Asymmetric Synthesis of Spirooxindole ε-Lactones through N-Heterocyclic Carbene Catalysis

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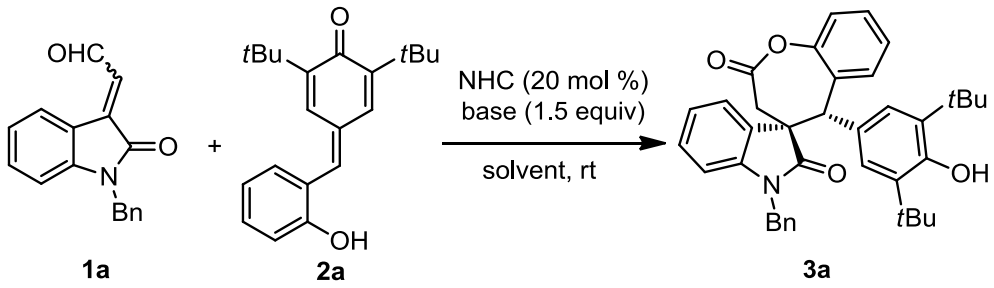
Contents

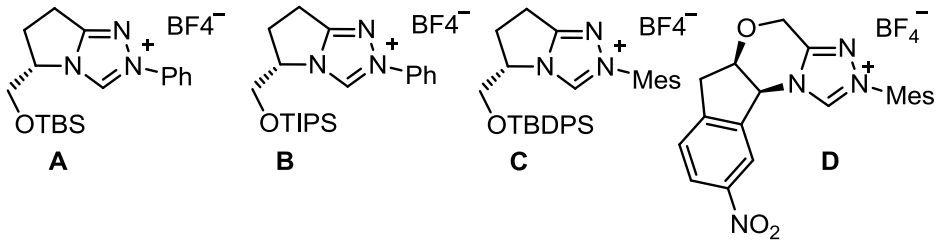
Part I General Information

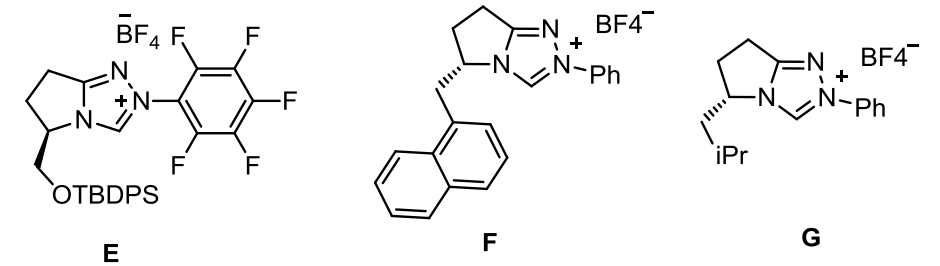
Unless otherwise indicated, all reactions were carried out with Ar protection with magnetic stirring. Chiral triazolium salts,[1] ortho-hydroxyphenyl-substituted para-quinone methides[2] and isatin-derived enals [3] were synthesized according to literature procedures. For preparative column chromatography SIL G-25 UV252 from Macherey & Nagel, particle size 0.040-0.063 nm (230-240 mesh. flash) was used. Visualization of the developed TLC plates was performed with UV irradiation (254 nm). Optical rotations were measured on a Perkin-Elmer 241 polarimeter and reported as follows: $[\alpha]_D^T$ (concentration (g/100 mL), solvent). High-resolution mass spectra (HRMS) were acquired on a Thermo Fisher Scientific Orbitrap XL spectrometer. IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum 100 using ATR-Unit. ^{1}H and ^{13}C spectra were recorded at ambient temperature on Inova 400, Varian VNMRS-400, or Varian VNMRS-600 spectrometers. Analytical HPLC was performed on a Hewlett-Packard 1100 Series instrument using chiral stationary phases (Daicel IA, and Daicel IC).

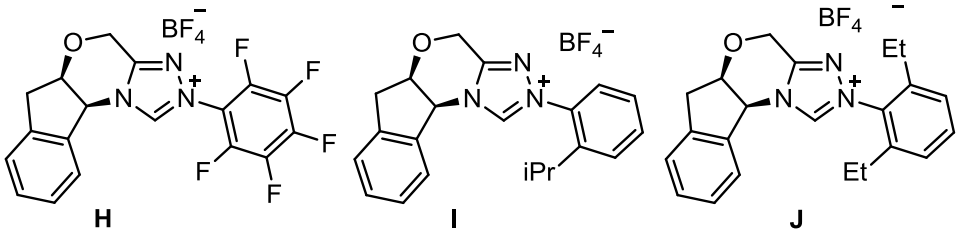
Part II Experimental part

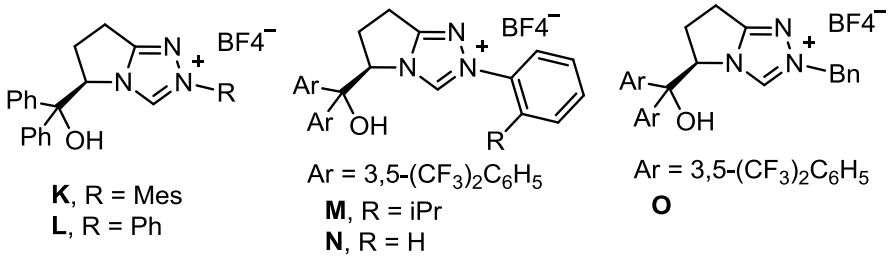
1 Optimization of the Reaction Conditions.

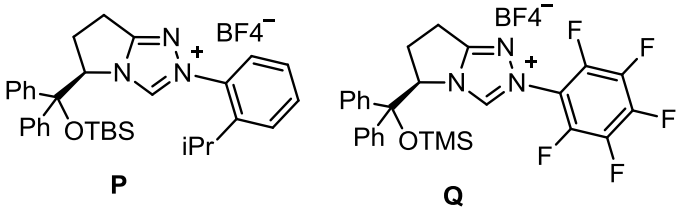










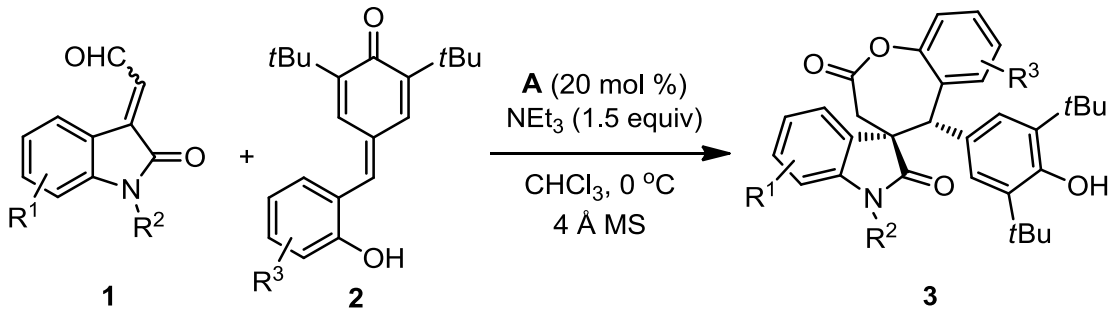


entry	cat	base	solvent	yield (%)	dr	er
1	A	NEt_3	DCM	85	7:1	89.5:11.5
2	B	NEt_3	DCM	83	7:1	88:12
3	C	NEt_3	DCM	62	3:1	85:15
4	D	NEt_3	DCM	52	2:1	-90:10
5	E	NEt_3	DCM	80	6:1	-76.5:23.5
6	F	NEt_3	DCM	82	7:1	-76:24
7	G	NEt_3	DCM	80	6:1	76:24
8	H	NEt_3	DCM	trace	--	--
9	I	NEt_3	DCM	trace	--	--
10	J	NEt_3	DCM	trace	--	--
11	K	NEt_3	DCM	trace	--	--
12	L	NEt_3	DCM	trace	--	--
13	M	NEt_3	DCM	trace	--	--
14	N	NEt_3	DCM	trace	--	--
15	O	NEt_3	DCM	trace	--	--
16	P	NEt_3	DCM	trace	--	--
17	Q	NEt_3	DCM	trace	--	--
18	A	NEt_3	DCE	60	6:1	87.5:12.5
19	A	NEt_3	$CHCl_3$	81	7:1	90.5:9.5
20	A	NEt_3	CCl_4	72	7:1	90:10
21	A	NEt_3	THF	trace	_	_
22	A	NEt_3	dioxane	trace	_	_
23	A	NEt_3	DME	trace	_	_
24	A	NEt_3	toluene	58	7:1	90:10
25	A	NEt_3	MTBE	50	7:1	89.5:10.5
26	A	NEt_3	CH_3CN	trace	_	_
27	A	DIPEA	$CHCl_3$	76	7:1	90:10

26	A	TMEDA	$CHCl_3$	72	7:1	90:10
28	A	DMAP	$CHCl_3$	66	7:1	91:9
29	A	DABCO	$CHCl_3$	75	7:1	90:10
30	A	KOAc	$CHCl_3$	66	6:1	90:10
31	A	K_2CO_3	$CHCl_3$	68	6:1	90:10
32	A	K_3PO_4	$CHCl_3$	78	6:1	90:10
33	A	NaOAc	$CHCl_3$	65	6:1	89:11
34	A	Na_2CO_3	$CHCl_3$	62	6:1	90:10
35[a]	A	NEt_3	$CHCl_3$	85	7:1	91:9
36[a,b]	A	NEt_3	$CHCl_3$	84	7:1	94:6

[a]4 Å molecular sieves were added. [b]The reaction was carried out at 0 °C.

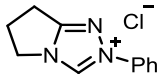
2 Asymmetric Synthesis of Spirooxindole ε-Lactones



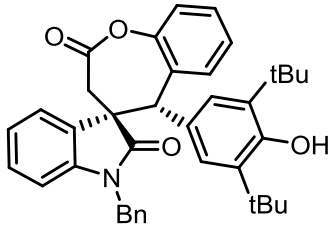
To a solution of isatin-derived enal 1 (0.3 mmol, 1.5 equiv) in $CHCl_3$ (2 mL), was added the substrates **2** (0.2 mmol, 1.0 equiv), NHC precursor **A** (0.04 mmol, 0.2 equiv), Et_3N (0.3 mmol, 1.5 equiv) and 4 Å molecular sieves. The resulting mixture was stirred at 0 °C for 24 h. The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (pentane/EtOAc as the eluent, typically 20:1-10:1) to furnish the corresponding products.

All racemic samples were obtained according to the general procedure by

using NHC precursor **R**.



R



3a

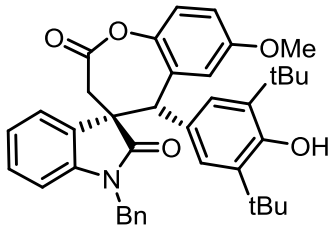
(*4S*,*5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro[benzo[b] oxepine-4,3'-indoline]-2,2'(3H)-dione (3a)

Yield: 96 mg, 84%; dr = 7:1, white solid, mp 205-207 ^{o}C; $[\alpha]_D^{21}$ 167.5 (*c* = 1.0, CH_2Cl_2); 96:4 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 6.60 min, $t_{r\,maj}$ = 27.23 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.29 – 7.19 (m, 5H), 7.11 – 7.01 (m, 4H), 6.98 (s, 2H), 6.43 (d, *J* = 6.0 Hz, 1H), 5.28 (d, *J* = 15.6 Hz, 1H), 5.08 (s, 1H), 4.75 (s, 1H), 4.15 (d, *J* = 15.6 Hz, 1H), 3.45 (d, *J* = 12.6 Hz, 1H), 2.36 (d, *J* = 12.6 Hz, 1H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 168.8, 153.0, 151.0, 141.1, 135.2 (2C), 135.2, 130.7, 129.9, 129.6, 128.8 (2C), 128.6, 128.4, 127.7, 127.2 (2C), 127.1 (2C), 126.0, 124.7, 123.4, 122.8, 119.6, 109.1, 56.5, 51.2, 43.8, 39.9, 34.2 (2C), 30.3 (6C) ppm. IR (KBr) 3450, 2955, 2328, 2178, 1973, 1750, 1700, 1610, 1450, 1375, 1286, 1188, 1019, 919, 840, 751, 704 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{39}NO_4Na$ $[M + Na]^+$: 596.2771, found 596.2766.

The 1.0 mmol scale reaction for the synthesis of **3a** was carried out in a similar manner.

To a solution of isatin-derived enal **1a** (1.5 mmol, 1.5 equiv, 395 mg) in $CHCl_3$ (10 mL), was added the substrates **2a** (1 mmol, 1.0 equiv, 310 mg), NHC precursor **A** (0.2 mmol, 0.2 equiv, 83 mg), Et_3N (1.5 mmol, 1.5 equiv, 210ul) and 4 Å molecular sieves. The resulting mixture was stirred at 0 ^{o}C for 24 h.

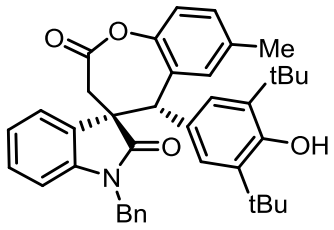
The reaction mixture was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel (pentane/EtOAc = 15:1) to furnish the products **3a** (78%, 7:1 dr, 91:9 er). The analytical data of the gram scale reaction of **3a** are consistent with those of the 0.2 mmol scale experiment



3b

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-7-methoxy-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3b)

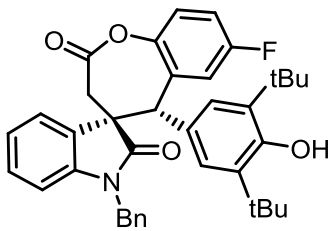
Yield: 101 mg, 84%; dr = 6:1, white solid, mp 133-135 ^{o}C; $[\alpha]_D^{21}$ +113.2 (*c* = 1.0, CH_2Cl_2); 89:11 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min) $t_{r\,min}$ = 8.58 min, $t_{r\,maj}$ = 13.69 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.52 – 7.47 (m, 1H), 7.25 – 7.18 (m, 3H), 7.17 – 7.13 (m, 2H), 7.08 – 7.01 (m, 4H), 6.99 (s, 2H), 6.85 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.40 (d, *J* = 7.2 Hz, 1H), 5.24 (d, *J* = 15.6 Hz, 1H), 5.08 (s, 1H), 4.68 (s, 1H), 4.16 (d, *J* = 15.6 Hz, 1H), 3.76 (s, 3H), 3.47 (d, *J* = 12.6 Hz, 1H), 2.33 (d, *J* = 12.6 Hz, 1H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 169.3, 157.0, 153.0, 144.8, 141.2, 135.2 (2C), 135.1, 130.8, 130.5, 128.8 (2C), 128.4, 127.7, 127.2 (2C), 127.1 (2C), 124.6, 123.4, 122.8, 120.3, 115.4, 113.5, 109.1, 56.5, 55.4, 51.4, 43.8, 39.6, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3751, 3629, 3418, 3213, 2954, 2866, 2605, 2309, 2195, 2081, 2051, 2006, 1935, 1867, 1759, 1708, 1609, 1486, 1436, 1363, 1312, 1231, 1181, 1140, 1039, 973, 913, 886, 849, 820, 748, 697 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{41}NO_5Na$ $[M + Na]^+$: 626.2877, found 626.2873.



3c

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-7-methyl-5H-spiro [benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3c)

Yield: 106 mg, 90%; dr = 6:1, white solid mp 199-201 ^{o}C; $[\alpha]_D^{21}$ +171.4 (*c* = 1.0, CH_2Cl_2); 88.5:11.5 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min) $t_{r\,min}$ = 6.90 min, $t_{r\,maj}$ = 9.51 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.2 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.25 – 7.18 (m, 3H), 7.17 – 7.10 (m, 2H), 7.07 – 7.01 (m, 4H), 6.99 (s, 2H), 6.40 (d, *J* = 7.2 Hz, 1H), 5.23 (d, *J* = 15.6 Hz, 1H), 5.09 (s, 1H), 4.70 (s, 1H), 4.16 (d, *J* = 15.6 Hz, 1H), 3.46 (d, *J* = 12.6 Hz, 1H), 2.37 – 2.31 (m, 4H), 1.32 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 169.1, 152.9, 149.0, 141.2, 135.3, 135.2, 135.1 (2C), 130.8, 130.5, 129.1, 128.9, 128.8 (2C), 128.4, 127.7, 127.4 (2C), 127.1 (2C), 124.6, 123.4, 122.8, 119.3, 109.1, 56.7, 51.2, 43.8, 39.6, 34.3 (2C), 30.3 (6C), 21.4 ppm. IR (KBr) 3627, 3207, 2953, 2308, 2143, 2105, 2019, 1956, 1760, 1709, 1609, 1483, 1440, 1364, 1313, 1232, 1183, 1141, 1108, 1017, 913, 822, 748, 695 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{41}NO_4Na$ $[M + Na]^+$: 610.2928, found 610.2919.

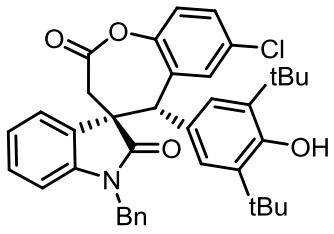


3d

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-7-fluoro-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3d)

Yield: 86 mg, 73%; dr = 10:1, white solid, mp 246-248 ^{o}C; $[\alpha]_D^{21}$ +131.4 (*c* = 1.0,

CH_2Cl_2); 89:11 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min) $t_{r\ min}$ = 7.00 min, $t_{r\ maj}$= 8.46 min, T= 30 ^oC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.46 (m, 1H), 7.30 (dd, *J* = 9.6, 3.0 Hz, 1H), 7.26 – 7.17 (m, 4H), 7.08 – 7.02 (m, 5H), 6.96 (s, 2H), 6.44 – 6.40 (m, 1H), 5.26 (d, *J* = 15.6 Hz, 1H), 5.11 (s, 1H), 4.69 (s, 1H), 4.16 (d, *J* = 15.6 Hz, 1H), 3.45 (d, *J* = 12.6 Hz, 1H), 2.37 (d, *J* = 12.6 Hz, 1H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.8, 168.5, 160.8 ($J_{C\text{-}F}$ = 244.8 Hz), 153.2, 146.9, 141.2, 135.5 (2C), 135.0, 131.8 ($J_{C\text{-}F}$ = 8.0 Hz), 130.4, 128.8 (2C), 128.6, 127.7, 127.1 (2C), 127.0 (2C), 124.1, 123.4, 122.9, 120.9 ($J_{C\text{-}F}$ = 8.6 Hz), 117.3 ($J_{C\text{-}F}$ = 25.7 Hz), 115.3 ($J_{C\text{-}F}$ = 23.7 Hz), 109.2, 56.4, 51.2, 43.8, 39.6, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3730, 3643, 2959, 2872, 2616, 2285, 2221, 2183, 2084, 2032, 2008, 1969, 1913, 1762, 1710, 1612, 1478, 1437, 1363, 1315, 1267, 1233, 1177, 1139, 1023, 977, 914, 848, 753, 728, 695 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4FNa$ $[M + Na]^+$: 614.2677, found 614.2676.

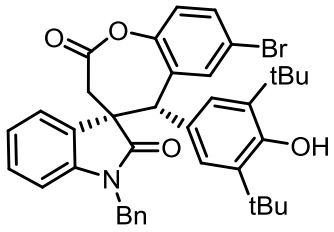


3e

(*4S,5S*)-1'-Benzyl-7-chloro-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3e)

Yield: 97 mg, 80%; dr = 7:1, white solid, mp 186-188 ^{o}C; $[\alpha]_D^{21}$ +122.2 (*c* = 1.0, CH_2Cl_2); 94:6 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min) $t_{r\ min}$ = 7.12 min, $t_{r\ maj}$ = 8.88 min, T= 30 ^oC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (d, *J* = 2.4 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.32 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.07 – 7.02 (m, 4H), 6.96 (s, 2H), 6.44 – 6.39 (m, 1H), 5.23 (d, *J* = 15.6 Hz, 1H), 5.12 (s, 1H), 4.68 (s, 1H), 4.17 (d, *J* = 15.6 Hz, 1H), 3.45 (d, *J* = 12.6 Hz, 1H), 2.38 (d, *J* = 12.6 Hz, 1H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.7, 168.2, 153.2, 149.5,

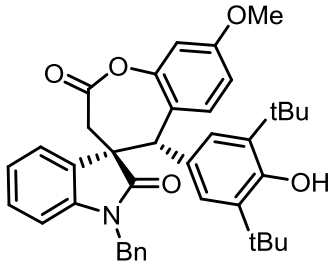
141.2, 135.4 (2C), 135.0, 131.4, 130.4, 130.3, 128.8 (2C), 128.6, 128.6, 127.7, 127.2 (2C), 127.1 (2C), 123.9, 123.4, 122.9, 120.9, 115.0, 109.2, 56.5, 51.1, 43.8, 39.6, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3862, 3625, 2953, 2441, 2285, 2211, 2107, 2050, 2007, 1905, 1764, 1708, 1610, 1471, 1366, 1222, 1177, 1109, 1018, 901, 822, 740 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4ClNa$ [M + Na]$^+$: 630.2382, found 630.2374.



3f

(*4S,5S*)-1'-Benzyl-7-bromo-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro [benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3f)

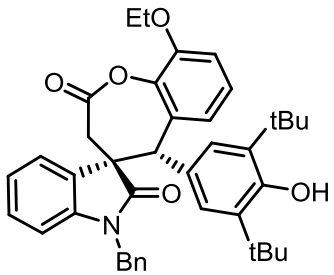
Yield: 120 mg, 92%; dr = 3:1, white solid, mp 186-188 ^oC; $[\alpha]_D^{21}$ +98.1 (*c* = 1.0, CH_2Cl_2); 94:6 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min) $t_{r\,min}$ = 7.47 min, $t_{r\,maj}$ = 9.41 min, T= 30 ^oC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.75 (m, 1H), 7.51 – 7.45 (m, 2H), 7.25 – 7.18 (m, 3H), 7.11 (d, *J* = 9.0 Hz, 1H), 7.08 – 7.01 (m, 4H), 6.96 (s, 2H), 6.43 – 6.38 (m, 1H), 5.22 (d, *J* = 15.6 Hz, 1H), 5.13 (s, 1H), 4.68 (s, 1H), 4.18 (d, *J* = 15.6 Hz, 1H), 3.46 (d, *J* = 12.6 Hz, 1H), 2.38 (d, *J* = 12.6 Hz, 1H), 1.32 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.7, 168.1, 153.2, 150.1, 141.2, 135.4 (2C), 135.0, 133.3, 131.7, 131.6, 130.4, 128.8 (2C), 128.6, 127.7, 127.2 (2C), 127.1 (2C), 123.8, 123.4, 122.9, 121.3, 119.2, 109.2, 56.5, 51.1, 43.8, 39.6, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3858, 3624, 2651, 2289, 2179, 2105, 2059, 1977, 1886, 1765, 1709, 1610, 1467, 1366, 1219, 1175, 1017, 899, 817, 745 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4BrNa$ [M + Na]$^+$: 674.1876, found 674.1876.



3g

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-8-methoxy-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3g)

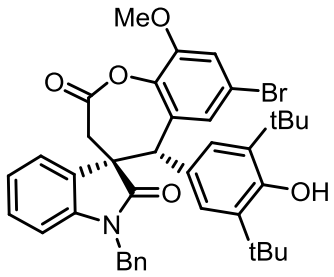
Yield: 112 mg, 93%; dr = 3:1, white solid, mp 249-251 ^{o}C; $[\alpha]_D^{21}$ +76.0 (c = 1.0, CH_2Cl_2); 93.5:6.5 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 7.71 min, $t_{r\,maj}$ = 17.45 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 2H), 7.25 – 7.18 (m, 3H), 7.06 (d, *J* = 7.2 Hz, 2H), 7.05 – 7.00 (m, 2H), 6.96 (s, 2H), 6.83 – 6.77 (m, 2H), 6.43 – 6.39 (m, 1H), 5.27 (d, *J* = 15.6 Hz, 1H), 5.07 (s, 1H), 4.67 (s, 1H), 4.14 (d, *J* = 15.6 Hz, 1H), 3.83 (s, 3H), 3.45 (d, *J* = 12.6 Hz, 1H), 2.35 (d, *J* = 12.6 Hz, 1H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 168.9, 152.9, 151.6, 141.1, 135.2, 135.2 (2C), 130.8, 130.4, 128.8 (2C), 128.4, 127.7, 127.2 (2C), 127.1 (2C), 124.9, 123.4, 122.8, 121.4, 111.2, 109.0, 105.7, 56.8, 55.6, 55.6, 50.9, 43.8, 39.9, 34.2 (2C), 30.3 (6C) ppm. IR (KBr) 3641, 2959, 2254, 1972, 1713, 1613, 1494, 1439, 1360, 1279, 1234, 1178, 1105, 1031, 971, 909, 855, 801, 727 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{41}NO_5Na$ $[M + Na]^+$: 626.2877, found 626.2875.



3h

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-9-ethoxy-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3h)

Yield: 99 mg, 80%; dr = 4:1, white solid, mp 240-242 ^{o}C; $[\alpha]_D^{21}$ +152.3 (*c* = 1.0, CH_2Cl_2); 94:6 er as determined by HPLC (Chiralcel IB, 97:3 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 7.93 min, $t_{r\,maj}$ = 8.63 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 – 7.47 (m, 1H), 7.25 – 7.18 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 2H), 7.06 – 7.00 (m, 2H), 6.99 – 6.94 (m, 3H), 6.47 – 6.39 (m, 1H), 5.30 (d, *J* = 15.6 Hz, 1H), 5.06 (s, 1H), 4.75 (s, 1H), 4.17 – 4.11 (m, 3H), 3.46 (d, *J* = 12.6 Hz, 1H), 2.34 (d, *J* = 12.6 Hz, 1H), 1.47 (t, *J* = 7.2 Hz, 3H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 168.7, 152.9, 149.0, 141.1, 140.2, 135.3, 135.2 (2C), 131.0, 130.8, 128.8 (2C), 128.4, 127.7, 127.2 (2C), 127.1 (2C), 125.8, 125.0, 123.5, 122.8, 121.3, 113.0, 109.0, 64.8, 56.4, 51.2, 43.8, 40.0, 34.2 (2C), 30.3 (6C), 14.9 ppm. IR (KBr) 3604, 3419, 3068, 2961, 2553, 2284, 2183, 2106, 2055, 1974, 1898, 1761, 1714, 1606, 1461, 1360, 1279, 1179, 1232, 1069, 1020, 923, 849, 743, 668 cm^{-1}; HRMS (ESI) calcd for $C_{40}H_{43}NO_5Na$ $[M + Na]^+$: 640.3033, found 640.3035.

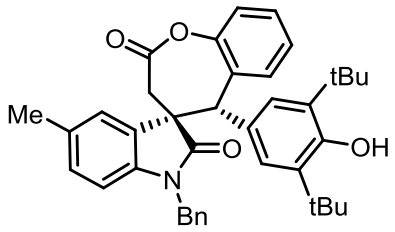


3i

(4S,5R)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-9-ethoxy-5H-spiro [benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3i)

Yield: 115 mg, 84%; dr = 4:1, white solid, mp 277-279 ^{o}C; $[\alpha]_D^{21}$ +123.5 (*c* = 1.0, CH_2Cl_2); 93.5:6.5 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 7.46 min, $t_{r\,maj}$ = 11.46 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.46 (m, 1H), 7.35 – 7.31 (m, 1H), 7.25 – 7.18 (m, 3H), 7.12 – 7.08 (m, 1H), 7.07 – 7.00 (m, 4H), 6.94 (s, 2H), 6.43 – 6.38 (m, 1H), 5.24 (d, *J* = 15.6 Hz, 1H), 5.11 (s, 1H), 4.69 (s, 1H), 4.16 (d, *J* = 15.6 Hz,

1H), 3.91 (s, 3H), 3.46 (d, *J* = 12.6 Hz, 1H), 2.36 (d, *J* = 12.6 Hz, 1H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.7, 167.9, 153.1, 150.3, 141.1, 139.1, 135.3 (2C), 135.1, 132.4, 130.4, 128.8 (2C), 128.5, 127.7, 127.2 (2C), 127.1 (2C), 124.6, 124.1, 123.4, 122.9, 118.9, 115.1, 109.1, 56.5, 56.4, 51.0, 43.8, 39.6, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3605, 3081, 2954, 2323, 2163, 1974, 1760, 1701, 1604, 1438, 1370, 1296, 1175, 1123, 1014, 905, 845, 736, 695 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{40}NO_5BrNa$ [M + Na]$^+$: 704.1982, found 704.1981.

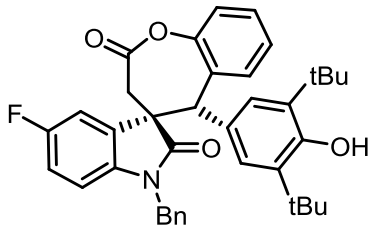


3j

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5'-methyl-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3j)

Yield: 103 mg, 88%; dr = 6:1, white solid, mp 234-236 ^{o}C; $[\alpha]_D^{21}$ +111.6 (*c* = 1.0, CH_2Cl_2); 91:9 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 5.71 min, $t_{r\,maj}$ = 12.51 min, T= 30 ^oC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.8 Hz, 1H), 7.39 – 7.33 (m, 1H), 7.31 (s, 1H), 7.28 – 7.18 (m, 5H), 7.07 (d, *J* = 7.2 Hz, 2H), 6.98 (s, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.30 (d, *J* = 7.8 Hz, 1H), 5.28 (d, *J* = 15.6 Hz, 1H), 5.08 (s, 1H), 4.74 (s, 1H), 4.10 (d, *J* = 15.6 Hz, 1H), 3.44 (d, *J* = 12.6 Hz, 1H), 2.36 (d, *J* = 12.6 Hz, 1H), 2.32 (s, 3H), 1.32 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.9, 168.9, 152.9 151.0, 138.8, 135.3, 135.2 (2C), 132.4, 130.7, 129.8, 129.6, 128.7 (2C), 128.7, 128.6, 127.6, 127.2 (4C), 125.9, 124.8, 124.2, 119.6, 108.8, 56.6, 51.2, 43.8, 39.9, 34.2 (2C), 30.3 (6C), 21.1 ppm. IR (KBr) 3616, 3403, 2958, 2916, 2650, 2321, 2170, 2082, 2050, 1978, 1925, 1759, 1704, 1603, 1493, 1439,1364, 1316, 1284, 1217, 1170, 1098, 1016, 903, 813, 730, 703 cm^{-1}; HRMS (ESI)

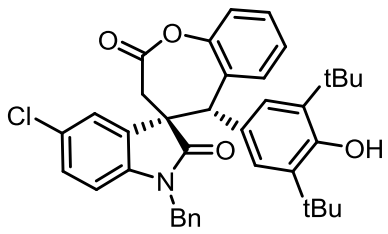
calcd for $C_{39}H_{41}NO_4Na$ [M + Na]$^+$: 610.2928, found 610.2929.



3k

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5'-fluoro-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3k)

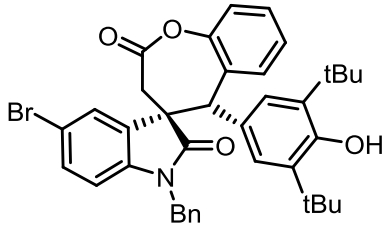
Yield: 98 mg, 83%; dr = 7:1, white solid, mp 251-253 ^{o}C; $[\alpha]_D^{21}$ +141.4 (*c* = 1.0, CH_2Cl_2); 94:6 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 6.32 min, $t_{r\,maj}$ = 12.40 min, T= 30 ^oC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.30 – 7.20 (m, 6H), 7.05 (d, *J* = 7.2 Hz, 2H), 7.00 (s, 2H), 6.78 – 6.71 (m, 1H), 6.34 (dd, *J* = 9.0, 4.2 Hz, 1H), 5.31 (d, *J* = 15.6 Hz, 1H), 5.12 (s, 1H), 4.70 (s, 1H), 4.11 (d, *J* = 15.6 Hz, 1H), 3.45 (d, *J* = 12.6 Hz, 1H), 2.37 (d, *J* = 12.6 Hz, 1H), 1.33 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.7, 168.5, 160.1 ($J_{C\text{-}F}$ = 243.1 Hz), 158.5, 153.1, 150.9, 137.1 ($J_{C\text{-}F}$ = 1.8 Hz), 135.4 (2C), 134.8, 132.4 ($J_{C\text{-}F}$ = 7.9 Hz), 129.9, 129.2, 128.9 (2C), 128.8, 127.9, 127.1 (2C), 127.0, 126.0, 124.4, 119.6, 114.8 ($J_{C\text{-}F}$ = 24.0 Hz), 111.8 ($J_{C\text{-}F}$ = 25.2 Hz), 109.7 ($J_{C\text{-}F}$ = 7.9 Hz), 56.8, 51.2, 43.9, 39.8, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3592, 3081, 2964, 2298, 2202, 2052, 1921, 1758, 1706, 1621, 1489, 1440, 1363, 1342, 1285, 1258, 1238, 1209, 1174, 1124, 1097, 1012, 971, 926, 895, 870, 811, 750, 700, 655 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4FNa$ [M + Na]$^+$: 614.2677, found 614.2676.



