A Tandem Dearomatization/Rearomatization Strategy: Enantioselective N-Heterocyclic Carbene-Catalyzed α-Arylation

Zijun Wu[†] and Jian Wang*[,†]

†School of Pharmaceutical Sciences, Key Laboratory of Bioorganic Phosphorous Chemistry & Chemical Biology (Ministry of Education), Tsinghua University, Beijing, 100084 (China)

*Wangjian012@tsinghua.edu.cn

Supporting Information

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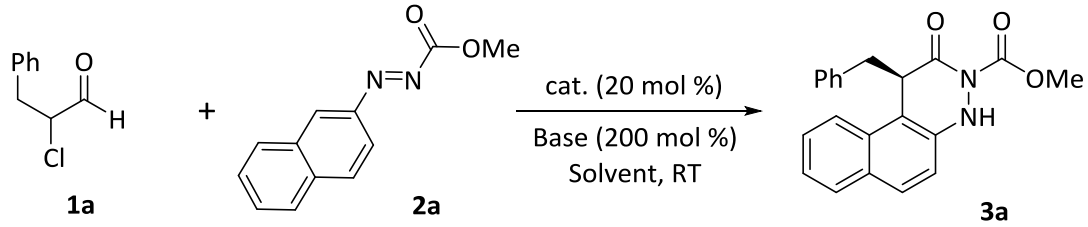
1. General information

Chemicals were purchased from commercial suppliers and used without further purification unless otherwise stated. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ACF400 (400 MHz) spectrometer. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.0) or tetramethylsilane (TMS δ 0.00) was used as a reference. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), bs (broad singlet). Coupling constants were reported in Hertz (Hz). Low resolution mass spectra were obtained on a Finnigan/MAT LCQ spectrometer in ESI mode, and a Finnigan/MAT 95XL-T mass spectrometer in EI mode. All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T spectrometer. For thin layer chromatography (TLC), Visualization on TLC was achieved by use of UV light (254 nm). Flash column chromatography was performed using Tsingdao silica gel (60, particle size 0.040-0.063 mm). The enantiomeric excesses of products were determined by chiral phase HPLC analysis. Optical rotations were recorded on Jasco DIP-1000 polarimeter. α-Chloro aldehyde substrates[1] and azonaphthalenes[2] were prepared according to literature procedures.

2. Screening of catalysts and condition optimization[a]



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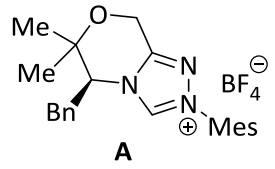
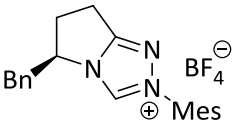


A



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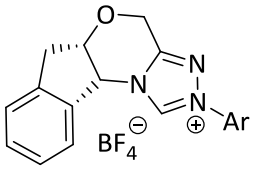
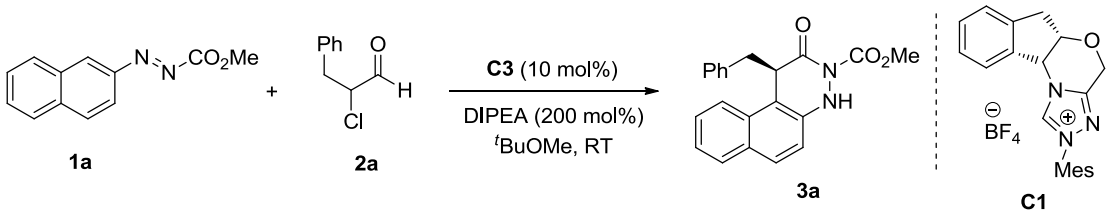


C1: Ar = Mes
C2: Ar = Ph
C3: Ar = 2,6-$(Et)_2C_6H_3$

entry	cat.	solvent	base	yield (%)[b]	*ee* (%)[c]
1	**A**	THF	DIPEA	8	--
2	**B**	THF	DIPEA	58	88
3	**C1**	THF	DIPEA	76	99
4	**C2**	THF	DIPEA	73	90
5	**C3**	THF	DIPEA	71	99
6	**C1**	THF	Et_3N	66	96
7	**C1**	THF	DBU	trace	--
8	**C1**	THF	NaOAc	43	80
9	**C1**	THF	Cs_2CO_3	22	24
10	**C1**	THF	DMAP	trace	--
11	**C1**	THF	K_3PO_4	74	99
12	**C1**	THF	Li_2CO_3	15	94
13	**C1**	1,4-Dioxane	DIPEA	54	98
14	**C1**	DCM	DIPEA	77	97
15	**C1**	EtOAc	DIPEA	83	98
16	**C1**	toluene	DIPEA	65	98
17	**C1**	^{t}BuOMe	DIPEA	90	99
18	**C1**	CH_3CN	DIPEA	71	82
19[d]	**C1**	^{t}BuOMe	DIPEA	89	99
20[e]	**C1**	^{t}BuOMe	DIPEA	61	99

[a]Reaction conditions: α-chloroaldehyde **1a** (0.20 mmol, 2.0 equiv), azonaphthalene **2a** (0.10 mmol, 1.0 equiv), cat. (0.02 mmol), base (0.20 mmol), solvent (1.0 mL), 10 h, room temperature. [b] Yields of isolated products after column chromatography. [c] The *ee* values were determined by HPLC using a chiral stationary phase. [d] **C1** (10 mol %), 16 h. [e] **C1** (5 mol %), 24 h.

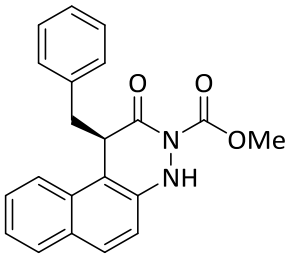
3. General procedure for the synthesis of products 3 and 4



To a flame-dried Schlenk reaction tube equipped with a magnetic stir bar, was added the azolium precatalyst **C1** (4.2 mg, 0.01 mmol), azonaphthalene **1a** (21.4 mg, 0.10 mmol). The Schlenk tube was closed with a septum, evacuated and refilled with Ar. α-Chloro aldehyde **2a** (33.6 mg, 0.20 mmol), DIPEA ($^{i}Pr_2NEt$, 25.8 mg, 33 μL, 0.20 mmol) and freshly distilled ^{t}BuOMe (1.0 mL) was added. The mixture was then stirred at room temperature until TLC indicated that **1** disappeared. Subsequently, the reaction mixture was directly purified through preparative thin layer chromatography on silica gel to afford pure products **3a**.

4: Characterization data.

Methyl (*R*)-1-benzyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3a)

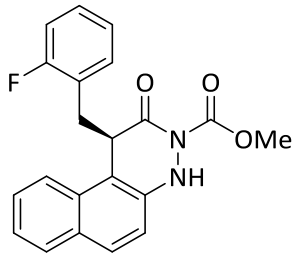


According to the general procedure, **3a** was obtained in 89% yield (30.8 mg) with 99% *ee* as a white solid. m.p. 168-169 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 – 7.75 (m, 2H), 7.49 – 7.46 (m, 1H), 7.37 – 7.33 (m, 2H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.14 – 7.08 (m, 3H), 6.94 (dd, *J* = 7.3, 2.0 Hz, 2H), 4.66 (t, *J* = 8.0 Hz, 1H), 4.04 (s, 3H), 3.25 (ddd, *J* = 21.2, 13.2, 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 152.5, 138.8, 137.3, 130.9, 130.4, 129.3, 128.7, 128.6, 128.3, 127.0, 126.7, 124.3, 121.4, 116.8, 115.4, 55.2, 47.9, 35.6. HRMS (ESI): calcd for $C_{21}H_{19}N_2O_3^+$ ($M+H^+$): 347.1390, found 347.1385. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 16.1 min, t_R (major) = 30.6 min, *ee* = 99%. $[\alpha]_D^{25}$ = - 69.0 (*c* = 1.2 in $CHCl_3$)

Methyl

(*R*)-1-(2-fluorobenzyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

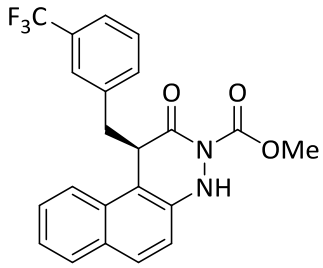
(3b)



According to the general procedure, **3b** was obtained in 81% yield (29.5 mg) with 98% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.71 (m, 3H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.21 (d, *J* = 8.7 Hz, 1H), 7.17 – 7.11 (m, 1H), 6.97 – 6.88 (m, 3H), 4.73 (t, *J* = 7.9 Hz, 1H), 4.04 (s, 3H), 3.34 (dd, *J* = 13.4, 8.3 Hz, 1H),

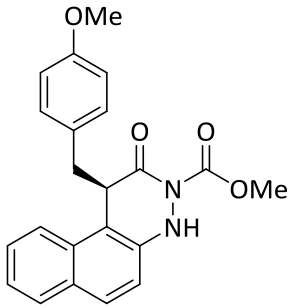
3.17 (dd, J = 13.6, 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 162.7, 160.3, 152.6, 138.8, 131.5 (d, J_{CF} 3.0), 130.8, 130.4, 128.8, 128.7 (d, J_{CF} 3.0), 127.2, 124.5 (d, J_{CF} 12.0), 124.3, 123.9 (d, J_{CF} 3.0), 121.2, 116.5, 115.3, 115.1, 55.3, 46.5, 28.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -118.43. HRMS (ESI): calcd for $C_{21}H_{18}FN_2O_3^+$ ($M+H^+$): 365.1296, found 365.1288. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 14.7 min, t_R (major) = 27.5 min, *ee* = 98%. $[\alpha]_D^{25}$ = -91.2 (c = 1.0 in $CHCl_3$).

Methyl (*R*)-2-oxo-1-(3-(trifluoromethyl)benzyl)-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3c)



According to the general procedure, **3c** was obtained in 88% yield (36.4 mg) with 94% *ee* as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 – 7.75 (m, 2H), 7.69 (s, 1H), 7.35 – 7.32 (m, 3H), 7.30 – 7.28 (m, 1H), 7.21 – 7.18 (m, 2H), 7.17 – 7.06 (m, 2H), 4.65 (dd, J = 8.5, 6.6 Hz, 1H), 4.06 (s, 3H), 3.35 – 3.24 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.6, 152.4, 138.8, 138.2, 132.7, 130.9, 130.3, 129.0, 128.7, 128.6, 127.1, 126.2, 126.2, 124.3, 123.5, 123.5, 121.0, 115.4, 115.0, 55.3, 47.6, 34.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -62.84. HRMS (ESI): calcd for $C_{22}H_{18}F_3N_2O_3^+$ ($M+H^+$): 415.1270, found 415.1261. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 10.4 min, t_R (major) = 14.8 min, *ee* = 94%. $[\alpha]_D^{25}$ = -64.9 (c = 3.0 in $CHCl_3$).

Methyl (*R*)-1-(4-methoxybenzyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3d)

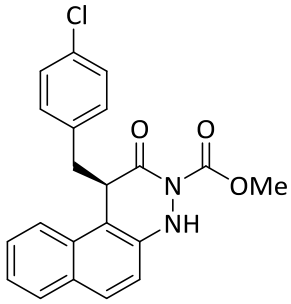


According to the general procedure, **3d** was obtained in 80% yield (30.1 mg) with 99% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.74 (m, 2H), 7.53 – 7.50 (m, 1H), 7.41 – 7.35 (m, 3H), 7.19 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 4.62 (t, *J* = 7.3 Hz, 1H), 4.04 (s, 3H), 3.73 (s, 3H), 3.19 (ddd, *J* = 21.2, 13.4, 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 158.5, 152.6, 138.7, 130.9, 130.4, 130.3, 129.4, 128.7, 127.1, 124.3, 121.5, 117.0, 115.6, 113.7, 55.2, 55.2, 48.1, 34.9. HRMS (ESI): calcd for $C_{22}H_{21}N_2O_4^+$ ($M+H^+$): 377.1501, found 377.1506. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 22.8 min, t_R (major) = 47.3 min, *ee* = 99%. $[\alpha]_D^{25}$ = -23.8 (*c* = 1.1 in $CHCl_3$).

Methyl

(*R*)-1-(4-chlorobenzyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

(3e)



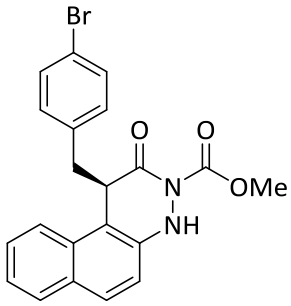
According to the general procedure, **3e** was obtained in 88% yield (33.5 mg) with 95% *ee* as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.75 (m, 2H), 7.61 (s, 1H), 7.48 – 7.45 (m, 1H), 7.39 – 7.35 (m, 2H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.08 (d, *J* = 8.3 Hz, 2H), 6.87 (d, *J* = 8.3 Hz, 2H), 4.62 (t, *J* = 7.4 Hz, 1H), 4.05 (s, 3H), 3.20 (ddd, *J* = 21.4, 13.3, 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8, 152.5, 138.8,

135.8, 132.7, 130.8, 130.6, 130.4, 128.9, 128.7, 128.4, 127.2, 124.4, 121.2, 116.1, 115.2, 55.3, 47.8, 34.8. HRMS (ESI): calcd for $C_{21}H_{18}ClN_2O_3^+$ ($M+H^+$): 381.1006, found 381.1012. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 18.8 min, t_R (major) = 39.6 min, *ee* = 95%. $[\alpha]_D^{25}$ = -88.4 (*c* = 0.9 in $CHCl_3$).

Methyl

(*R*)-1-(4-bromobenzyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

(3f)

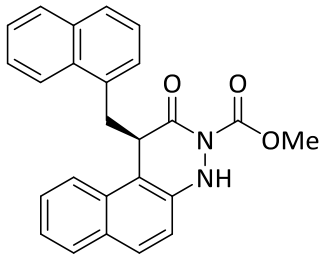


According to the general procedure, **3f** was obtained in 85% yield (36.1 mg) with 95% *ee* as a yellow solid. m.p. 155-156 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 – 7.75 (m, 2H), 7.62 (s, 1H), 7.47 (dd, *J* = 5.9, 3.9 Hz, 1H), 7.39 – 7.35 (m, 2H), 7.25 – 7.18 (m, 3H), 6.83 – 6.81 (m, 2H), 4.62 (t, *J* = 8.0 Hz, 1H), 4.05 (s, 3H), 3.23 (dd, *J* = 13.3, 6.8 Hz, 1H), 3.13 (dd, *J* = 13.3, 8.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8, 152.4, 138.8, 136.4, 131.3, 131.0, 130.8, 130.3, 128.9, 128.8, 127.3, 124.4, 121.2, 120.8, 116.1, 115.2, 55.3, 47.7, 34.8. HRMS (ESI): calcd for $C_{21}H_{18}BrN_2O_3^+$ ($M+H^+$): 425.0501, 427.0480, found 425.0505, 427.0484. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 19.9 min, t_R (major) = 35.6 min, *ee* = 95%. $[\alpha]_D^{25}$ = -67.5 (*c* = 0.8 in $CHCl_3$).

Methyl

(*R*)-1-(naphthalen-1-ylmethyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carbox

ylate (3g)

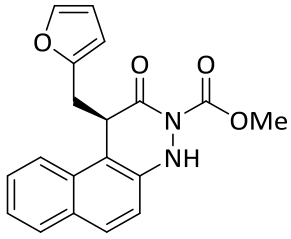


According to the general procedure, **3g** was obtained in 88% yield (34.8 mg) with 99% *ee* as a light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.0 Hz, 1H), 7.81 – 7.79 (m, 1H), 7.70 (t, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.22 (ddd, *J* = 12.3, 7.4, 4.0 Hz, 2H), 7.10 – 7.00 (m, 3H), 6.89 – 6.87 (m, 1H), 4.82 (dd, *J* = 9.0, 5.9 Hz, 1H), 4.04 (s, 3H), 3.85 (dd, *J* = 13.4, 5.9 Hz, 1H), 3.58 (dd, *J* = 13.5, 9.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.1, 152.5, 138.7, 133.7, 133.4, 132.0, 131.1, 130.2, 128.8, 128.7, 128.4, 127.7, 126.7, 125.5, 125.1, 124.1, 123.1, 121.2, 116.9, 115.0, 55.2, 47.1, 32.1. HRMS (ESI): calcd for $C_{25}H_{21}N_2O_3^+$ ($M+H^+$): 397.1552, found 397.1548. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 9.3 min, t_R (major) = 38.6 min, *ee* = 99%. $[\alpha]_D^{25}$ = -121.4 (*c* = 1.1 in $CHCl_3$).

Methyl

(*R*)-1-(furan-2-ylmethyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

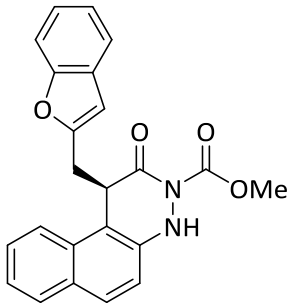
(3h)



According to the general procedure, **3h** was obtained in 73% yield (24.5 mg) with 96% *ee* as a light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (t, *J* = 9.3 Hz, 1H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.46 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.39 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.28 (d, *J* = 0.8 Hz, 2H), 7.19 (d, *J* = 8.7 Hz, 1H), 6.13 (dd, *J* = 3.1, 1.9 Hz, 1H), 5.82 (dd, *J* = 3.2, 0.5 Hz, 1H), 4.77 (t, *J* = 7.5 Hz, 1H), 4.05 (s, 3H), 3.41 – 3.27 (m, 1H), 3.23 – 3.07 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ =

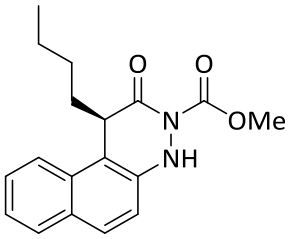
165.6, 152.5, 151.0, 141.7, 138.7, 130.8, 130.4, 128.8, 128.7, 127.3, 124.4, 121.2, 116.4, 115.2, 110.5, 107.8, 55.3, 45.7, 27.6. HRMS (ESI): calcd for $C_{19}H_{17}N_2O_4^+$ ($M+H^+$): 337.1188, found 337.1189. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 19.1 min, t_R (major) = 33.2 min, *ee* = 96%. $[\alpha]_D^{25}$ = +17.1 (*c* = 1.2 in $CHCl_3$).

Methyl (*R*)-1-(benzofuran-2-ylmethyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3i)



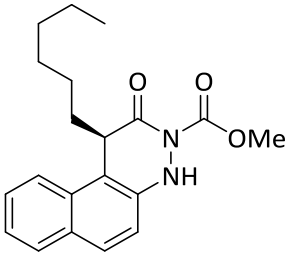
According to the general procedure, **3i** was obtained in 78% yield (30.1 mg) with 95% *ee* as a light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.73 (m, 4H), 7.41 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.37 – 7.32 (m, 3H), 7.24 – 7.19 (m, 2H), 7.14 (td, *J* = 7.5, 0.9 Hz, 1H), 6.28 (s, 1H), 4.94 (t, *J* = 7.5 Hz, 1H), 4.05 (d, *J* = 1.9 Hz, 3H), 3.48 (dd, *J* = 14.8, 7.6 Hz, 1H), 3.26 (dd, *J* = 14.8, 7.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.2, 154.9, 154.1, 152.5, 138.9, 130.7, 130.4, 129.0, 128.5, 127.4, 124.5, 123.7, 122.5, 121.1, 120.6, 116.2, 115.1, 110.9, 109.7, 104.8, 55.3, 45.1, 28.1. HRMS (ESI): calcd for $C_{23}H_{19}N_2O_4^+$ ($M+H^+$): 387.1345, found 387.1342. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 15.1 min, t_R (major) = 24.2 min, *ee* = 95%. $[\alpha]_D^{25}$ = +55.8 (*c* = 1.0 in $CHCl_3$).

Methyl (*R*)-1-butyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3j)



According to the general procedure, **3j** was obtained in 93% yield (29.0 mg) with 96% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 12.1, 8.4 Hz, 2H), 7.75 (d, *J* = 8.6 Hz, 2H), 7.63 – 7.51 (m, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 4.43 (t, *J* = 7.7 Hz, 1H), 4.05 (s, 3H), 2.11 – 1.92 (m, 1H), 1.89 – 1.72 (m, 1H), 1.54 – 1.28 (m, 4H), 0.87 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 152.6, 138.5, 130.8, 130.5, 128.9, 128.4, 127.4, 124.4, 121.5, 117.6, 115.3, 55.2, 45.7, 29.6, 29.3, 22.6, 13.9. HRMS (ESI): calcd for $C_{18}H_{21}N_2O_3^+$ ($M+H^+$): 313.1552, found 313.1556. HPLC analysis: (Chiralpak AS-H, isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 8.9 min, t_R (minor) = 13.7 min, *ee* = 96%. $[\alpha]_D^{25}$ = +28.3 (*c* = 0.9 in $CHCl_3$).

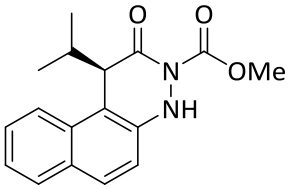
Methyl (*R*)-1-hexyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3k)



According to the general procedure, **3k** was obtained in 90% yield (30.6 mg) with 95% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 12.1, 8.3 Hz, 2H), 7.78 – 7.68 (m, 2H), 7.56 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.49 – 7.37 (m, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 4.47 – 4.36 (m, 1H), 4.05 (s, 3H), 2.12 – 1.94 (m, 1H), 1.87 – 1.71 (m, 1H), 1.54 – 1.20 (m, 8H), 0.86 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 152.6, 138.5, 130.8, 130.5, 128.9, 128.4, 127.3, 124.4, 121.5, 117.6, 115.3, 55.2, 45.8, 31.6, 29.5, 29.2, 27.5, 22.6, 14.1. HRMS (ESI): calcd for $C_{20}H_{25}N_2O_3^+$ ($M+H^+$): 341.1865, found 341.1864. HPLC analysis: (Chiralpak AS-H, isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 6.6 min,

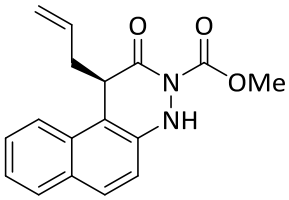
t_R (minor) = 10.9 min, *ee* = 95%. $[\alpha]_D^{25}$ = +98.2 (*c* = 1.0 in $CHCl_3$).

Methyl (*R*)-1-isopropyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3l)



According to the general procedure, **3l** was obtained in 51% yield (15.2 mg) with 91% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 1H), 7.76 (d, *J* = 8.6 Hz, 1H), 7.71 (s, 1H), 7.57 – 7.50 (m, 1H), 7.43 (dd, *J* = 11.0, 3.9 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 4.14 (d, *J* = 9.4 Hz, 1H), 4.05 (s, 3H), 2.54 – 2.41 (m, 1H), 1.22 (d, *J* = 6.7 Hz, 3H), 0.83 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 152.7, 138.9, 131.8, 130.5, 128.8, 128.5, 127.2, 124.3, 122.3, 117.4, 115.4, 55.2, 53.0, 28.5, 21.5, 21.1. HRMS (ESI): calcd for $C_{17}H_{19}N_2O_3^+$ ($M+H^+$): 299.1396, found 299.1386. HPLC analysis: (Chiralpak AS-H, isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 8.6 min, t_R (minor) = 15.8 min, *ee* = 91%. $[\alpha]_D^{25}$ = +13.5 (*c* = 1.0 in $CHCl_3$).

Methyl (*R*)-1-allyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3m)



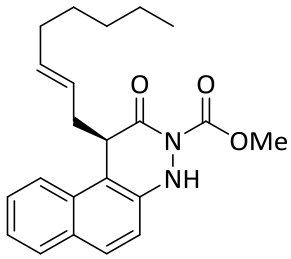
According to the general procedure, **3m** was obtained in 88% yield (26.4 mg) with 95% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (t, *J* = 8.1 Hz, 2H), 7.76 (d, *J* = 8.7 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 5.87 – 5.76 (m, 1H), 5.06 (dd, *J* = 24.8, 13.5 Hz, 2H), 4.51 (t, *J* = 7.7 Hz, 1H), 4.05 (s, 3H), 2.84 – 2.67 (m, 1H), 2.62 (dt, *J* = 14.0, 7.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 152.5, 138.6, 134.2, 130.7, 130.5, 128.9, 128.7, 127.4, 124.5, 121.6, 118.0, 116.6, 115.3, 55.3, 46.0, 33.7. HRMS (ESI): calcd for $C_{17}H_{17}N_2O_3^+$ ($M+H^+$): 297.1239, found 297.1241. HPLC analysis: (Chiralpak AS-H,

isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 10.5 min, t_R (minor) = 16.8 min, *ee* = 95%. $[\alpha]_D^{25}$ = +55.5 (*c* = 1.0 in $CHCl_3$).

Methyl

(*R*,*E*)-1-(oct-2-en-1-yl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

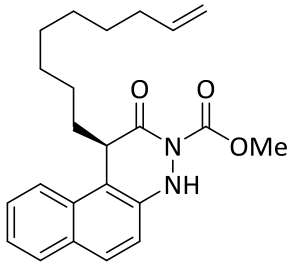
(3n)



According to the general procedure, **3n** was obtained in 87% yield (31.8 mg) with 95% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (t, *J* = 7.1 Hz, 2H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.59 – 7.48 (m, 1H), 7.42 (dd, *J* = 11.2, 4.1 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 5.46 – 5.29 (m, 2H), 4.46 (t, *J* = 7.6 Hz, 1H), 4.04 (s, 3H), 2.78 – 2.64 (m, 1H), 2.64 – 2.52 (m, 1H), 1.85 (d, *J* = 5.8 Hz, 2H), 1.23 (dq, *J* = 14.0, 7.2 Hz, 2H), 1.14 (tt, *J* = 10.9, 5.6 Hz, 4H), 0.86 (dd, *J* = 8.6, 5.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.3, 152.5, 138.5, 134.4, 130.9, 130.5, 128.8, 128.5, 127.1, 125.3, 124.3, 121.9, 116.8, 115.2, 55.2, 46.4, 32.7, 32.4, 31.2, 28.7, 22.5, 14.1. HRMS (ESI): calcd for $C_{22}H_{27}N_2O_3^+$ ($M+H^+$): 367.2022, found 367.2028. HPLC analysis: (Chiralpak AS-H, isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 6.9 min, t_R (minor) = 11.5 min, *ee* = 95%. $[\alpha]_D^{25}$ = +87.2 (*c* = 0.7 in $CHCl_3$).

Methyl

(*R*)-1-(non-8-en-1-yl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3o)

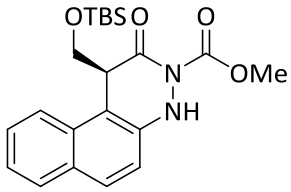


According to the general procedure, **3o** was obtained in 91% yield (34.6 mg) with 95%

ee as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, *J* = 10.9, 8.6 Hz, 2H), 7.79 – 7.64 (m, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 8.7 Hz, 1H), 5.80 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.08 – 4.76 (m, 2H), 4.42 (t, *J* = 7.7 Hz, 1H), 4.05 (s, 3H), 2.08 – 1.96 (m, 3H), 1.86 – 1.73 (m, 1H), 1.54 – 1.26 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 152.6, 139.2, 138.5, 130.8, 130.5, 128.9, 128.4, 127.4, 124.4, 121.5, 117.6, 115.3, 114.2, 55.2, 45.8, 33.8, 29.5, 29.4, 29.2, 29.0, 28.8, 27.5. HRMS (ESI): calcd for $C_{23}H_{29}N_2O_3^+$ ($M+H^+$): 381.2178, found 381.2180. HPLC analysis: (Chiralpak AS-H, isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 6.3 min, t_R (minor) = 10.9 min, *ee* = 95%. $[\alpha]_D^{25}$ = +100.2 (*c* = 0.6 in $CHCl_3$).

Methyl

(*S*)-1-(((tert-butyldimethylsilyl)oxy)methyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3p)

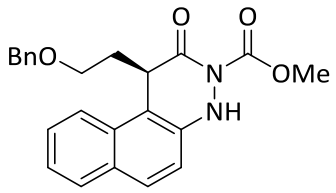


According to the general procedure, **3p** was obtained in 71% yield (28.4 mg) with 91% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 1H), 7.60 – 7.52 (m, 2H), 7.47 – 7.41 (m, 1H), 7.20 (d, *J* = 8.7 Hz, 1H), 4.68 (t, *J* = 6.8 Hz, 1H), 4.12 (dd, *J* = 9.8, 6.9 Hz, 1H), 4.10 – 4.02 (m, 4H), 0.77 (s, 9H), -0.15 (s, 3H), -0.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.5, 152.6, 139.0, 131.3, 130.6, 128.9, 128.8, 127.3, 124.5, 121.9, 115.8, 115.4, 61.6, 55.1, 49.0, 25.7, 18.1, -5.8, -5.8. HRMS (ESI): calcd for $C_{21}H_{29}NO_4Si^+$ ($M+H^+$): 401.1897, found 401.1891. HPLC analysis: (Chiralpak AS-H, isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 8.3 min, t_R (minor) = 11.6 min, *ee* = 91%. $[\alpha]_D^{25}$ = -43.9 (*c* = 0.8 in $CHCl_3$).

Methyl

(*R*)-1-(2-(benzyloxy)ethyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

(3q)

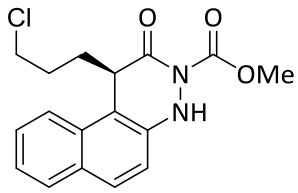


According to the general procedure, **3q** was obtained in 92% yield (35.9 mg) with 94% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.78 – 7.49 (m, 2H), 7.46 – 7.44 (m, 1H), 7.42 – 7.40 (m, 1H), 7.39 (d, *J* = 4.4 Hz, 4H), 7.35 – 7.30 (m, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 4.72 (t, *J* = 7.4 Hz, 1H), 4.47 (s, 2H), 4.01 (s, 3H), 3.58 – 3.54 (m, 1H), 3.41 – 3.37 (m, 1H), 2.33 (dtd, *J* = 11.8, 7.4, 4.5 Hz, 1H), 2.27 – 2.09 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.7, 152.5, 138.9, 138.4, 131.1, 130.5, 128.8, 128.6, 128.4, 127.6, 127.5, 127.4, 124.5, 121.8, 117.2 115.4, 72.9, 67.1, 55.1, 42.7, 29.6. HRMS (ESI): calcd for $C_{23}H_{23}N_2O_4^+$ ($M+H^+$): 391.1658, found 391.1657. HPLC analysis: (Chiralpak AS-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 12.4 min, t_R (minor) = 24.7 min, *ee* = 94%. $[\alpha]_D^{25}$ = -108.0 (*c* = 1.1 in $CHCl_3$).

Methyl

(*R*)-1-(3-chloropropyl)-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

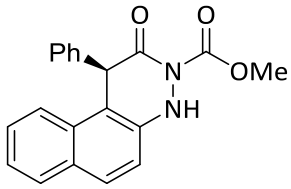
(3r)



According to the general procedure, **3r** was obtained in 86% yield (28.6 mg) with 96% *ee* as a white solid. m.p. 161-162 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, *J* = 11.7, 8.4 Hz, 2H), 7.77 (d, *J* = 8.6 Hz, 2H), 7.58 (dd, *J* = 11.3, 4.0 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 4.46 (dd, *J* = 8.8, 6.2 Hz, 1H), 4.06 (s, 3H), 3.65 – 3.55 (m, 2H), 2.17 (dd, *J* = 19.0, 9.0 Hz, 1H), 2.06 – 1.88 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 152.4, 138.6, 130.6, 130.6, 129.0, 128.8, 127.6, 124.5, 121.3, 116.7, 115.2, 55.3, 44.8, 44.3, 30.0, 26.4. HRMS (ESI): calcd for

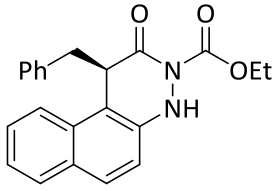
$C_{17}H_{18}ClN_2O_3^+$ ($M+H^+$): 333.1006, found 333.1010. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 29.5 min, t_R (major) = 33.0 min, *ee* = 96%. $[\alpha]_D^{25}$ = +70.5 (*c* = 0.8 in $CHCl_3$).

Methyl (*R*)-2-oxo-1-phenyl-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (3s)



According to the general procedure, **3s** was obtained in 76% yield (25.2 mg) with 57% *ee* as a light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (t, *J* = 8.6 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.71 – 7.68 (m, 1H), 7.53 – 7.42 (m, 2H), 7.28 – 7.21 (m, 5H), 5.75 (s, 1H), 4.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 152.5, 139.1, 134.5, 131.2, 130.6, 129.4, 128.9, 128.9, 127.9, 127.7, 127.7, 124.7, 121.6, 115.4, 115.4, 55.3, 50.3. HRMS (ESI): calcd for $C_{20}H_{17}N_2O_3^+$ ($M+H^+$): 333.1239, found 333.1237. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 29.8 min, t_R (minor) = 47.1 min, *ee* = 57%. $[\alpha]_D^{25}$ = -44.1 (*c* = 1.0 in $CHCl_3$).

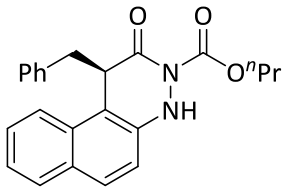
Ethyl (*R*)-1-benzyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4a)



According to the general procedure, **4a** was obtained in 88% yield (31.7 mg) with 98% *ee* as a white solid. m.p. 163-164 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 – 7.74 (m, 2H), 7.45 (dd, *J* = 6.4, 2.9 Hz, 1H), 7.34 – 7.30 (m, 3H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.15 – 7.07 (m, 3H), 6.93 (dd, *J* = 7.4, 1.9 Hz, 2H), 4.64 (dd, *J* = 8.1, 6.6 Hz, 1H), 4.49 (q, *J* = 7.1 Hz, 2H), 3.29 (dd, *J* = 13.1, 6.5 Hz, 1H), 3.20 (dd, *J* = 13.1, 8.2 Hz, 1H), 1.45 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2, 151.9, 138.8, 137.4, 131.0, 130.3, 129.3, 128.7, 128.6, 128.2, 127.0, 126.7, 124.2, 121.4, 116.8, 115.4, 64.9, 48.0, 35.6, 14.4. HRMS (ESI): calcd for $C_{22}H_{21}N_2O_3^+$ ($M+H^+$): 361.1552, found

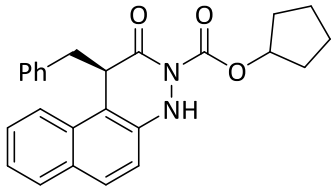
361.1558. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 14.0 min, t_R (major) = 30.4 min, *ee* = 98%. $[\alpha]_D^{25}$ = -109.2 (*c* = 1.2 in $CHCl_3$).

Propyl (*R*)-1-benzyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4b)



According to the general procedure, **4b** was obtained in 87% yield (32.6 mg) with 99% *ee* as a white solid. m.p. 138-140 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 – 7.74 (m, 2H), 7.50 (s, 1H), 7.45 (dd, *J* = 6.2, 3.1 Hz, 1H), 7.37 – 7.31 (m, 3H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.13 – 7.09 (m, 2H), 6.94 – 6.92 (m, 2H), 4.64 (dd, *J* = 8.1, 6.6 Hz, 1H), 4.38 (t, *J* = 6.6 Hz, 2H), 3.29 (dd, *J* = 13.1, 6.5 Hz, 1H), 3.20 (dd, *J* = 13.1, 8.2 Hz, 1H), 1.88 – 1.79 (m, 2H), 1.04 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2, 152.1, 138.8, 137.4, 131.0, 130.3, 129.3, 128.6, 128.6, 128.3, 127.0, 126.7, 124.2, 121.4, 116.8, 115.4, 70.2, 48.1, 35.6, 22.0, 10.3. HRMS (ESI): calcd for $C_{23}H_{23}N_2O_3^+$ ($M+H^+$): 375.1709, found 375.1711. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 12.9 min, t_R (major) = 29.1 min, *ee* = 99%. $[\alpha]_D^{25}$ = -35.2 (*c* = 0.7 in $CHCl_3$).

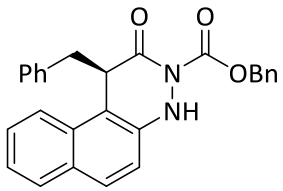
Cyclopentyl (*R*)-1-benzyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4c)



According to the general procedure, **4c** was obtained in 83% yield (33.2 mg) with 99% *ee* as a white solid. m.p. 161-162 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 – 7.73 (m, 2H), 7.53 (s, 1H), 7.43 – 7.41 (m, 1H), 7.37 – 7.28 (m, 3H), 7.19 (d, *J* = 8.7 Hz, 1H), 7.12 – 7.08 (m, 2H), 6.92 (dd, *J* = 7.4, 1.6 Hz, 2H), 5.41 – 5.39 (m, 1H), 4.61 (dd, *J* = 8.3, 6.4 Hz, 1H), 3.28 (dd, *J* = 13.1, 6.3 Hz, 1H), 3.19 (dd, *J* = 13.1, 8.4 Hz, 1H), 1.89

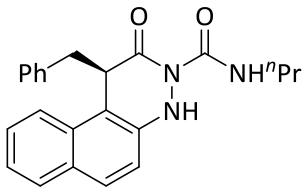
(dddd, J = 24.4, 18.9, 11.7, 4.8 Hz, 6H), 1.87 – 1.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 151.7, 138.9, 137.5, 131.0, 130.3, 129.3, 128.6, 128.5, 128.2, 126.9, 126.7, 124.2, 121.4, 116.7, 115.4, 82.4, 48.1, 35.6, 32.7, 23.6, 23.6. HRMS (ESI): calcd for $C_{25}H_{25}N_2O_3^+$ ($M+H^+$): 401.1865, found 401.1860. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 12.2 min, t_R (major) = 22.5 min, *ee* = 99%. $[\alpha]_D^{25}$ = -90.5 (*c* = 0.9 in $CHCl_3$).

Benzyl (*R*)-1-benzyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4d)



According to the general procedure, **4d** was obtained in 85% yield (35.9 mg) with 99% *ee* as a white solid. m.p. 155-156 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 – 7.73 (m, 2H), 7.51 – 7.33 (m, 9H), 7.17 (d, J = 8.7 Hz, 1H), 7.13 – 7.07 (m, 3H), 6.94 – 6.92 (m, 2H), 5.46 (s, 2H), 4.67 – 4.64 (m, 1H), 3.25 (ddd, J = 21.2, 13.1, 7.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.2, 151.8, 138.7, 137.4, 134.8, 130.9, 130.4, 129.3, 128.7, 128.6, 128.6, 128.3, 128.3, 128.0, 127.0, 126.7, 124.3, 121.4, 116.7, 115.5, 69.8, 48.0, 35.7. HRMS (ESI): calcd for $C_{27}H_{23}N_2O_3^+$ ($M+H^+$): 423.1709, found 423.1709. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 24.2 min, t_R (major) = 47.1 min, *ee* = 99%. $[\alpha]_D^{25}$ = -13.5 (*c* = 0.8 in $CHCl_3$).

