Supplementary Information (SI) for Green Chemistry.

Oxidative Dearomatization of 3-Substituted Indoles with Sulfonium Salts: Direct Access to 3-Hydroxyoxindoles

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Supporting Information Placeholder

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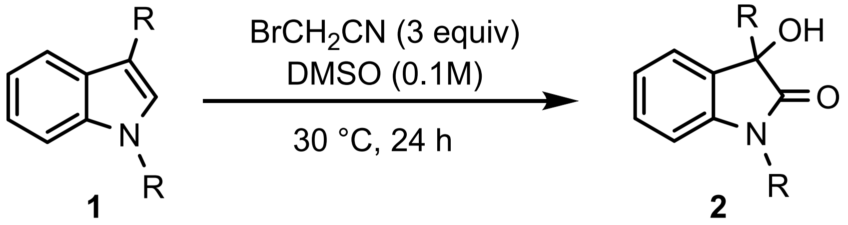
General information

Unless noted otherwise, all reagents and solvents were purchased from commercial sources and used as received. The glassware to be used in the reaction was thoroughly washed and dried in an oven and the experiments were carried out with the required precautions. Chemicals were purchased from BLD Pharma, Chempure, Spectrochem and TCI, solvent were purchased from Chempure Pvt. Ltd. and Spectrochem Pvt. Ltd.

Reactions were monitored by TLC, which was performed with 0.2 mm Merck pre-coated silica gel 60 F254 Aluminium sheets. TLC plates were visualized with UV light and column chromatography was performed using silica gel (60-120, 100-200, or 230-400 mesh).

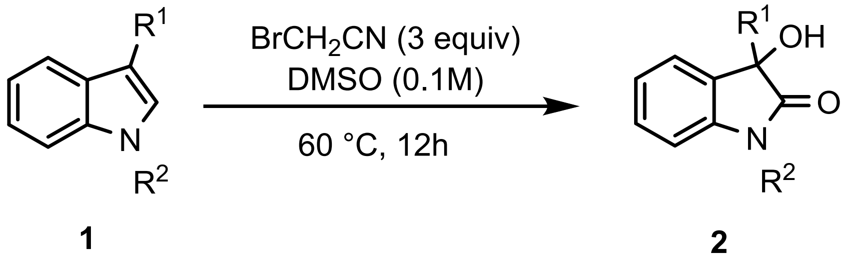
^{1}H NMR, ^{13}C NMR, and HRMS data. High-Resolution Mass Spectra (HRMS) were obtained using the Electron spin ionization (ESI) technique and as a TOF mass analyzer on a 6200 series TOF/6500 series Q-TOF (11.0.230.2). ^{1}H and ^{13}C spectra were recorded on Jeol 500, 600 MHz, and 125, 150 MHz NMR spectrometers in $CDCl_3$ and DMSO-d_6 with residual undeuterated solvent using TMS as an internal standard. Chemical shifts (δ) are given in ppm and *J* values are given in Hz, pattern was designated as s, singlet; bs, broad singlet; d, doublet; dd, doublet of doublet; dt, triplet of doublet; t, triplet; m, multiplet.

General Procedure for the synthesis of 3-Hydroxy-3-alkyl-2-oxyindole derivatives



Procedure A

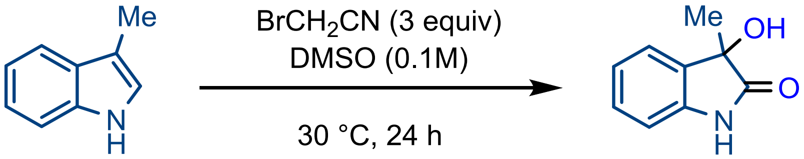
To a screw cap reaction tube charged with a magnetic stir-bar, substrate **1** (0.25 mmol) and bromoacetonitrile (0.75 mmol) were added. Then, 2.5 mL DMSO was added. The reaction mixture was kept at 30 °C and stirred vigorously for completion of the reaction (24h). Then the reaction mixture was diluted with 20 mL of water and extracted with 3*20 mL of EtOAc. Afterward, the extracted organic layer was dried over Na_2SO_4 and concentrated and the product was purified by column chromatography using silica gel (100-200 mesh) and EtOAc / Hexane as eluent.



Procedure B

To a screw cap reaction tube charged with a magnetic stir-bar, substrate **1** (0.25 mmol) and bromoacetonitrile (0.75 mmol) were added. Then, 2.5 mL DMSO was added. The reaction mixture was kept at 60 °C and stirred vigorously for completion of the reaction (12h). Then the reaction mixture was diluted with 20 mL of water and extracted with 3*20 mL of EtOAc. Afterward, the extracted organic layer was dried over Na_2SO_4 and concentrated and the product was purified by column chromatography using silica gel (100-200 mesh) and EtOAc / Hexane as eluent.

Table 1: Optimization of reaction conditions[a]

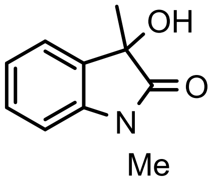


1m **2m**

Entry	Alkyl halide (x equiv)	Additive (x)	Solvent	Yield (%)
1	$BrCH_2CN$ (3 equiv)	-	DMSO	73
2	$BrCH_2CN$ (2 equiv)	-	DMSO	52
3	$BrCH_2CN$ (3 equiv)	Et_3N (2 equiv)	DMSO	55
4	$BrCH_2CN$ (3 equiv)	$NaHCO_3$ (2 equiv)	DMSO	0
5	$BrCH_2CN$ (3 equiv)	$FeCl_3$ (0.2 equiv)	DMSO	49
6	$BrCH_2CN$ (3 equiv)	-	20 equiv DMSO + 1 mL PhCl	10
7b	$BrCH_2CN$ (3 equiv)	-	PhCl	30
8[b]	$BrCH_2CN$ (3 equiv)	-	CH_2Cl_2	20
9	$BrCH_2CN$ (3 equiv)	-	CH_3CN	0
10	$BrCH_2CN$ (3 equiv)	-	DMF	0
11	$BrCH_2CN$ (3 equiv)	-	DMF: H_20 = 1:1	0
12	$BrCH_2CN$ (3 equiv)	-	EtOH	0
13	4-$BrPhCH_2Br$ (3 equiv)	-	DMSO	66
14	nC_4H_9Br (3 equiv)	-	DMSO	0
15	$BrC(Me)_2CO_2{}^tBu$ (3 equiv)		DMSO	46
16	$BrCH_2CO_2{}^tBu$ (3 equiv)		DMSO	70
17	$BrCF_2CO_2Et$ (3 equiv)		DMSO	43
18	$BrCH_2CH=CH_2$ (3 equiv)		DMSO	65
19[c]	$BrCH_2CN$ (3 equiv)		DMSO	40
20[d]	$BrCH_2CN$ (3 equiv)		DMSO (dry)	0
21[e]	$BrCH_2CN$ (3 equiv)		DMSO (1 mL)	64
22[f]	$BrCH_2CN$ (3 equiv)		DMSO	82

[a]Reaction conditions: **1** (0.25 mmol), $BrCH_2CN$ (x mmol), wet DMSO (2 mL), 30 °C, 24 h. [b]20 equiv. of DMSO was used as a reagent. [c]Reaction was performed at 0 °C instead of 30 °C. [d]Reaction was carried out with dry DMSO and 4Å MS (150 mg), 36 h. Isolated yield was given. [e]1 mL DMSO was used. [f]N-Methy-3-methylindole was used.

Characterization data



3-Hydroxy-1,3-dimethylindolin-2-one (2a)

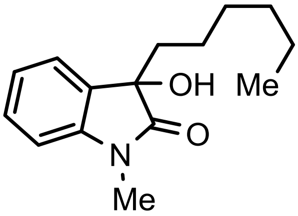
Compound **2a** was obtained by using the general procedure **A** from 1,3-dimethyl-1H-indole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (30:70 v/v); yellow solid with 82 % yield (36.2 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.34 (d, *J* = 7.3 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 5.92 (s,1H), 3.10 (s, 3H), 1.38 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.8, 142.6, 132.9, 128.9, 123.0, 122.3, 108.5, 72.3, 25.8, 24.5 ppm.

Rf: 0.28 (EtOAc/Hexane (40:60 v/v)

The spectral data are consistent with those reported in the literature[1]



3-Hexyl-3-hydroxy-1-methylindolin-2-one (2b)

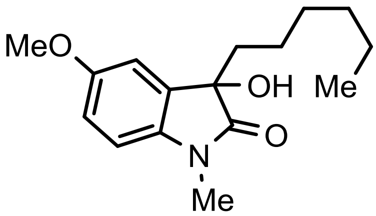
Compound **2b** was obtained by using the general procedure **A** from 3-hexyl-1-methyl-1H-indole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (25:75 v/v); white solid with 54% yield (33.4 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.30 (dd, *J* = 9.3, 7.6 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.97 (d, *J* = 7.7 Hz, 1H), 5.88 (s, 1H), 3.09 (s, 3H), 1.82 – 1.73 (m, 2H), 1.19 – 1.08 (m, 6H), 1.01 – 0.92 (m, 1H), 0.92 – 0.84 (m, 1H), 0.79 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.5, 143.2, 131.5, 128.9, 123.4, 122.2, 108.3, 75.4, 37.7, 30.9, 28.7, 25.7, 22.6, 21.9, 13.8 ppm.

Rf: 0.3 (EtOAc/Hexane (30:70 v/v)

HRMS: calc. for $[M+H]^+$ $C_{15}H_{21}N_2O_2$: 248.1651 found: 248.1652.



3-Hexyl-3-hydroxy-5-methoxy-1-methylindolin-2-one (2c)

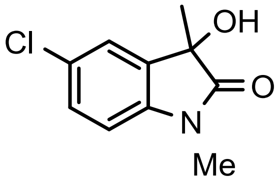
Compound **2c** was obtained by using the general procedure **A** from 3-hexyl-5-methoxy-1-methyl-1H-indole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (25:75 v/v); white solid with 48% yield (33.0 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 6.91 (d, *J* = 2.2 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.85 (dd, *J* = 8.4, 2.3 Hz, 1H), 5.88 (s, 1H), 3.73 (s, 3H), 3.06 (s, 3H), 1.82 – 1.70 (m, 2H), 1.21 – 1.06 (m, 6H), 0.98 – 0.90 (m, 1H), 0.90 – 0.83 (m, 1H), 0.79 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.2, 155.5, 136.6, 132.8, 113.0, 110.7, 108.7, 75.8, 55.5, 37.7, 30.9, 28.7, 25.8, 22.6, 21.9, 13.8 ppm.

Rf: 0.27 (EtOAc/Hexane (30:70 v/v)

HRMS: calc. for $[M+H]^+$ $C_{16}H_{24}NO_3$: 278.1756 found: 278.1775.



5-Chloro-3-hydroxy-1,3-dimethylindolin-2-one (2d)

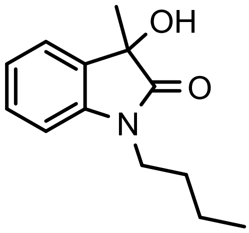
Compound **2d** was obtained by using the general procedure **A** from 5-chloro-1,3-dimethyl-1H-indole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (25:75 v/v); white solid with 77% yield (61.5 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.39 (d, *J* = 1.9 Hz, 1H), 7.36 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.02 (d, *J* = 8.3 Hz, 1H), 6.06 (s, 1H), 3.10 (s, 3H), 1.39 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.4, 141.5, 134.9, 128.7, 126.5, 110.1, 72.5, 25.9, 24.1 ppm

Rf: 0.29 (EtOAc/Hexane (30:70 v/v)

The spectral data are consistent with those reported in the literature.[2]



1-Butyl-3-hydroxy-3-methylindolin-2-one (2f)

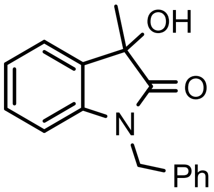
Compound **2f** was obtained by using the general procedure **B** from 1-butyl-3-methyl-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid with 45% yield (24.7 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.34 (d, *J* = 6.5 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.05 – 7.00 (m, 2H), 5.93 (s, 1H), 3.65 – 3.59 (m, 2H), 1.59 – 1.50 (m, 2H), 1.37 (s, 3H), 1.33 – 1.26 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.8, 141.9, 133.1, 128.9, 123.2, 122.1, 108.7, 72.3, 38.7, 29.0, 24.7, 19.5, 13.7 ppm.

Rf: 0.39 (EtOAc/Hexane (20:80 v/v)

The spectral data are consistent with those reported in the literature.[3]



1-Benzyl-3-hydroxy-3-methylindolin-2-one (2g)

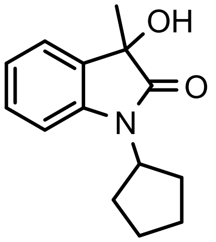
Compound **2g** was obtained by using the general procedure **B** from 1-benzyl-3-methyl-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid with 70% yield (44.3 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.37 (d, *J* = 7.2 Hz, 1H), 7.35 – 7.30 (m, 4H), 7.29 – 7.24 (m, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.09 (s, 1H), 4.86 (s, 2H), 1.44 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 178.0, 141.5, 136.4, 132.9, 128.8, 128.6, 127.3, 127.1, 123.2, 122.5, 109.1, 72.5, 42.4, 24.7 ppm.

Rf: 0.37 (EtOAc/Hexane (30:70 v/v)

The spectral data are consistent with those reported in the literature.[4]



1-Cyclopentyl-3-hydroxy-3-methylindolin-2-one (2h)

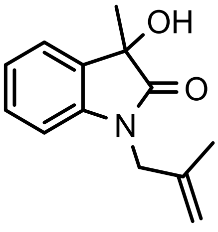
Compound **2h** was obtained by using the general procedure **B** from 1-cyclopentyl-3-methyl-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); dense liquid with 52% yield (30.0 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.35 (d, *J* = 6.7 Hz, 1H), 7.27 (td, *J* = 7.8, 1.2 Hz, 1H), 7.03 (t, *J* = 7.3 Hz, 2H), 5.90 (s, 1H), 4.63 (p, *J* = 8.8 Hz, 1H), 1.98 (m, 2H), 1.93 – 1.85 (m, 2H), 1.85 – 1.77 (m, 2H), 1.64 (m, 2H), 1.35 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.8, 141.1, 133.3, 128.8, 123.4, 121.9, 109.6, 72.1, 51.6, 27.4, 27.1, 24.7 ppm.

Rf: 0.28 (EtOAc/Hexane (30:70 v/v)

HRMS: calc. for [M+H]$^+$ $C_{14}H_{18}NO_2$: 232.1338 found: 232.1343.



3-Hydroxy-3-methyl-1-(2-methylallyl)indolin-2-one (2i)

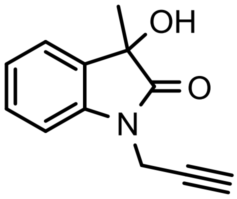
Compound **2i** was obtained by using the general procedure **B** from 3-methyl-1-(2-methylallyl)-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid with 52% yield (28.25 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.36 (d, *J* = 6.9 Hz, 1H), 7.25 (t, *J* = 7.7 Hz 1H), 7.04 (t, *J* = 7.3 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.01 (s, 1H), 4.86 (s, 1H), 4.78 (s, 1H), 4.18 (dd, *J* = 41.5, 16.4 Hz, 2H), 1.69 (s, 3H), 1.41 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.7, 141.7, 139.2, 132.8, 128.8, 123.1, 122.3, 111.5, 109.2, 72.3, 44.5, 24.8, 19.8 ppm.

Rf: 0.28 (EtOAc/Hexane (30:70 v/v)

HRMS: calc. for $[M+H]^+$ $C_{13}H_{16}NO_2$: 218.1181 found: 218.1174.



3-Hydroxy-3-methyl-1-(prop-2-yn-1-yl)indolin-2-one (2j)

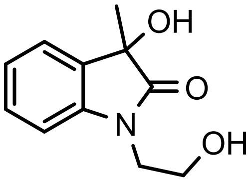
Compound **2j** was obtained by using the general procedure **B** from 3-methyl-1-(prop-2-yn-1-yl)-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid with 39% yield (20.0 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.38 (d, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 6.6 Hz, 1H), 7.11 – 7.04 (m, 2H), 6.07 (s, 1H), 4.49 (qd, *J* = 17.9, 2.5 Hz, 2H), 3.27 (t, *J* = 2.4 Hz, 1H), 1.39 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.0, 140.6, 132.8, 128.9, 123.2, 122.7, 109.2, 78.1, 74.4, 72.4, 28.6, 24.6 ppm.

Rf: 0.35 (EtOAc/Hexane (30:70 v/v)

HRMS: calc. for $[M+H]^+$ $C_{12}H_{12}NO_2$: 202.0868 found: 202.0863.



3-Hydroxy-1-(2-hydroxyethyl)-3-methylindolin-2-one (2k)

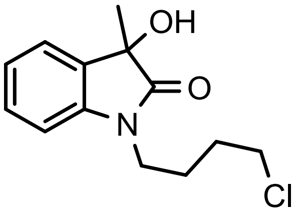
Compound **2k** was obtained by using the general procedure **B** from 2-(3-methyl-1H-indol-1-yl)ethan-1-ol (0.25 mmol).The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid with 38% yield (19.0 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.33 (d, *J* = 7.2 Hz, 1H), 7.28 (t, *J* = 0.7 Hz, 1H), 7.03 (m, 2H), 5.89 (s, 1H), 4.82 (t, *J* = 5.6 Hz, 1H), 3.76 – 3.69 (m, 1H), 3.67 – 3.61 (m, 1H), 3.60 – 3.54 (m, 2H), 1.38 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.9, 142.4, 132.9, 128.8, 123.0, 122.0, 109.0, 72.3, 58.1, 41.9, 24.6 ppm.

Rf: 0.32 (EtOAc/Hexane (30:70 v/v)

HRMS: calc. for $[M+H]^+$ $C_{11}H_{14}NO_3$: 209.0974 found: 209.0976.



1-(4-Chlorobutyl)-3-hydroxy-3-methylindolin-2-one (2l)

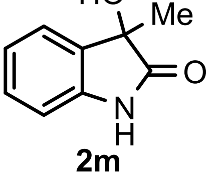
Compound **2l** was obtained by using the general procedure **B** from 1-(4-chlorobutyl)-3-methyl-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (30:70 v/v); white solid with 62% yield (39.25 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.36 – 7.33 (m, 1H), 7.29 (td, *J* = 7.7, 1.0 Hz, 1H), 7.06 – 7.01 (m, 2H), 5.95 (s, 1H), 3.72 – 3.61 (m, 3H), 3.57 (t, *J* = 6.6 Hz, 1H), 1.82 (dd, *J* = 8.5, 6.8 Hz, 1H), 1.77 – 1.67 (m, 3H), 1.37 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.9, 141.7, 133.1, 128.9, 123.2, 122.3, 108.7, 72.3, 45.0, 38.2, 29.3, 24.6, 24.3 ppm.

Rf: 0.34 (EtOAc/Hexane (40:60 v/v)

HRMS: calc. for $[M+H]^+$ $C_{13}H_{17}ClNO_2$: 254.0948 found: 254.0950.



2m

3-Hydroxy-3-methylindolin-2-one (2m)

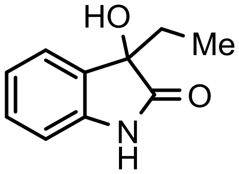
Compound **2m** was obtained by using the general procedure **A** from 3-methylindole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); yellow solid (29.8 mg) with 73% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.20 (s,1H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.18 (t, *J* = 7.3 Hz, 1H), 6.96 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 5.84 (s, 1H), 1.35 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 179.7, 141.1, 133.6, 128.8, 123.4, 121.6, 109.6, 72.6, 24.5 ppm

Rf: 0.37 (EtOAc/Hexane (50:50 v/v)

The spectral data are consistent with those reported in the literature.[4]



3-Ethyl-3-hydroxyindolin-2-one (2n)

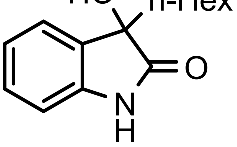
Compound **2n** was obtained by using the general procedure **A** from 3-ethyl-1H-indole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (24 mg) with 54% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.21 (s, 1H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.19 (td, *J* = 7.7, 1.2 Hz, 1H), 6.96 (td, *J* = 7.5, 0.8 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 5.81 (s, 1H), 1.85 – 1.67 (m, 2H), 0.61 (t, *J* = 7.5 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 179.3, 141.9, 131.8, 128.8, 123.8, 121.6, 109.4, 76.2, 30.6, 7.5 ppm.

Rf: 0.39 (EtOAc/Hexane (50:50 v/v)

The spectral data are consistent with those reported in the literature.[4]



3-Hexyl-3-hydroxyindolin-2-one (2o)

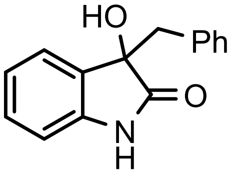
Compound **2o** was obtained by using the general procedure **B** from 3-hexyl-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid with 63% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.19 (s, 1H), 7.23 (d, *J* = 7.3 Hz, 1H), 7.18 (td, *J* = 7.6, 0.9 Hz, 1H), 6.95 (t, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 5.80 (s, 1H), 1.79 – 1.69 (m, 2H), 1.21 – 1.09 (m, 6H), 1.02 (m, 1H), 0.89 (m, 1H), 0.79 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 179.4, 141.8, 132.2, 128.8, 123.8, 121.5, 109.4, 75.7, 37.7, 31.0, 28.7, 22.6, 21.9, 13.9 ppm.

Rf: 0.35 (EtOAc/Hexane (30:70 v/v)

The spectral data are consistent with those reported in the literature.[5]



3-Benzyl-3-hydroxyindolin-2-one (2p)

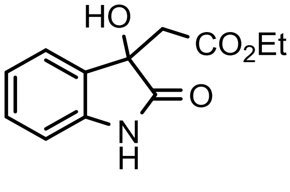
Compound **2p** was obtained by using the general procedure **A** from 3-benzyl-1H-indole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid (24.5mg) with 41% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.03 (s,1H), 7.12 – 7.06 (m, 5H), 6.92 – 6.87 (m, 3H), 6.59 (d, *J* = 7.5 Hz, 1H), 6.10 (s, 1H), 3.15 (d, *J* = 12.7 Hz, 1H), 2.99 (d, *J* = 12.7 Hz, 1H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 178.8, 141.7, 135.1, 130.9, 130.1, 128.8, 127.5, 126.3, 124.6, 121.2, 109.3, 76.6, 43.4 ppm.

Rf: 0.34 (EtOAc/Hexane (30:70 v/v)

The spectral data are consistent with those reported in the literature.[4]



ethyl 2-(3-hydroxy-2-oxoindolin-3-yl)acetate (2q)

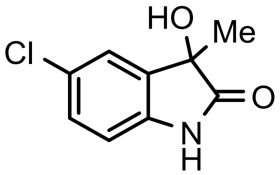
Compound **2q** was obtained by using the general procedure **A** from ethyl 2-(1H-indol-3-yl)acetate (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (22.32) with 38% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.27 (s, 1H), 7.30 (d, *J* = 7.1 Hz, 1H), 7.19 (td, *J* = 7.7, 1.2 Hz, 1H), 6.93 (td, *J* = 7.5, 0.9 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 6.13 (s, 1H), 3.87 – 3.75 (m, 2H), 2.95 (d, *J* = 2.2 Hz, 2H), 0.92 (t, *J* = 7.1 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 177.9, 168.5, 142.6, 130.8, 129.3, 124.1, 121.3, 109.5, 72.7, 59.8, 41.7, 13.6 ppm.

Rf: 0.37 (EtOAc/Hexane (50:50 v/v)

The spectral data are consistent with those reported in the literature.[6]



5-Chloro-3-hydroxy-3-methylindolin-2-one (2r)

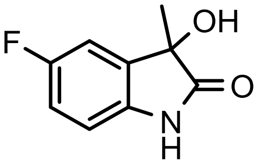
Compound **2r** was obtained by using the general procedure **B** from 5-chloro-3-methyl-1H-indole (0.25 mmol). The reaction was carried out at 60 °C for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (35.5 mg) with 72% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.35 (s, 1H), 7.33 (d, *J* = 2.1 Hz, 1H), 7.24 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 5.99 (s, 1H), 1.36 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 179.3, 139.9, 135.7, 128.6, 125.7, 123.7, 111.1, 72.8, 24.2 ppm.

Rf: 0.38 (EtOAc/Hexane (50:50 v/v)

The spectral data are consistent with those reported in the literature.[4]



5-fluoro-3-hydroxy-3-methylindolin-2-one (2s)

Compound **2s** was obtained by using the general procedure **A** from 5-chloro-1,3-dimethyl-1H-indole (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (35:65 v/v); white solid with 62% yield (28.05mg).

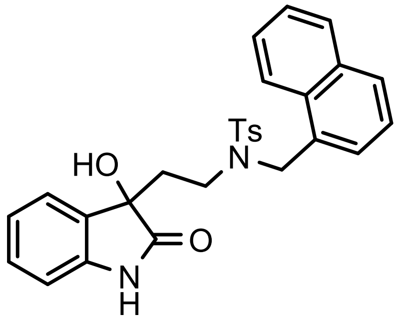
^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.24 (s, 1H), 7.16 (dd, *J* = 8.1, 2.7 Hz, 1H), 7.05 – 6.98 (m, 1H), 6.79 (dd, *J* = 8.4, 4.3 Hz, 1H), 5.98 (s, 1H), 1.36 (s, 1H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 179.6, 158.9, 137.2, 135.4, 115.0, 111.3, 110.4, 72.9, 24.3 ppm.

^{19}F NMR (565 MHz, DMS0-D$_6$) δ -121.74, -121.76, -121.76, -121.77, -121.78 ppm.

Rf: 0.28 (EtOAc/Hexane (40:60 v/v)

The spectral data are consistent with those reported in the literature.[7]



N-(2-(3-Hydroxy-2-oxoindolin-3-yl)ethyl)-4-methyl-*N*-(naphthalen-1-ylmethyl)benzenesulfonamide (2t)

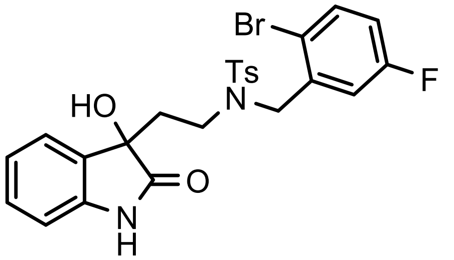
Compound **2t** was obtained by using the general procedure **A** from *N*-(2-(1H-indol-3-yl)ethyl)-4-methyl-*N*-(naphthalen-1-ylmethyl)benzenesulfonamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (86.26 mg) with 71% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.13 (s, 1H), 8.30 (d, J = 8.1 Hz, 1H), 7.95 (d, J = 7.2 Hz, 1H), 7.88 (dd, J = 6.8, 2.8 Hz, 1H), 7.71 (d, J = 7.9 Hz, 2H), 7.56 (dq, J = 13.5, 6.8 Hz, 2H), 7.46 (d, J = 7.8 Hz, 2H), 7.38 (d, J = 6.8 Hz, 2H), 7.15 (ddd, J = 8.2, 5.4, 3.4 Hz, 1H), 6.90 (d, J = 5.6 Hz, 2H), 6.69 (d, J = 7.7 Hz, 1H), 5.80 (s, 1H), 4.69 (q, J = 14.3 Hz, 2H), 3.00 (m, 1H), 2.82 (m, 1H), 2.43 (s, 3H), 1.51 (dd, J = 11.5, 5.8 Hz, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.3, 143.5, 141.2, 135.5, 133.3, 131.2, 131.1, 129.9, 129.0, 128.6, 127.6, 127.1, 126.3, 125.9, 125.3, 123.7, 123.7, 121.6, 109.5, 73.8, 50.2, 42.1, 35.7, 21.0 ppm.

Rf: 0.39 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{28}H_{27}N_2O_4S$: 487.1692 found: 487.1708.



***N*-(2-Bromo-5-fluorobenzyl)-*N*-(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)-4-methylbenzenesulfonamide (2u)**

Compound **2u** was obtained by using the general procedure **A** from *N*-(2-(1H-indol-3-yl)ethyl)-*N*-(2-bromo-5-fluorobenzyl)-4-methylbenzenesulfonamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (92 mg) with 69% yield.

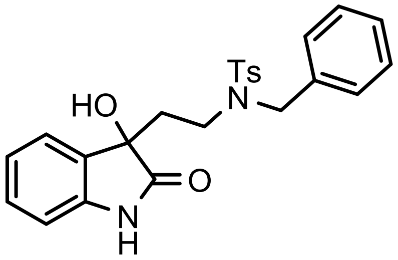
^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.24 (s, 1H), 7.65 (d, J = 8.2 Hz, 3H), 7.43 (d, J = 8.0 Hz, 2H), 7.17 (dtd, J = 22.8, 8.1, 5.8 Hz, 3H), 7.09 (d, J = 7.3 Hz, 1H), 6.94 (t, J = 7.5 Hz, 1H), 6.76 (d, J = 7.7 Hz, 1H), 5.96 (s, 1H), 4.30 (s, 2H), 3.23 – 3.09 (m, 1H), 3.06 (m, 1H), 2.41 (s, 3H), 1.75 (dt, J = 11.6, 5.5 Hz, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.4, 162.3, 160.6, 143.7, 141.2, 138.4, 135.5, 134.4, 134.4, 131.3, 130.0, 129.1, 127.0, 123.7, 121.7, 116.8, 116.7, 116.5, 109.7, 73.7, 51.5, 43.3, 35.9, 21.0 ppm.

^{19}F NMR (565 MHz, DMSO-D$_6$) δ -113.81, -113.82, -113.83, -113.85 ppm.

Rf: 0.38 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{24}H_{23}FN_2O_4S$: 533.0546 found: 533.0541



***N*-Benzyl-*N*-(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)-4-methylbenzenesulfonamide (2v)**

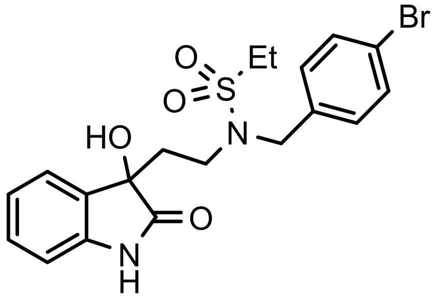
Compound **2v** was obtained by using the general procedure **A** *N*-(2-(1H-indol-3-yl)ethyl)-*N*-benzyl-4-methylbenzenesulfonamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (77.36 mg) with 71% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.20 (s, 1H), 7.63 (d, J = 8.1 Hz, 2H), 7.41 (d, J = 8.1 Hz, 2H), 7.30 (dd, J = 8.0, 6.3 Hz, 2H), 7.28 – 7.25 (m, 1H), 7.23 – 7.20 (m, 2H), 7.19 (td, J = 7.6, 1.2 Hz, 1H), 7.06 (d, J = 7.3 Hz, 1H), 6.94 (t, J = 7.6 Hz, 1H), 6.74 (d, J = 7.7 Hz, 1H), 5.91 (s, 1H), 4.25 (d, J = 11.2 Hz, 2H), 3.11 – 3.00 (m, 1H), 2.95 – 2.86 (m, 1H), 2.41 (s, 3H), 1.71 (dt, J = 10.6, 4.8 Hz, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.4, 143.3, 141.3, 136.6, 136.5, 131.3, 129.9, 129.1, 128.4, 128.0, 127.5, 126.8, 123.7, 121.7, 109.6, 73.8, 50.9, 42.0, 41.3, 35.5, 20.9 ppm.

Rf: 0.39 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{24}H_{25}N_2O_4S$: 437.1457 found: 437.1458.



***N*-(4-Bromobenzyl)-*N*-(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)ethanesulfonamide (2w)**

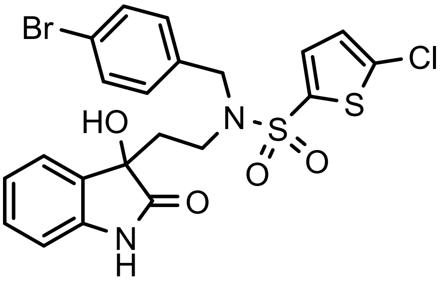
Compound **2w** was obtained by using the general procedure **A** *N*-(2-(1H-indol-3-yl)ethyl)-*N*-(4-bromobenzyl)ethanesulfonamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid with 63% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.26 (s, 1H), 7.52 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 7.20 – 7.16 (m, 2H), 6.95 (t, J = 7.5 Hz, 1H), 6.77 (d, J = 7.7 Hz, 1H), 5.98 (s, 1H), 4.28 (s, 2H), 3.10 (dqd, J = 14.6, 7.8, 7.2, 3.0 Hz, 3H), 3.05 – 2.97 (m, 1H), 1.92 (dd, J = 10.0, 6.6 Hz, 2H), 1.19 (t, J = 7.3 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.5, 141.3, 136.6, 131.4, 131.3, 130.2, 129.1, 123.9, 121.7, 120.6, 109.7, 73.9, 49.6, 45.8, 41.5, 35.9, 7.9 ppm.