3l

(4S,5R)-1'-Benzyl-5'-chloro-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro [benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3l)

Yield: 109 mg, 90%; dr = 4:1, white solid, mp 228-230 ^{o}C; $[\alpha]_D^{21}$ +92.1 (*c* = 1.0, CH_2Cl_2); 92:8 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 6.28 min, $t_{r\,maj}$ = 12.48 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.29 – 7.19 (m, 5H), 7.05 (d, *J* = 6.6 Hz, 2H), 7.03 – 6.94 (m, 3H), 6.32 (d, *J* = 8.4 Hz, 1H), 5.31 (d, *J* = 15.6 Hz, 1H), 5.12 (s, 1H), 4.70 (s, 1H), 4.07 (d, *J* = 15.6 Hz, 1H), 3.45 (d, *J* = 12.6 Hz, 1H), 2.38 (d, *J* = 12.6 Hz, 1H), 1.34 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.5, 168.5, 153.1, 150.9 139.7, 135.4 (2C), 134.7, 132.4, 129.8, 129.0, 128.9 (2C), 128.8, 128.5, 128.4, 127.9, 127.1 (2C), 127.1 (2C), 126.0, 124.3, 124.1, 119.6, 110.0, 56.8, 51.4, 43.9, 39.6, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3621, 3412, 2956, 2324, 2062, 1989, 1934, 1756, 1707, 1605, 1480, 1441, 1357, 1216, 1167, 1097, 922, 815, 745, 700 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4ClNa$ $[M + Na]^+$: 630.2382, found 630.2377.

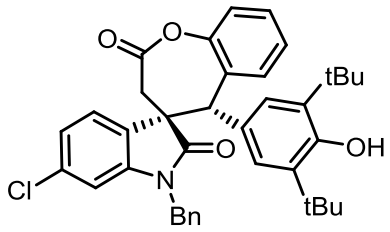


3m

(*4S,5S*)-1'-Benzyl-5'-bromo-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro [benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3m)

Yield: 111 mg, 85%; dr = 4:1, white solid, mp 236-238 ^{o}C; $[\alpha]_D^{21}$ +56.6 (*c* = 1.0, CH_2Cl_2); 92:8 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 6.36 min, $t_{r\,maj}$ = 13.28 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 – 7.60 (m, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.30 – 7.20 (m, 5H), 7.15 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.04 (d, *J* = 7.1 Hz, 2H), 6.98 (s, 2H), 6.27 (d, *J* = 8.4 Hz, 1H), 5.31 (d, *J* = 15.6 Hz, 1H), 5.11 (s, 1H),

4.69 (s, 1H), 4.05 (d, *J* = 15.6 Hz, 1H), 3.44 (d, *J* = 12.6 Hz, 1H), 2.38 (d, *J* = 12.6 Hz, 1H), 1.34 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.4, 168.5, 153.1, 150.9, 140.2, 135.4 (2C), 134.7, 132.8, 131.3, 129.8, 128.9, 128.9 (2C), 128.9, 127.9, 127.1 (4C), 126.8, 126.0, 124.2, 119.7, 115.7, 110.4, 56.7, 51.4, 43.9, 39.5, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3621, 3207, 2957, 2333, 2178, 2120, 2062, 2006, 1759, 1709, 1603, 1443, 1354, 1170, 1015, 914, 811, 739 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4BrNa$ [M + Na]$^+$: 674.1876, found 674.1875.

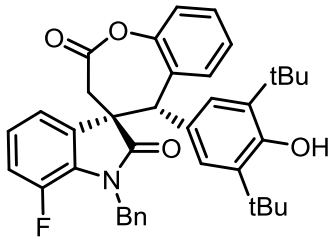


3n

(*4S,5S*)-1'-Benzyl-6'-chloro-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro [benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3n)

Yield: 102 mg, 84%; dr = 6:1, white solid, mp 176-178 ^{o}C; $[\alpha]_D^{21}$ +103.6 (*c* = 1.0, CH_2Cl_2); 91.5:8.5 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\ min}$ = 6.09 min, $t_{r\ maj}$ = 15.9 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.28 – 7.20 (m, 5H), 7.07 (d, *J* = 7.2 Hz,, 2H), 7.03 (dd, *J* = 7.8, 1.2 Hz, 1H), 6.96 (s, 2H), 6.42 (d, *J* = 1.2 Hz, 1H), 5.29 (d, *J* = 15.6 Hz, 1H), 5.12 (s, 1H), 4.69 (s, 1H), 4.06 (d, *J* = 15.6 Hz, 1H), 3.43 (d, *J* = 12.6 Hz, 1H), 2.33 (d, *J* = 12.6 Hz, 1H), 1.34 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.9, 168.6, 153.1, 150.9, 142.4, 135.4 (2C), 134.6, 134.3, 129.8, 129.2 (2C), 129.0 (2C), 128.8, 128.0, 127.1 (2C), 127.0 (2C), 126.0, 124.4, 124.3, 122.7, 119.6, 109.6, 56.3, 51.2, 43.9, 39.8, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3607, 2957, 2664, 2067, 1902, 1722, 1604, 1443, 1370, 1338, 1145, 928, 870, 806, 742, 663 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4ClNa$ [M + Na]$^+$:

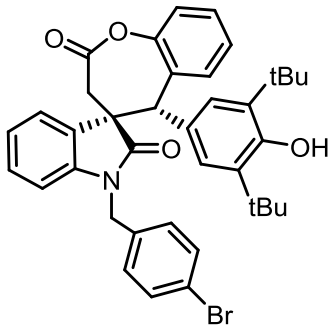
630.2382, found 630.2364.



3o

(*4S,5S*)-1'-Benzyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-7'-fluoro-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3o)

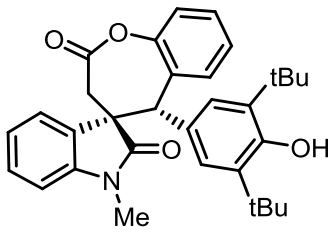
Yield: 101 mg, 85%; dr = 6:1, white solid, mp 237-239 ^{o}C; $[\alpha]_D^{21}$ +137.3 (*c* = 0.5, CH_2Cl_2); 93.5:6.5 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 5.87 min, $t_{r\,maj}$ = 10.43 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.39 – 7.34 (m, 1H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.25 – 7.19 (m, 4H), 7.19 – 7.14 (m, 2H), 7.02 – 6.98 (m, 1H), 6.96 (s, 2H), 6.83 (dd, *J* = 11.4, 8.4 Hz, 1H), 5.32 (d, *J* = 15.6 Hz, 1H), 5.11 (s, 1H), 4.71 (s, 1H), 4.44 (d, *J* = 15.6 Hz, 1H), 3.40 (d, *J* = 12.6 Hz, 1H), 2.32 (d, *J* = 12.6 Hz, 1H), 1.33 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.8, 168.5, 153.1, 150.9, 148.0 ($J_{C\text{-}F}$ = 244.6 Hz), 136.5, 135.4 (2C), 133.7 ($J_{C\text{-}F}$ = 2.9 Hz), 129.9, 129.2, 128.8, 128.6 (2C), 127.9 ($J_{C\text{-}F}$ = 8.6 Hz), 127.7, 127.4 (2C), 126.8, 126.0, 124.4, 123.6 ($J_{C\text{-}F}$ = 6.5 Hz), 119.6 (2C), 119.4 ($J_{C\text{-}F}$ = 2.9 Hz), 116.6 ($J_{C\text{-}F}$ = 19.5 Hz), 56.8, 51.4, 45.4, 40.0, 34.3 (2C), 30.3 (6C) ppm. IR (KBr) 3597, 2962, 2322, 1979, 1761, 1708, 1632, 1480, 1439, 1355, 1312, 1288, 1240, 1212, 1170, 1145, 1096, 1032, 925, 897, 840, 758, 732, 702 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4FNa$ $[M + Na]^+$: 614.2677, found 614.2675.



3p

(*4S,5S*)-1'-(4-bromobenzyl)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro [benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3p)

Yield: 116 mg, 89%; dr = 7:1, white solid, mp 121-123 ^{o}C; $[\alpha]_D^{21}$ +127.1 (*c* = 1.0, CH_2Cl_2); 91.5:8.5 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 6.66 min, $t_{r\,maj}$ = 17.42 min, T= 30 *^{o}C*; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.39 – 7.33 (m, 3H), 7.28 – 7.22 (m, 2H), 7.10 – 7.02 (m, 2H), 6.97 (s, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 6.42 – 6.36 (m, 1H), 5.17 (d, *J* = 15.6 Hz, 1H), 5.08 (s, 1H), 4.74 (s, 1H), 4.14 (d, *J* = 15.6 Hz, 1H), 3.43 (d, *J* = 12.6 Hz, 1H), 2.33 (d, *J* = 12.6 Hz, 1H), 1.30 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.0, 168.6, 153.0, 151.0, 140.8, 135.2 (2C), 134.2, 131.9 (2C), 130.7, 129.8, 129.4, 128.9 (2C), 128.7, 128.5, 127.2, 126.0, 124.6, 123.6, 123.0, 121.7, 119.7, 108.9, 56.6, 51.3, 43.3, 39.8, 34.2 (2C), 30.3 (6C) ppm. IR (KBr) 3624, 3066, 2955, 2658, 2324, 2066, 1911, 1758, 1707, 1608, 1480, 1440, 1364, 1303, 1217, 1176, 1139, 1011, 910, 734 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{38}NO_4BrNa$ $[M + Na]^+$: 674.1876, found 674.1878.

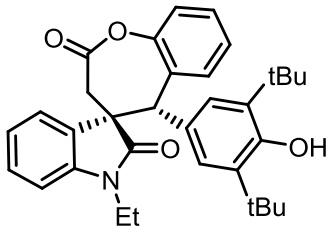


3q

(*4S,5S*)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-1'-Methyl-5H-spiro[benzo[b]

oxepine-4,3'-indoline]-2,2'(3H)-dione (3q)

Yield: 78 mg, 78%; dr = 7:1, white solid, mp 235-237 ^{o}C; $[\alpha]_D^{21}$ +158.2 (*c* = 1.0, CH_2Cl_2); 95:5 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 7.09 min, $t_{r\,maj}$ = 9.28 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.25 – 7.19 (m, 2H), 7.17 – 7.12 (m, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.91 (s, 2H), 6.52 (d, *J* = 7.8 Hz, 1H), 5.03 (s, 1H), 4.68 (s, 1H), 3.37 (d, *J* = 12.6 Hz, 1H), 3.03 (s, 3H), 2.34 (d, *J* = 12.6 Hz, 1H), 1.29 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.6, 169.1 152.9, 150.9, 142.1, 135.1 (2C), 130.8, 129.8 (2C), 128.6, 128.5, 127.0 (2C), 125.9, 124.5, 123.3, 122.8, 119.5, 107.7, 56.6, 51.6, 39.4, 34.2 (2C), 30.3 (6C), 26.3 ppm. IR (KBr) 3573, 2948, 2660, 2065, 1921, 1753, 1707, 1606, 1441, 1357, 1282, 1214, 1132, 1026, 929, 845, 747, 661 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{35}NO_4Na$ $[M + Na]^+$: 520.2458, found 520.2446.

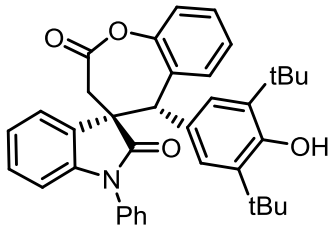


3r

(*4S,5S*)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-1'-Ethyl-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3r)

Yield: 81 mg, 79%; dr = 7:1, white solid, mp 194-196 ^{o}C; $[\alpha]_D^{21}$ +106.3 (*c* = 1.0, CH_2Cl_2); 92:8 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 5.45 min, $t_{r\,maj}$ = 7.62 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.25 – 7.19 (m, 2H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.92 (s, 2H), 6.57 (d, *J* = 7.2 Hz, 1H), 5.02 (s, 1H), 4.69 (s, 1H), 3.93 (dq, *J* = 21.6, 7.2 Hz, 1H), 3.36 (d, *J* = 12.6 Hz, 1H), 3.22 (dq, *J* = 21.6, 7.2 Hz, 1H), 2.30 (d, *J* = 12.6 Hz, 1H), 1.29 (s, 18H), 1.13 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C NMR (151

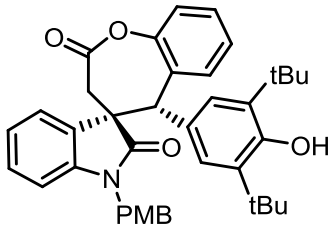
MHz, $CDCl_3$) δ 175.3, 169.0, 152.9, 151.0, 141.2, 135.1, 131.0, 129.8 (2C), 129.6, 128.5, 128.4, 127.1 (2C), 125.9, 124.6, 123.5, 122.6, 119.5, 108.0, 56.4, 51.2, 39.8, 34.8, 34.3 (2C), 30.2 (6C), 12.6 ppm. IR (KBr) 3537, 2954, 2325, 2071, 1907, 1755, 1694, 1609, 1440, 1374, 1284, 1209, 1136, 1021, 910, 744 cm^{-1}; HRMS (ESI) calcd for $C_{33}H_{37}NO_4Na$ [M + Na]$^+$: 534.2615, found 534.2598.



3s

(*4S,5S*)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-1'-Phenyl-5H-spiro[benzo[b] oxepine-4,3'-indoline]-2,2'(3H)-dione (3s)

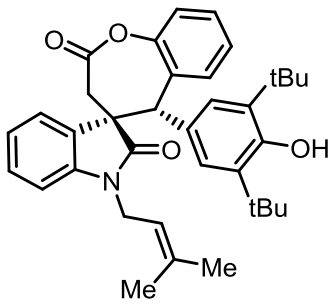
Yield: 84 mg, 75%; dr = 7:1, white solid, mp 214-216 ^oC; $[\alpha]_D^{21}$ +158.9 (*c* = 1.0, CH_2Cl_2); 92:8 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 5.62 min, $t_{r\,maj}$ = 6.03 min, T= 30 ^oC; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 – 7.55 (m, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.35 (dd, *J* = 13.8, 7.2 Hz, 2H), 7.25 – 7.19 (m, 2H), 7.19 – 7.09 (m, 4H), 7.00 (s, 2H), 6.65 (d, *J* = 7.2 Hz, 1H), 5.09 (s, 1H), 4.78 (s, 1H), 3.47 (d, *J* = 12.6 Hz, 1H), 2.48 (d, *J* = 12.6 Hz, 1H), 1.24 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.9, 168.8, 153.1, 151.0, 141.8, 135.3 (2C), 133.8, 130.6, 129.9, 129.4, 129.3 (2C), 128.6, 128.4, 127.8, 127.4, 125.9 (4C), 124.5, 123.6, 123.3, 119.6, 109.4, 56.6, 51.5, 40.1, 34.2 (2C), 30.2 (6C) ppm. IR (KBr) 3597, 3058, 2964, 2875, 2324, 2174, 2014, 1924, 1750, 1719, 1604, 1441, 1370, 1319, 1285, 1182, 1144, 1099, 1030, 908, 838, 796, 748, 697 cm^{-1}; HRMS (ESI) calcd for $C_{37}H_{37}NO_4Na$ [M + Na]$^+$: 582.2615, found 582.2605.



3t

(*4S,5S*)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-1'-(4-methoxybenzyl)-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3t)

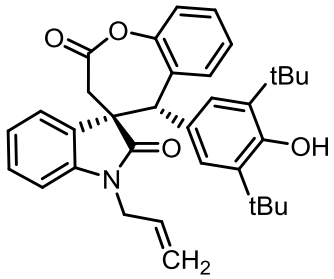
Yield: 106 mg, 88%; dr = 8:1, white solid, mp 124-126 ^{o}C; $[\alpha]_D^{21}$ +143.8 (*c* = 1.0, CH_2Cl_2); 91: 9 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,mn}$ = 6.53 min, $t_{r\,maj}$ = 26.83 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.8 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.38 – 7.33 (m, 1H), 7.24 (t, *J* = 7.8 Hz, 2H), 7.06 – 7.02 (m, 2H), 7.01 (d, *J* = 9.0 Hz, 2H), 6.97 (s, 2H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.47 – 6.43 (m, 1H), 5.22 (d, *J* = 15.6 Hz, 1H), 5.07 (s, 1H), 4.74 (s, 1H), 4.08 (d, *J* = 15.6 Hz, 1H), 3.73 (s, 3H), 3.42 (d, *J* = 12.6 Hz, 1H), 2.32 (d, *J* = 12.6 Hz, 1H), 1.31 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.9, 168.8, 159.0, 152.9, 151.0, 141.2, 135.2 (2C), 130.7, 129.9, 129.6, 128.6, 128.6 (2C), 128.4, 127.3, 127.1 (2C), 125.9, 124.7, 123.4, 122.8, 119.6, 114.1 (2C), 109.1, 56.5, 55.2, 51.2, 43.3, 39.9, 34.2 (2C), 30.3 (6C) ppm. IR (KBr) 3625, 2956, 2323, 2065, 1904, 1759, 1705, 1610, 1443, 1364, 1291, 1239, 1175, 1138, 1027, 911, 833, 734 cm^{-1}; HRMS (ESI) calcd for $C_{39}H_{41}NO_5Na$ $[M + Na]^+$: 626.2877, found 626.2880.



3u

(*4S,5S*)-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-1'-(3-methylbut-2-en-1-yl)-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3u)

Yield: 95 mg, 86%; dr = 7:1, white solid, mp 171-173 ^{o}C; $[\alpha]_D^{21}$ +140.2 (*c* = 1.0, CH_2Cl_2); 91:9 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 5.26 min, $t_{r\,maj}$ = 7.61 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 1H), 7.25 – 7.19 (m, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.8 Hz, 1H), 6.93 (s, 2H), 6.52 (d, *J* = 7.2 Hz, 1H), 5.04 (s, 1H), 4.92 (t, *J* = 6.6 Hz, 1H), 4.69 (s, 1H), 4.47 (dd, *J* = 15.6, 6.6 Hz, 1H), 3.78 (dd, *J* = 15.6, 6.6 Hz, 1H), 3.36 (d, *J* = 12.6 Hz, 1H), 2.31 (d, *J* = 12.6 Hz, 1H), 1.73 (s, 3H), 1.66 (s, 3H), 1.30 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.2, 169.0, 152.9, 151.0, 141.5, 136.8, 135.1 (2C), 130.9, 129.8 (2C), 129.6, 128.5, 128.4, 127.1, 125.9, 124.6, 123.3, 122.6, 119.5, 118.0, 108.7, 56.5, 51.2, 39.7, 38.2, 34.2 (2C), 30.3 (6C), 25.5, 18.1 ppm. IR (KBr) 3621, 2961, 2324, 2056, 1902, 1759, 1704, 1609, 1483, 1437, 1366, 1315, 1292, 1213, 1174, 1142, 1100, 1044, 973, 908, 836, 734 cm^{-1}; HRMS (ESI) calcd for $C_{36}H_{41}NO_4Na$ $[M + Na]^+$: 574.2928, found 574.2926.



3v

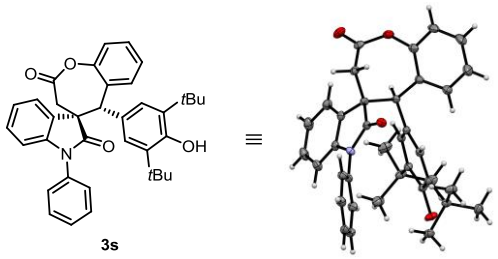
(*4S,5S*)-1'-Allyl-5-(3,5-di-tert-butyl-4-hydroxyphenyl)-5H-spiro[benzo[b]oxepine-4,3'-indoline]-2,2'(3H)-dione (3v)

Yield: 83 mg, 79%; dr = 7:1, white solid, mp 115-117 ^{o}C; $[\alpha]_D^{21}$ +124.5 (*c* = 1.0, CH_2Cl_2); 91:9 er as determined by HPLC (Chiralcel IA, 9:1 *n*-heptane/iPrOH, 1.0 mL/min), $t_{r\,min}$ = 5.85 min, $t_{r\,maj}$ = 7.19 min, T= 30 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.8 Hz,

1H), 7.26 – 7.20 (m, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.94 (s, 2H), 6.56 (d, *J* = 7.2 Hz, 1H), 5.68 – 5.59 (m, 1H), 5.12 (d, *J* = 10.2 Hz, 1H), 5.04 (s, 1H), 5.01 (d, *J* = 16.2 Hz, 1H), 4.71 (s, 1H), 4.52 – 4.45 (m, 1H), 3.83 (dd, *J* = 16.2, 5.4 Hz, 1H), 3.38 (d, *J* = 12.6 Hz, 1H), 2.32 (d, *J* = 12.6 Hz, 1H), 1.29 (s, 18H) ppm. ^{13}C NMR (151 MHz, $CDCl_3$) δ 175.4, 168.8, 152.9, 151.0, 141.3, 135.2, 130.9 (2C), 130.7, 129.8 (2C), 129.5, 128.6, 128.4, 127.1, 125.9, 124.6, 123.4, 122.8, 119.6, 117.9, 109.0, 56.5, 51.2, 42.3, 39.9, 34.2 (2C), 30.3 (6C) ppm. IR (KBr) 3634, 3065, 2958, 2253, 1994, 1758, 1704, 1611, 1484, 1437, 1365, 1315, 1287, 1215, 1187, 1140, 1101, 1014, 975, 910, 840, 730, 676 cm^{-1}; HRMS (ESI) calcd for $C_{34}H_{37}NO_4Na$ [M + Na]$^+$: 546.2615, found 546.12613.

3. X-ray structure of compound 3s

The crystal suitable for X-ray analysis was prepared by slow evaporation of the solvent of the solution of **3s** in pentan/DCM (10/1) at room temperature.



