}H NMR of compound **2aa**



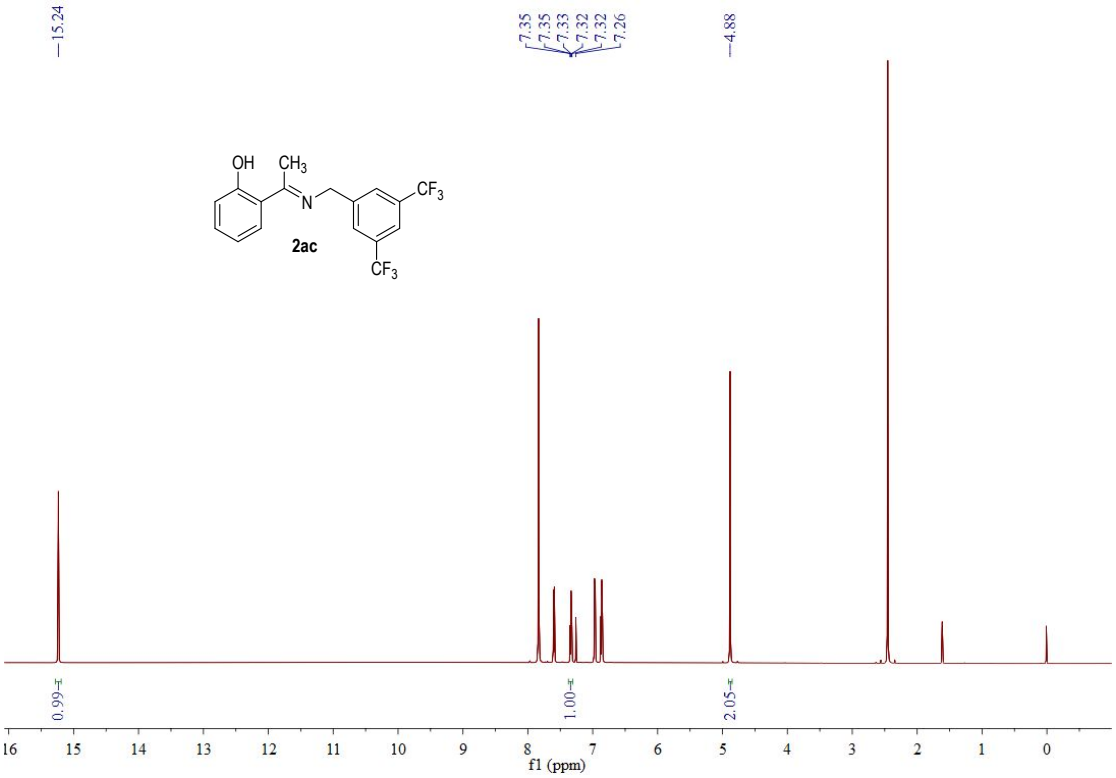
^{1}H NMR of the reaction mixture



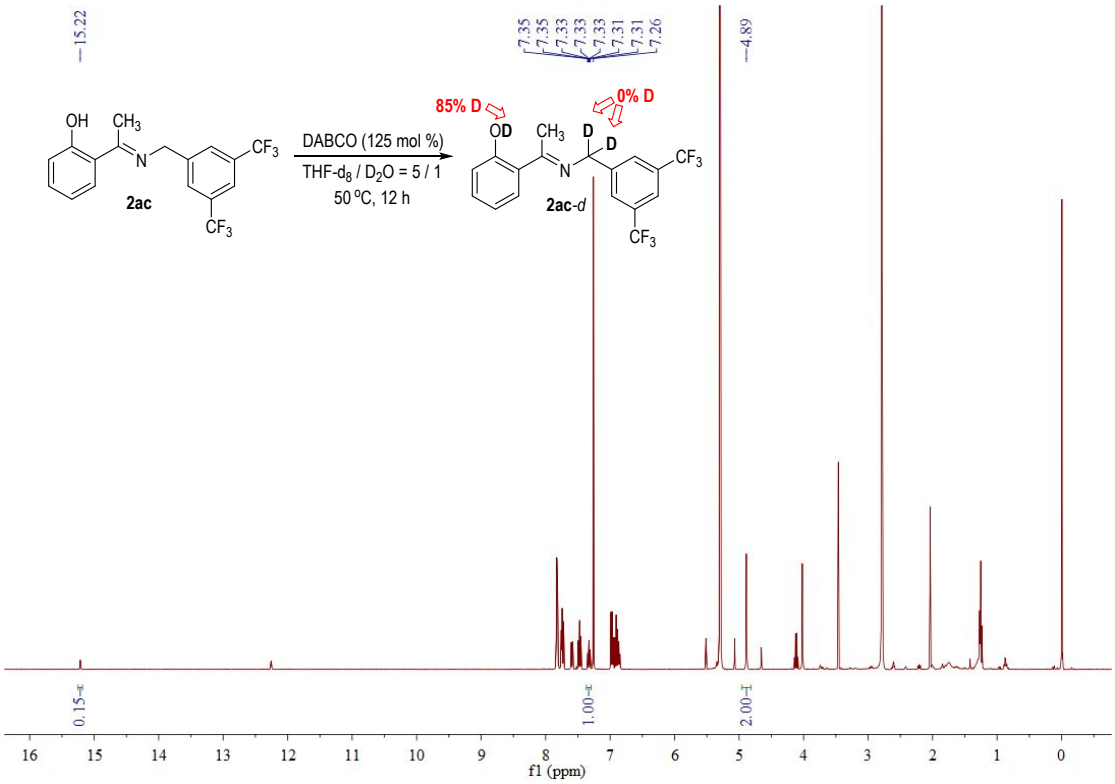