Rf: 0.39 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{19}H_{22}{}^{79}BrN_2O_4S$: 453.0484 found: 453.0480



N-(4-Bromobenzyl)-5-chloro-N-(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)thiophene-2-sulfonamide (2x)

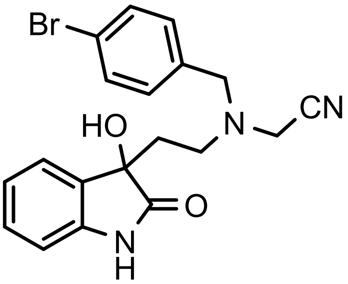
Compound **2x** was obtained by using the general procedure **A** *N*-(2-(1H-indol-3-yl)ethyl)-N-(4-bromobenzyl)-5-chlorothiophene-2-sulfonamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (82.65 mg) with 61% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.25 (s, 1H), 7.55 (d, J = 4.1 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 4.0 Hz, 1H), 7.19 (dd, J = 8.0, 6.5 Hz, 3H), 7.11 (d, J = 7.3 Hz, 1H), 6.94 (t, J = 7.5 Hz, 1H), 6.76 (d, J = 7.7 Hz, 1H), 5.98 (s, 1H), 4.27 (q, J = 15.3 Hz, 2H), 3.21 – 3.11 (m, 1H), 3.10 – 2.94 (m, 1H), 1.78 (td, J = 7.5, 6.3, 3.5 Hz, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.4, 141.2, 137.4, 135.7, 135.2, 132.3, 131.4, 131.3, 130.2, 129.1, 128.5, 123.7, 121.7, 120.8, 109.7, 73.7, 50.6, 42.9, 35.7 ppm

Rf: 0.35 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{21}H_{19}{}^{79}BrClN_2O_4S$: 540.9580 found: 540.9651



2-((4-Bromobenzyl)(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)amino)acetonitrile (2y)

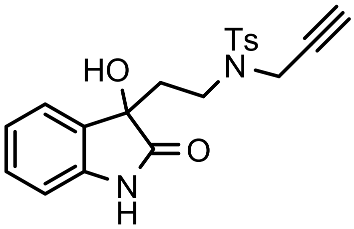
Compound **2y** was obtained by using the general procedure **A** (6 Eq. of $BrCH_2CN$ was taken) *N*-(4-bromobenzyl)-2-(1H-indol-3-yl)ethan-1-amine (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (65 mg) with 65% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.23 (s, 1H), 7.47 (d, J = 8.3 Hz, 2H), 7.22 (d, J = 7.4 Hz, 1H), 7.19 (td, J = 7.7, 1.3 Hz, 1H), 7.15 (d, J = 8.3 Hz, 2H), 6.93 (t, J = 7.5 Hz, 1H), 6.78 (d, J = 7.7 Hz, 1H), 5.93 (s, 1H), 3.59 (d, J = 17.7 Hz, 1H), 3.53 – 3.47 (m, 2H), 3.40 (d, J = 13.7 Hz, 1H), 2.40 – 2.31 (m, 3H), 2.00 (m, 1H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.9, 141.7, 136.8, 131.5, 131.2, 130.7, 128.9, 123.9, 121.6, 120.3, 115.6, 109.6, 74.4, 57.3, 47.9, 41.2, 34.8 ppm.

Rf: 0.36 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for [M+H]$^+$ C19H18BrN3O2: 400.0582 found: 400.0591



_N_-(2-(3-Hydroxy-2-oxoindolin-3-yl)ethyl)-4-methyl-_N_-(prop-2-yn-1-yl)benzenesulfonamide (2z)

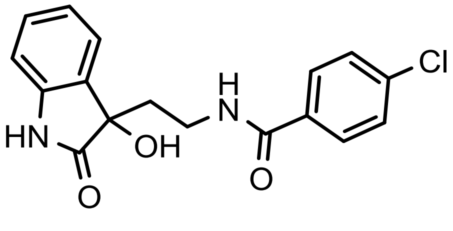
Compound **2z** was obtained by using the general procedure **A** *N*-(2-(1H-indol-3-yl)ethyl)-4-methyl-*N*-(prop-2-yn-1-yl)benzenesulfonamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (60 mg) with 62% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.29 (s, 1H), 7.59 (d, J = 8.2 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.28 – 7.14 (m, 2H), 6.99 (t, J = 7.5 Hz, 1H), 6.81 (d, J = 7.7 Hz, 1H), 6.03 (s, 1H), 4.06 (s, 2H), 3.24 – 3.10 (m, 2H), 2.38 (s, 3H), 1.97 (m, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.5, 143.4, 141.4, 135.5, 131.6, 129.6, 129.1, 127.2, 123.8, 121.7, 109.7, 77.4, 76.1, 73.9, 41.4, 36.5, 35.7, 20.9 ppm.

Rf: 0.37 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for [M+H]$^+$ $C_{20}H_{21}N_2O_4S$: 385.1144 found: 385.1152



4-Chloro-*N*-(2-(3-hydroxy-2-oxoindolin-3-yl)ethyl)benzamide (2aa)

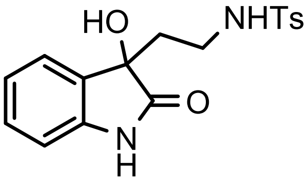
Compound **2aa** was obtained by using the general procedure **A** *N*-(2-(1H-indol-3-yl)ethyl)-4-chlorobenzamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (43.25 mg) with 53% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.31 (s, 1H), 8.43 (s, 1H), 7.77 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.98 (t, *J* = 7.3 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 6.01 (s, 1H), 3.19 (dd, *J* = 14.2, 6.4 Hz, 2H), 2.15 – 1.85 (m, 2H) ppm

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 179.0, 164.9, 141.5, 135.8,, 133.2, 131.9, 129.0, 128.3, 124.0, 121.7, 109.7, 74.5, 37.1, 34.4 ppm

Rf: 0.38 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{17}H_{16}ClN_2O_3$: 331.0771 found: 331.0843.



***N*-(2-(3-Hydroxy-2-oxoindolin-3-yl)ethyl)-4-methylbenzenesulfonamide (2ab)**

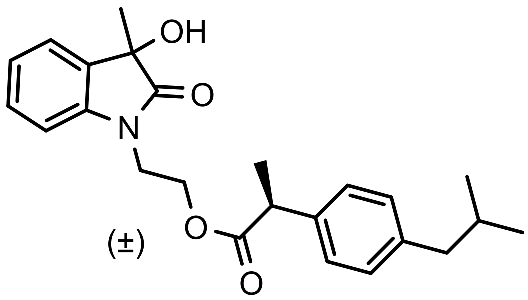
Compound **2ab** was obtained by using the general procedure **A** *N*-(2-(1H-indol-3-yl)ethyl)-4-methylbenzenesulfonamide (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (52 mg) with 60% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.25 (s, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.45 (t, *J* = 5.6 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 7.3 Hz, 1H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 7.7 Hz, 1H), 5.97 (s, 1H), 2.78 – 2.65 (m, 2H), 2.38 (s, 3H), 1.83 (m, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.6, 142.6, 141.3, 137.3, 131.6, 129.6, 129.1, 126.5, 123.8, 121.7, 109.7, 73.9, 42.1, 37.3, 20.9 ppm.

Rf: 0.39 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{17}H_{19}N_2O_4S$: 347.0987 found: 347.1061.



2-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)ethyl 2-(4-isobutylphenyl)propanoate (2ac)

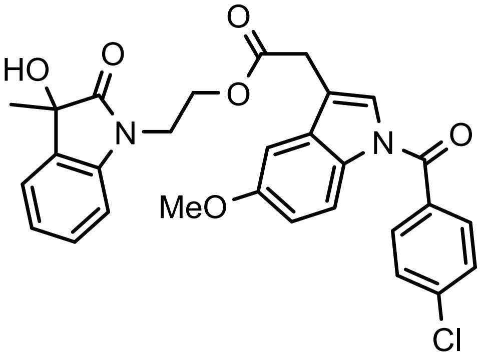
Compound **2ac** was obtained by using the general procedure **B** from 2-(3-methyl-1*H*-indol-1-yl)ethyl 2-(4-isobutylphenyl)propanoate (0.25 mmol). The reaction was carried out at 60 ^oC for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (30:70 v/v); dense liquid with 55% yield (54.3 mg).

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.34 (d, *J* = 7.1 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 7.09 – 6.99 (m, 6H), 5.95 (s, 1H), 4.37 – 4.22 (m, 1H), 4.21 – 4.08 (m, 1H), 3.95 (m, 1H), 3.83 (m, 1H), 3.59 (dq, *J* = 14.2, 7.1 Hz, 1H), 2.38 (d, *J* = 7.2 Hz, 2H), 1.78 (dp, *J* = 13.2, 6.6 Hz, 1H), 1.32 (d, *J* = 9.4 Hz, 3H), 1.29 (d, *J* = 7.2 Hz, 1.51H), 1.23 (d, *J* = 7.2 Hz, 1.53H), 0.84 (d, *J* = 1.7 Hz, 3H), 0.83 (d, *J* = 1.7 Hz, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 178.1, 173.8, 141.7, 139.7, 137.5, 137.5, 132.9, 129.0, 128.9, 127.0, 123.2, 122.3, 108.8, 72.3, 61.3, 44.2, 44.1, 38.3, 29.6, 24.6, 22.2, 18.3 ppm.

Rf: 0.35 (EtOAc/Hexane (40:60 v/v)

HRMS: calc. for $[M+H]^+$ $C_{24}H_{29}NO_4$: 396.2175 found: 396.2179.



2-(3-Hydroxy-3-methyl-2-oxoindolin-1-yl)ethyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (2ad)

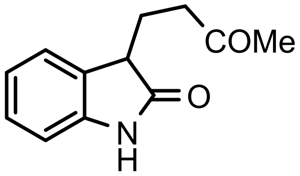
Compound **2ad** was obtained by using the general procedure **B** from 2-(3-methyl-1H-indol-1-yl)ethyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate (0.25 mmol).The reaction was carried out at 60 ^oC for 12 hours. The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (30:70 v/v); yellowish solid (86.5 mg) with 65% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.70 – 7.60 (m, 4H), 7.33 (d, *J* = 6.7 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.1 Hz, 2H), 6.99 (d, *J* = 2.3 Hz, 1H), 6.93 (d, *J* = 9.0 Hz, 1H), 6.71 (dd, *J* = 9.0, 2.4 Hz, 1H), 5.96 (s, 1H), 4.28 (m, 2H), 3.97 (m, 1H), 3.91 – 3.84 (m, 1H), 3.74 (s, 3H), 3.65 (dd, *J* = 32.0, 16.8 Hz, 2H), 2.10 (s, 3H), 1.33 (s, 3H) ppm.

^{13}C NMR (151 MHz, DMS0-D$_6$) δ 178.2, 170.4, 167.8, 155.6, 141.6, 137.6, 135.5, 134.1, 132.9, 131.2, 130.5, 130.2, 129.1, 128.8, 123.2, 122.3, 114.6, 112.3, 111.5, 108.6, 101.6, 72.3, 61.2, 55.4, 38.4, 29.1, 24.5, 13.1 ppm.

Rf: 0.34 (EtOAc/Hexane (40:60 v/v)

HRMS: calc. for $[M+H]^+$ $C_{29}H_{26}ClN_2O_4$: 533.1479 found: 533.1570.



3-(3-Oxobutyl)indolin-2-one (4a)

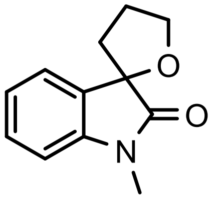
Compound **4a** was obtained by using the general procedure **A** 4-(1H-indol-3-yl)butan-2-one (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (25.9 mg) with 51% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.38 (s, 1H), 7.24 (d, *J* = 7.3 Hz, 1H), 7.17 (t, *J* = 7.7 Hz, 1H), 6.97 – 6.91 (m, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 3.42 (t, *J* = 6.3 Hz, 1H), 2.48 – 2.38 (m, 2H), 2.04 (s, 2H), 2.02 – 1.93 (m, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 207.7, 178.6, 142.7, 129.3, 127.7, 124.0, 121.3, 109.2, 44.1, 38.8, 29.8, 23.9 ppm.

Rf: 0.35 (EtOAc/Hexane (50:50 v/v)

The spectral data are consistent with those reported in the literature.[8]



1'-Methyl-4,5-dihydro-3H-spiro[furan-2,3'-indolin]-2'-one (4b)

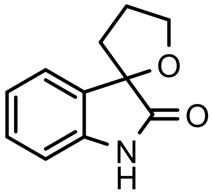
Compound **4b** was obtained by using the general procedure **A** 3-(1-methyl-1H-indol-3-yl)propyl 4-methylbenzenesulfonate (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (10:90 v/v); white solid (23.3 mg) with 46% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 7.33 (m, 2H), 7.05 (t, *J* = 7.7 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 4.16 – 4.01 (m, 2H), 3.08 (s, 3H), 2.32 – 2.25 (m, 1H), 2.19 (m, 2H), 2.11 – 2.03 (m, 1H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 176.9, 143.3, 130.3, 129.5, 123.5, 122.6, 108.6, 82.1, 69.5, 35.5, 26.0, 25.8 ppm.

Rf: 0.35 (EtOAc/Hexane (20:80 v/v)

The spectral data are consistent with those reported in the literature.[9]



4,5-dihydro-3H-spiro[furan-2,3'-indolin]-2'-one (4c)

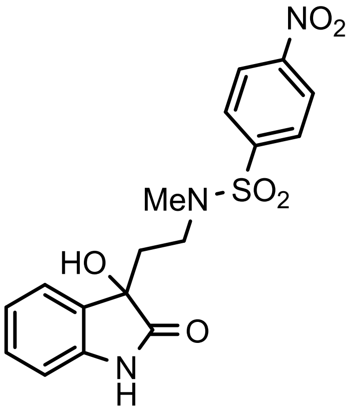
Compound **4c** was obtained by using the general procedure **A** 3-(1H-indol-3-yl)propan-1-ol (0.25 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (20:80 v/v); white solid (21.25 mg) with 45% yield.

^{1}H NMR (600 MHz, DMSO-D$_6$) δ 10.29 (s, 1H), 7.28 (d, *J* = 7.3 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 6.96 (t, *J* = 7.2 Hz, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 4.17 – 3.99 (m, 2H), 2.31 – 2.22 (m, 1H), 2.22 – 2.11 (m, 2H), 2.08 – 1.95 (m, 1H) ppm

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.9, 141.8, 131.0, 129.4, 123.9, 122.0, 109.7, 82.4, 69.4, 35.5, 25.9 ppm.

Rf: 0.36 (EtOAc/Hexane (30:70 v/v)

The spectral data are consistent with those reported in the literature.[10]



N-(2-(3-Hydroxy-2-oxoindolin-3-yl)ethyl)-N-methyl-4-nitrobenzenesulfonamide (7)

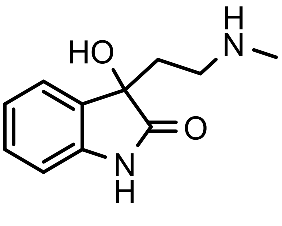
Compound **7** was obtained by using the general procedure **A** *N*-(2-(1H-Indol-3-yl)ethyl)-*N*-methyl-4-nitrobenzenesulfonamide (1 mmol). The product was isolated by column chromatography with silica gel. Eluent: EtOAc/Hexane (40:60 v/v); white solid (274 mg) with 70% yield. (65% for 1 gram-scale reaction)

^{1}H NMR (600 MHz, DMSO-D_6) δ 10.29 (s, 1H), 8.41 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 8.8 Hz, 2H), 7.28 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.21 (dd, *J* = 7.6, 1.3 Hz, 1H), 6.98 (td, *J* = 7.5, 1.0 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 6.03 (s, 1H), 3.17 (m, *J* = 13.5, 10.4, 6.0 Hz, 1H), 3.13 – 3.07 (m, 1H), 2.69 (s, 3H), 1.92 (m, *J* = 13.2, 11.0, 6.9 Hz, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 178.6, 149.9, 142.7, 141.4, 131.6, 129.2, 128.6, 124.8, 123.9, 121.7, 109.8, 73.8, 44.6, 35.3, 34.5 ppm.

Rf: 0.38 (EtOAc/Hexane (50:50 v/v)

HRMS: calc. for $[M+H]^+$ $C_{17}H_{18}N_3O_6S$: 392.0916 found: 392.0898.



3-Hydroxy-3-(2-(methylamino)ethyl)indolin-2-one (8)

To a screw cap reaction tube charged with a magnetic stir-bar, substrate **7** (0.25 mmol) and Cs_2CO_3 (0.5 mmol, 2 equiv)) were added followed by the addition of Thiophenol (0.75 mmol, 3 equiv) Then, 1.5 mL DMF was added. The reaction mixture was kept at room temperature under a nitrogen atmosphere and stirred vigorously for completion of the reaction (1h). Then the reaction mixture was diluted with 20 mL of water and extracted with 3*20 mL of EtOAc.

Afterward, the extracted organic layer was dried over Na_2SO_4 and concentrated and the product was purified by column chromatography using silica gel (100-200 mesh) and EtOAc / Hexane as eluent (65:35 v/v); yellow solid (20.5 mg) with 40% yield.

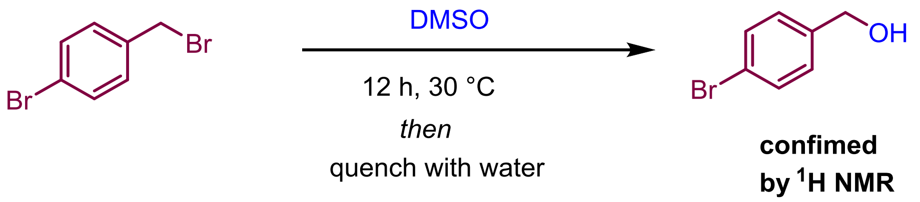
^{1}H NMR (600 MHz, DMSO-D$_6$) δ 6.99 – 6.93 (m, 1H), 6.68 – 6.65 (m, 2H), 6.45 (t, *J* = 7.4 Hz, 1H), 6.08 (s, 1H), 5.24 (br s, 2H), 3.30 – 3.24 (m, 1H), 2.99 (m, 1H), 2.85 (s, 3H), 2.43 (m, 1H), 2.16 (m, 1H) ppm.

^{13}C NMR (151 MHz, DMSO-D$_6$) δ 174.1, 147.1, 128.1, 125.9, 124.4, 116.2, 115.4, 78.8, 44.6, 33.4, 29.5 ppm.

Rf: 0.4 (EtOAc/Hexane (70:30 v/v)

The spectral data are consistent with those reported in the literature.[4]

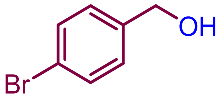
Mechanistic experiment:



i) Reaction with 4-BrPHCH$_2$Br

To a screw cap reaction tube charged with a magnetic stir-bar, substrate 4-bromobenylbromide (1 mmol) was added. Then, 2 mL DMSO was added. The reaction mixture was kept at 30 °C and stirred vigorously for 12 h. Then the reaction mixture was diluted with 20 mL of water and extracted with 3*20 mL of EtOAc. Afterward, the extracted organic layer was dried over Na_2SO_4 and concentrated and the product was purified by column chromatography using silica gel (100-200 mesh) and EtOAc / Hexane as eluent (20:80 v/v); colorless liquid (125 mg) with 67% yield.

(4-Bromophenyl)methanol



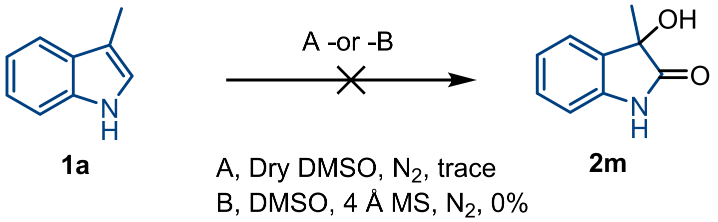
^{1}H NMR (600 MHz, DMSO-*D*$_6$) δ 7.50 (d, *J* = 7.9 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 5.28 (t, *J* = 5.7 Hz, 1H), 4.46 (d, *J* = 5.6 Hz, 2H) ppm.

^{13}C NMR (151 MHz, DMSO-*D*$_6$) δ 142.0, 130.9, 128.6, 119.5, 62.1 ppm.

Rf: 0.38 (EtOAc/Hexane (30:70 v/v)

The spectral data are consistent with those reported in the literature.

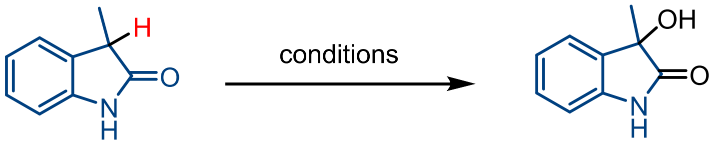
ii) Reaction with Dry DMSO and Molecular Sieve



To a screw cap reaction tube charged with a magnetic stir-bar, substrate **1a** (0.25 mmol) and bromoacetonitrile (0.75 mmol) were added. Then, 2 mL dry DMSO was added. The reaction mixture was kept at 30 °C and stirred vigorously for completion of the reaction (24h). Then the reaction mixture was diluted with 20 mL of water and extracted with 3*20 mL of EtOAc. Afterward, the extracted organic layer was dried over Na_2SO_4 and concentrated and the product was purified by column chromatography using silica gel (100-200 mesh) and EtOAc / Hexane as eluent. Finally, the reaction mixture was analysed by ^1H NMR of crude reaction mixture and the desired product was not found.

Similarly, when, the reaction was performed with DMSO with 4 Å MS, the desired product was not found, confirmed by TLC and ^1H NMR.

iii) Reaction with probable intermediate



1a'

A, Without $BrCH_2CN$, 0% yield

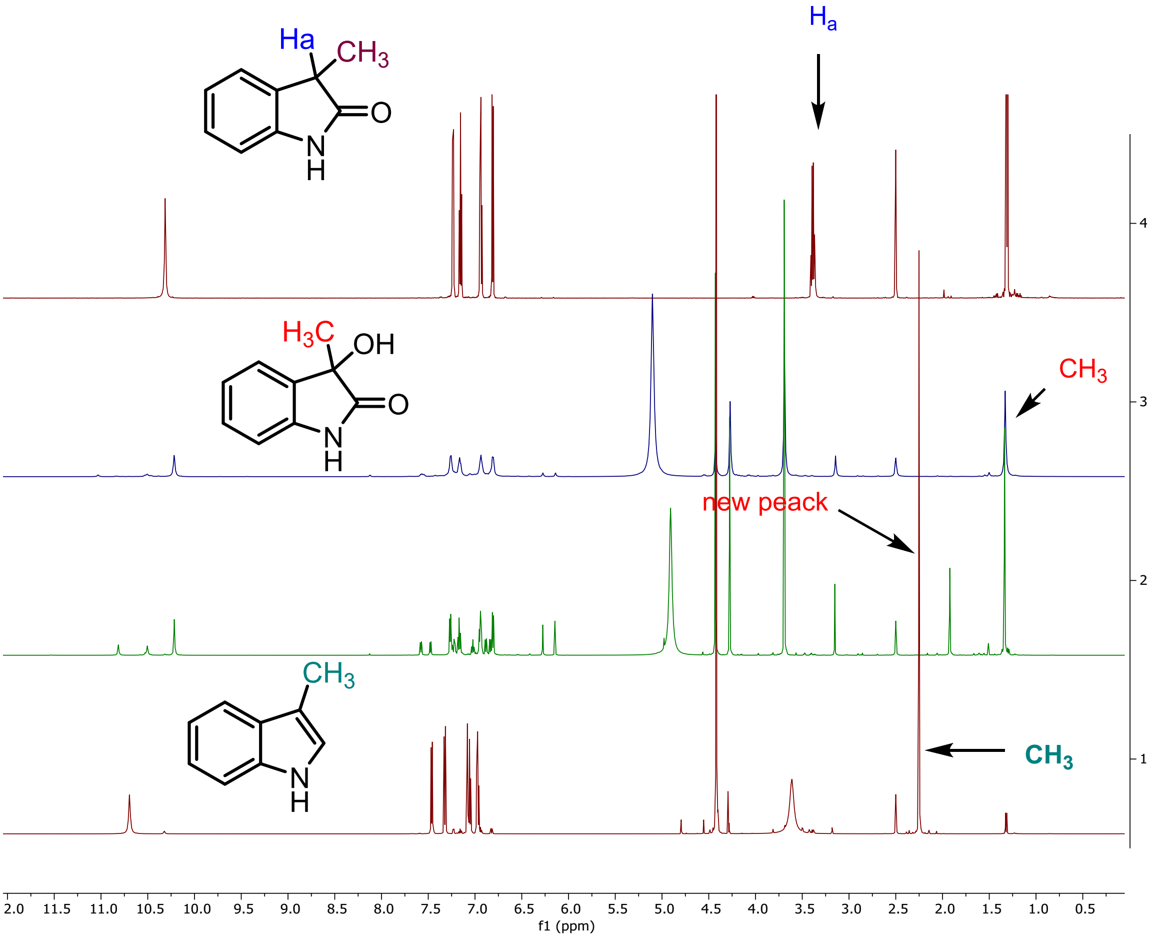
2m

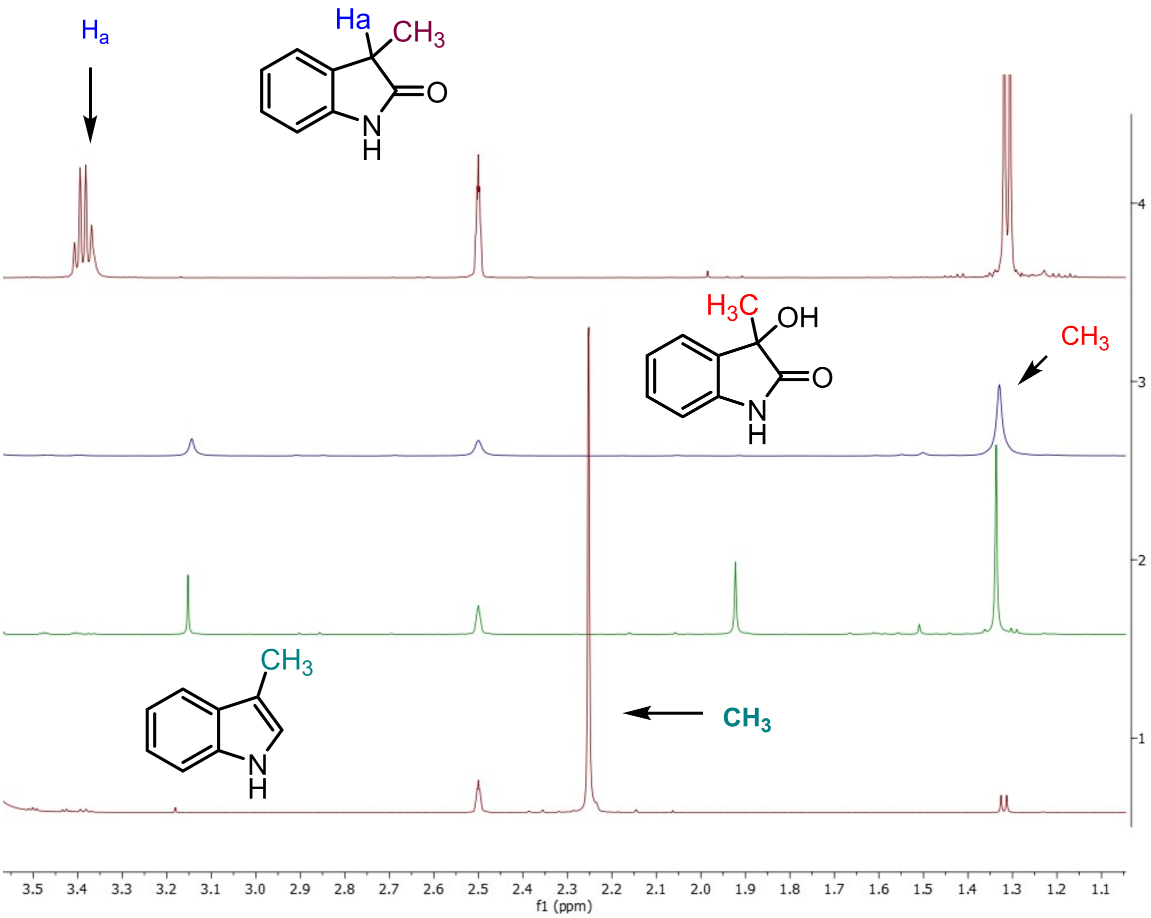
B, $BrCH_2CN$, 24 h, trace, 36 h, 20% yield

To a screw cap reaction tube charged with a magnetic stir-bar, substrate **1a'** (0.25 mmol) was added. Then, 2 mL normal DMSO was added. The reaction mixture was kept at 30 °C and stirred vigorously for completion of the reaction (24h). Then the reaction mixture was diluted with 20 mL of water and extracted with 3*20 mL of EtOAc. Afterward, the extracted organic layer was dried over Na_2SO_4 and concentrated and the product was purified by column chromatography using silica gel (100-200 mesh) and EtOAc / Hexane as eluent. Finally, the reaction mixture was analysed by ^1H NMR of crude reaction mixture and the desired product was not found.

Similarly, when, the reaction was carried out with 3 equiv of $BrCH_2CN$, the desired product was observed only 20% after 36 h, confirmed ^1H NMR

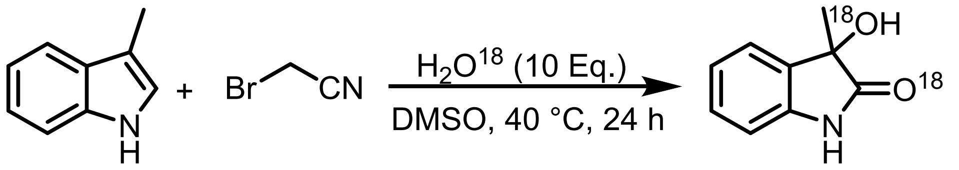
iv) NMR study of the crude reaction mixture



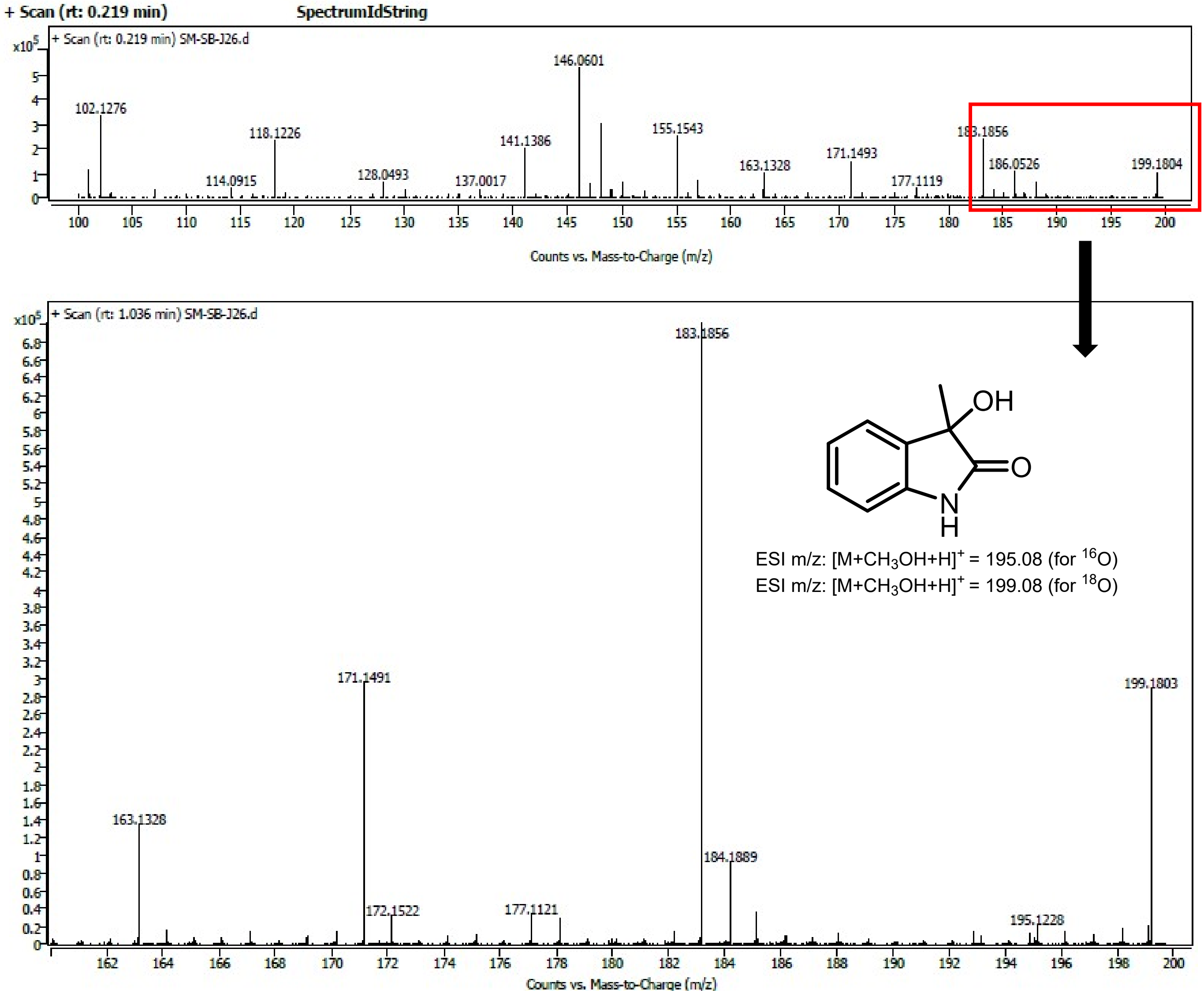


Conclusion: After 3 hours, two methyl peaks of the intended product and perhaps an intermediate were identified. After 6 hours, the methyl peak of the intermediate had vanished, leaving only the methyl peak of the desired product. During the 1H NMR analysis, we did not observe an oxindole signals.

v) **^{18}O labelling experiment with $^{18}OH_2$**



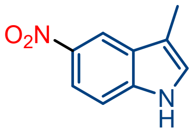
Confirmed by Mass data



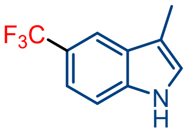
ESI m/z: $[M+CH_3OH+H]^+$ = 195.08 (for ^{16}O)

ESI m/z: $[M+CH_3OH+H]^+$ = 199.08 (for ^{18}O)

Unsuccessful Attempts:



0%



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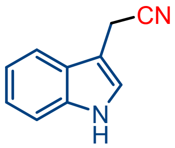

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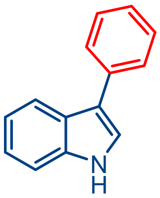

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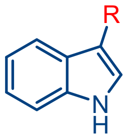
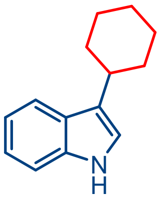


R = CN 0%

R = CHO 0%

R = CO_2Et 0%



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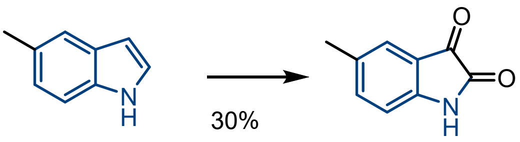

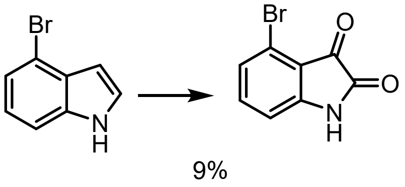

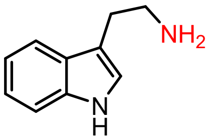

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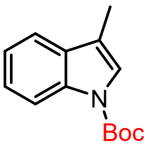
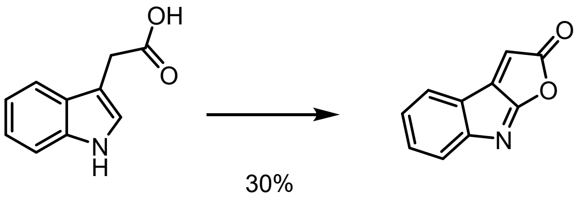
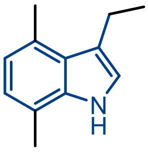


decomposed





complex mixtures

Green chemistry metrics comparison with previous works[11]

E-Factor = Amount of waste/Amount of final product (*Green Chem.*, **2025**, 10.1039/D4GC06205A)

AE = Molecular weight of product/Sum of molecular weight of reagent. (*Green Chem.*, **2025**, 10.1039/D4GC06205A)

Entry	**Work of different groups**	**AE**	**E-factor**	**Conditions**	**Ref^{n}**
1	Our method	97.88	1.16	Metal-free	-
2	Palaniappan	84.68	3.82	PANI, PCC	[12]
3	Yadav	41.64	4.18	$CeCl_3$•$7H_2O$ and IBX	[13]
4	Ren and others	73.31	3.86	$CuBr_2$+$Cu(ClO_4)_2$•$6H_2O$	[4]

Green Chemistry Metrics for our method [11,14]

a) Process Mass Intensity (PMI)

PMI = [Total mass used in the process (g/g)]/[Mass of product (g/g)]

PMI$_{\text{[Reaction]}}$ =[Mass$_{\text{[reactants]}}$ + Mass$_{\text{[reagents]}}$ + Mass$_{\text{[solvents]}}$]/ [Mass of product]

PMI$_{\text{[Workup \& column]}}$ = [Mass$_{\text{[workup solvents]}}$ + Mass$_{\text{[comumn solvents]}}$ /[Mass of product]

PMI$_{\text{[Total]}}$ = [Mass$_{\text{[reactants]}}$ + Mass$_{\text{[reagents]}}$ + Mass$_{\text{[solvents]}}$ + Mass$_{\text{[workup \& column solvents]}}$]/[Mass of product]

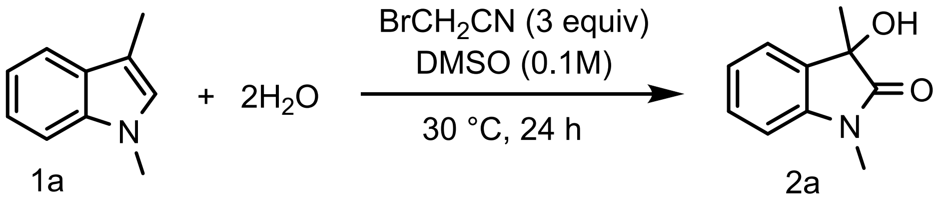
b) E-Factor = PMI-1

c) Atom Economy (AE) = [Molar Mass of desired product X 100]/ [Molar Mass of all reactants]

d) Reaction Mass Efficiency (RME) = [Mass of desired product X 100]/ [Mass of all reactants]

PMI Calculations:

The table below displays the detailed PMI calculations and other green chemistry parameters for the preparation of compound 2a in a 0.25 mmol scale.