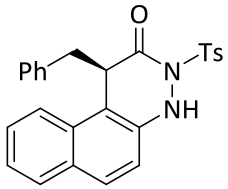
(*R*)-1-Benzyl-2-oxo-*N*-propyl-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxamide (4e)



According to the general procedure, **4e** was obtained in 91% yield (33.9 mg) with 99% *ee* as a white solid. m.p. 150-151 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.13 (t, J = 5.4

Hz, 1H), 8.46 (s, 0.7H), 7.81 – 7.74 (m, 2H), 7.53 (dd, *J* = 6.6, 2.7 Hz, 1H), 7.37 – 7.34 (m, 2H), 7.23 (d, *J* = 8.7 Hz, 1H), 7.18 – 7.15 (m, 3H), 7.04 (dd, *J* = 6.5, 3.0 Hz, 2H), 4.63 (t, *J* = 7.7 Hz, 1H), 3.40 – 3.34 (m, 2H), 3.24 (dd, *J* = 13.2, 7.6 Hz, 1H), 3.09 (dd, *J* = 13.2, 7.8 Hz, 1H), 1.66 – 1.61 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.9, 151.7, 139.1, 137.6, 130.9, 130.2, 129.3, 128.7, 128.6, 128.3, 127.0, 126.7, 124.0, 121.2, 115.5, 115.1, 47.4, 42.4, 35.0, 22.7, 11.4. HRMS (ESI): calcd for $C_{23}H_{24}N_3O_2^+$ ($M+H^+$): 374.1869, found 374.1873. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 12.2 min, t_R (major) = 63.7 min, *ee* = 99%. $[\alpha]_D^{25}$ = -69.1 (*c* = 1.8 in $CHCl_3$).

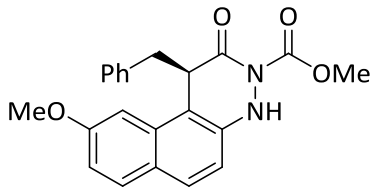
(*R*)-1-Benzyl-3-tosyl-3,4-dihydrobenzo[*f*]cinnolin-2(1*H*)-one (4f)



According to the general procedure, **4f** was obtained in 79% yield (35.0 mg) with 93% *ee* as a light yellow solid. m.p. 173-174 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 – 7.82 (m, 3H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.52 – 7.41 (m, 2H), 7.26 – 7.16 (m, 3H), 7.15 – 7.04 (m, 3H), 6.75 (d, *J* = 7.2 Hz, 2H), 5.84 (s, 1H), 4.54 (t, *J* = 6.0 Hz, 1H), 3.22 (ddd, *J* = 41.5, 13.3, 6.0 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6, 145.5, 138.2, 136.5, 134.1, 131.4, 130.5, 129.5, 129.3, 129.0, 128.9, 128.7, 128.2, 127.3, 127.2, 125.2, 121.5, 119.9, 118.2, 46.5, 37.6, 21.7. HRMS (ESI): calcd for $C_{26}H_{23}N_2O_3S^+$ ($M+H^+$): 443.1429, found 443.1435. HPLC analysis: (Chiralpak OD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 28.4 min, t_R (minor) = 36.9 min, *ee* = 93%. $[\alpha]_D^{25}$ = +132.0 (*c* = 1.5 in $CHCl_3$).

Methyl

(*R*)-1-benzyl-9-methoxy-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4g)

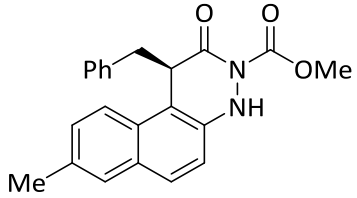


According to the general procedure, **4g** was obtained in 90% yield (33.8 mg) with 98% *ee* as a white solid. m.p. 157-158 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (t, *J* = 8.8 Hz, 2H), 7.12 – 7.05 (m, 4H), 6.93 (ddd, *J* = 9.2, 8.5, 2.0 Hz, 3H), 6.54 (d, *J* = 2.3 Hz, 1H), 4.55 (dd, *J* = 9.0, 5.7 Hz, 1H), 4.06 (s, 3H), 3.68 (s, 3H), 3.25 (qd, *J* = 12.9, 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.5, 158.5, 152.5, 139.3, 137.7, 132.6, 130.0, 129.4, 128.4, 128.3, 126.8, 125.7, 117.0, 115.7, 112.7, 100.1, 55.3, 55.0, 48.5, 35.4. HRMS (ESI): calcd for $C_{22}H_{21}N_2O_4^+$ ($M+H^+$): 377.1501, found 377.1506. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (major) = 24.5 min, t_R (minor) = 36.4 min, *ee* = 98%. $[\alpha]_D^{25}$ = -66.6 (*c* = 2.0 in $CHCl_3$).

Methyl

(*R*)-1-benzyl-8-methyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate

(4h)

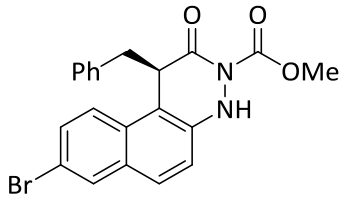


According to the general procedure, **4h** was obtained in 84% yield (30.2 mg) with 96% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.7 Hz, 1H), 7.57 (s, 1H), 7.38 (dd, *J* = 15.7, 6.2 Hz, 2H), 7.19 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.16 – 7.105 (m, 4H), 6.95 (dd, *J* = 7.1, 2.0 Hz, 2H), 4.64 (t, *J* = 7.3 Hz, 1H), 4.03 (s, 3H), 3.24 (ddd, *J* = 21.0, 13.2, 7.3 Hz, 2H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 152.6, 138.1, 137.4, 134.0, 130.7, 129.3, 129.0, 128.3, 128.0, 127.7, 126.8, 121.3, 117.1, 115.6, 55.2, 48.0, 35.7, 21.4. HRMS (ESI): calcd for $C_{22}H_{21}N_2O_3^+$ ($M+H^+$): 361.1552, found 361.1550. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 17.6 min, t_R (major) = 31.8

min, *ee* = 96%. $[\alpha]_D^{25}$ = +16.7 (*c* = 1.8 in $CHCl_3$).

Methyl

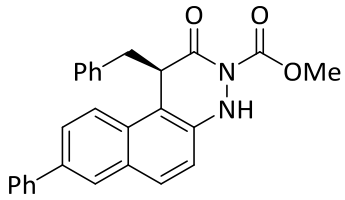
(*R*)-1-benzyl-8-bromo-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4i)



According to the general procedure, **4i** was obtained in 93% yield (39.5 mg) with 93% *ee* as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 2.0 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 1H), 7.58 (s, 1H), 7.33 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.22 (dd, *J* = 8.9, 3.8 Hz, 2H), 7.13 – 7.07 (m, 3H), 6.88 (dd, *J* = 7.8, 1.4 Hz, 2H), 4.57 (dd, *J* = 8.7, 6.1 Hz, 1H), 4.05 (s, 3H), 3.23 (ddd, *J* = 21.8, 13.1, 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.9, 152.4, 139.0, 137.1, 131.4, 130.5, 130.1, 129.6, 129.3, 128.3, 127.8, 126.9, 123.2, 118.0, 116.8, 116.4, 55.3, 48.1, 35.5. HRMS (ESI): calcd for $C_{21}H_{18}BrN_2O_3^+$ ($M+H^+$): 425.0501, 427.0480, found 425.0505, 427.0484. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 18.9 min, t_R (major) = 39.7 min, *ee* = 93%. $[\alpha]_D^{25}$ = -88.3 (*c* = 1.3 in $CHCl_3$).

Methyl

(*R*)-1-benzyl-2-oxo-8-phenyl-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4j)

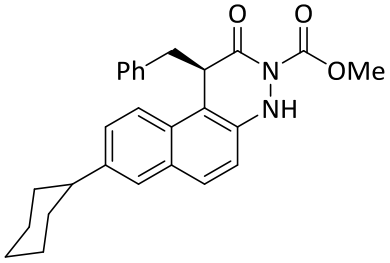


According to the general procedure, **4j** was obtained in 80% yield (33.8 mg) with 96% *ee* as a white solid. m.p. 172-173 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 1.8 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.70 – 7.68 (m, 2H), 7.61 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.53 – 7.48 (m, 3H), 7.40 (ddd, *J* = 7.4, 3.9, 1.2 Hz, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 7.16 – 7.09 (m, 3H), 6.96 (dd, *J* = 6.5, 3.0 Hz, 2H), 4.67 (dd, *J* = 8.0, 6.6 Hz, 1H), 4.05 (s, 3H), 3.31 (dd, *J* = 13.1, 6.5 Hz, 1H), 3.23 (dd, *J* = 13.2, 8.1 Hz, 1H). ^{13}C

NMR (100 MHz, $CDCl_3$): δ = 166.3, 152.5, 140.6, 138.8, 137.3, 136.9, 130.7, 130.1, 129.3, 129.0, 128.9, 128.3, 127.4, 127.2, 126.8, 126.6, 126.4, 122.0, 116.7, 115.9, 55.2, 48.0, 35.7. HRMS (ESI): calcd for $C_{27}H_{23}N_2O_3^+$ ($M+H^+$): 423.1709, found 423.1711. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 16.6 min, t_R (major) = 29.7 min, *ee* = 96%. $[\alpha]_D^{25}$ = -64.0 (*c* = 0.8 in $CHCl_3$).

Methyl

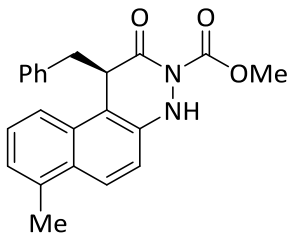
(*R*)-1-benzyl-8-cyclohexyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4k)



According to the general procedure, **4k** was obtained in 83% yield (35.6 mg) with 96% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.7 Hz, 1H), 7.59 (s, 1H), 7.46 (d, *J* = 8.8 Hz, 1H), 7.37 – 7.33 (m, 1H), 7.25 (d, *J* = 1.6 Hz, 1H), 7.14 (dt, *J* = 9.3, 4.7 Hz, 4H), 6.97 (dd, *J* = 6.9, 2.3 Hz, 2H), 4.63 (t, *J* = 7.2 Hz, 1H), 4.03 (s, 3H), 3.28 (dd, *J* = 13.2, 7.0 Hz, 1H), 3.18 (dd, *J* = 13.2, 7.5 Hz, 1H), 2.65 – 2.60 (m, 1H), 1.95 – 1.88 (m, 4H), 1.80 (d, *J* = 12.6 Hz, 1H), 1.54 – 1.40 (m, 4H), 1.35 – 1.27 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.6, 152.6, 144.1, 138.1, 137.4, 130.8, 129.3, 129.3, 128.4, 128.3, 127.4, 126.8, 125.3, 121.3, 117.0, 115.5, 55.1, 47.9, 44.3, 35.8, 34.3, 26.9, 26.2. HRMS (ESI): calcd for $C_{27}H_{29}N_2O_3^+$ ($M+H^+$): 429.2178, found 429.2170. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 16.6 min, t_R (major) = 31.3 min, *ee* = 96%. $[\alpha]_D^{25}$ = -137.4 (*c* = 1.4 in $CHCl_3$).

Methyl

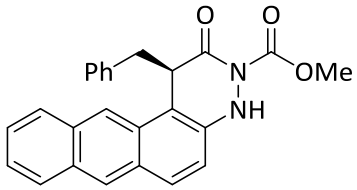
(*R*)-1-benzyl-7-methyl-2-oxo-1,4-dihydrobenzo[*f*]cinnoline-3(2*H*)-carboxylate (4l)



According to the general procedure, **4l** was obtained in 85% yield (30.6 mg) with 98% *ee* as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.9 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.28 – 7.20 (m, 3H), 7.15 – 7.12 (m, 3H), 6.97 (dd, *J* = 6.5, 2.9 Hz, 2H), 4.68 (t, *J* = 7.3 Hz, 1H), 4.04 (s, 3H), 3.29 (dd, *J* = 13.2, 6.9 Hz, 1H), 3.20 (dd, *J* = 13.2, 7.7 Hz, 1H), 2.69 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4, 152.6, 138.5, 137.4, 135.0, 131.0, 129.6, 129.3, 128.3, 126.8, 126.8, 125.4, 124.8, 119.8, 117.5, 115.1, 55.2, 48.1, 35.8, 19.8. HRMS (ESI): calcd for $C_{22}H_{21}N_2O_3^+$ ($M+H^+$): 361.1552, found 361.1550. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 13.8 min, t_R (major) = 21.8 min, *ee* = 98%. $[\alpha]_D^{25}$ = -117.5 (*c* = 1.3 in $CHCl_3$).

Methyl

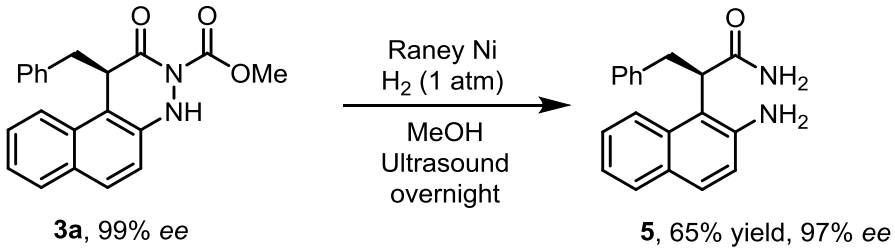
(*R*)-1-benzyl-2-oxo-1,4-dihydronaphtho[2,3-*f*]cinnoline-3(2*H*)-carboxylate (4m)



According to the general procedure, **4m** was obtained in 76% yield (30.1 mg) with 95% *ee* as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 8.01 (s, 1H), 7.97 – 7.91 (m, 2H), 7.83 (dd, *J* = 6.3, 3.0 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.17 (d, *J* = 8.9 Hz, 1H), 7.12 – 7.06 (m, 3H), 7.02 – 6.99 (m, 2H), 4.82 (t, *J* = 7.1 Hz, 1H), 4.06 (s, 3H), 3.36 (dd, *J* = 13.2, 6.5 Hz, 1H), 3.26 (dd, *J* = 13.2, 7.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.0, 152.5, 137.8, 137.5, 132.3, 130.4, 129.4, 129.0, 128.9, 128.2, 128.1, 128.0, 127.4, 126.9, 126.0, 125.2, 119.8, 116.3, 114.5, 55.2, 47.8, 35.8. HRMS (ESI): calcd for $C_{25}H_{21}N_2O_3^+$ ($M+H^+$): 397.1552, found 397.1552. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 20/80, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 26.0 min, t_R (major) = 66.4 min, *ee* = 95%. $[\alpha]_D^{25}$ = -18.2 (*c* = 1.1 in

$CHCl_3$).

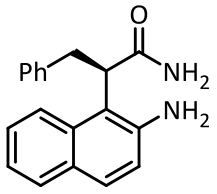
5. Cleavage of the N-N bond in 3a



3a, 99% *ee* **5**, 65% yield, 97% *ee*

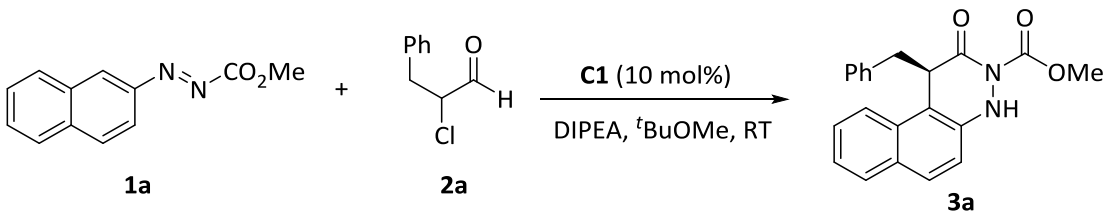
To the solution of **3a** (34.6 mg, 0.1 mmol, 99% ee) in MeOH (1.0 mL) was added Raney-Ni (~100 mg, washed with MeOH). The reaction vial was degassed with H_2 and back-filled with H_2. This reaction vial was immersed in an ultrasonic cleaner filled with water, and sonicated under H_2 atmosphere (1 atm) untill disappearance of the starting material. The reaction mixture was filtered through a Buchner funnel and the filtrate was evaporated in vacuo. The residue was purified by column chromatography (PE/EA = 20/1 to 8/1) on silica gel to afford **5** (18.8 mg, 65% yield, 97% ee) as a light yellow solid.

(*R*)-2-(2-aminonaphthalen-1-yl)-3-phenylpropanamide (5)



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.55 (dd, *J* = 9.6, 5.1 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.12 – 7.03 (m, 4H), 6.93 – 6.66 (m, 3H), 4.26 (t, *J* = 4.8 Hz, 1H), 3.90 – 3.71 (m, 2H), 3.65 (dd, *J* = 13.7, 4.8 Hz, 1H), 3.56 (dd, *J* = 13.7, 4.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 138.3, 136.9, 131.3, 130.8, 129.7, 129.2, 128.9, 128.5, 127.9, 127.2, 126.9, 124.8, 121.5, 118.4, 42.7, 38.3. HRMS (ESI): calcd for $C_{19}H_{19}N_2O^+$ ($M+H^+$): 291.1497, found 291.1487. HPLC analysis: (Chiralpak AD-H, isopropanol/hexane = 25/75, flow rate 1.0 mL/min, λ = 254 nm): t_R (minor) = 24.1 min, t_R (major) = 37.4 min, *ee* = 97%. $[\alpha]_D^{25}$ = +55.3 (*c* = 0.7 in $CHCl_3$).

6. Gram-scale synthesis



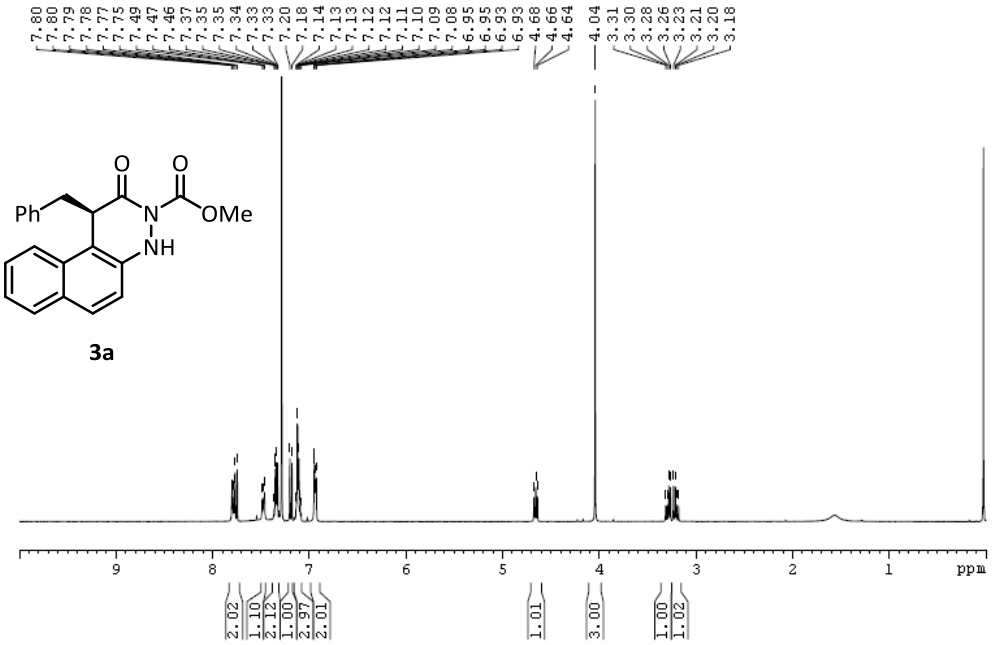
1a (750 mg, 3.5 mmol) + **2a** (1.18g, 7.0 mmol) → **3a** 90% yield (1.09g), 97% *ee*

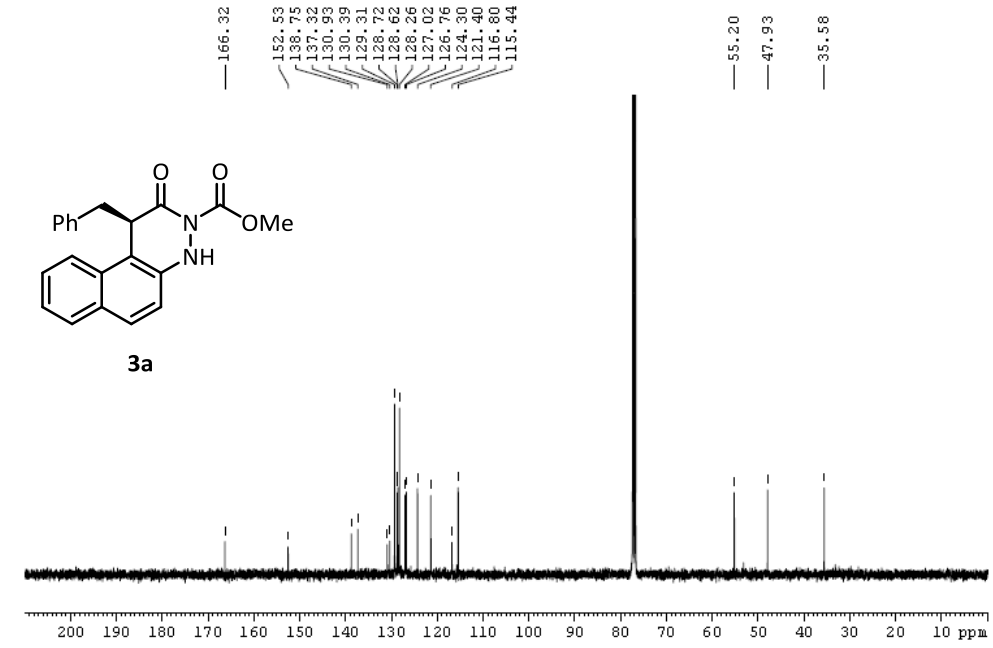
3a was synthesis under the corresponding optimal conditions with 90% yield, 97% *ee*.

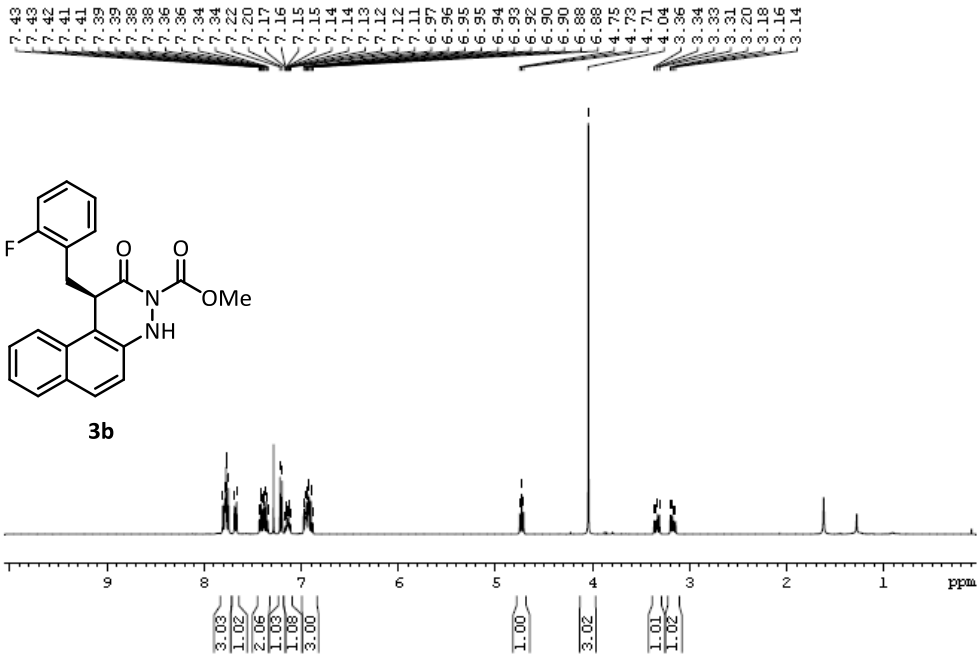
7. Reference

1) (a) Borg, T.; Danielsson, J.; Mohiti, M.; Restorp, P.; Somfai, P. *Adv. Synth. Catal*. **2011**, *353*, 2022. (b) Jing, Y.; Daniliuc, C. G.; Studer, A. *Org. Lett*. **2014**, *16*, 4932.
2) Qi, L.-W.; Mao, J.-H.; Zhang, J.; Tan, B. *Nat. Chem*. **2018**, *10*, 58.

8. ^{1}H and ^{13}C NMR spectra



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7.34
7.22
7.20
7.17
7.16
7.15
7.15
7.14
7.14
7.13
7.12
7.12
7.11
6.97
6.96
6.95
6.95
6.94
6.93
6.92
6.90
6.90
6.88
6.88
4.75
4.73
4.71
4.04
3.36
3.34
3.33
3.31
3.20
3.18
3.16
3.14
F
O
O
N
OMe
NH
3b
9
8
7
6
5
4
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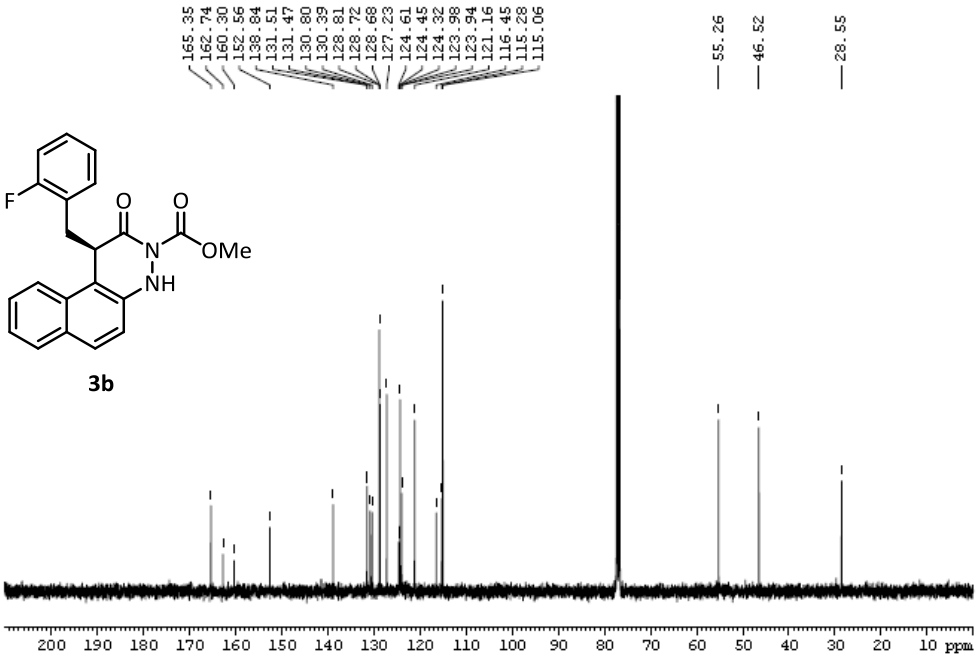
1.02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124.45
124.32
123.98
123.94
121.16
116.45
115.28
115.06
55.26
46.52
28.55
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O
O
N
OMe
NH
3b
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150
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F
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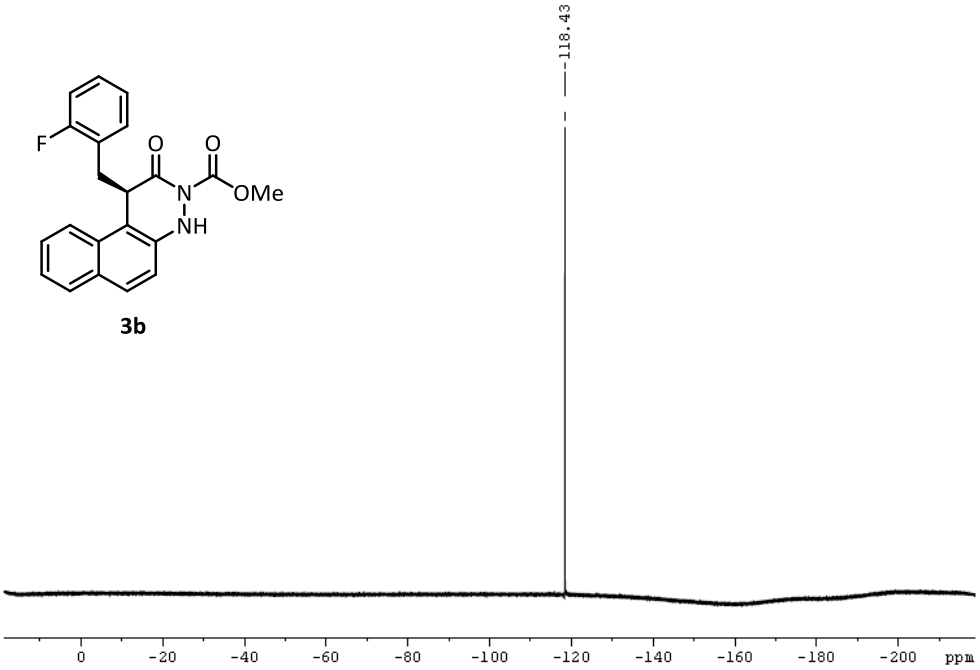
N
OMe
NH

3b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ppm


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7.76
7.75
7.69
7.35
7.33
7.32
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7.30
7.28
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7.17
7.11
7.09
7.06
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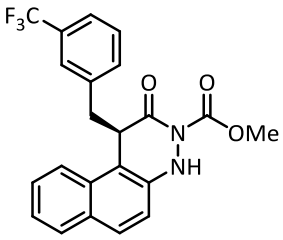
3.24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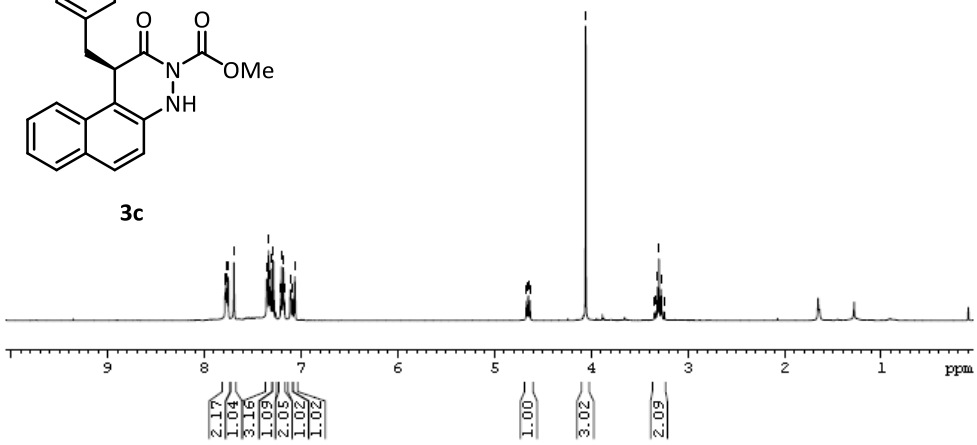
NH