^{1}H NMR of compound **2ab**



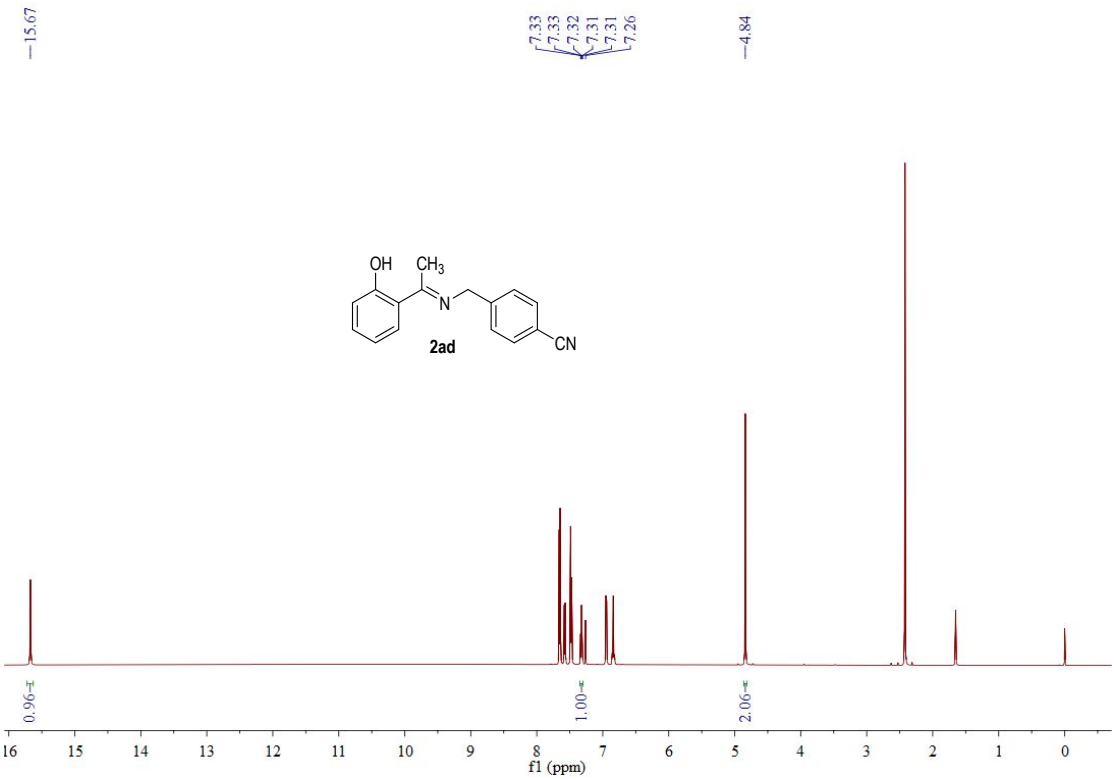
^{1}H NMR of the reaction mixture



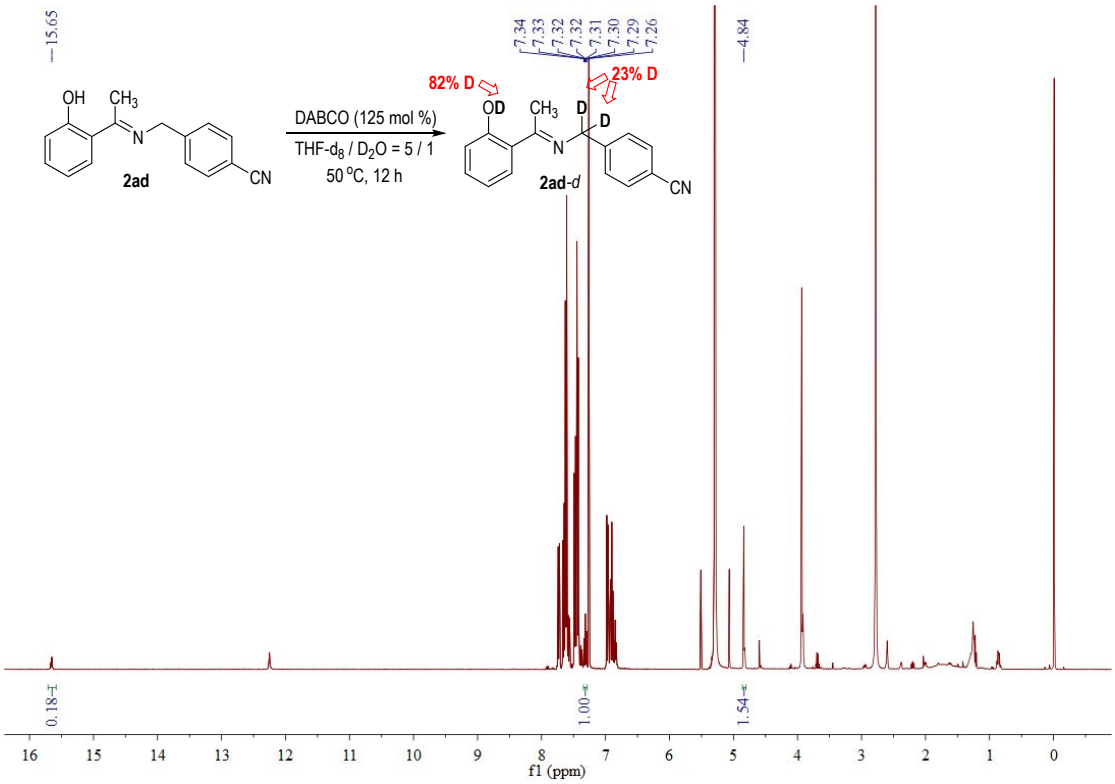