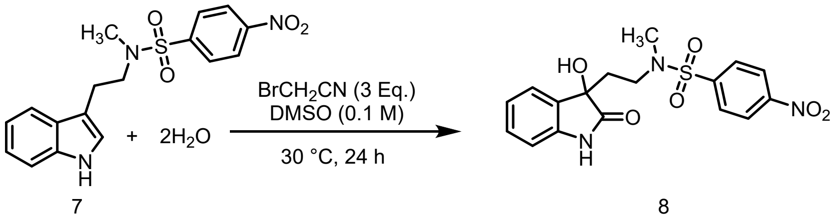


A) Reaction Stage

i)	**Substrate**	**Mass (g)**	**Mol. Wt.**	**Mol**
	1a	**0.036**	145.02	0.00025
ii)	**Reagents**	**Mass (g)**	**Mol. Wt.**	**Mol**
	$BrCH_2CN$	**0.089**	119.94	0.00075
iii)	**Reaction Solvents**	**Vol. (mL)**	**Density (g/mL)**	**Mass (g)**
	DMSO	2.5	1.10	2.750
	Total Reaction Materials	**2.875 g**		
B)	**Purification Stage (Work up & Column chromatography)**			
	Materials	**Vol. (mL)**	**Density (g/mL)**	**Mass (g)**
	H_2O	20	1.0	20
	AcOEt	180	0.902	162.36
	hexane	180	0.661	118.98
	Total purification Materials	**301.34 g**		
	Total Input Materials	**304.21 g**		
	Output Target Product	**Mass (g)**	**Mol. Wt.**	
	2a	**0.036**	177.2	
	Green Metrics Analysis			
	Yield (%)	**82**		
	Conversion (%)	**100**		
	AE (%)	**97.88**		
	RME (%)	**100**		
	PMI$_{\text{[Reaction]}}$	**79.86**		
	PMI$_{\text{[Workup \& column]}}$	**8370.55**		
	PMI$_{\text{[Total]}}$	**8450.27**		
	E-factor	**8449.27**		

PMI Calculations for step iii (7 to 8)

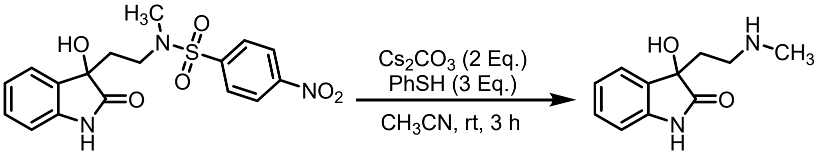
The table below displays the detailed PMI calculations and other green chemistry parameters for the preparation of compound 8 in a 0.25 mmol scale



A) Reaction Stage				
i)	**Substrate**	**Mass (g)**	**Mol. Wt.**	**Mol**
	7	**0.089**	359.40	0.25
ii)	**Reagents**	**Mass (g)**	**Mol. Wt.**	**Mol**
	$BrCH_2CN$	**0.089**	119.94	0.75
iii)	**Reaction Solvents**	**Vol. (mL)**	**Density (g/mL)**	**Mass (g)**
	DMSO	2.5	1.10	2.75
	Total Reaction Materials	**2.92 g**		
B) Purification Stage (Work up & Column chromatography)				
	Materials	**Vol. (mL)**	**Density (g/mL)**	**Mass (g)**
	H_2O	20	1.0	20
	AcOEt	180	0.902	162.36
	hexane	180	0.661	118.98
	Total purification Materials	**301.34 g**		
	Total Input Materials	**304.26 g**		
	Output Target Product	**Mass (g)**	**Mol. Wt.**	
	8	**0.068**	391.39	
	Green Metrics Analysis			
	Yield (%)	**70**		
	Conversion (%)	**100**		
	AE (%)	**98.98**		
	RME (%)	**76.40**		
	$PMI_{[Reaction]}$	**42.94**		
	$PMI_{[Workup\ \&\ column]}$	**4431.47**		
	$PMI_{[Total]}$	**4474.41**		
	E-factor	**4473.41**		

PMI Calculations for step iv (8 to 9)

The table below displays the detailed PMI calculations and other green chemistry parameters for the preparation of compound 9 (Donaxaridine) in a 0.25 mmol scale.

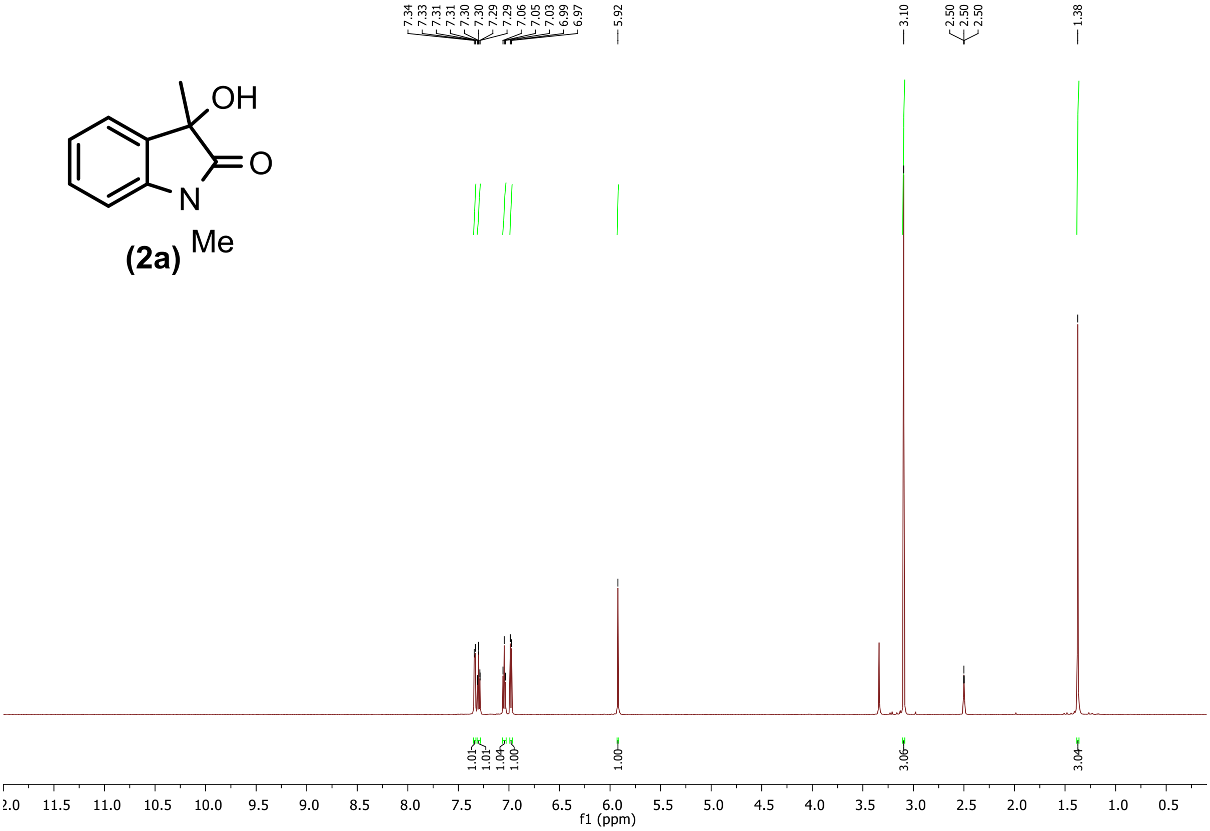


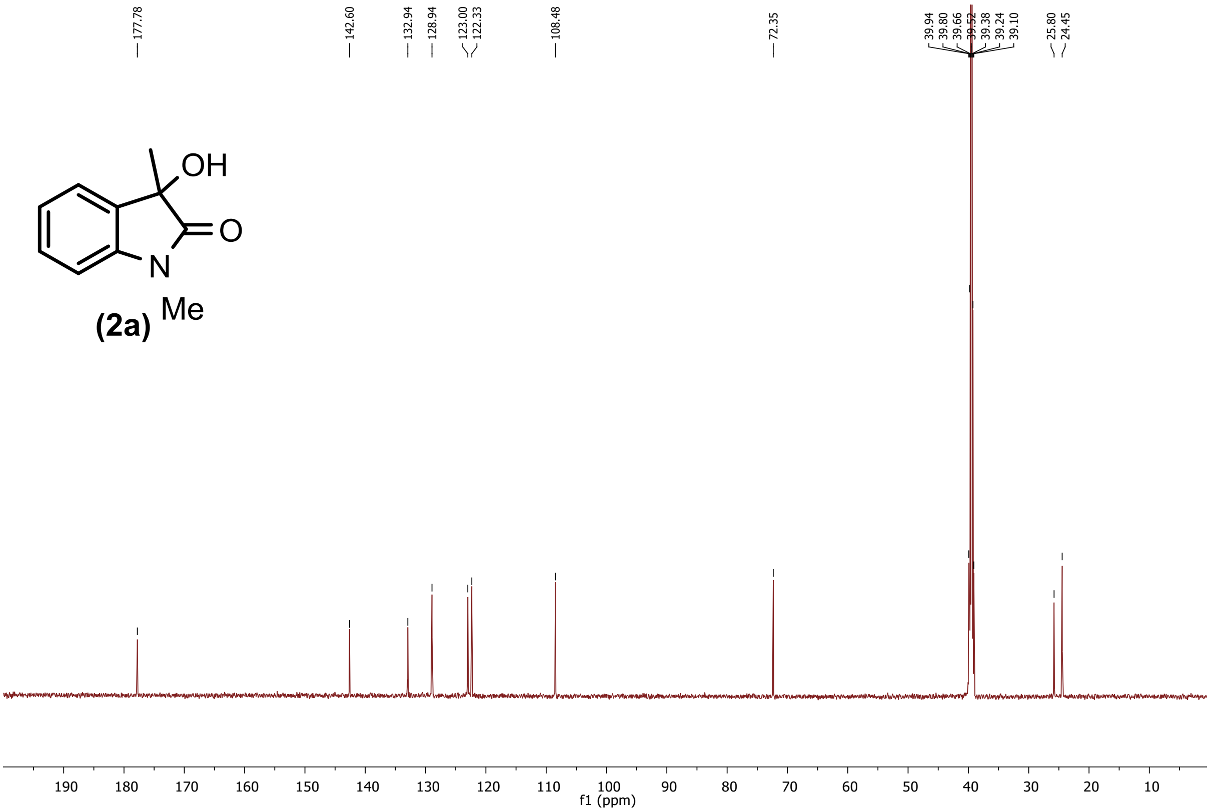
8 9

A) Reaction Stage				
i)	**Substrate**	**Mass (g)**	**Mol. Wt.**	**Mol**
	8	**0.097**	391.39	0.25
ii)	**Reagents**	**Mass (g)**	**Mol. Wt.**	**Mol**
	Cs_2CO_3	**0.162**	325.82	0.5
	PhSH	**0.082**	110.19	0.75
iii)	**Reaction Solvents**	**Vol. (mL)**	**Density (g/mL)**	**Mass (g)**
	CH_3CN	1.5	0.783	1.17
	Total Reaction Materials	**1.51 g**		
B) Purification Stage (Work up & Column chromatography)				
	Materials	**Vol. (mL)**	**Density (g/mL)**	**Mass (g)**
	H_2O	20	1.0	20
	AcOEt	180	0.902	162.36
	hexane	180	0.661	118.98
	Total purification Materials	**301.34 g**		
	Total Input Materials	**302.85 g**		
	Output Target Product	**Mass (g)**	**Mol. Wt.**	
	9	**0.023**	206.25	
	Green Metrics Analysis			
	Yield (%)	**45**		
	Conversion (%)	**100**		
	AE (%)	**52.69**		
	RME (%)	**23.71**		
	$PMI_{[Reaction]}$	**65.65**		
	$PMI_{[Workup\ \&\ column]}$	**13101.73**		
	$PMI_{[Total]}$	**13167.39**		
	E-factor	**13166.39**		

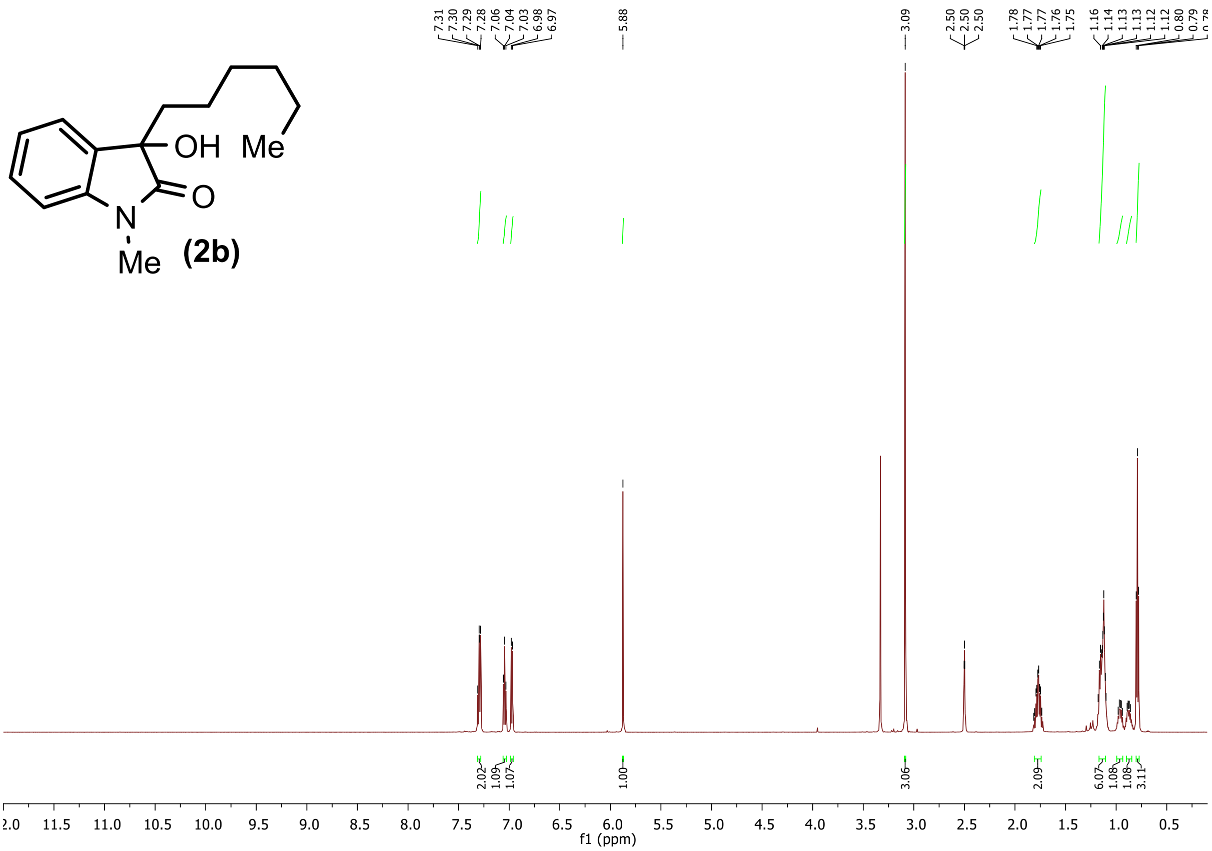
NMR spectra of synthesized compounds

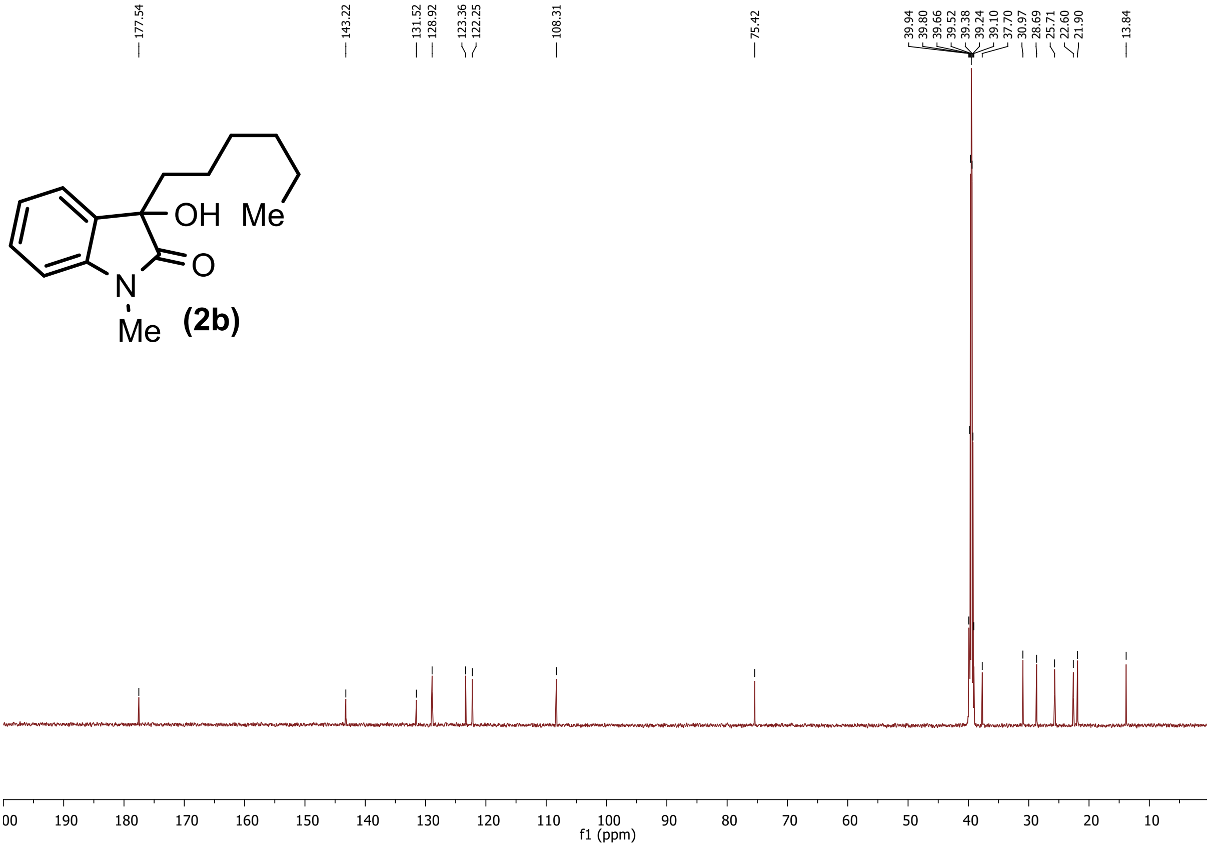
NMR of compound (**2a**)



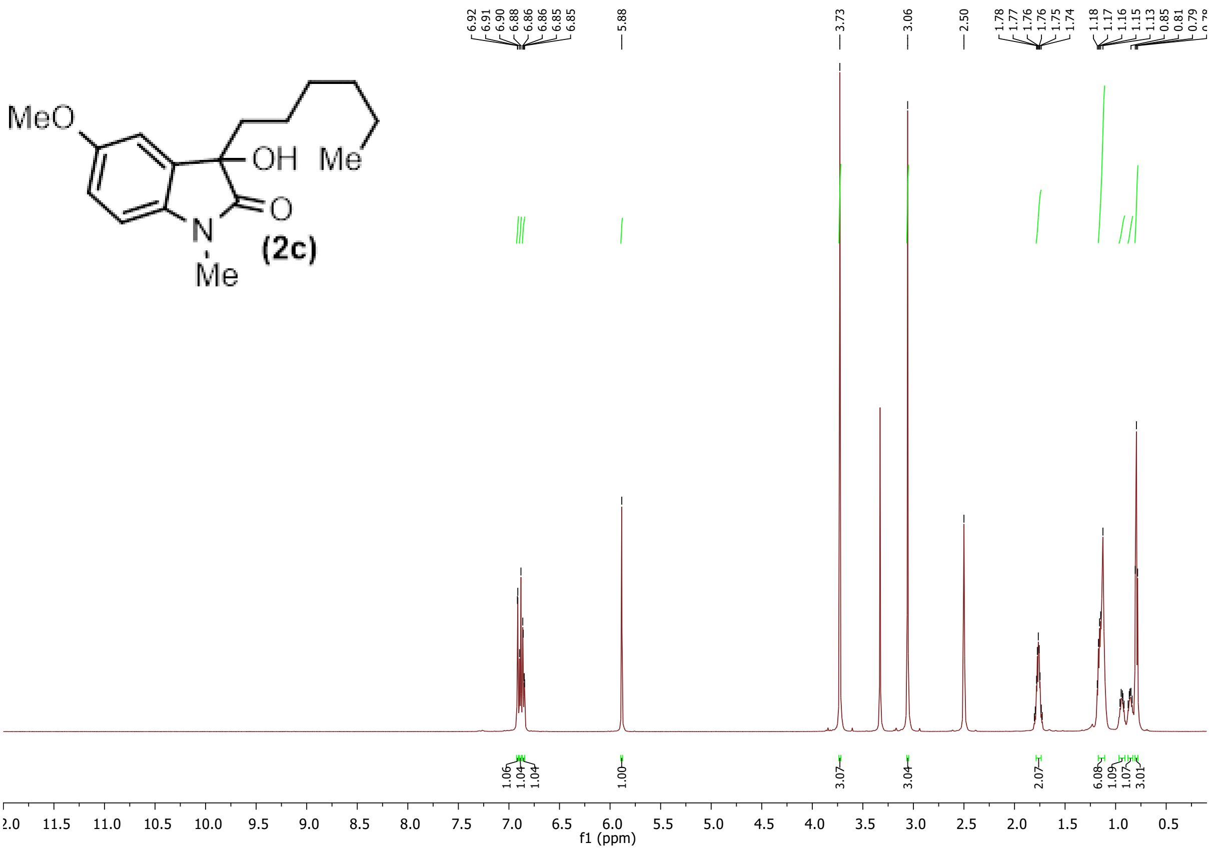


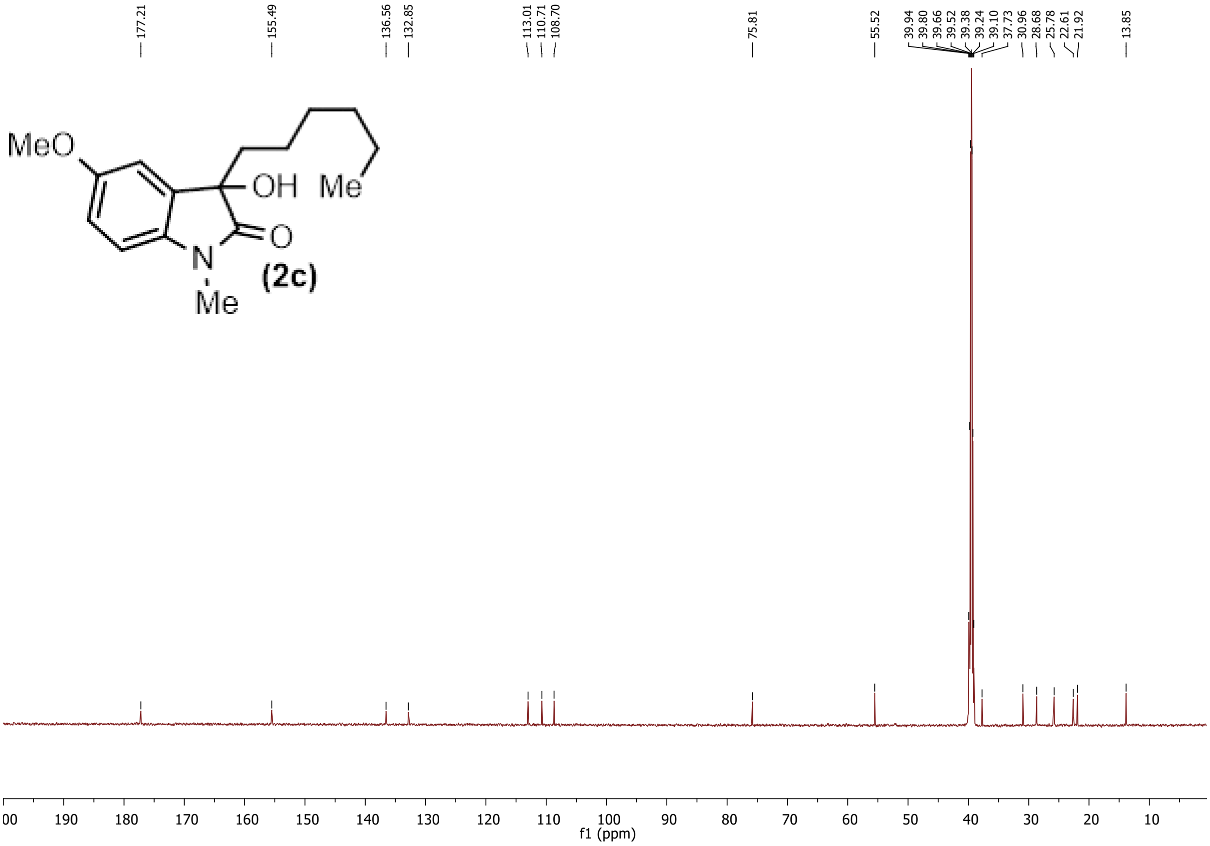
NMR of compound (**2b**)



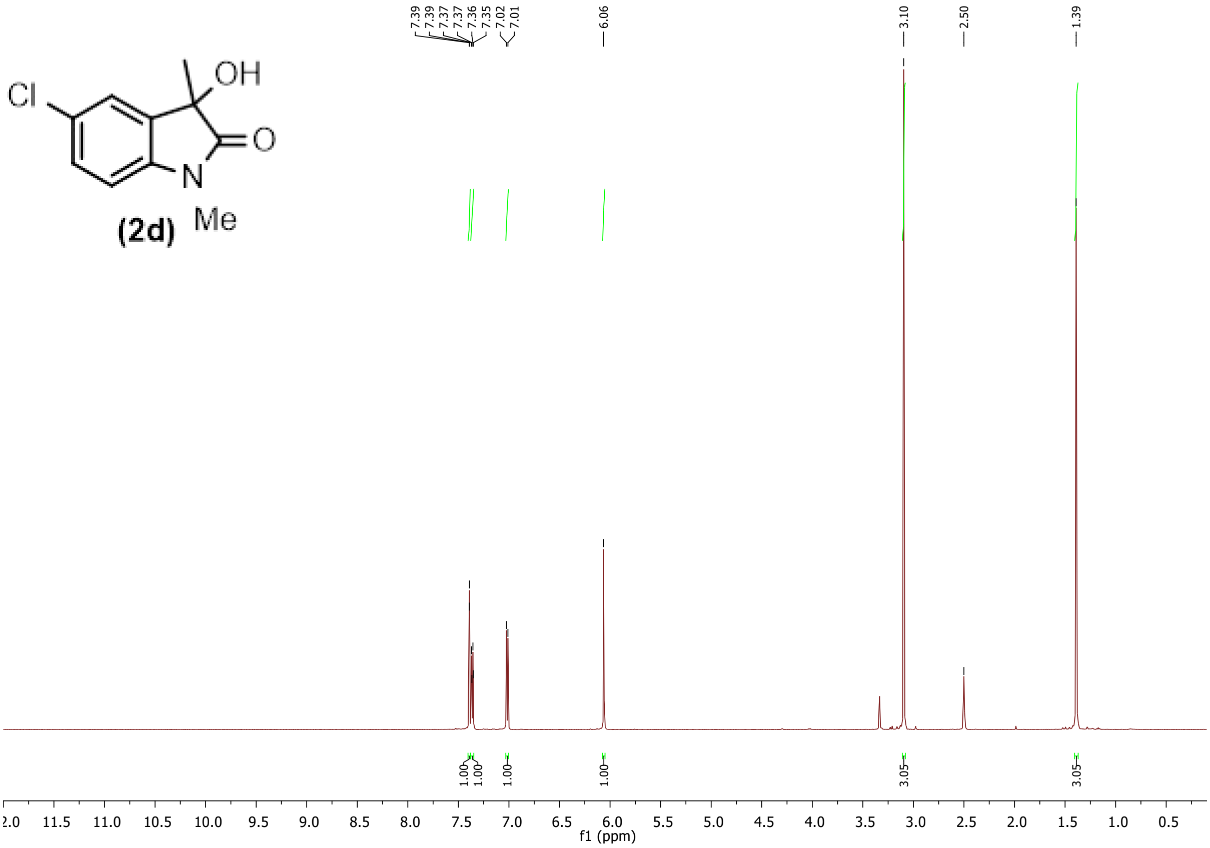


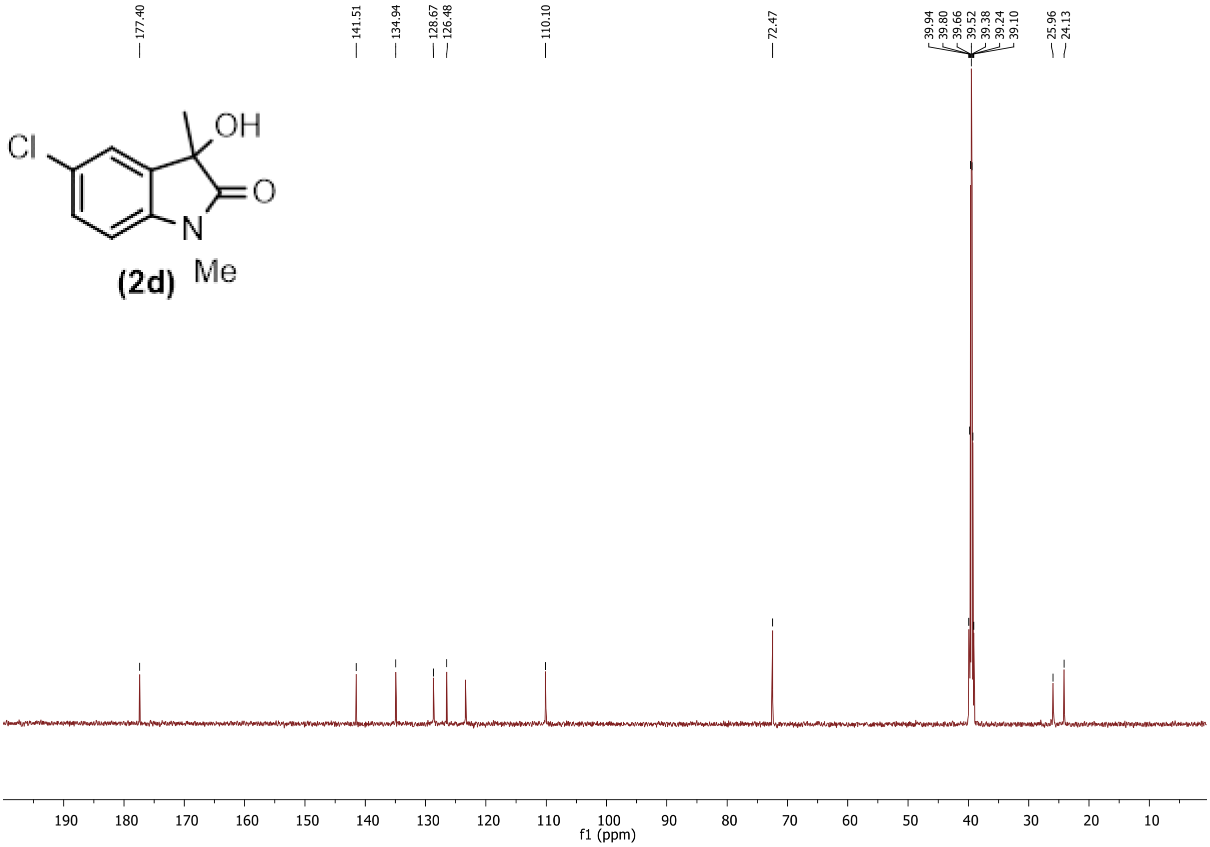
NMR of compound (**2c**)