3c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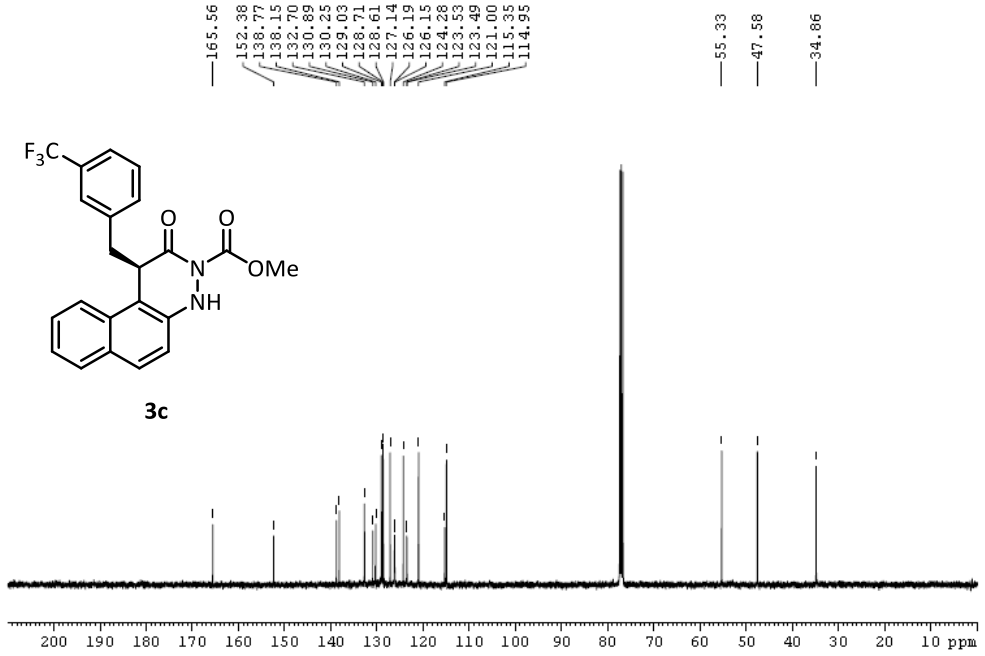
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124.28
123.53
123.49
121.00
115.35
114.95
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O
N
OMe
NH
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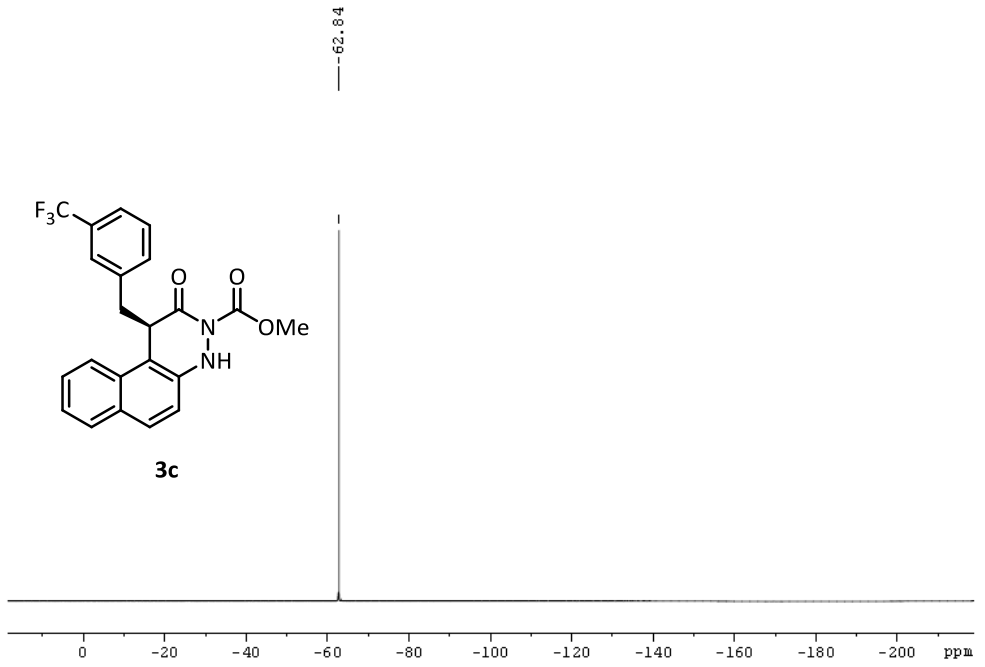
3c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NH
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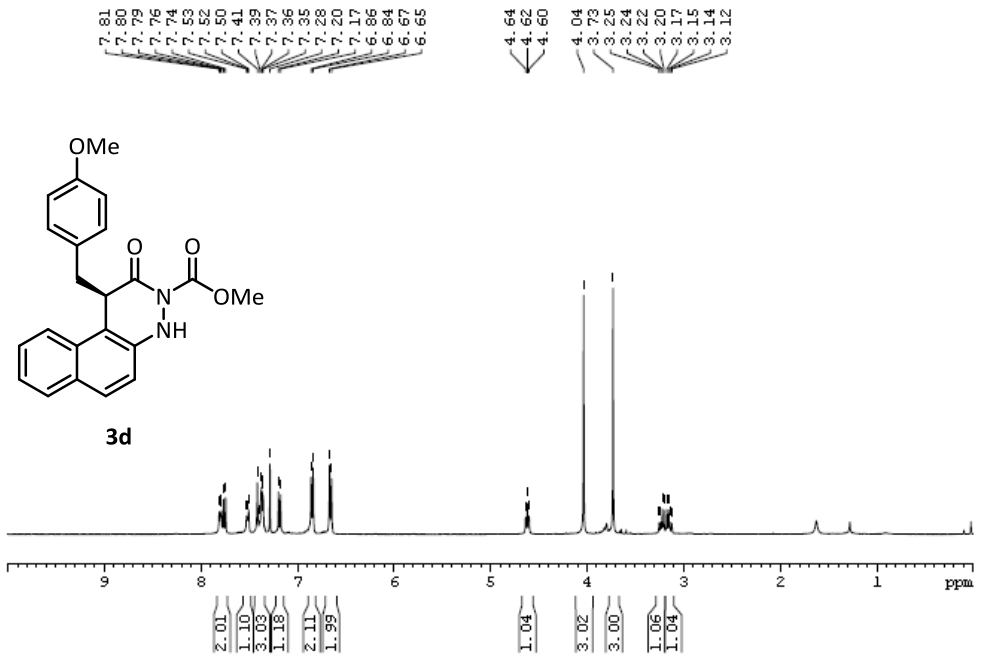
3c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7.17
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6.67
6.65
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4.62
4.60
4.04
3.73
3.25
3.24
3.22
3.20
3.17
3.15
3.14
3.12
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O
O
N
OMe
NH
3d
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8
7
6
5
4
3
2
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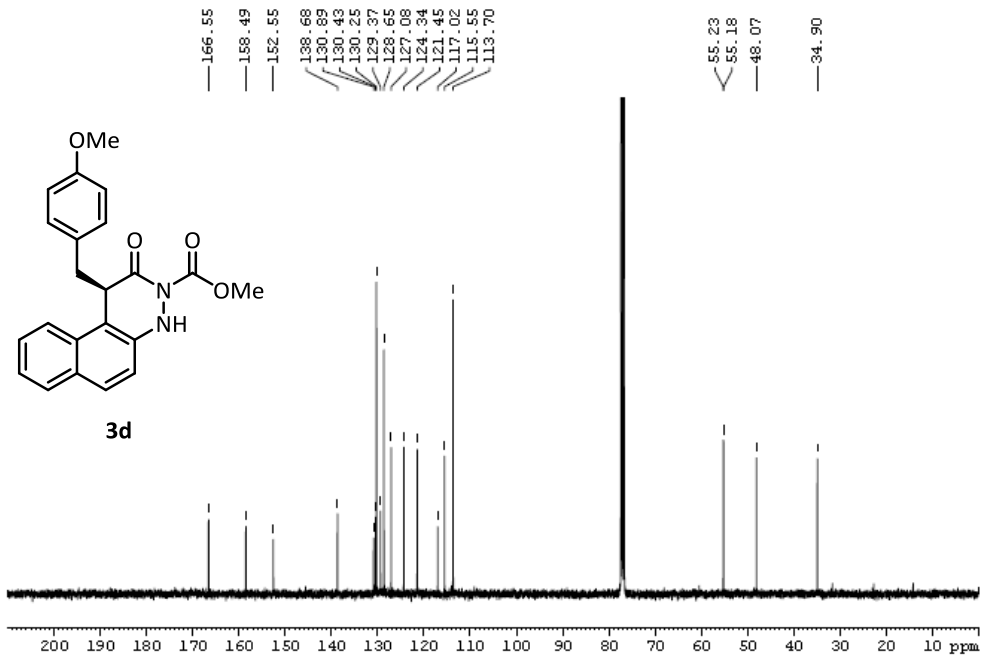
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55.18
48.07
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O
O
N
OMe
NH
3d
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100
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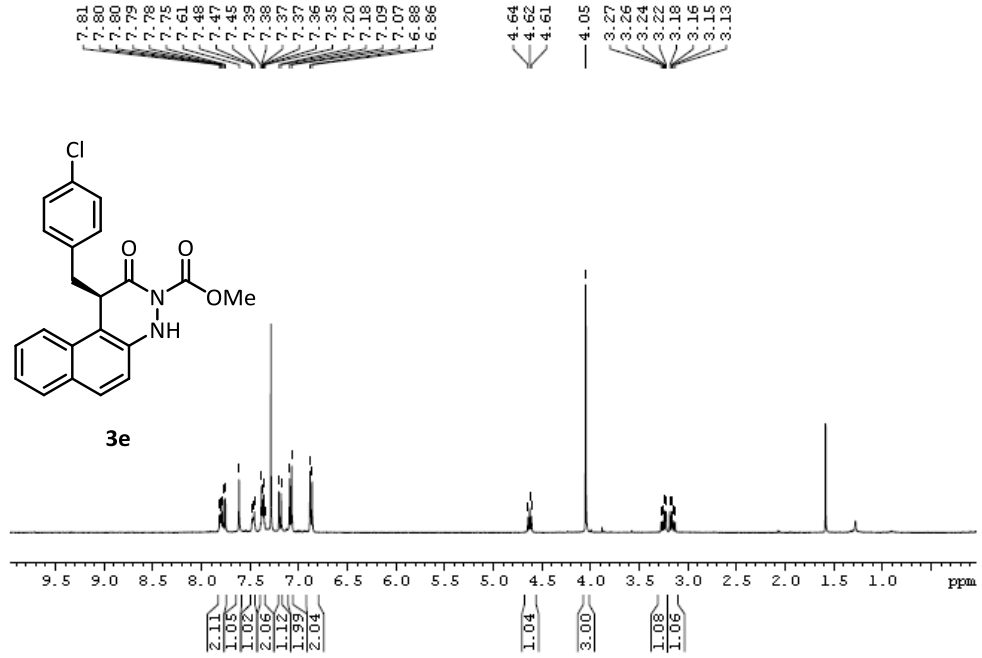
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4.61
4.05
3.27
3.26
3.24
3.22
3.18
3.16
3.15
3.13
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O
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OMe
NH
3e
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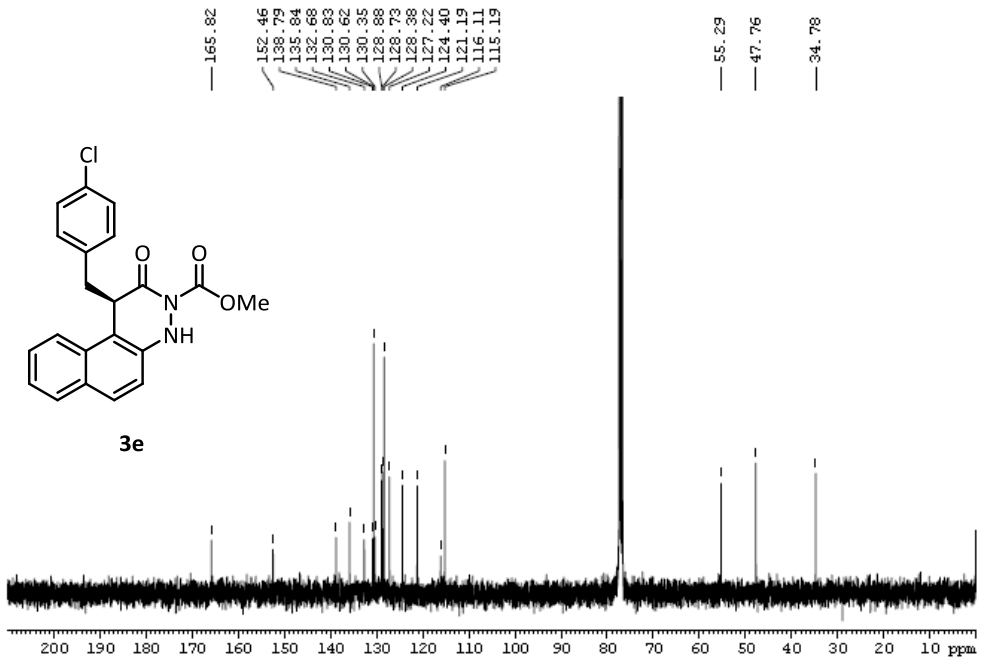
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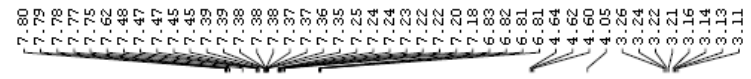
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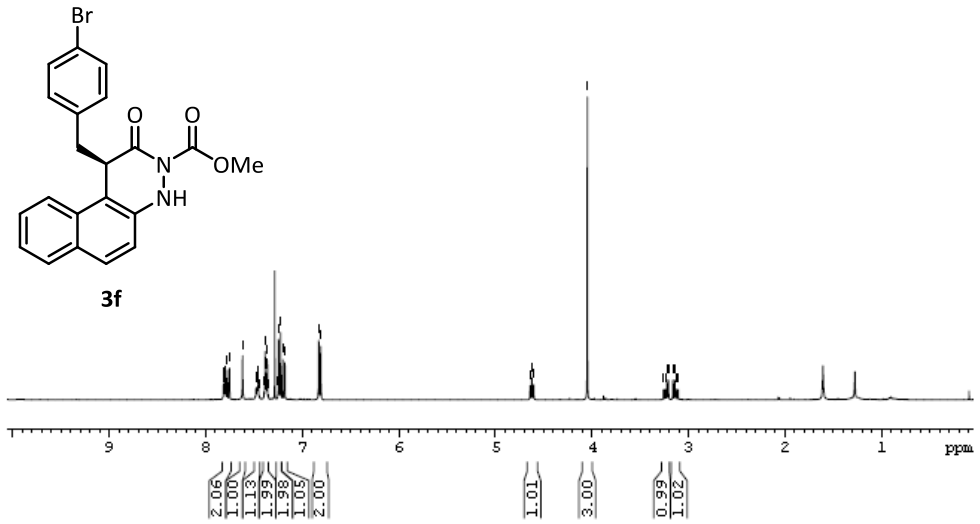
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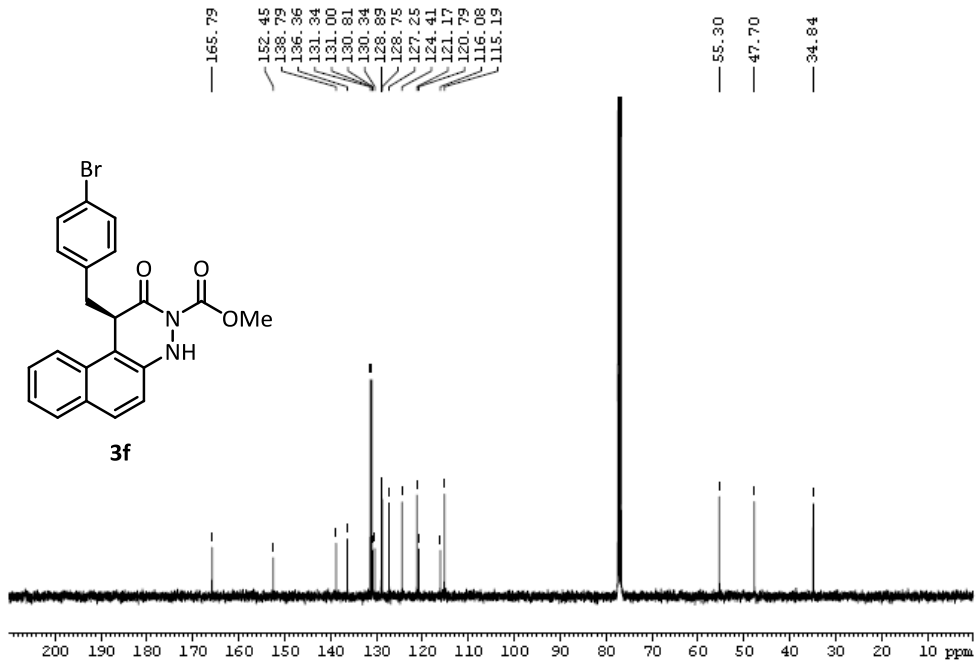
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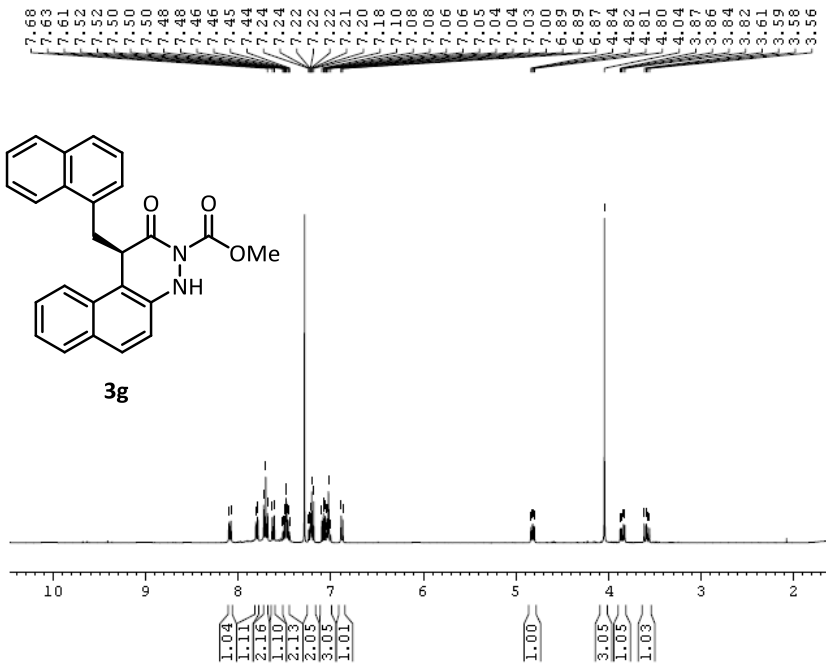
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7.06
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7.03
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3g
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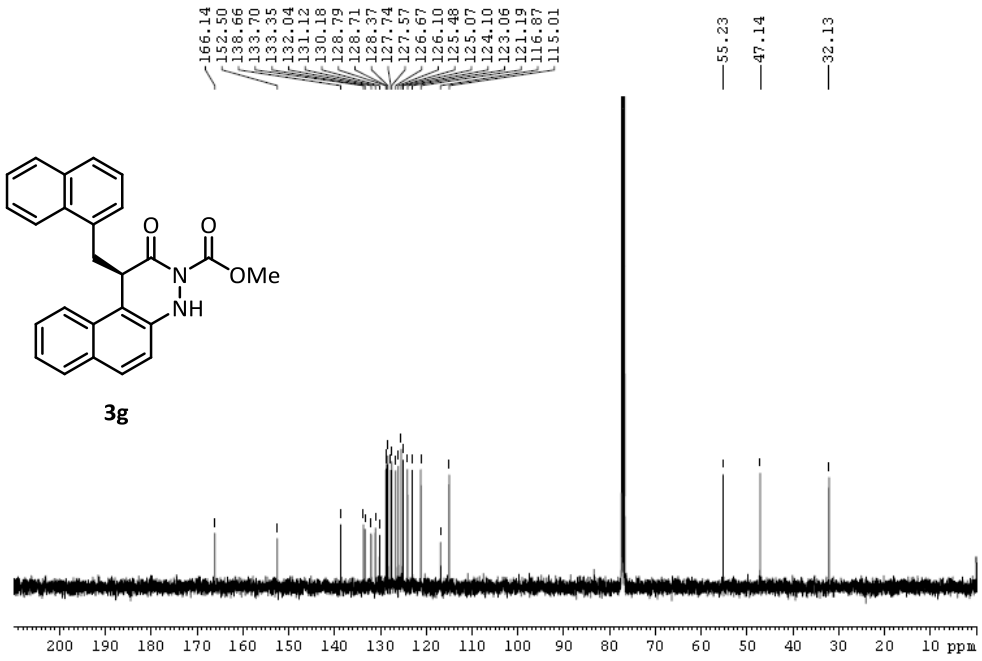
1.03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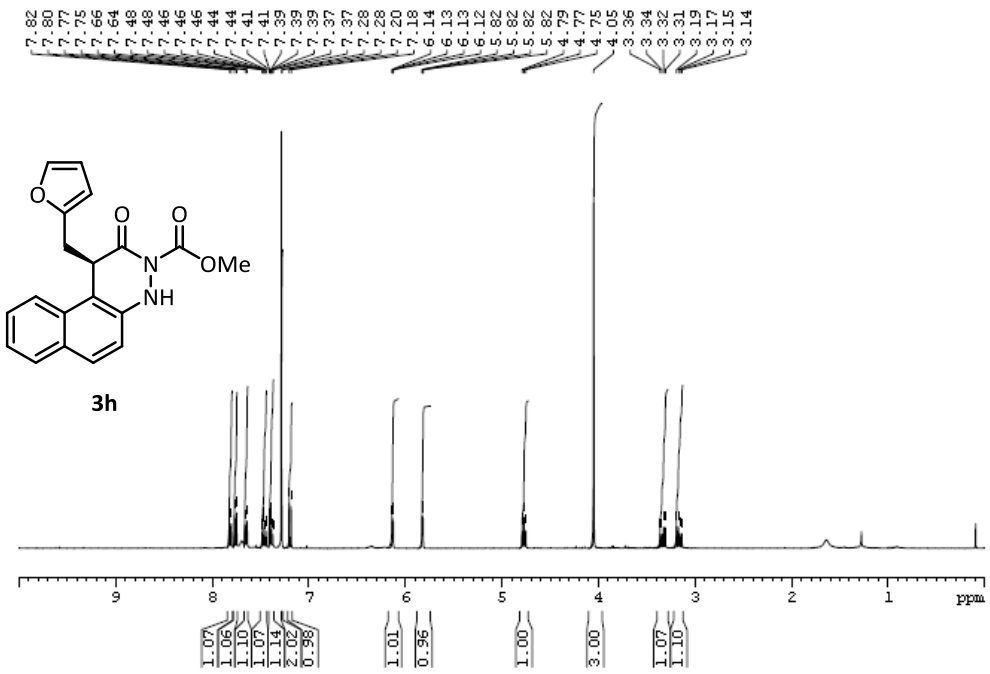
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5.82
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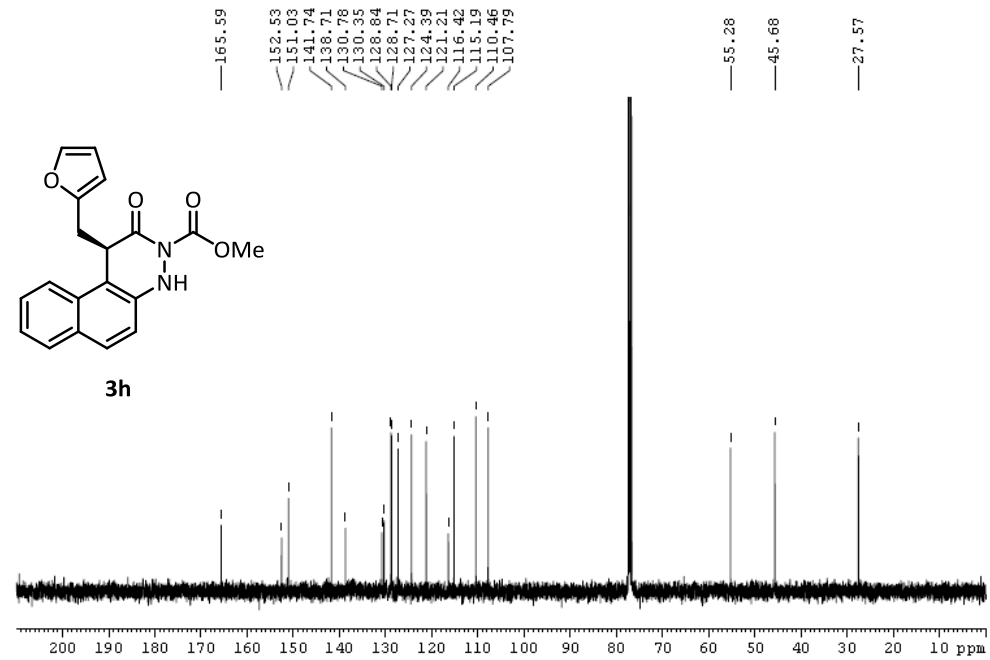
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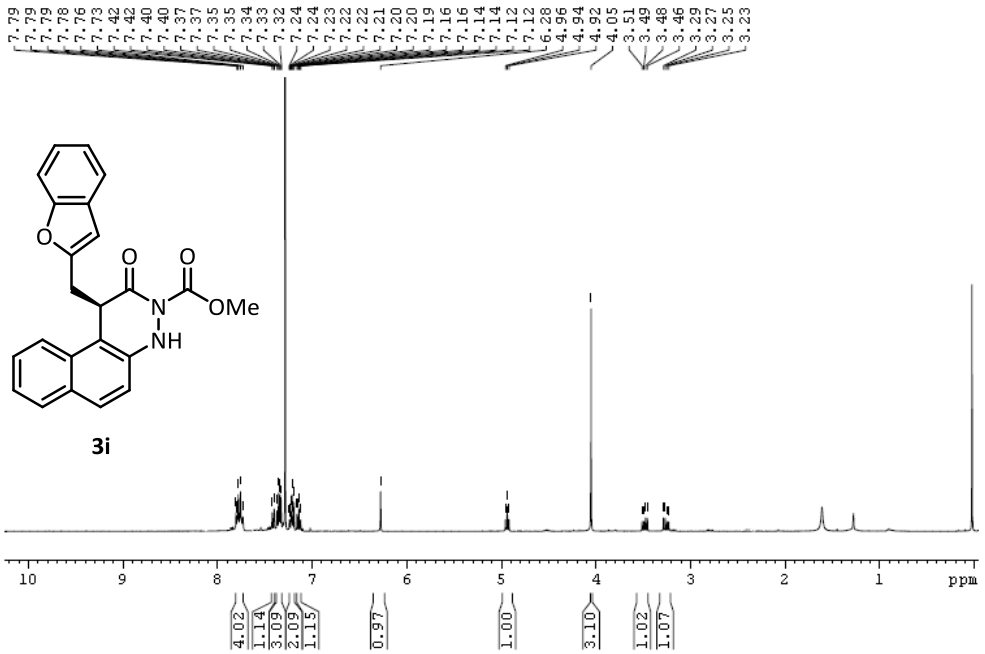
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7.16
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7.14
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7.12
6.28
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3.51
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NH
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9
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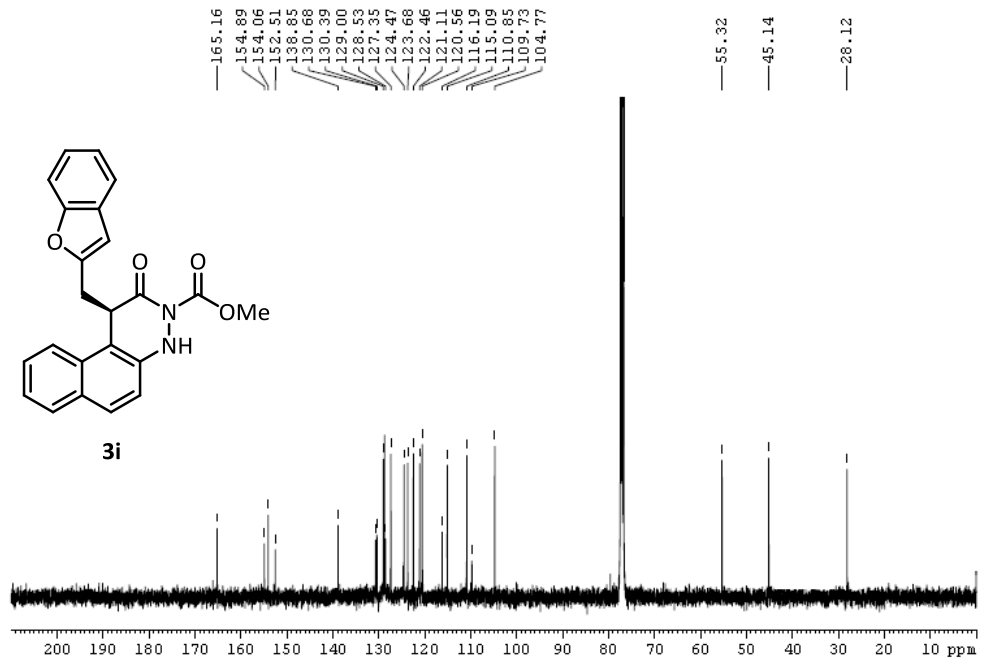
3i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120.56
116.19
115.09
110.85
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45.14
28.12
O
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O
N
OMe
NH
200
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60
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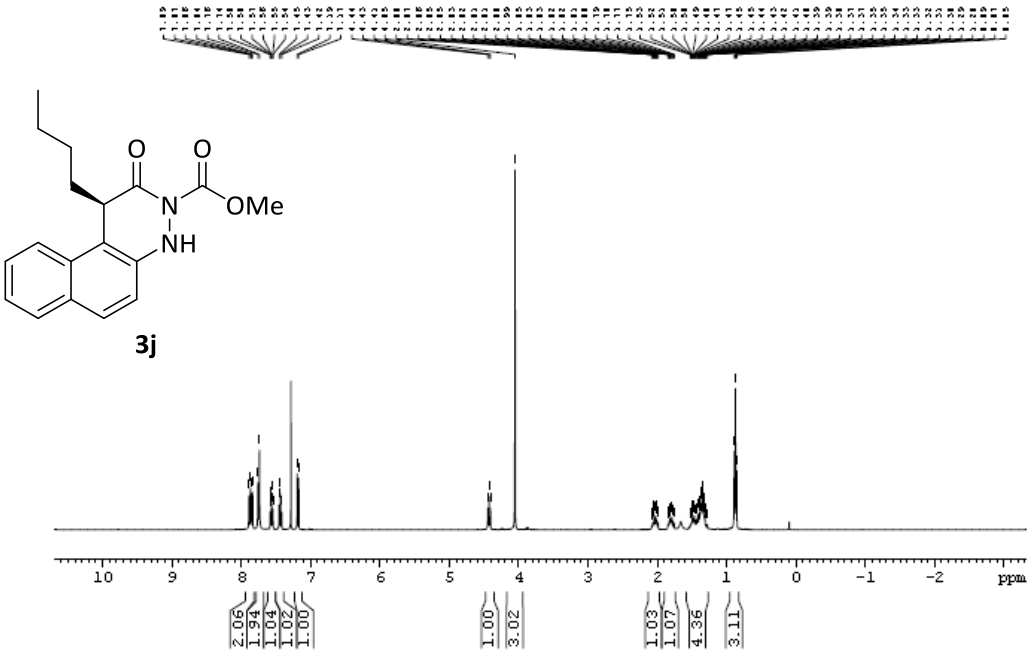
20
10 ppm

3i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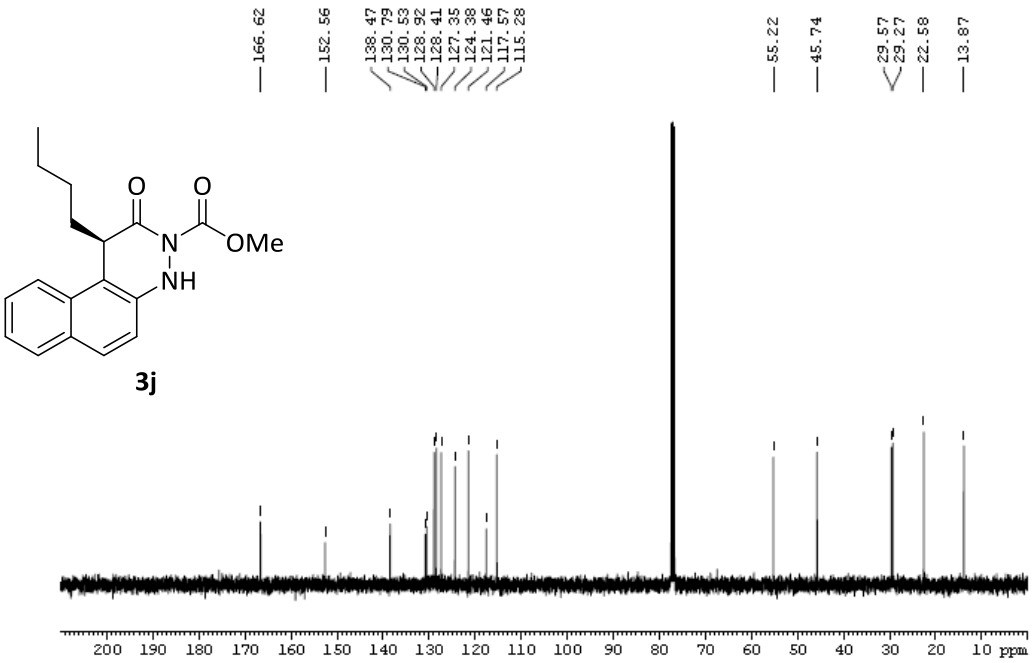
1.03
1.07
4.36
3.11

3j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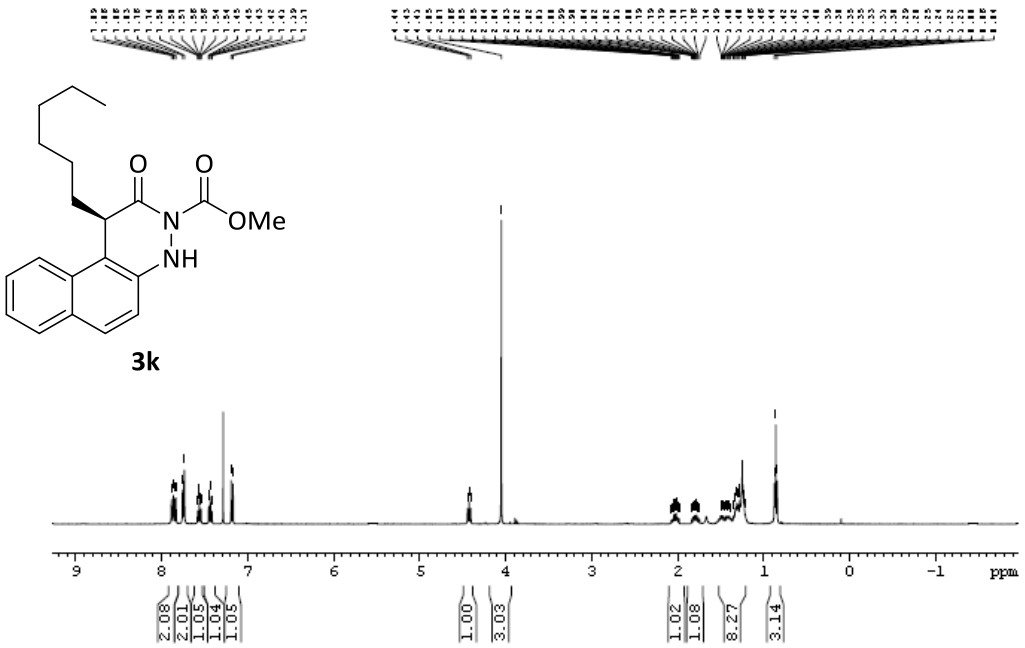
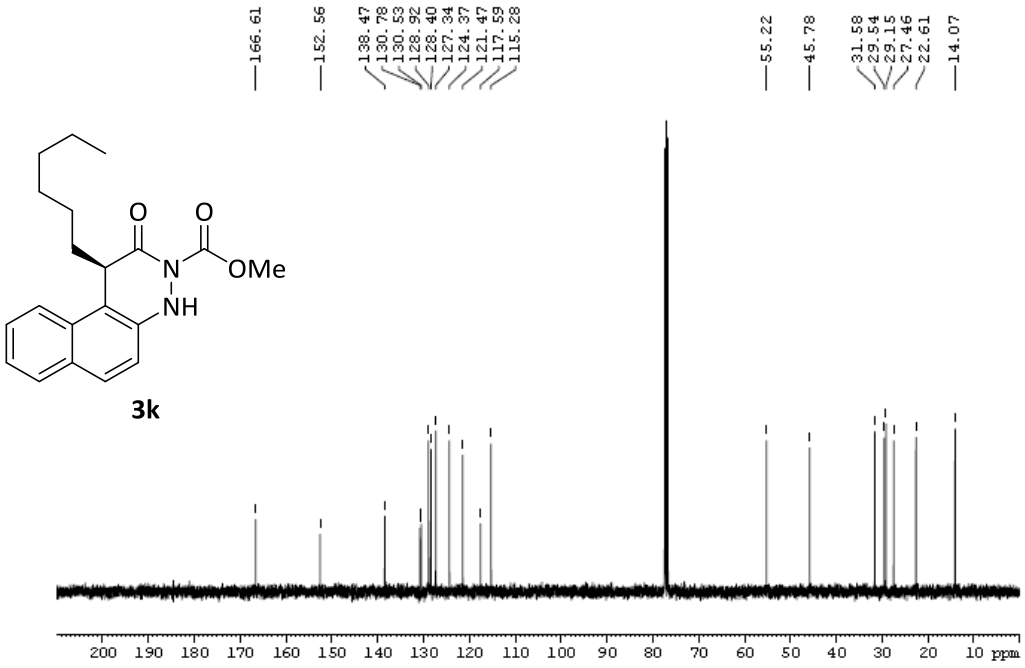
152.56
138.47
130.79
130.53
128.92
128.41
127.35
124.38
121.46
117.57
115.28
55.22
45.74
29.57
29.27
22.58
13.87
O
O
N
OMe
NH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

3j


O
O
N
OMe
NH
3k
9
8
7
6
5
4
3
2
1
0
−1
ppm
2.08
2.01
1.05
1.04
1.05
1.00
3.03
1.02
1.08
8.27
3.14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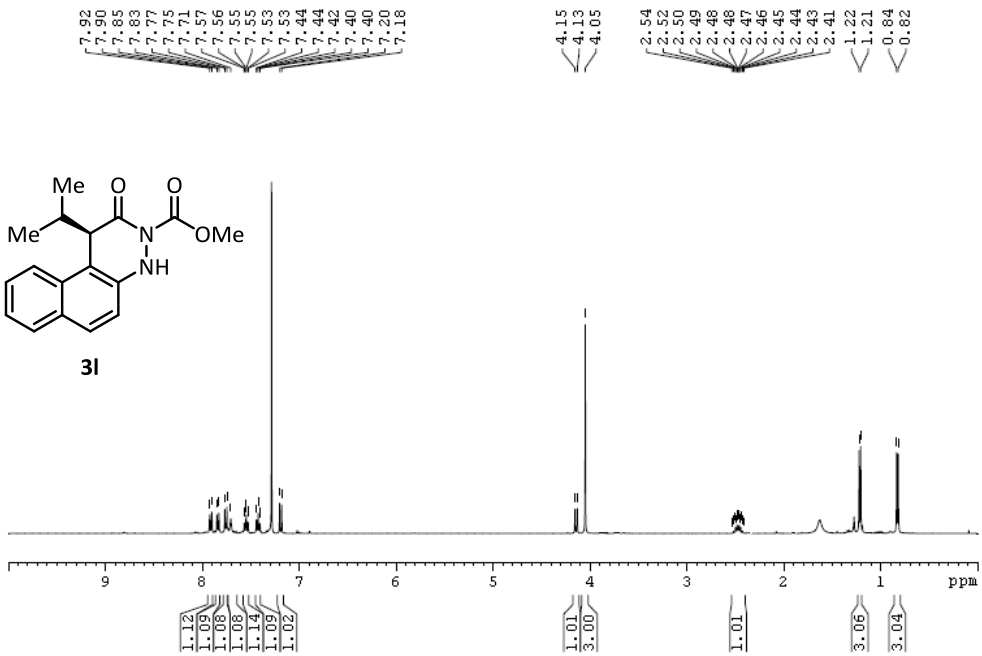
152.56
138.47
130.78
130.53
128.92
128.40
127.34
124.37
121.47
117.59
115.28
55.22
45.78
31.58
29.54
29.15
27.46
22.61
14.07
O
O
N
OMe
NH
3k
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


7.92
7.90
7.85
7.83
7.77
7.75
7.71
7.57
7.56
7.55
7.55
7.53
7.53
7.44
7.44
7.42
7.40
7.40
7.20
7.18
4.15
4.13
4.05
2.54
2.52
2.50
2.49
2.48
2.48
2.47
2.46
2.45
2.44
2.43
2.41
1.22
1.21
0.84
0.82
Me
O
O
Me
N
OMe
NH
3l
9
8
7
6
5
4
3
2
1
ppm
1.12
1.09
1.08
1.08
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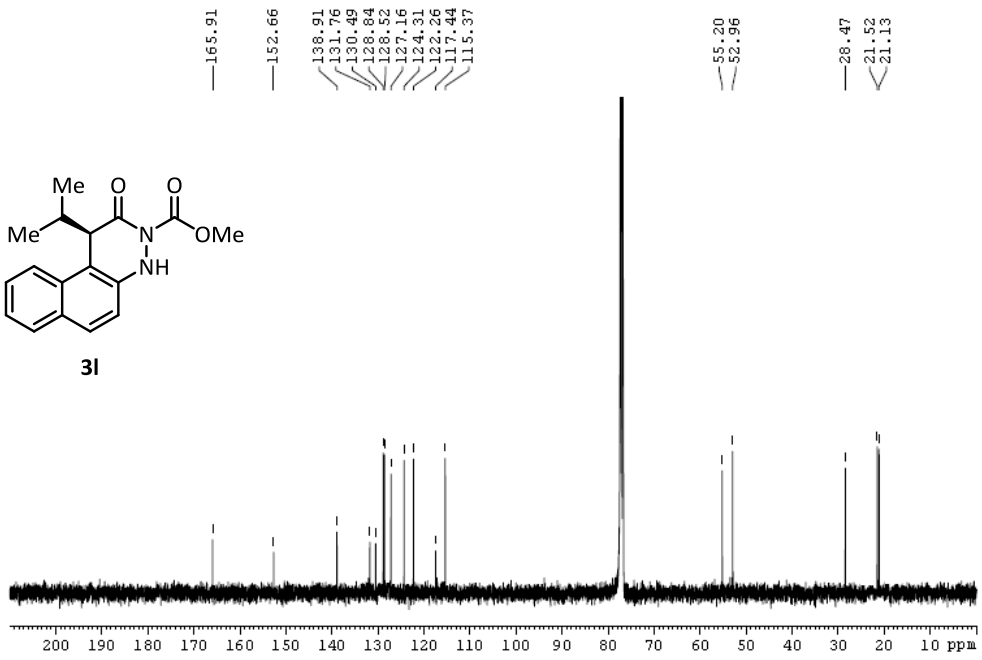
1.02
1.01
3.00
1.01
3.06
3.04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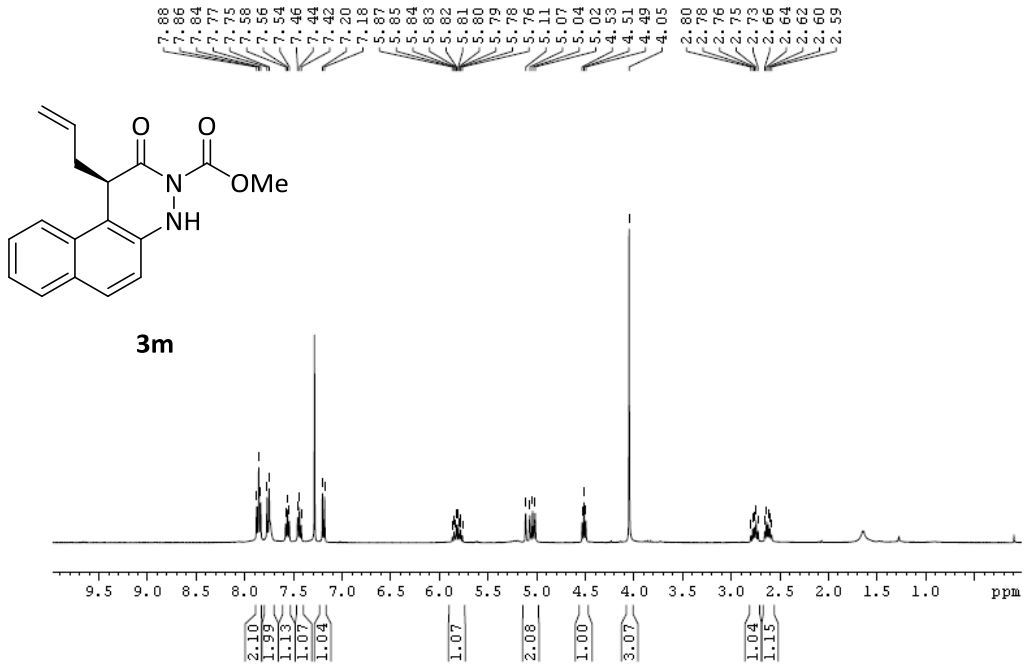
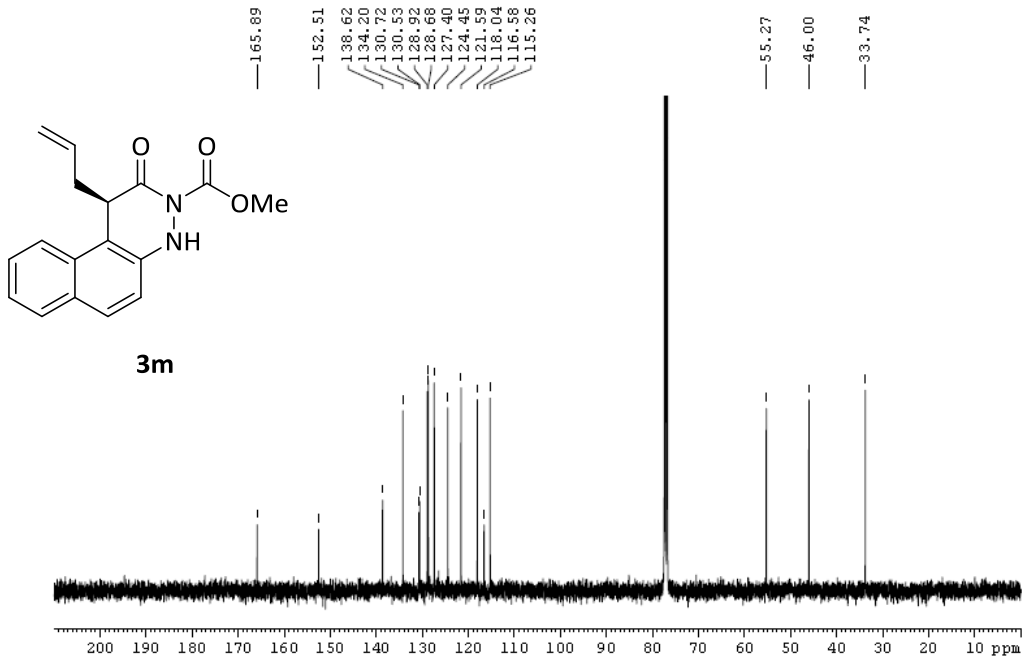
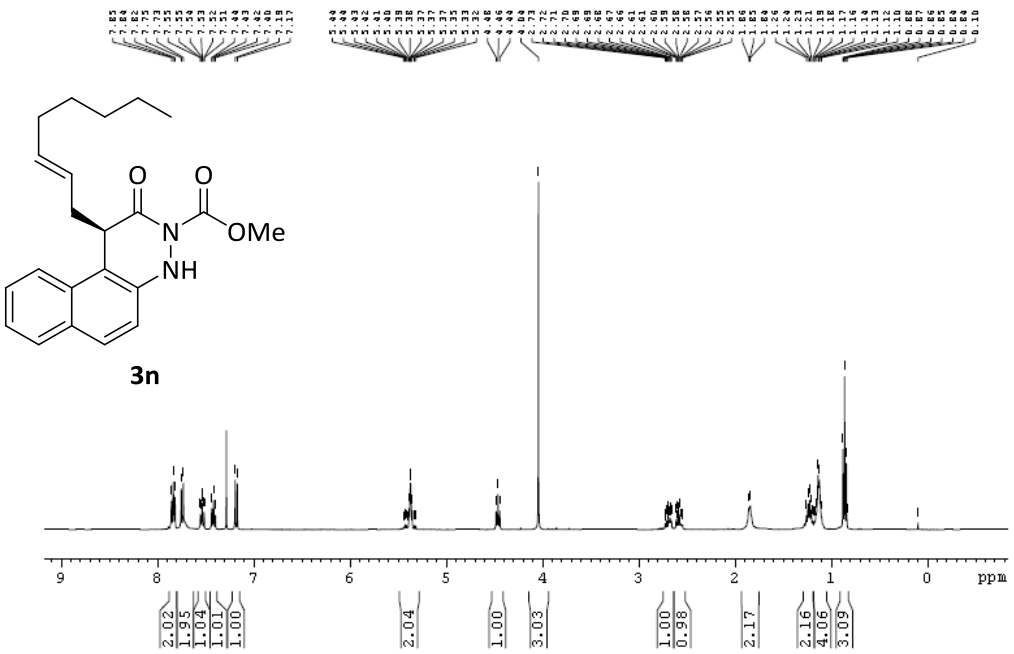
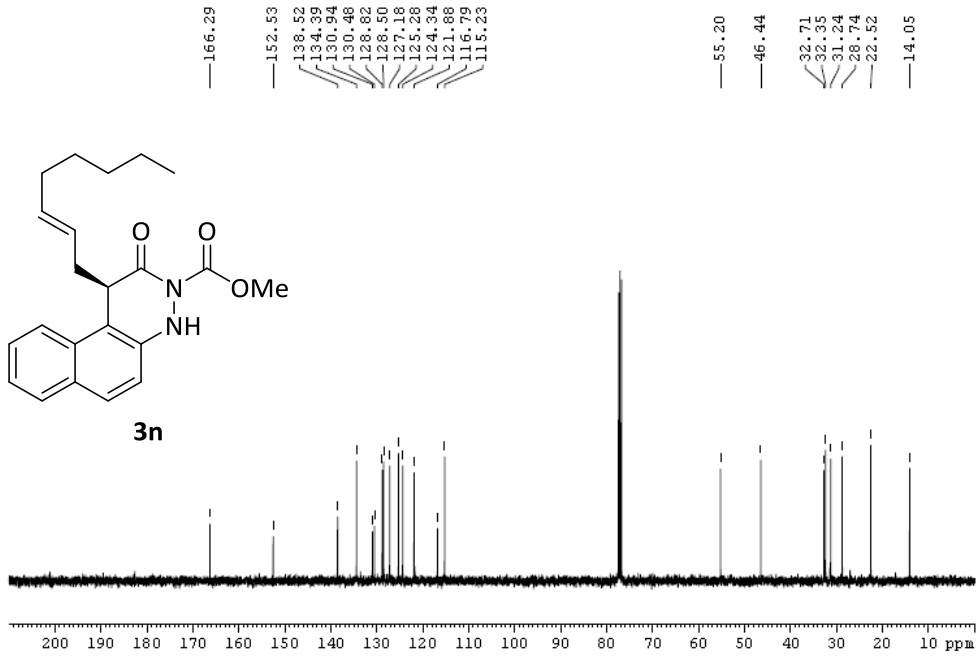
152.66
138.91
131.76
130.49
128.84
128.52
127.16
124.31
122.26
117.44
115.37
55.20
52.96
28.47
21.52
21.13
Me
O
O
Me
N
OMe
NH
3l
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