3s

Datablock: 3s

```
Bond precision:  C-C = 0.0021 A          Wavelength=1.54184

Cell:            a=10.7822(1)     b=15.2654(1)     c=18.4818(1)
                 alpha=90         beta=90          gamma=90
Temperature:     120 K

                Calculated                Reported
Volume          3042.01(4)                3042.00(4)
Space group     P 21 21 21                P 21 21 21
Hall group      P 2ac 2ab                 P 2ac 2ab
Moiety formula  C37 H37 N O4              C37 H37 N O4
Sum formula     C37 H37 N O4              C37 H37 N O4
Mr              559.68                    559.67
Dx,g cm-3       1.222                     1.222
Z               4                         4
Mu (mm-1)       0.623                     0.623
F000            1192.0                    1192.0
F000'           1195.44
h,k,lmax        13,19,23                  13,19,23
Nref            6416[ 3600]               6398
Tmin,Tmax       0.765,0.800               0.951,0.963
Tmin'           0.765

Correction method= # Reported T Limits: Tmin=0.951 Tmax=0.963
AbsCorr = ANALYTICAL

Data completeness= 1.78/1.00      Theta(max)= 76.891

R(reflections)= 0.0309( 6373)     wR2(reflections)= 0.0779( 6398)

S = 1.075                 Npar= 386
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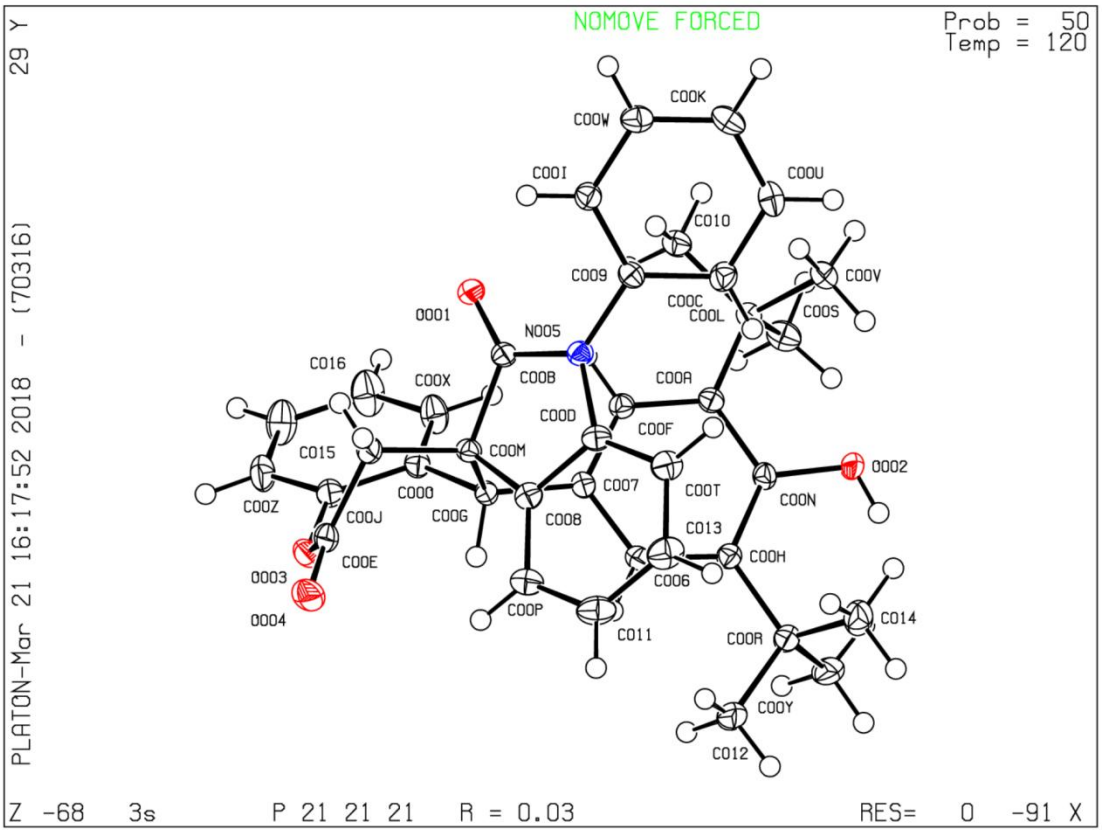


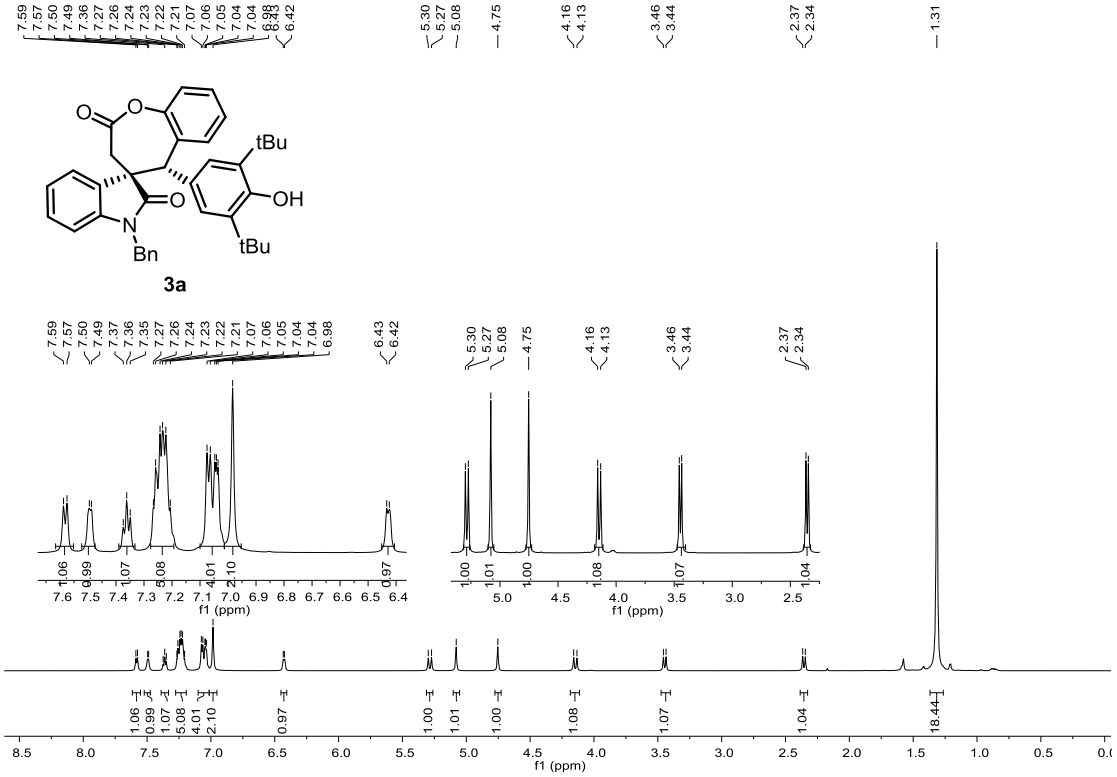
4. References

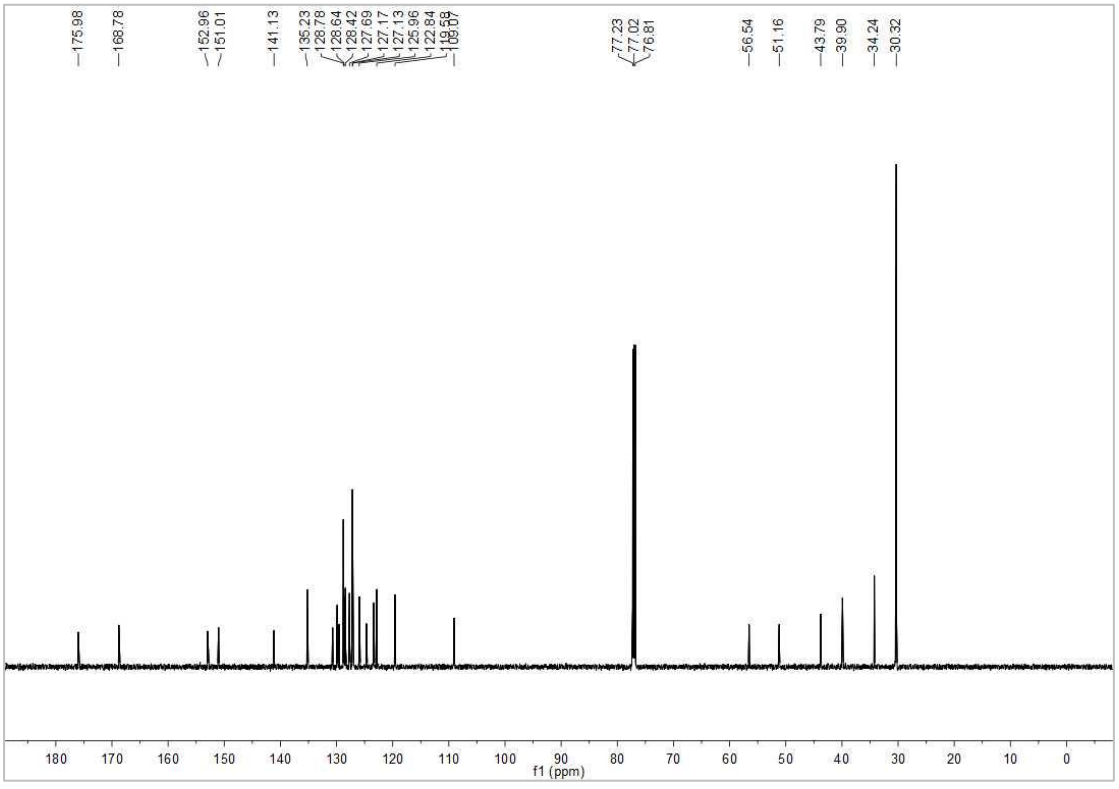
[1] a) A. K. Ghosh, S. P. McKee, W. M. Sanders, *Tetrahedron Lett.* **1991**, *32*, 711; b) M. S. Kerr, J. Read de Alaniz, T. Rovis, *J. Org. Chem.* **2005**, *70*, 5725; c) D. Enders, O. Niemeier, T. Balensiefer, *Angew. Chem. Int. Ed*. **2006**, *45*, 1463; d) M. He, J. R. Struble, J. W. Bode, *J. Am. Chem. Soc.* **2006**, *128*, 8418; e) C. Zhao, F. Li, J. Wang, *Angew. Chem. Int. Ed.* **2016**, *55*, 1820; f) X. Wu, Y. Zhang, Y. Wang, J. Ke, M. Jeret, R. N. Reddi, S. Yang, B. A. Song, Y. R. Chi, *Angew. Chem. Int. Ed.* **2017**, *56*, 2942.

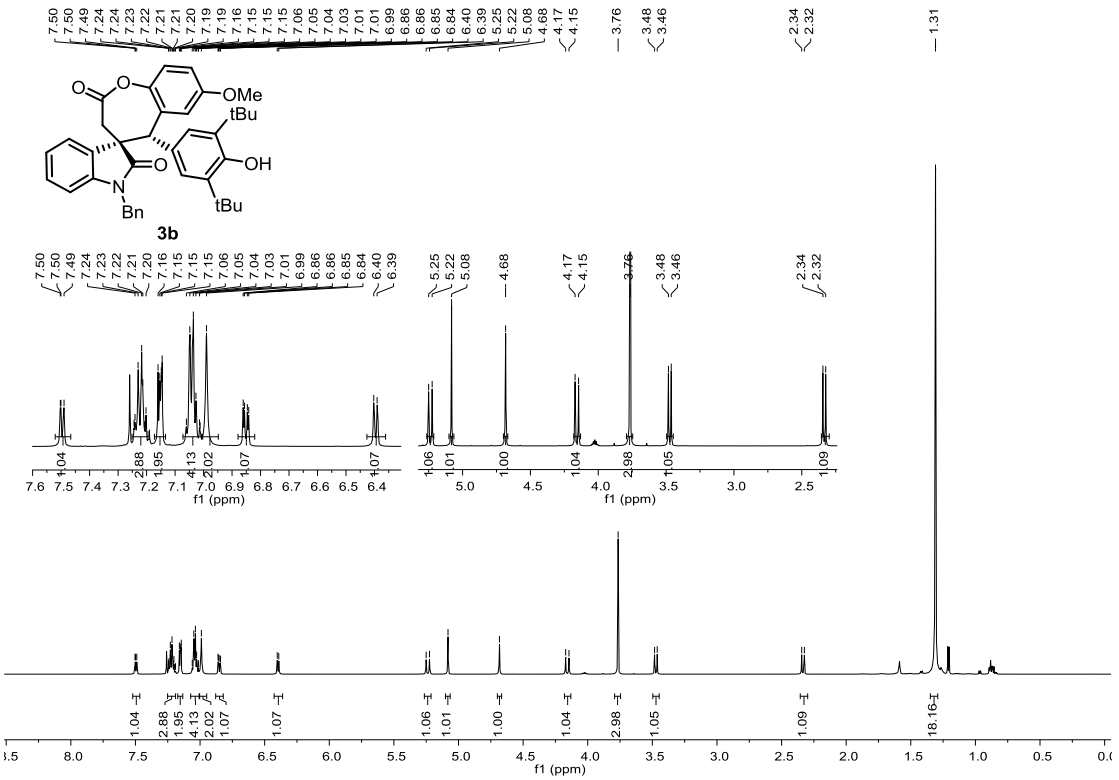
[2] Kun Zhao, Ying Zhi, Tao Shu, Arto Valkonen, Kari Rissanen, and Dieter Enders. *Angew. Chem. Int. Ed.* **2016**, *55*, 12104 –12108.

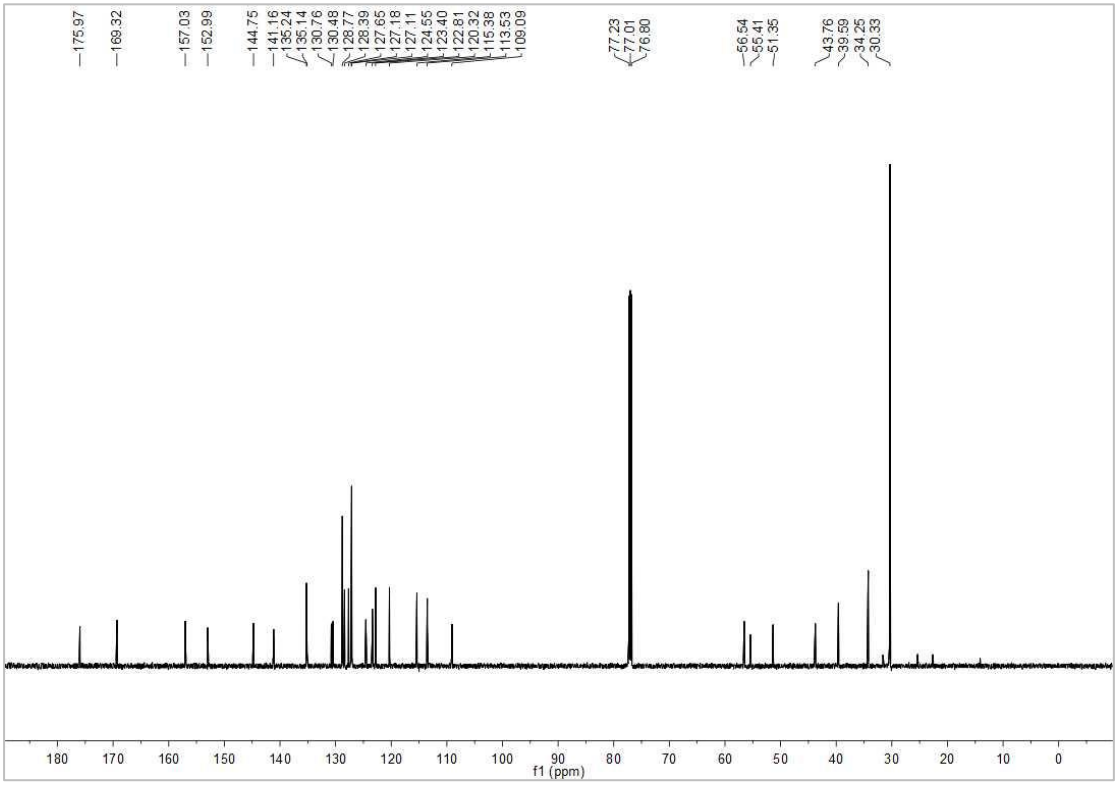
[3] T. Mukaiyama, K. Ogata, I. Sato, Y. Hayashi, *Chem. Eur. J.* **2014**, *20*, 13583 – 13588.

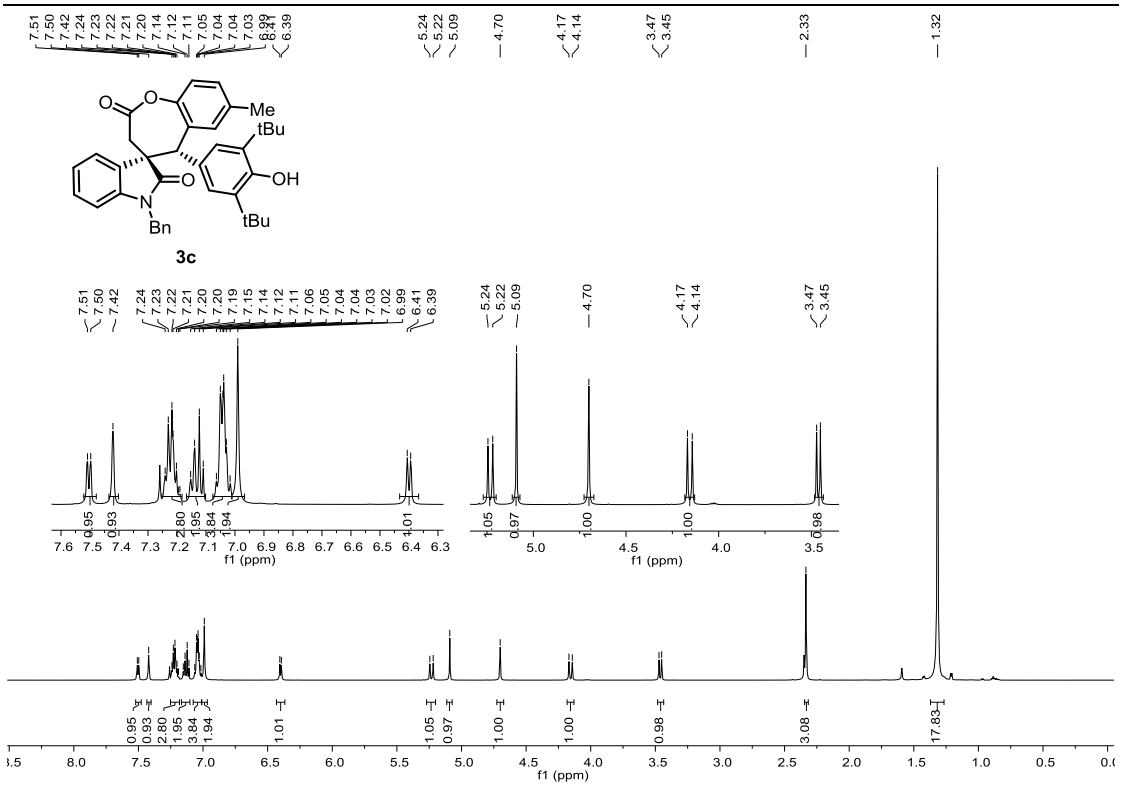
Part III NMR Spectra

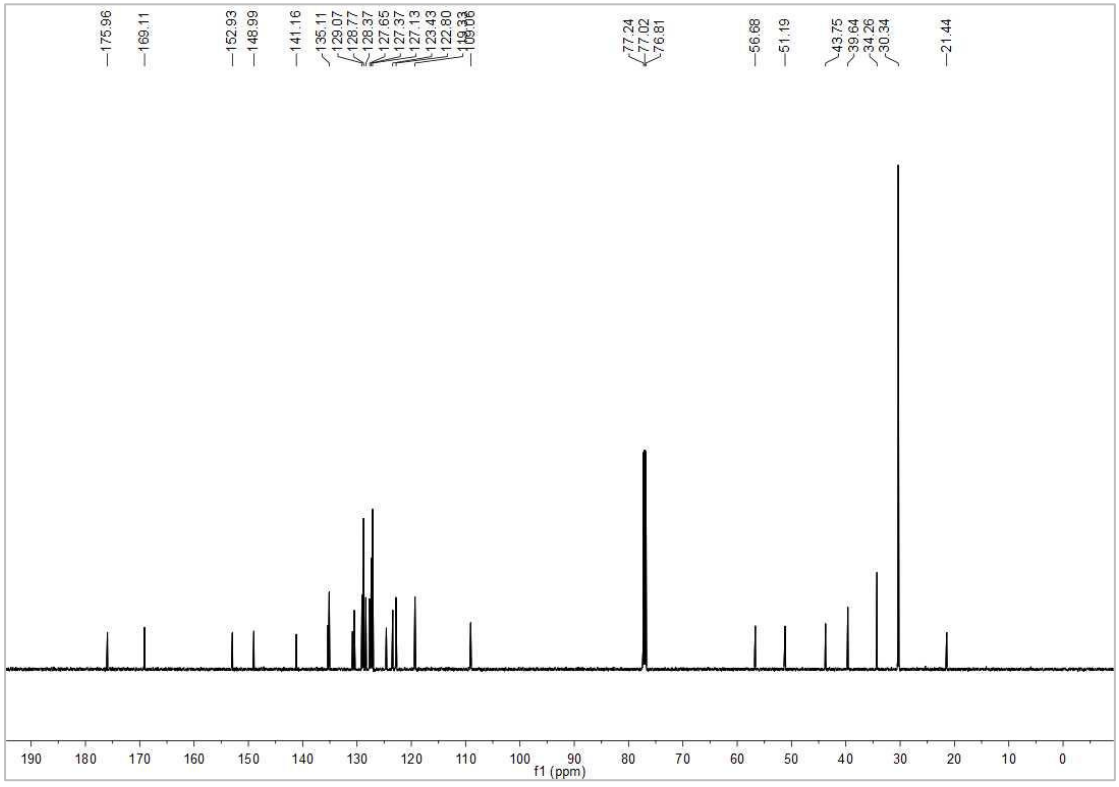


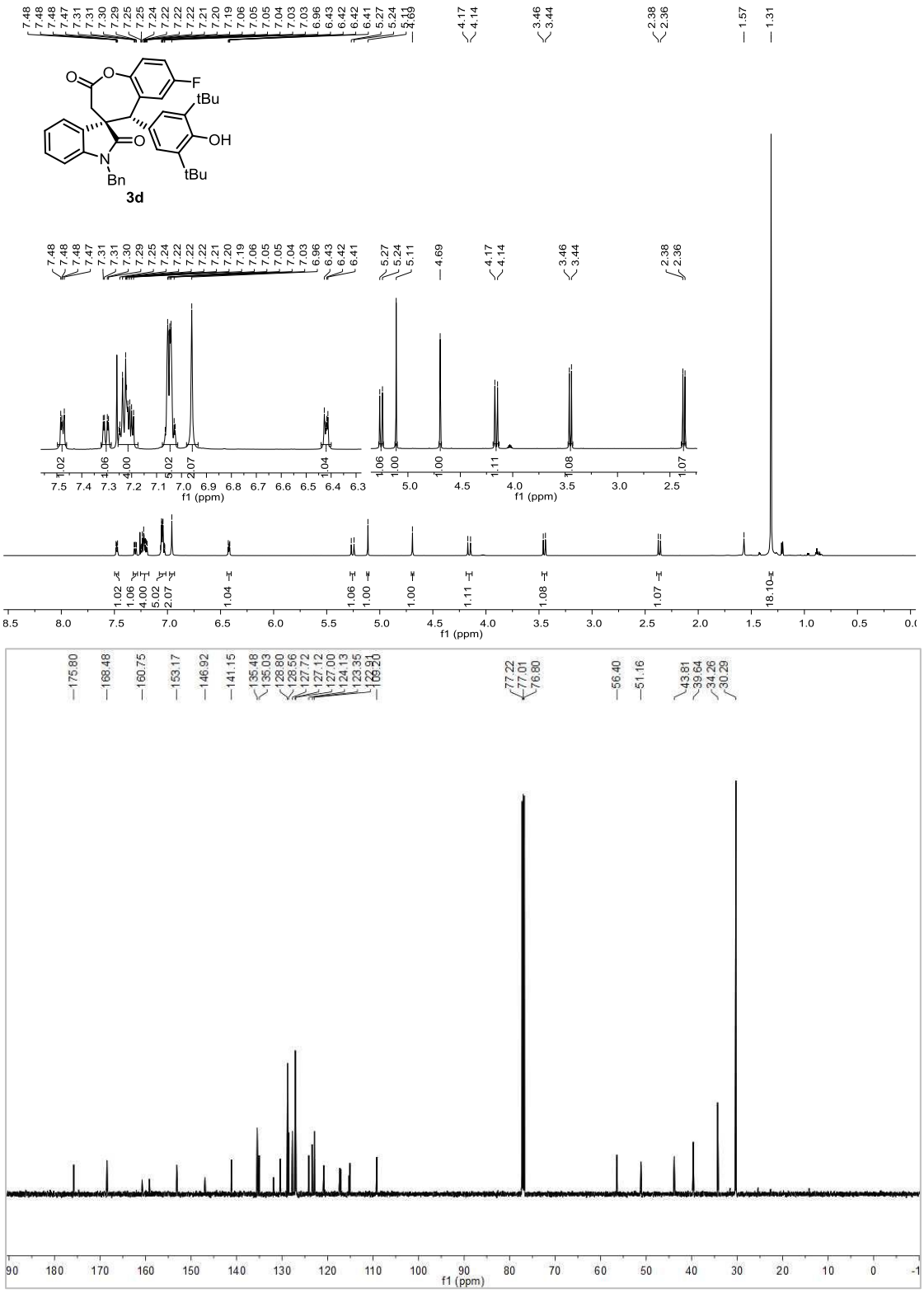


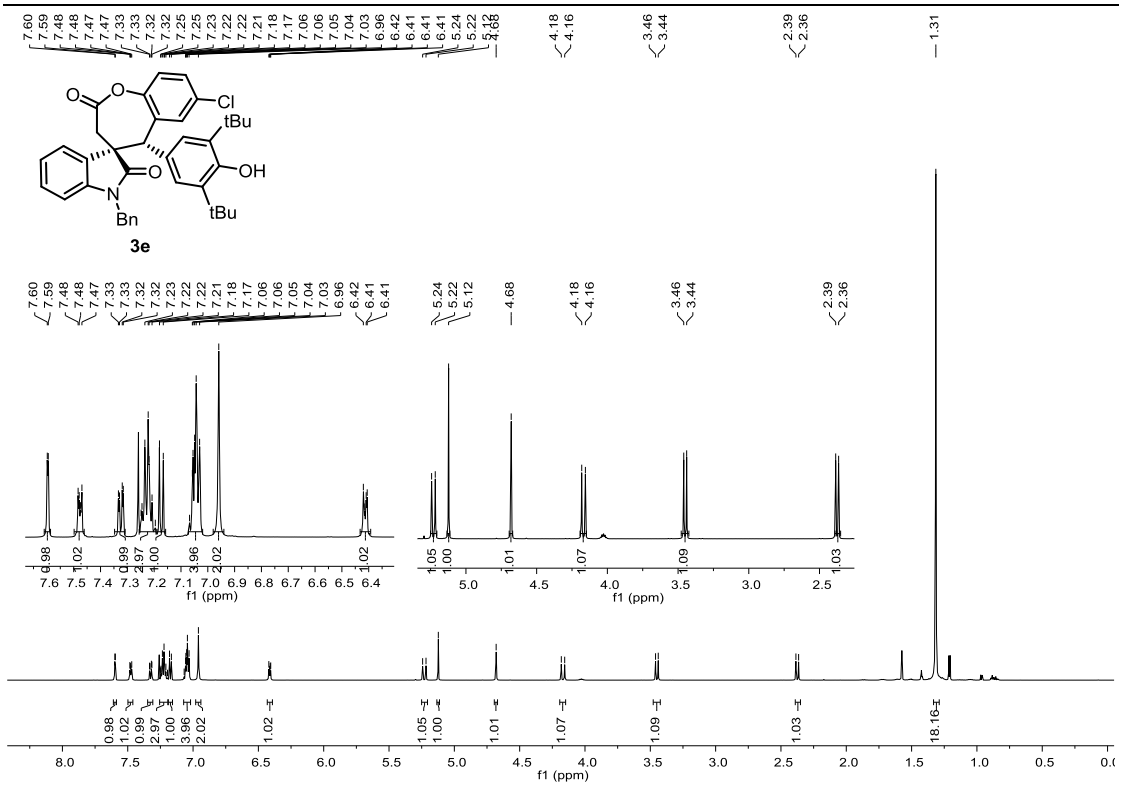

OMe
tBu
OH
tBu
O
O
O
N
Bn
3b
f1 (ppm)

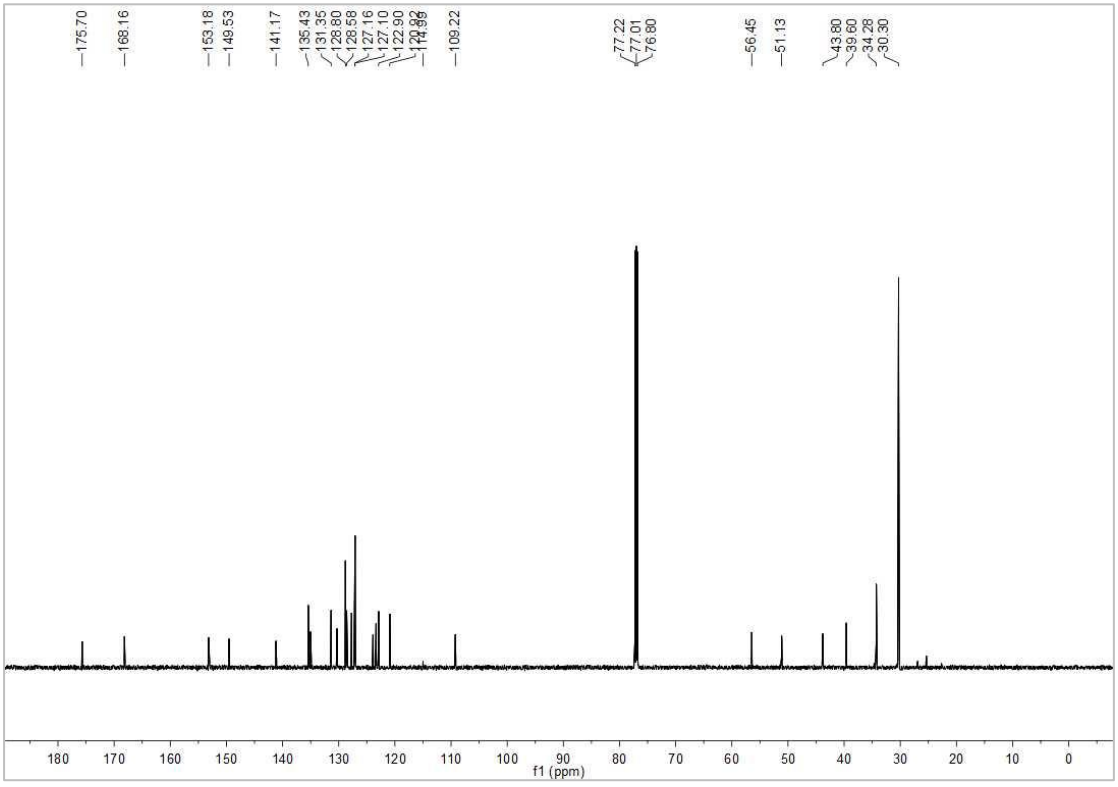

f1 (ppm)

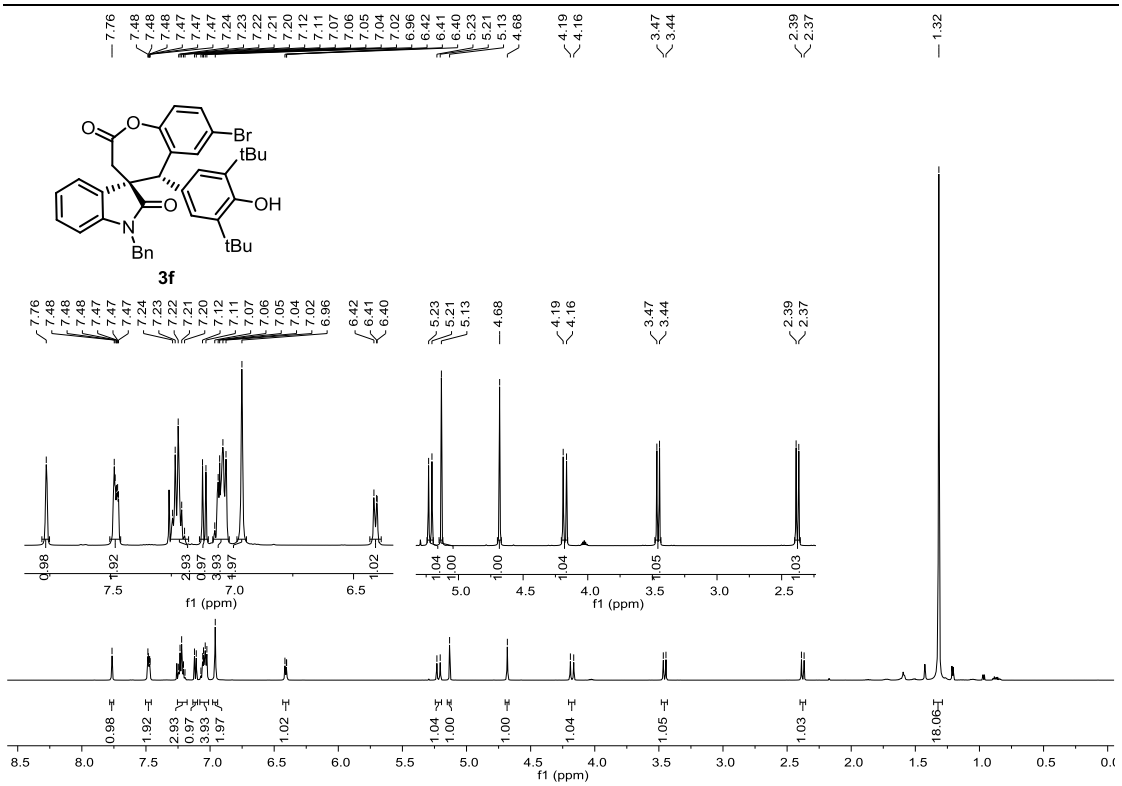

Me
tBu
OH
tBu
Bn
3c
f1 (ppm)


f1 (ppm)


3d
f1 (ppm)


Cl
tBu
OH
tBu
N
Bn
O
O
O
3e
f1 (ppm)


f1 (ppm)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7.48
7.48
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7.47
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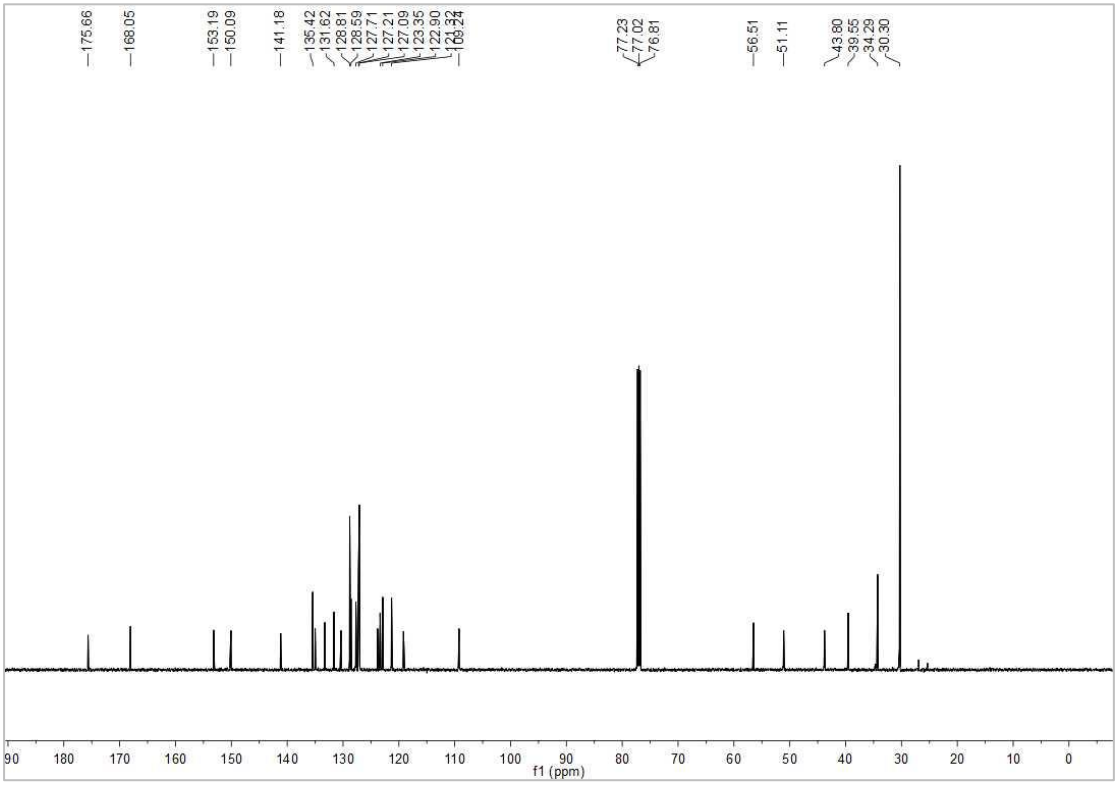
7.20
7.12
7.11
7.07
7.06
7.05
7.04
7.02
6.96
6.42
6.41
6.40
5.23
5.21
5.13
4.68
4.19
4.16
3.47
3.44
2.39
2.37
1.32
Br
tBu
OH
tBu
Bn
3f
0.98
1.92
2.93
0.97
3.93
1.97
1.02
1.04
1.00
1.00
1.04
1.05
1.03
18.06
f1 (ppm)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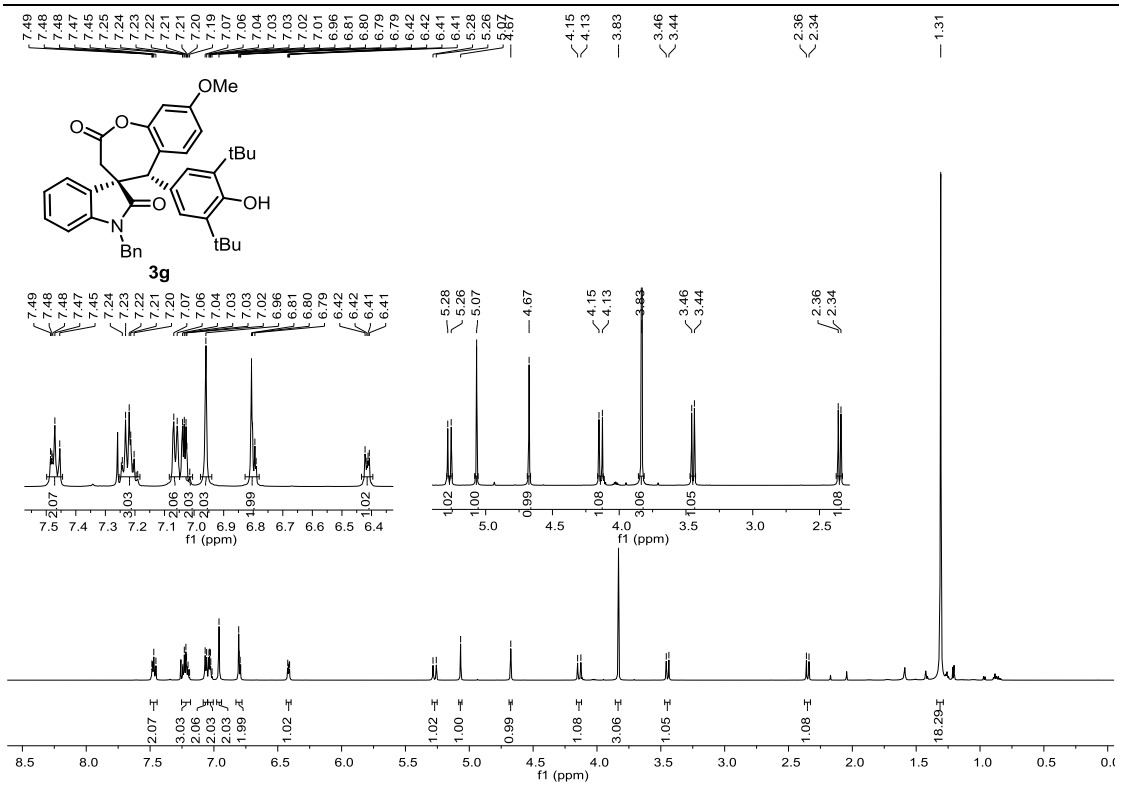