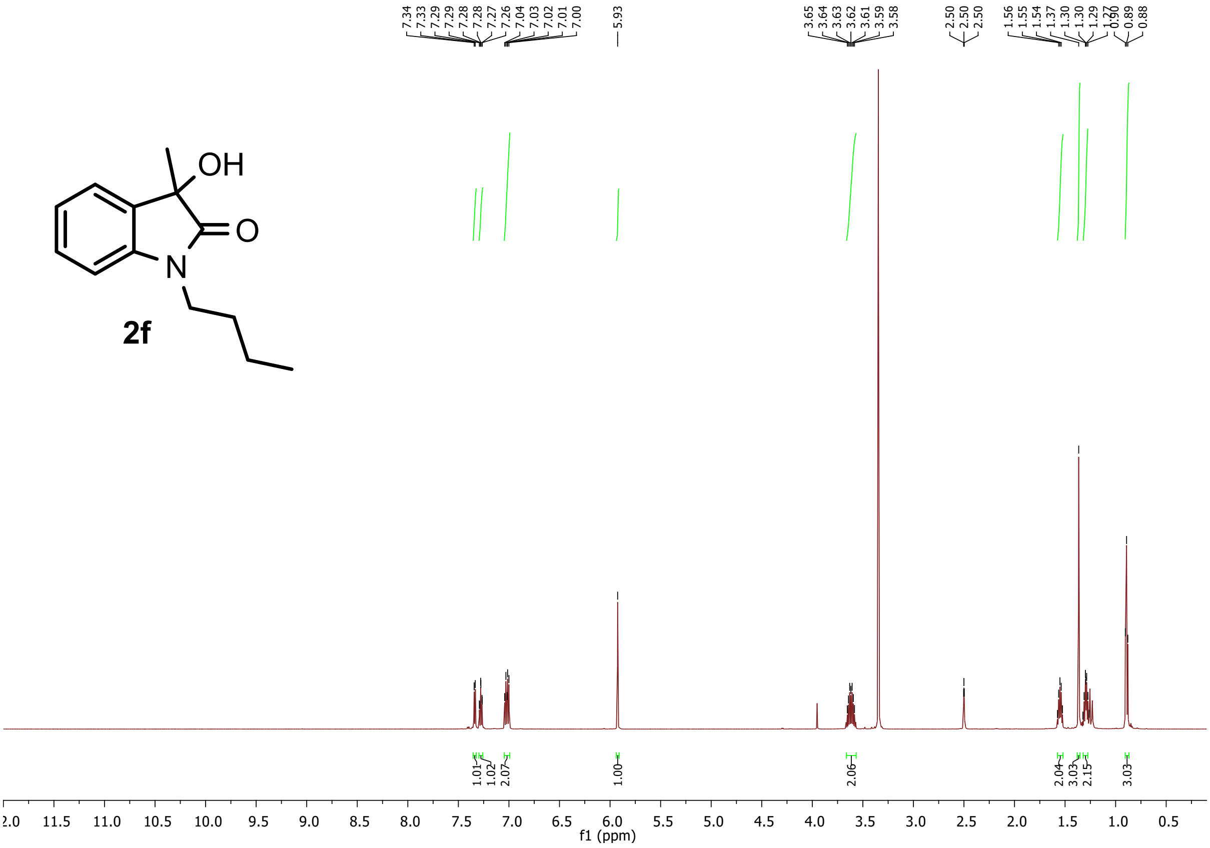


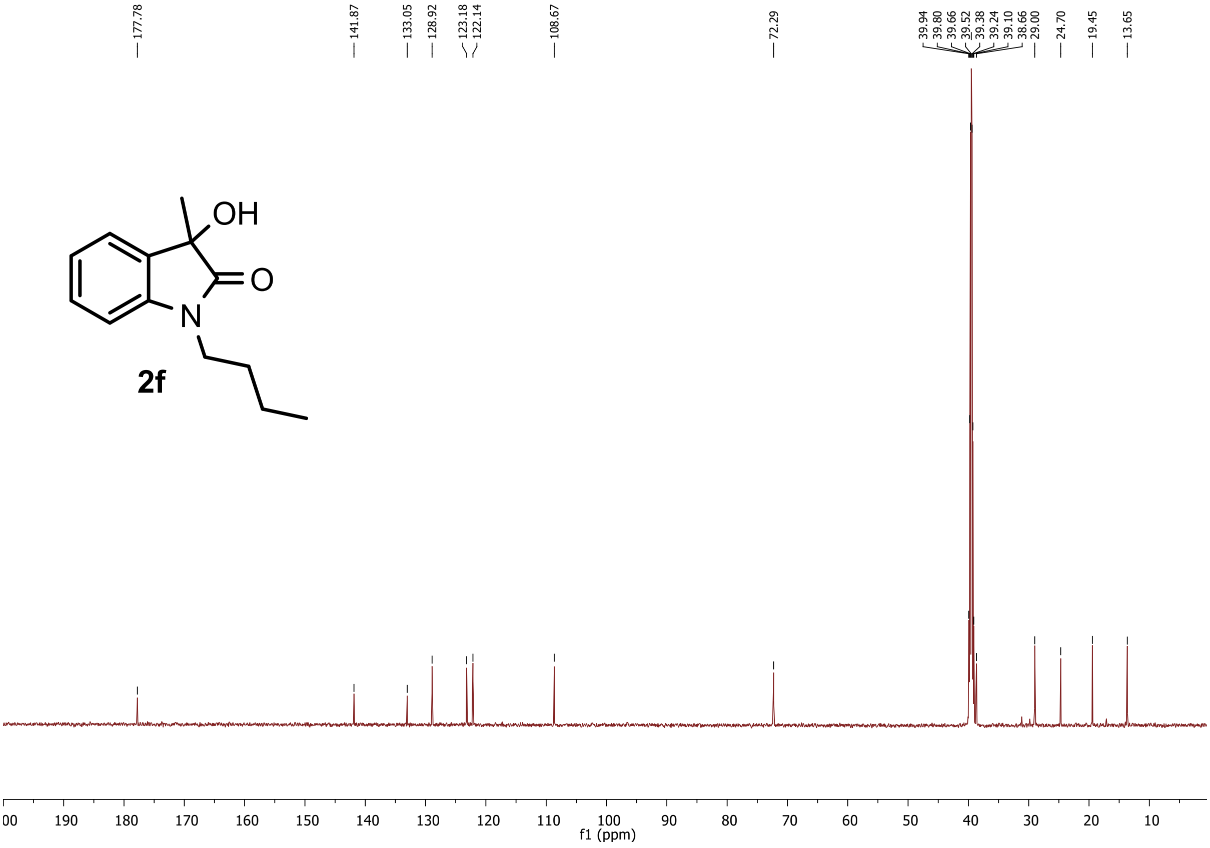
NMR of compound (**2d**)



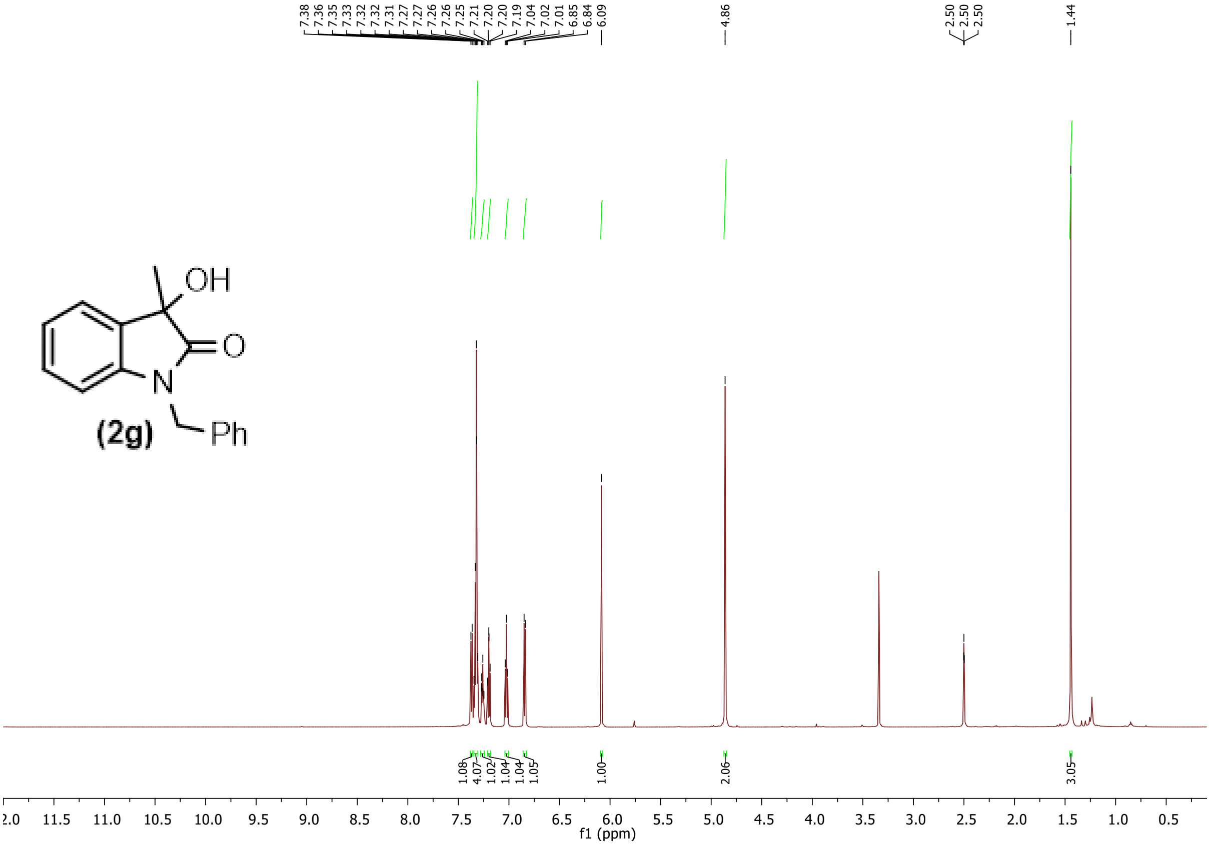


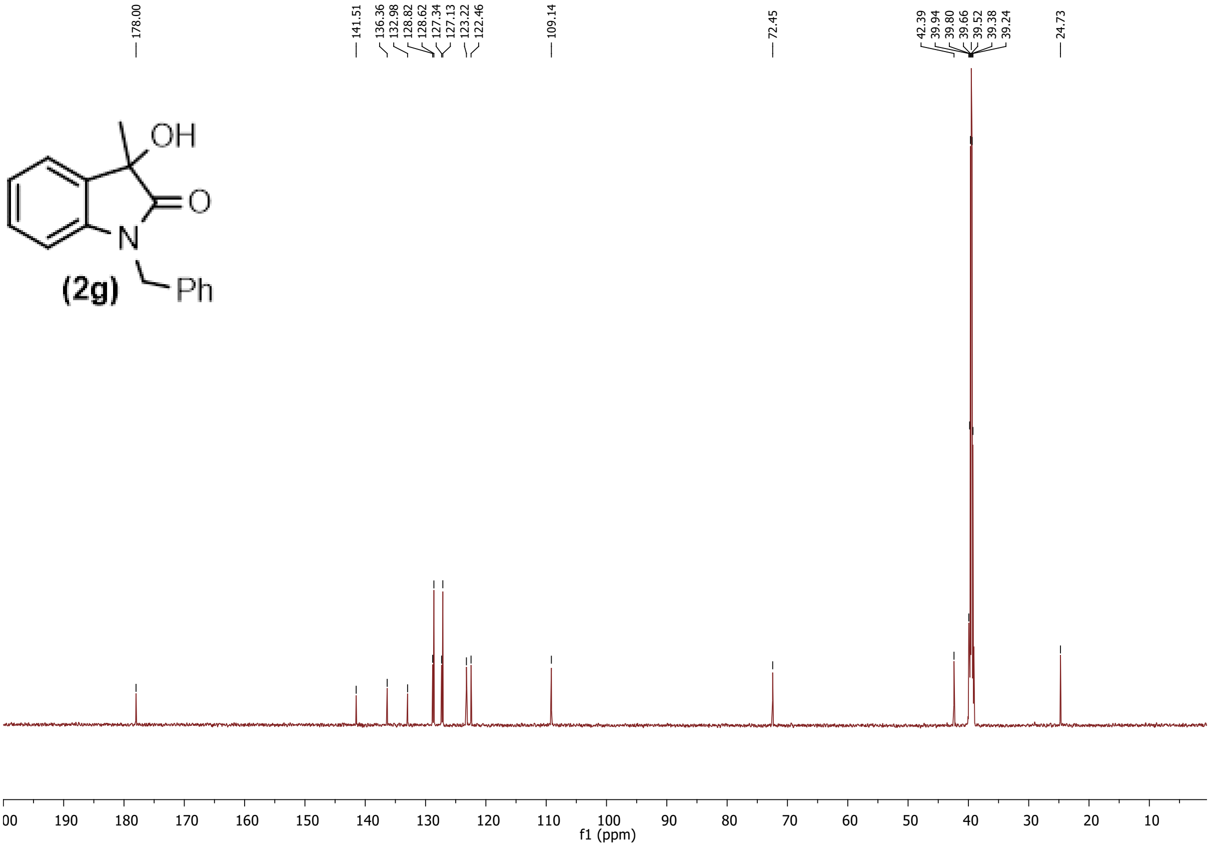
NMR of compound (**2f**)



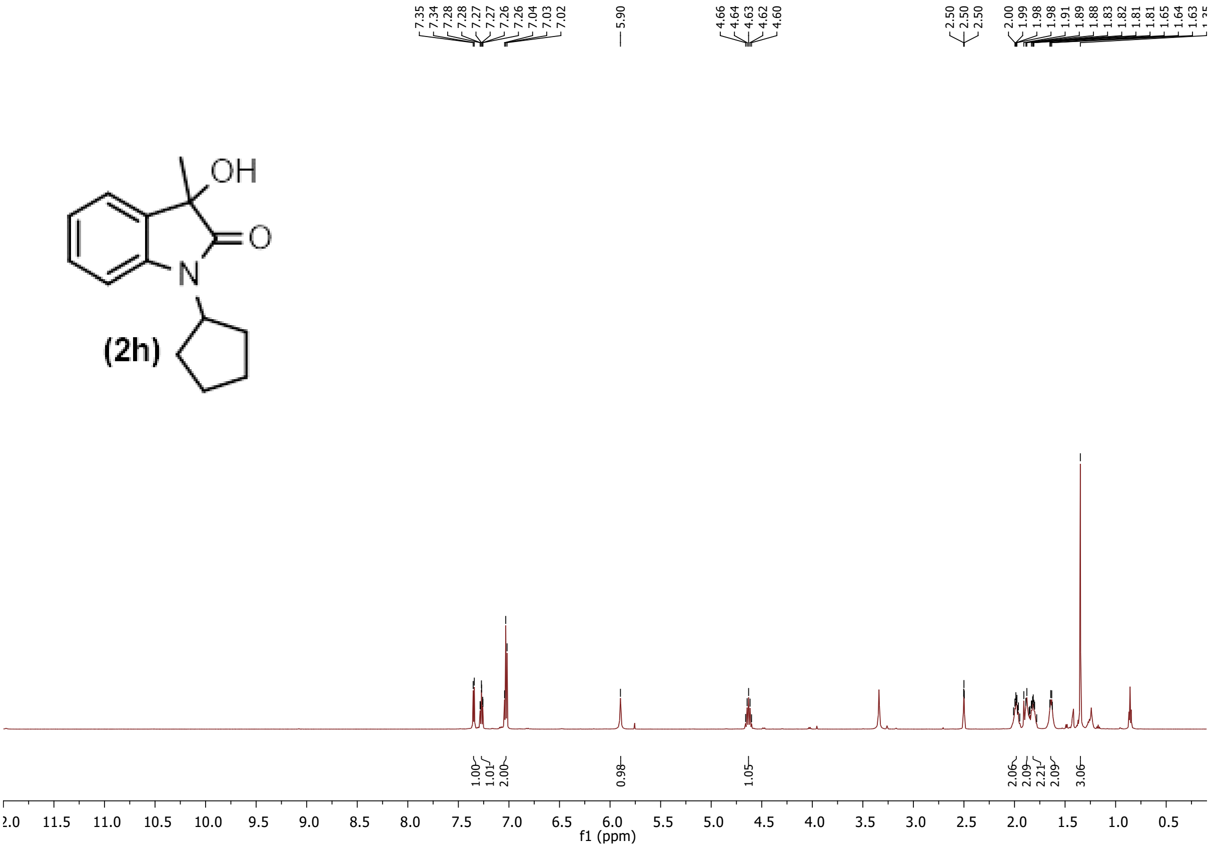


NMR of compound (**2g**)

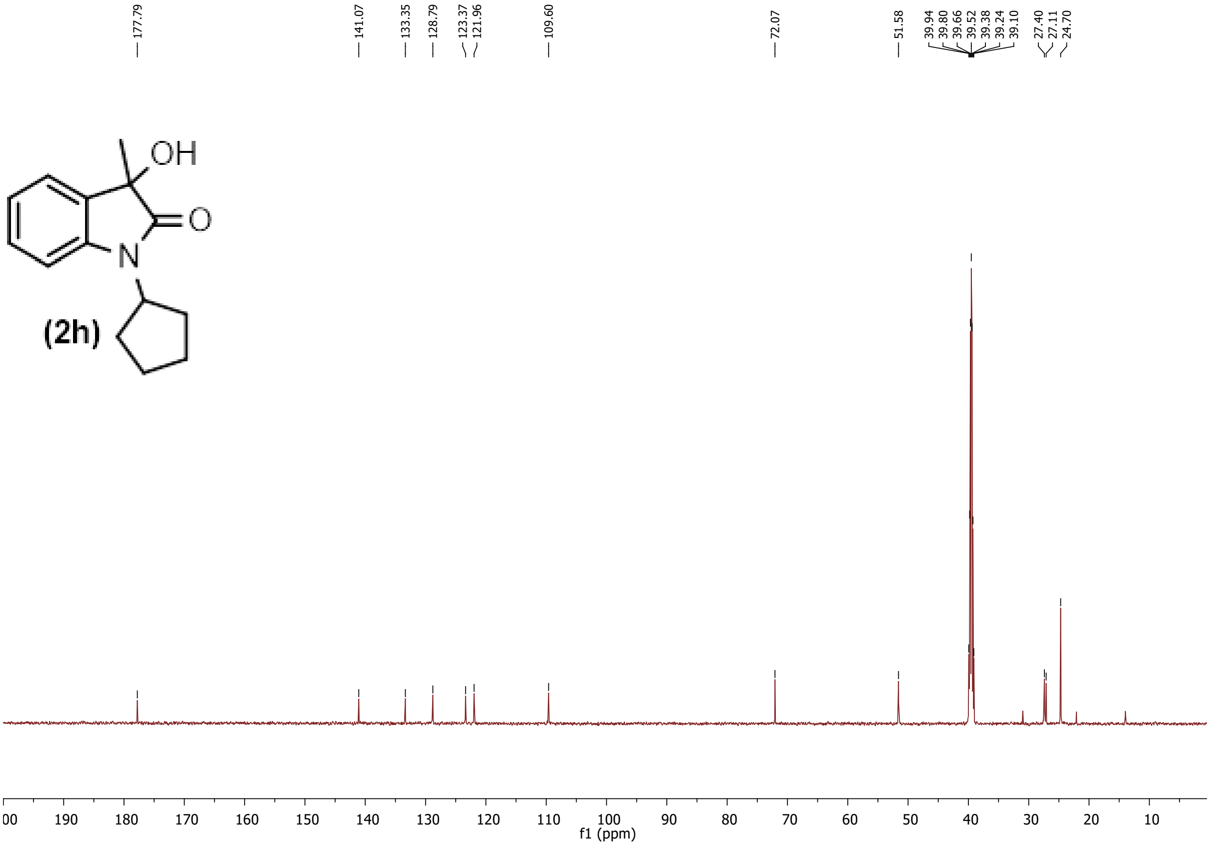




NMR of compound (**2h**)

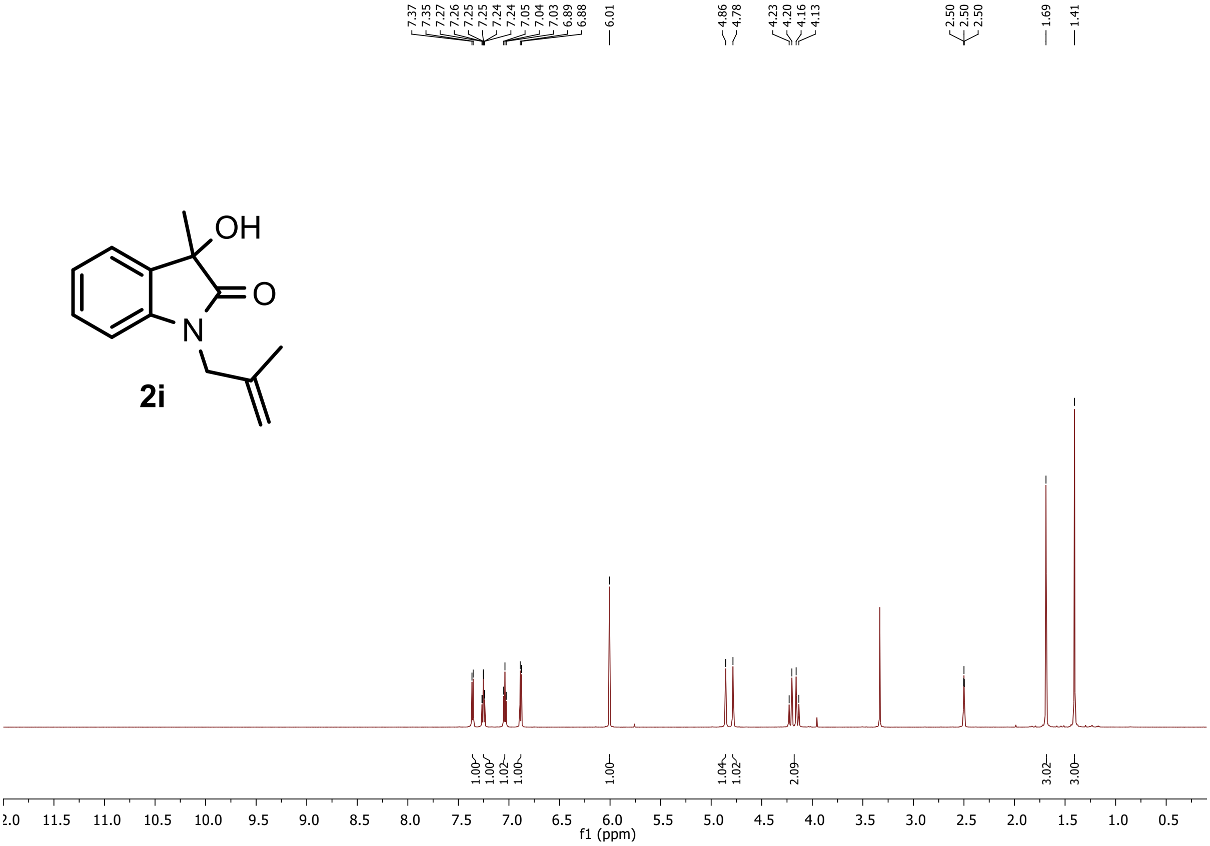


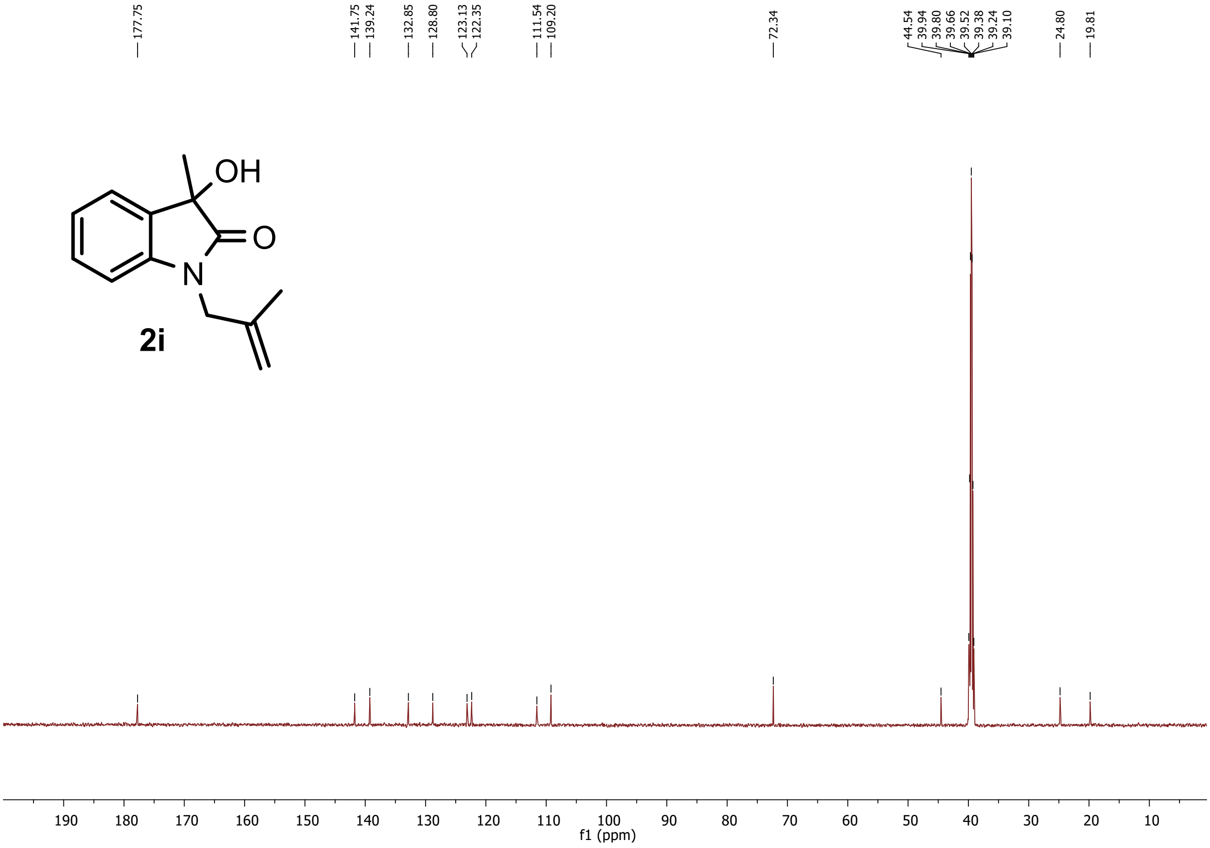
(2h)



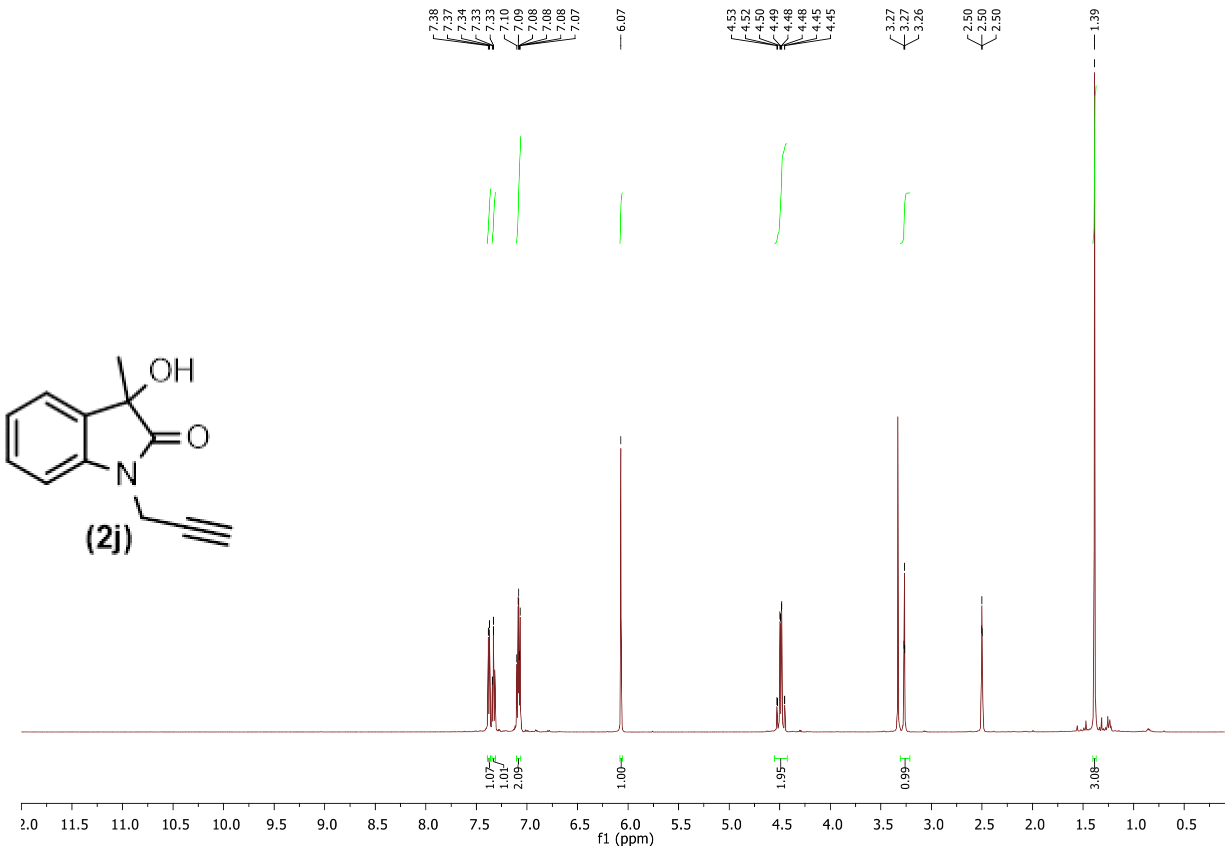
(2h)

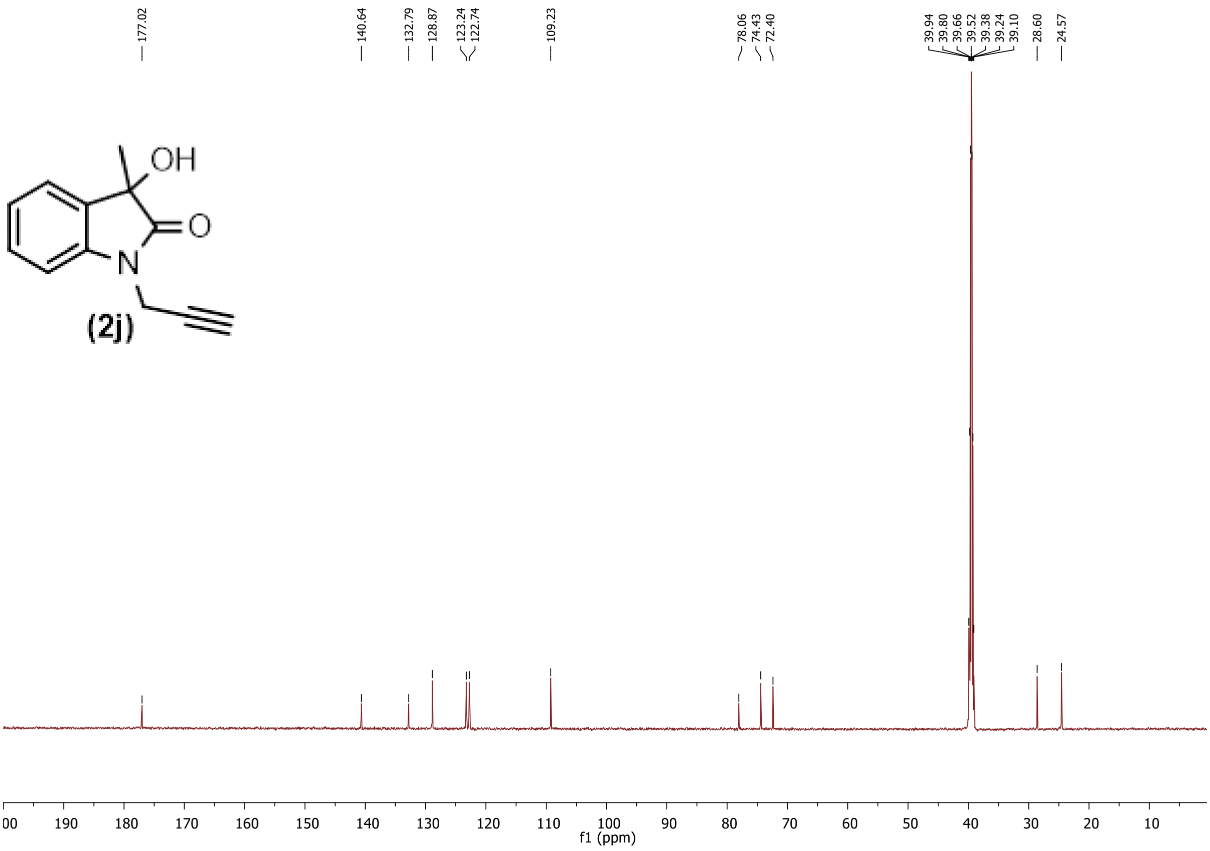
NMR of compound (**2i**)