^{1}H NMR of compound **2ac**



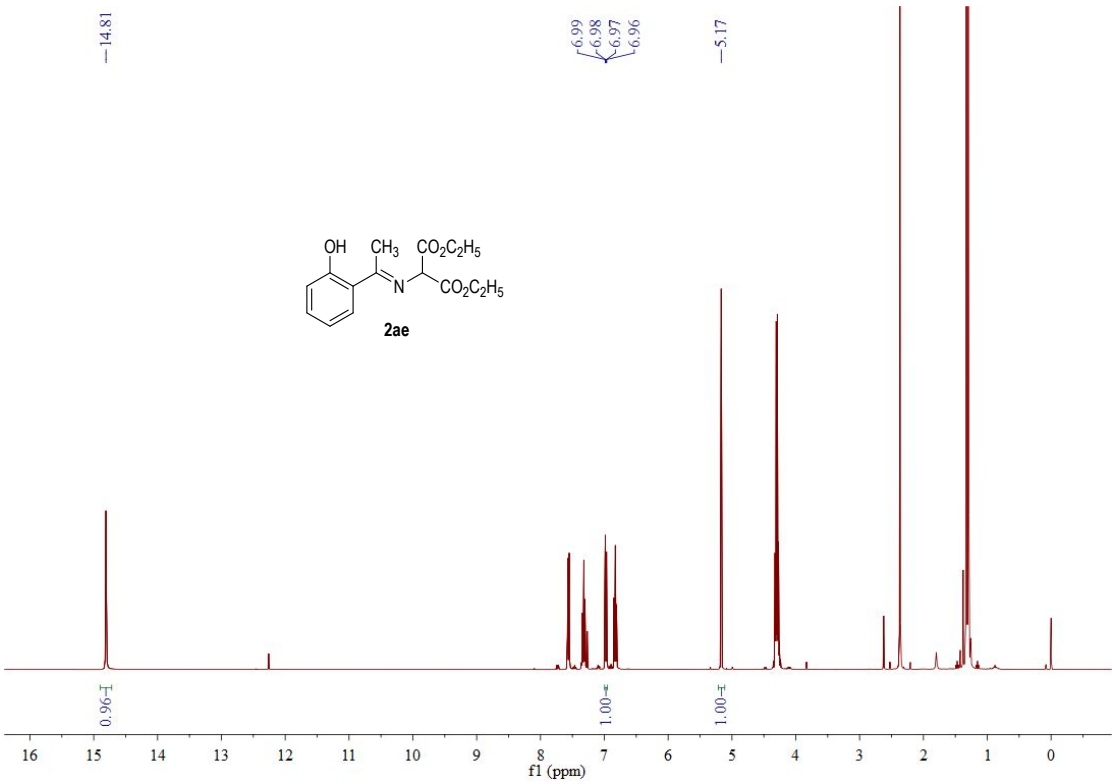
^{1}H NMR of the reaction mixture



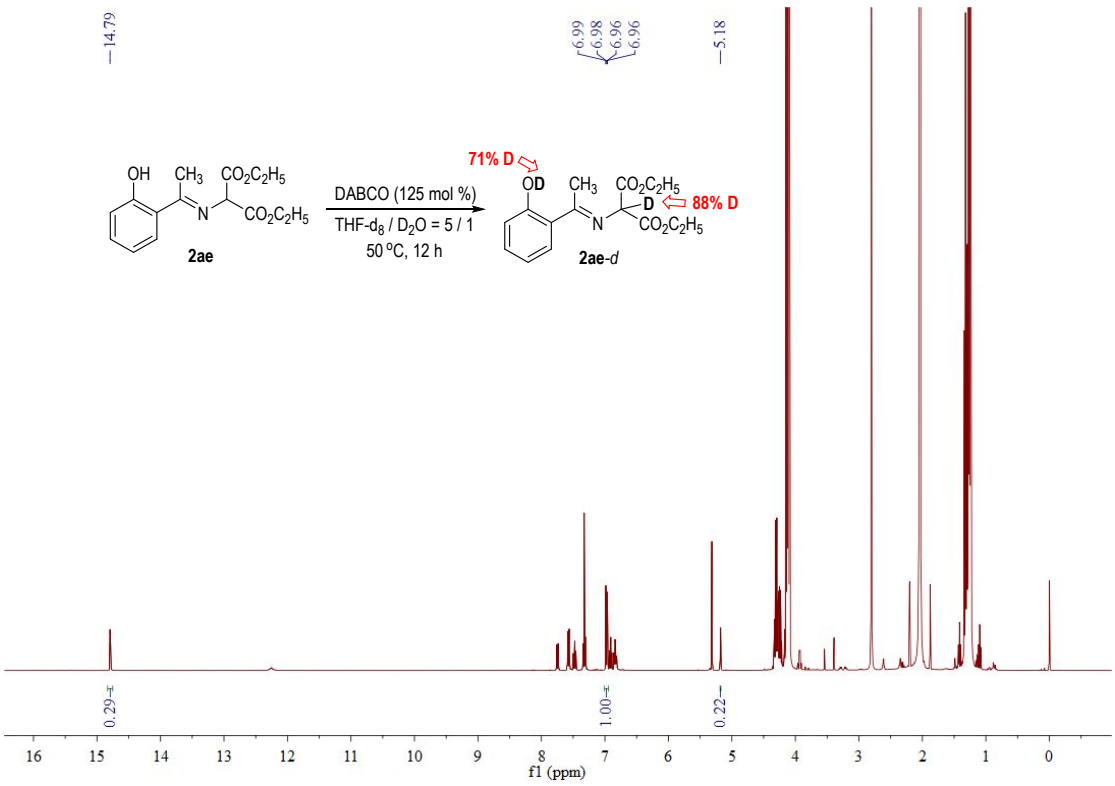
^{1}H NMR of compound **2ad**



^{1}H NMR of the reaction mixture



^{1}H NMR of compound **2ae**



^{1}H NMR of the reaction mixture