153.19
150.09
141.18
135.42
131.62
128.81
128.59
127.71
127.21
127.09
123.35
122.90
77.23
77.02
76.81
56.51
51.11
43.80
39.55
34.29
30.30
f1 (ppm)


OMe
O
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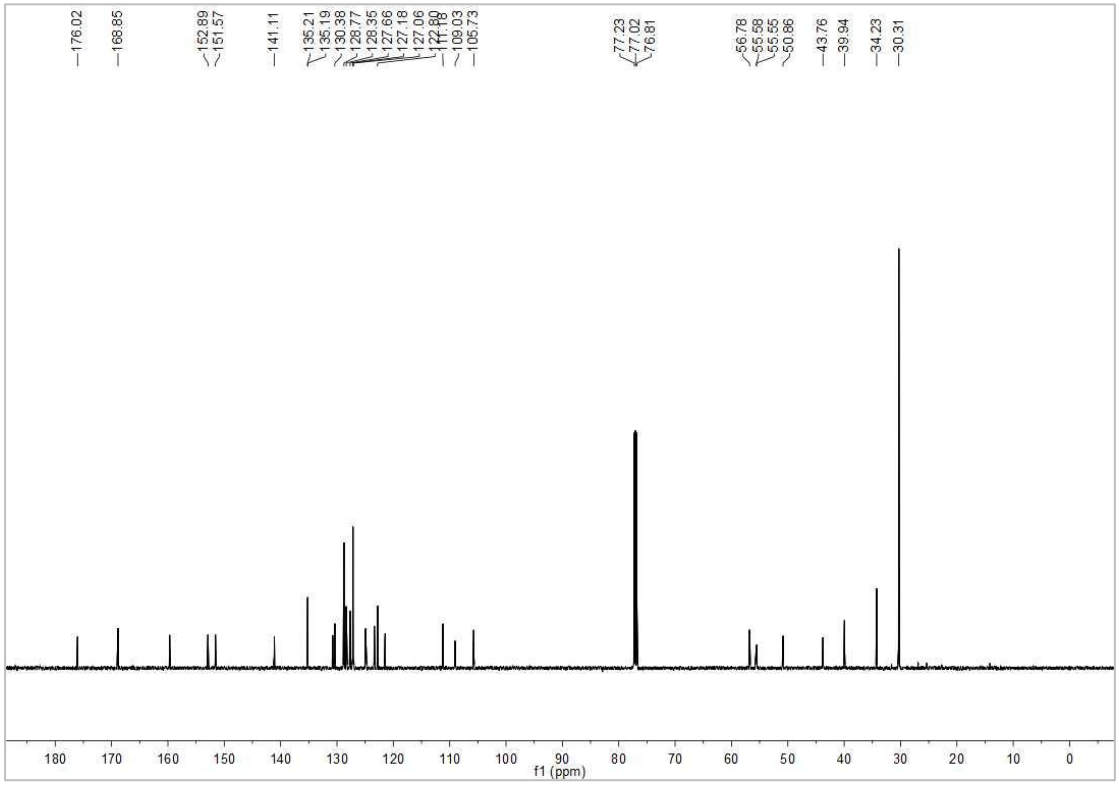
OH
O
N
Bn
tBu
3g
f1 (ppm)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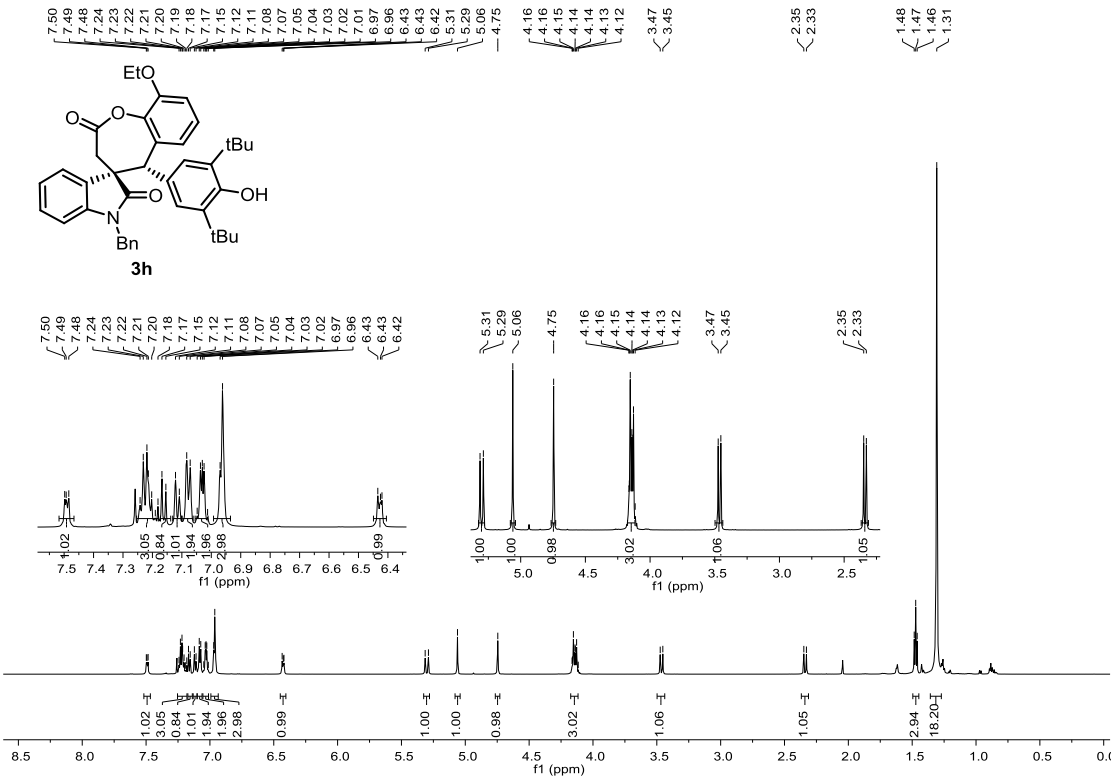
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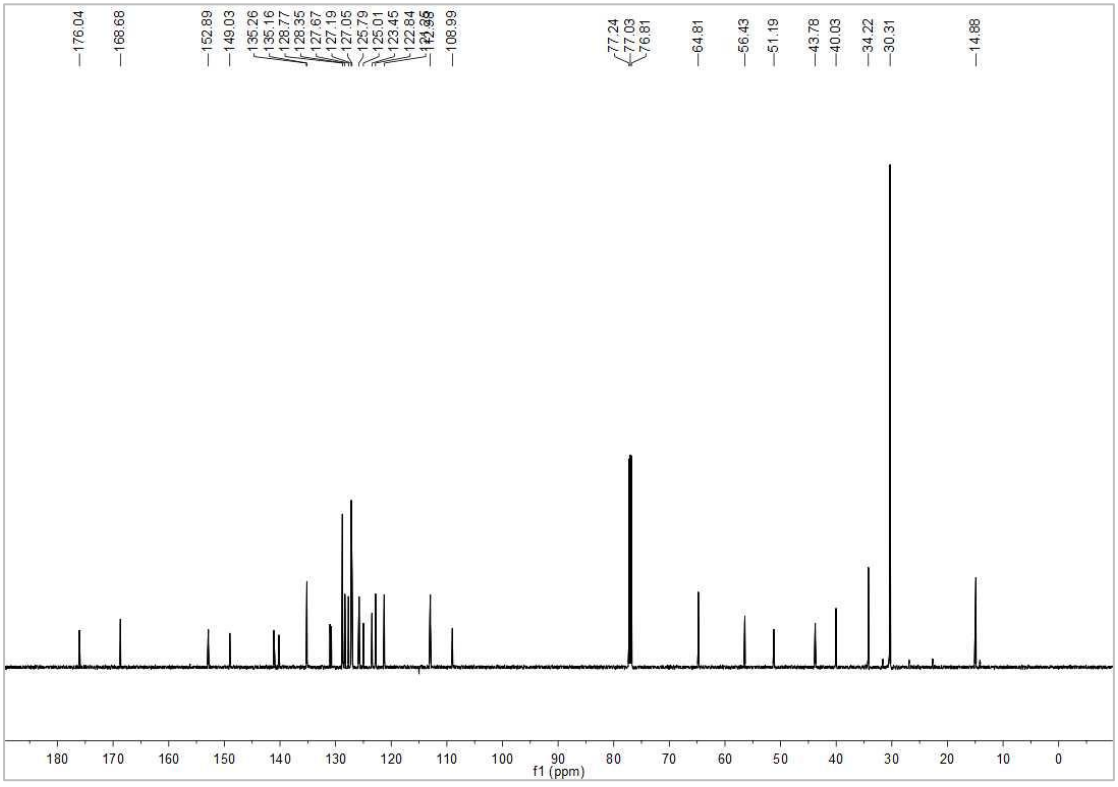
OH
O
N
Bn
tBu
3h
f1 (ppm)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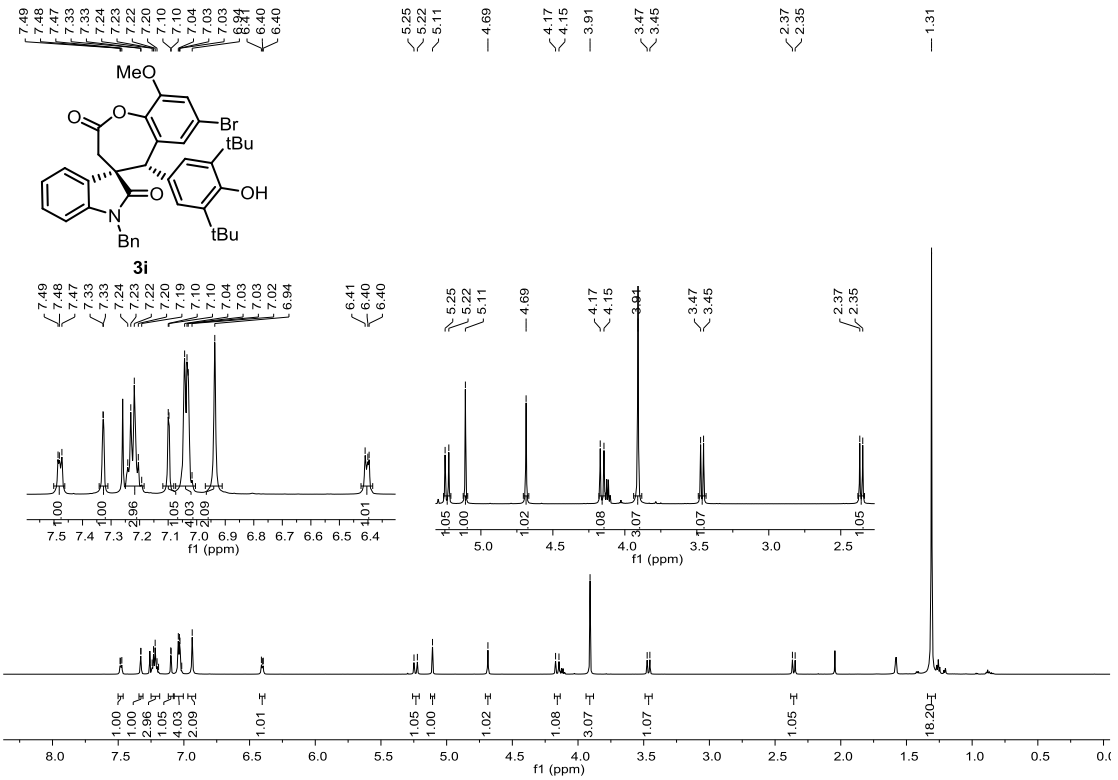
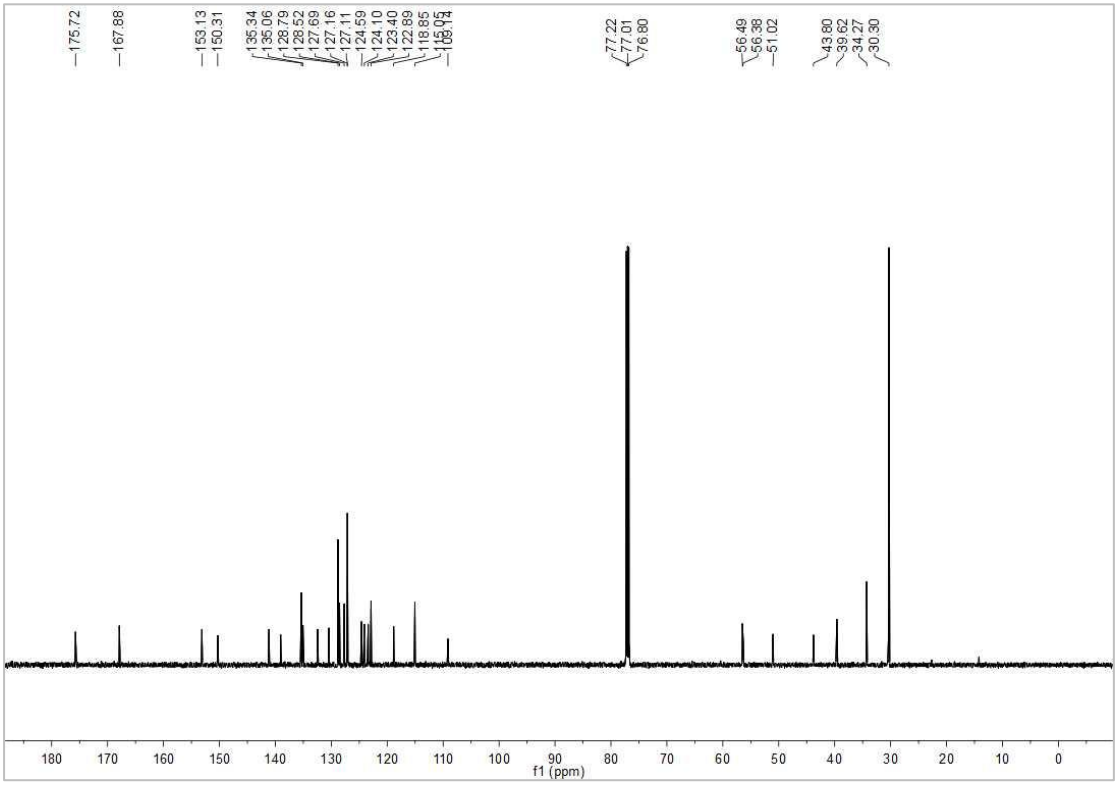
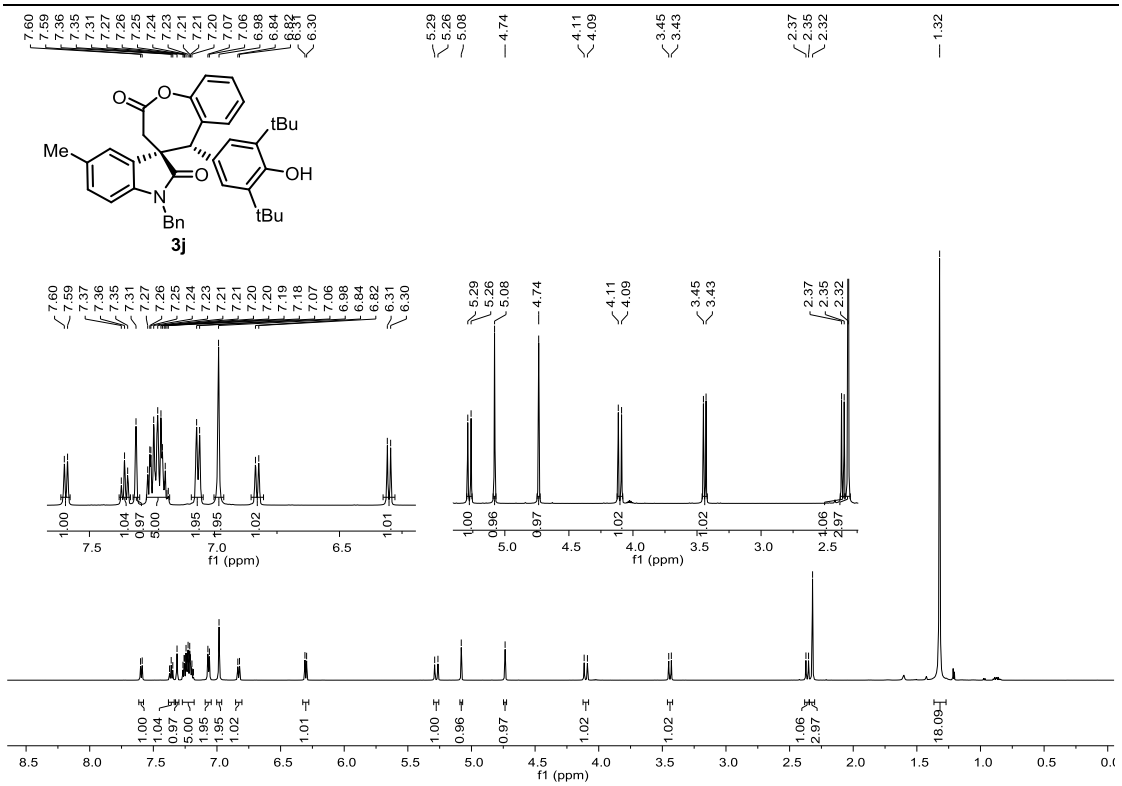
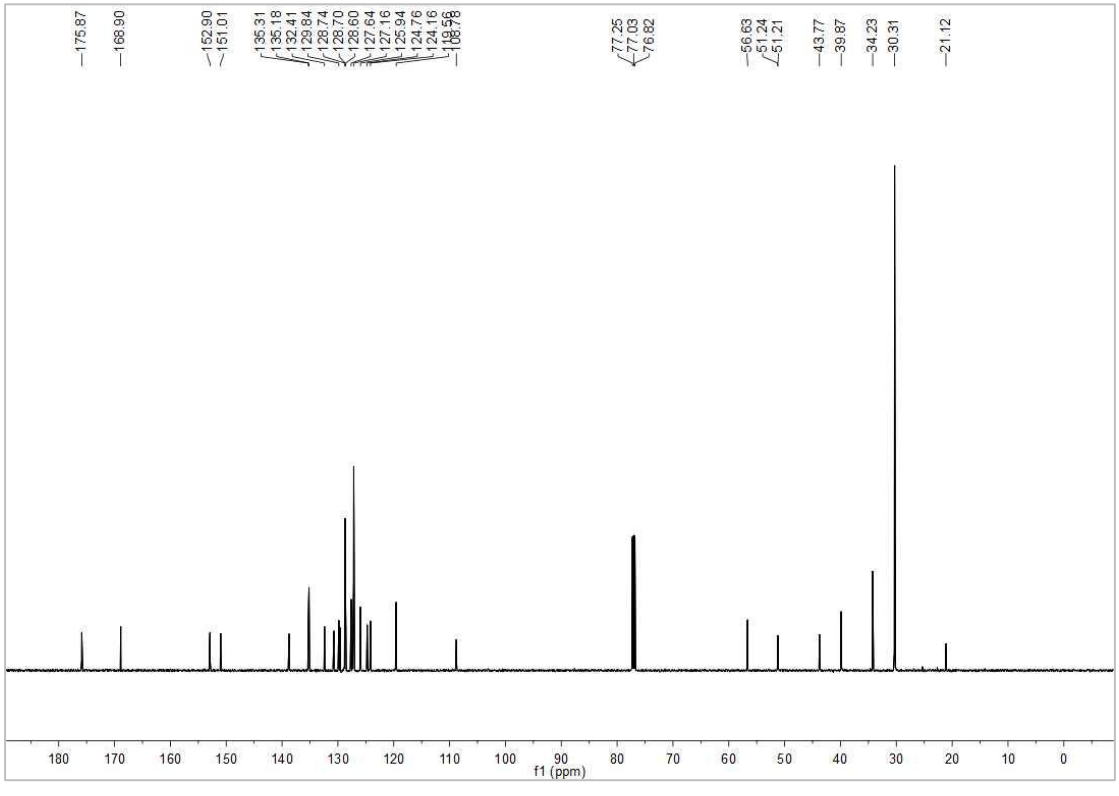

MeO
Br
tBu
OH
tBu
Bn
3i
f1 (ppm)


f1 (ppm)


7.60 7.59 7.36 7.35 7.31 7.27 7.26 7.25 7.24 7.23 7.21 7.21 7.20 7.07 7.06 6.98 6.84 6.82 6.30
5.29 5.26 5.08
4.74
4.11 4.09
3.45 3.43
2.37 2.35 2.32
1.32
O
O
tBu
Me
O
OH
N
Bn
tBu
3j
f1 (ppm)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168.90
152.90 151.01
135.31 135.18 132.41 129.84 128.74 128.70 128.60 127.64 127.16 125.94 124.76 124.16 119.56 108.78
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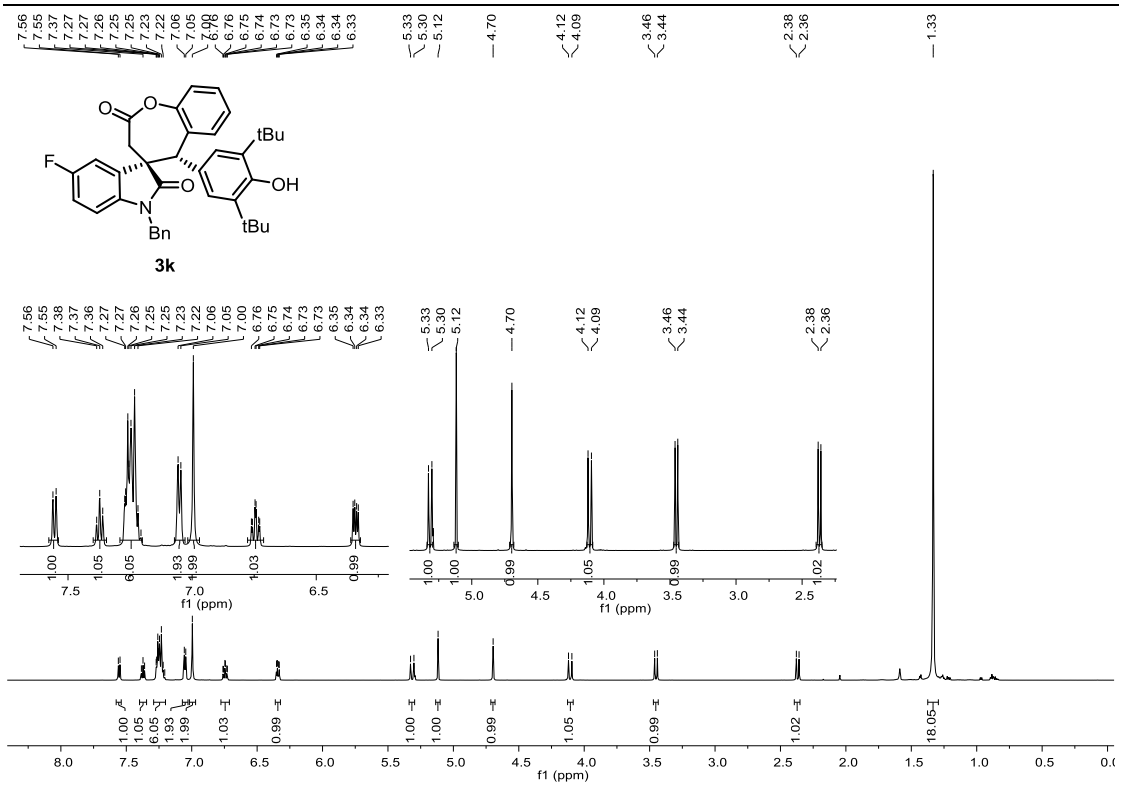
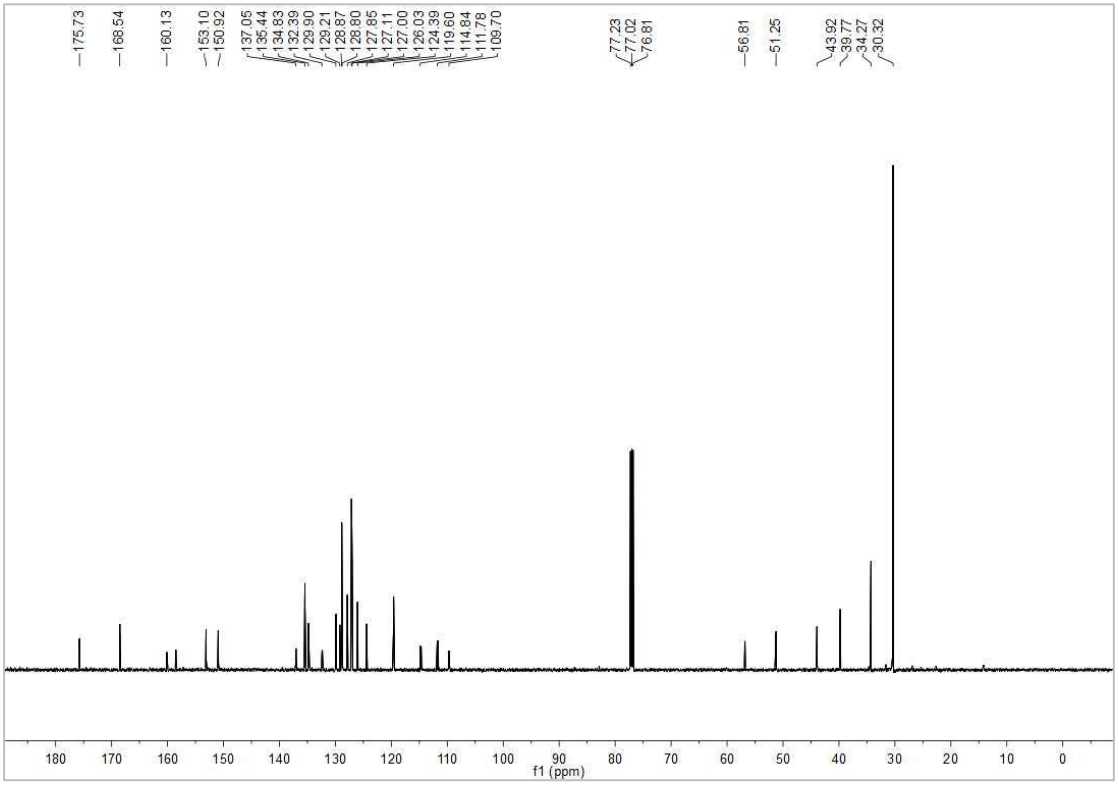
43.77 39.87 34.23 30.31
21.12
f1 (ppm)


7.56 7.55 7.37 7.27 7.27 7.26 7.25 7.25 7.23 7.22 7.06 7.05 7.00 6.76 6.75 6.74 6.73 6.73 6.35 6.34 6.34 6.33
5.33 5.30 5.12
4.70
4.12 4.09
3.46 3.44
2.38 2.36
1.33
O
O
tBu
F
OH
O
N
Bn
tBu
1.00 1.05 6.05 1.93 1.99 1.03 0.99 1.00 1.00 0.99 1.05 0.99 1.02 18.05
f1 (ppm)

3k


175.73 168.54 160.13 153.10 150.92 137.05 135.44 134.83 132.39 129.90 129.21 128.87 128.80 127.85 127.11 127.00 126.03 124.39 119.60 114.84 111.78 109.70
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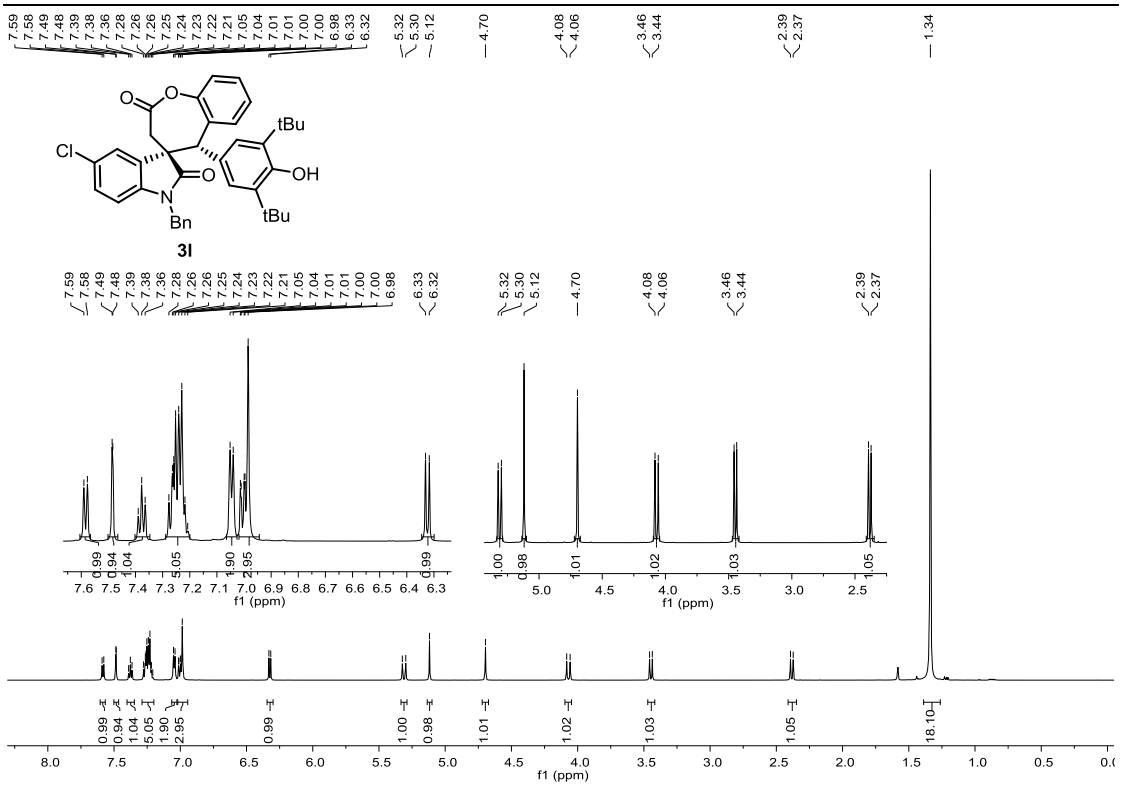
56.81 51.25
43.92 39.77 34.27 30.32
f1 (ppm)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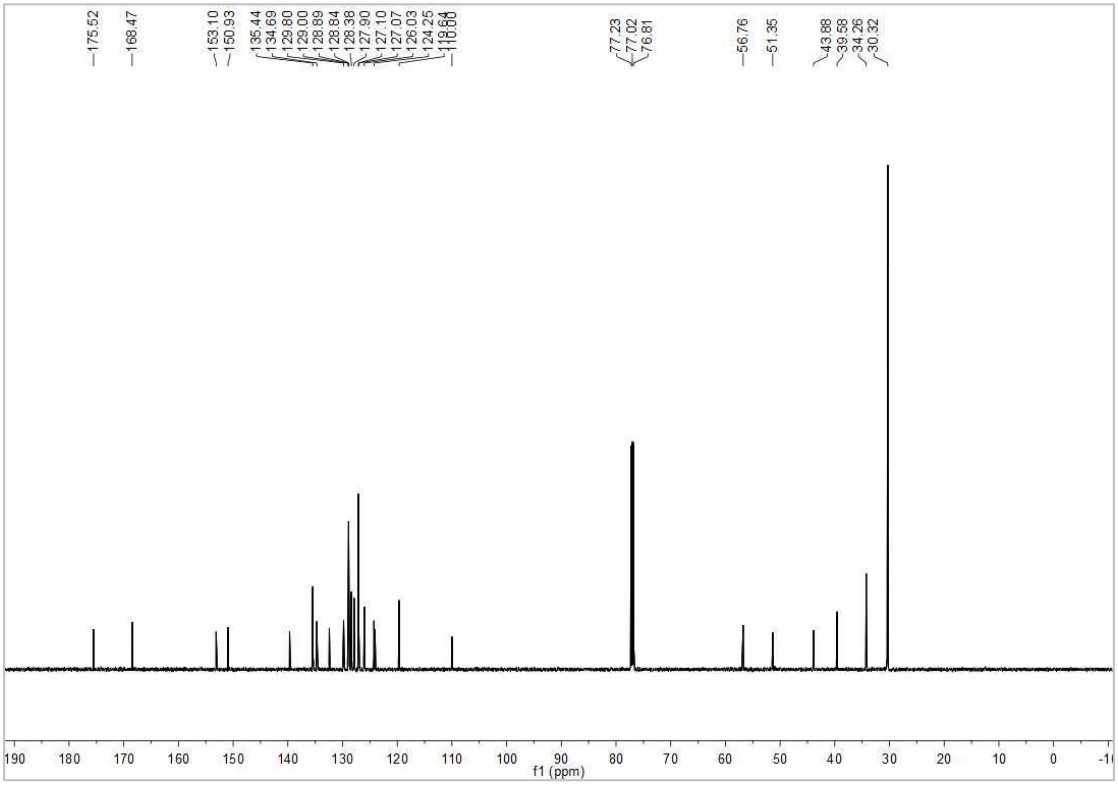
5.32 5.30 5.12
4.70
4.08 4.06
3.46 3.44
2.39 2.37
1.34
O
O
tBu
Cl
O
OH
N
Bn
tBu
3l
0.99 0.94 1.04 5.05 1.90 2.95 0.99 1.00 0.98 1.01 1.02 1.03 1.05 18.10
f1 (ppm)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129.00
128.89
128.84
128.38
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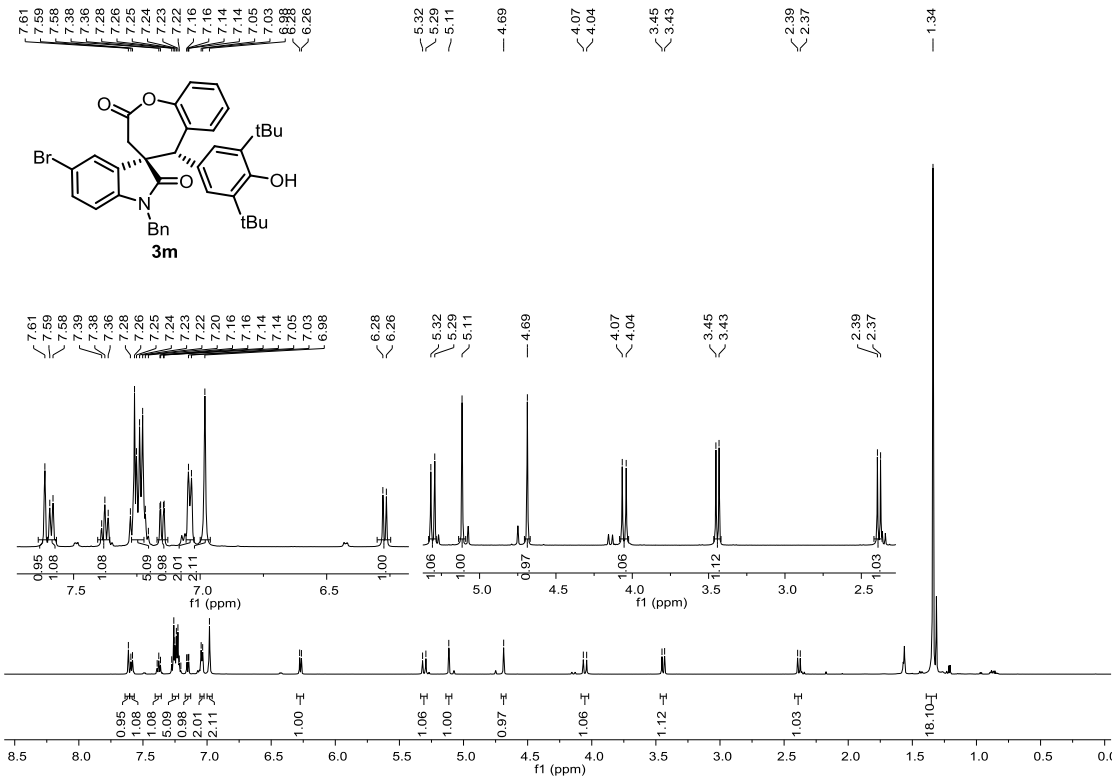
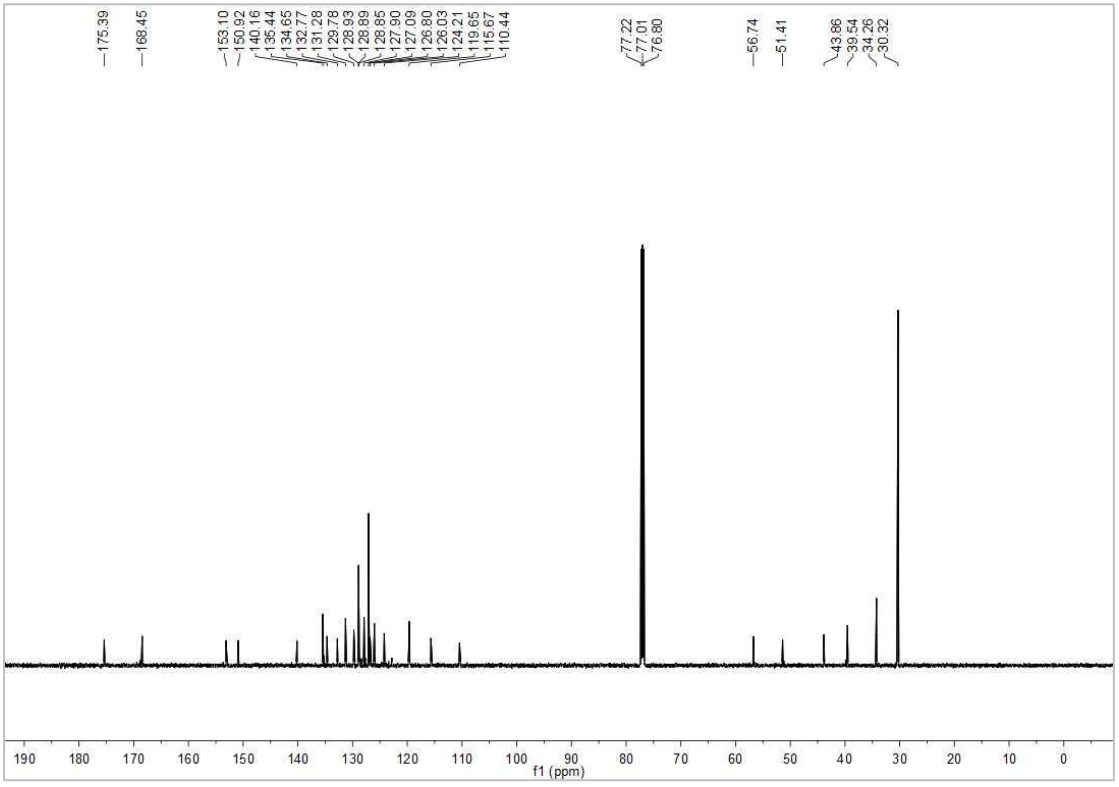
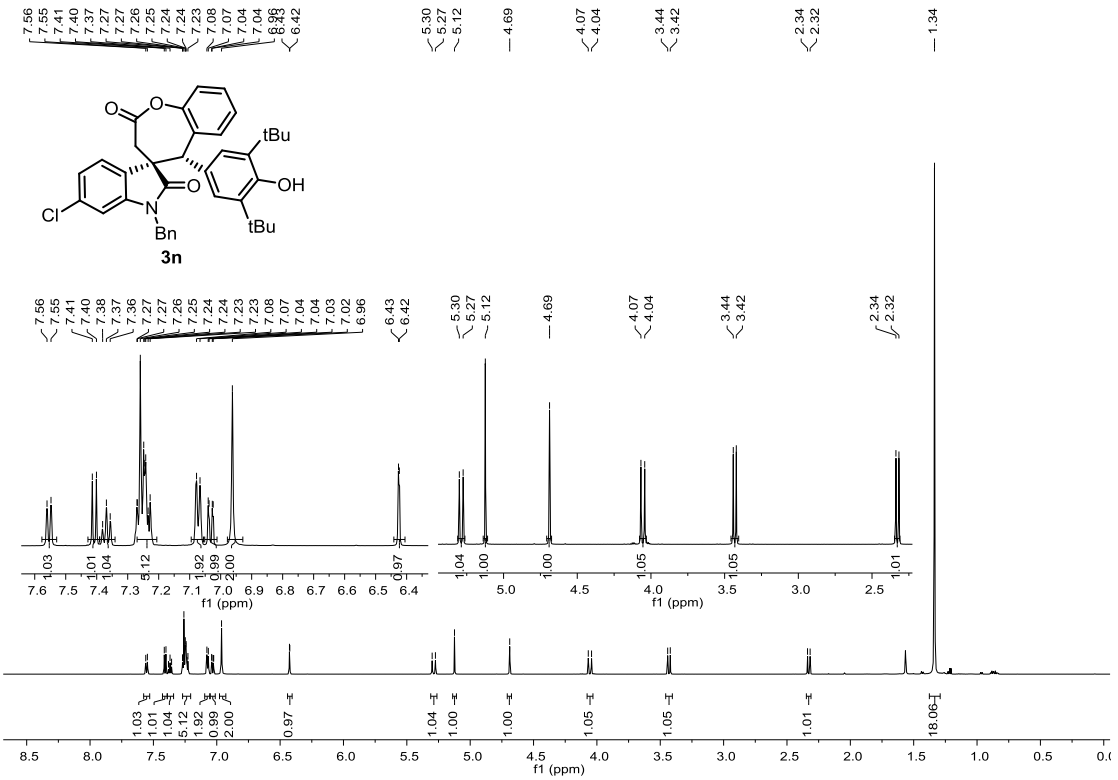
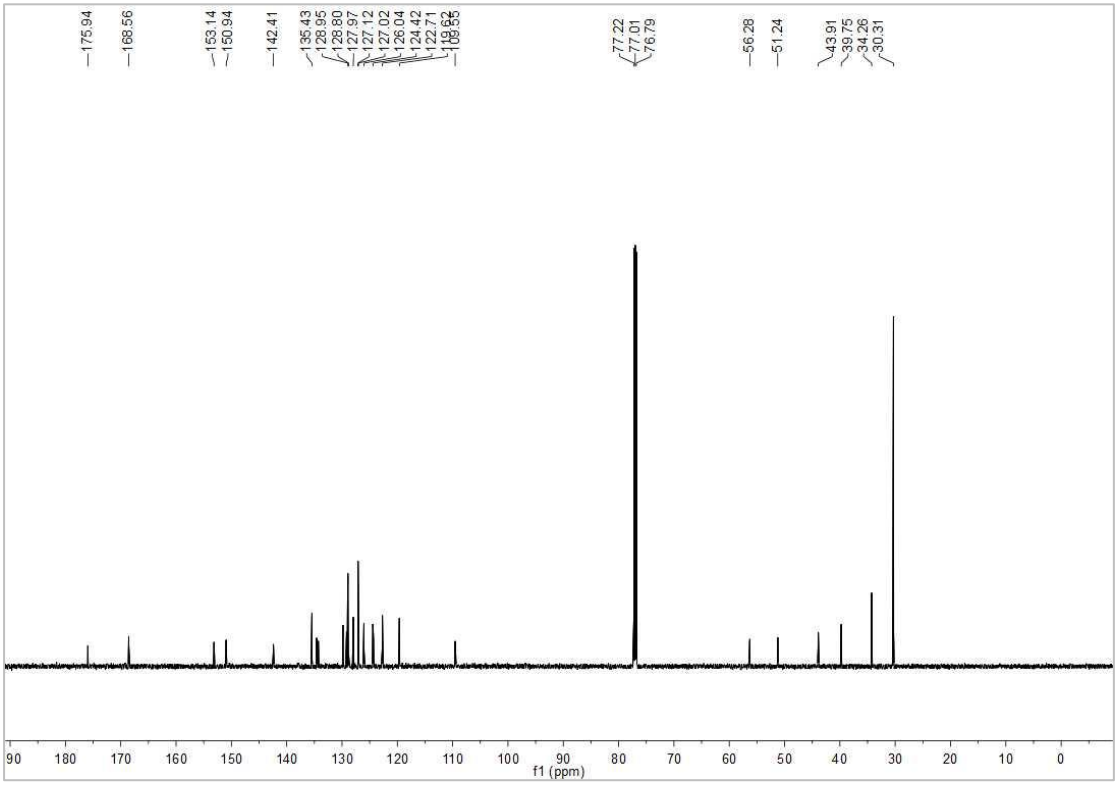
127.10
127.07
126.03
124.25
119.64
110.00
77.23
77.02
76.81
56.76
51.35
43.88
39.58
34.26
30.32
f1 (ppm)


7.61 7.59 7.58 7.38 7.36 7.28 7.26 7.25 7.24 7.23 7.22 7.16 7.16 7.14 7.14 7.05 7.03 6.98 6.26
5.32 5.29 5.11
4.69
4.07 4.04
3.45 3.43
2.39 2.37
1.34
O
O
tBu
Br
O
OH
N
Bn
tBu
3m
0.95 1.08 1.08 5.09 0.98 2.01 2.11 1.00 1.06 1.00 0.97 1.06 1.12 1.03 18.10
f1 (ppm)


175.39 168.45 153.10 150.92 140.16 135.44 134.65 132.77 131.28 129.78 128.93 128.89 128.85 127.90 127.09 126.80 126.03 124.21 119.65 115.67 110.44
77.22 77.01 76.80
56.74 51.41
43.86 39.54 34.26 30.32
f1 (ppm)


tBu
OH
tBu
Cl
Bn
3n
f1 (ppm)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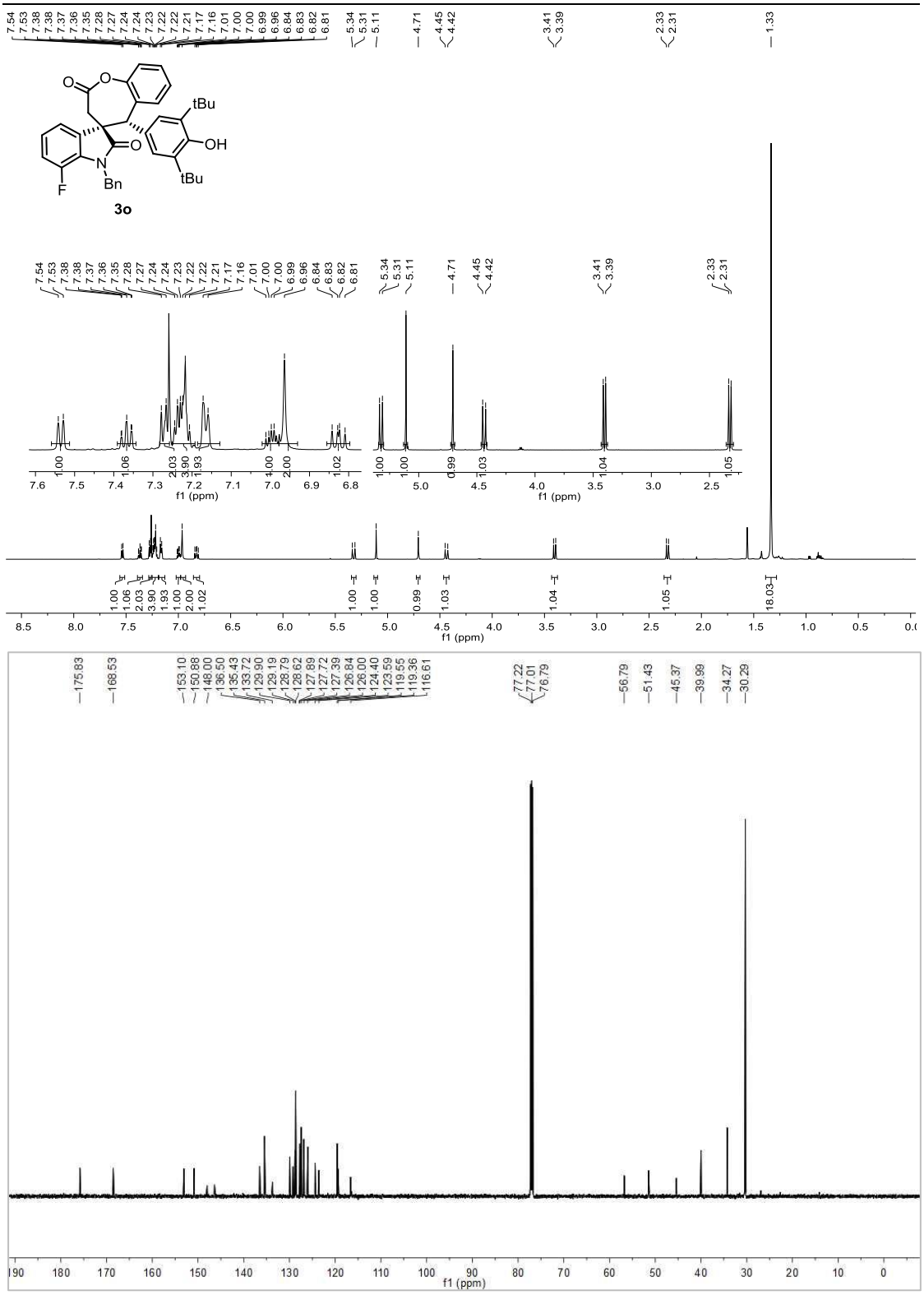
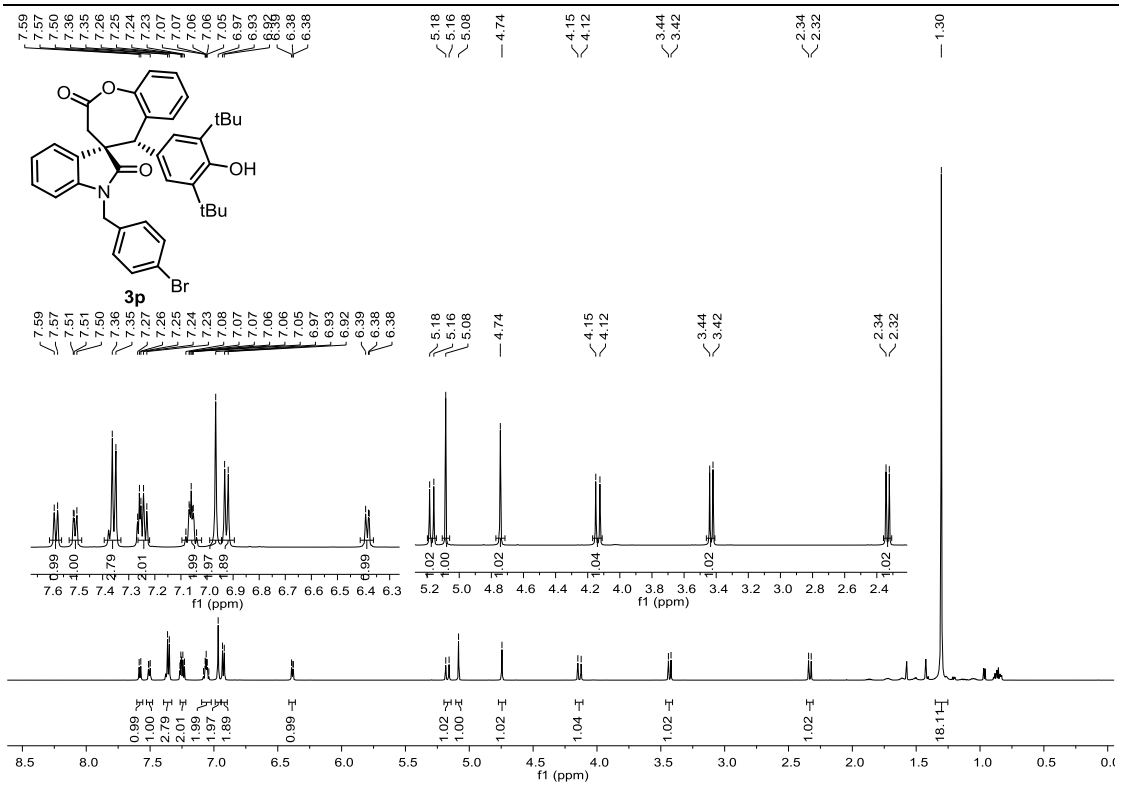

3o