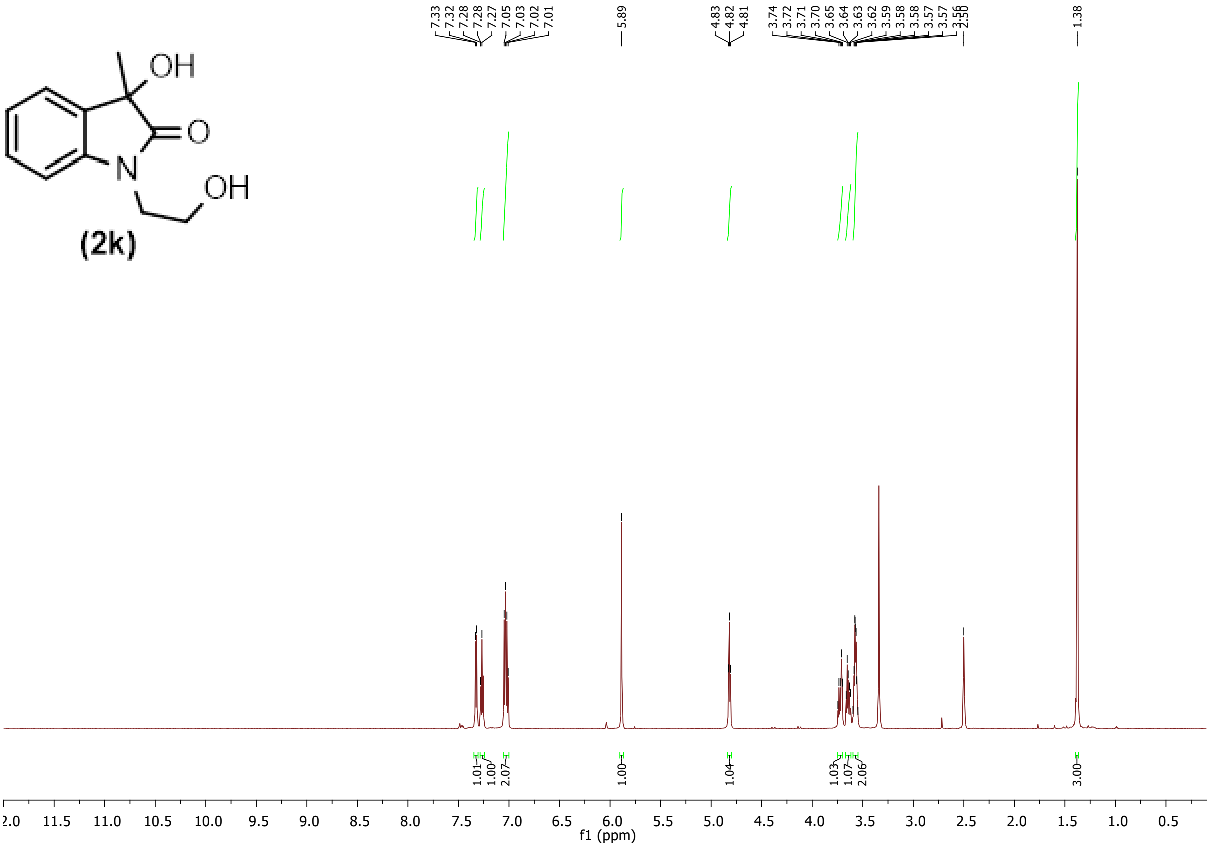


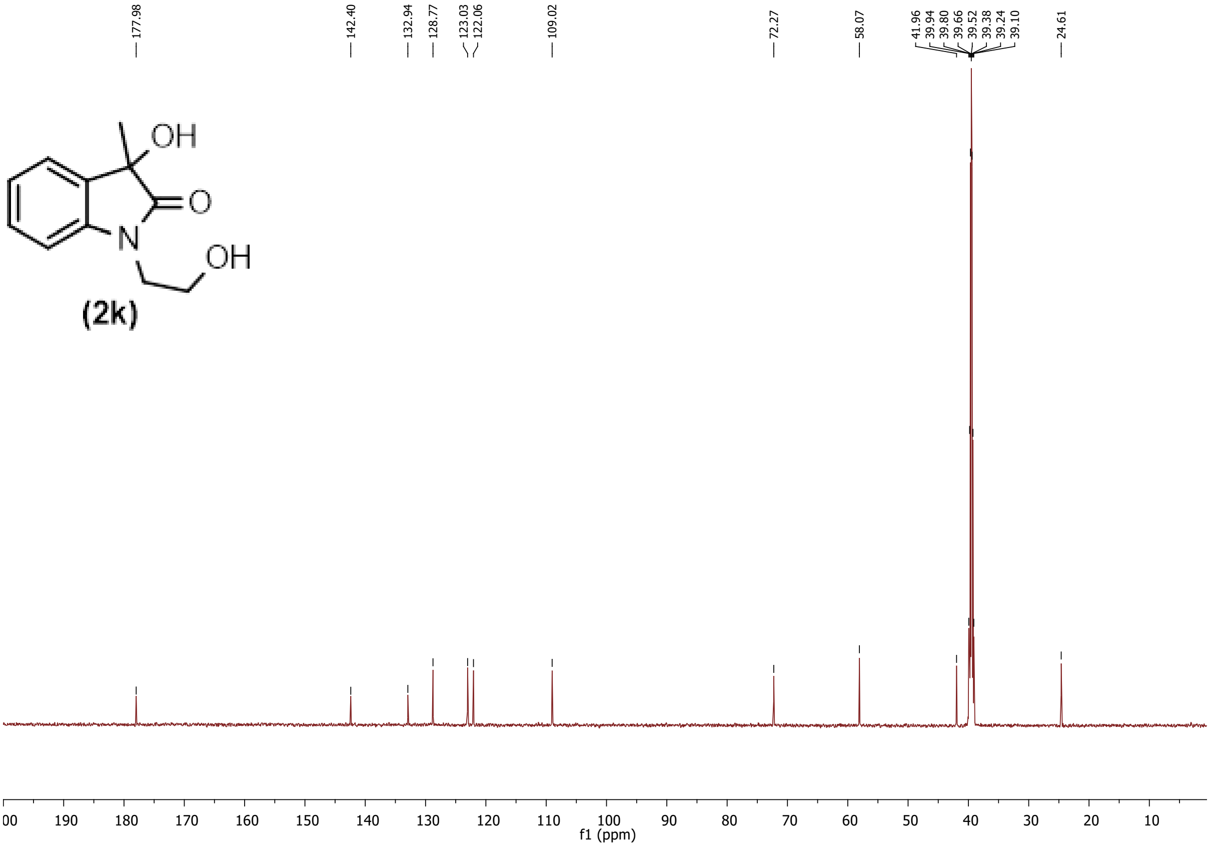
NMR of compound (**2j**)





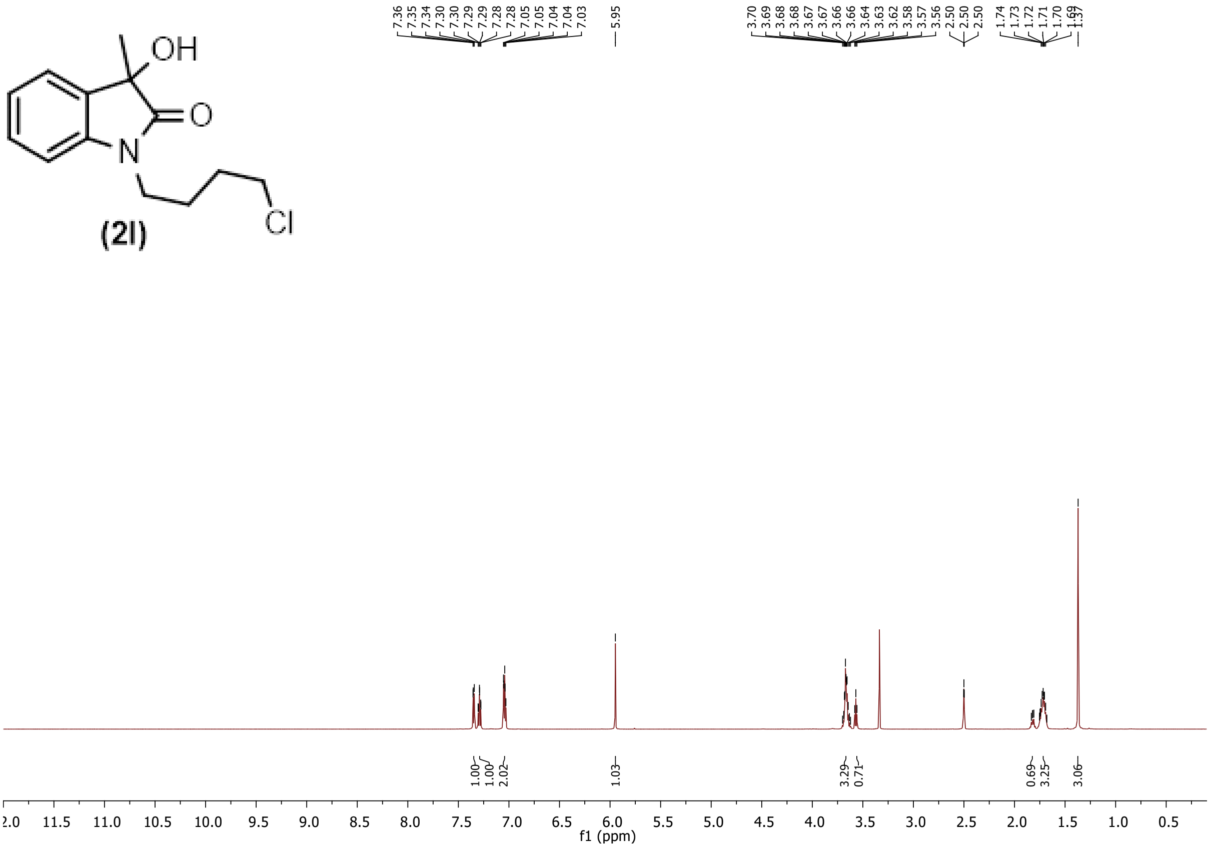
NMR of compound (**2K**)



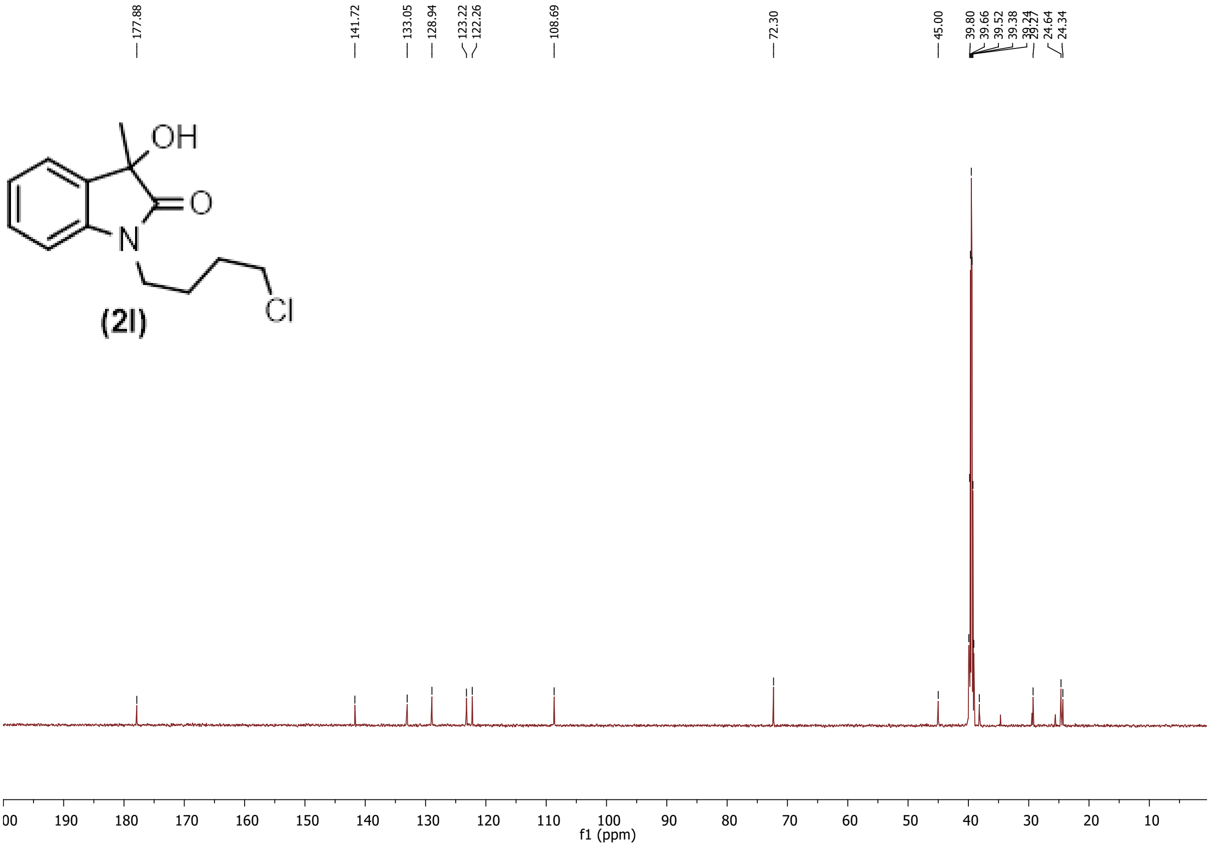


NMR of compound (**2l**)

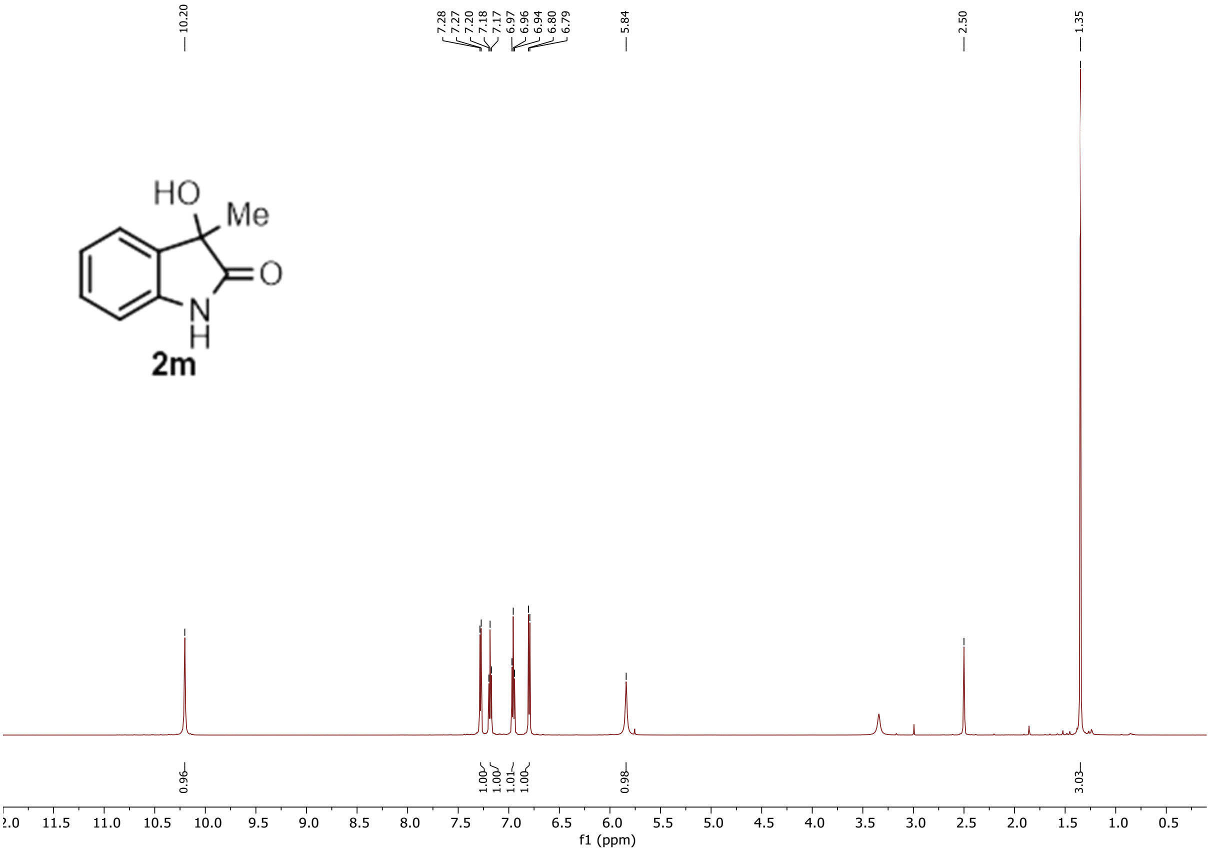
(2l)

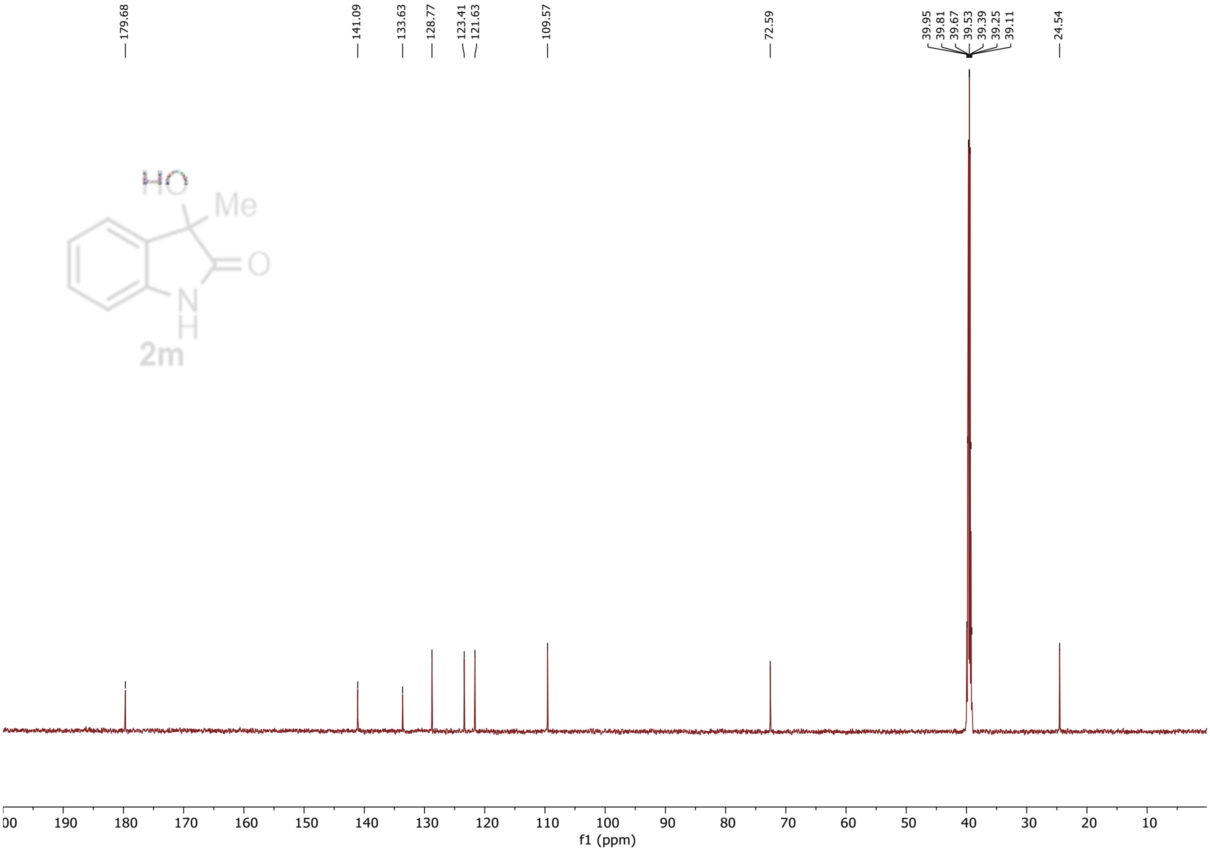


(2l)

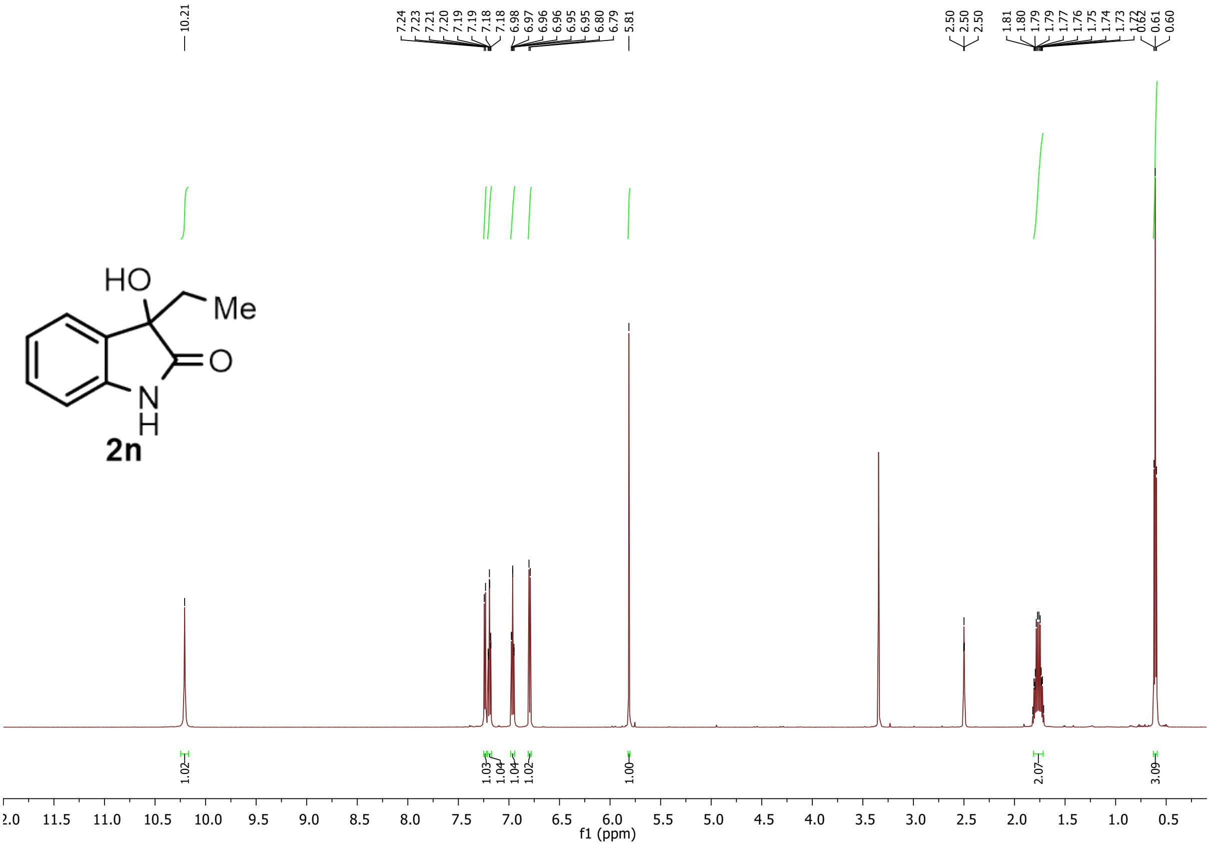


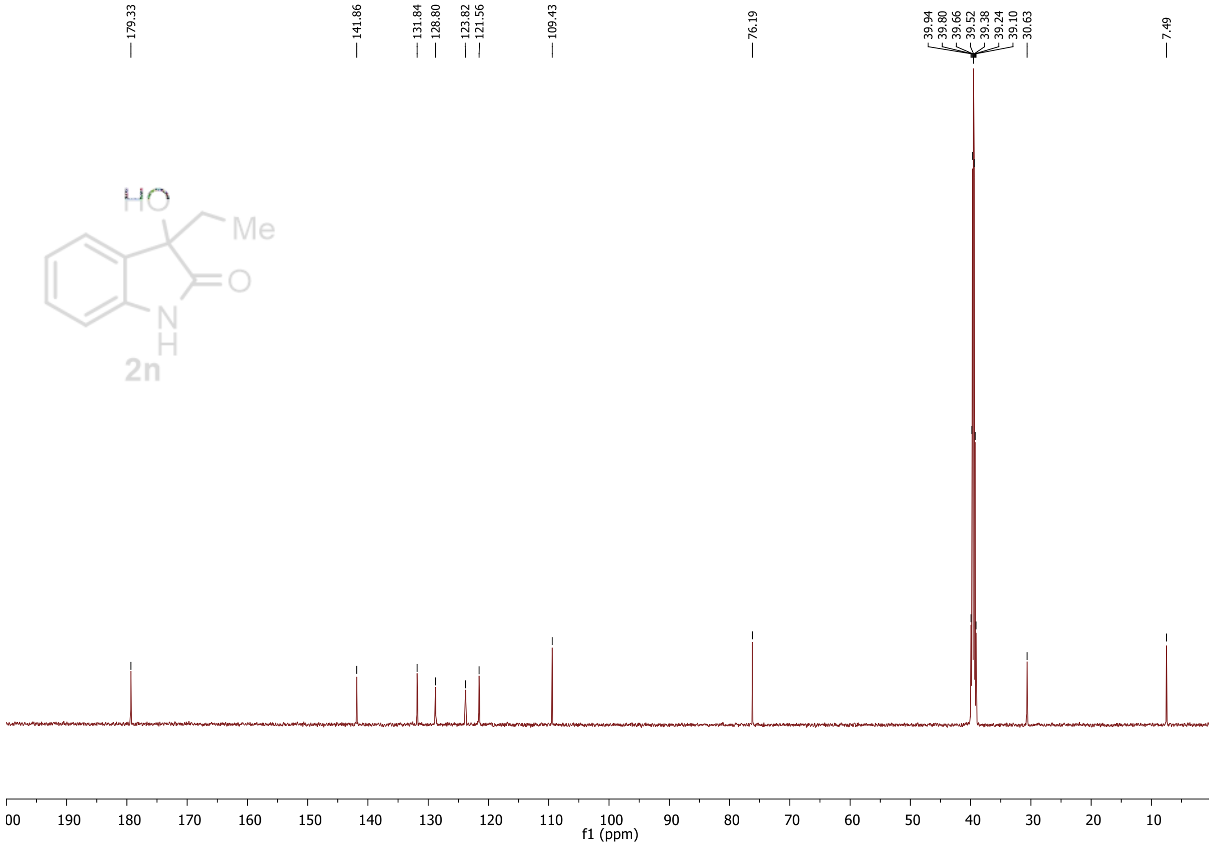
NMR of compound (**2m**)



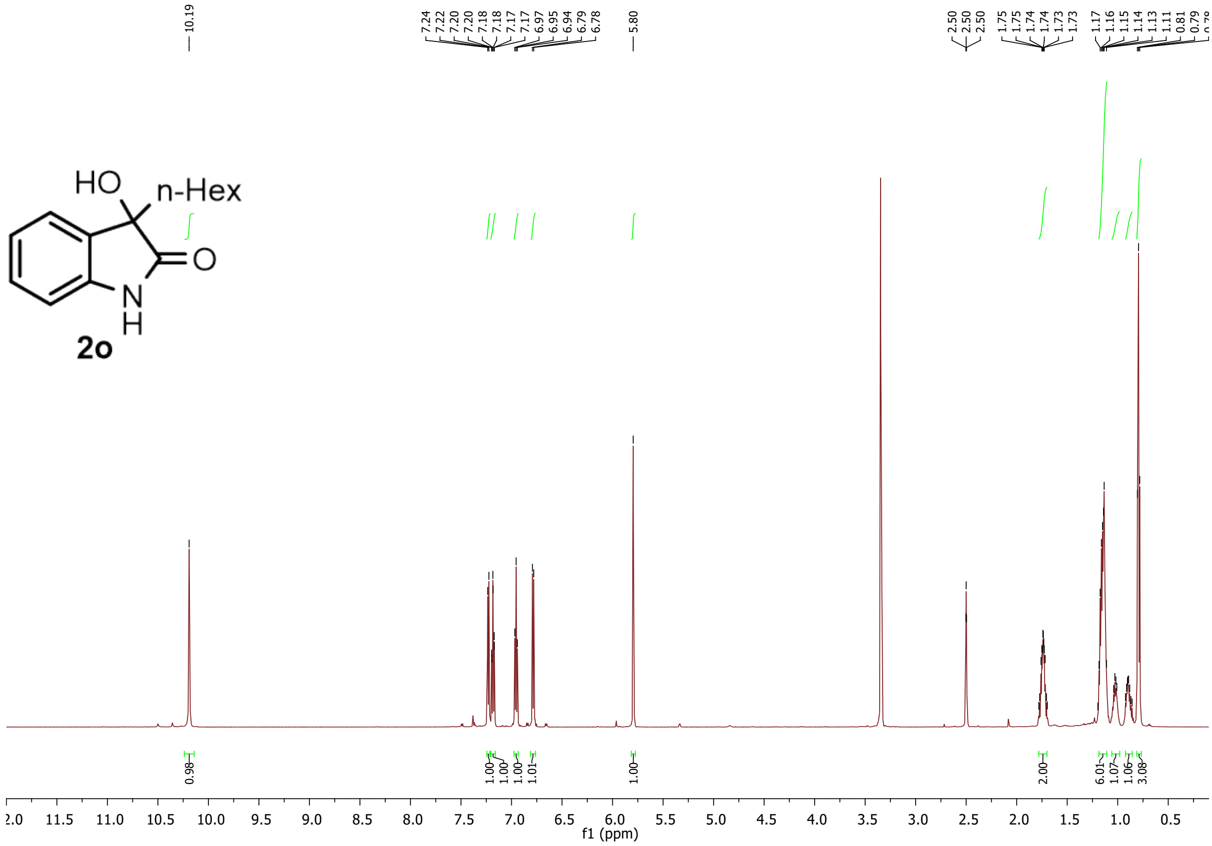


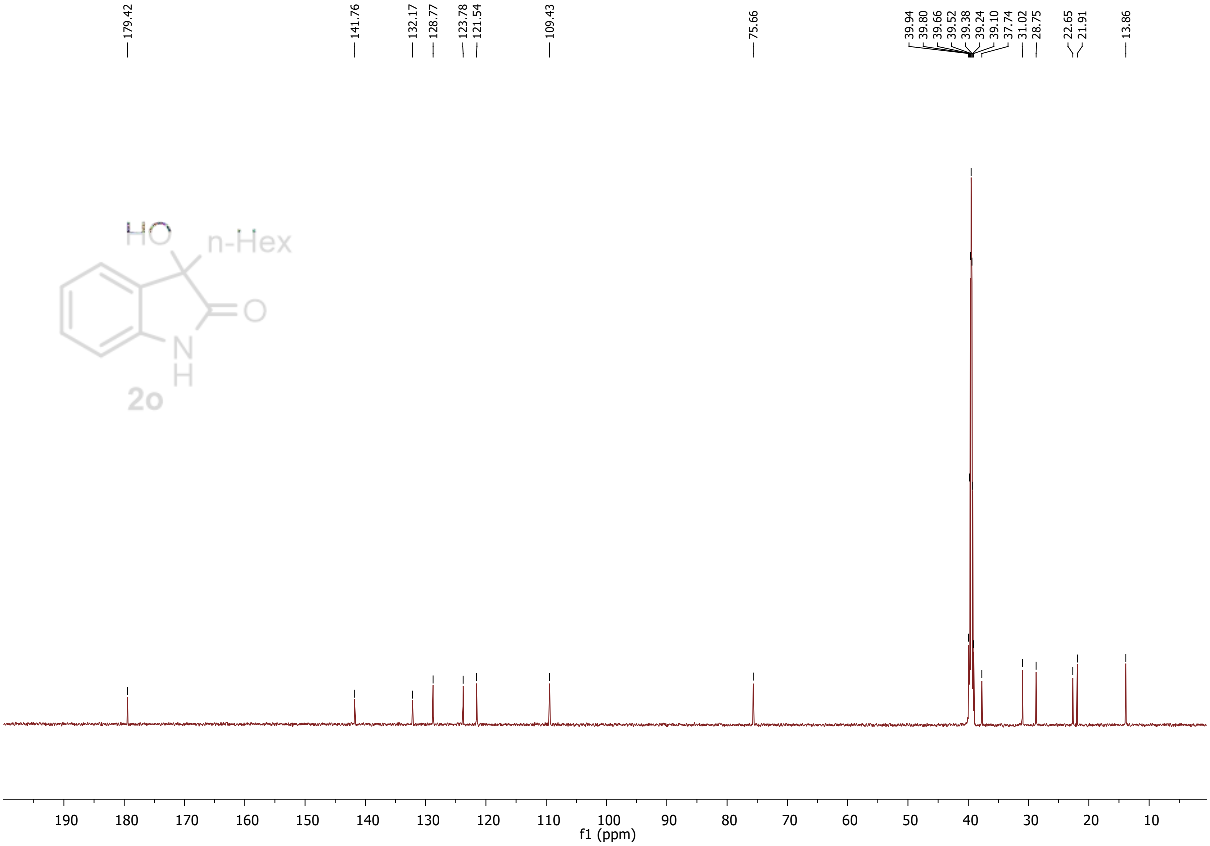
NMR of compound (**2n**)