7.88
7.86
7.84
7.77
7.75
7.58
7.56
7.54
7.46
7.44
7.42
7.20
7.18
5.87
5.85
5.84
5.83
5.82
5.81
5.80
5.79
5.78
5.76
5.11
5.07
5.04
5.02
4.53
4.51
4.49
4.05
2.80
2.78
2.76
2.75
2.73
2.66
2.64
2.62
2.60
2.59
O
O
N
OMe
NH
3m
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.10
1.99
1.13
1.07
1.04
1.07
2.08
1.00
3.07
1.04
1.15

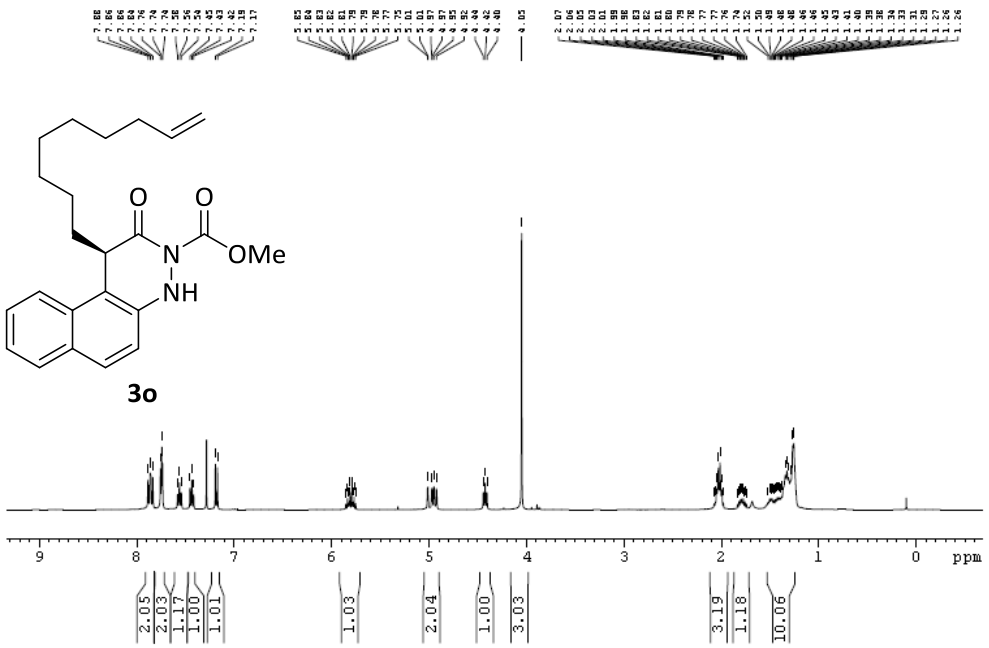

165.89
152.51
138.62
134.20
130.72
130.53
128.92
128.68
127.40
124.45
121.59
118.04
116.58
115.26
55.27
46.00
33.74
O
O
N
OMe
NH
3m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

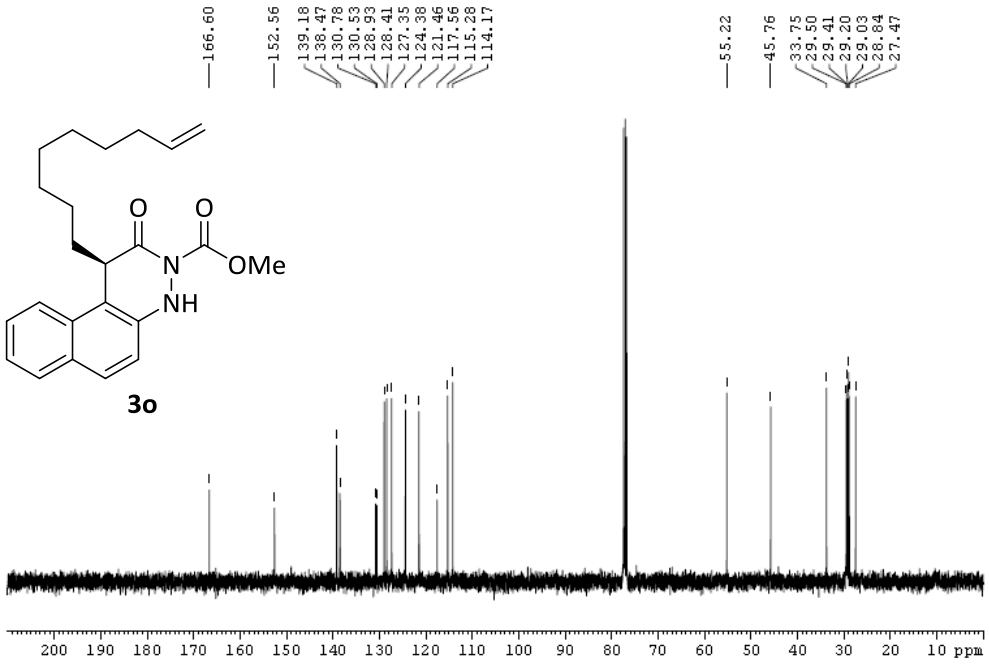

O
O
N
OMe
NH
9
8
7
6
5
4
3
2
1
0
ppm
2.02
1.95
1.04
1.01
1.00
2.04
1.00
3.03
1.00
0.98
2.17
2.16
4.06
3.09

3n


166.29
152.53
138.52
134.39
130.94
130.48
128.82
128.50
127.18
125.28
124.34
121.88
116.79
115.23
55.20
46.44
32.71
32.35
31.24
28.74
22.52
14.05
O
O
N
OMe
NH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

3n


O
O
N
OMe
NH
3o
9
8
7
6
5
4
3
2
1
0
ppm
2.05
2.03
1.17
1.00
1.01
1.03
2.04
1.00
3.03
3.19
1.18
10.06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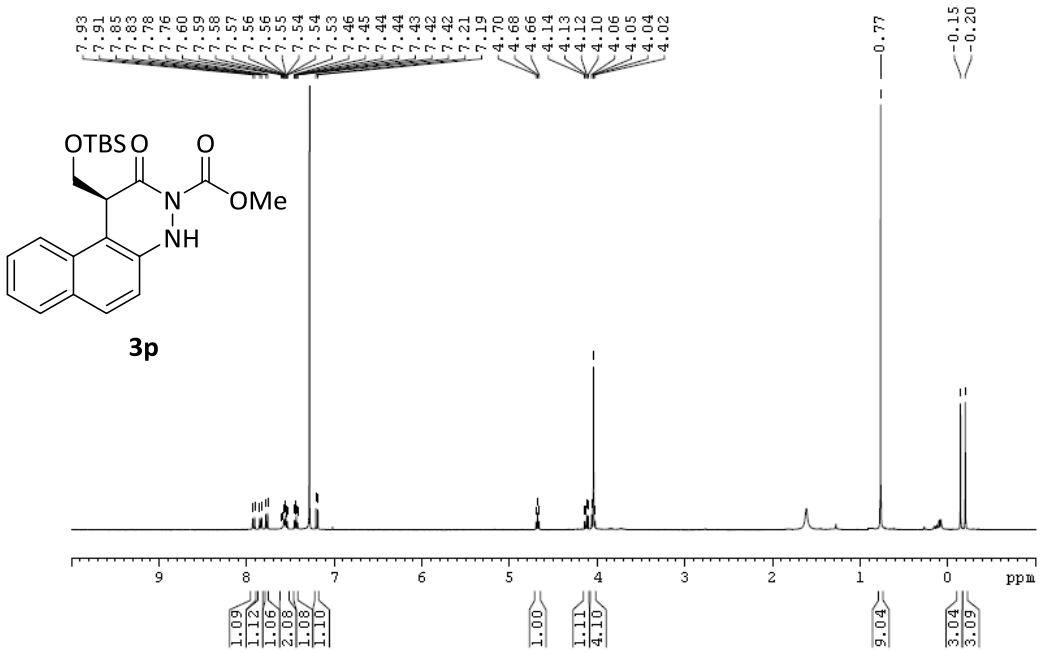
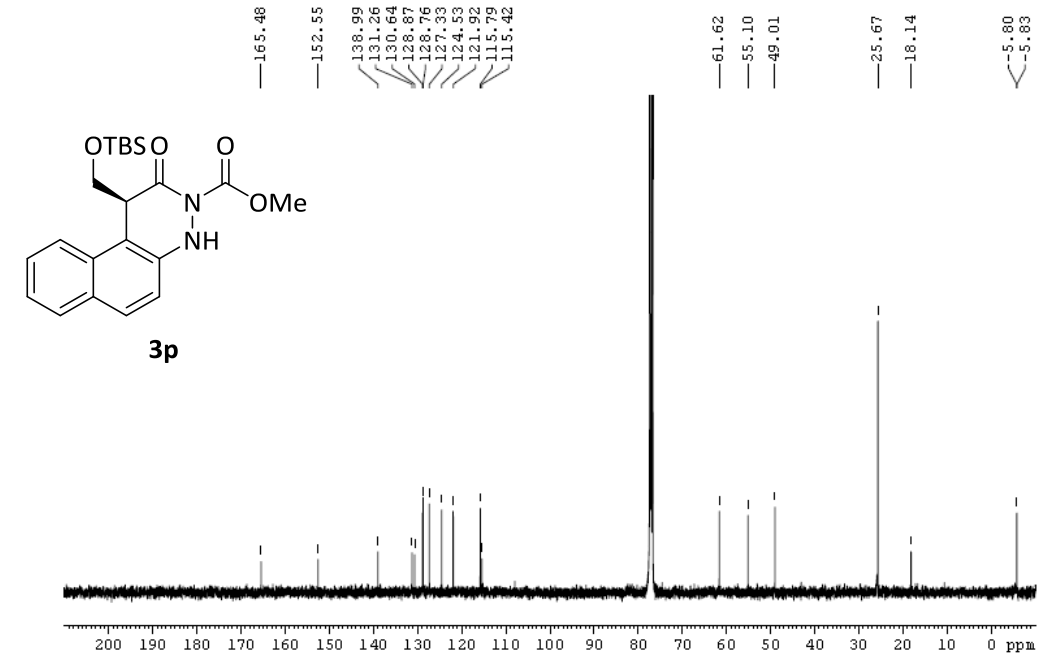
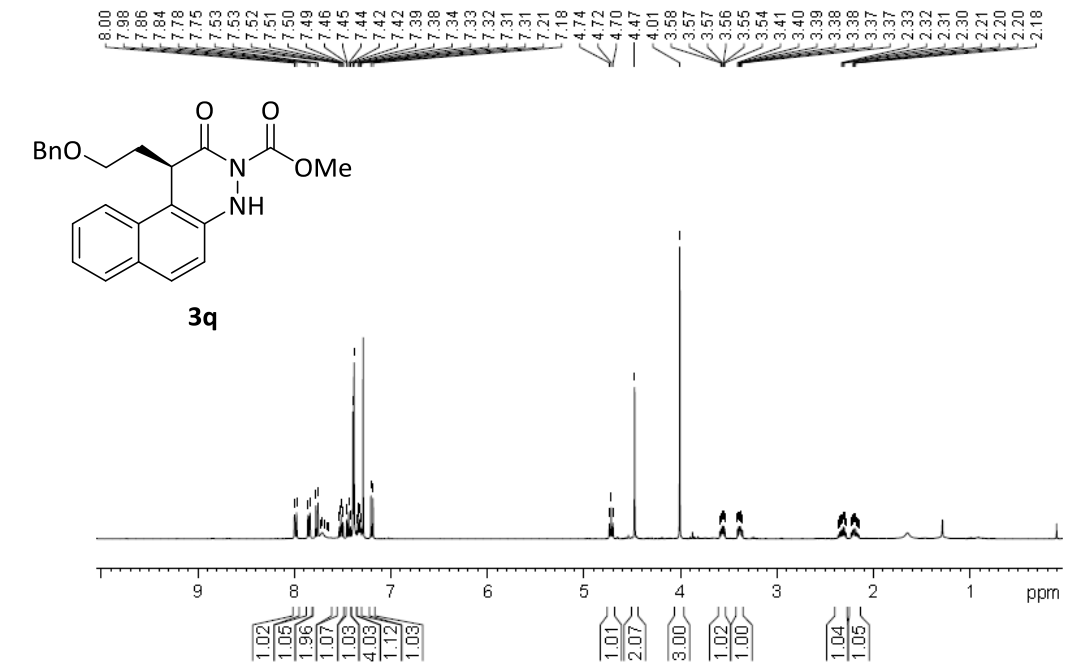
152.56
139.18
138.47
130.78
130.53
128.93
128.41
127.35
124.38
121.46
117.56
115.28
114.17
55.22
45.76
33.75
29.50
29.41
29.20
29.03
28.84
27.47
O
O
N
OMe
NH
3o
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

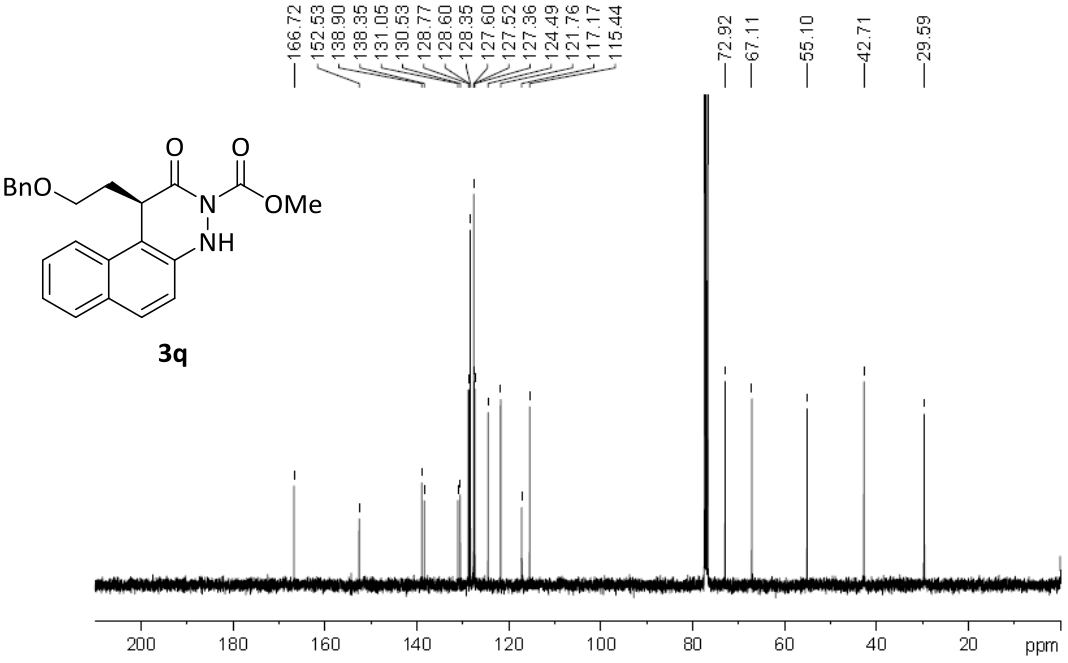

7.93
7.91
7.85
7.83
7.78
7.76
7.60
7.59
7.58
7.57
7.56
7.56
7.55
7.54
7.54
7.53
7.46
7.45
7.44
7.44
7.43
7.42
7.42
7.21
7.19
4.70
4.68
4.66
4.14
4.13
4.12
4.10
4.06
4.05
4.04
4.02
0.77
0.15
0.20
OTBS
O
O
N
OMe
NH
ppm
1.09
1.12
1.06
2.08
1.08
1.10
1.00
1.11
4.10
9.04
3.04
3.09

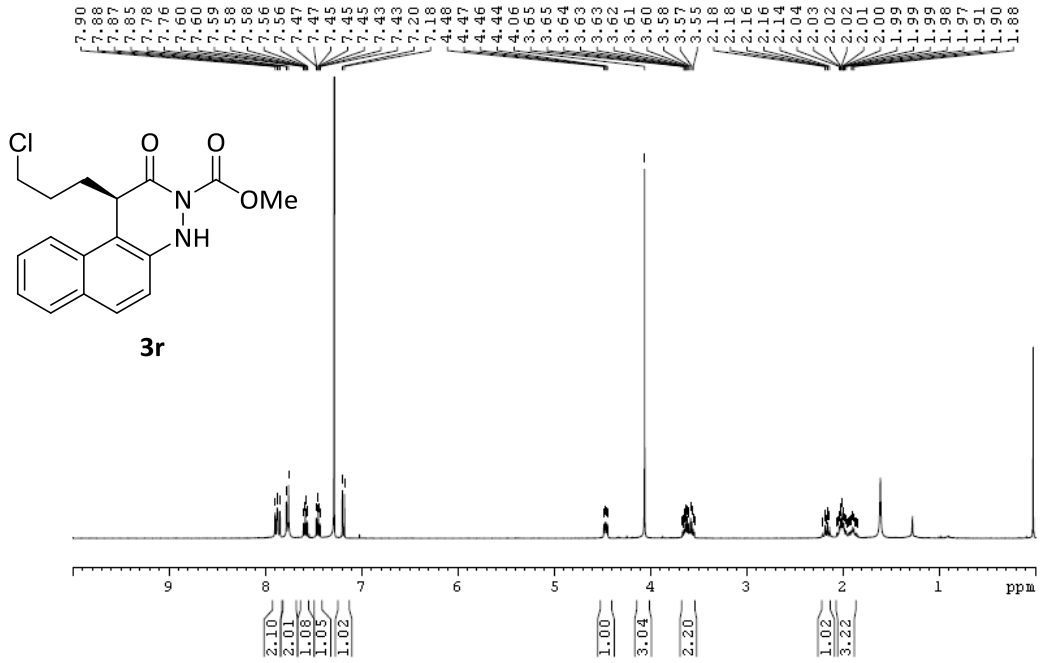
3p


165.48
152.55
138.99
131.26
130.64
128.87
128.76
127.33
124.53
121.92
115.79
115.42
61.62
55.10
49.01
25.67
18.14
5.80
5.83
OTBS
O
O
N
OMe
NH
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

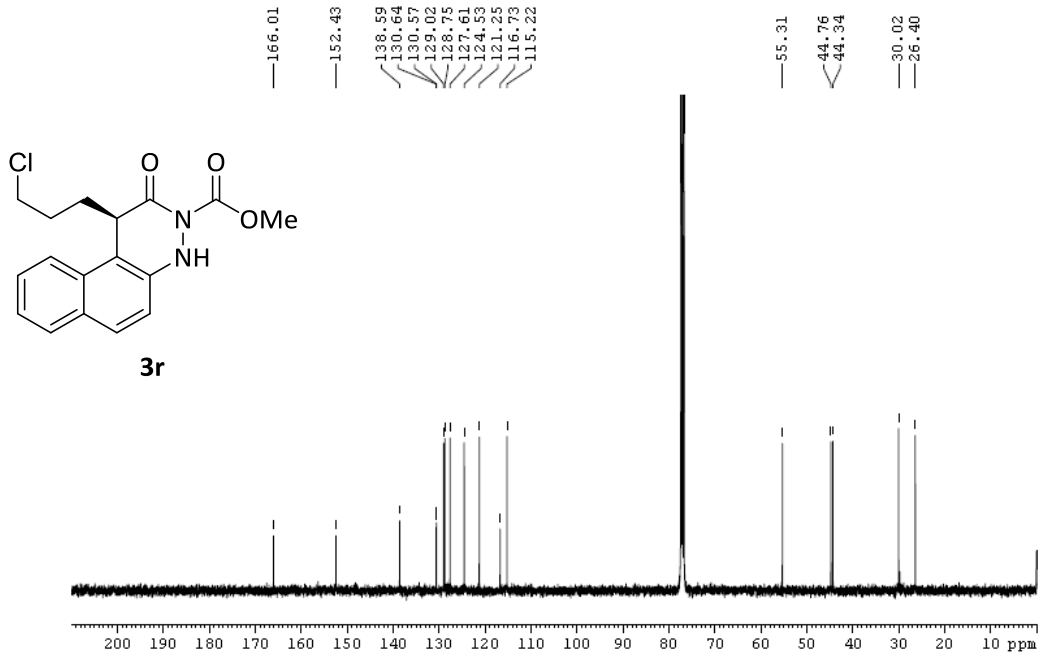
3p


8.00
7.98
7.86
7.84
7.78
7.75
7.53
7.53
7.52
7.51
7.50
7.49
7.46
7.45
7.44
7.42
7.42
7.39
7.38
7.34
7.33
7.32
7.31
7.31
7.21
7.18
4.74
4.72
4.70
4.47
4.01
3.58
3.57
3.57
3.56
3.55
3.54
3.41
3.40
3.39
3.38
3.38
3.37
3.37
2.33
2.32
2.31
2.30
2.21
2.20
2.20
2.18
BnO
O
O
N
OMe
NH
3q
9
8
7
6
5
4
3
2
1
ppm
1.02
1.05
1.96
1.07
1.03
4.03
1.12
1.03
1.01
2.07
3.00
1.02
1.00
1.04
1.05

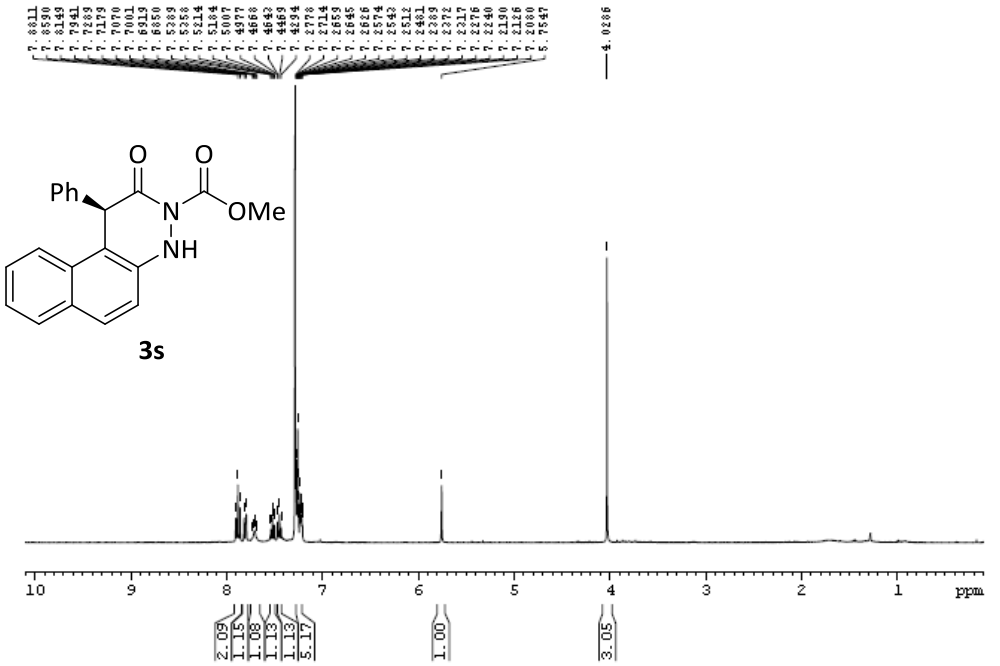

166.72
152.53
138.90
138.35
131.05
130.53
128.77
128.60
128.35
127.60
127.52
127.36
124.49
121.76
117.17
115.44
72.92
67.11
55.10
42.71
29.59
BnO
O
O
N
OMe
NH
3q
200
180
160
140
120
100
80
60
40
20
ppm

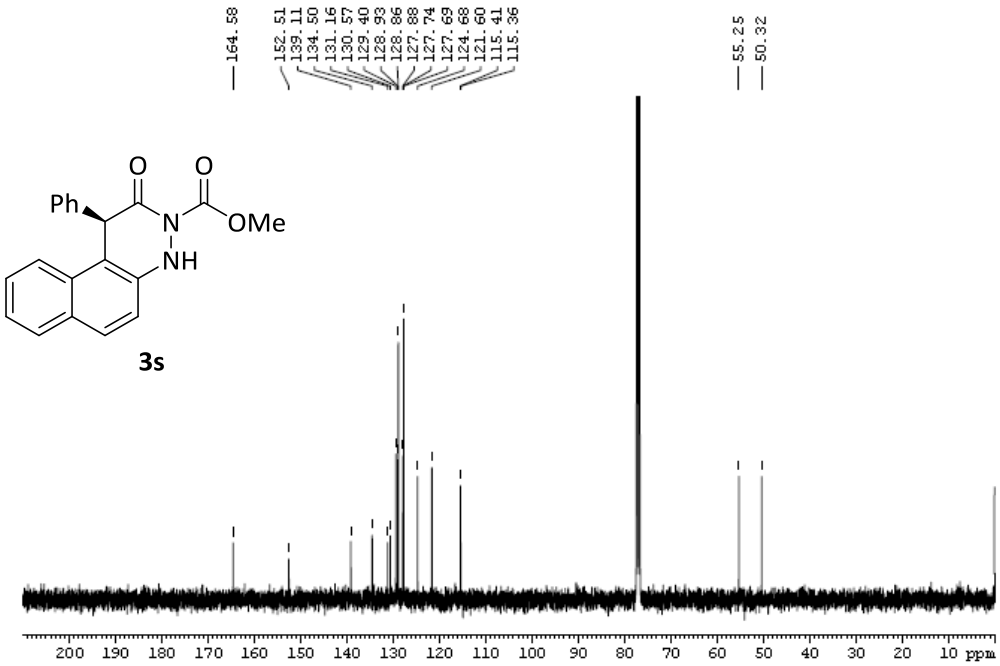

7.90 7.88 7.87 7.85 7.78 7.76 7.60 7.60 7.59 7.58 7.58 7.56 7.56 7.47 7.47 7.45 7.45 7.45 7.43 7.43 7.20 7.18 4.48 4.47 4.46 4.44 4.06 3.65 3.65 3.64 3.63 3.63 3.62 3.61 3.60 3.58 3.57 3.55 2.18 2.18 2.16 2.16 2.14 2.04 2.03 2.02 2.02 2.01 2.00 1.99 1.99 1.99 1.98 1.97 1.91 1.90 1.88
Cl
O
O
N
OMe
NH
9 8 7 6 5 4 3 2 1 ppm
2.10 2.01 1.08 1.05 1.02 1.00 3.04 2.20 1.02 3.22

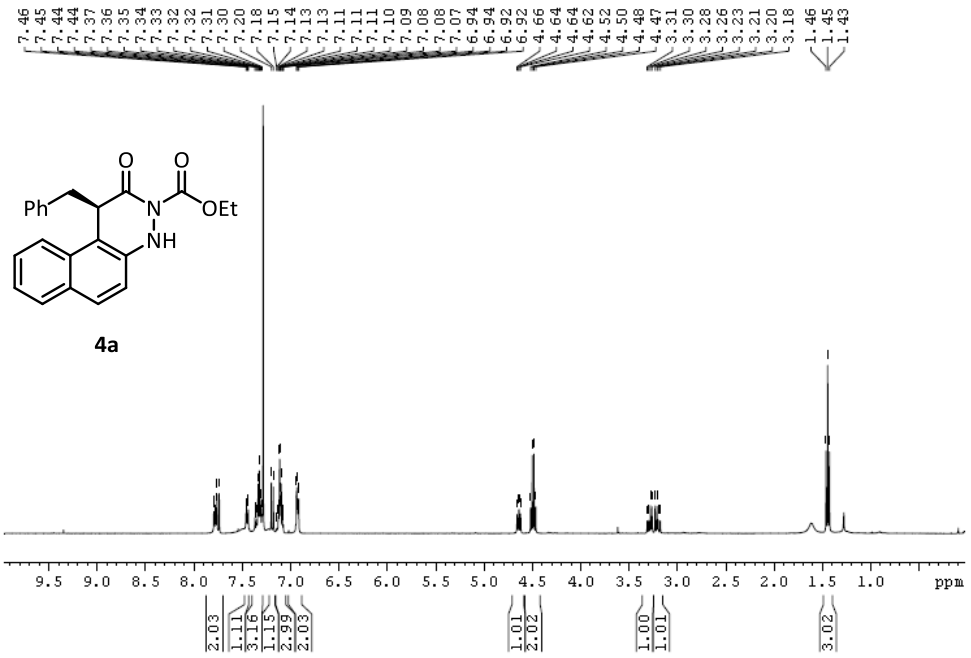
3r

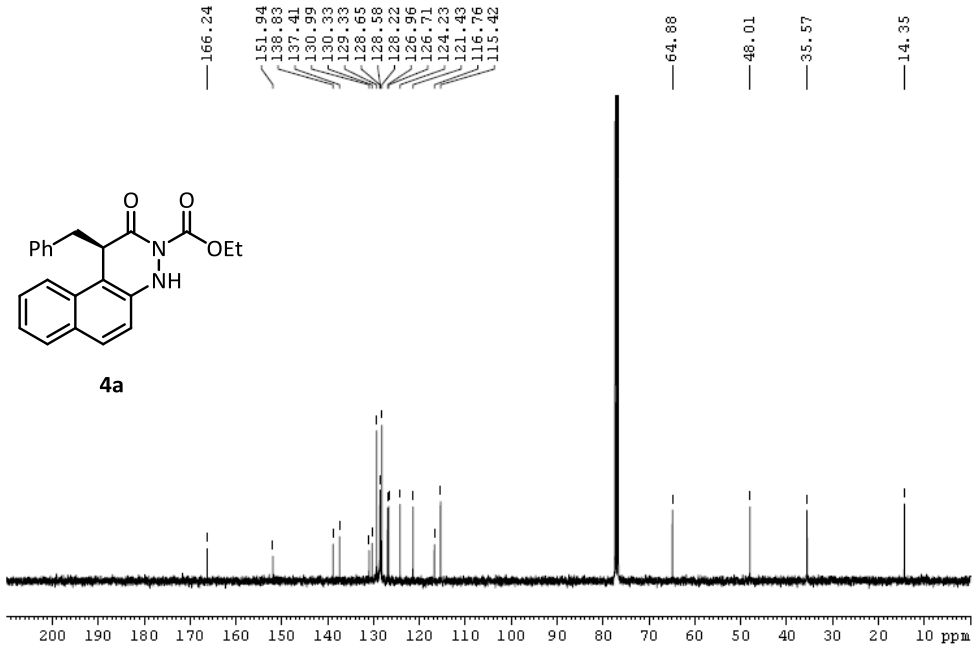

166.01 152.43 138.59 130.64 130.57 129.02 128.75 127.61 124.53 121.25 116.73 115.22 55.31 44.76 44.34 30.02 26.40
Cl
O
O
N
OMe
NH
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

3r


Ph
O
O
N
OMe
NH
3s
4.0286
10
9
8
7
6
5
4
3
2
1
ppm
2.09
1.15
1.08
1.13
1.13
5.17
1.00
3.05


Ph
O
O
N
OMe
NH
3s
164.58
152.51
139.11
134.50
131.16
130.57
129.40
128.93
128.86
127.88
127.74
127.69
124.68
121.60
115.41
115.36
55.25
50.32
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


7.46
7.45
7.44
7.44
7.37
7.36
7.35
7.34
7.33
7.32
7.32
7.31
7.30
7.20
7.18
7.15
7.14
7.13
7.13
7.11
7.11
7.11
7.10
7.09
7.08
7.08
7.07
6.94
6.94
6.92
6.92
4.66
4.64
4.64
4.62
4.52
4.50
4.48
4.47
3.31
3.30
3.28
3.26
3.23
3.21
3.20
3.18
1.46
1.45
1.43
O
O
Ph
N
OEt
NH
4a
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.03
1.11
3.16
1.15
2.99
2.03
1.01
2.02
1.00
1.01
3.02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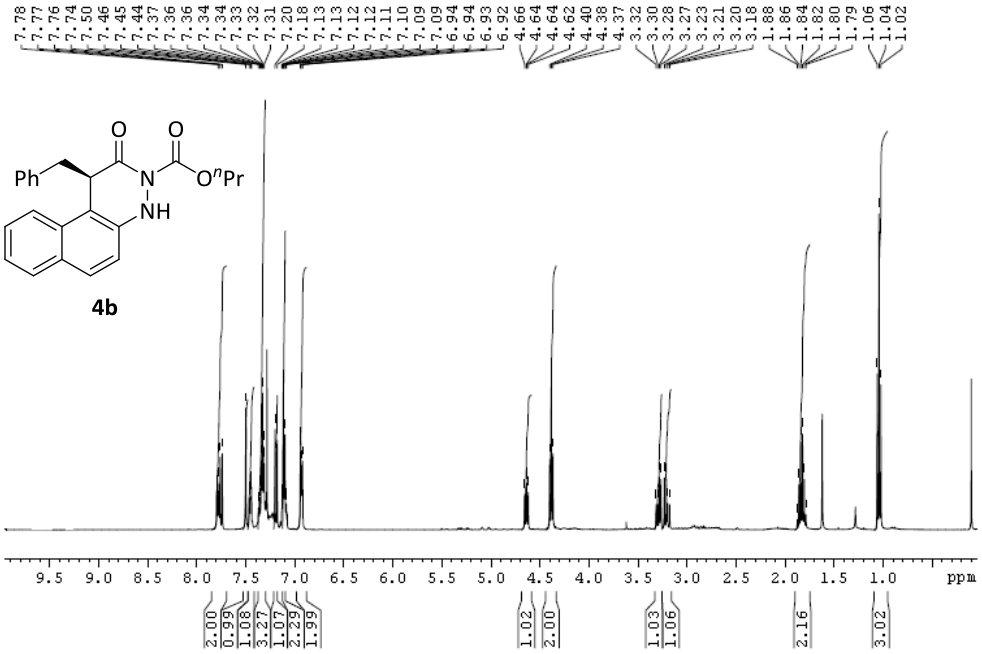
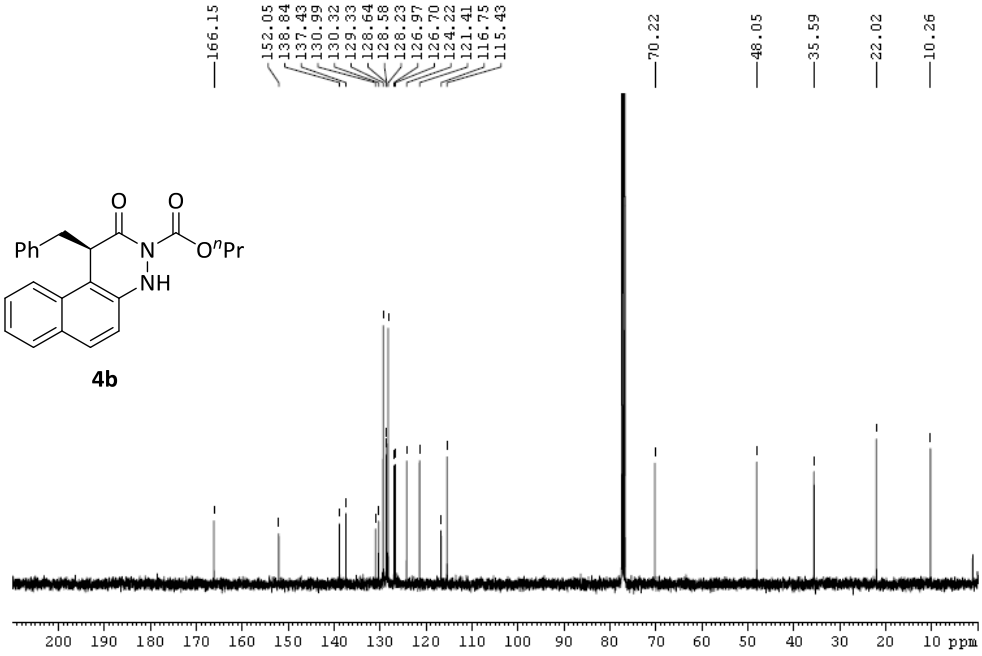
138.83
137.41
130.99
130.33
129.33
128.65
128.58
128.22
126.96
126.71
124.23
121.43
116.76
115.42
64.88
48.01
35.57
14.35
O
O
Ph
N
OEt
NH
4a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.78 7.77 7.76 7.74 7.50 7.46 7.45 7.44 7.37 7.36 7.36 7.34 7.34 7.33 7.32 7.31 7.20 7.18 7.13 7.13 7.12 7.12 7.11 7.10 7.09 7.09 6.94 6.94 6.93 6.92 4.66 4.64 4.64 4.62 4.40 4.38 4.37 3.32 3.30 3.28 3.27 3.23 3.21 3.20 3.18 1.88 1.86 1.84 1.82 1.80 1.79 1.06 1.04 1.02
O
O
Ph
N
O^{n}Pr
NH
4b
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.00 0.99 1.08 3.27 1.07 2.29 1.99 1.02 2.00 1.03 1.06 2.16 3.02


166.15
152.05 138.84 137.43 130.99 130.32 129.33 128.64 128.58 128.23 126.97 126.70 124.22 121.41 116.75 115.43
70.22
48.05
35.59
22.02
10.26
O
O
Ph
N
O^{n}Pr
NH
4b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