f1 (ppm)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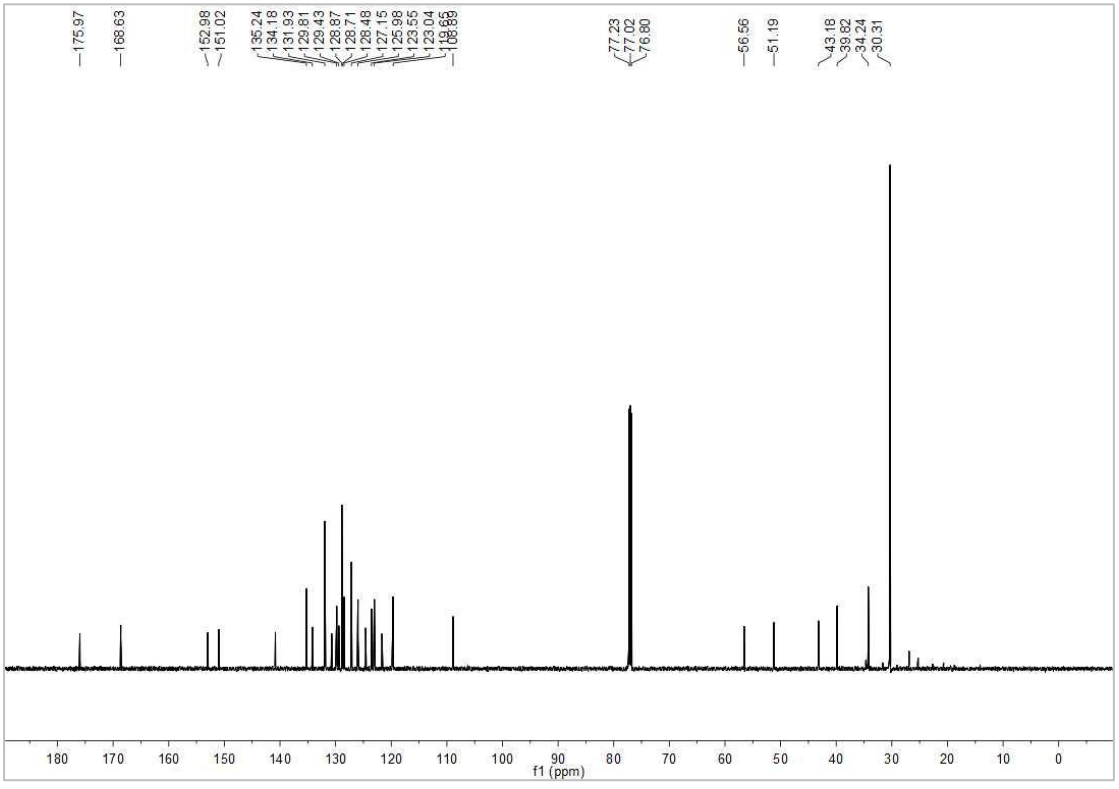
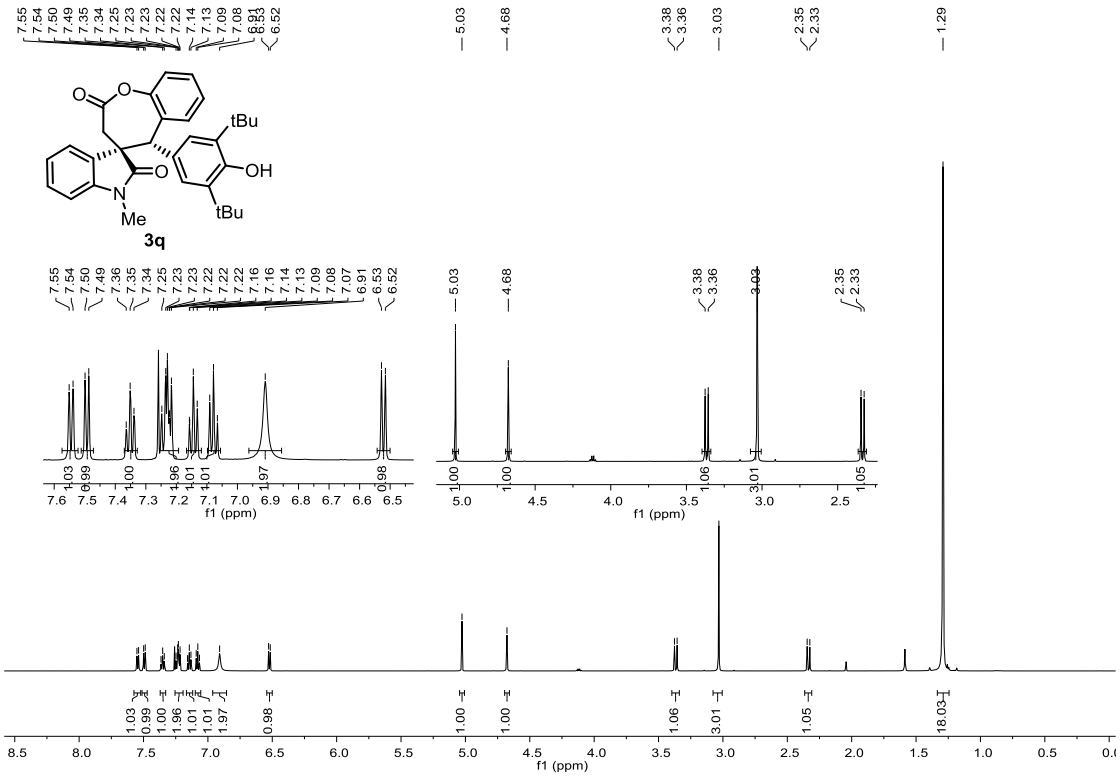
f1 (ppm)


f1 (ppm)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7.35
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7.25
7.23
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7.22
7.22
7.14
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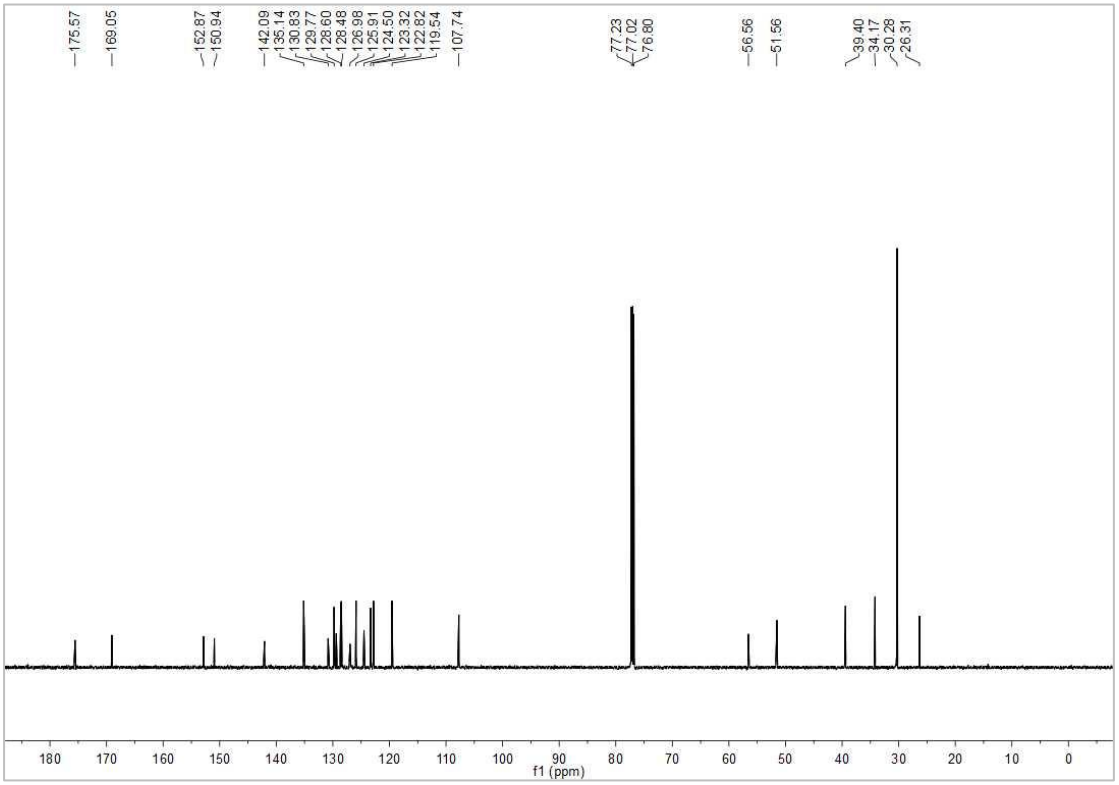
7.09
7.08
6.91
6.53
6.52
5.03
4.68
3.38
3.36
3.03
2.35
2.33
1.29
tBu
OH
tBu
O
O
O
N
Me
3q
1.03
0.99
1.00
1.96
1.01
1.01
1.97
0.98
1.00
1.00
1.06
3.01
1.05
18.03
f1 (ppm)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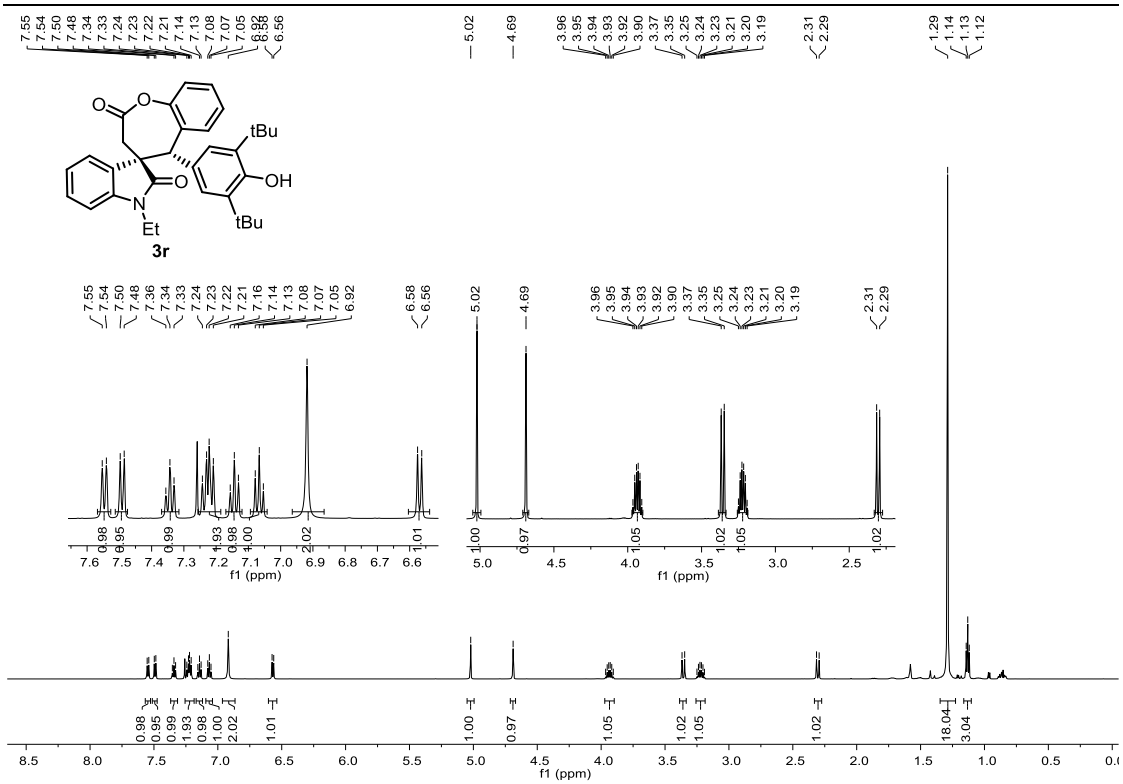
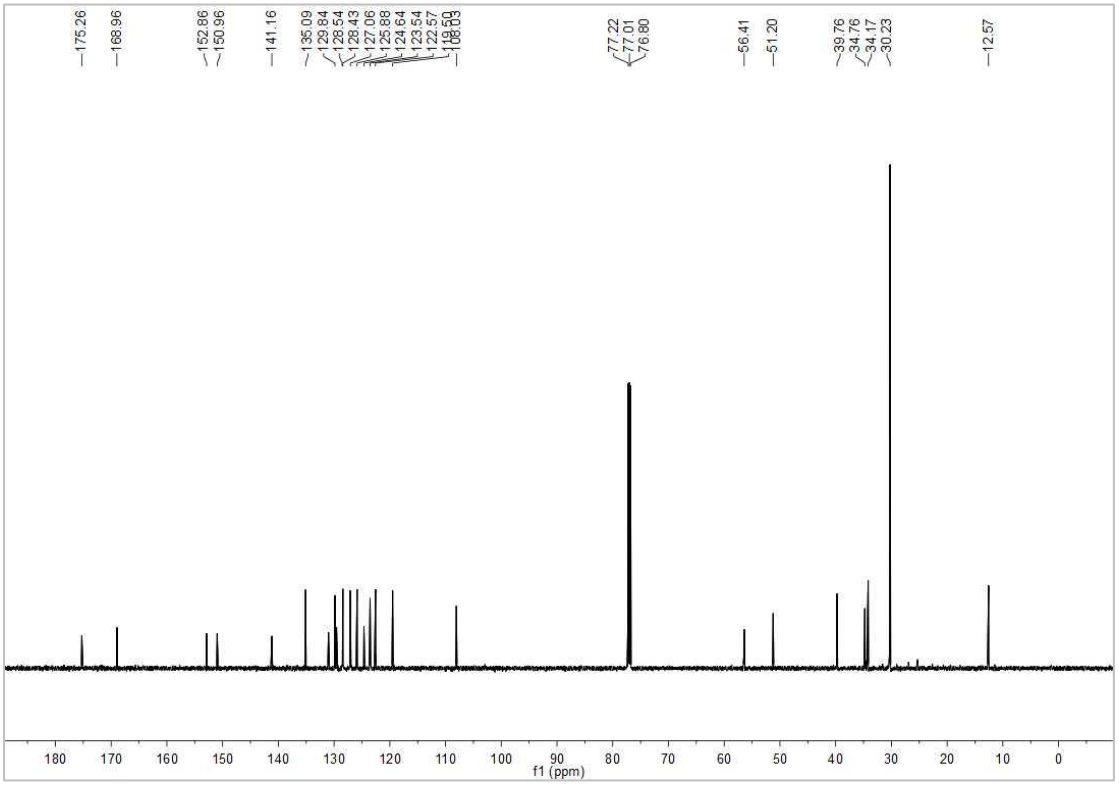
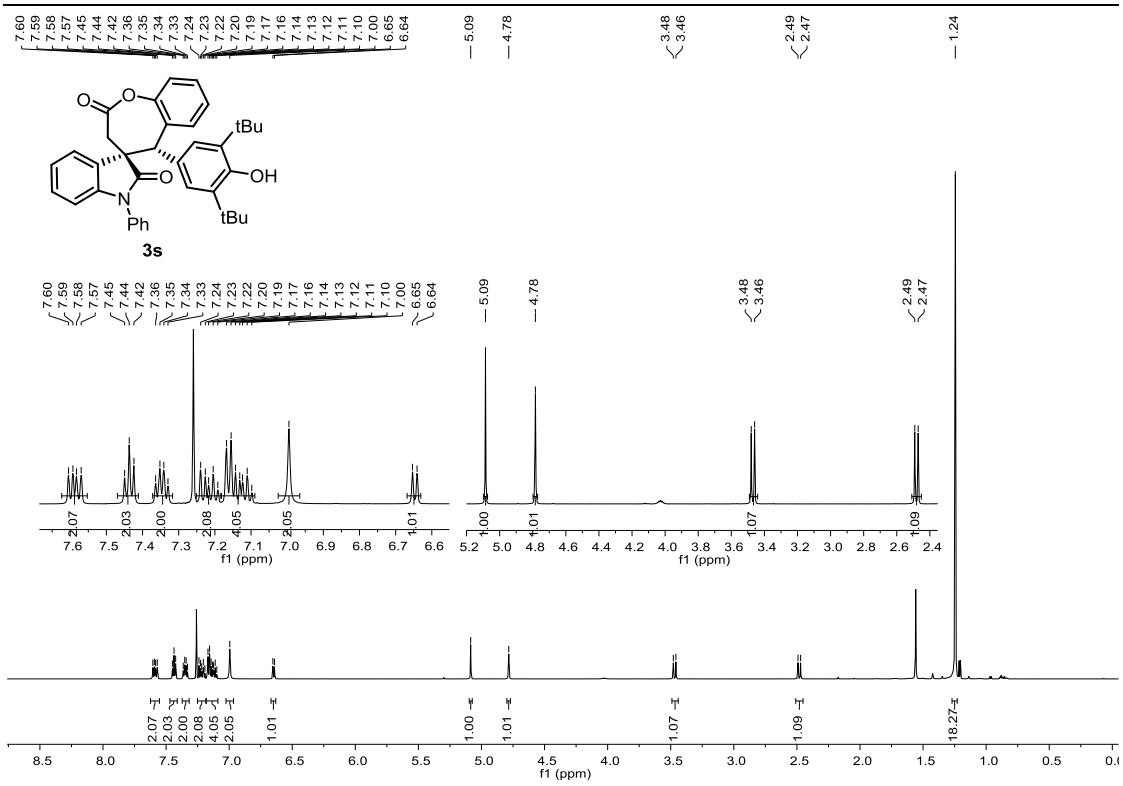
142.09
135.14
130.83
129.77
128.60
128.48
126.98
125.91
124.50
123.32
122.82
119.54
107.74
77.23
77.02
76.80
56.56
51.56
39.40
34.17
30.28
26.31
f1 (ppm)


3r
f1 (ppm)


f1 (ppm)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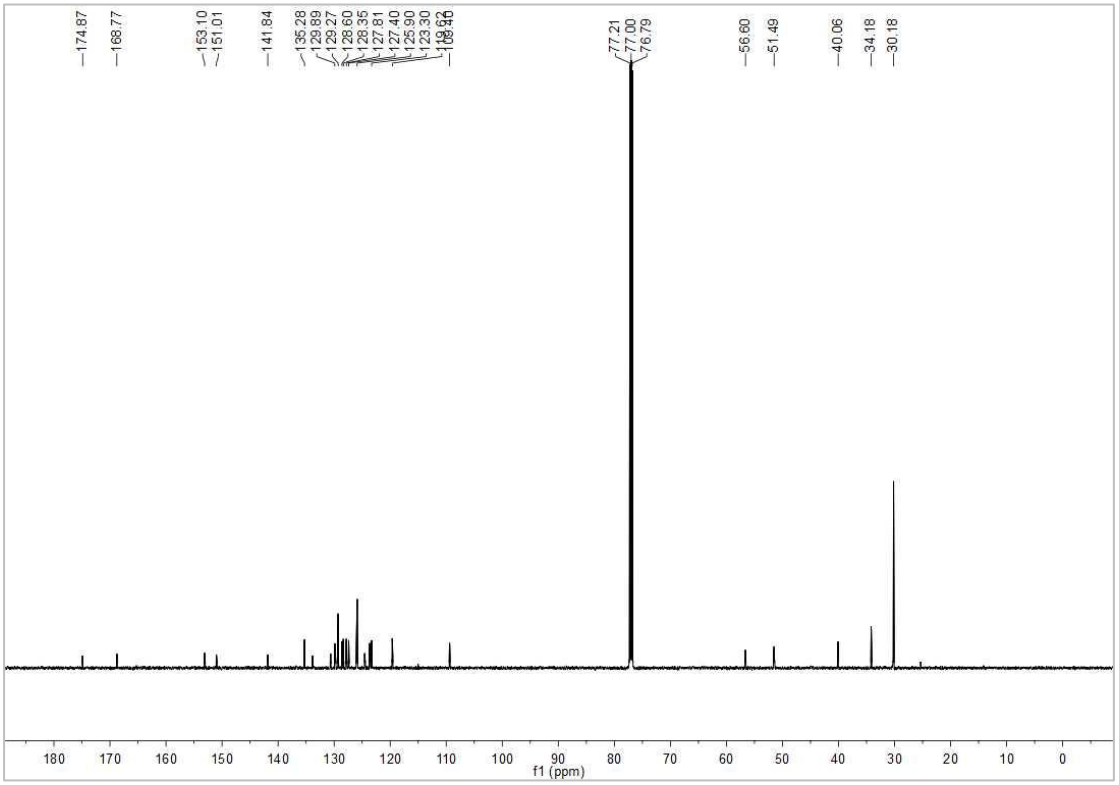
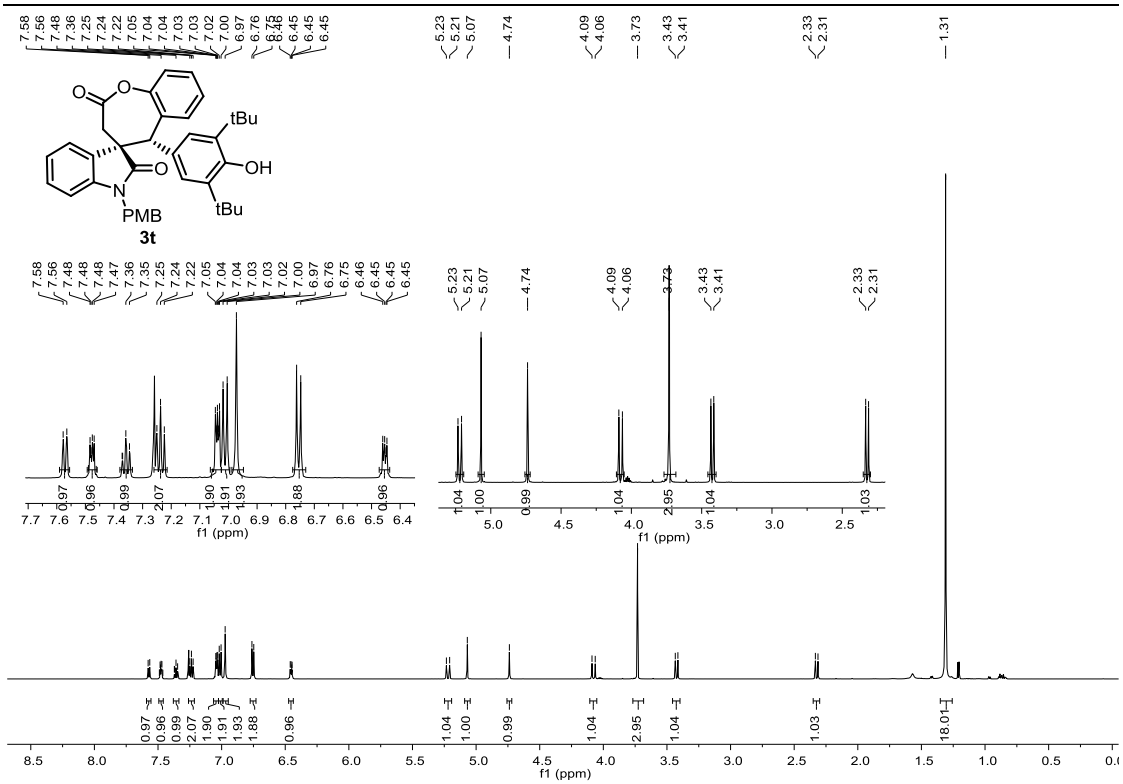
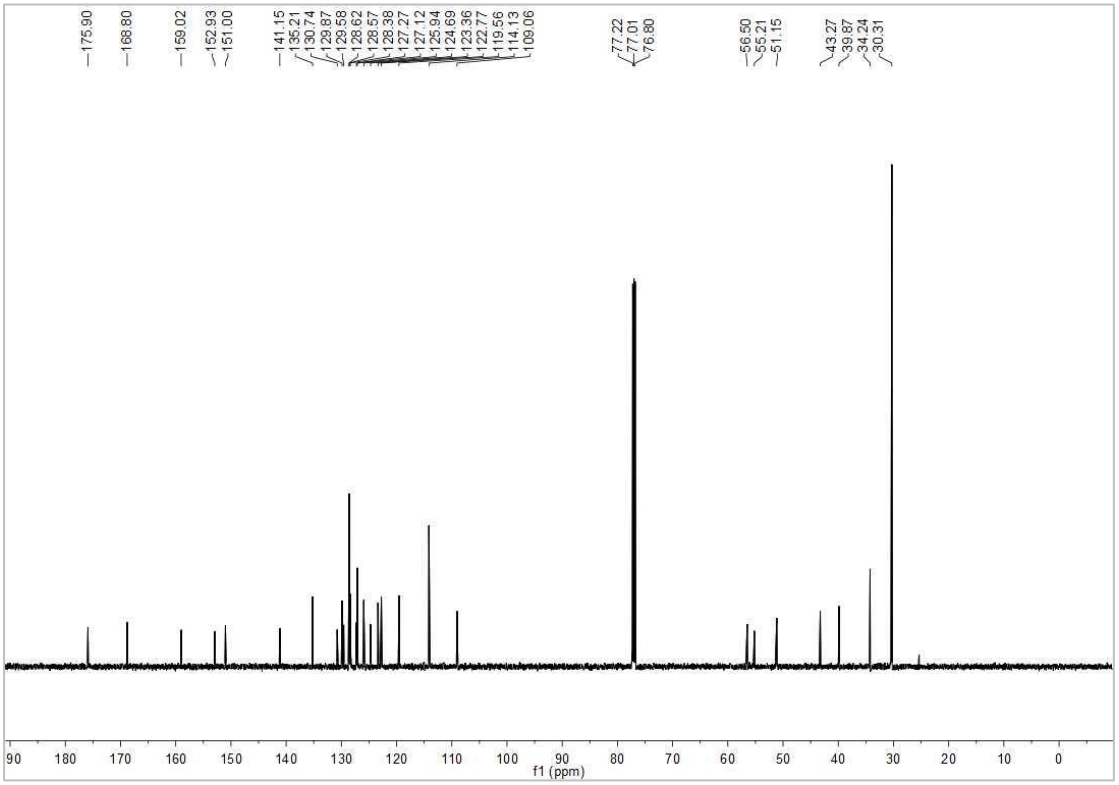
OH
tBu
O
O
O
N
Ph
3s
f1 (ppm)


f1 (ppm)


tBu
OH
tBu
O
O
O
N
PMB
3t
f1 (ppm)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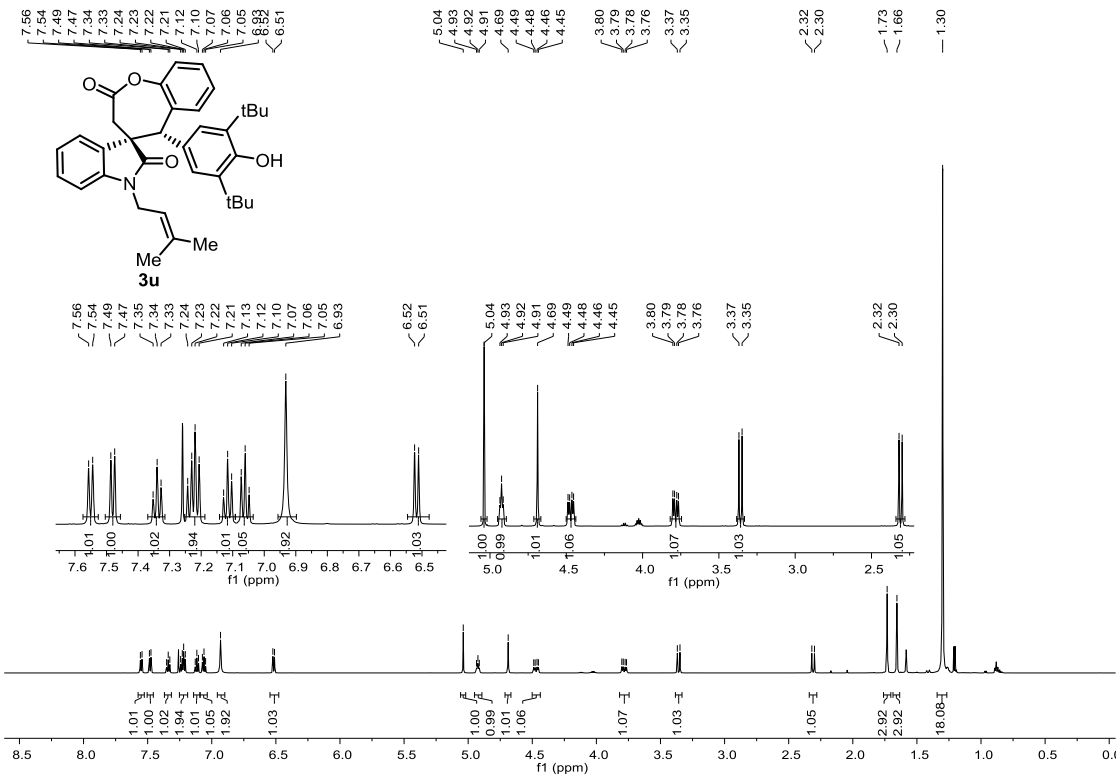
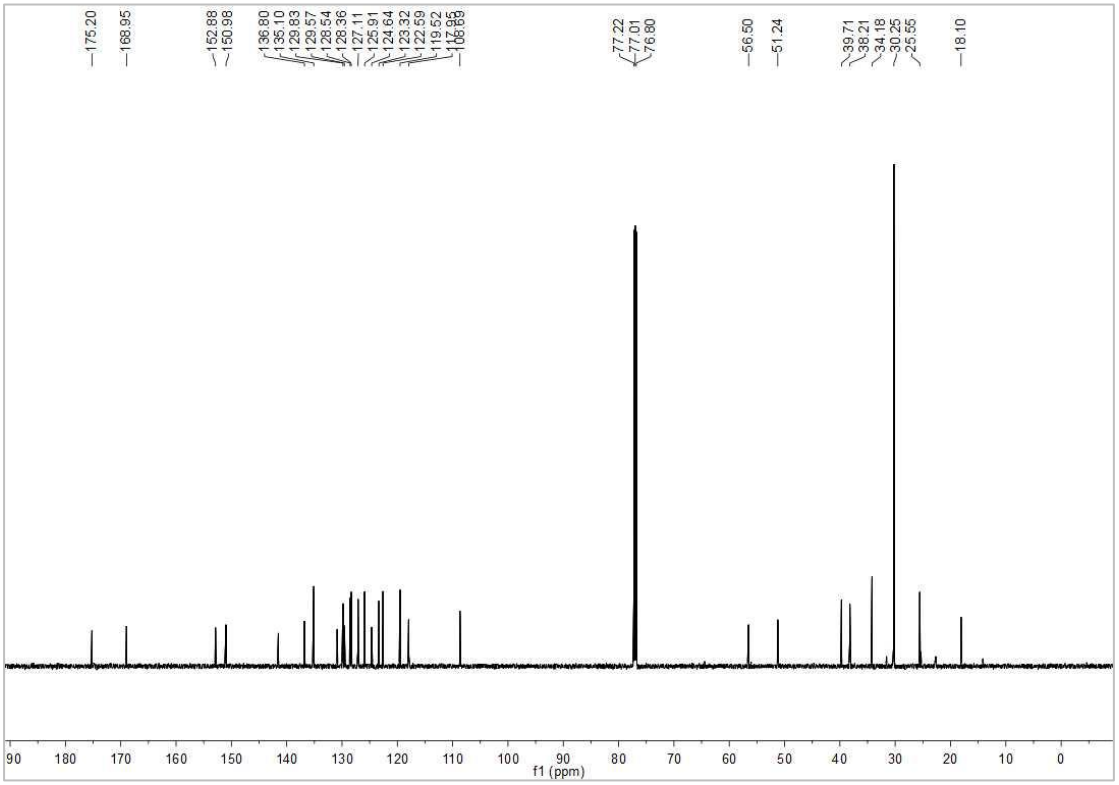
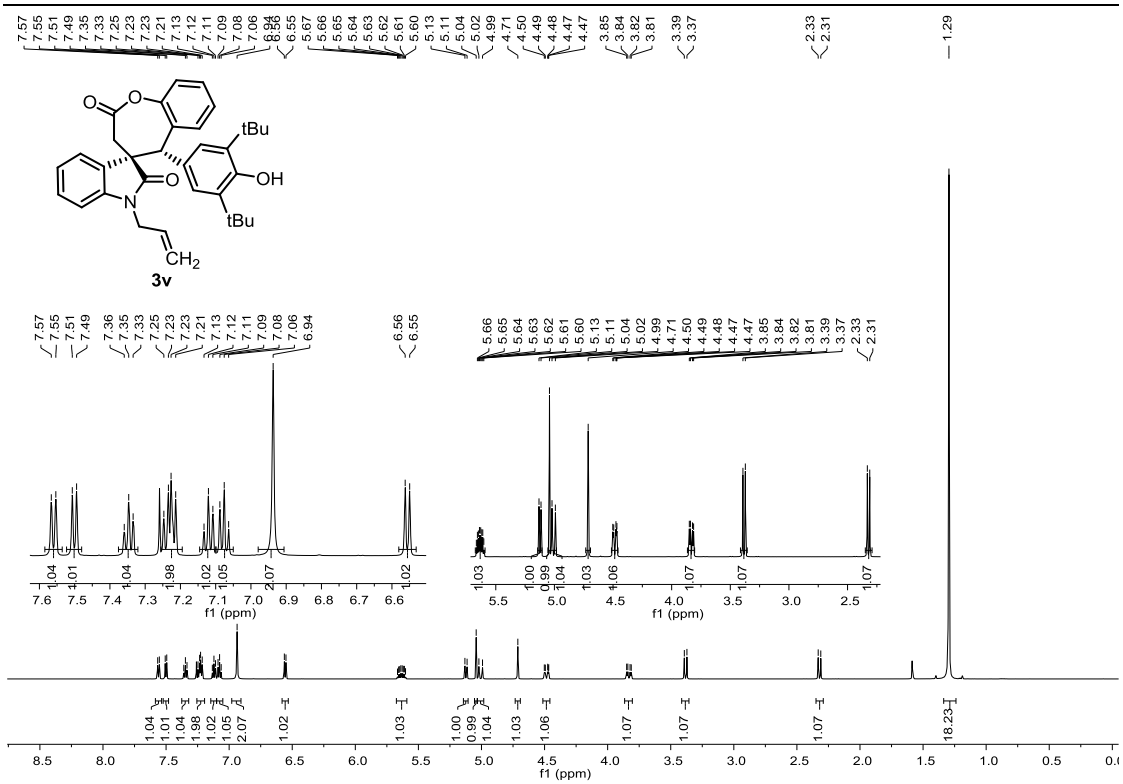
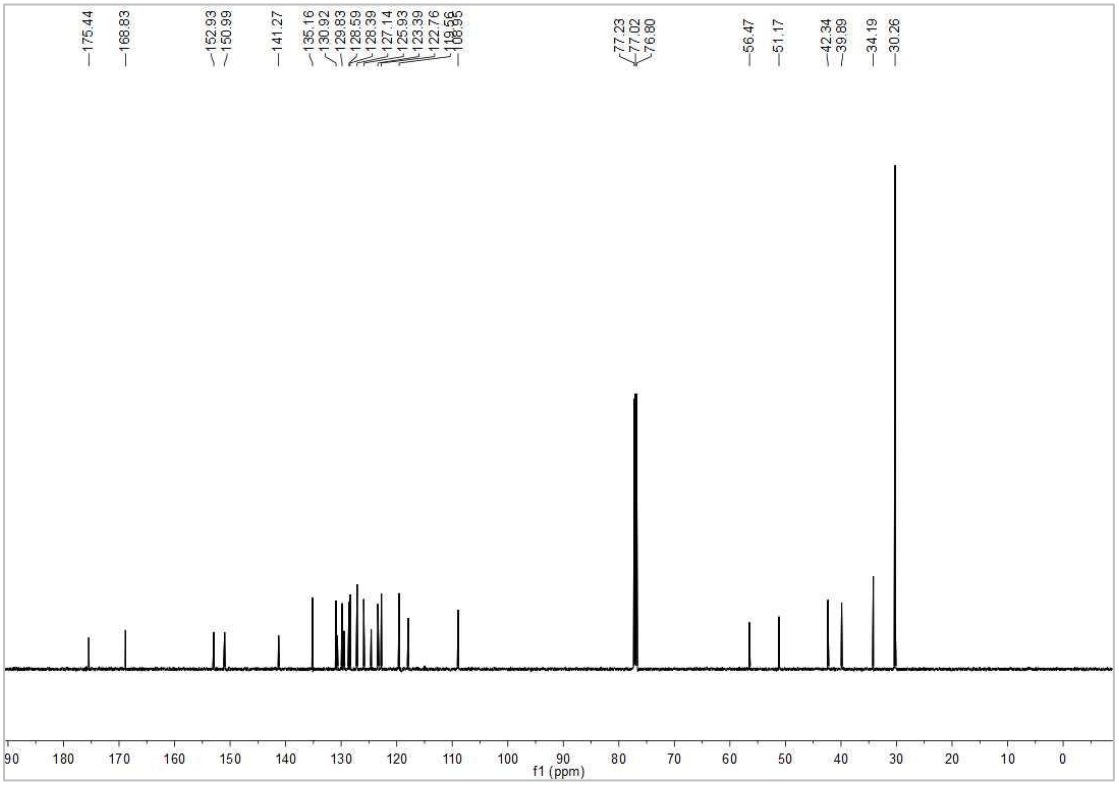
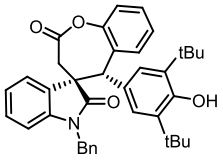

7.56 7.54 7.49 7.47 7.34 7.33 7.24 7.23 7.22 7.21 7.12 7.10 7.07 7.06 7.05 6.93 6.52 6.51
5.04 4.93 4.92 4.91 4.69 4.49 4.48 4.46 4.45
3.80 3.79 3.78 3.76 3.37 3.35
2.32 2.30
1.73 1.66
1.30
O
O
O
N
tBu
OH
tBu
Me
Me
3u
1.01 1.00 1.02 1.94 1.01 1.05 1.92 1.03
1.00 0.99 1.01 1.06 1.07 1.03 1.05 2.92 2.92 18.08
f1 (ppm)


175.20 168.95 152.88 150.98 136.80 135.10 129.83 129.57 128.54 128.36 127.11 125.91 124.64 123.32 122.59 119.52 77.22 77.01 76.80 56.50 51.24 39.71 38.21 34.18 30.25 25.55 18.10
f1 (ppm)


tBu
OH
tBu
CH2
3v
f1 (ppm)


f1 (ppm)

Part IV HPLC Data



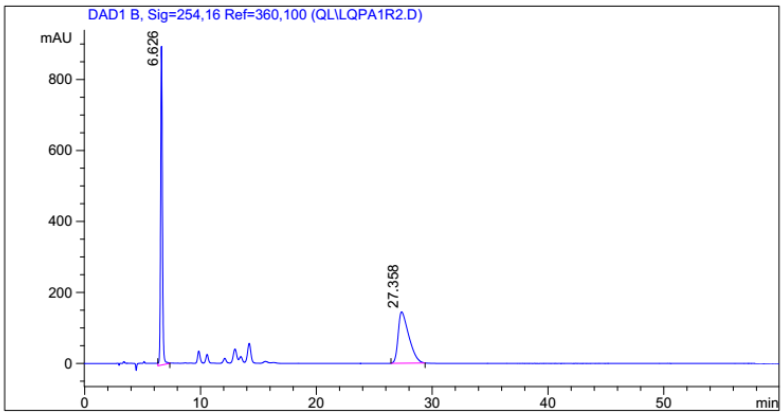
3a

Sample Name: LQ-P-A1 rac
Data file: D:\GONZO\QL\LQPA1R2.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

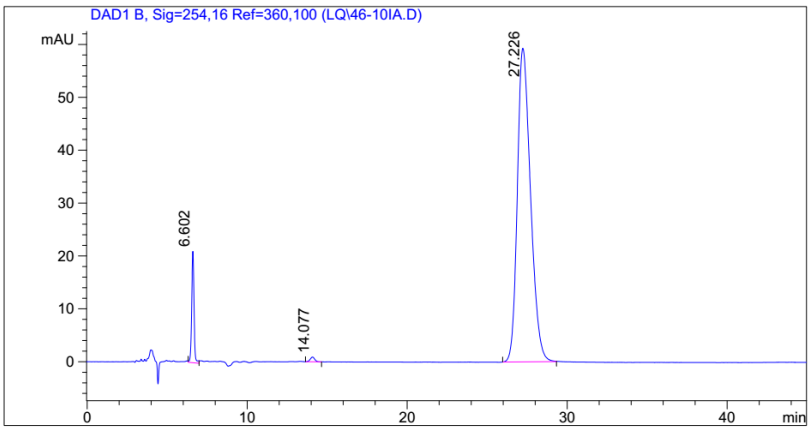
Column: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 14:00:29
Injektion Date: 08.12.2017

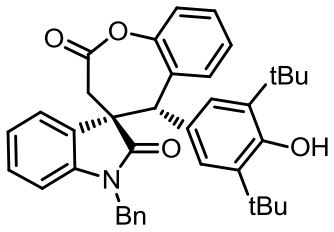
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.6	46.7
Flow in ml/min:	1.0	1.0



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.63	0.16	898.41	9575.01	50.87
2	27.36	0.91	144.84	9247.29	49.13
Total				18822.29	100.00

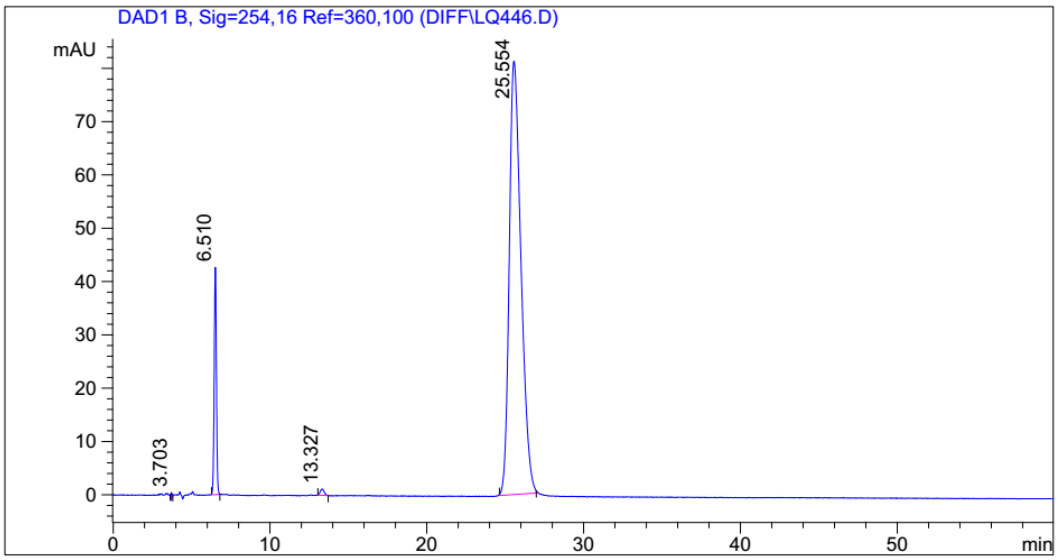


#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.60	0.16	21.07	214.80	5.92
2	14.08	0.30	0.89	17.63	0.49
3	27.23	0.88	59.33	3396.73	93.60
Total				3629.16	100.00

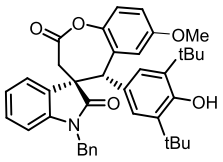


3a, 1 mmol scale

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	45.8	46.6
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.70	0.07	1.28	6.77	0.15
2	6.51	0.15	42.65	415.91	8.92
3	13.33	0.24	1.16	20.85	0.45
4	25.55	0.77	81.31	4216.70	90.48
Total				4660.22	100.00



3b

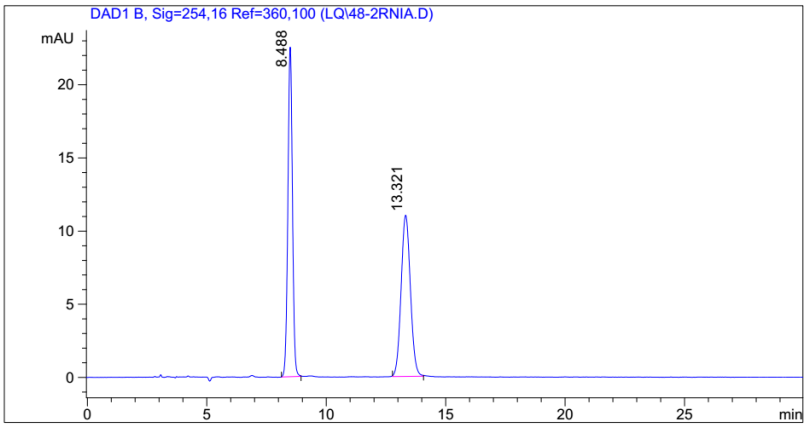
HEWLETT PACKARD