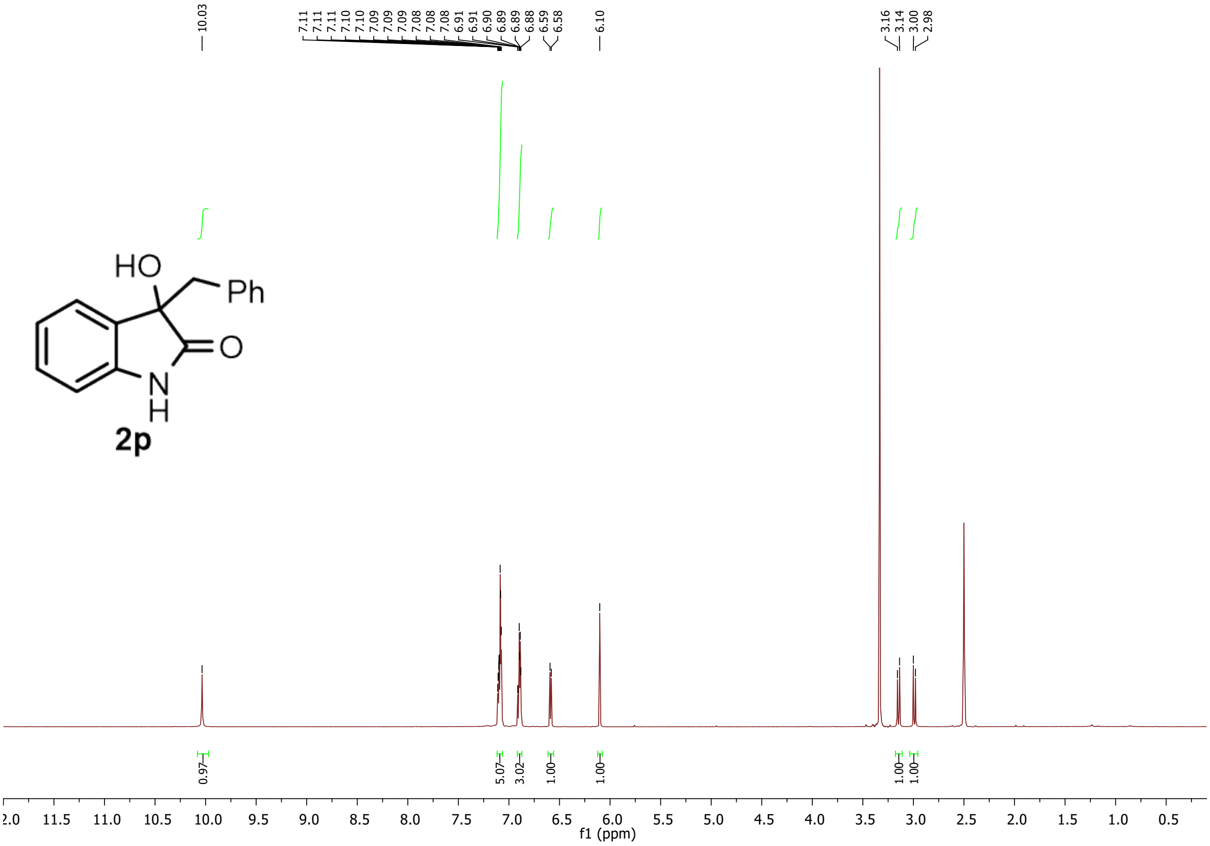


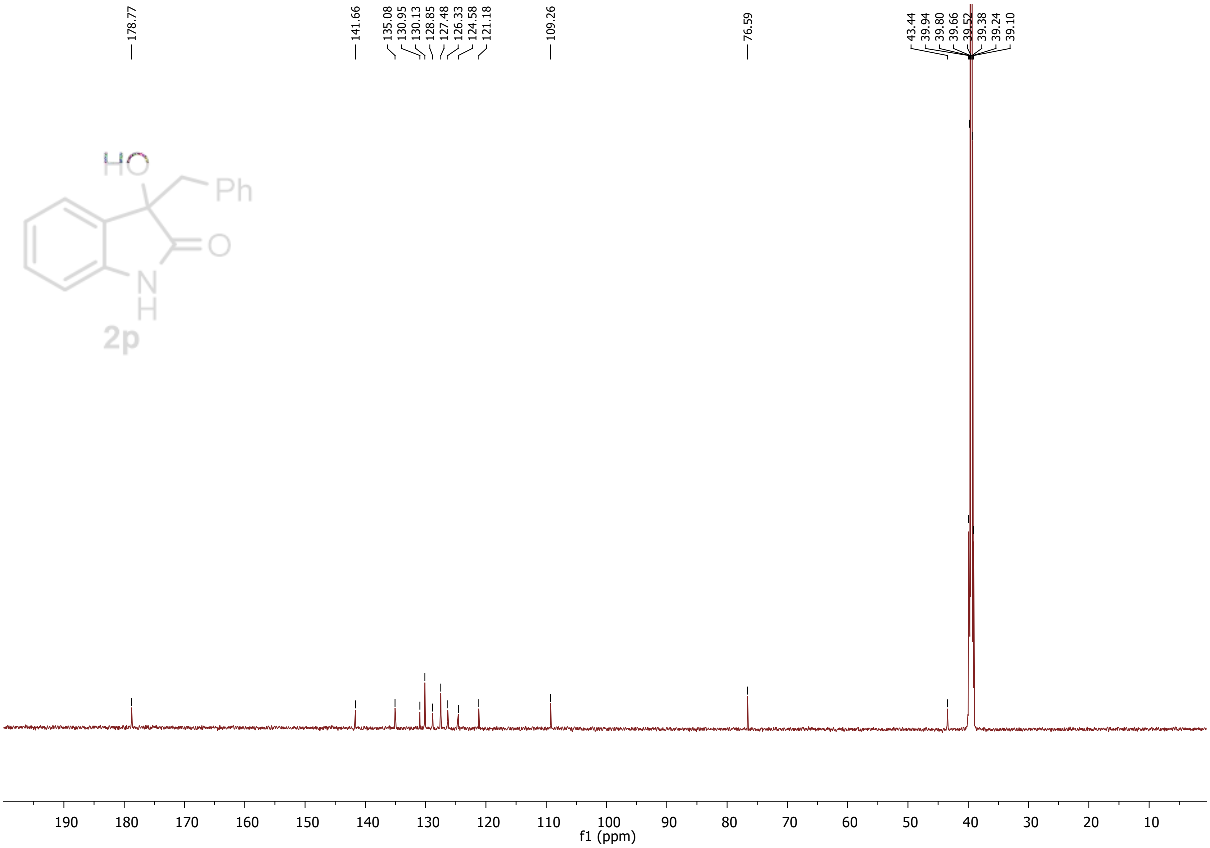
NMR of compound (**2o**)



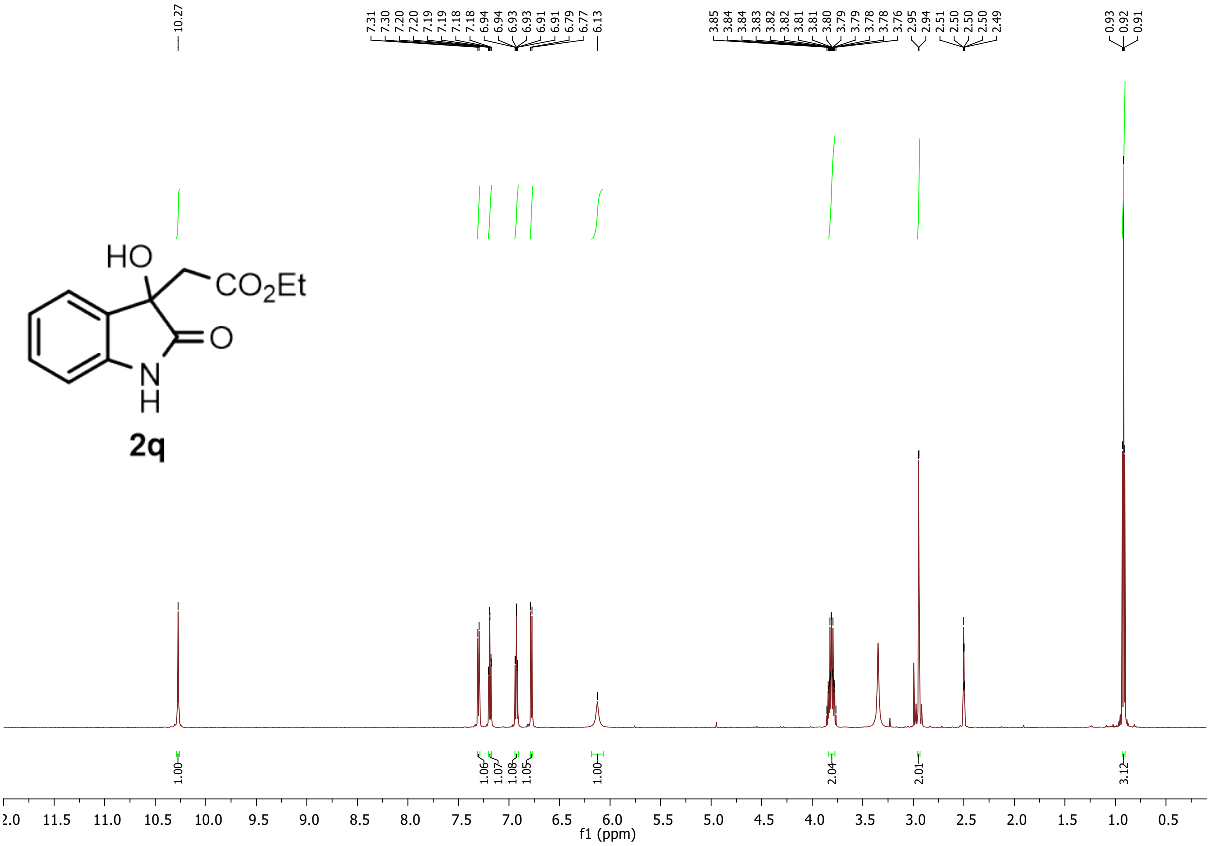


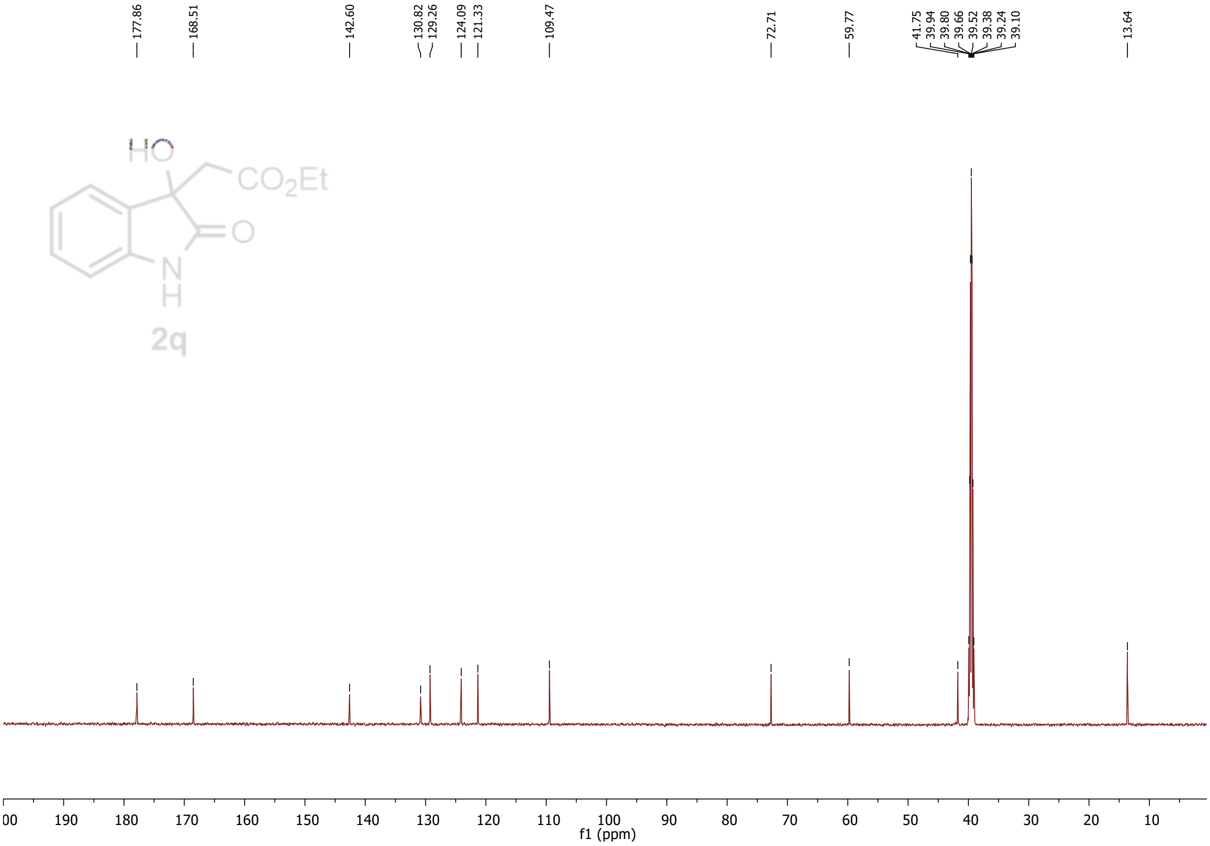
NMR of compound (**2p**)



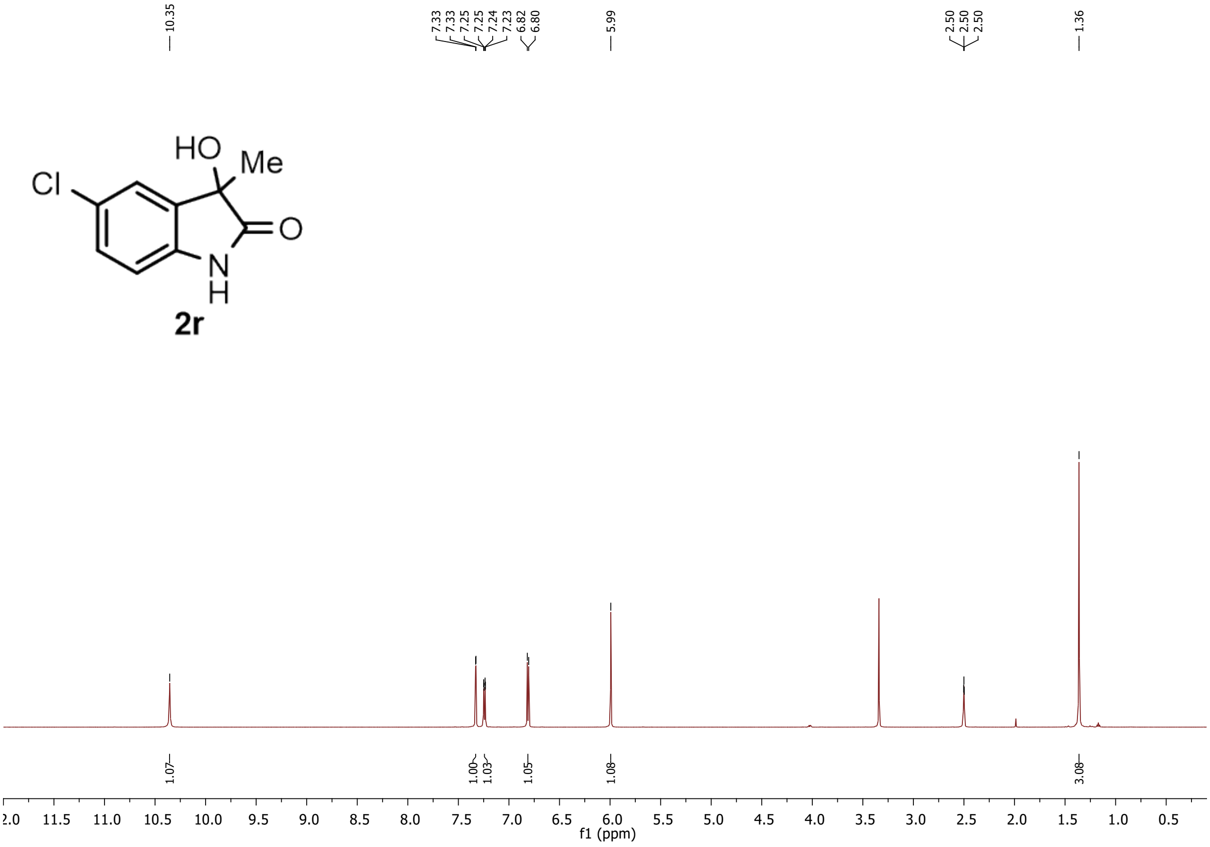


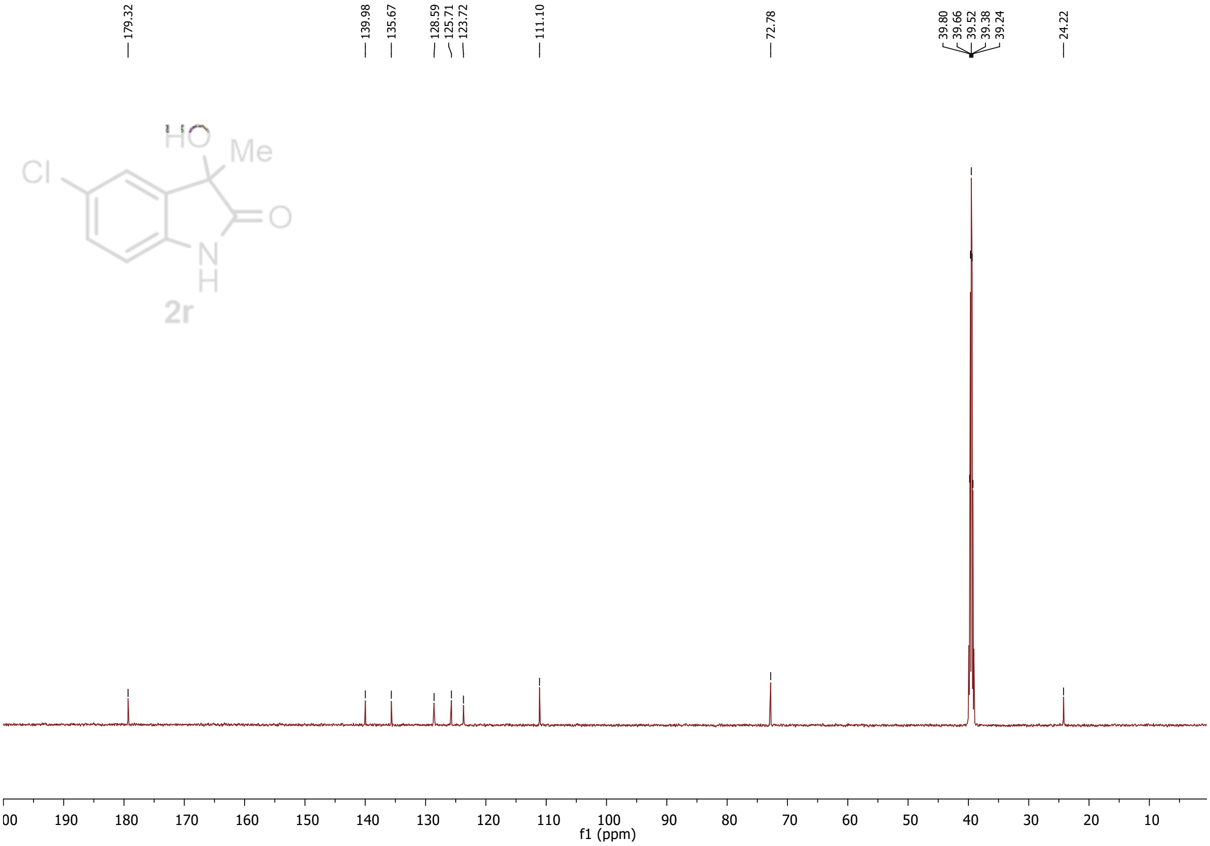
NMR of compound (**2q**)



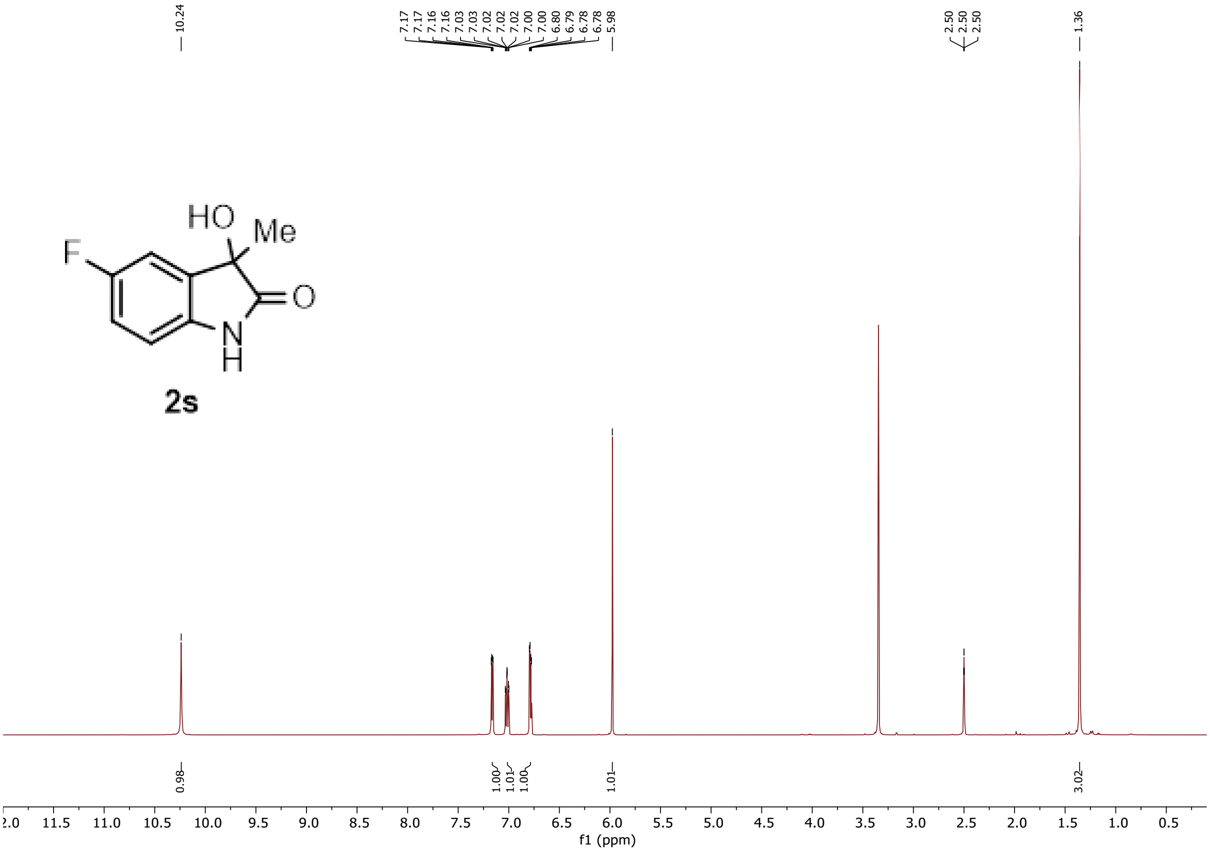


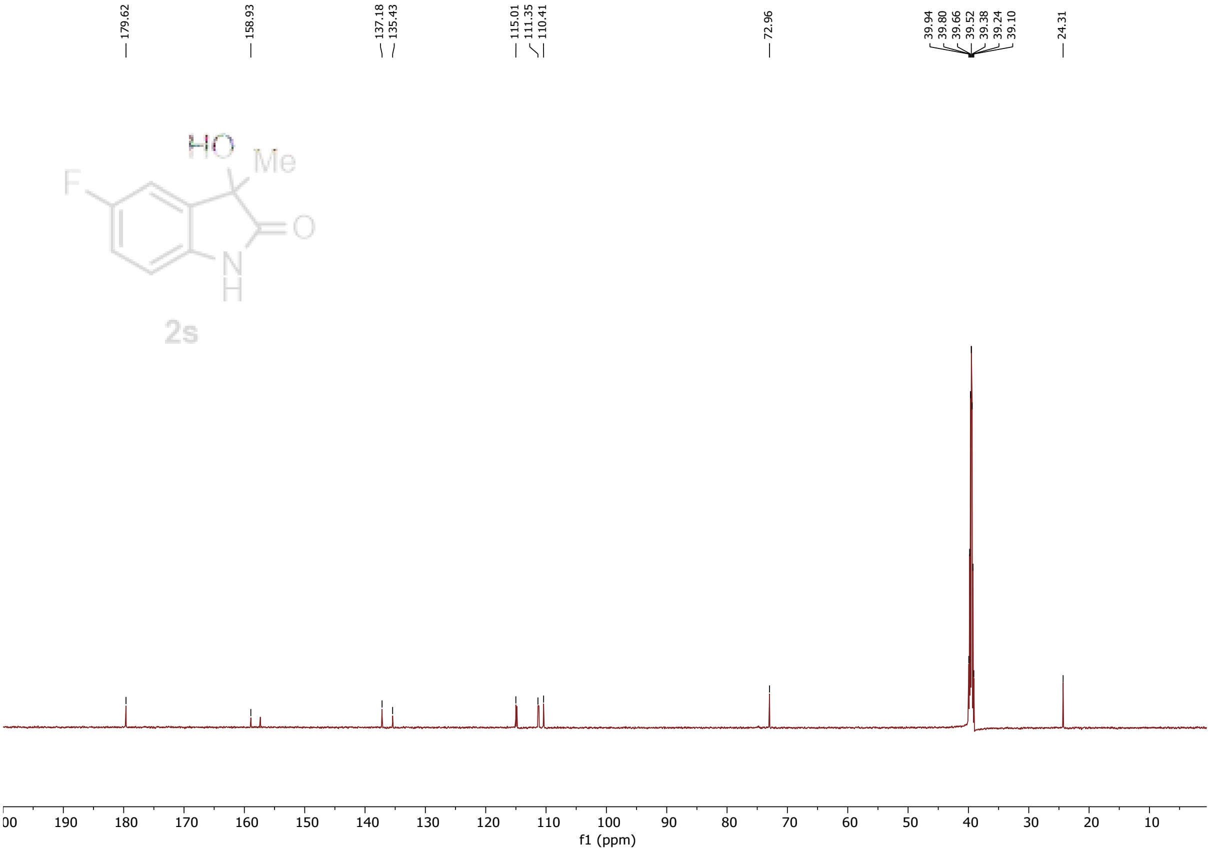
NMR of compound (**2r**)

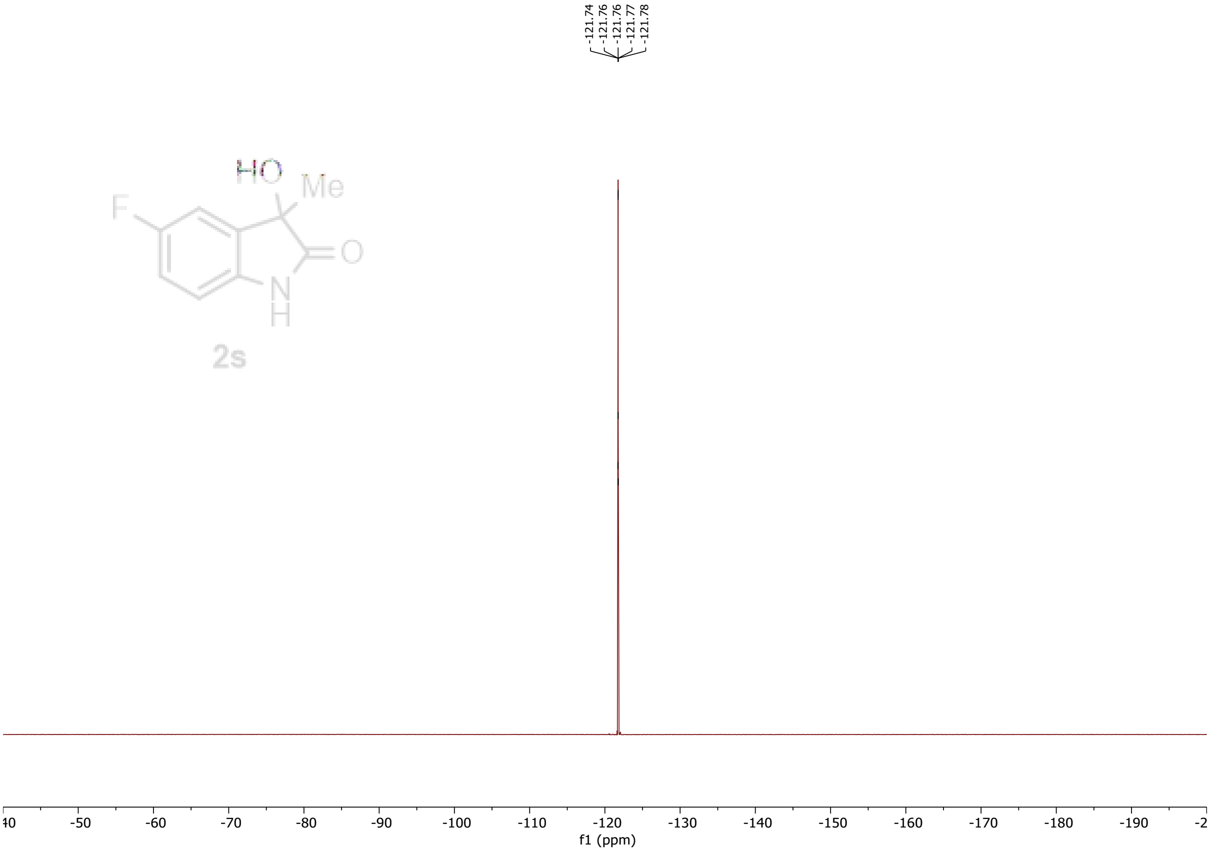




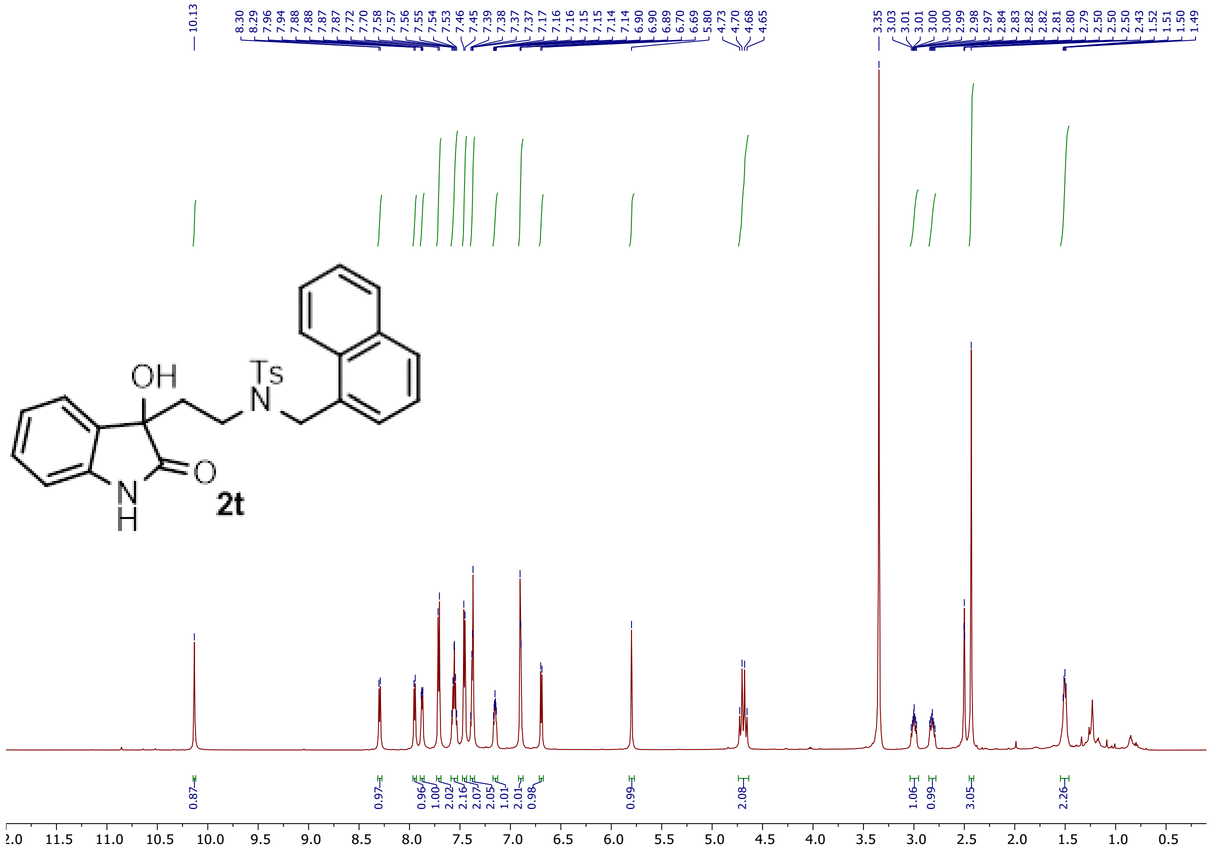
NMR of compound (**2s**)

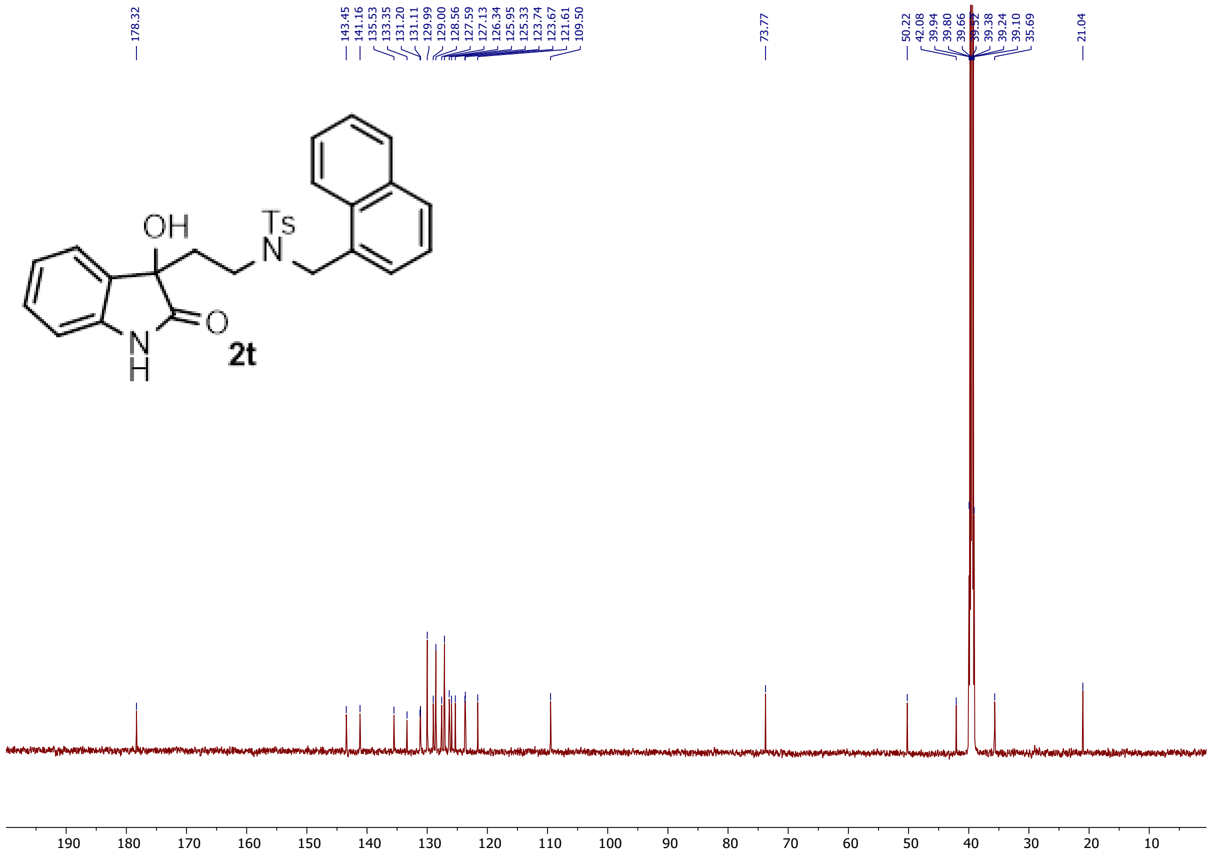



179.62
158.93
137.18
135.43
115.01
111.35
110.41
72.96
39.94
39.80
39.66
39.52
39.38
39.24
39.10
24.31
HO
Me
F
O
N
H
2s
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