7.79
7.78
7.76
7.76
7.73
7.53
7.43
7.41
7.41
7.37
7.35
7.34
7.33
7.33
7.32
7.31
7.31
7.30
7.29
7.28
7.20
7.18
7.12
7.11
7.09
7.08
6.93
6.93
6.91
6.91
5.41
5.40
5.39
4.62
4.61
4.60
4.59
3.28
3.26
3.22
3.20
1.99
1.98
1.96
1.93
1.92
1.90
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1.89
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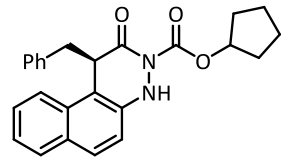
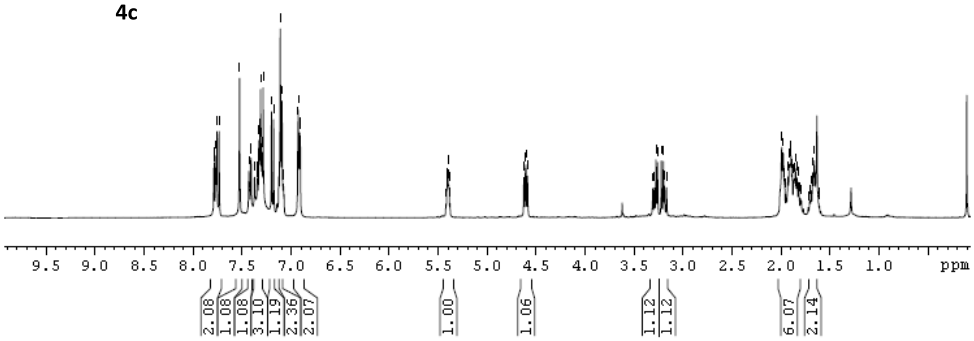
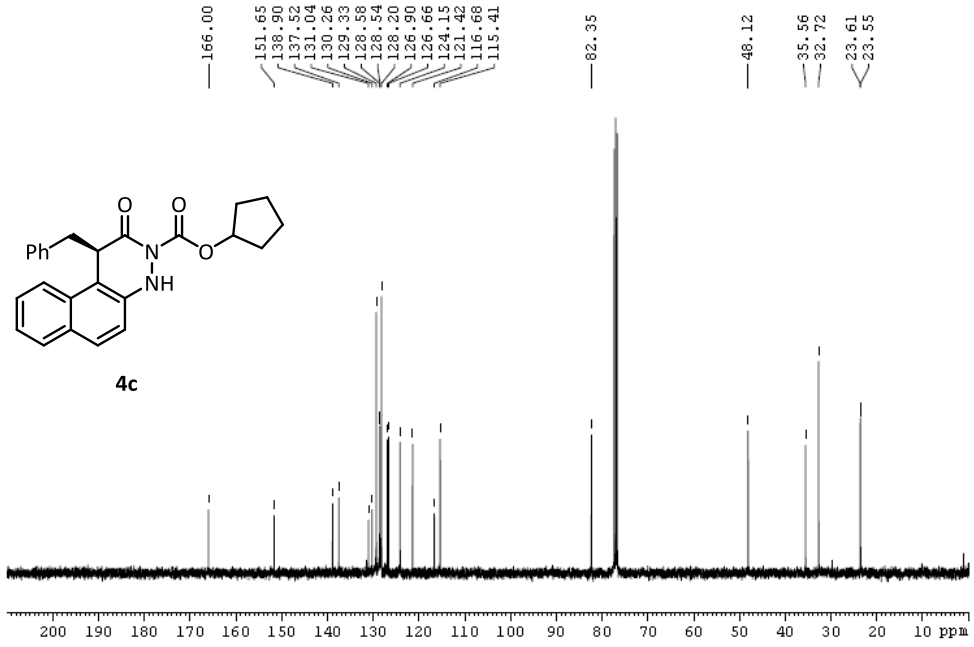
1.86
1.85
1.84
1.82
1.68
1.66
1.64


O
O
Ph
N
O
NH

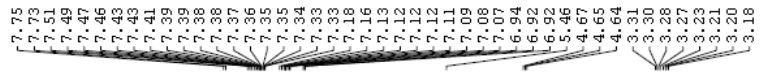
4c

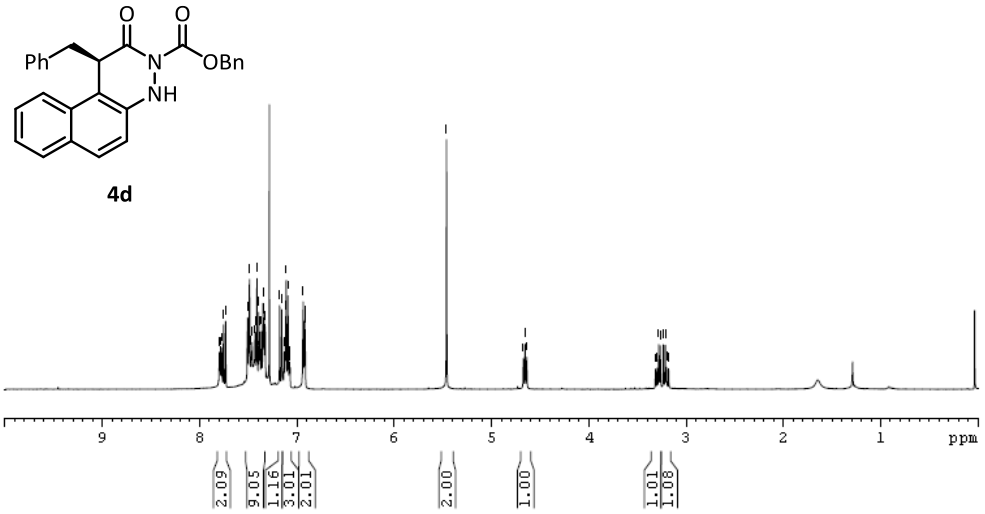

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.08
1.08
1.08
3.10
1.19
2.36
2.07
1.00
1.06
1.12
1.12
6.07
2.14


166.00
151.65
138.90
137.52
131.04
130.26
129.33
128.58
128.54
128.20
126.90
126.66
124.15
121.42
116.68
115.41
82.35
48.12
35.56
32.72
23.61
23.55
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

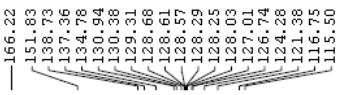
O
O
Ph
N
O
NH

4c


7.75
7.73
7.51
7.49
7.47
7.46
7.43
7.43
7.41
7.39
7.39
7.38
7.38
7.37
7.36
7.35
7.35
7.34
7.33
7.33
7.18
7.16
7.13
7.12
7.12
7.12
7.11
7.09
7.08
7.07
6.94
6.92
6.92
5.46
4.67
4.65
4.64
3.31
3.30
3.28
3.27
3.23
3.21
3.20
3.18


O
O
Ph
N
OBn
NH
9
8
7
6
5
4
3
2
1
ppm
2.09
9.05
1.16
3.01
2.01
2.00
1.00
1.01
1.08

4d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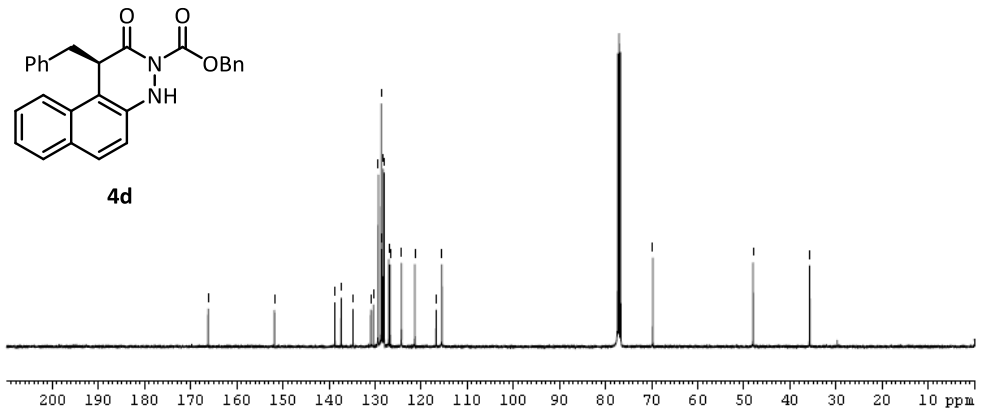
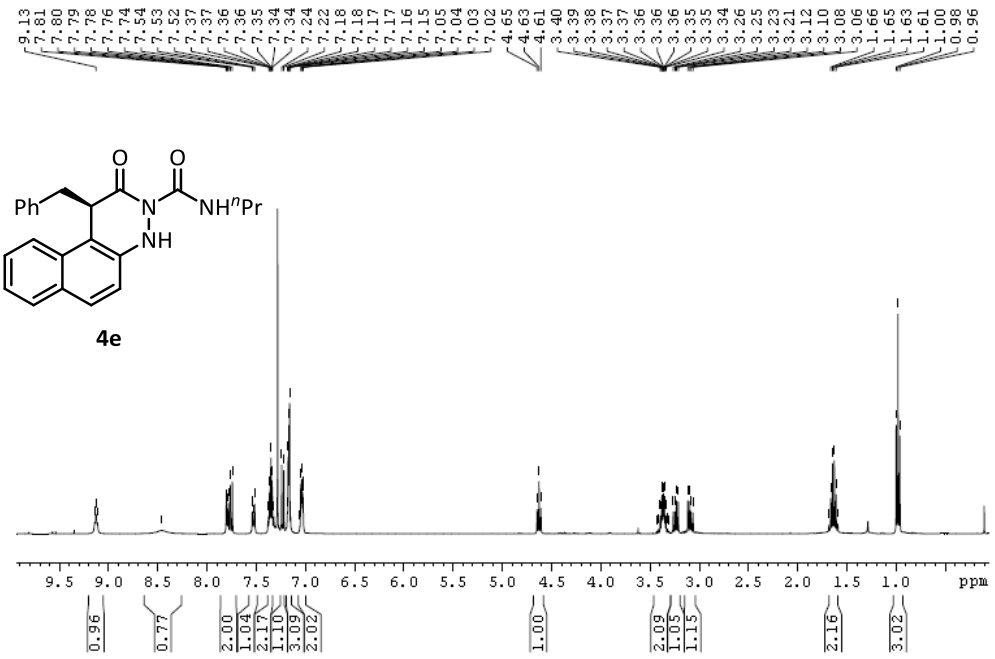
151.83
138.73
137.36
134.78
130.94
130.38
129.31
128.68
128.61
128.57
128.29
128.25
128.03
127.01
126.74
124.28
121.38
116.75
115.50
69.77
48.00
35.72


O
O
Ph
N
OBn
NH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

4d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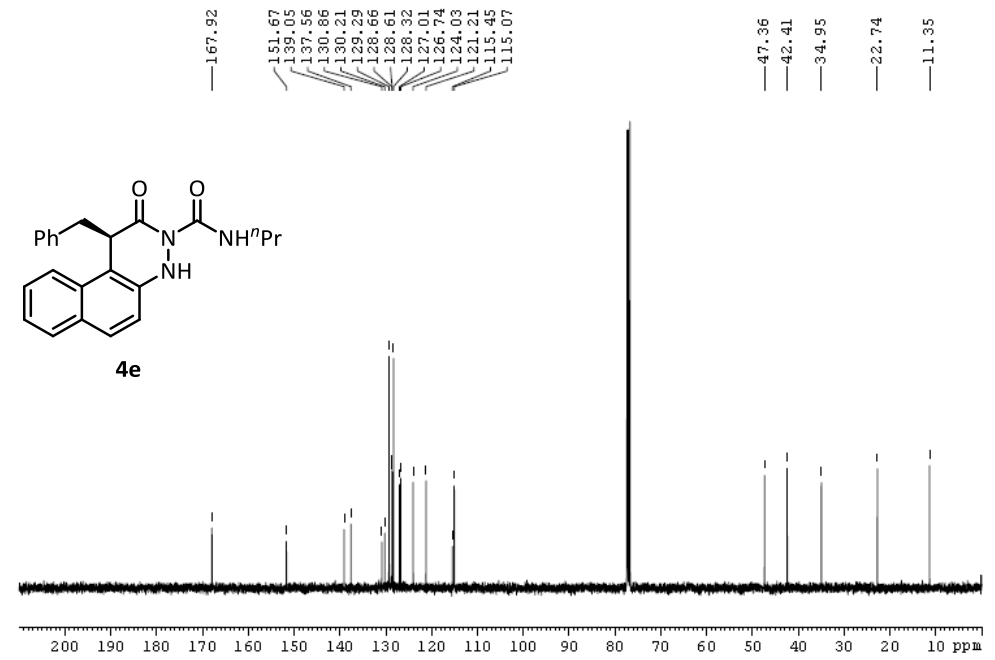
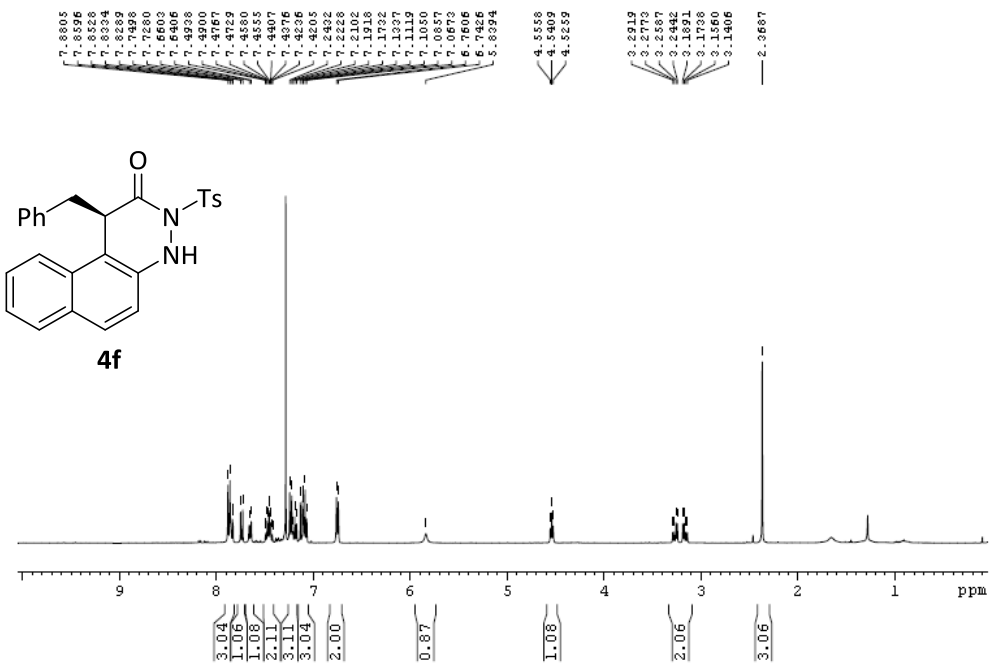
7.81
7.80
7.79
7.78
7.76
7.74
7.54
7.53
7.52
7.37
7.37
7.36
7.36
7.35
7.34
7.34
7.24
7.22
7.18
7.18
7.17
7.17
7.16
7.15
7.05
7.04
7.03
7.02
4.65
4.63
4.61
3.40
3.39
3.38
3.37
3.37
3.36
3.36
3.36
3.35
3.35
3.34
3.26
3.25
3.23
3.21
3.12
3.10
3.08
3.06
1.66
1.65
1.63
1.61
1.00
0.98
0.96
O
O
Ph
N
NH^{n}Pr
NH
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
0.96
0.77
2.00
1.04
2.17
1.10
3.09
2.02
1.00
2.09
1.05
1.15
2.16
3.02

4e


167.92
151.67
139.05
137.56
130.86
130.21
129.29
128.66
128.61
128.32
127.01
126.74
124.03
121.21
115.45
115.07
47.36
42.41
34.95
22.74
11.35
O
O
Ph
N
NH^{n}Pr
NH
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

4e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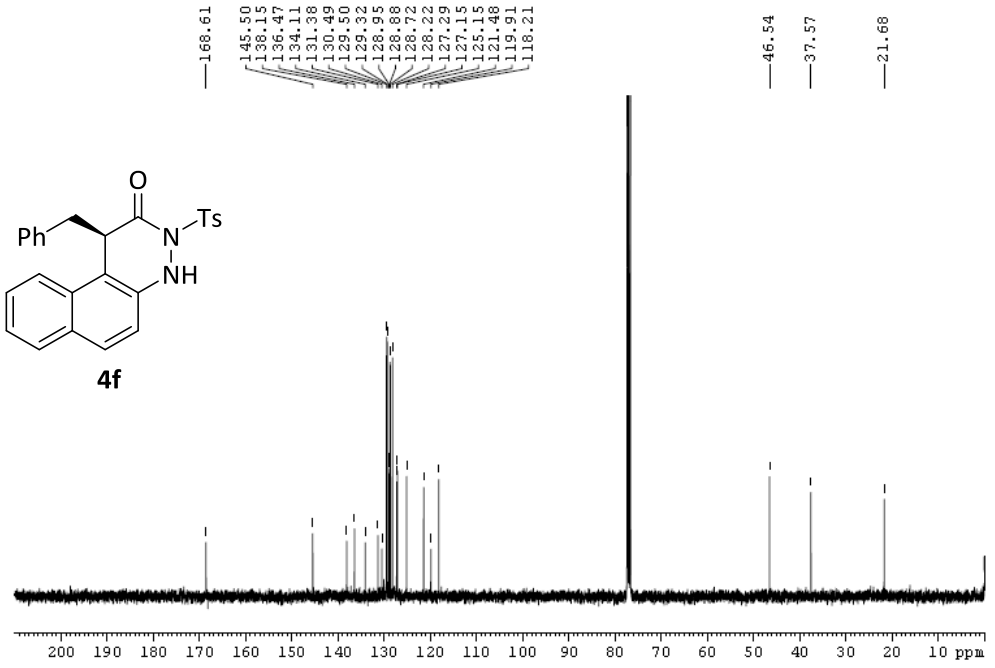
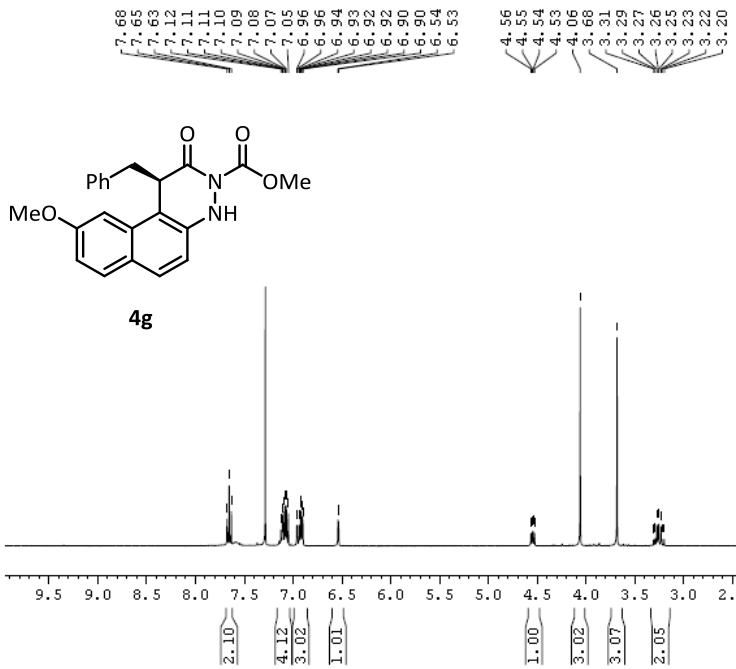
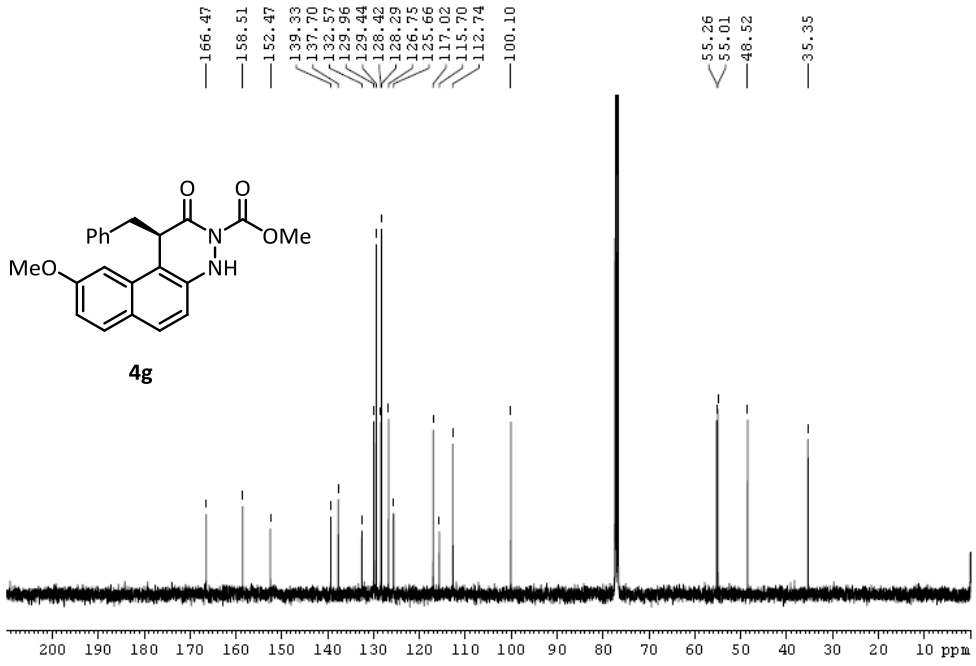
7.8596
7.8528
7.8334
7.8289
7.7498
7.7280
7.6603
7.6406
7.4938
7.4900
7.4767
7.4729
7.4580
7.4555
7.4407
7.4376
7.4236
7.4205
7.2492
7.2228
7.2102
7.1918
7.1732
7.1537
7.1113
7.1050
7.0857
7.0673
6.7606
6.7426
5.8394
4.5558
4.5409
4.5259
3.2919
3.2773
3.2587
3.2442
3.1891
3.1738
3.1560
3.1406
2.3667
O
Ph
N
Ts
NH
4f
9
8
7
6
5
4
3
2
1
ppm
3.04
1.06
1.08
2.11
3.04
2.00
0.87
1.08
2.06
3.06

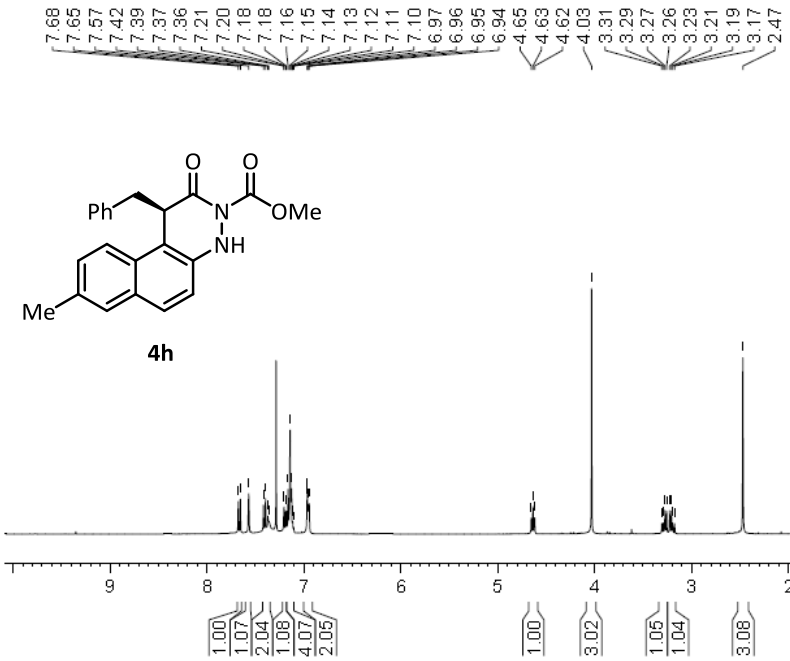

168.61
145.50
138.15
136.47
134.11
131.38
130.49
129.50
129.32
128.95
128.88
128.72
128.22
127.29
127.15
125.15
121.48
119.91
118.21
46.54
37.57
21.68
O
Ph
N
Ts
NH
4f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm

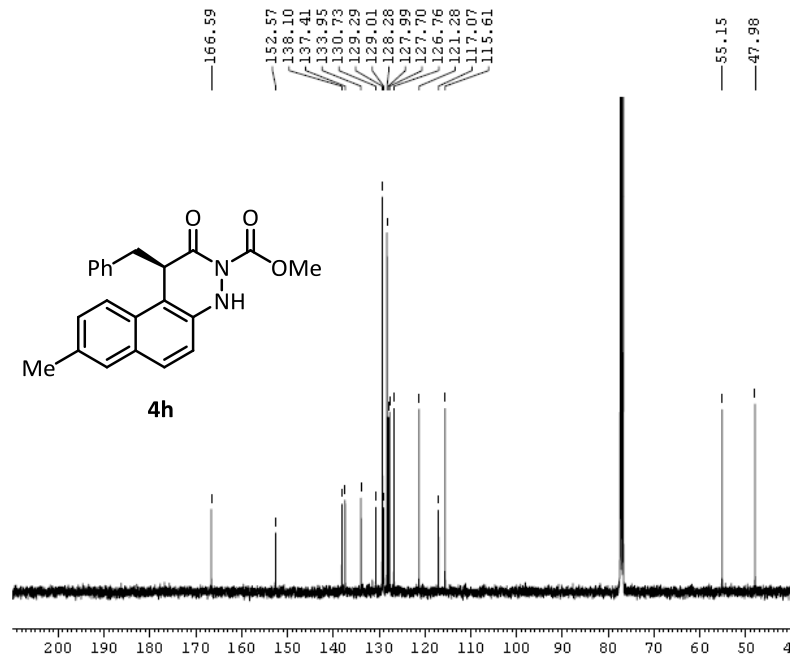

7.68
7.65
7.63
7.12
7.11
7.11
7.10
7.09
7.08
7.07
7.05
6.96
6.96
6.94
6.93
6.92
6.92
6.90
6.90
6.54
6.53
4.56
4.55
4.54
4.53
4.06
3.68
3.31
3.29
3.27
3.26
3.25
3.23
3.22
3.20
O
O
Ph
N
OMe
MeO
NH
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.10
4.12
3.02
1.01
1.00
3.02
3.07
2.05

4g


166.47
158.51
152.47
139.33
137.70
132.57
129.96
129.44
128.42
128.29
126.75
125.66
117.02
115.70
112.74
100.10
55.26
55.01
48.52
35.35
O
O
Ph
N
OMe
MeO
NH
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

4g


7.68
7.65
7.57
7.42
7.39
7.37
7.36
7.21
7.20
7.18
7.18
7.16
7.15
7.14
7.13
7.12
7.11
7.10
6.97
6.96
6.95
6.94
4.65
4.63
4.62
4.03
3.31
3.29
3.27
3.26
3.23
3.21
3.19
3.17
2.47
O
O
Ph
N
OMe
NH
Me
4h
9
8
7
6
5
4
3
2
1
ppm
1.00
1.07
2.04
1.08
4.07
2.05
1.00
3.02
1.05
1.04
3.08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152.57
138.10
137.41
133.95
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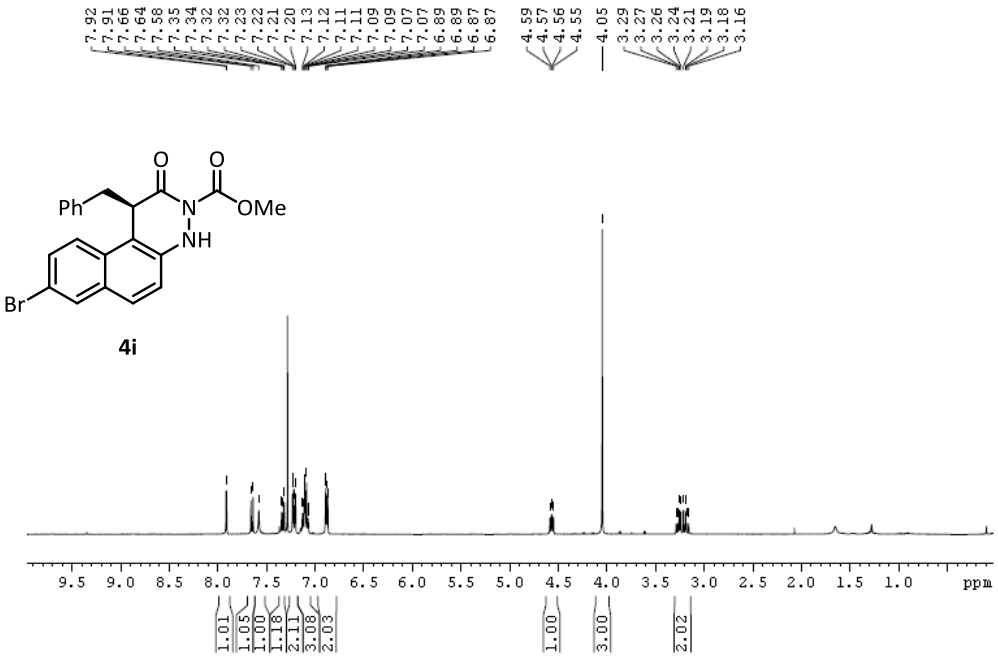
129.29
129.01
128.28
127.99
127.70
126.76
121.28
117.07
115.61
55.15
47.98
35.69
21.38
O
O
Ph
N
OMe
NH
Me
4h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm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7.91
7.66
7.64
7.58
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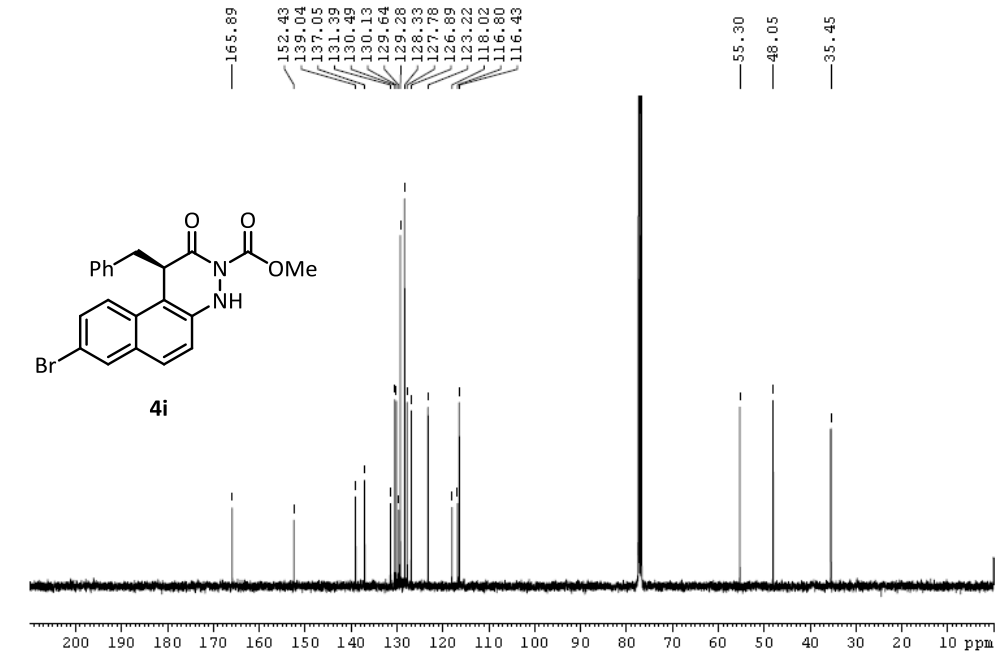
7.34
7.32
7.32
7.23
7.22
7.21
7.20
7.13
7.12
7.11
7.11
7.09
7.09
7.07
7.07
6.89
6.89
6.87
6.87
4.59
4.57
4.56
4.55
4.05
3.29
3.27
3.26
3.24
3.21
3.19
3.18
3.16
Ph
N
NH
OMe
Br
4i
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.01
1.05
1.00
1.18
2.11
3.08
2.03
1.00
3.00
2.02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137.05
131.39
130.49
130.13
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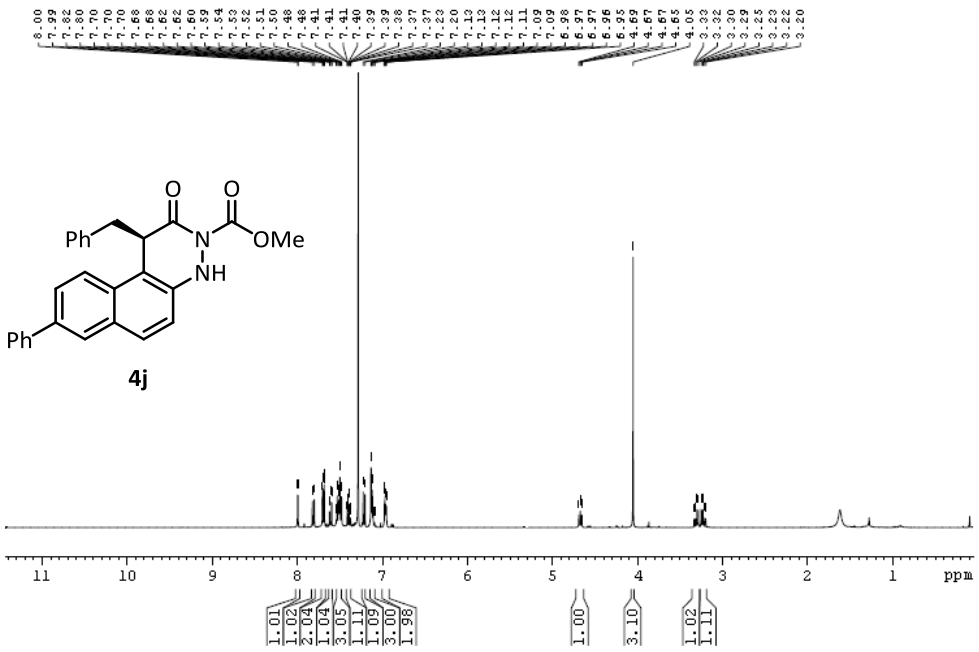
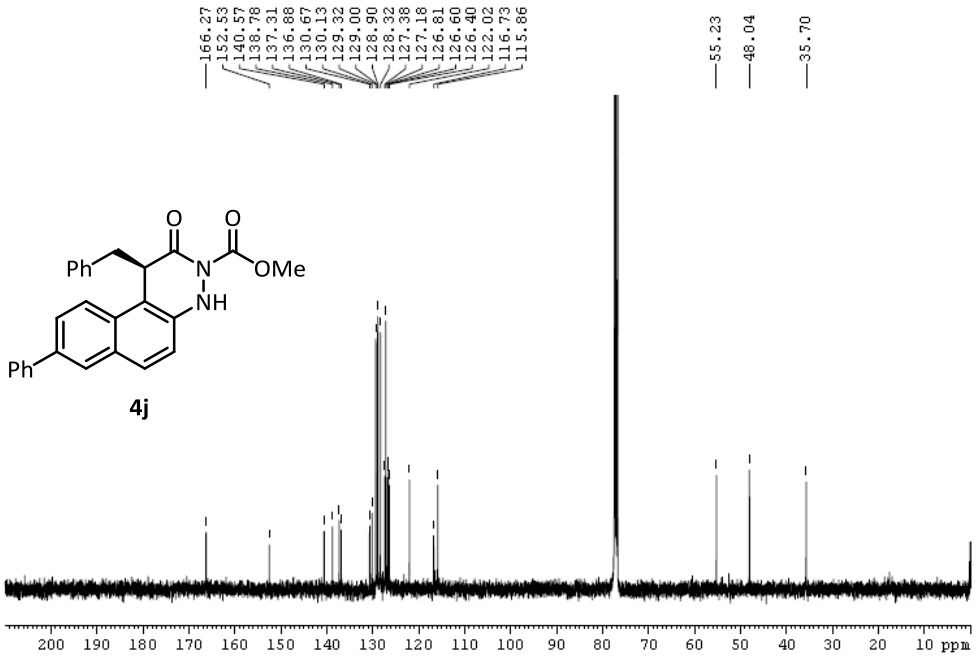
129.28
128.33
127.78
126.89
123.22
118.02
116.80
116.43
55.30
48.05
35.45
Ph
N
NH
OMe
Br
4i
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Ph
O
O
N
NH
OMe
Ph
4j
11
10
9
8
7
6
5
4
3
2
1
ppm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138.78
137.31
136.88
130.67
130.13
129.32
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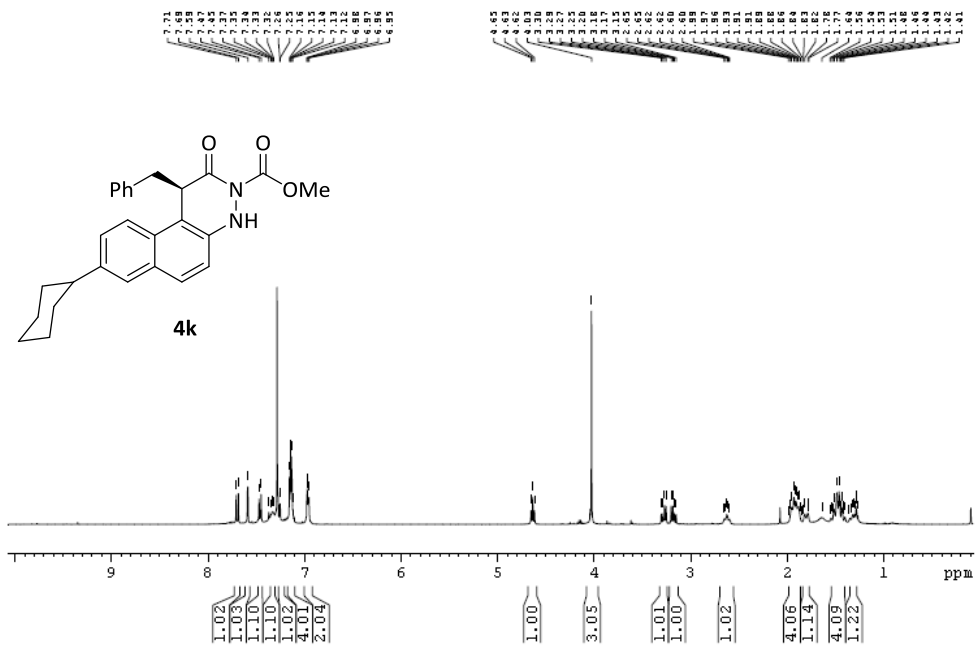
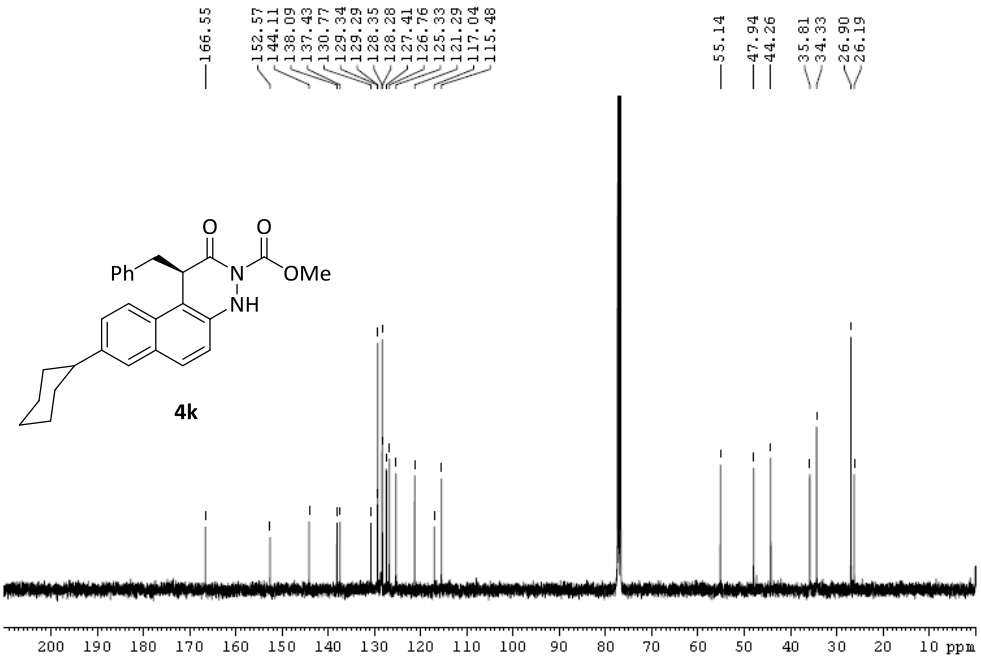
128.90
128.32
127.38
127.18
126.81
126.60
126.40
122.02
116.73
115.86
55.23
48.04
35.70
Ph
O
O
N
NH
OMe
Ph
4j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10 ppm