```
Sample Name:          LQ 48-2rac
Data file:            D:\GONZO\LQ\48-2RNIA.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 9:1;
                      The sample is solved in MP

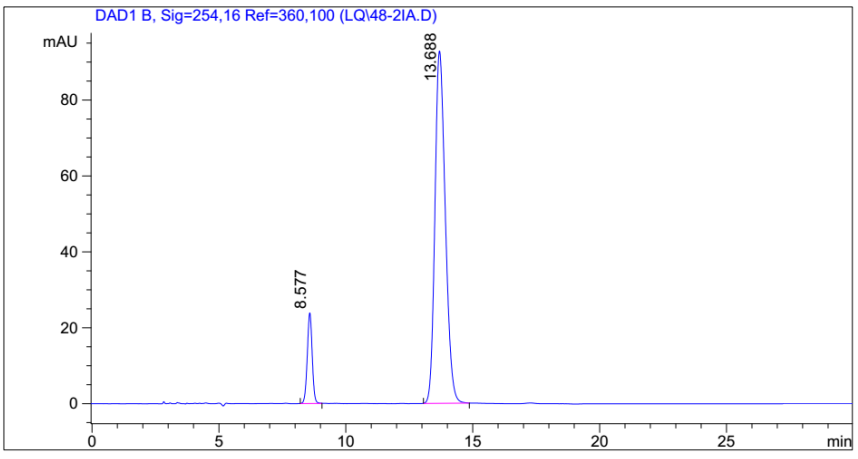
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       11:34:28
 Injektion Date:       23.02.2018