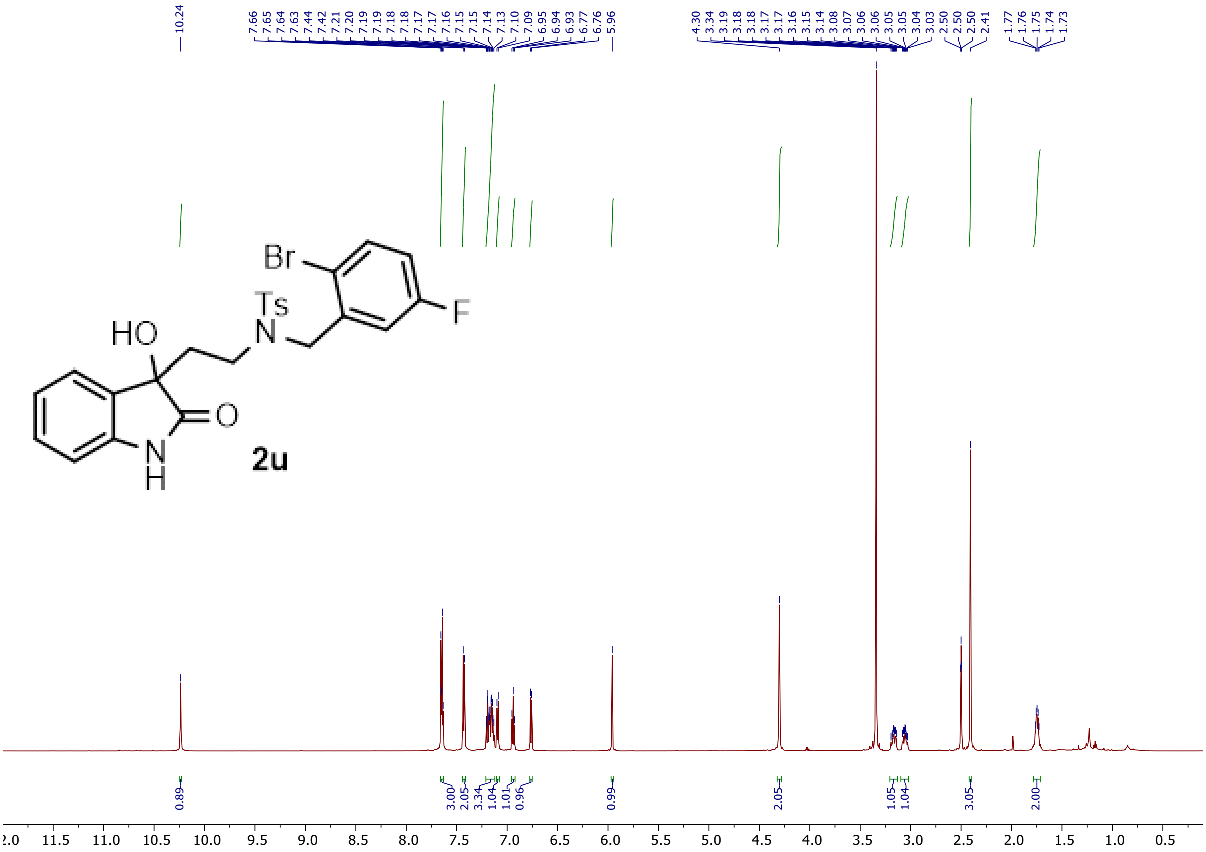

-121.74
-121.76
-121.76
-121.77
-121.78
HO
Me
F
O
N
H
2s
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

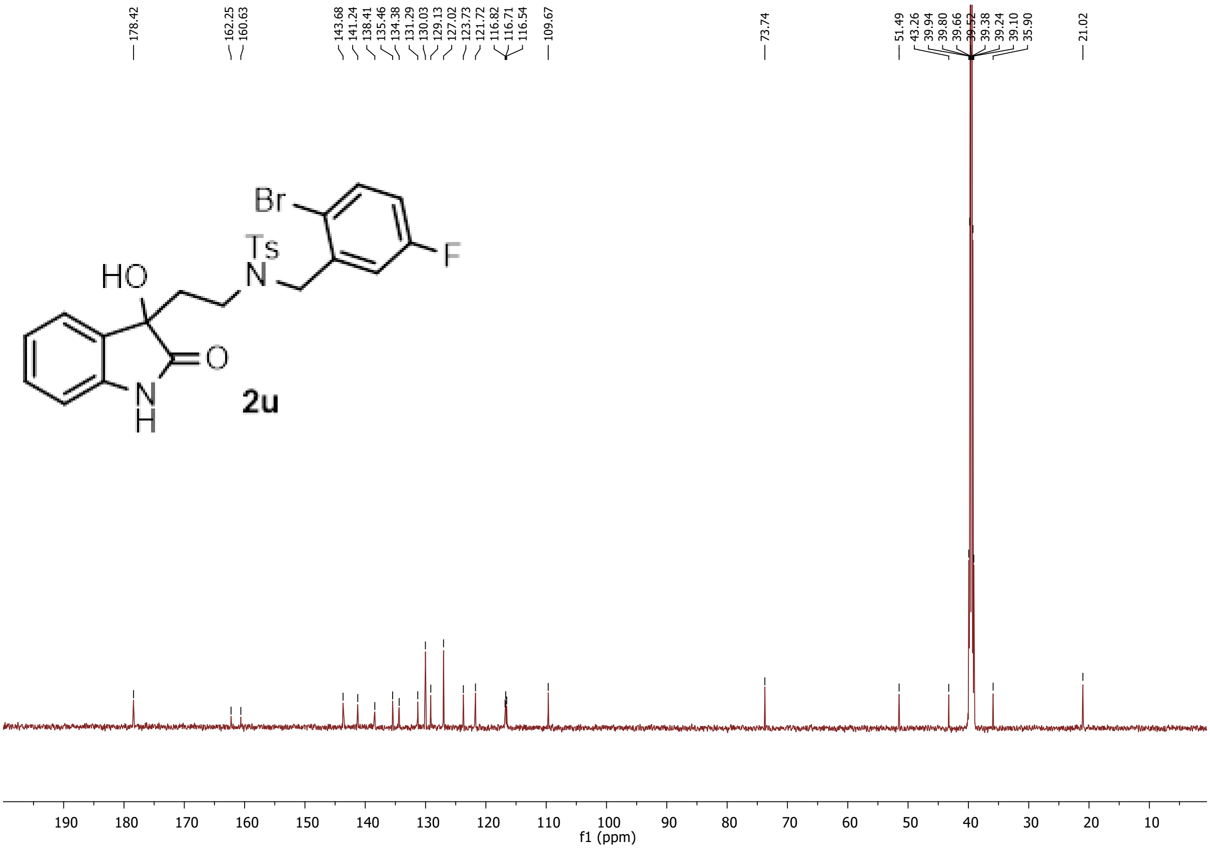
NMR of compound (**2t**)

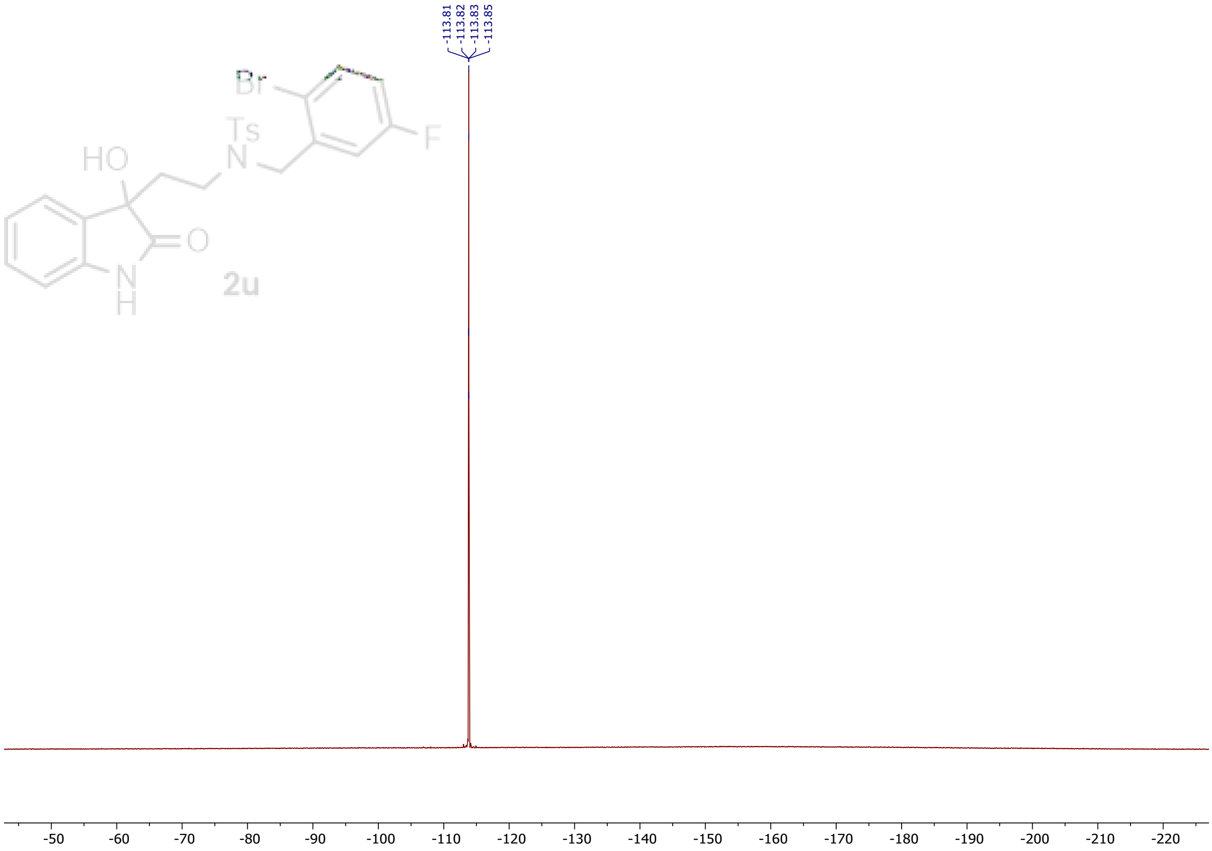




NMR of compound (**2u**)

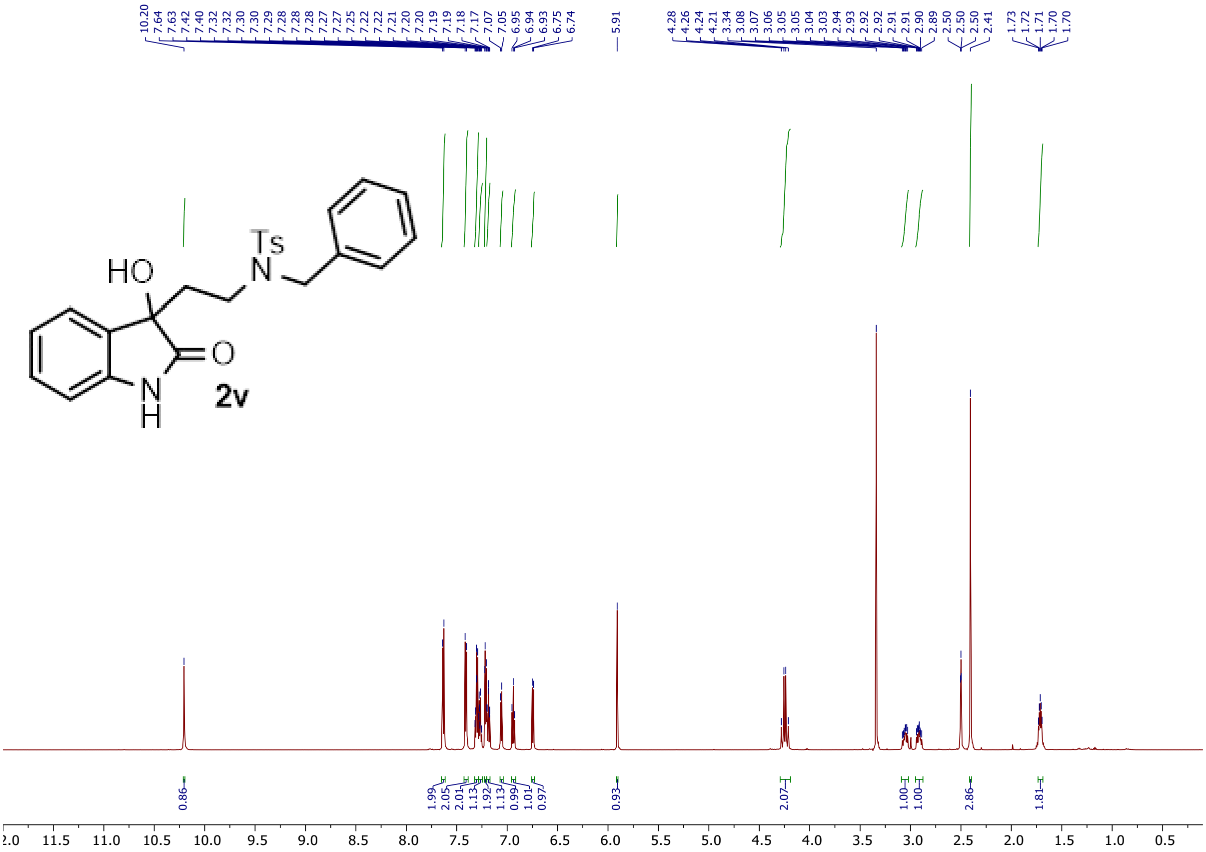

10.24
7.66 7.65 7.64 7.63 7.44 7.42 7.21 7.20 7.19 7.19 7.18 7.18 7.17 7.17 7.16 7.15 7.15 7.14 7.13 7.10 7.09 6.95 6.94 6.93 6.77 6.76
5.96
4.30 3.34 3.19 3.18 3.18 3.17 3.17 3.16 3.15 3.14 3.08 3.07 3.06 3.05 3.05 3.04 3.03 2.50 2.50 2.50 2.41
1.77 1.76 1.75 1.74 1.73
Br
F
Ts
N
HO
O
N
H
2u
0.89
3.00 2.05 3.34 1.04 1.01 0.96
0.99
2.05
1.05 1.04
3.05
2.00
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5

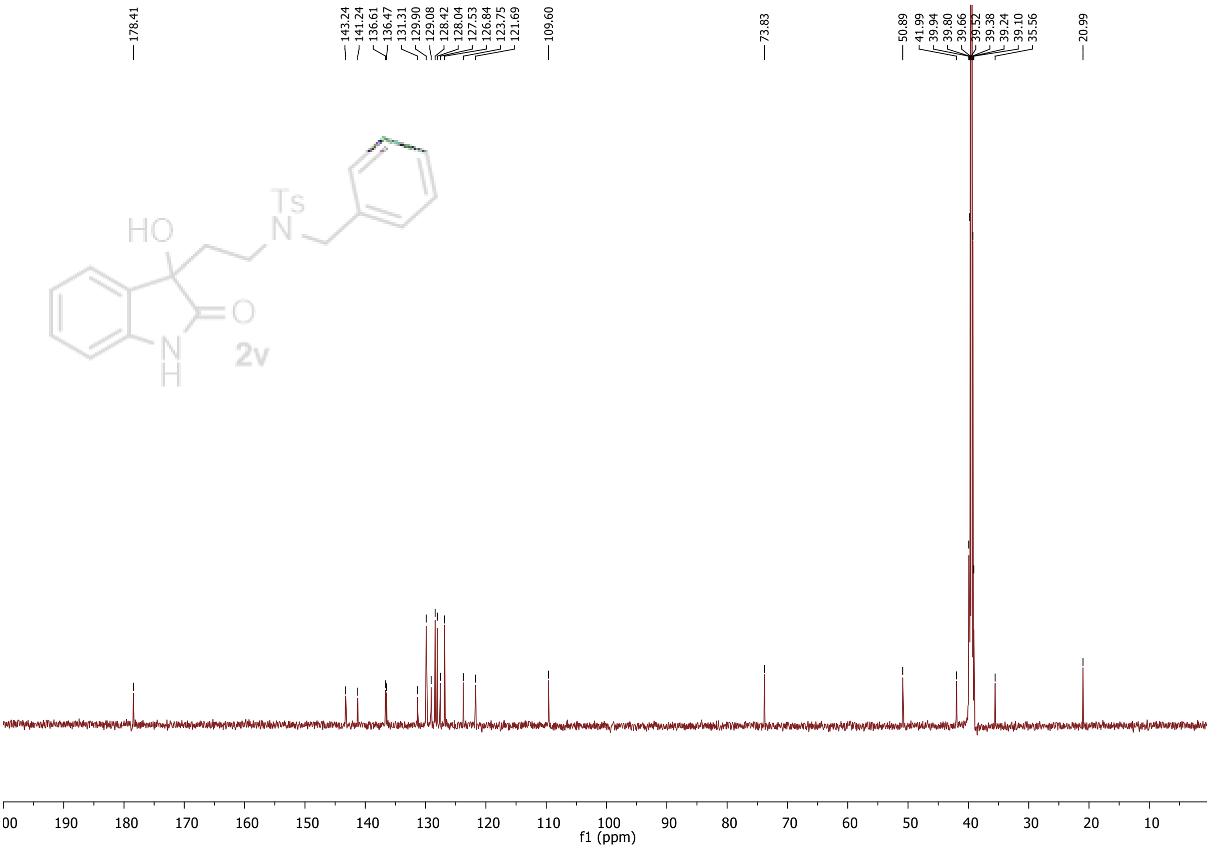

178.42
162.25 160.63
143.68 141.24 138.41 135.46 134.38 131.29 130.03 129.13 127.02 123.73 121.72 116.82 116.71 116.54
109.67
73.74
51.49 43.26 39.94 39.80 39.66 39.52 39.38 39.24 39.10 35.90
21.02
Br
F
Ts
N
HO
O
N
H
2u
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


-113.81
-113.82
-113.83
-113.85
Br
Ts
N
HO
O
F
N
H
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
-220

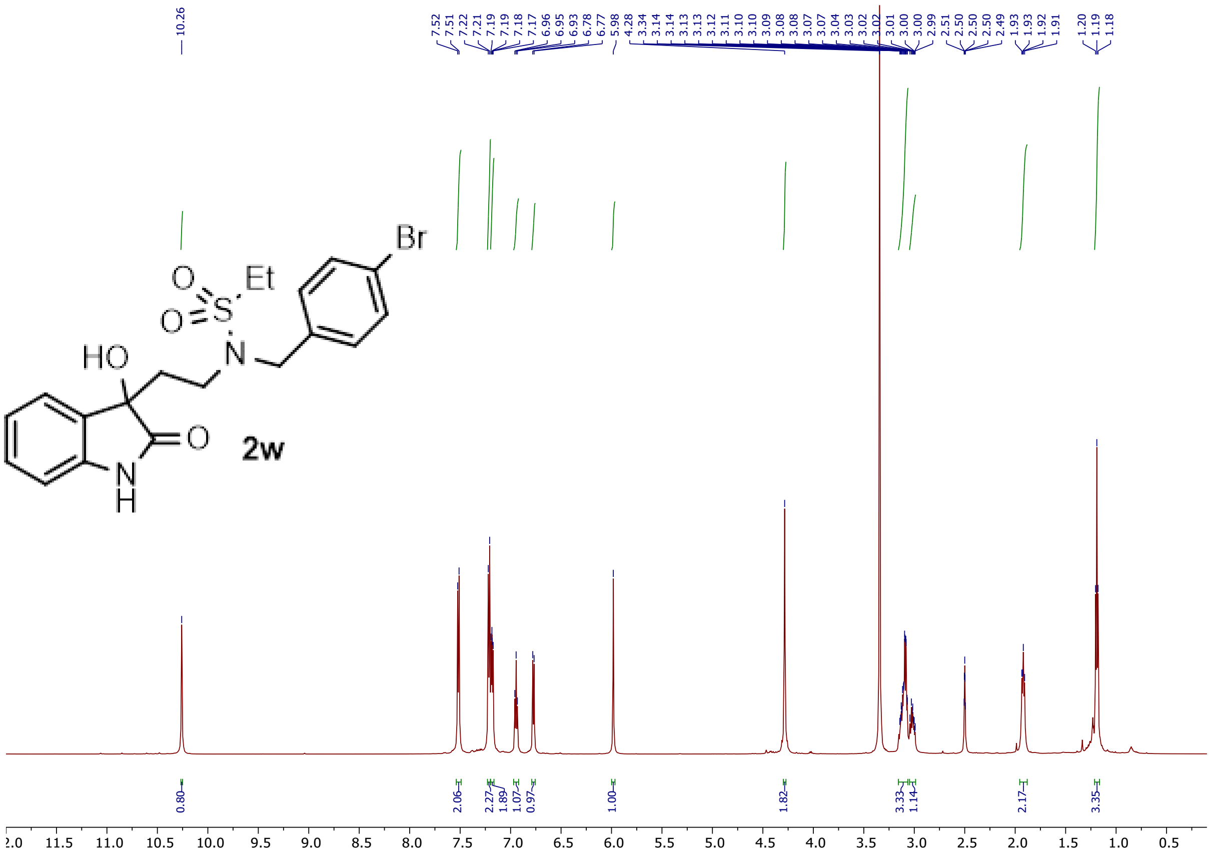
2u

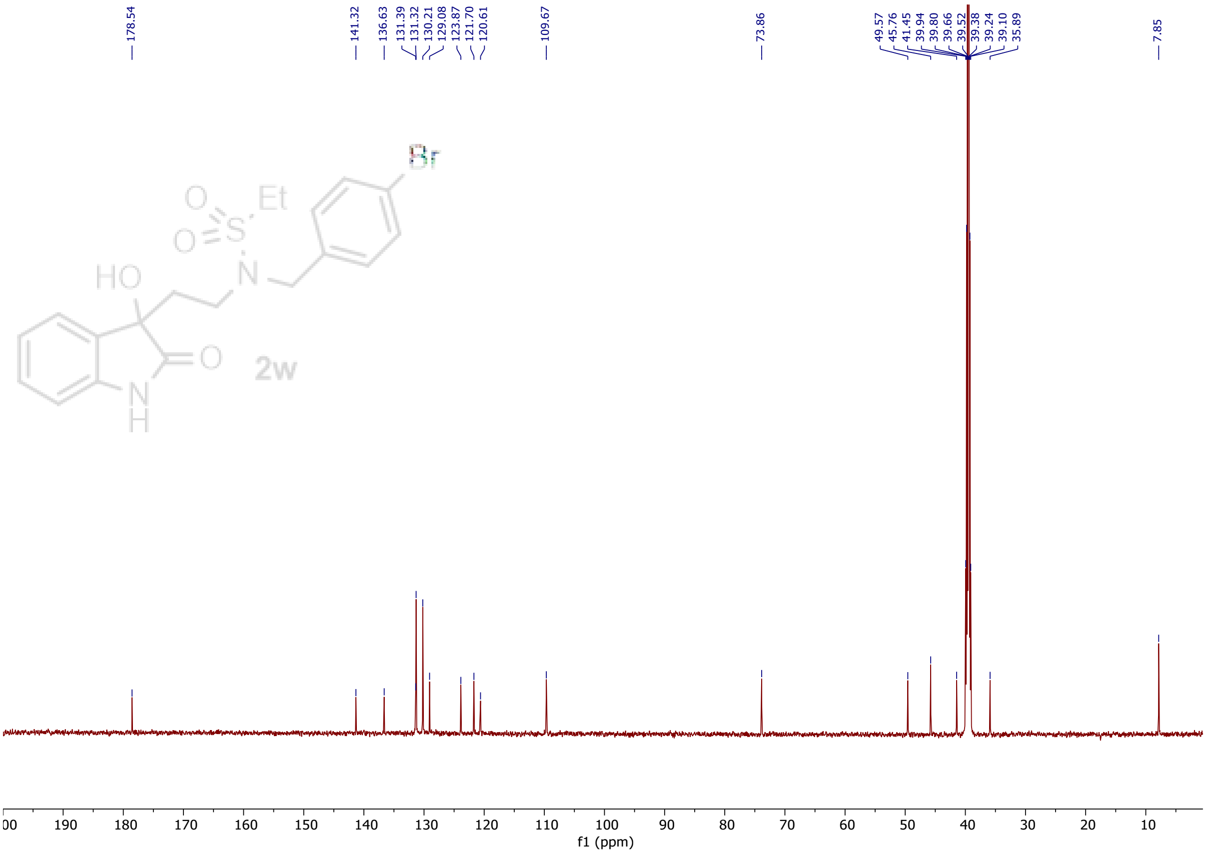
NMR of compound (**2v**)



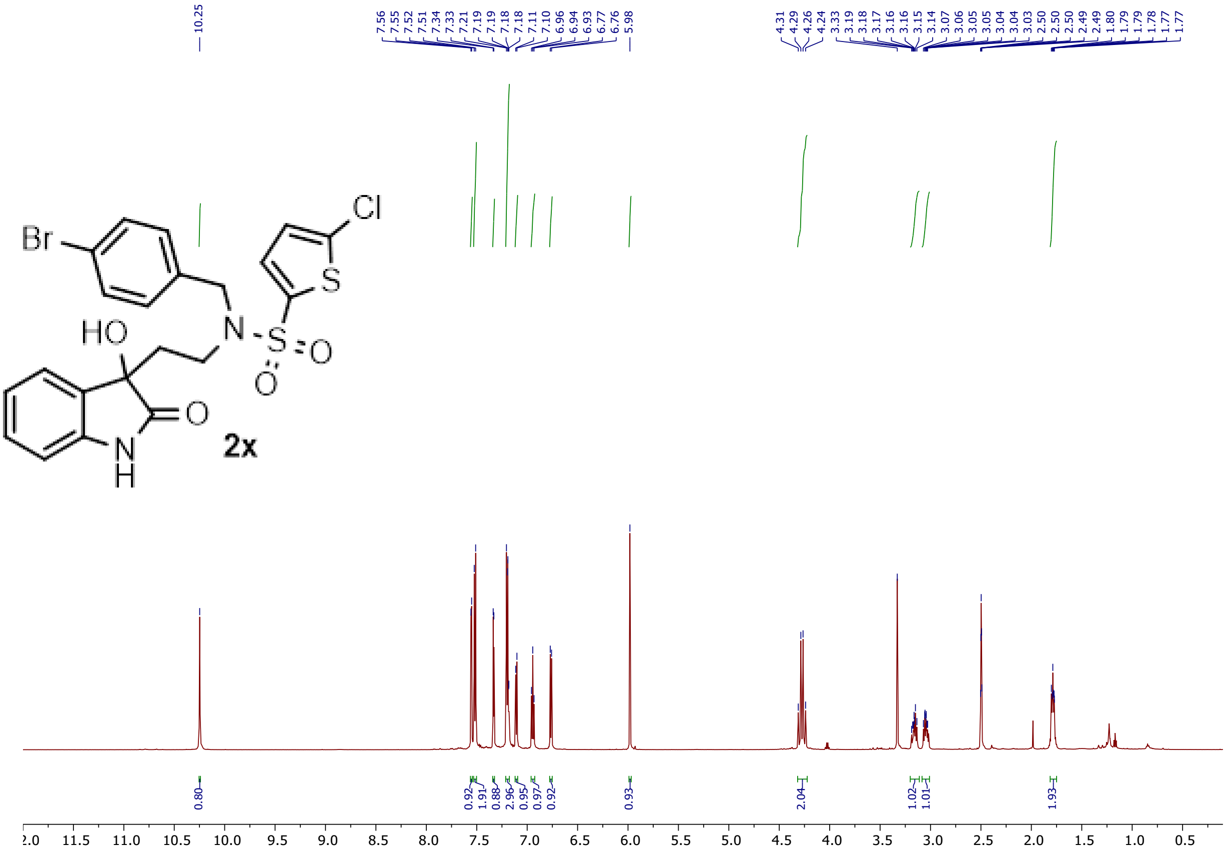


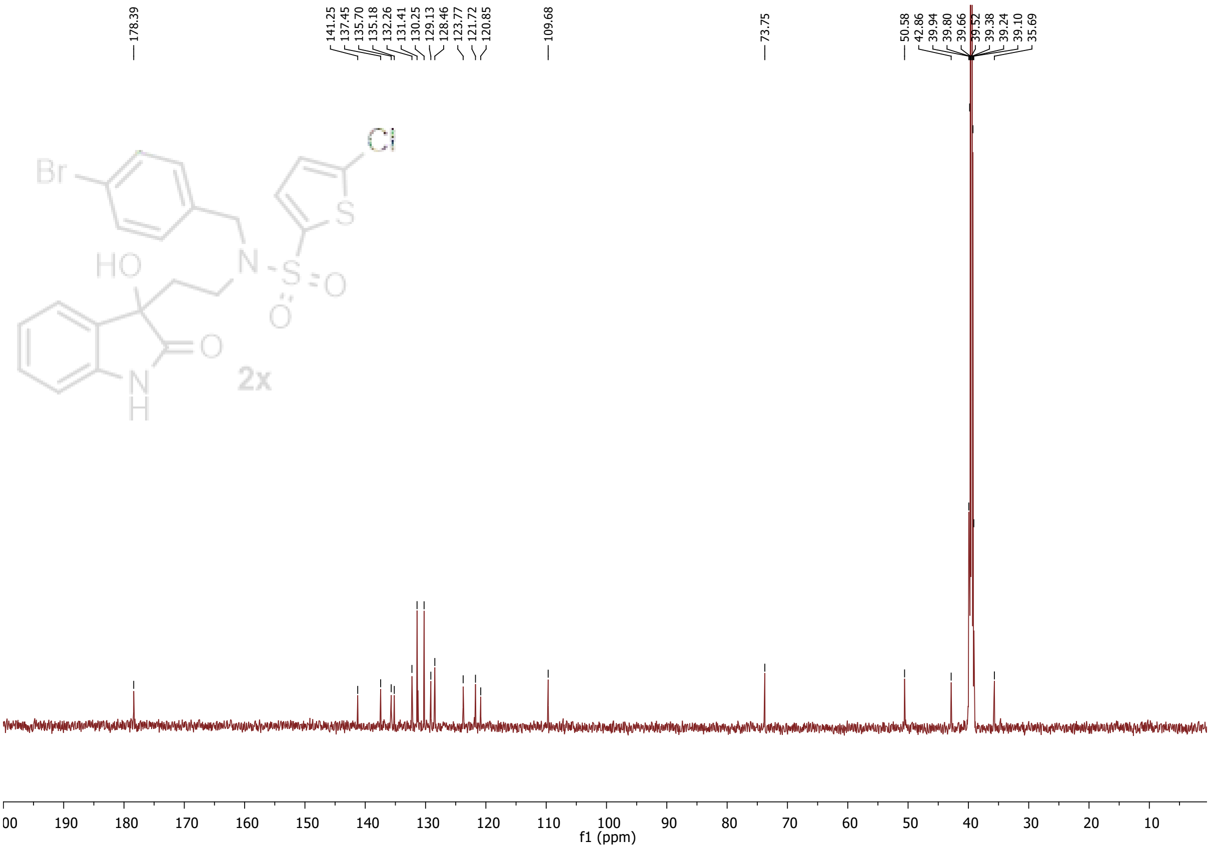
NMR of compound (**2w**)