Ph
O
O
N
OMe
NH
4k
ppm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137.43
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129.29
128.35
128.28
127.41
126.76
125.33
121.29
117.04
115.48
55.14
47.94
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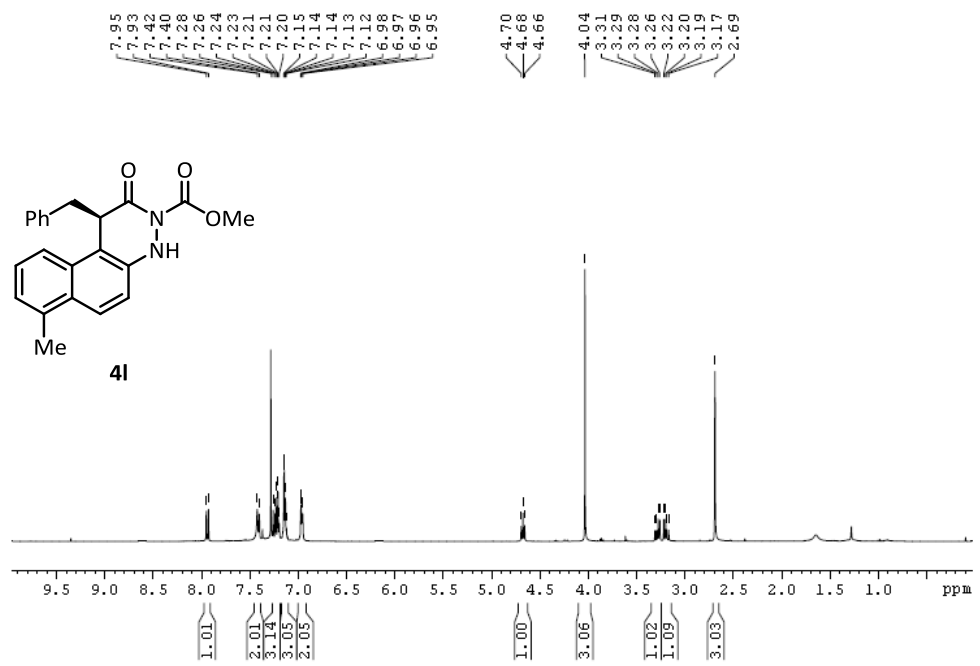
35.81
34.33
26.90
26.19
Ph
O
O
N
OMe
NH
4k
ppm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7.93
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7.40
7.28
7.26
7.24
7.23
7.21
7.21
7.20
7.15
7.14
7.14
7.13
7.12
6.98
6.97
6.96
6.95
4.70
4.68
4.66
4.04
3.31
3.29
3.28
3.26
3.22
3.20
3.19
3.17
2.69
Ph
O
O
N
OMe
NH
Me
4l
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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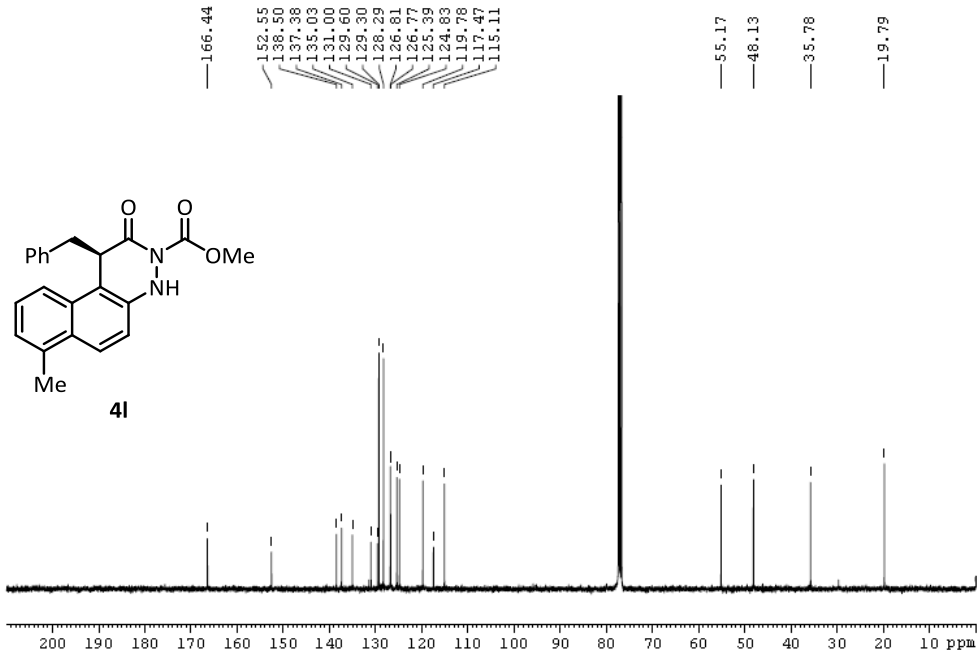
2.01
3.14
3.05
2.05
1.00
3.06
1.02
1.09
3.03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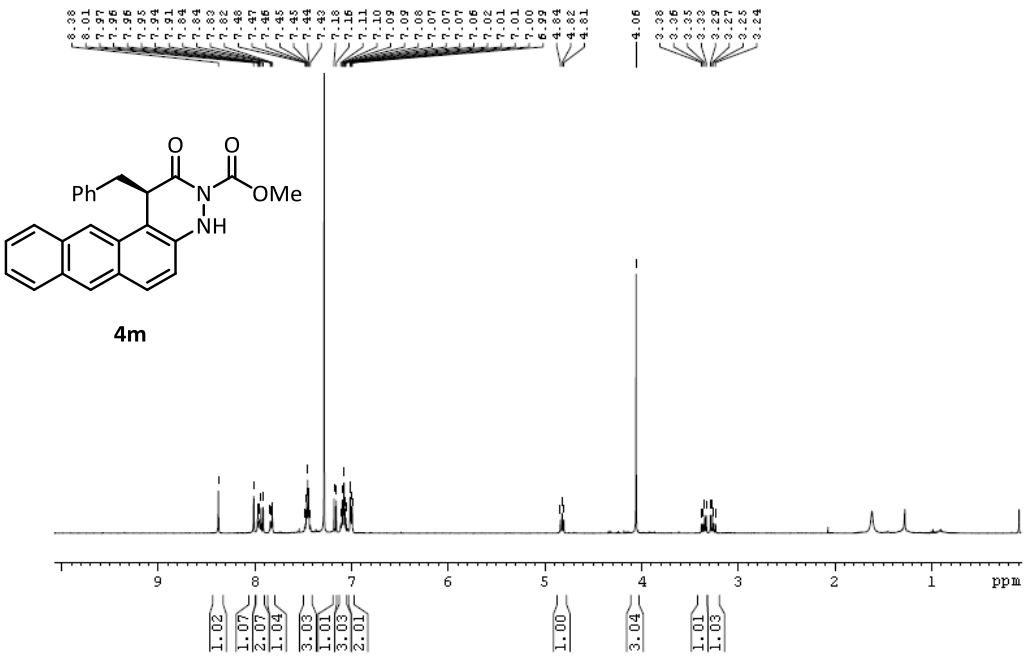
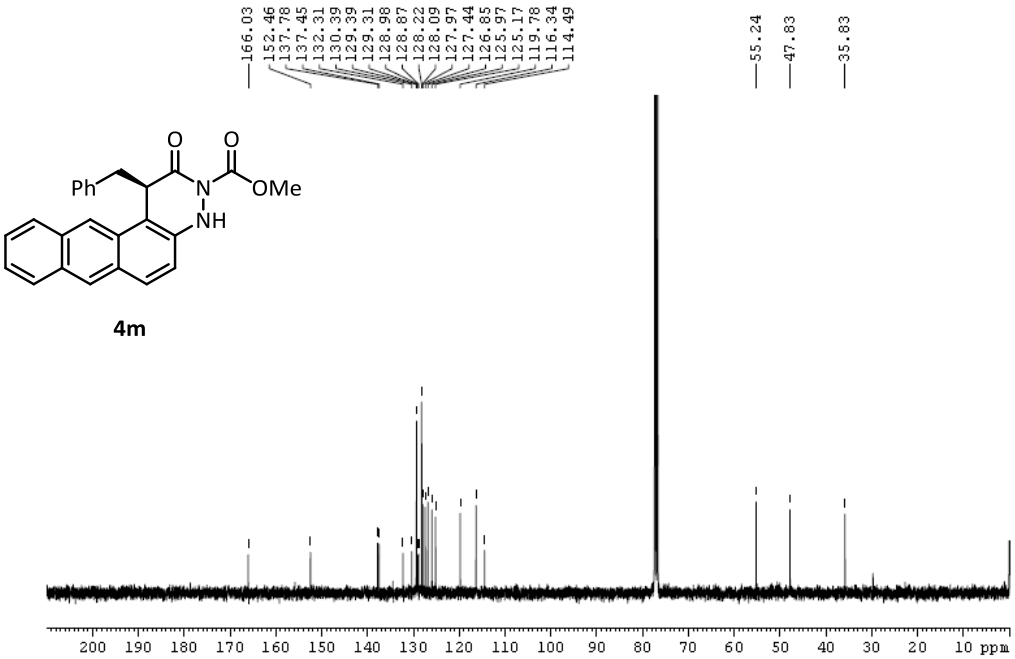
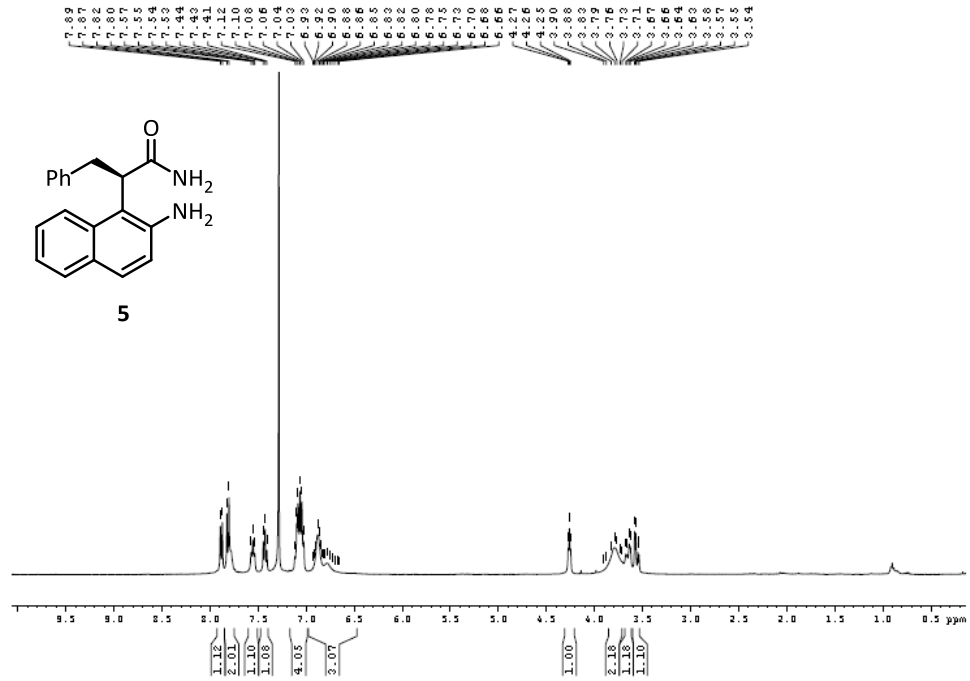
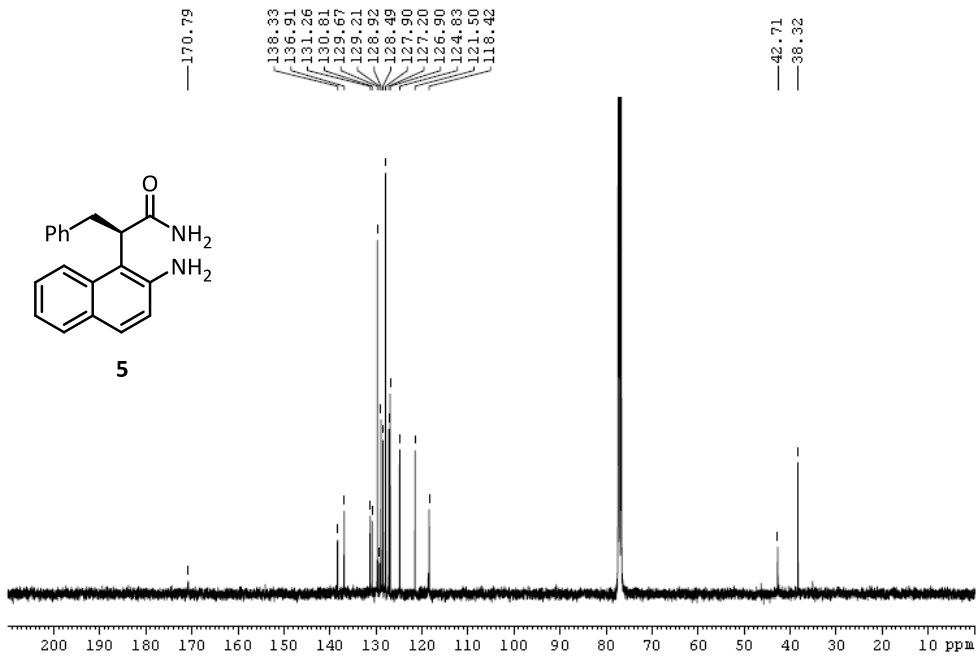
137.38
135.03
131.00
129.60
129.30
128.29
126.81
126.77
125.39
124.83
119.78
117.47
115.11
55.17
48.13
35.78
19.79
Ph
O
O
N
OMe
NH
Me
4l
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Ph
N
NH
OMe
O
O
4m
ppm


Ph
N
NH
OMe
O
O
4m
ppm

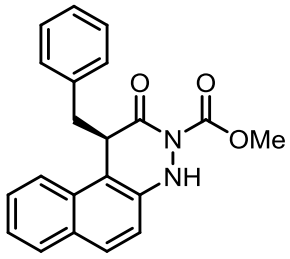


5



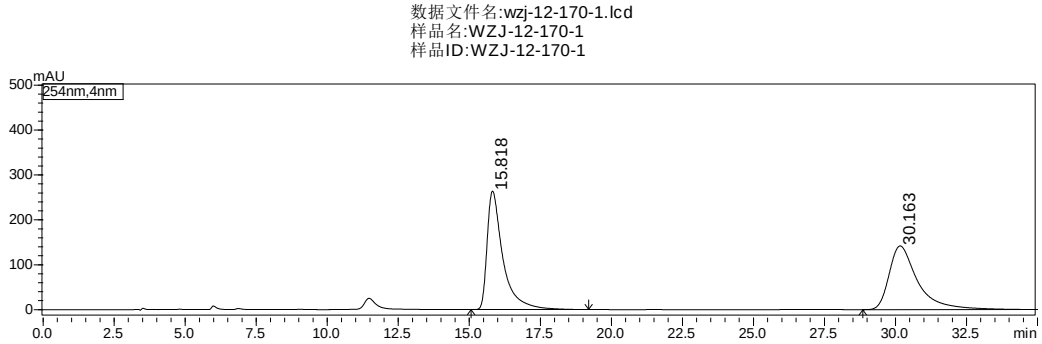
5

9. HPLC spectra



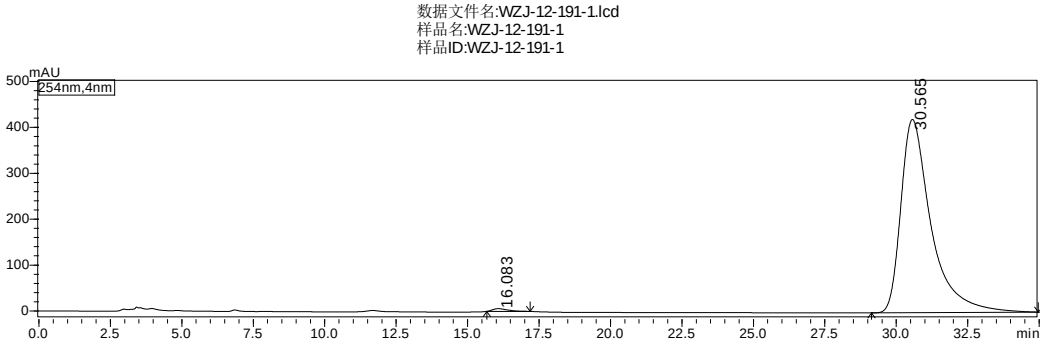
3a

Chiral HPLC spectrum of racemic **3a**

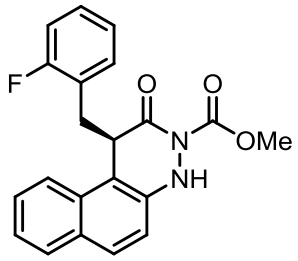


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.818	10237325	263999	50.714	65.045
2	30.163	9949073	141874	49.286	34.955
Total		20186398	405873	100.000	100.000

Chiral HPLC spectrum of **3a**

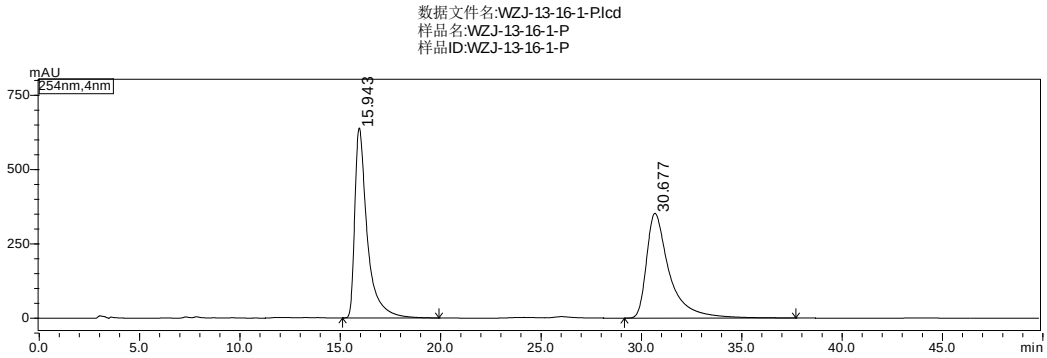


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.083	176753	5486	0.568	1.286
2	30.565	30943761	421108	99.432	98.714
Total		31120515	426594	100.000	100.000



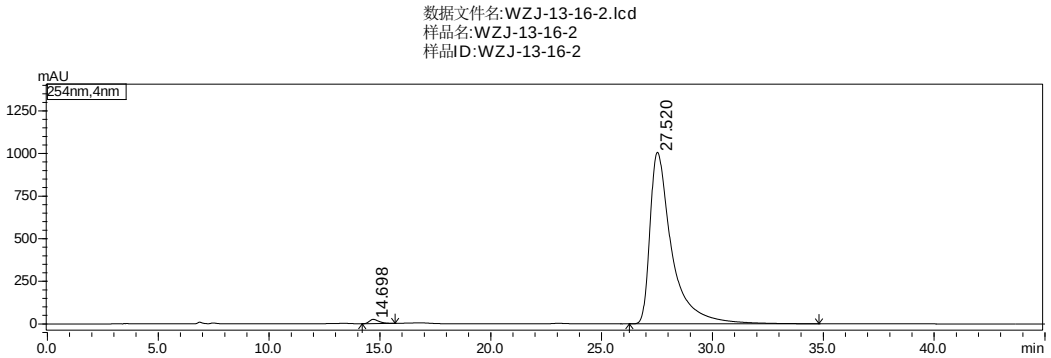
3b

Chiral HPLC spectrum of racemic **3b**

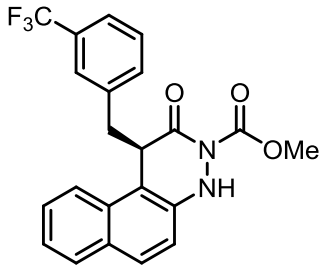


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.943	27604629	639040	49.671	64.446
2	30.677	27970809	352551	50.329	35.554
Total		55575438	991592	100.000	100.000

Chiral HPLC spectrum of **3b**

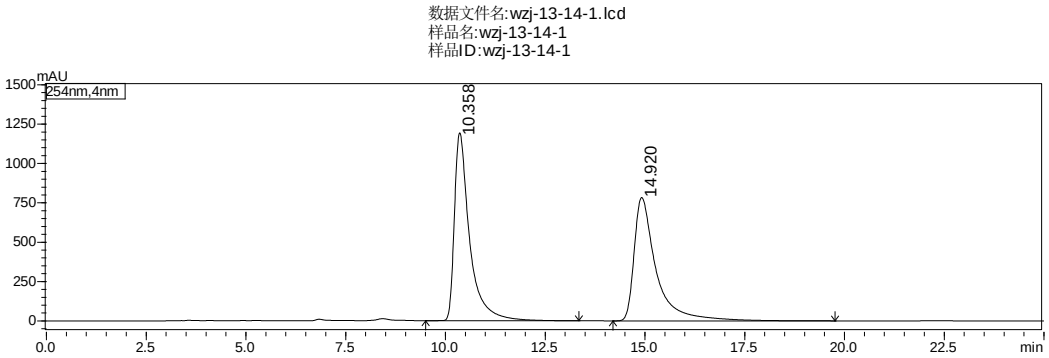


Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.698	769250	25448	1.101	2.465
2	27.520	69119210	1006897	98.899	97.535
Total		69888461	1032346	100.000	100.000



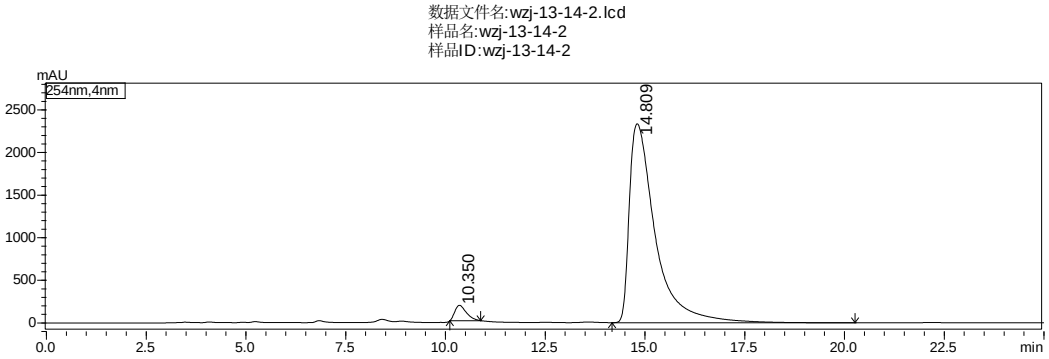
3c

Chiral HPLC spectrum of racemic **3c**

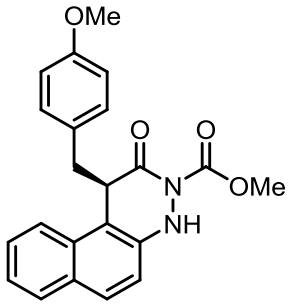


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.358	30010195	1180794	50.641	60.198
2	14.920	29251050	780734	49.359	39.802
总计		59261245	1961529	100.000	100.000

Chiral HPLC spectrum of **3c**

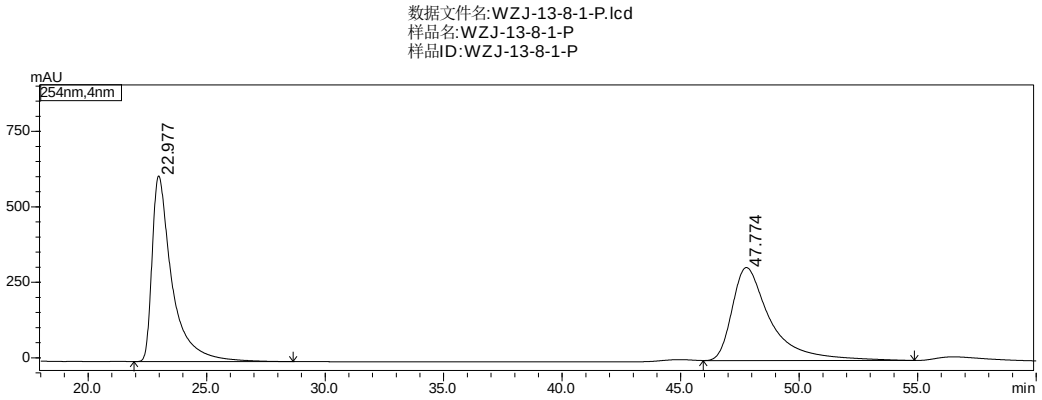


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.350	3630911	180138	3.316	7.165
2	14.809	105852721	2333930	96.684	92.835
Total		109483632	2514068	100.000	100.000



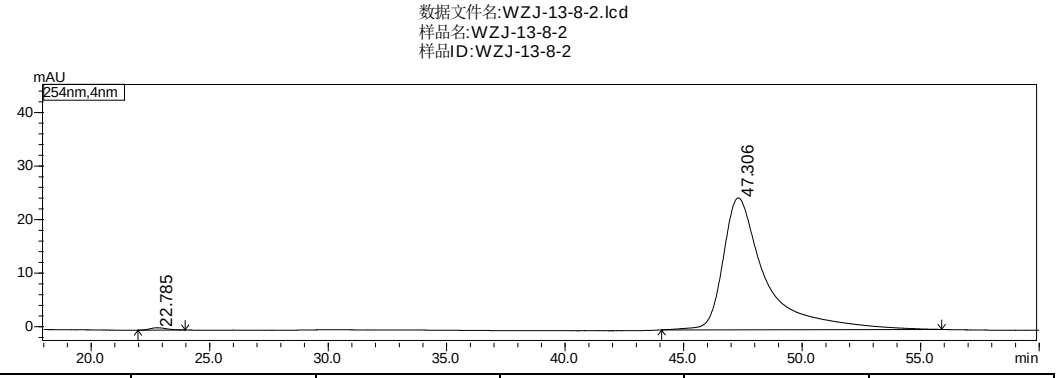
3d

Chiral HPLC spectrum of racemic **3d**

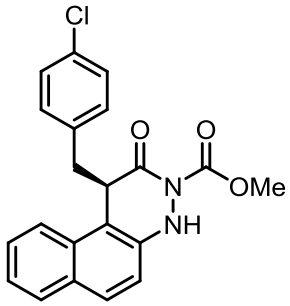


Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.977	36129091	615004	50.916	66.604
2	47.774	34829014	308366	49.084	33.396
Total		70958105	923370	100.000	100.000

Chiral HPLC spectrum of **3d**

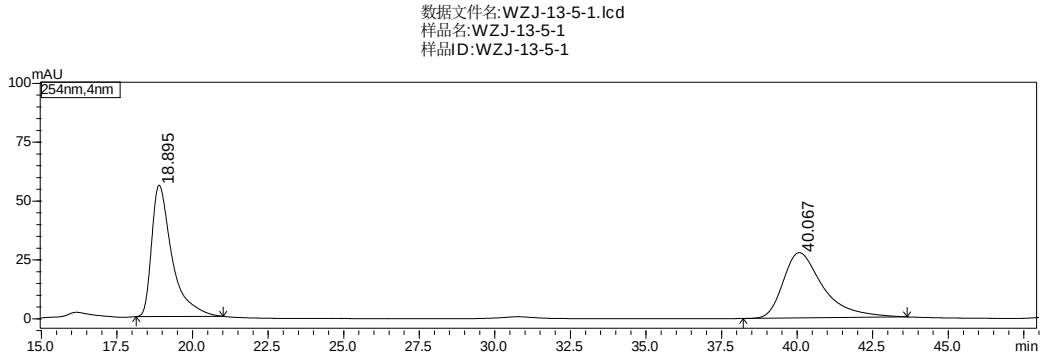


Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.785	15389	371	0.496	1.485
2	47.306	3084970	24620	99.504	98.515
Total		3100360	24991	100.000	100.000



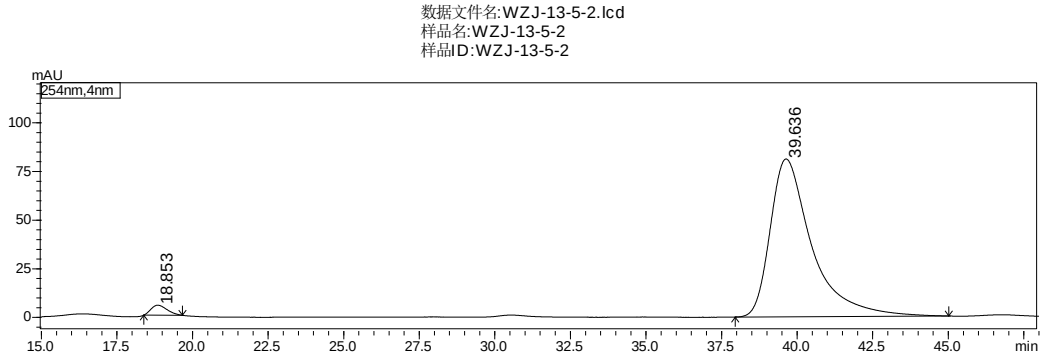
3e

Chiral HPLC spectrum of racemic **3e**

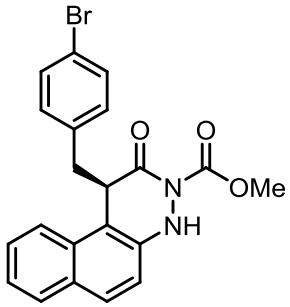


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.895	2605885	55811	50.511	66.784
2	40.067	2553175	27759	49.489	33.216
Total		5159059	83570	100.000	100.000

Chiral HPLC spectrum of **3e**

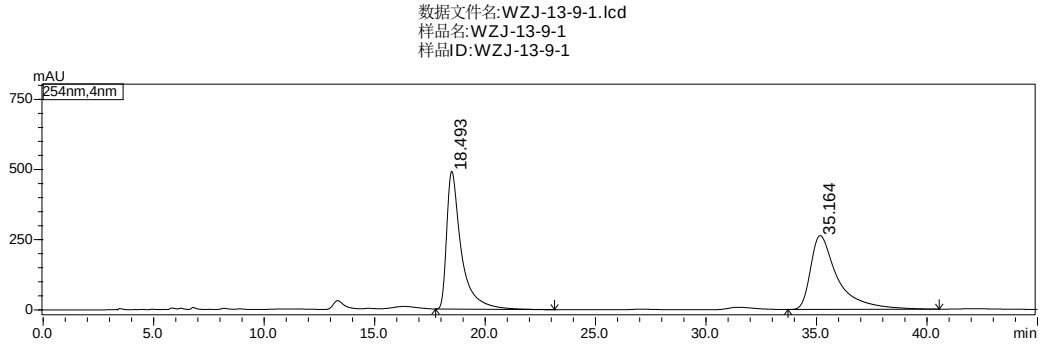


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.853	191127	5153	2.397	5.974
2	39.636	7782525	81108	97.603	94.026
Total		7973652	86261	100.000	100.000



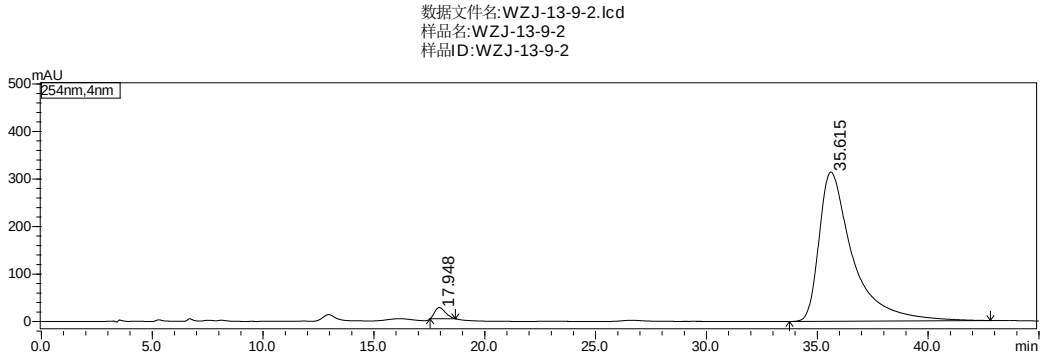
3f

Chiral HPLC spectrum of **3f**

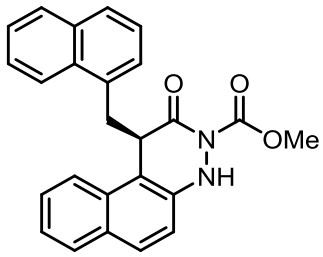


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.493	22605980	491010	50.227	65.093
2	35.164	22401702	263313	49.773	34.907
Total		45007683	754323	100.000	100.000

Chiral HPLC spectrum of **3f**

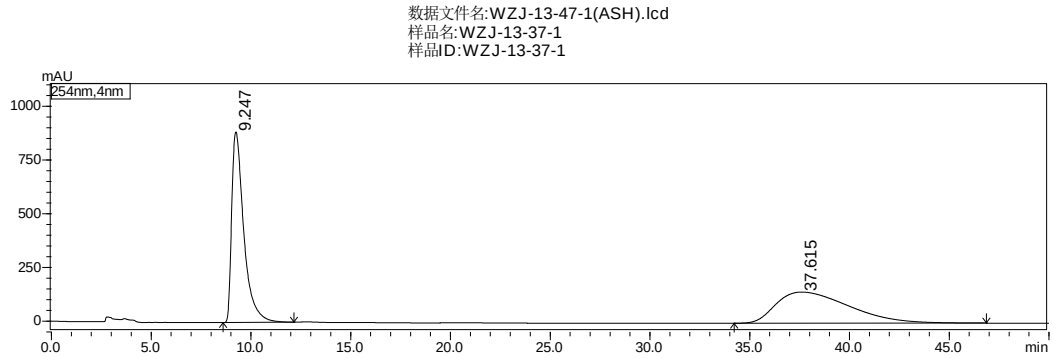


Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.878	1223419	32597	2.509	6.124
2	35.615	47531664	499708	97.491	93.876
Total		48755082	532305	100.000	100.000



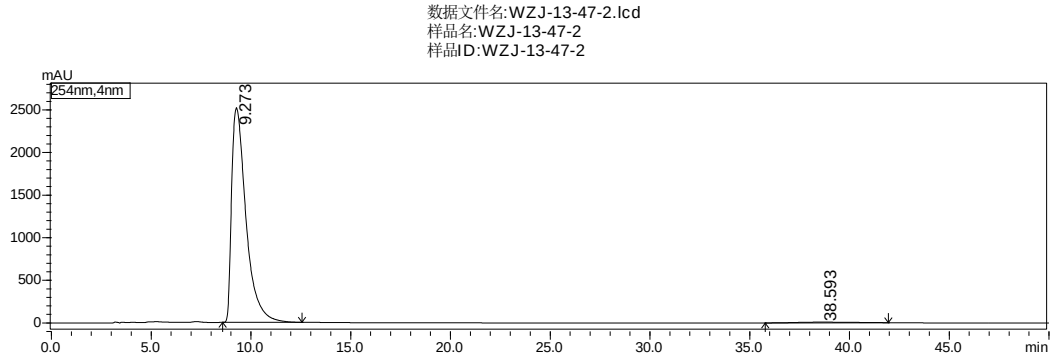
3g

Chiral HPLC spectrum of racemic **3g**

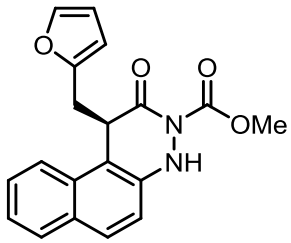


Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.247	37462887	887214	50.359	85.952
2	37.615	36928056	145003	49.641	14.048
Total		74390943	1032218	100.000	100.000

Chiral HPLC spectrum of **3g**

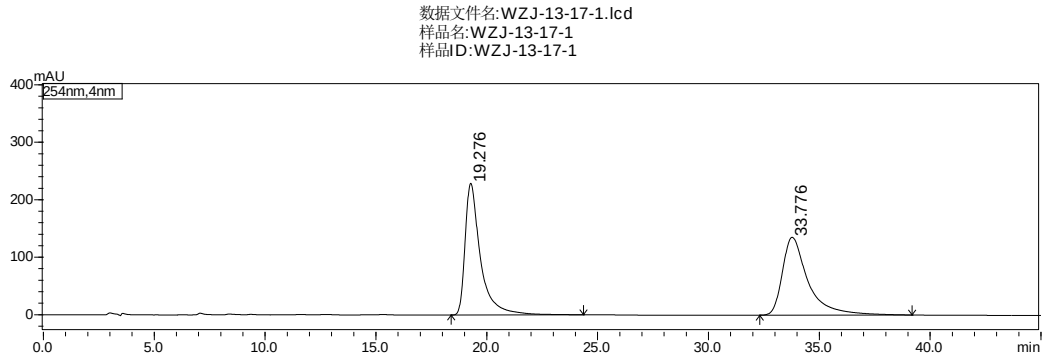


Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.273	126386530	2519813	99.522	99.825
2	38.593	606949	4417	0.478	0.175
Total		126993479	2524231	100.000	100.000



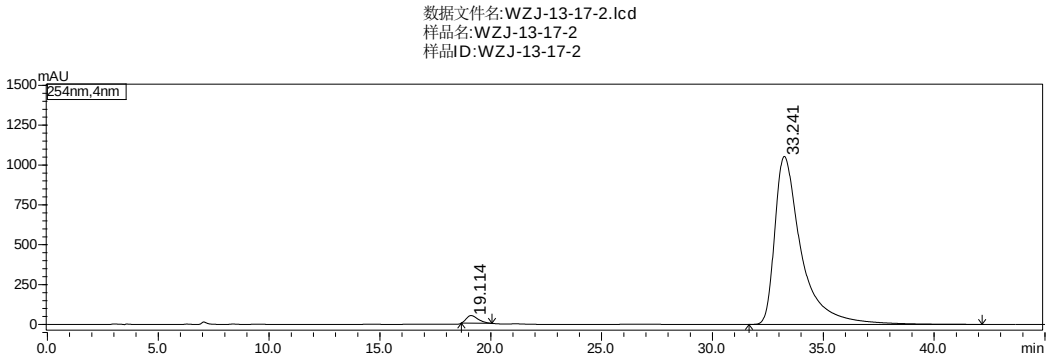
3h

Chiral HPLC spectrum of racemic **3h**

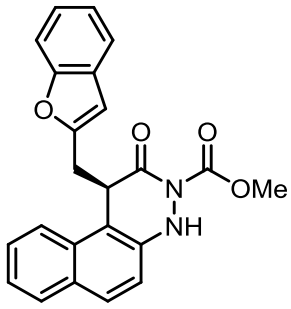


Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.276	11100192	229235	50.426	62.859
2	33.776	10912444	135449	49.574	37.141
Total		22012636	364684	100.000	100.000

Chiral HPLC spectrum of **3h**

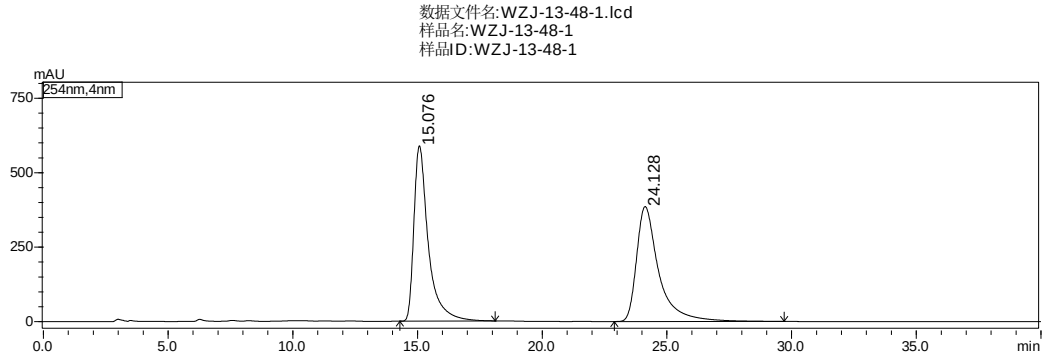


Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.114	1783619	48165	1.987	4.371
2	33.241	87992518	1053658	98.013	95.629
Total		89776137	1101824	100.000	100.000