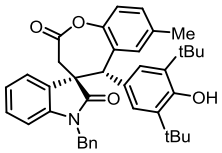
 Instrument Conditions:   At Start             At Stop
 Temperature in°C:          30.0                 30.0
 Pressure in bar:           46.1                 46.5
 Flow in ml/min:            1.00                 1.00
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	8.49	0.21	22.53	299.94	50.17
2	13.32	0.42	11.03	297.89	49.83
Total				597.83	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	8.58	0.21	23.89	322.25	10.86
2	13.69	0.44	92.88	2645.68	89.14
Total				2967.93	100.00



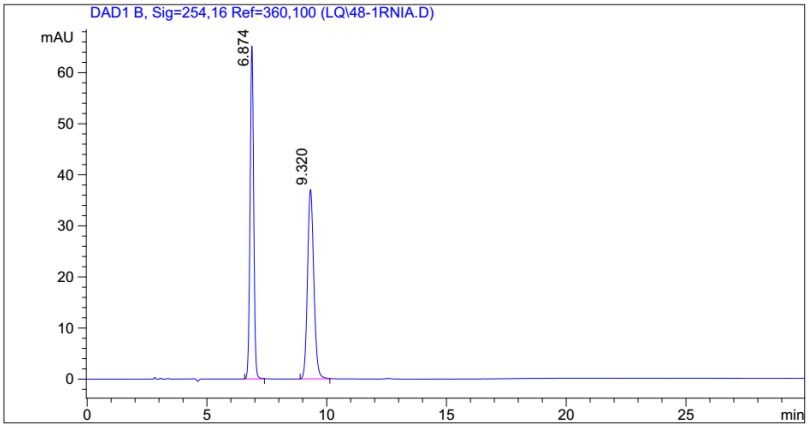
3c

Sample Name: LQ 48-1rac
Data file: D:\GONZO\LQ\48-1RNIA.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

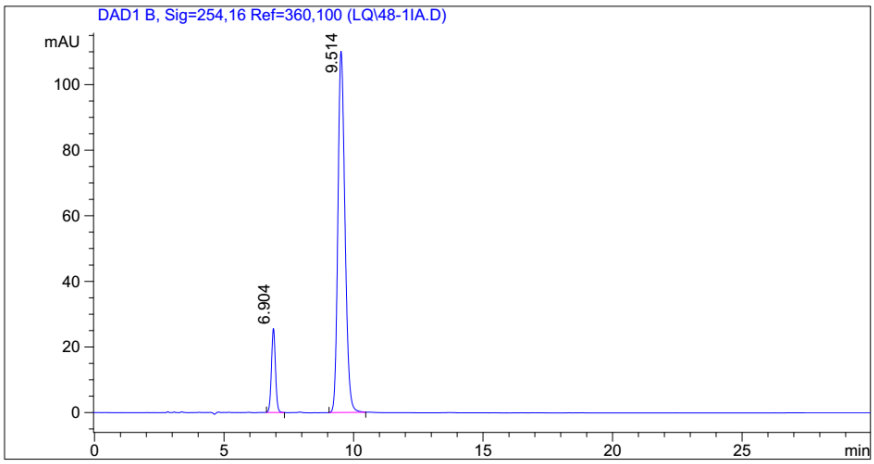
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 11:03:10
Injektion Date: 23.02.2018

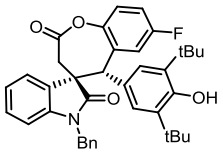
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.6	47.0
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.87	0.16	65.22	682.34	50.06
2	9.32	0.28	37.11	680.71	49.94
Total				1363.05	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.90	0.17	25.62	277.52	11.71
2	9.51	0.29	110.19	2092.22	88.29
Total				2369.73	100.00



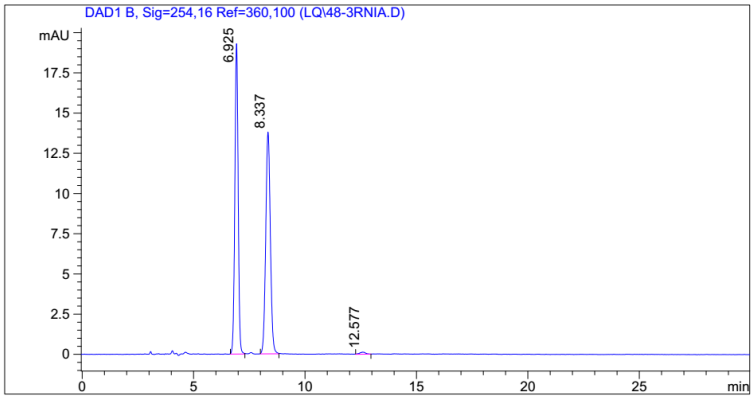
3d

Sample Name: LQ 48-3 rac
Data file: D:\GONZO\LQ\48-3RNIA.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

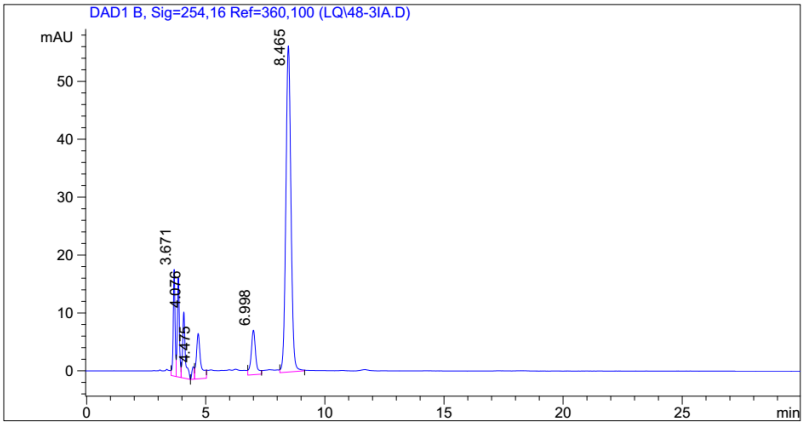
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 12:05:41
Injektion Date: 23.02.2018

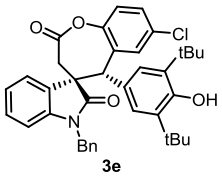
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.6	47.0
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.92	0.16	19.30	199.18	49.77
2	8.34	0.22	13.79	198.61	49.62
3	12.58	0.31	0.13	2.45	0.61
Total				400.24	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.67	0.08	18.44	97.90	7.30
2	3.85	0.09	17.20	102.58	7.65
3	4.08	0.11	11.42	89.58	6.68
4	4.47	0.11	2.15	14.75	1.10
5	4.68	0.18	7.85	99.89	7.45
6	7.00	0.20	7.71	100.87	7.52
7	8.46	0.23	56.35	835.29	62.29
Total				1340.86	100.00



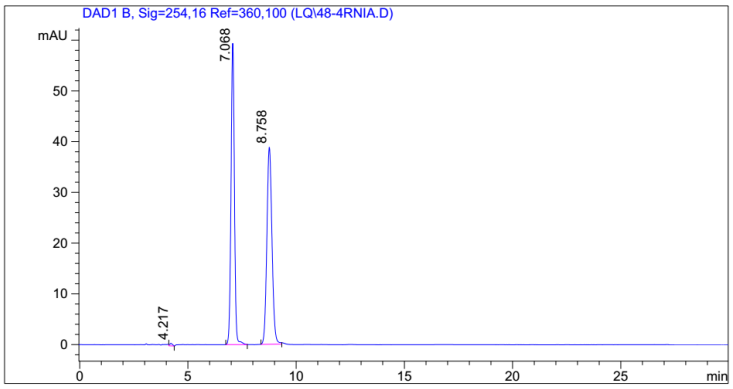
3e

Sample Name: LQ 48-4 rac
Data file: D:\GONZO\LQ\48-4RNIA.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

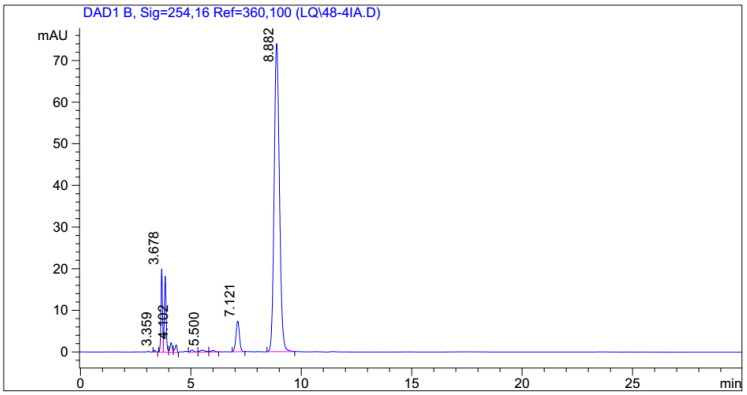
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 12:36:53
Injektion Date: 23.02.2018

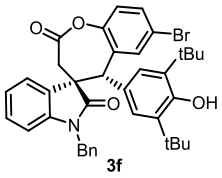
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.2	46.4
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.22	0.12	0.51	4.41	0.34
2	7.07	0.17	59.37	647.77	50.19
3	8.76	0.26	38.86	638.38	49.47
Total				1290.56	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.36	0.08	0.50	2.72	0.17
2	3.68	0.08	20.01	98.83	6.32
3	3.84	0.09	18.30	103.85	6.64
4	4.10	0.10	2.35	15.67	1.00
5	4.33	0.10	1.86	12.68	0.81
6	5.06	0.18	0.54	6.67	0.43
7	5.50	0.23	0.50	8.31	0.53
8	6.00	0.19	0.34	4.42	0.28
9	7.12	0.17	7.35	81.09	5.19
10	8.88	0.26	74.03	1229.74	78.63
Total				1563.97	100.00

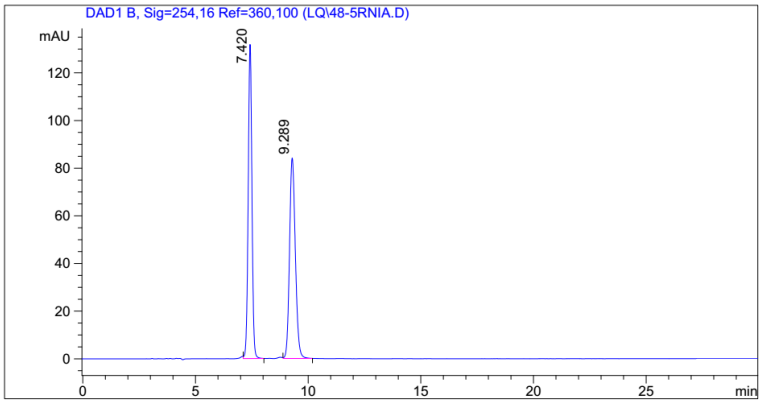


3f

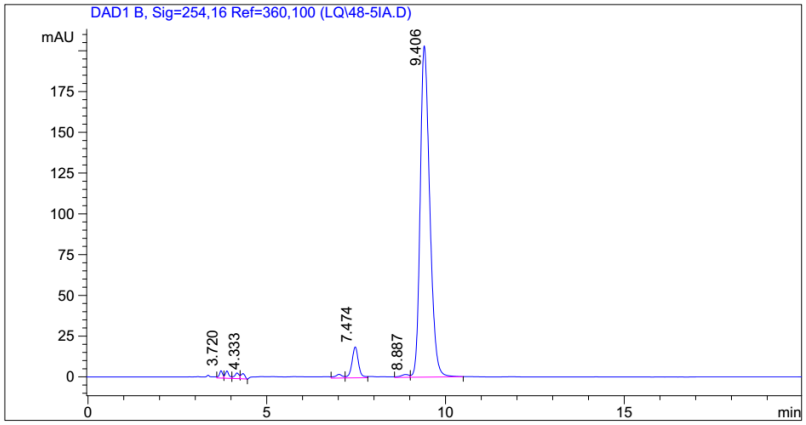
HEWLETT PACKARD

Sample Name:	LQ 48-5 rac
Data file:	D:\GONZO\LQ\48-5RNIA.D
Sample Info:	Mobile phase: n-Heptan/iPrOH 9:1; The sample is solved in MP
Methode file:	IA.M
Column-info:	Chiralpak IA (250x4,6)mm
Operator:	Analytical Lab 4.03 - 4.04
Injektion Time:	13:08:03
Injektion Date:	23.02.2018

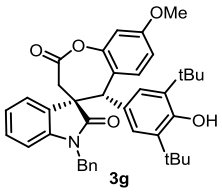
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.3	46.8
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	7.42	0.18	131.88	1518.26	50.06
2	9.29	0.28	84.13	1514.91	49.94
Total				3033.17	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.72	0.09	4.55	28.82	0.69
2	3.89	0.11	4.53	33.22	0.79
3	4.17	0.13	3.52	31.34	0.75
4	4.33	0.12	3.27	24.90	0.59
5	7.02	0.20	2.32	33.45	0.80
6	7.47	0.19	19.05	241.11	5.75
7	8.89	0.25	1.80	30.26	0.72
8	9.41	0.28	203.26	3770.79	89.91
Total				4193.88	100.00



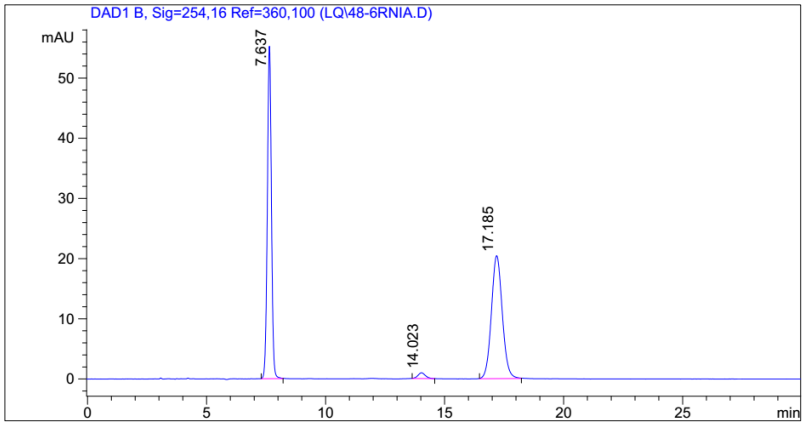
3g

Sample Name: LQ 48-6 rac
Data file: D:\GONZO\LQ\48-6RNIA.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

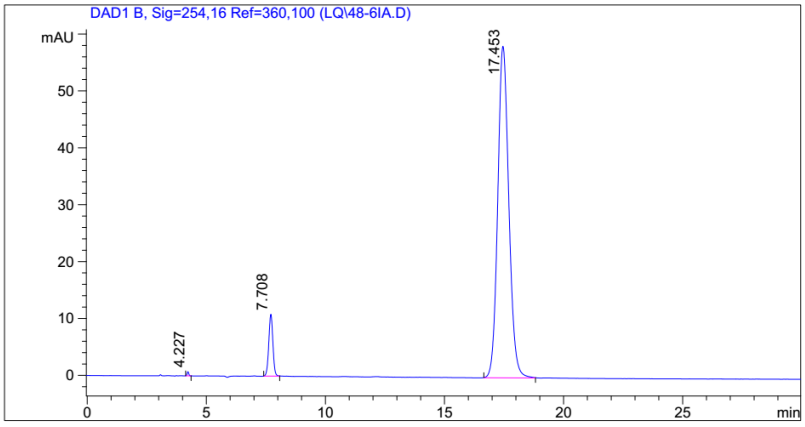
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 13:39:15
Injektion Date: 23.02.2018

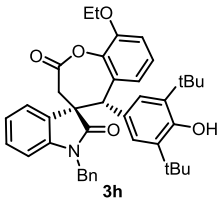
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.2	46.3
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	7.64	0.18	55.27	658.57	49.49
2	14.02	0.33	0.97	21.70	1.63
3	17.19	0.49	20.44	650.58	48.88
Total				1330.85	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.23	0.07	0.74	3.54	0.18
2	7.71	0.19	10.88	130.49	6.47
3	17.45	0.50	58.29	1883.80	93.36
Total				2017.84	100.00



3h

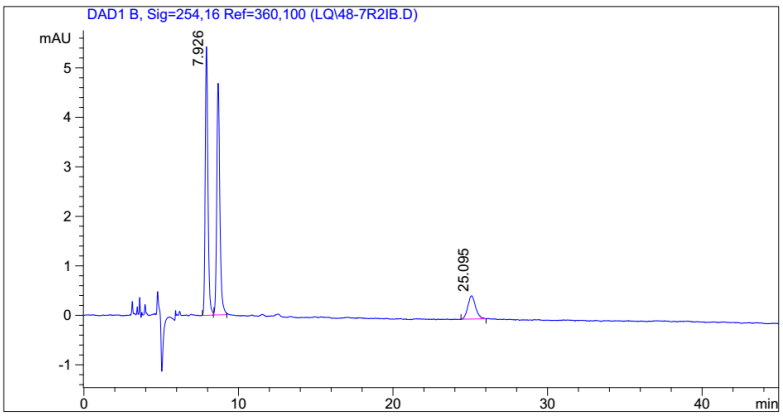
HEWLETT PACKARD

```
Sample Name:          LQ 48-7 rac
Data file:            D:\GONZO\LQ\48-7R2IB.D
Sample Info:          Mobile phase: n-Heptan/EtOH 97:3;
                      The sample is solved in MP

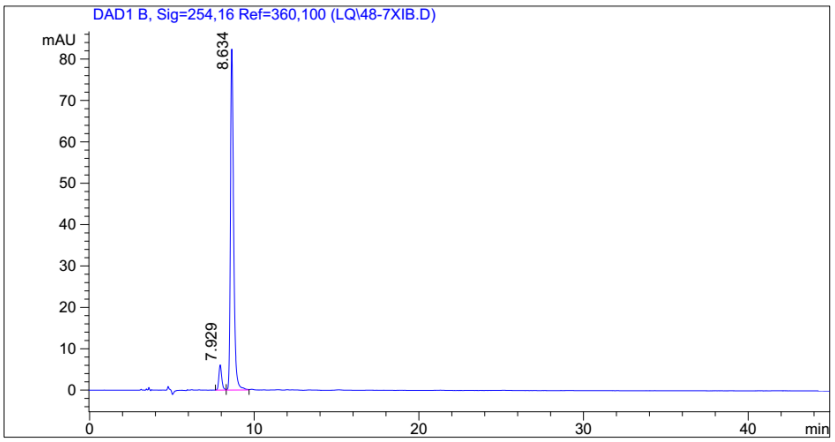
Methode file:         IB.M
Column-info:          Chiralpak IB (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       13:58:32
 Injektion Date:       27.02.2018

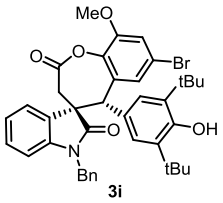
 Instrument Conditions:   At Start             At Stop
 Temperature in°C:          30.0                 30.0
 Pressure in bar:           43.3                 43.7
 Flow in ml/min:            1.00                 1.00
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	7.93	0.19	5.43	65.72	44.53
2	8.68	0.21	4.68	65.50	44.38
3	25.09	0.43	0.47	16.38	11.09
Total				147.60	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	7.93	0.19	6.10	74.22	6.26
2	8.63	0.21	82.48	1111.34	93.74
Total				1185.55	100.00



3i

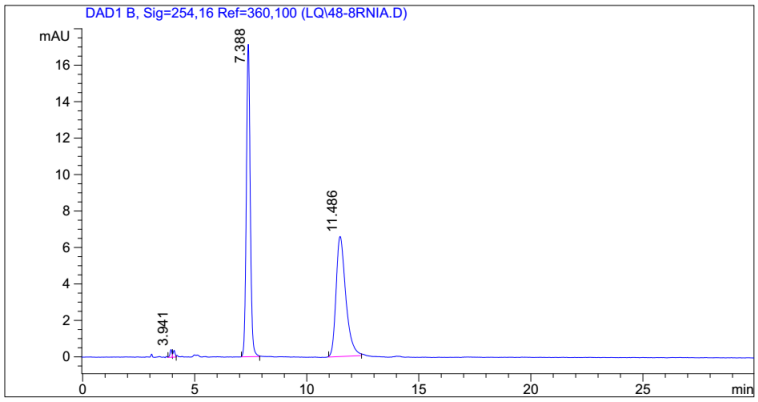
HEWLETT PACKARD

```
Sample Name:          LQ 48-8 rac
Data file:            D:\GONZO\LQ\48-8RNIA.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 9:1;
                      The sample is solved in MP

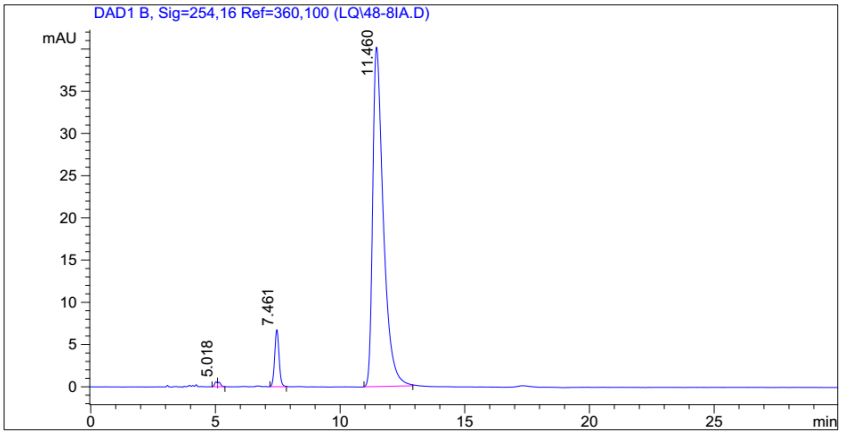
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       14:10:29
 Injektion Date:       23.02.2018

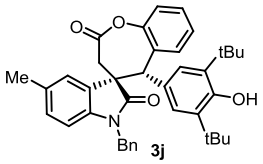
 Instrument Conditions:   At Start              At Stop
 Temperature in°C:          30.0                  30.0
 Pressure in bar:           46.3                  46.6
 Flow in ml/min:            1.00                  1.00
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.94	0.09	0.42	2.51	0.61
2	4.08	0.09	0.37	2.32	0.56
3	7.39	0.18	17.15	207.06	50.39
4	11.49	0.45	6.59	199.05	48.44
Total				410.93	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.02	0.11	0.59	4.28	0.33
2	5.15	0.12	0.55	4.57	0.35
3	7.46	0.19	6.75	82.67	6.41
4	11.46	0.44	40.21	1198.24	92.90
Total				1289.77	100.00



3j

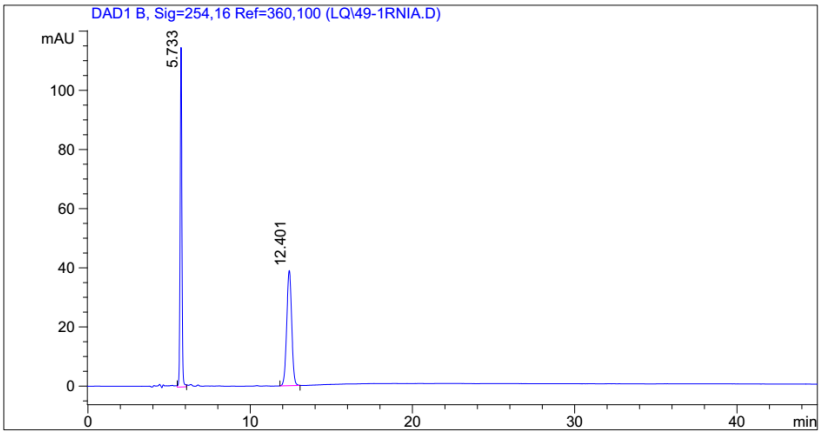
HEWLETT PACKARD

```
Sample Name:          LQ 49-1 rac
Data file:            D:\GONZO\LQ\49-1RNIA.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 7:3;
                      The sample is solved in MP

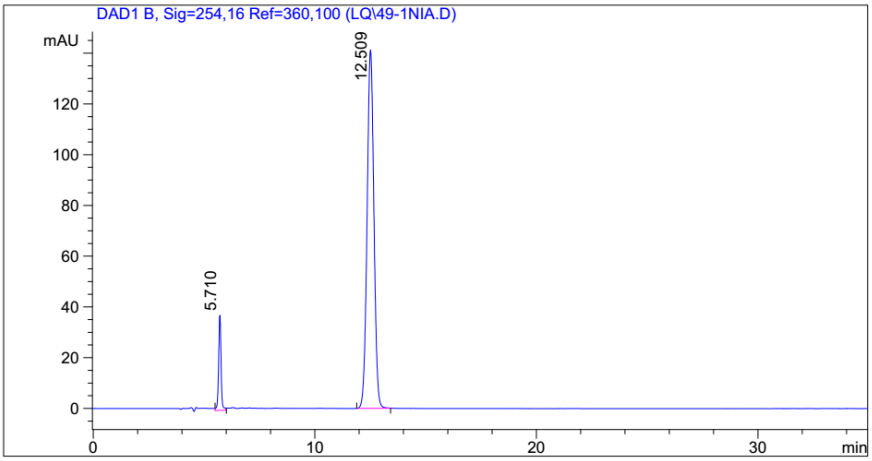
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       11:42:24
 Injektion Date:       20.02.2018

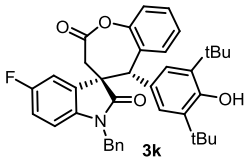
 Instrument Conditions:   At Start            At Stop
 Temperature in°C:          30.0                30.0
 Pressure in bar:           40.8                40.9
 Flow in ml/min:            0.70                0.70
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.73	0.11	114.84	845.21	50.47
2	12.40	0.33	38.97	829.58	49.53
Total				1674.79	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.71	0.12	37.49	288.54	8.75
2	12.51	0.33	141.26	3009.41	91.25
Total				3297.95	100.00



3k

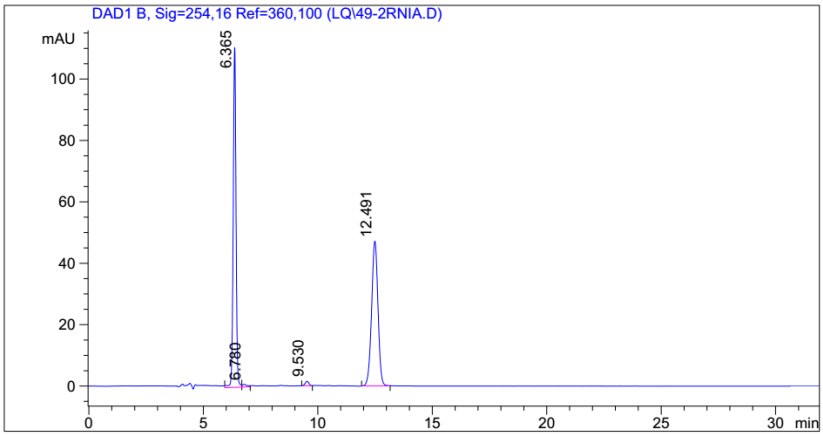
HEWLETT PACKARD

```
Sample Name:          LQ 49-2 rac
Data file:            D:\GONZO\LQ\49-2RNIA.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 7:3;
                      The sample is solved in MP

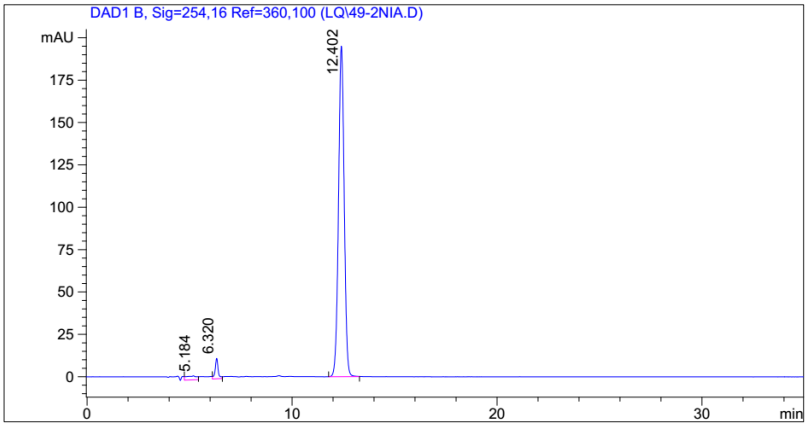
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       12:28:39
 Injektion Date:       20.02.2018

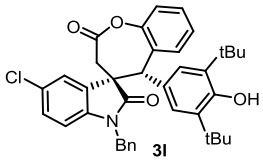
 Instrument Conditions:   At Start            At Stop
 Temperature in°C:          30.0                30.0
 Pressure in bar:           40.9                41.4
 Flow in ml/min:            0.70                0.70
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.37	0.13	110.80	935.01	49.78
2	6.78	0.20	0.85	12.72	0.68
3	9.53	0.18	1.45	16.85	0.90
4	12.49	0.30	47.16	913.87	48.65
Total				1878.44	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.18	0.44	2.40	85.28	2.15
2	6.32	0.15	12.09	124.86	3.15
3	12.40	0.30	195.05	3756.20	94.70
Total				3966.34	100.00



3l

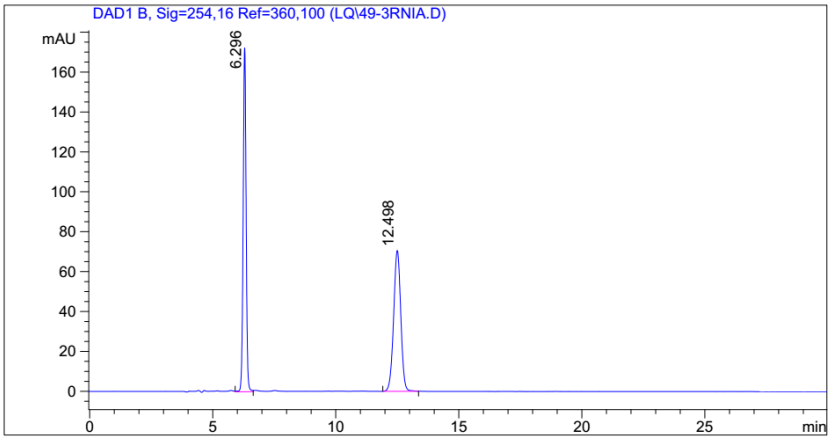
HEWLETT PACKARD

```
Sample Name:          LQ 49-3 rac
Data file:            D:\GONZO\LQ\49-3RNIA.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 7:3;
                      The sample is solved in MP

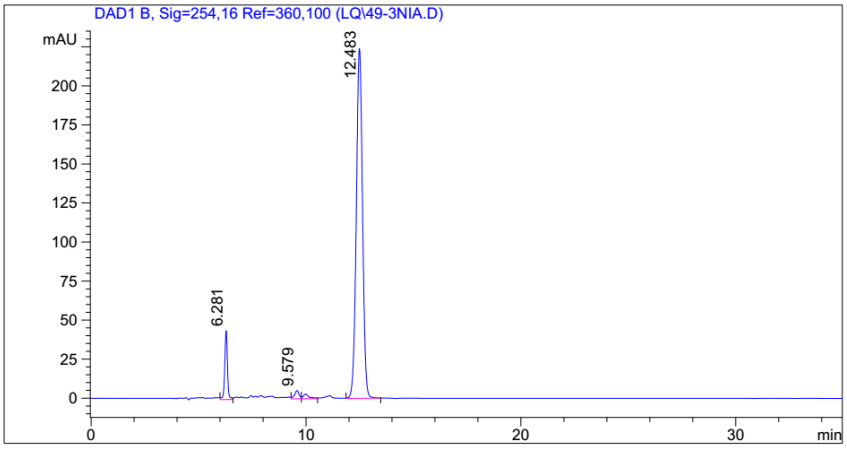
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       13:01:51
 Injektion Date:       20.02.2018

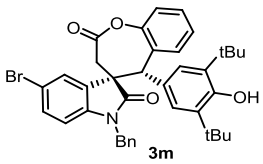
 Instrument Conditions:   At Start            At Stop
 Temperature in°C:          30.0                30.0
 Pressure in bar:           41.1                41.1
 Flow in ml/min:            0.70                0.70
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.30	0.13	172.52	1434.20	50.18
2	12.50	0.31	70.59	1424.05	49.82
Total				2858.26	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.28	0.13	44.02	389.38	7.74
2	9.58	0.22	5.36	79.99	1.59
3	9.98	0.28	3.08	61.13	1.22
4	12.48	0.31	224.04	4497.07	89.45
Total				5027.56	100.00



3m

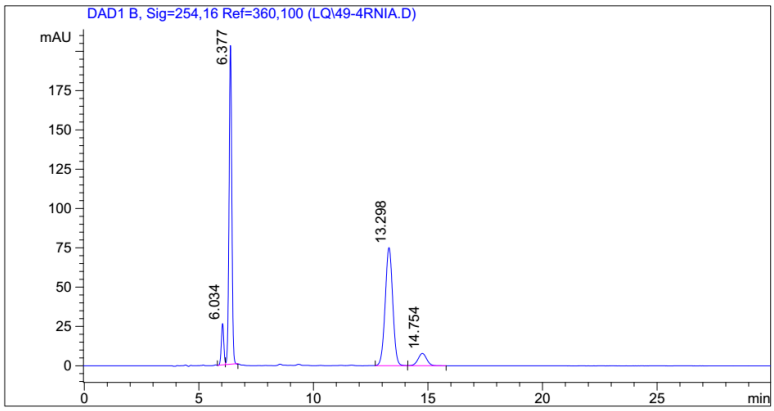
HEWLETT PACKARD

```
Sample Name:          LQ 49-4 rac
Data file:            D:\GONZO\LQ\49-4RNIA.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 7:3;
                      The sample is solved in MP

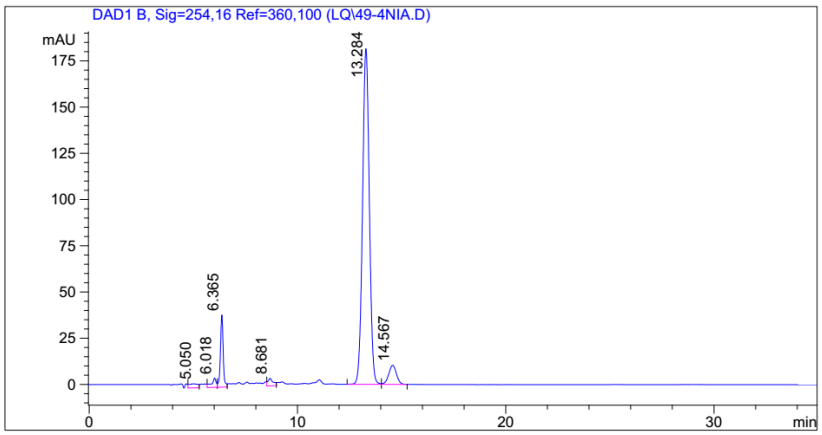
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       13:33:03
 Injektion Date:       20.02.2018

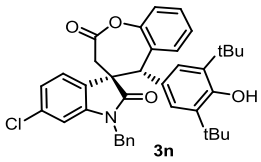
 Instrument Conditions:   At Start            At Stop
 Temperature in°C:          30.0                30.0
 Pressure in bar:           40.8                41.0
 Flow in ml/min:            0.70                0.70
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.03	0.12	26.37	194.74	5.10
2	6.38	0.14	202.98	1694.20	44.40
3	13.30	0.35	75.16	1719.65	45.06
4	14.75	0.41	7.84	207.58	5.44
Total				3816.17	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.05	0.37	2.22	66.79	1.34
2	6.02	0.21	5.06	77.79	1.57
3	6.36	0.14	39.09	364.09	7.33
4	8.68	0.24	4.11	72.66	1.46
5	13.28	0.35	181.58	4116.40	82.88
6	14.57	0.40	10.35	269.14	5.42
Total				4966.87	100.00



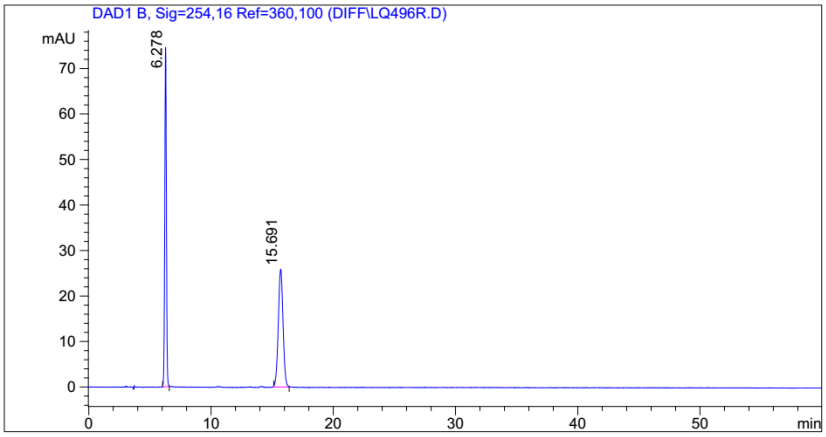
3n

```
Sample Name:          LQ-49-6
Data file:            D:\GONZO\DIFF\LQ496R.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 9:1;
                      The sample is solved in MP

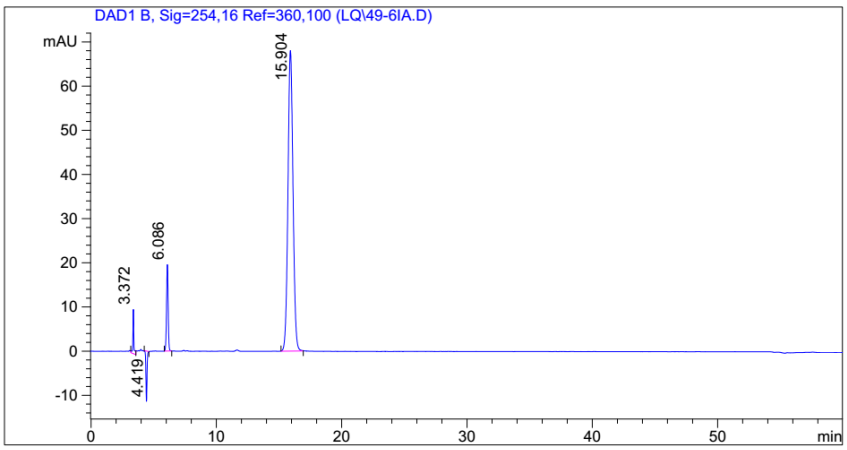
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       17:21:25
 Injektion Date:       16.01.2018

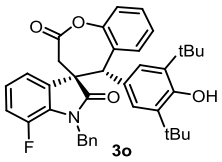
 Instrument Conditions:   At Start            At Stop
 Temperature in°C:          30.0                30.0
 Pressure in bar:           46.2                46.7
 Flow in ml/min:            1.00                1.00
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.28	0.14	74.57	699.30	50.15
2	15.69	0.41	25.89	695.10	49.85
Total				1394.40	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	3.37	0.09	10.06	52.57	2.39
2	4.42	0.10	11.42	67.88	3.08
3	6.09	0.14	19.59	176.17	8.00
4	15.90	0.43	68.06	1906.48	86.54
Total				2203.10	100.00



3o

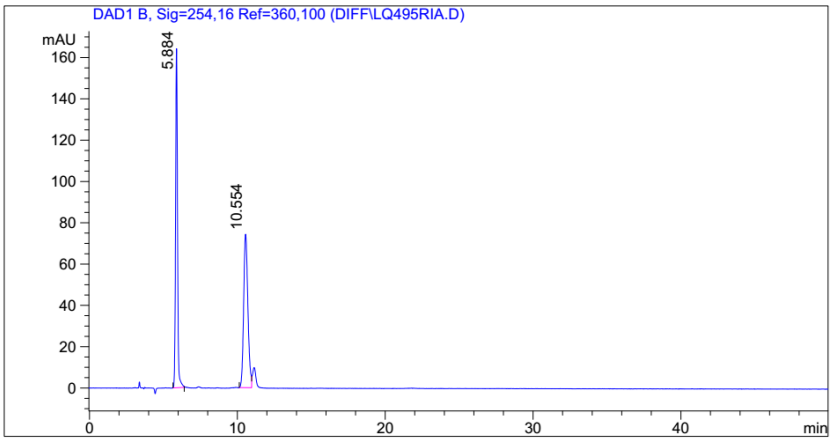
HEWLETT PACKARD

```
Sample Name:          LQ-49-5 rac
Data file:            D:\GONZO\DIFF\LQ495RIA.D
Sample Info:          Mobile phase: n-Heptan/iPrOH 9:1;
                      The sample is solved in MP

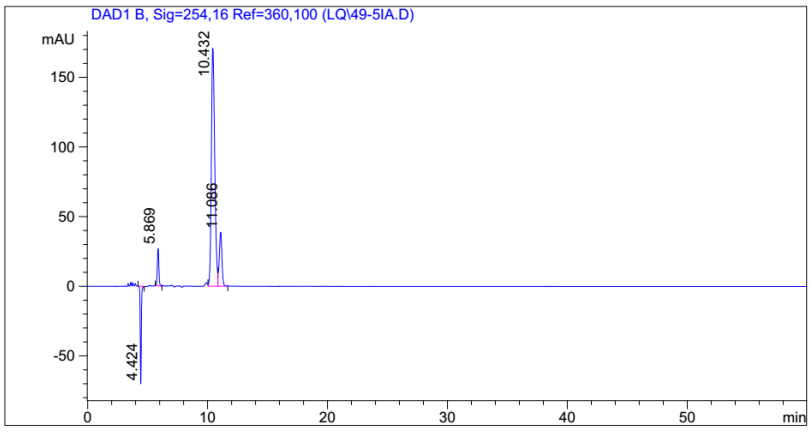
Methode file:         IA.M
Column-info:          Chiralpak IA (250x4,6)mm
Operator:             Analytical Lab 4.03 - 4.04

 Injektion Time:       20:25:12
 Injektion Date:       09.01.2018

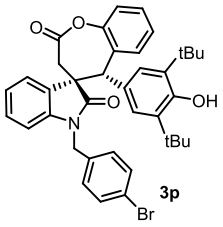
 Instrument Conditions:   At Start            At Stop
 Temperature in°C:          30.0                30.0
 Pressure in bar:           45.5                46.2
 Flow in ml/min:            1.00                1.00
```



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.88	0.14	164.23	1497.95	50.29
2	10.55	0.30	74.35	1480.82	49.71
Total				2978.76	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.42	0.10	70.39	417.09	9.06
2	5.87	0.15	26.59	236.56	5.14
3	10.43	0.30	171.00	3350.92	72.82
4	11.09	0.24	38.66	596.81	12.97
Total				4601.38	100.00



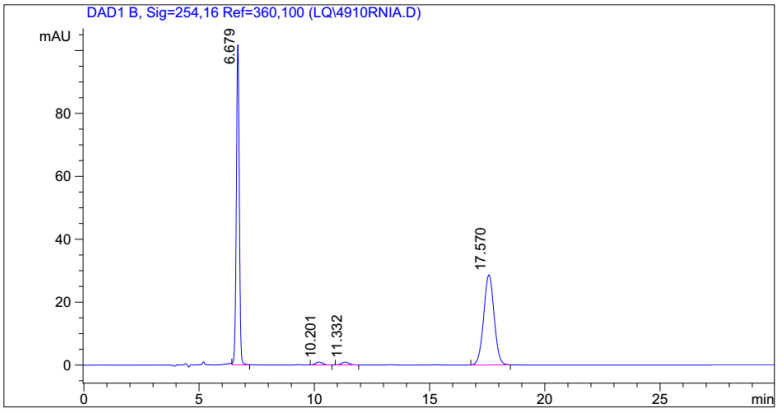
3p

Sample Name: LQ 49-10 rac
Data file: D:\GONZO\LQ\4910RNIA.D
Sample Info: Mobile phase: n-Heptan/iPrOH 7:3;
The sample is solved in MP

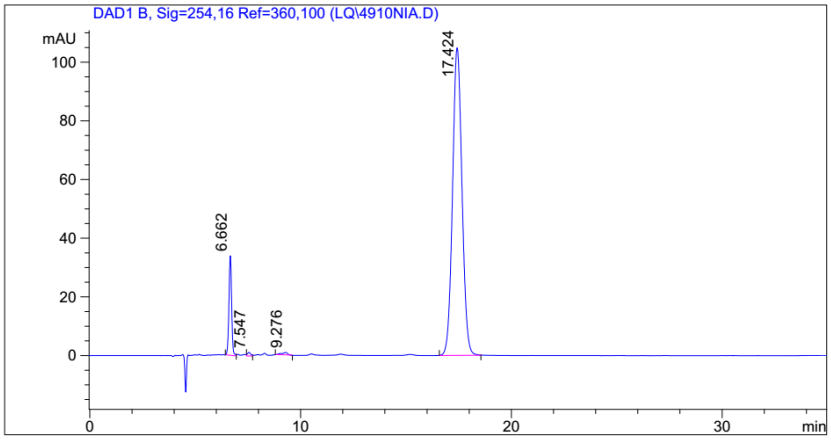
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 14:04:15
Injektion Date: 20.02.2018

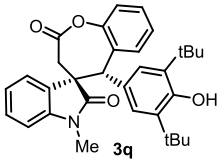
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	40.8	41.2
Flow in ml/min:	0.70	0.70



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.68	0.14	101.89	908.70	49.01
2	10.20	0.33	0.92	20.09	1.08
3	11.33	0.36	0.90	20.95	1.13
4	17.57	0.49	28.69	904.41	48.78
Total				1854.14	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.66	0.15	33.95	302.12	8.39
2	7.55	0.18	1.22	13.03	0.36
3	9.28	0.34	0.86	17.36	0.48
4	17.42	0.48	104.89	3267.28	90.76
Total				3599.79	100.00



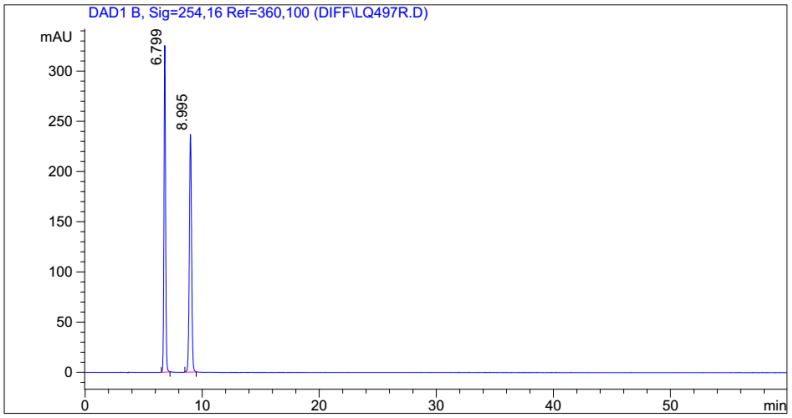
3q

Sample Name: LQ-49-7
Data file: D:\GONZO\DIFF\LQ497R.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

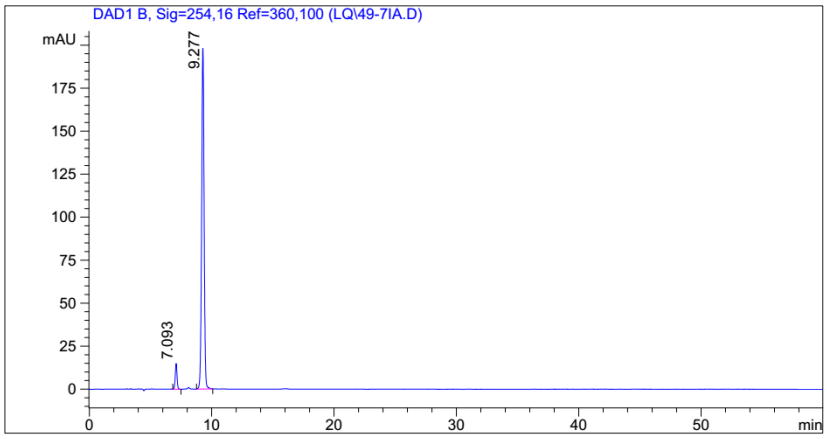
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 18:22:38
Injektion Date: 16.01.2018

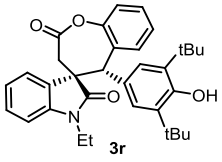
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.3	46.8
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.80	0.15	325.68	3179.91	49.94
2	8.99	0.21	236.82	3187.82	50.06
Total				6367.73	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	7.09	0.16	14.92	153.15	5.26
2	9.28	0.21	198.16	2759.91	94.74
Total				2913.06	100.00



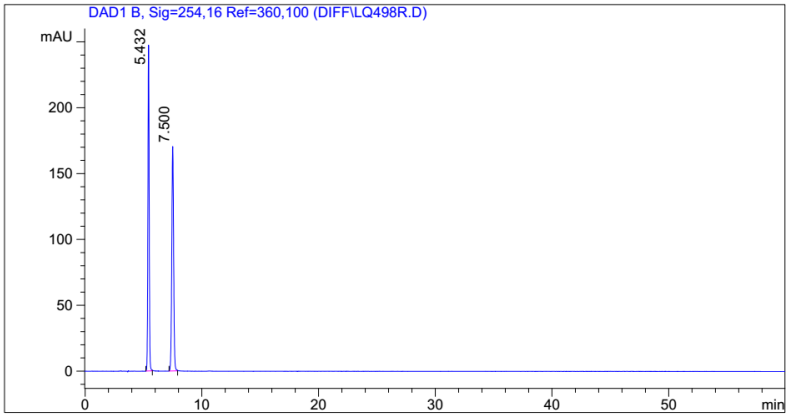
3r

Sample Name: LQ-49-8
Data file: D:\GONZO\DIFF\LQ498R.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

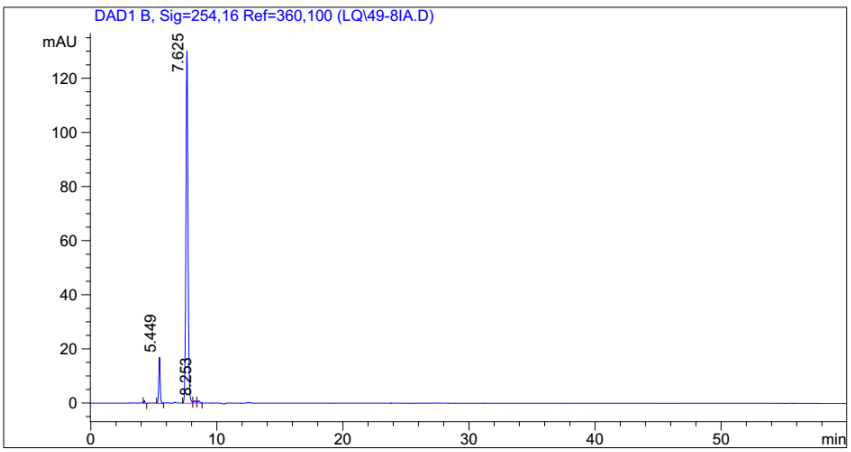
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 19:23:50
Injektion Date: 16.01.2018

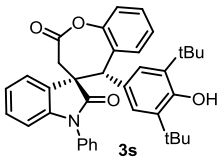
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.2	46.7
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.43	0.12	247.95	1900.11	50.00
2	7.50	0.17	170.51	1900.39	50.00
Total				3800.51	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.25	0.09	1.04	6.19	0.37
2	5.45	0.12	17.08	133.14	8.05
3	7.62	0.18	130.21	1493.47	90.25
4	8.25	0.18	0.94	11.62	0.70
5	8.55	0.18	0.85	10.30	0.62
Total				1654.73	100.00



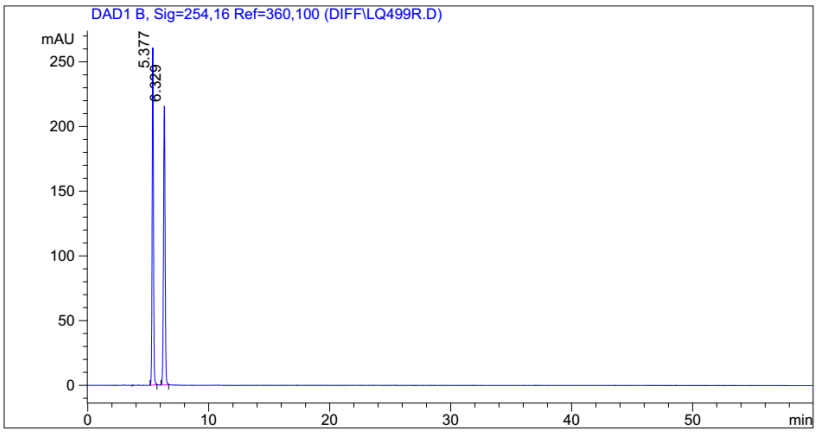
3s

Sample Name: LQ-49-9
Data file: D:\GONZO\DIFF\LQ499R.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

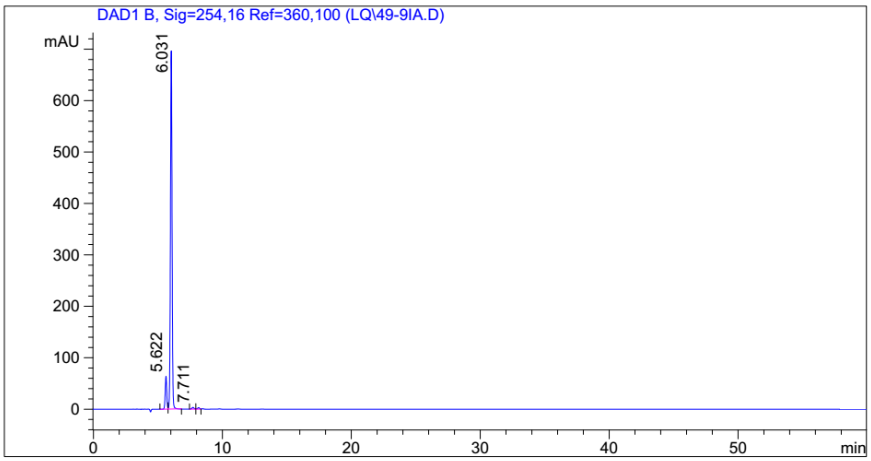
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 20:25:05
Injektion Date: 16.01.2018

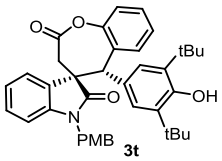
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.2	46.7
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.38	0.12	260.75	1999.32	49.98
2	6.33	0.14	215.48	2000.81	50.02
Total				4000.13	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.62	0.14	63.88	519.15	7.83
2	6.03	0.14	696.78	6044.59	91.11
3	7.71	0.17	3.43	38.87	0.59
4	8.16	0.17	2.82	31.47	0.47
Total				6634.08	100.00



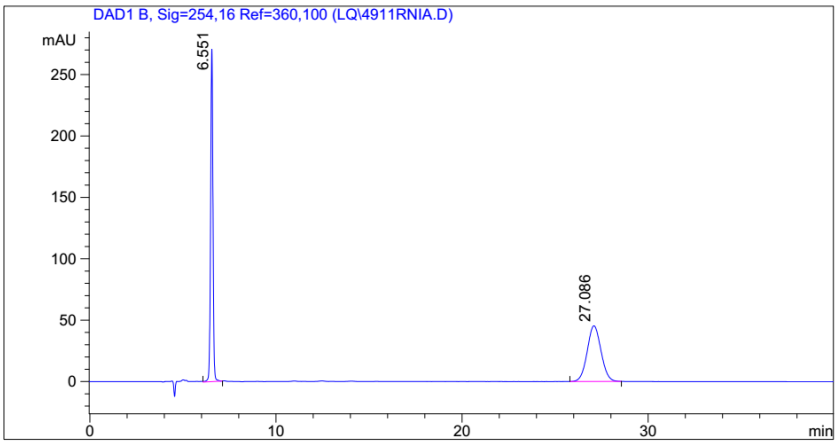
3t

Sample Name: LQ 49-11 rac
Data file: D:\GONZO\LQ\4911RNIA.D
Sample Info: Mobile phase: n-Heptan/iPrOH 7:3;
The sample is solved in MP

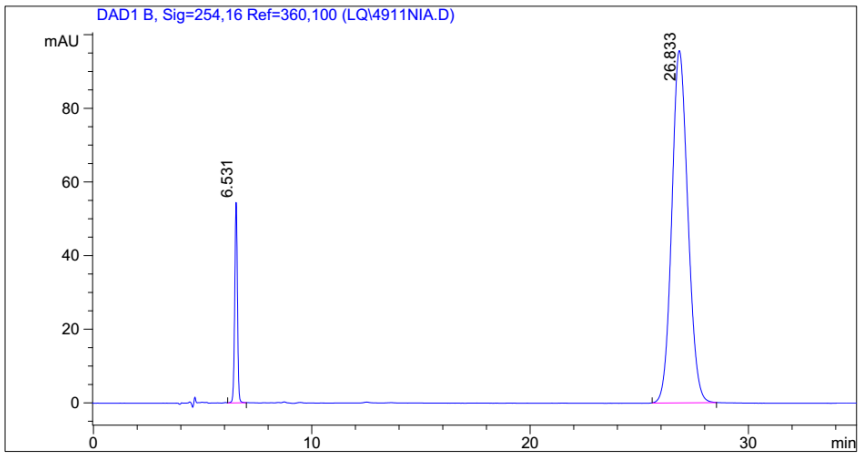
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 14:35:26
Injektion Date: 20.02.2018

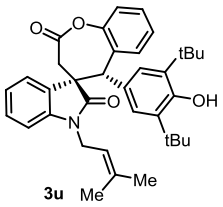
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	40.5	41.0
Flow in ml/min:	0.70	0.70



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.55	0.15	271.30	2373.96	50.30
2	27.09	0.79	45.39	2345.33	49.70
Total				4719.29	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	6.53	0.13	54.47	471.41	8.77
2	26.83	0.79	95.73	4901.90	91.23
Total				5373.31	100.00



3u

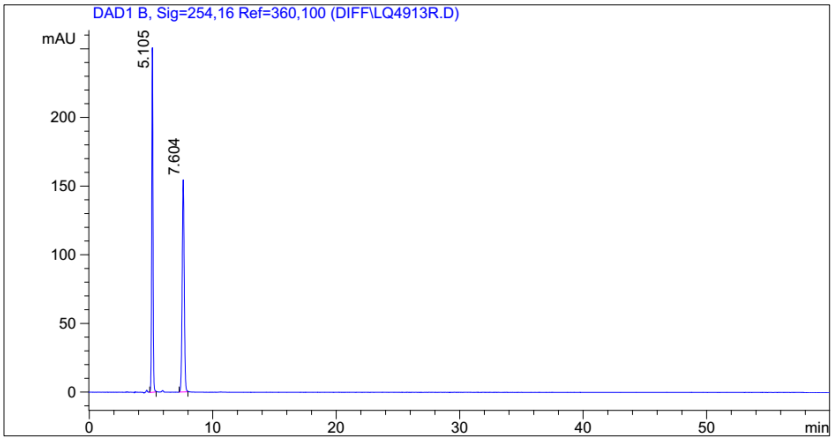
Sample Name: LQ-49-13
Data file: D:\GONZO\DIFF\LQ4913R.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

HEWLETT PACKARD

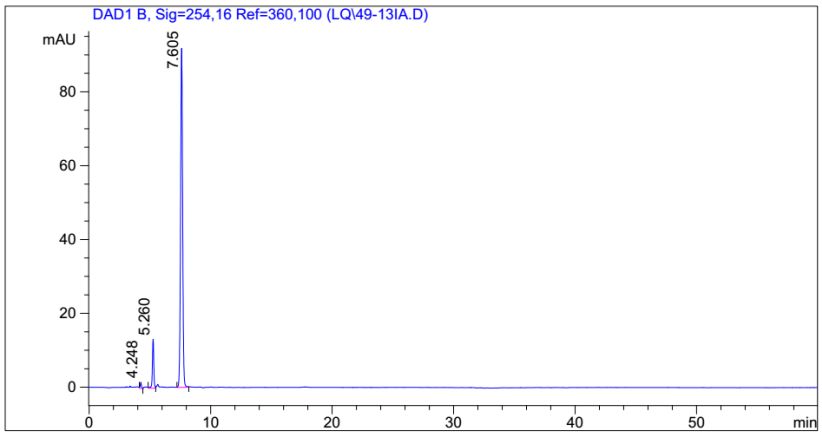
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 23:28:53
Injektion Date: 16.01.2018

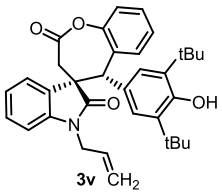
Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	45.9	46.8
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.11	0.11	251.15	1814.11	50.09
2	7.60	0.18	154.66	1807.84	49.91
Total				3621.95	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	4.25	0.10	1.69	11.42	0.95
2	5.26	0.13	13.22	107.78	8.96
3	7.61	0.18	91.74	1084.01	90.09
Total				1203.21	100.00



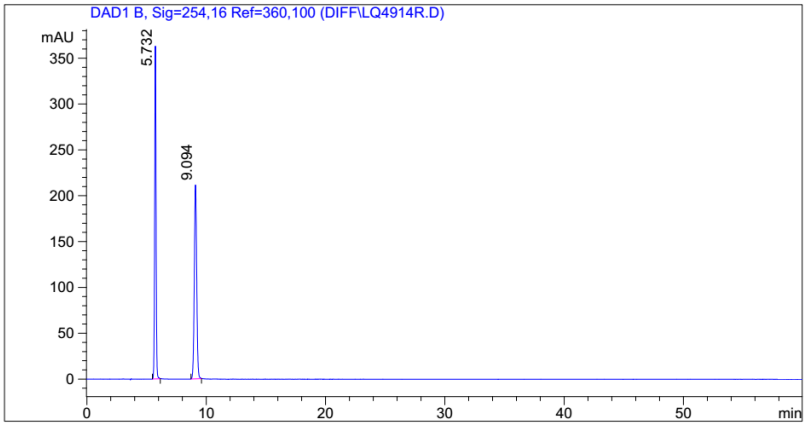
Sample Name: LQ-49-14
Data file: D:\GONZO\DIFF\LQ4914R.D
Sample Info: Mobile phase: n-Heptan/iPrOH 9:1;
The sample is solved in MP

HEWLETT PACKARD

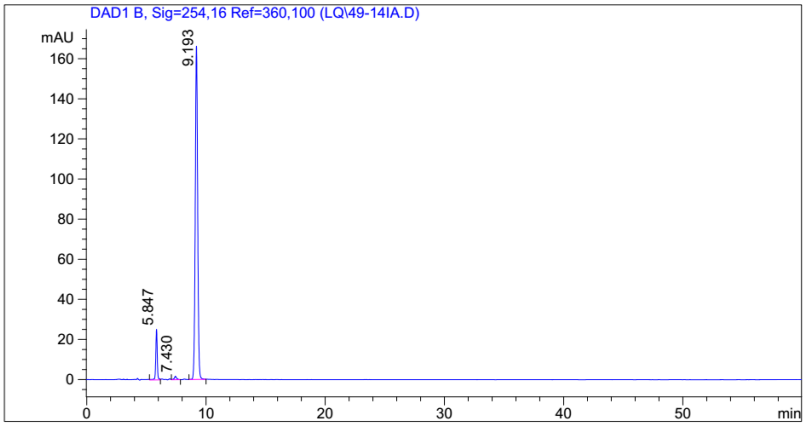
Methode file: IA.M
Column-info: Chiralpak IA (250x4,6)mm
Operator: Analytical Lab 4.03 - 4.04

Injektion Time: 00:30:17
Injektion Date: 17.01.2018

Instrument Conditions:	At Start	At Stop
Temperature in°C:	30.0	30.0
Pressure in bar:	46.3	46.7
Flow in ml/min:	1.00	1.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.73	0.13	363.20	2970.51	50.04
2	9.09	0.22	211.83	2966.35	49.96
Total				5936.86	100.00



#	Ret. Time (min)	Width	Height (mAU)	Area (mAU*s)	Area %
1	5.85	0.14	25.18	222.37	8.57
2	7.43	0.21	1.69	24.43	0.94
3	9.19	0.22	166.18	2346.61	90.48
Total				2593.41	100.00