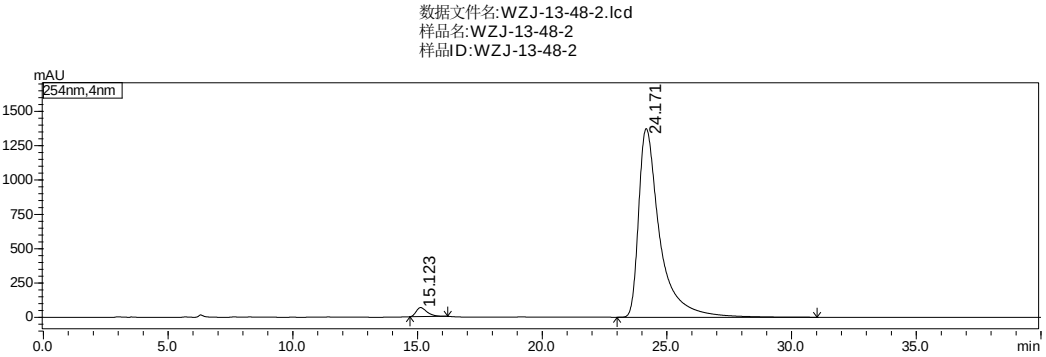
3i

Chiral HPLC spectrum of racemic **3i**

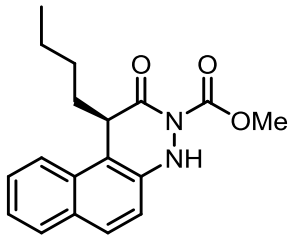


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.076	23652408	588768	49.668	60.387
2	24.128	23968650	386219	50.332	39.613
Total		47621058	974987	100.000	100.000

Chiral HPLC spectrum of **3i**

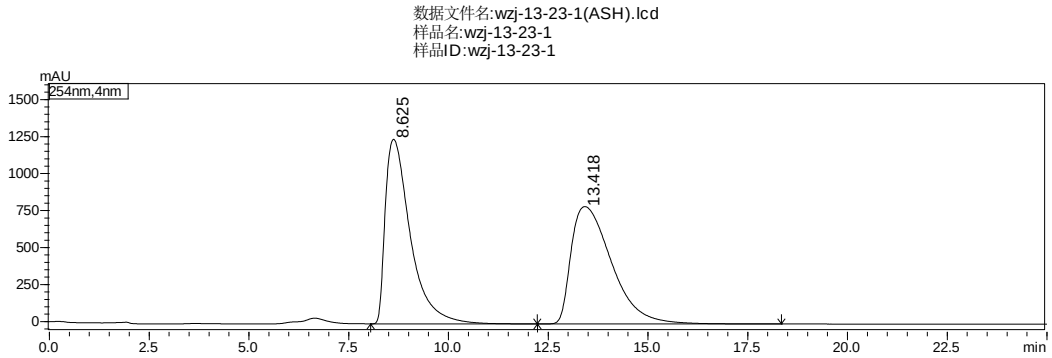


Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.123	2010731	65920	2.419	4.577
2	24.171	81104198	1374215	97.581	95.423
Total		83114929	1440135	100.000	100.000



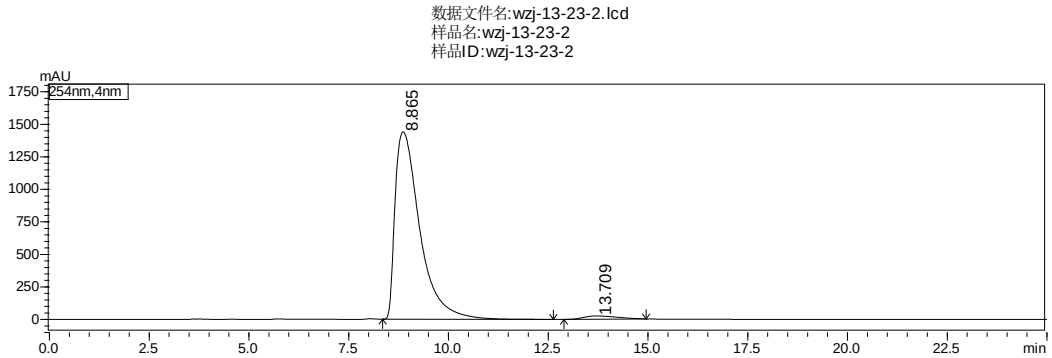
3j

Chiral HPLC spectrum of racemic **3j**

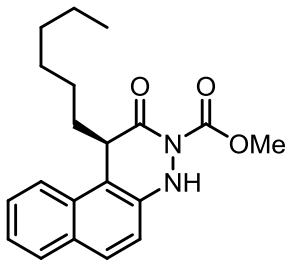


Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.625	54760773	1247340	49.385	61.123
2	13.418	56123675	793364	50.615	38.877
Total		110884448	2040704	100.000	100.000

Chiral HPLC spectrum of **3j**

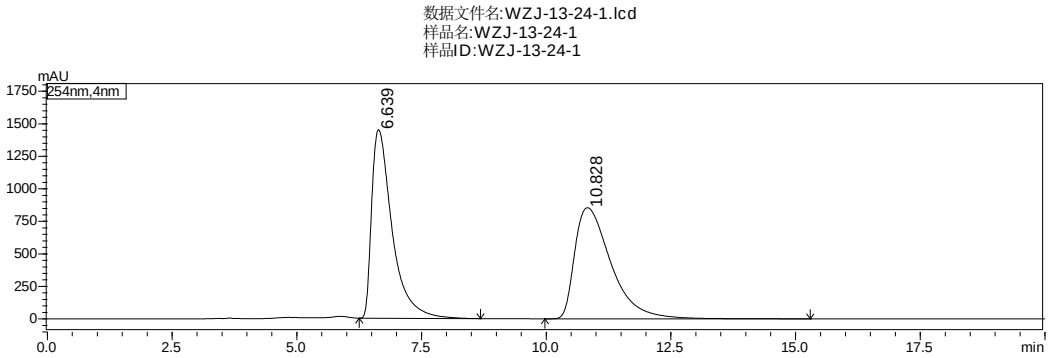


Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.865	62189443	1440589	97.850	98.346
2	13.709	1366520	24225	2.150	1.654
Total		63555963	1464814	100.000	100.000



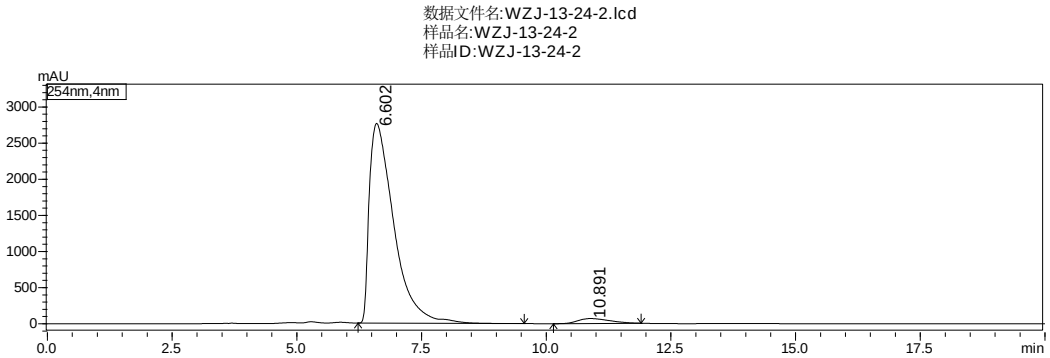
3k

Chiral HPLC spectrum of racemic **3k**

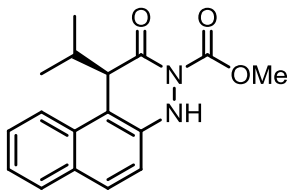


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.639	41567017	1449989	49.314	62.984
2	10.828	42723439	852178	50.686	37.016
Total		84290457	2302167	100.000	100.000

Chiral HPLC spectrum of **3k**

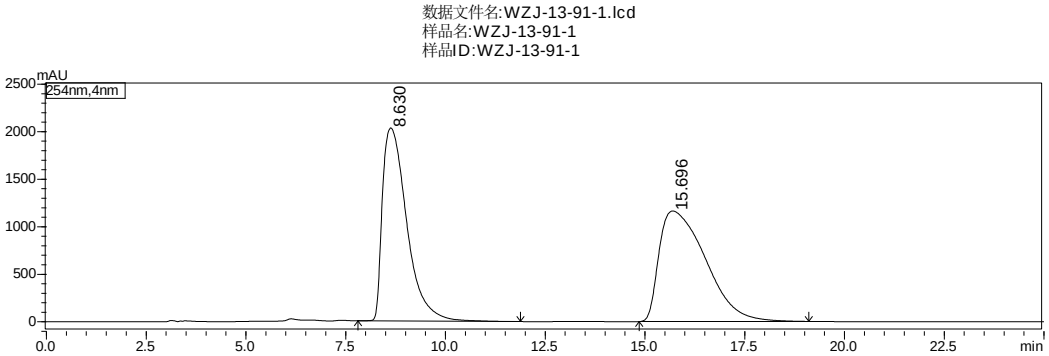


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.602	94795282	2768129	97.350	97.752
2	10.891	2580670	63659	2.650	2.248
Total		97375951	2831788	100.000	100.000



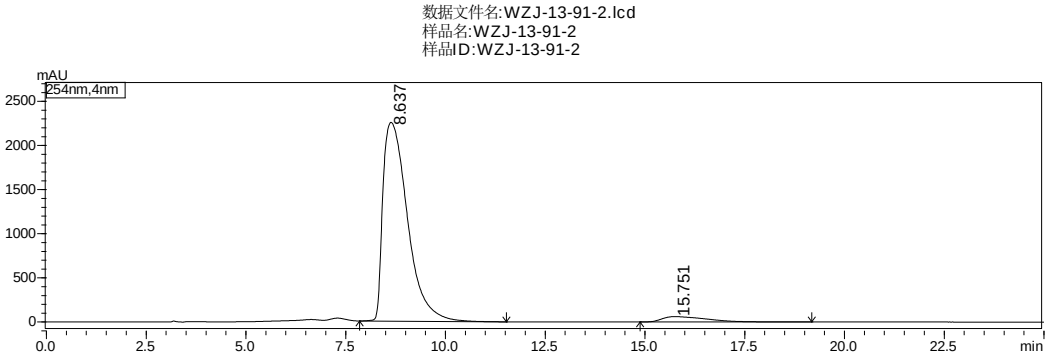
3l

Chiral HPLC spectrum of racemic **3l**

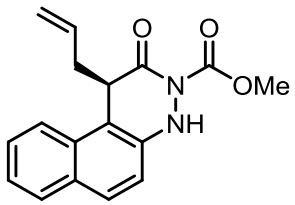


Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.630	86741690	2031581	49.360	64.066
2	15.696	88989716	1139479	50.640	35.934
Total		175731407	3171060	100.000	100.000

Chiral HPLC spectrum of **3l**

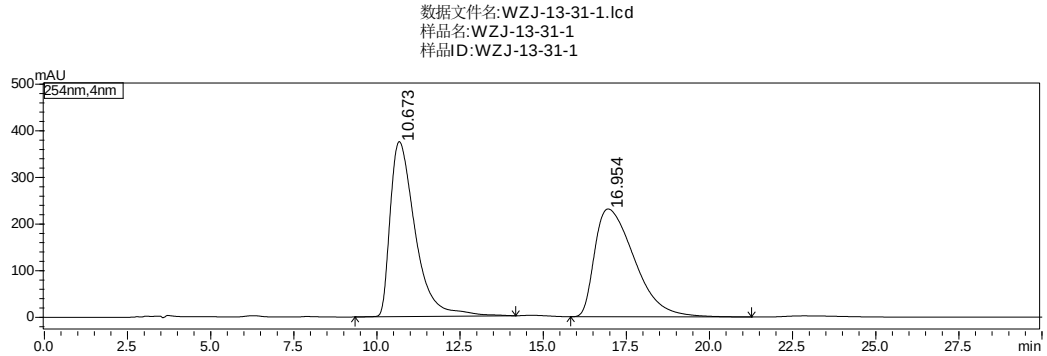


Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.637	96936138	2252862	95.428	97.381
2	15.751	4644238	60590	4.572	2.619
Total		101580376	2313452	100.000	100.000



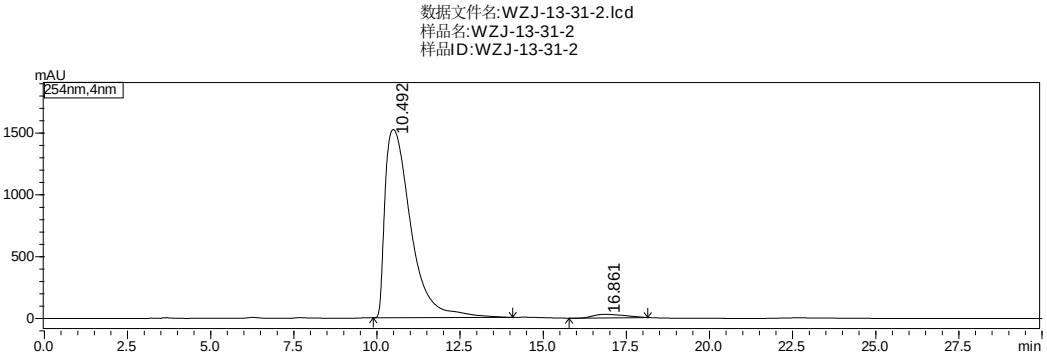
3m

Chiral HPLC spectrum of racemic **3m**

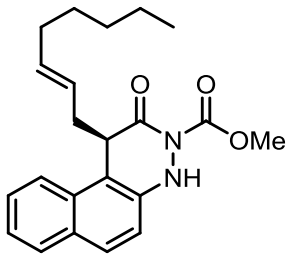


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.673	19726794	375394	50.587	61.870
2	16.954	19269153	231355	49.413	38.130
Total		38995947	606749	100.000	100.000

Chiral HPLC spectrum of **3m**

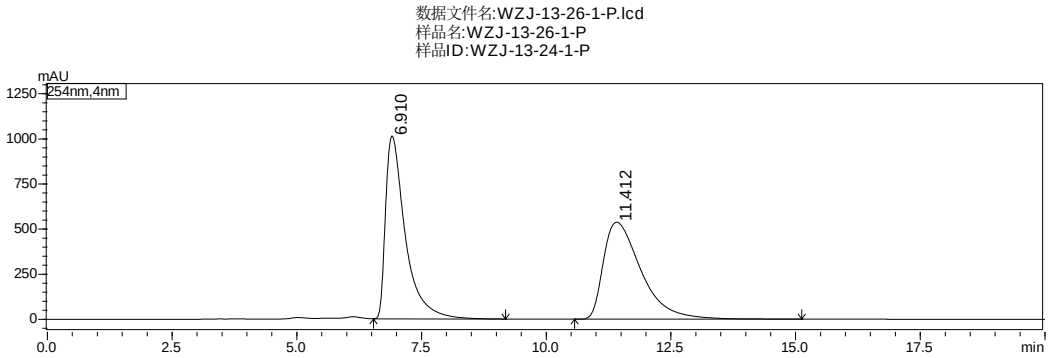


Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.492	82348377	1523724	97.761	98.161
2	16.861	1885635	28553	2.239	1.839
Total		84234012	1552277	100.000	100.000



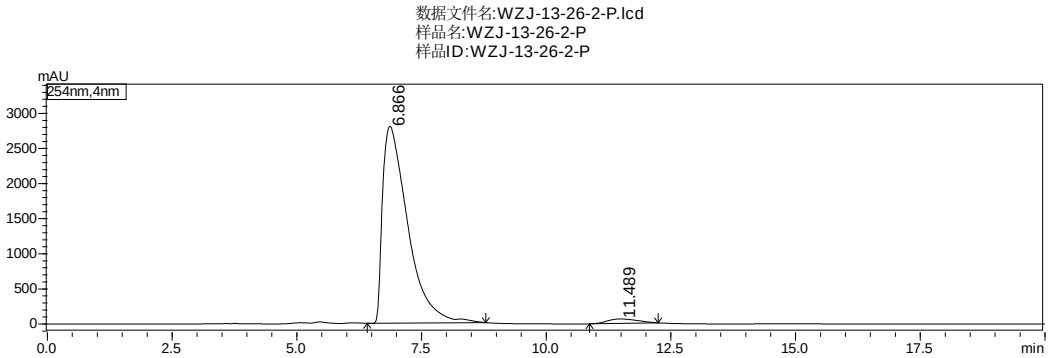
3n

Chiral HPLC spectrum of racemic **3n**

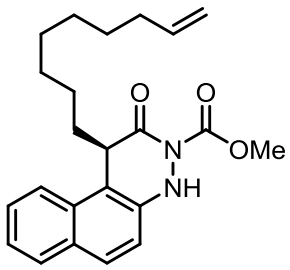


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.910	27925843	1014033	49.626	65.353
2	11.412	28346224	537598	50.374	34.647
Total		56272067	1551631	100.000	100.000

Chiral HPLC spectrum of **3n**

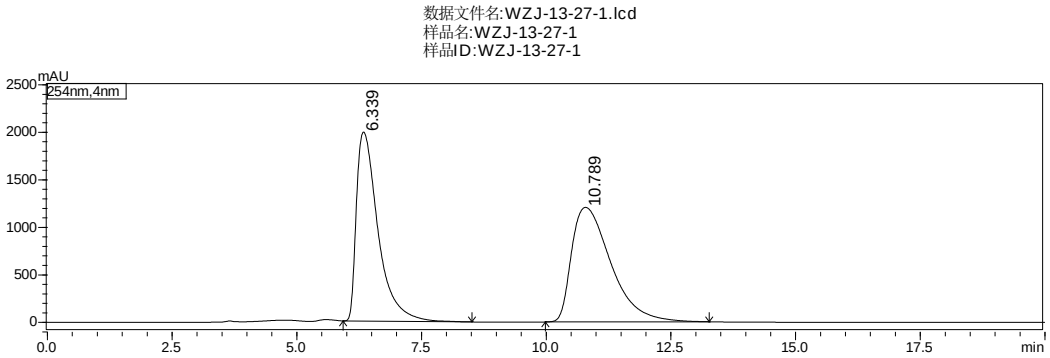


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.866	98865051	2802281	97.411	97.796
2	11.489	2627629	63146	2.589	2.204
Total		101492680	2865427	100.000	100.000



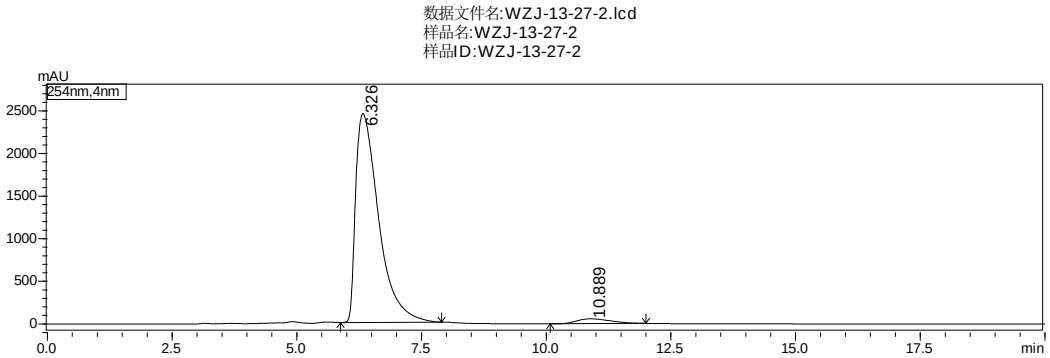
3o

Chiral HPLC spectrum of racemic **3o**

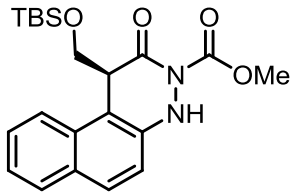


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.339	60215725	1988977	50.524	63.277
2	10.789	58967010	1154286	49.476	36.723
Total		119182735	3143263	100.000	100.000

Chiral HPLC spectrum of **3o**

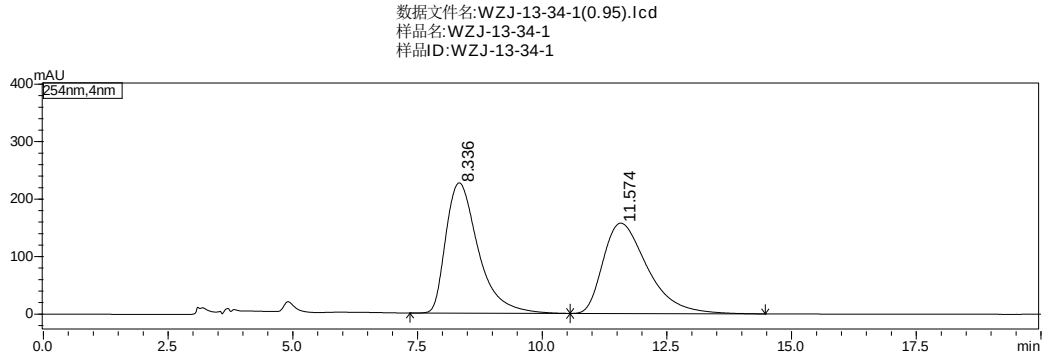


Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.326	78669981	2451834	97.528	98.072
2	10.889	1994114	48211	2.472	1.928
Total		80664095	2500045	100.000	100.000



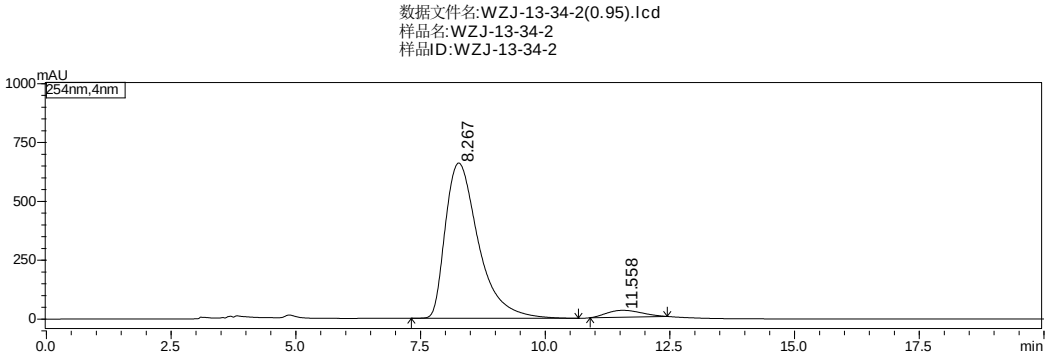
3p

Chiral HPLC spectrum of racemic **3p**

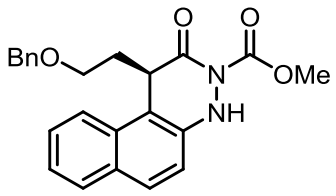


Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.336	9666842	223314	49.769	58.676
2	11.574	9756555	157275	50.231	41.324
Total		19423397	380589	100.000	100.000

Chiral HPLC spectrum of **3p**

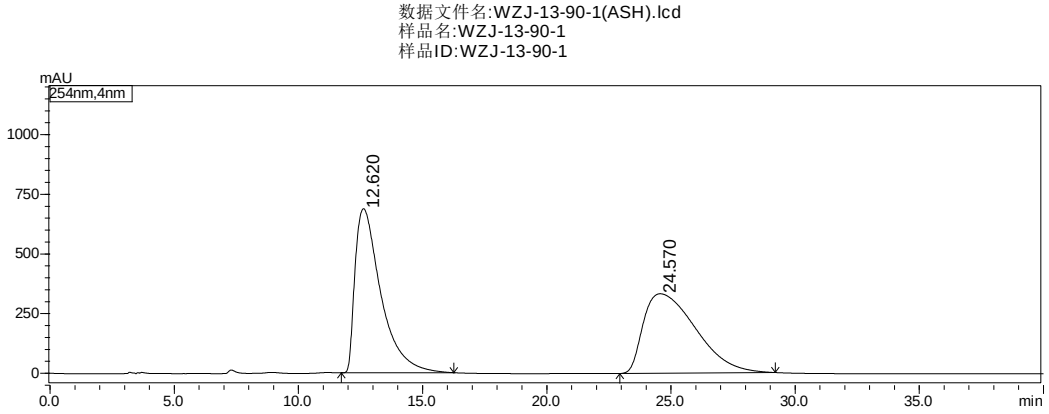


Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.267	30483532	660017	95.511	95.754
2	11.558	1432814	29267	4.489	4.246
Total		31916346	689284	100.000	100.000



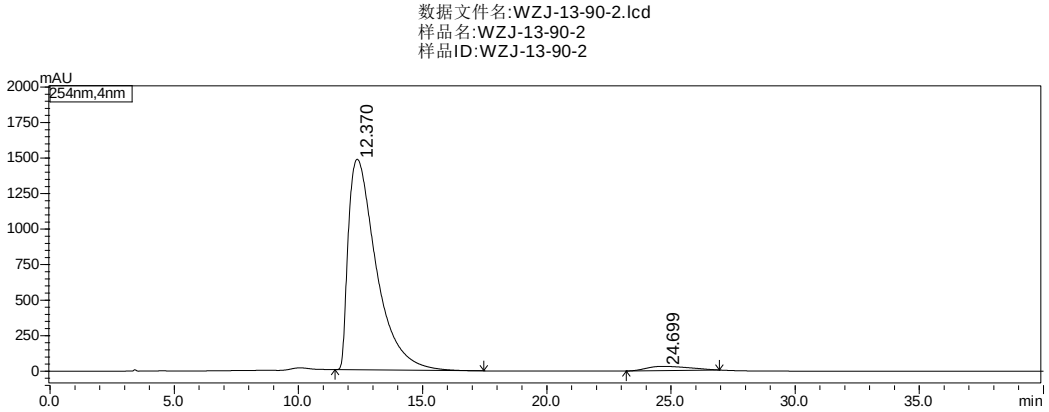
3q

Chiral HPLC spectrum of racemic **3q**

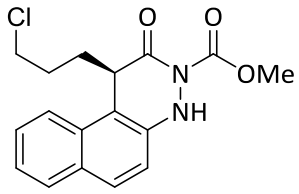


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.620	49958178	687916	50.489	67.368
2	24.570	48989988	333220	49.511	32.632
Total		98948166	1021135	100.000	100.000

Chiral HPLC spectrum of **3q**

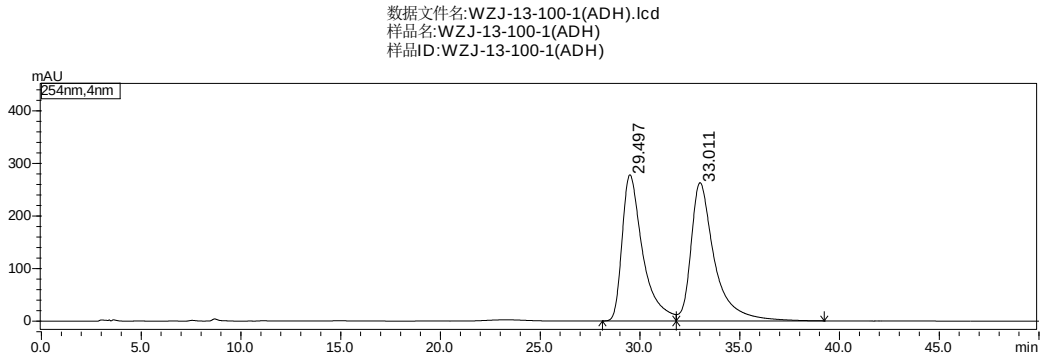


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.370	116394347	1482555	97.006	98.003
2	24.699	3592316	30217	2.994	1.997
Total		119986663	1512772	100.000	100.000



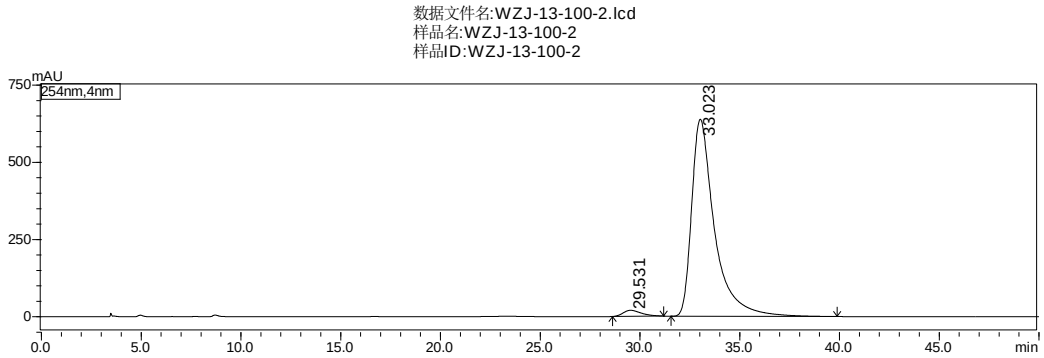
3r

Chiral HPLC spectrum of racemic **3r**

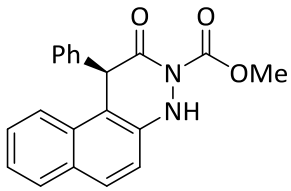


Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.497	20010472	277816	48.095	51.377
2	33.011	21595419	262927	51.905	48.623
Total		41605891	540743	100.000	100.000

Chiral HPLC spectrum of **3r**

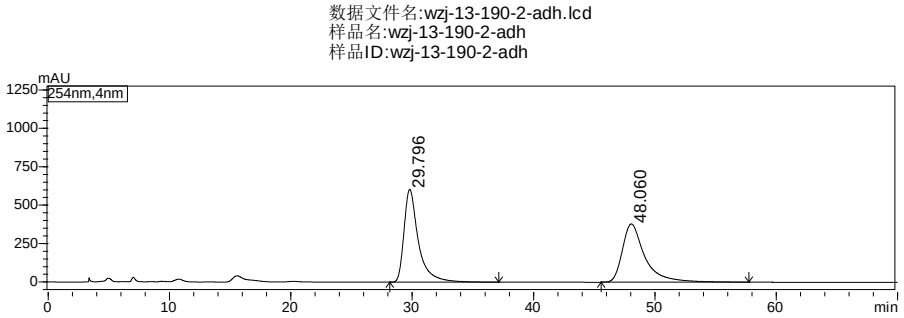


Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.531	1237969	19591	2.374	2.980
2	33.023	50898123	637894	97.626	97.020
Total		52136092	657485	100.000	100.000



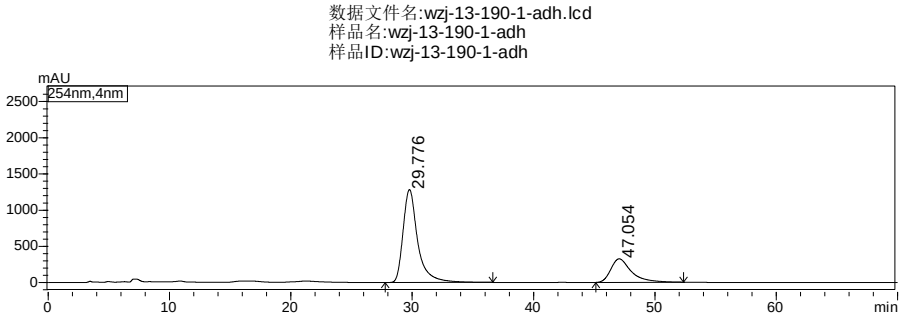
3s

Chiral HPLC spectrum of racemic **3s**

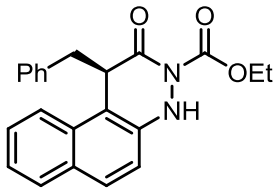


Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.796	50056138	604848	50.502	61.442
2	48.060	49061638	379567	49.498	38.558
Total		99117775	984415	100.000	100.000

Chiral HPLC spectrum of **3s**

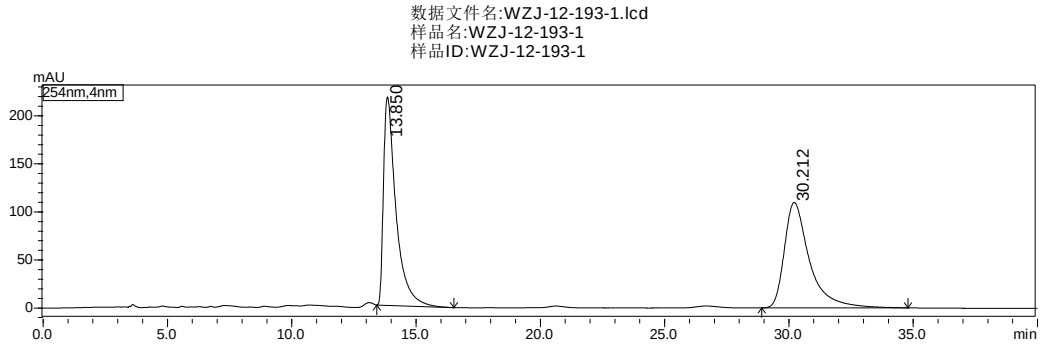


Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.776	107778962	1282439	78.226	81.118
2	47.054	29999147	298522	21.774	18.882
Total		137778108	1580960	100.000	100.000



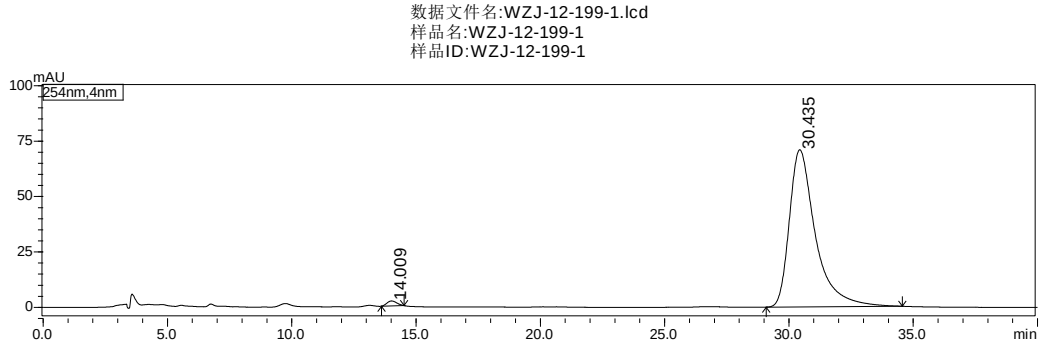
4a

Chiral HPLC spectrum of racemic **4a**

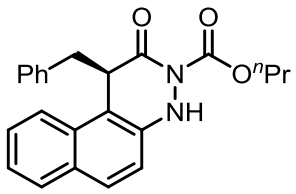


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.850	7584582	217112	49.525	66.426
2	30.212	7730035	109734	50.475	33.574
Total		15314617	326846	100.000	100.000

Chiral HPLC spectrum of **4a**

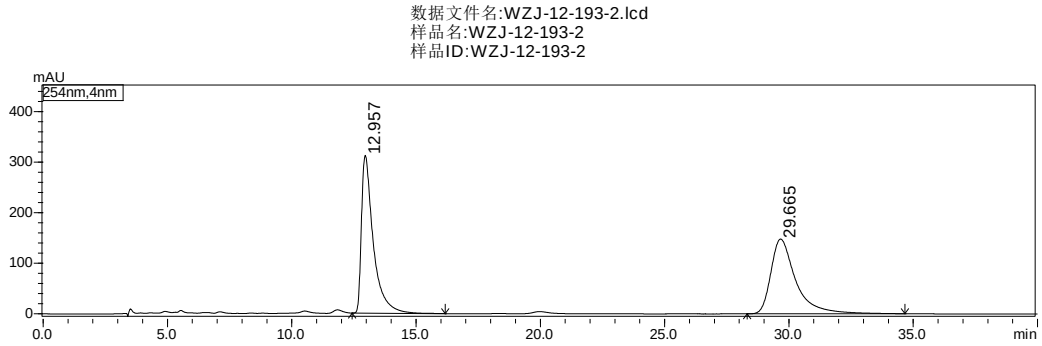


Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.009	61894	2254	1.183	3.080
2	30.435	5171889	70918	98.817	96.920
Total		5233782	73172	100.000	100.000



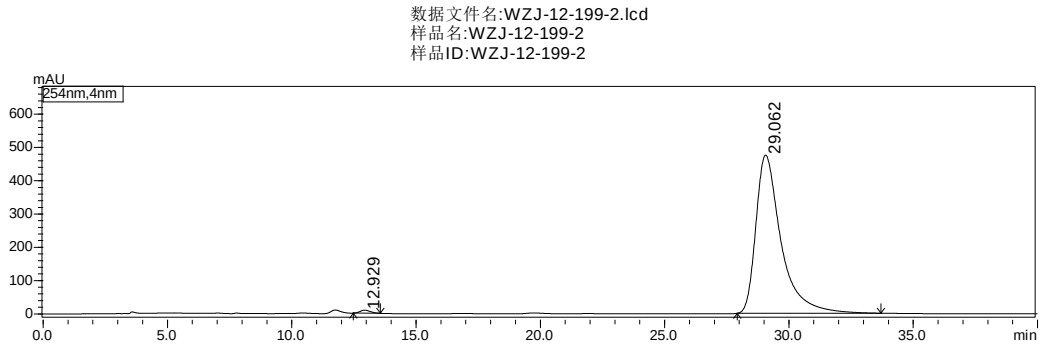
4b

Chiral HPLC spectrum of racemic **4b**

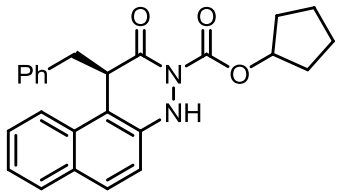


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.957	10349943	311884	50.062	67.853
2	29.665	10324168	147762	49.938	32.147
Total		20674111	459646	100.000	100.000

Chiral HPLC spectrum of **4b**

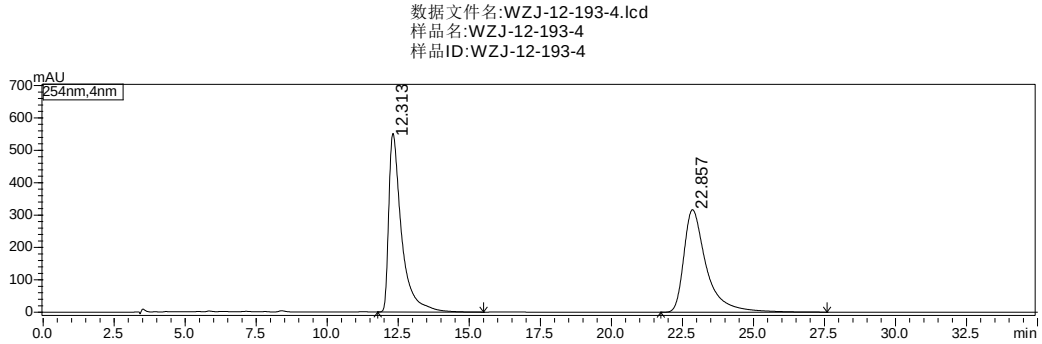


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.929	226889	8534	0.661	1.758
2	29.062	34093649	476809	99.339	98.242
Total		34320538	485343	100.000	100.000



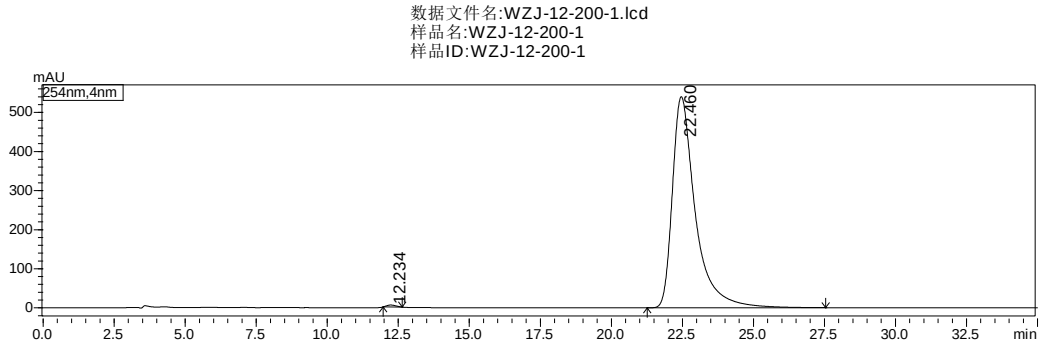
4c

Chiral HPLC spectrum of racemic **4c**

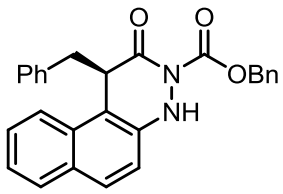


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.313	17303729	551050	49.742	63.500
2	22.857	17483009	316740	50.258	36.500
Total		34786739	867789	100.000	100.000

Chiral HPLC spectrum of **4c**

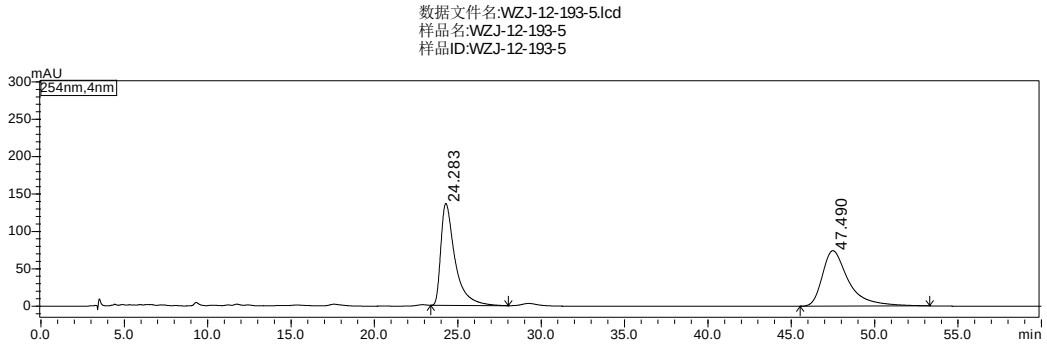


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.234	110444	4956	0.362	0.909
2	22.460	30377126	540322	99.638	99.091
Total		30487570	545278	100.000	100.000



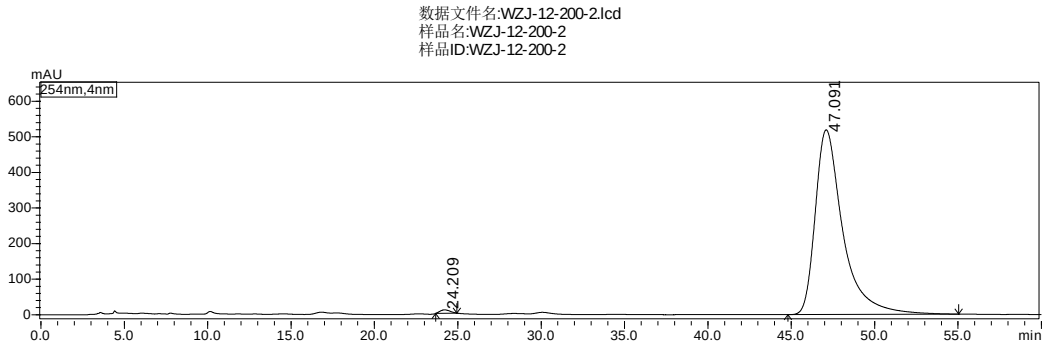
4d

Chiral HPLC spectrum of racemic **4d**

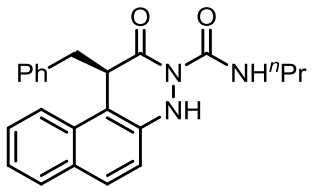


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.283	8073450	136483	49.867	64.773
2	47.490	8116455	74228	50.133	35.227
Total		16189905	210712	100.000	100.000

Chiral HPLC spectrum of **4d**

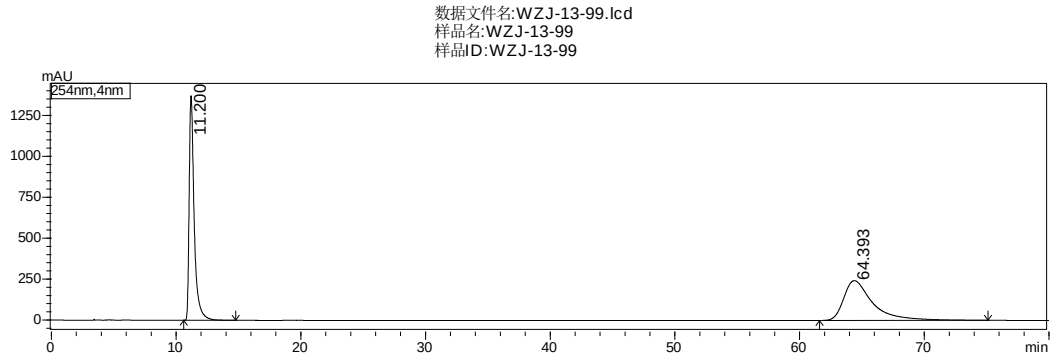


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.209	406246	9797	0.675	1.852
2	47.091	59789154	519221	99.325	98.148
Total		60195400	529018	100.000	100.000



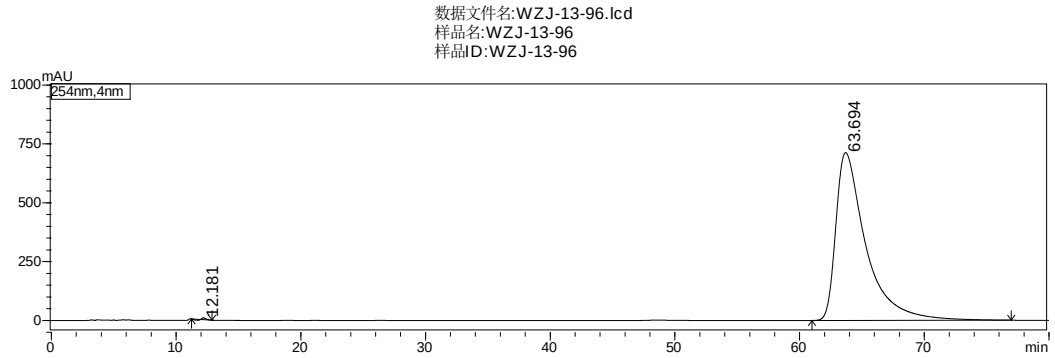
4e

Chiral HPLC spectrum of racemic **4e**

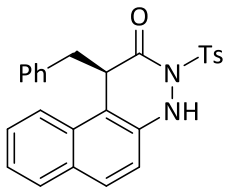


Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.200	38504449	1371415	49.527	84.944
2	64.393	39239360	243077	50.473	15.056
Total		77743809	1614493	100.000	100.000

Chiral HPLC spectrum of **4e**

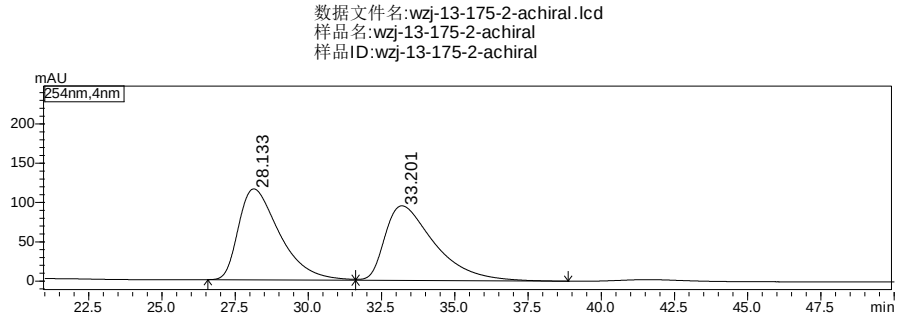


Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.181	49110	7559	0.041	1.049
2	63.694	119353002	713012	99.959	98.951
Total		119402112	720571	100.000	100.000



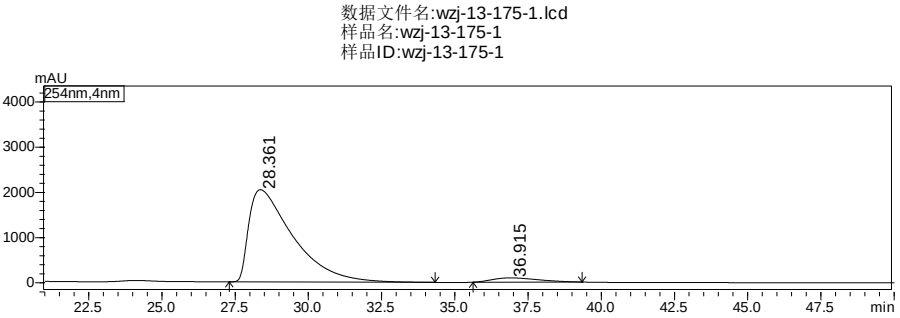
4f

Chiral HPLC spectrum of racemic **4f**

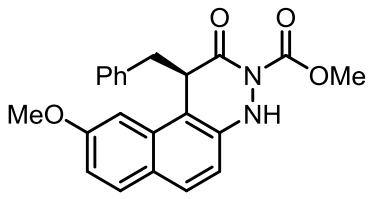


Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.133	11342400	115816	50.157	54.908
2	33.201	11271373	95112	49.843	45.092
Total		22613772	210928	100.000	100.000

Chiral HPLC spectrum of **4f**

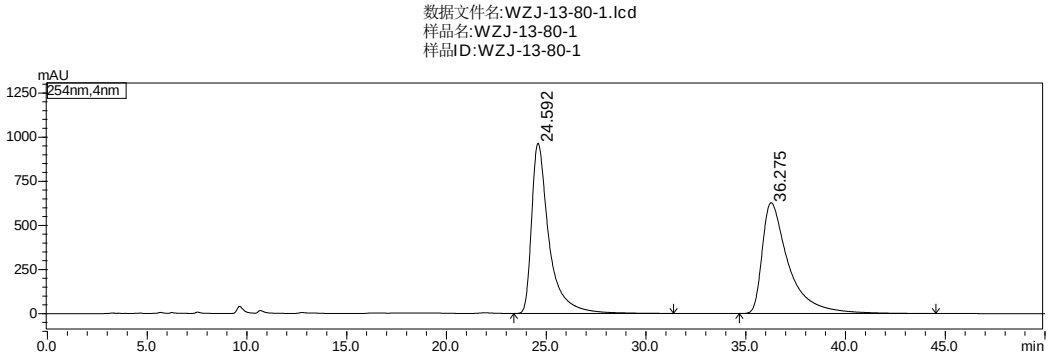


Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.361	214187296	2039222	96.346	95.957
2	36.915	8122125	85913	3.654	4.043
Total		222309421	2125135	100.000	100.000



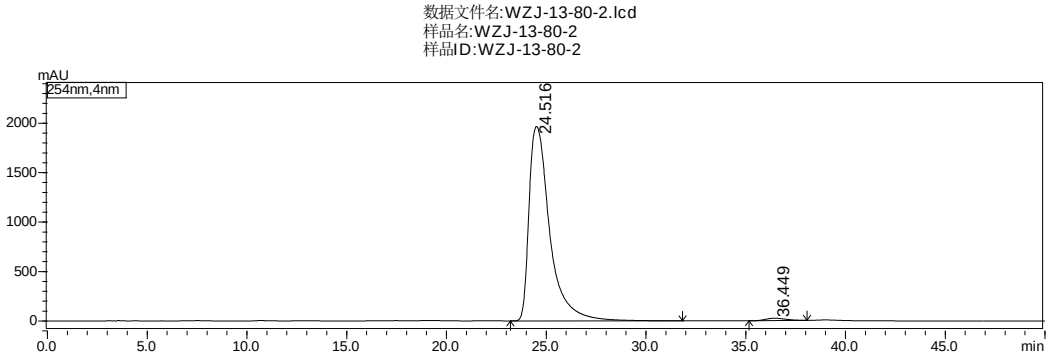
4g

Chiral HPLC spectrum of racemic **4g**

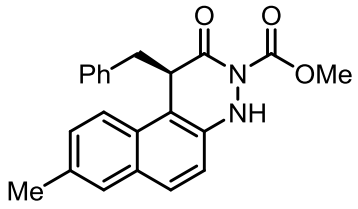


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.592	58457923	964094	50.216	60.562
2	36.275	57954668	627828	49.784	39.438
Total		116412591	1591921	100.000	100.000

Chiral HPLC spectrum of **4g**

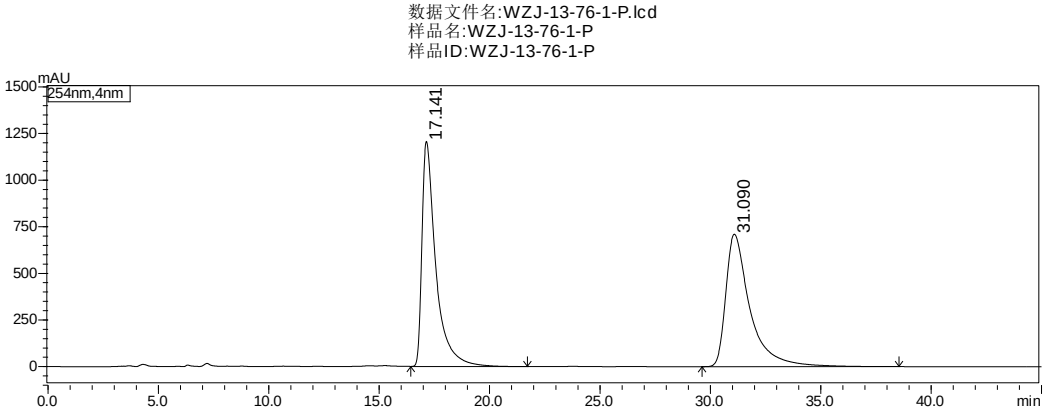


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.516	142210890	1966098	98.772	98.763
2	36.449	1768074	24628	1.228	1.237
Total		143978965	1990726	100.000	100.000



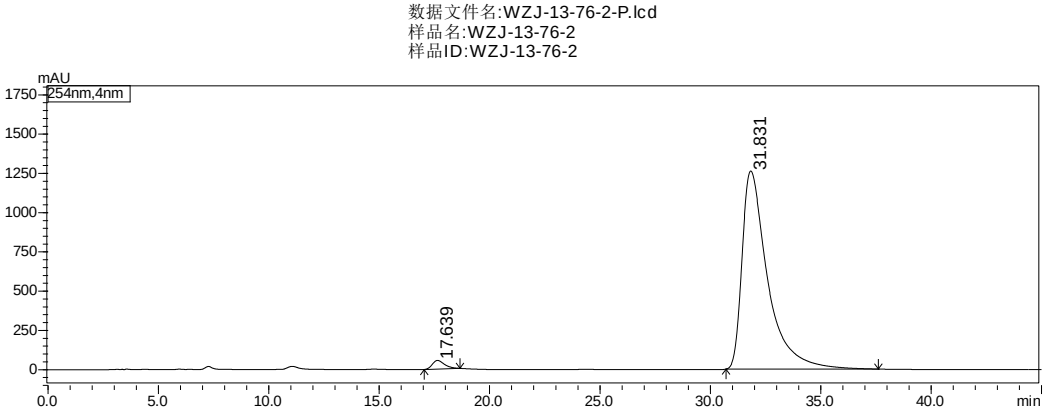
4h

Chiral HPLC spectrum of racemic **4h**

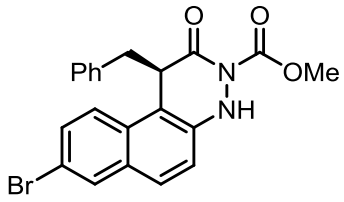


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.141	52724473	1206945	49.365	62.949
2	31.090	54081526	710406	50.635	37.051
Total		106805999	1917352	100.000	100.000

Chiral HPLC spectrum of **4h**

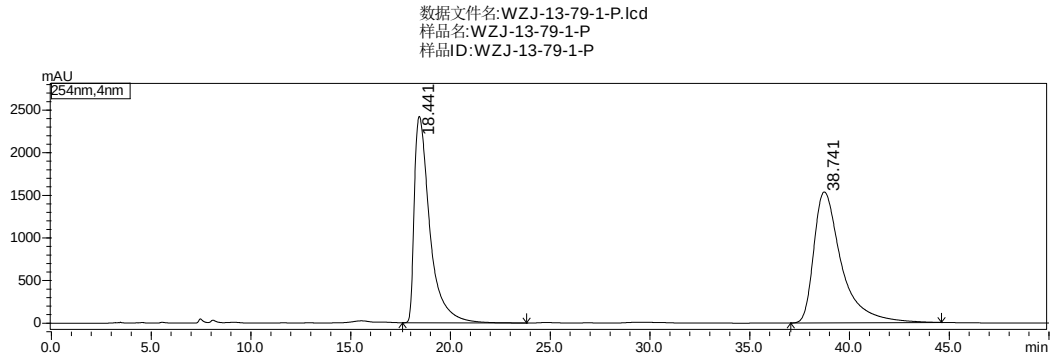


Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.639	2123755	55252	2.043	4.195
2	31.831	101840873	1261985	97.957	95.805
Total		103964627	1317237	100.000	100.000



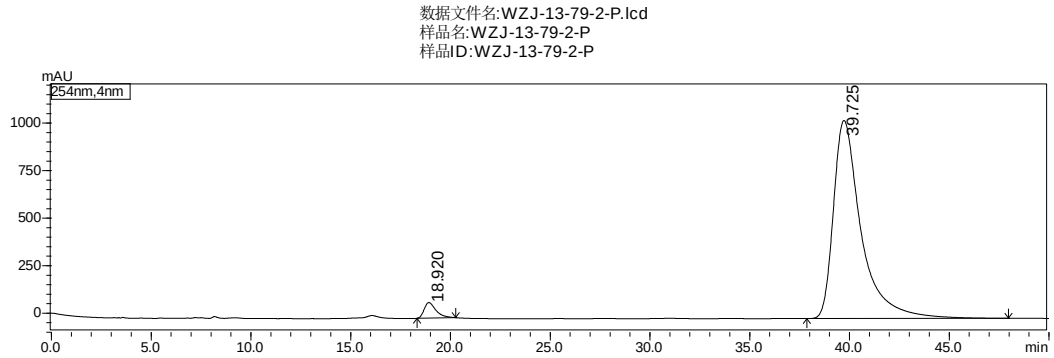
4i

Chiral HPLC spectrum of racemic **4i**

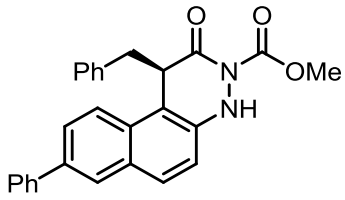


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.441	131211987	2422516	49.362	61.857
2	38.741	134603412	1493777	50.638	38.143
Total		265815399	3916293	100.000	100.000

Chiral HPLC spectrum of **4i**

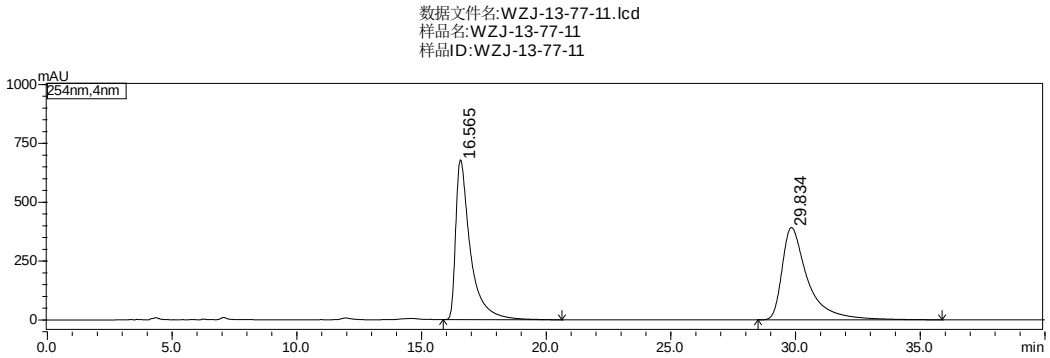


Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.920	3412950	82138	3.279	7.309
2	39.725	100669239	1041644	96.721	92.691
Total		104082190	1123781	100.000	100.000



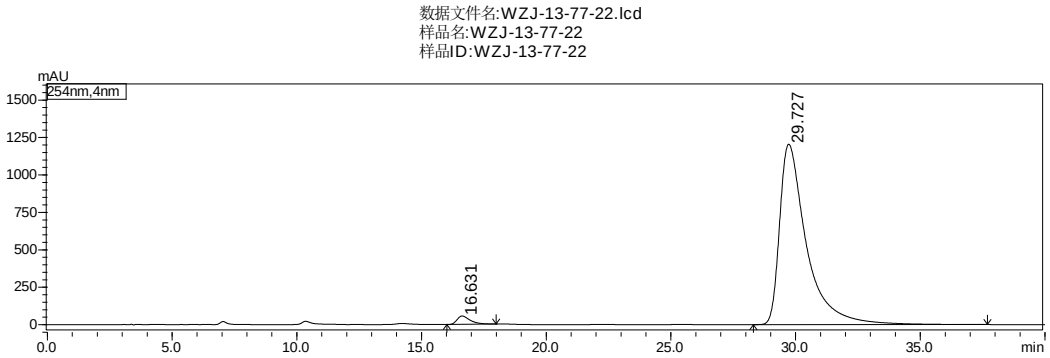
4j

Chiral HPLC spectrum of racemic **4j**

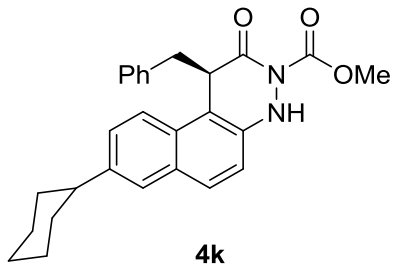


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.565	27662951	678711	49.656	63.364
2	29.834	28045930	392423	50.344	36.636
Total		55708881	1071134	100.000	100.000

Chiral HPLC spectrum of **4j**

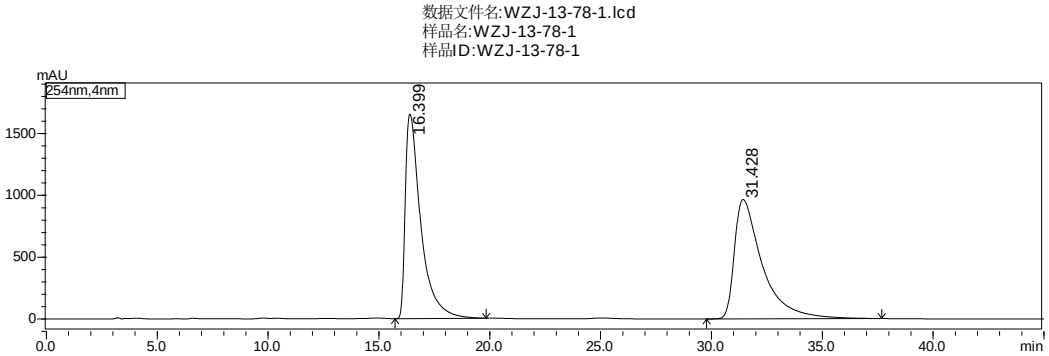


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.631	1870780	54550	2.030	4.332
2	29.727	90276022	1204623	97.970	95.668
Total		92146802	1259173	100.000	100.000



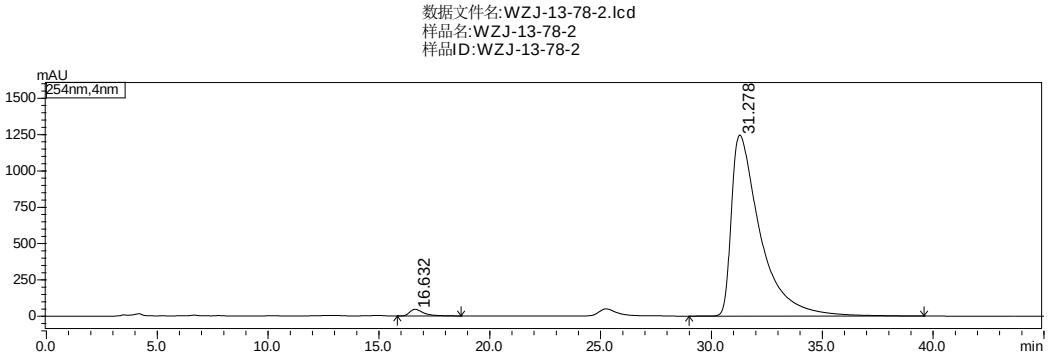
4k

Chiral HPLC spectrum of racemic **4k**

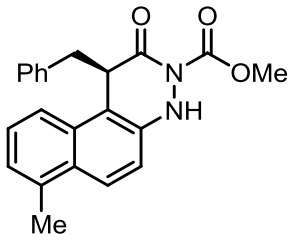


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.399	80872247	1655243	50.201	63.497
2	31.428	80223698	951576	49.799	36.503
Total		161095945	2606819	100.000	100.000

Chiral HPLC spectrum of **4k**

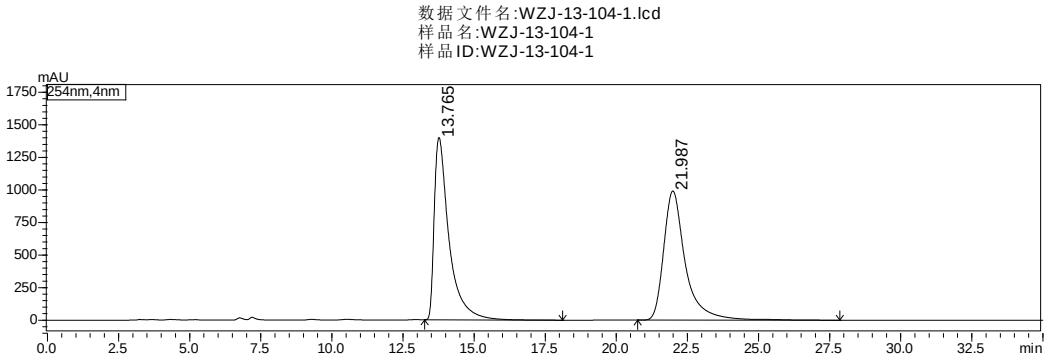


Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.632	2039043	46423	1.770	3.593
2	31.278	113181206	1245763	98.230	96.407
Total		115220249	1292186	100.000	100.000



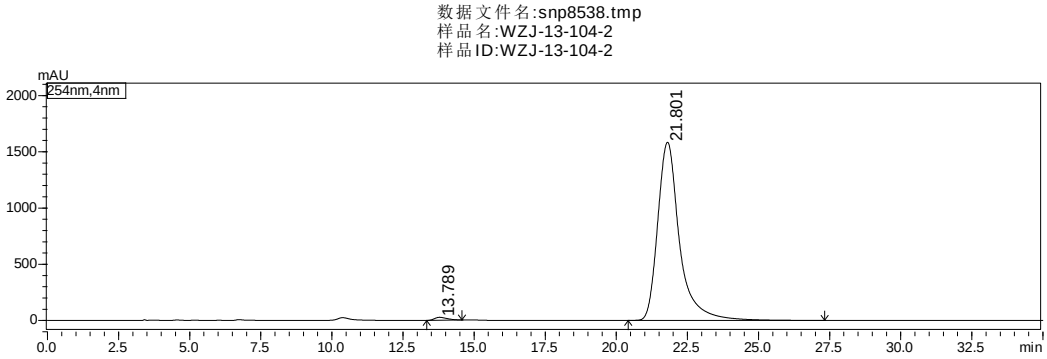
4l

Chiral HPLC spectrum of racemic **4l**

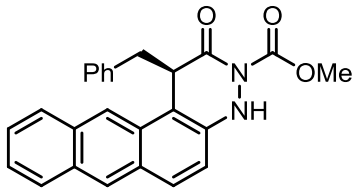


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.765	50780188	1400853	49.074	58.549
2	21.987	52696417	991756	50.926	41.451
Total		103476605	2392608	100.000	100.000

Chiral HPLC spectrum of racemic **4l**

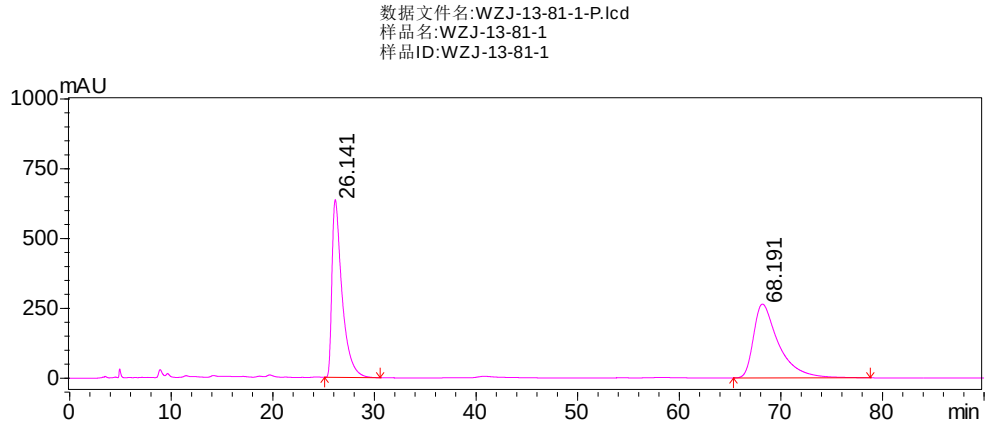


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.789	815329	26377	0.956	1.638
2	21.801	84430708	1583928	99.044	98.362
Total		85246037	1610305	100.000	100.000



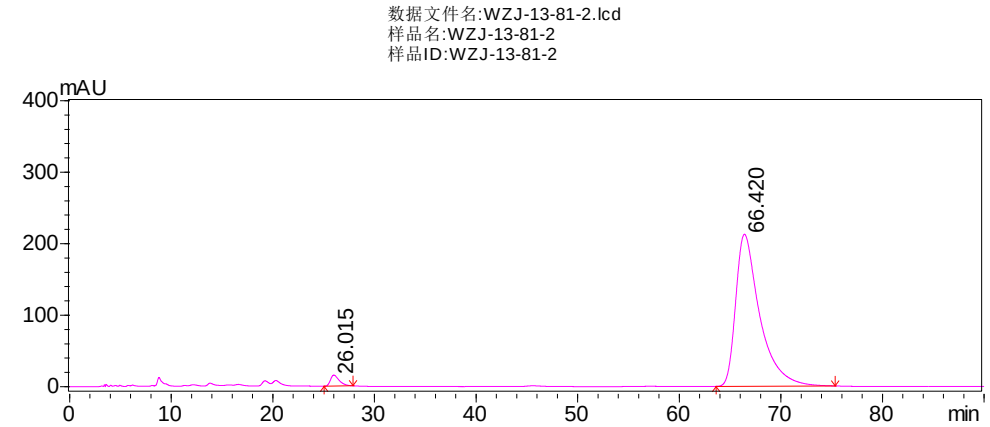
4m

Chiral HPLC spectrum of racemic **4m**

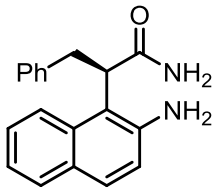


Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.141	44009688	636984	49.227	70.650
2	68.191	45391061	264615	50.773	29.350
Total		89400749	901599	100.000	100.000

Chiral HPLC spectrum of **4m**

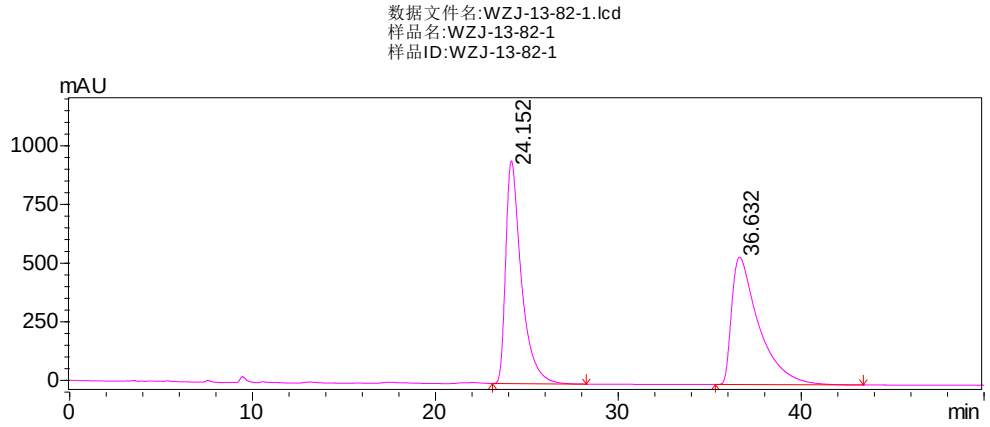


Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.015	882236	15261	2.461	6.698
2	66.420	34967988	212588	97.539	93.302
Total		35850224	227849	100.000	100.000



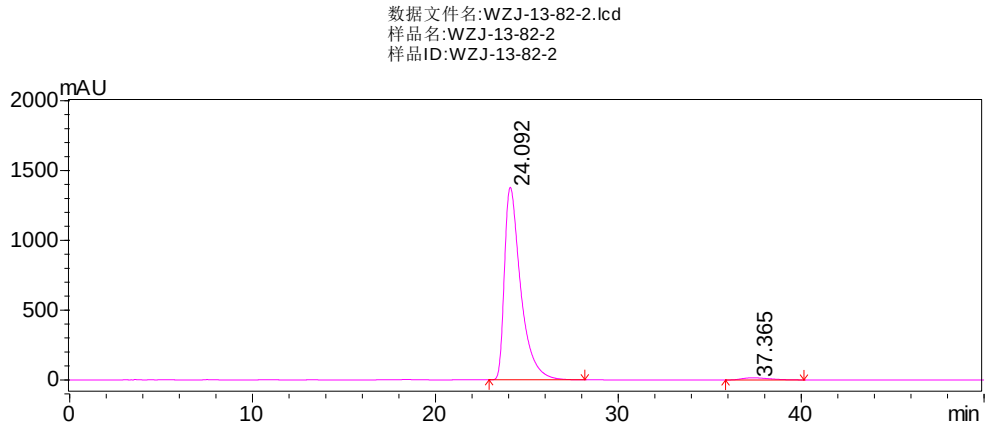
5

Chiral HPLC spectrum of racemic **5**



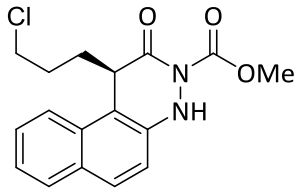
Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.152	56422446	950003	50.140	63.609
2	36.632	56107806	543499	49.860	36.391
Total		112530252	1493502	100.000	100.000

Chiral HPLC spectrum of **5**

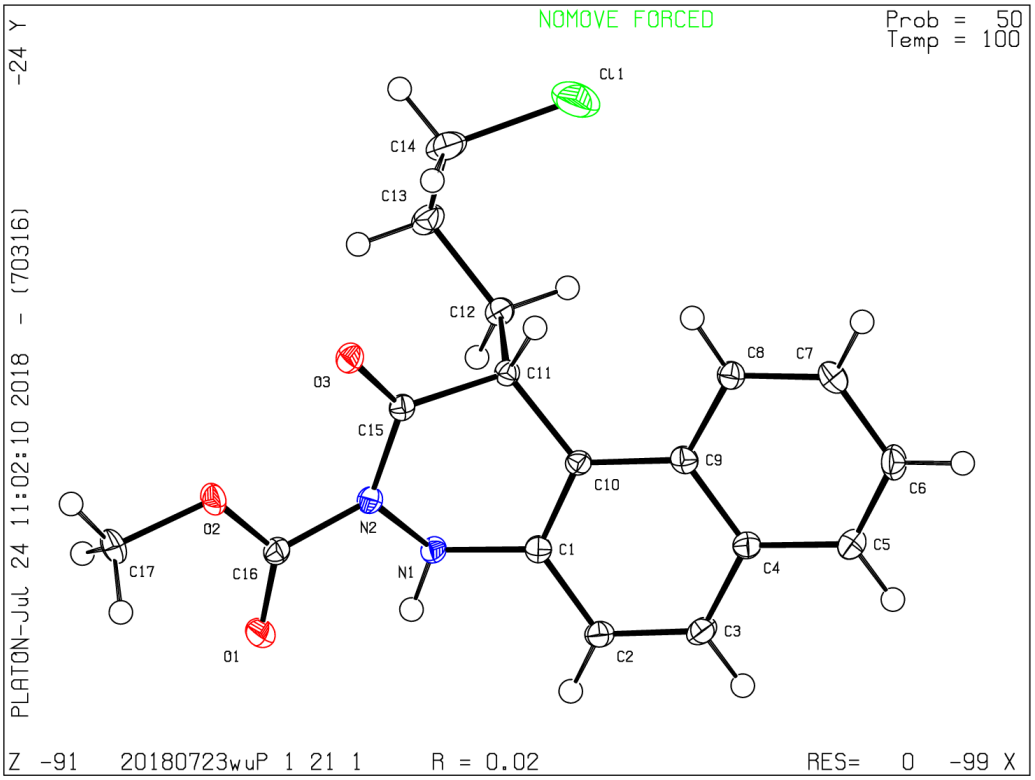


Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.092	85134231	1379699	98.648	99.050
2	37.365	1167030	13235	1.352	0.950
Total		86301261	1392935	100.000	100.000

10. X-ray single crystal data for compound 3r



3r



checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: 20180723wuzijun

```
Bond precision:  C-C = 0.0028 A          Wavelength=1.54184

Cell:            a=7.5990(1)    b=10.2490(1)        c=10.4880(1)
                 alpha=90       beta=109.100(1)     gamma=90
Temperature:     100 K

                 Calculated                Reported
Volume           771.861(15)               771.861(15)
Space group      P 21                      P 1 21 1
Hall group       P 2yb                     P 2yb
Moiety formula   C17 H17 Cl N2 O3          C17 H17 Cl N2 O3
Sum formula      C17 H17 Cl N2 O3          C17 H17 Cl N2 O3
Mr               332.78                    332.77
Dx,g cm-3        1.432                     1.432
Z                2                         2
Mu (mm-1)        2.342                     2.342
F000             348.0                     348.0
F000'            349.72
h,k,lmax         9,12,12                   9,12,12
Nref             2997[ 1588]               2950
Tmin,Tmax        0.430,0.473               0.811,1.000
Tmin'            0.303

Correction method= # Reported T Limits: Tmin=0.811 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 1.86/0.98      Theta(max)= 71.200

R(reflections)= 0.0244( 2941)     wR2(reflections)= 0.0629( 2950)

S = 1.087                 Npar= 209
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level G

```
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms .............          1 Report
PLAT012_ALERT_1_G No       _shelx_res_checksum Found in CIF ......     Please Check
PLAT142_ALERT_4_G s.u. on b - Axis Small or Missing ..............    0.00010 Ang.
PLAT143_ALERT_4_G s.u. on c - Axis Small or Missing ..............    0.00010 Ang.
PLAT791_ALERT_4_G Model has Chirality at C11        (Chiral SPGR)          R Verify
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   0 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   5 ALERT level G = General information/check it is not something unexpected

   1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   0 ALERT type 2 Indicator that the structure model may be wrong or deficient
   0 ALERT type 3 Indicator that the structure quality may be low
   3 ALERT type 4 Improvement, methodology, query or suggestion
   1 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 14/07/2018; check.def file version of 05/06/2018