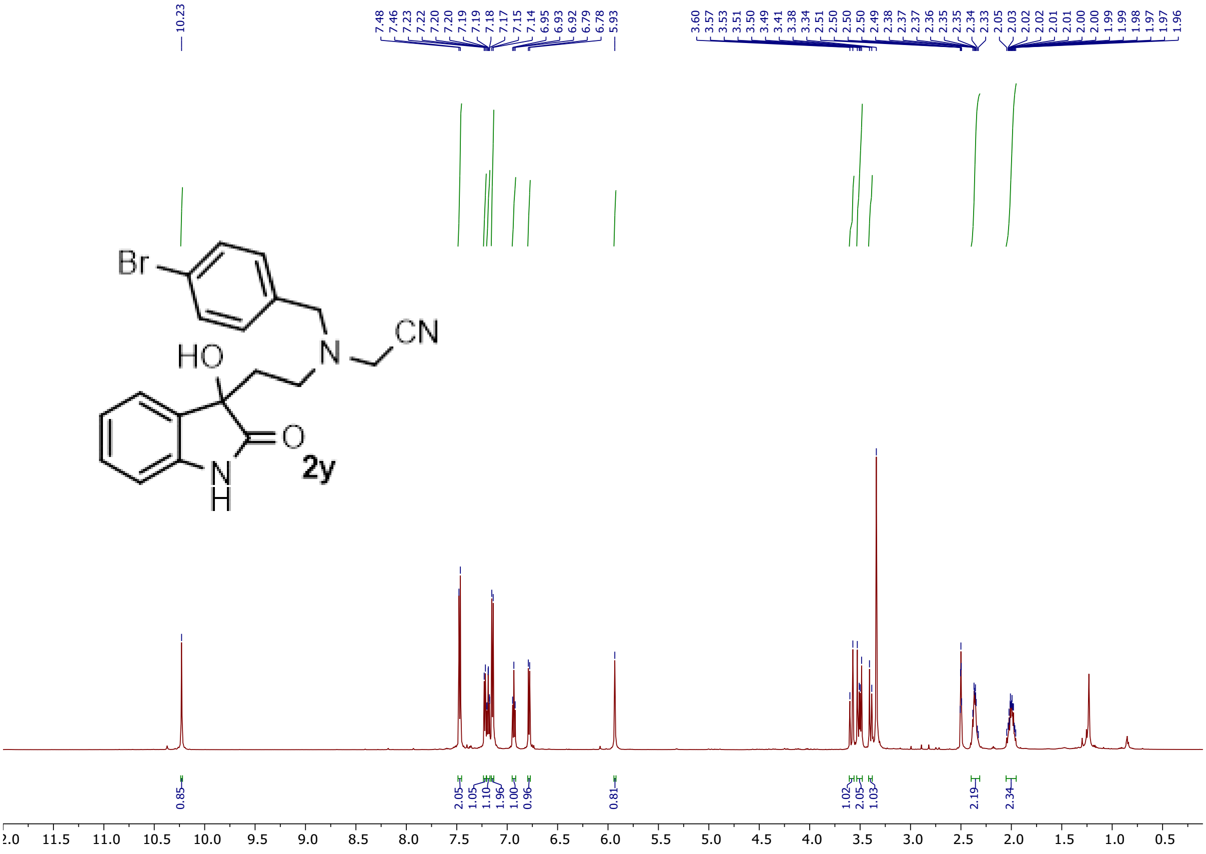


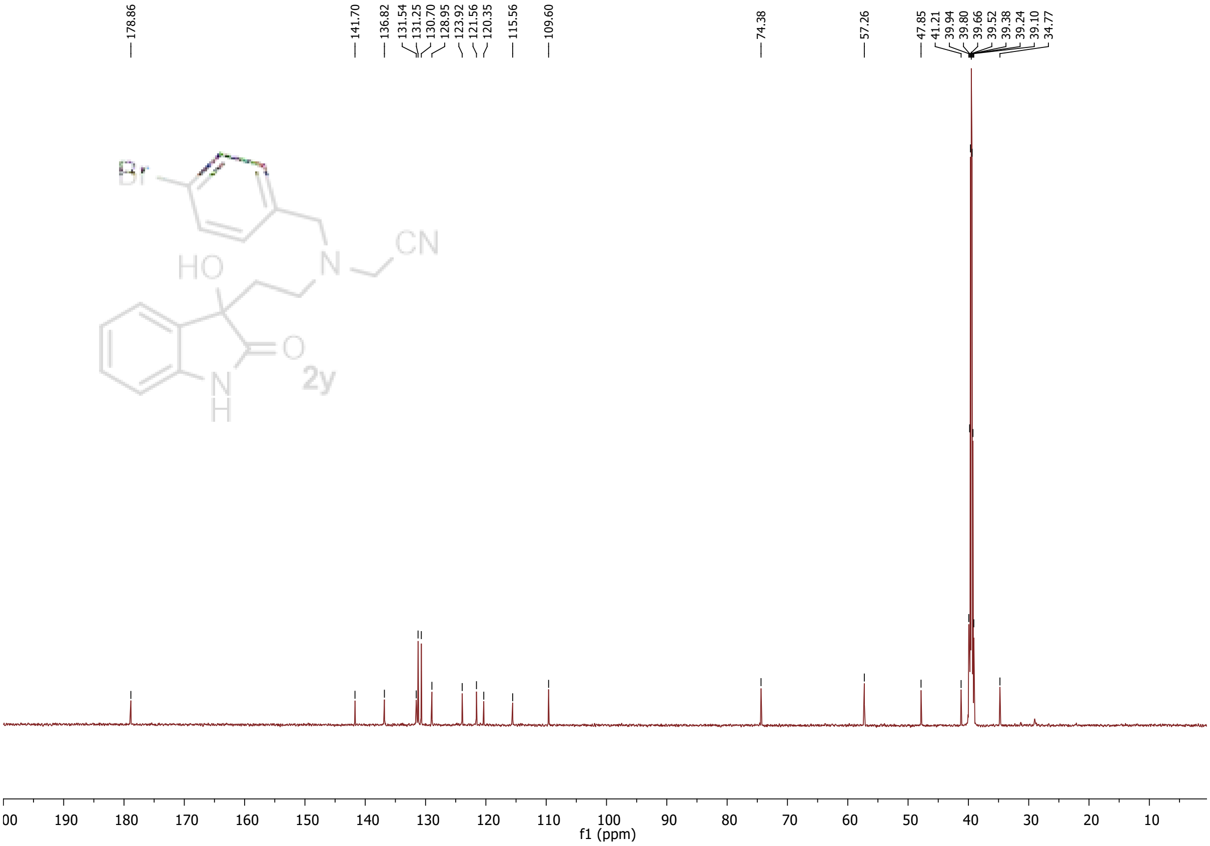
NMR of compound (**2x**)



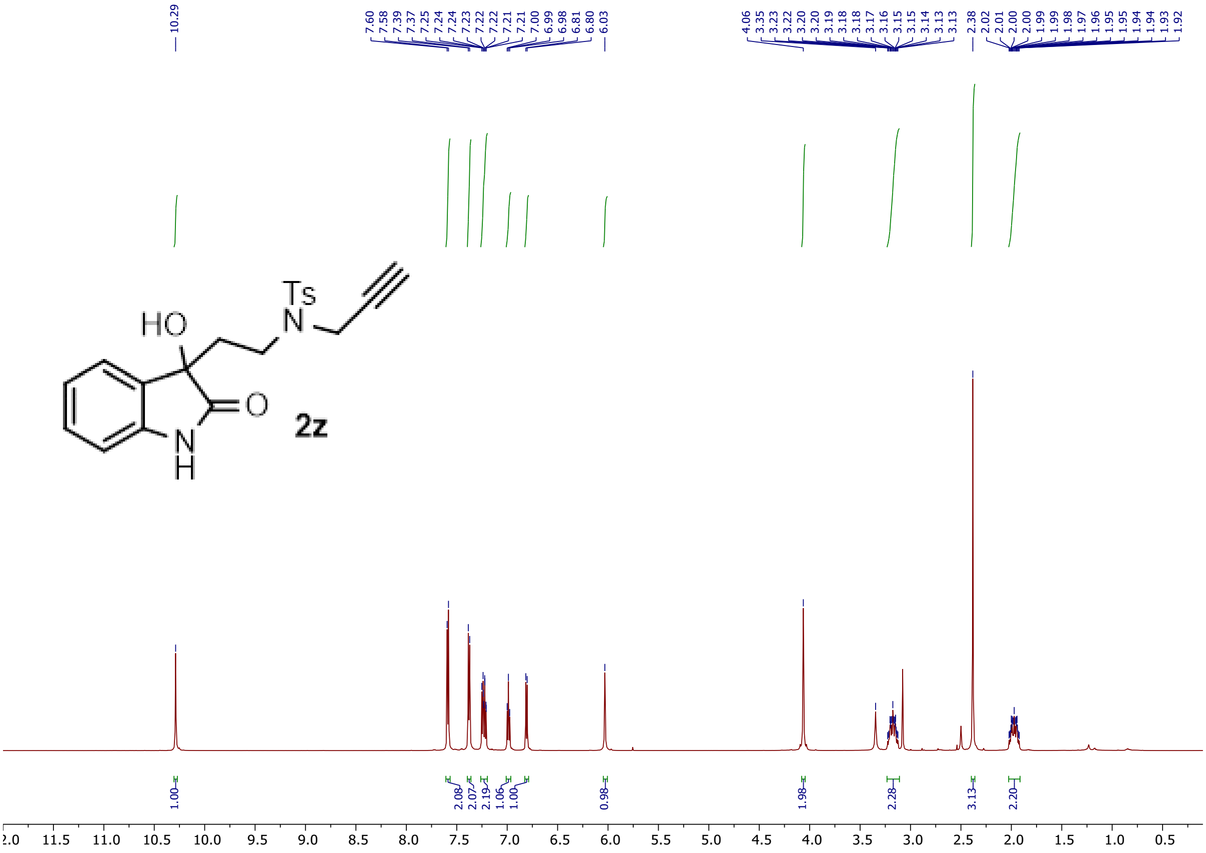


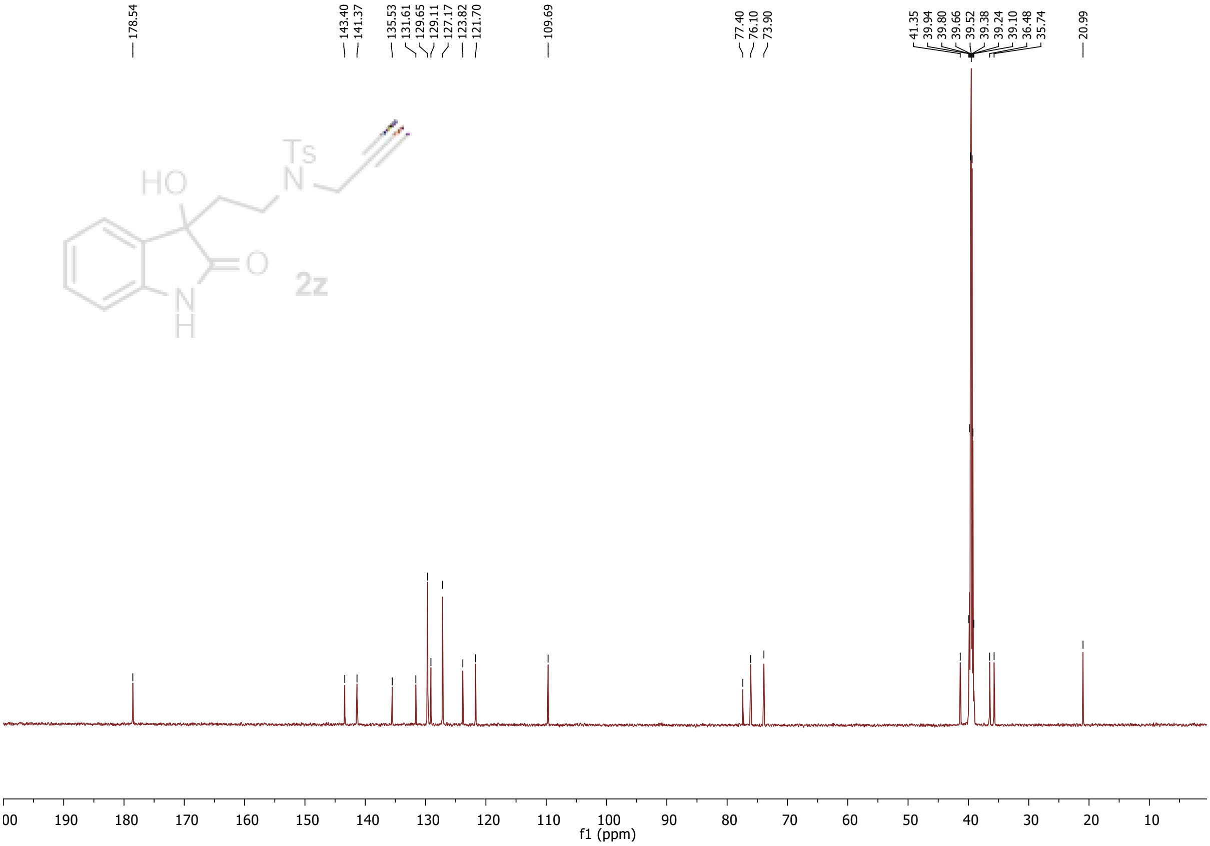
NMR of compound (**2y**)



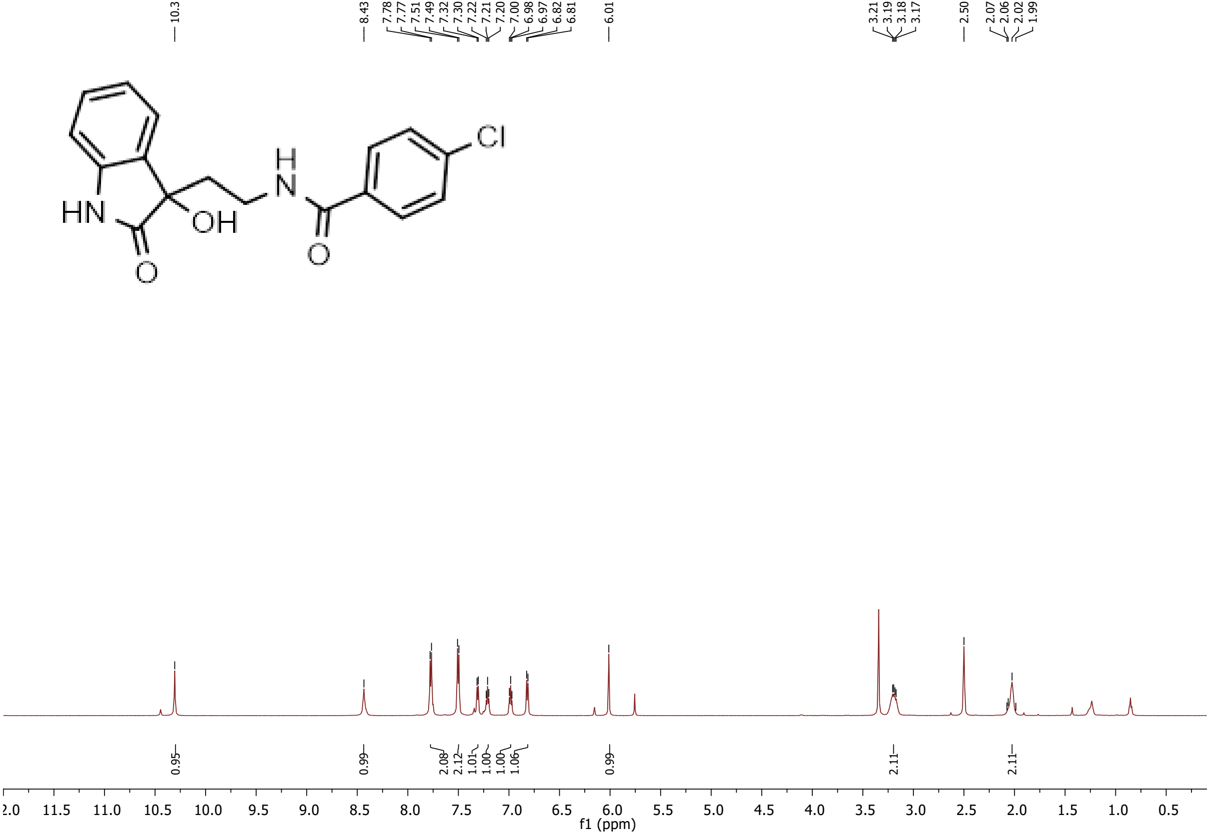


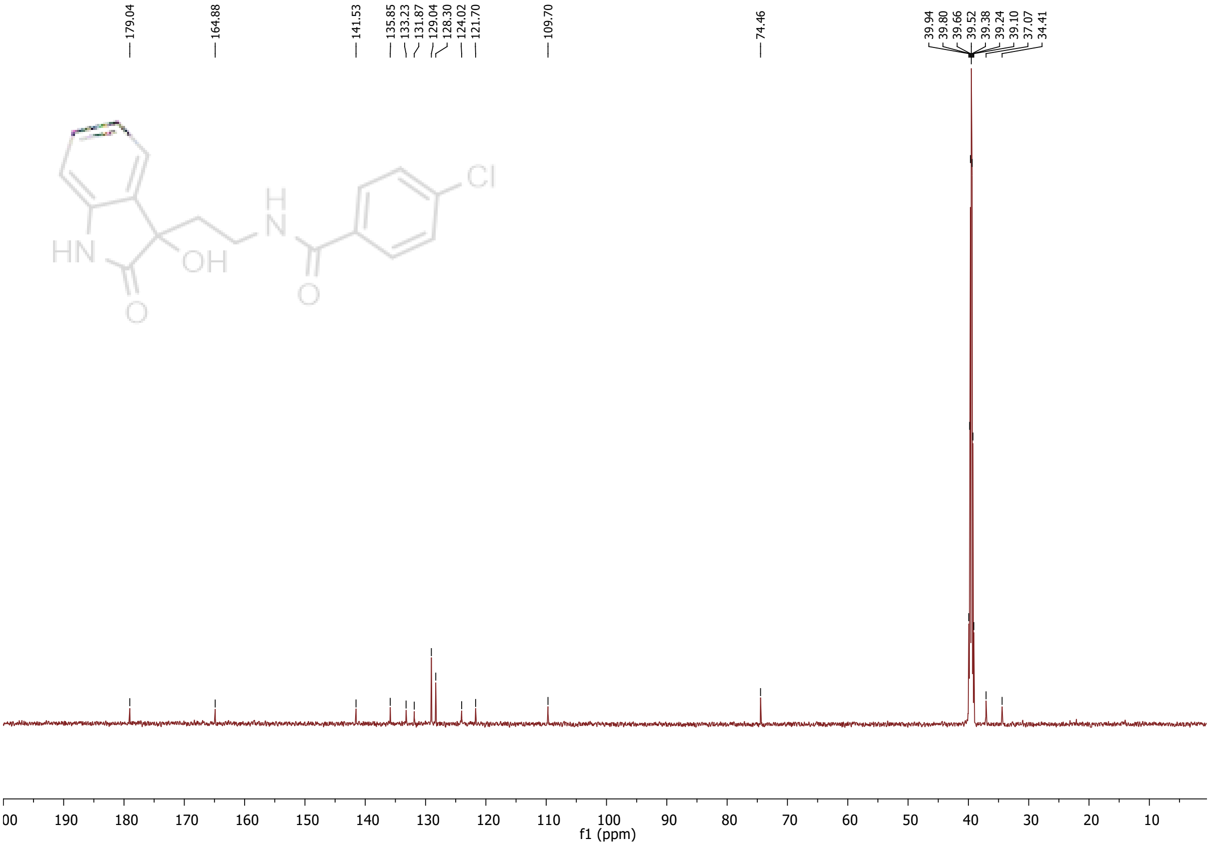
NMR of compound (**2z**)



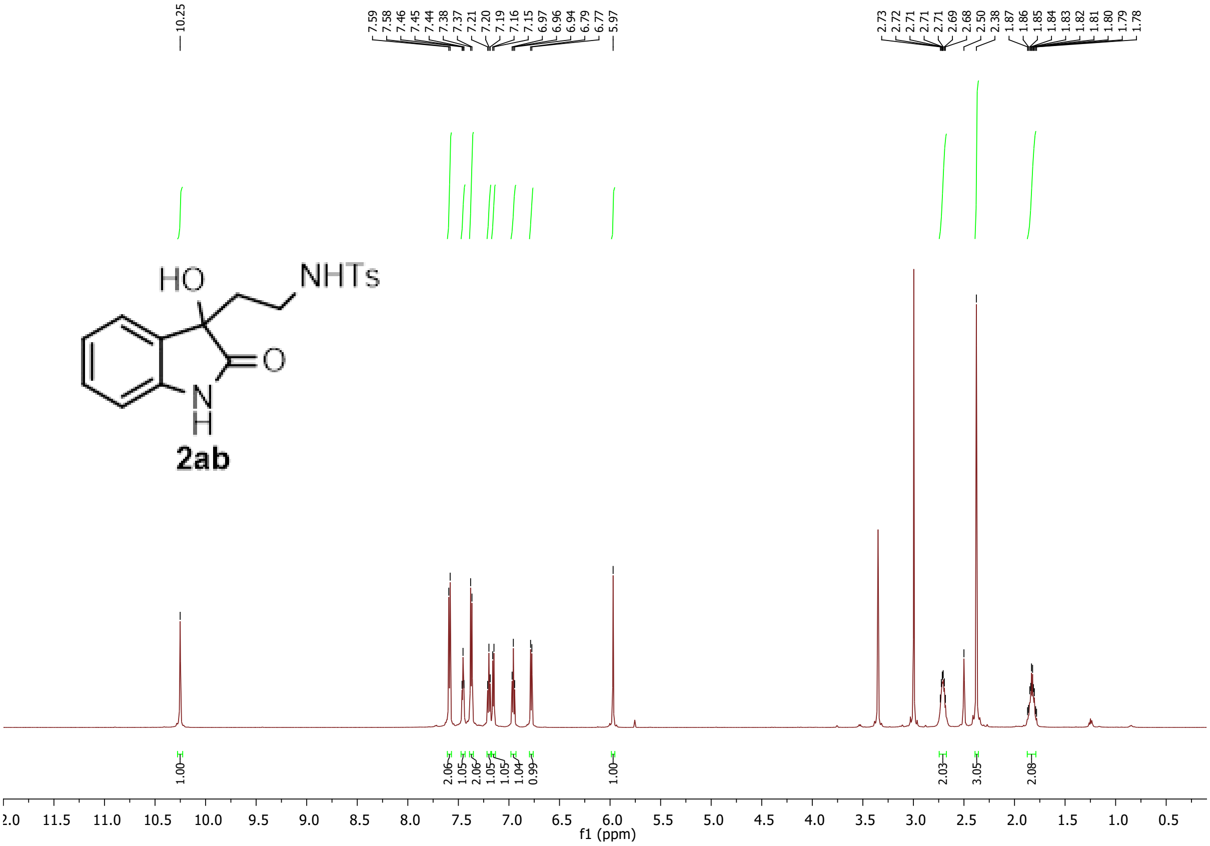


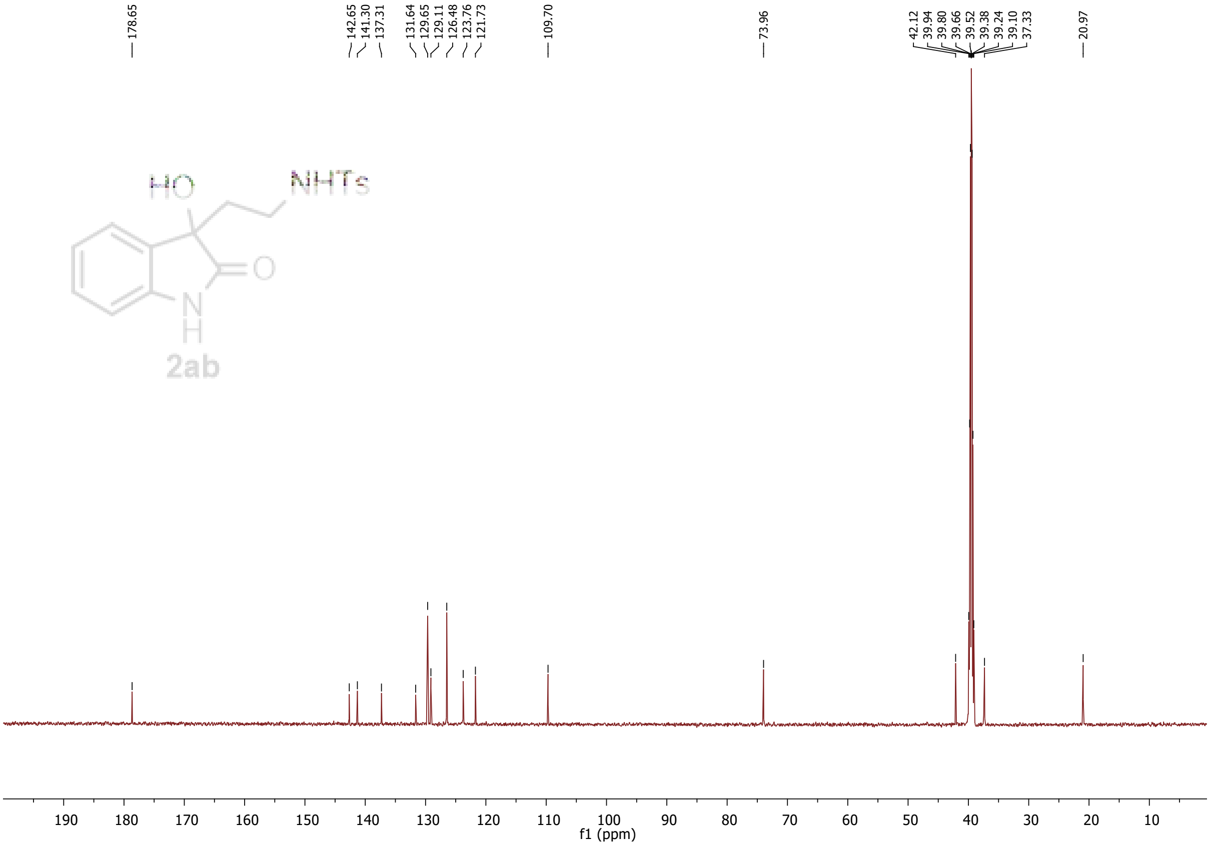
NMR of compound (**2aa**)



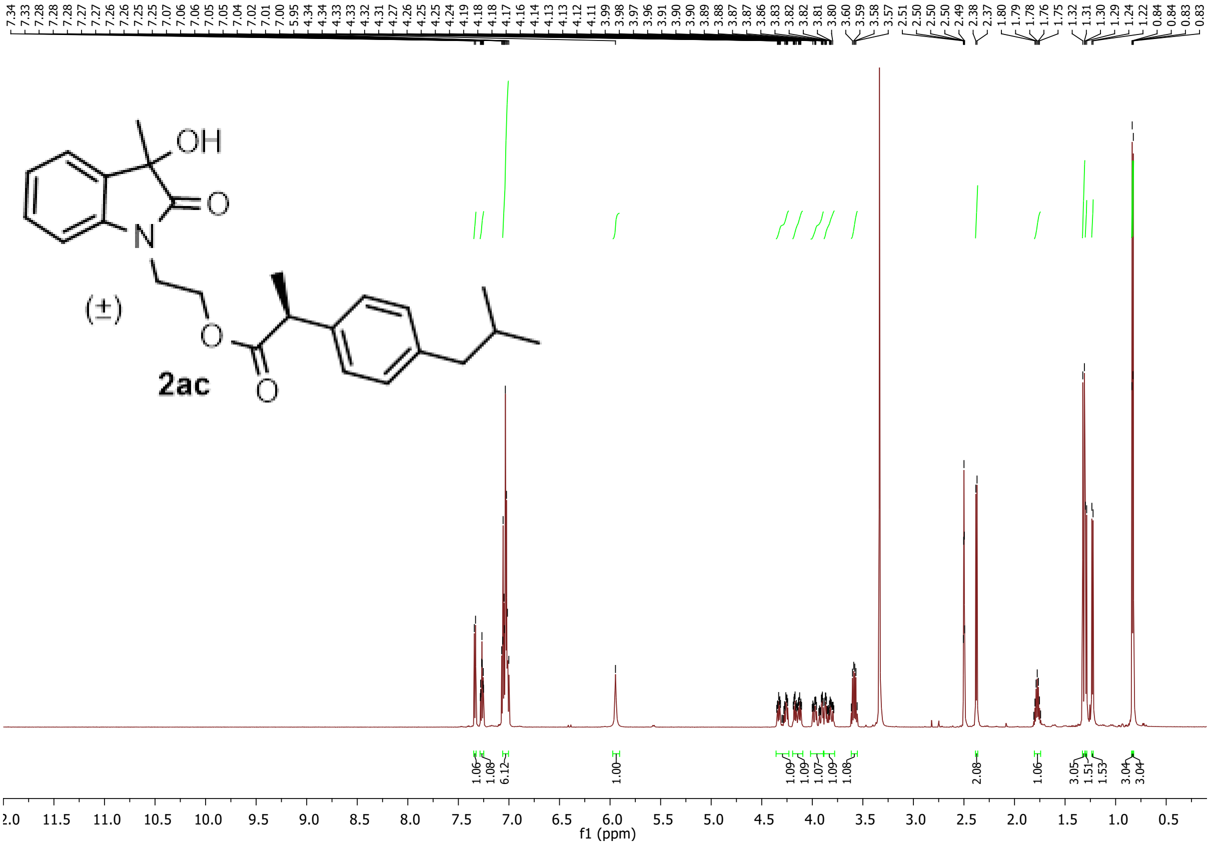


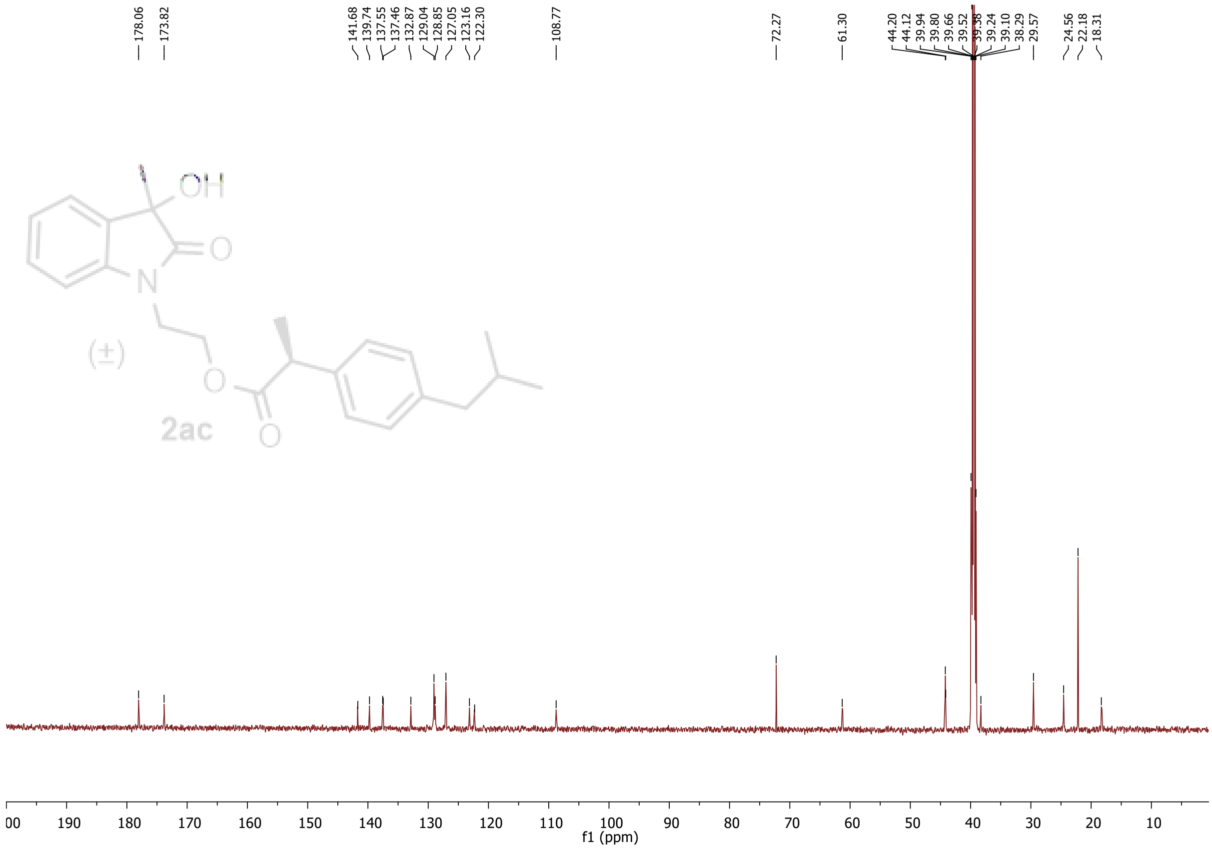
NMR of compound (**2ab**)



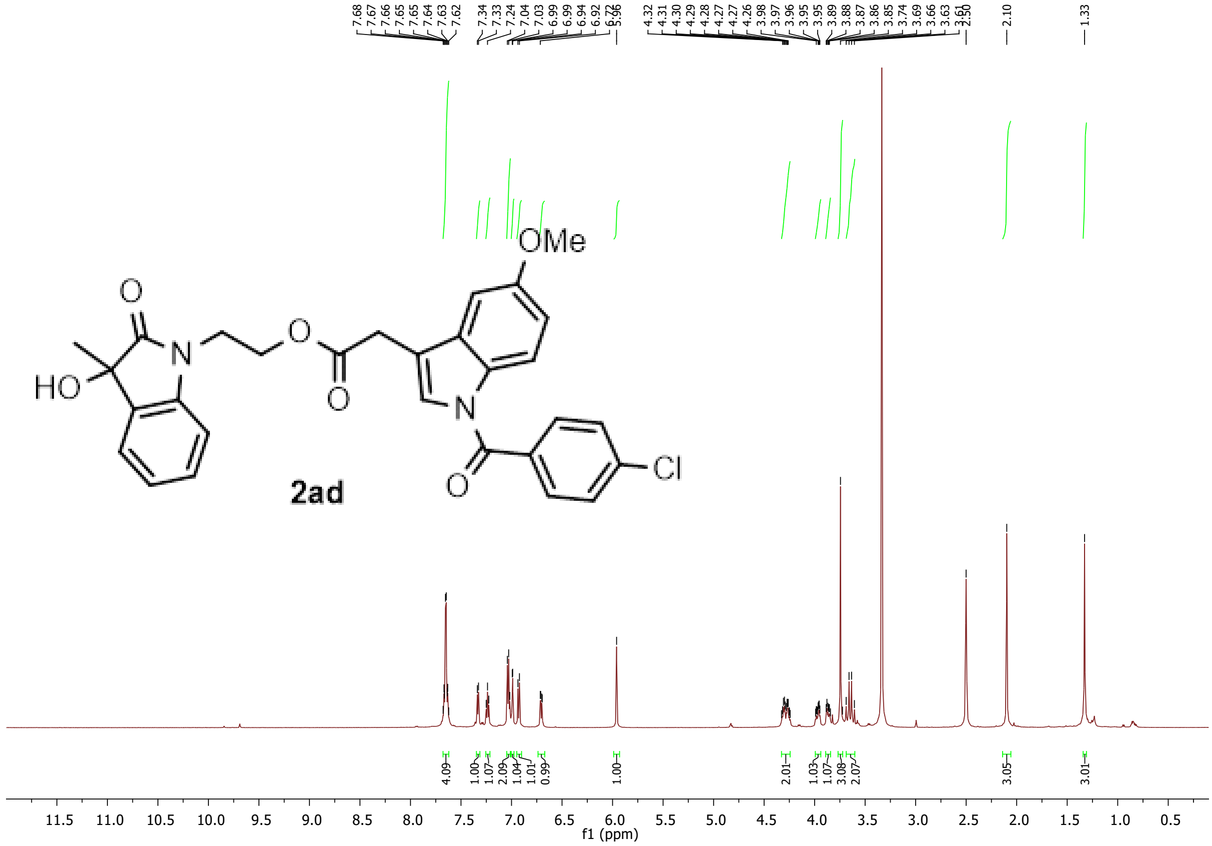


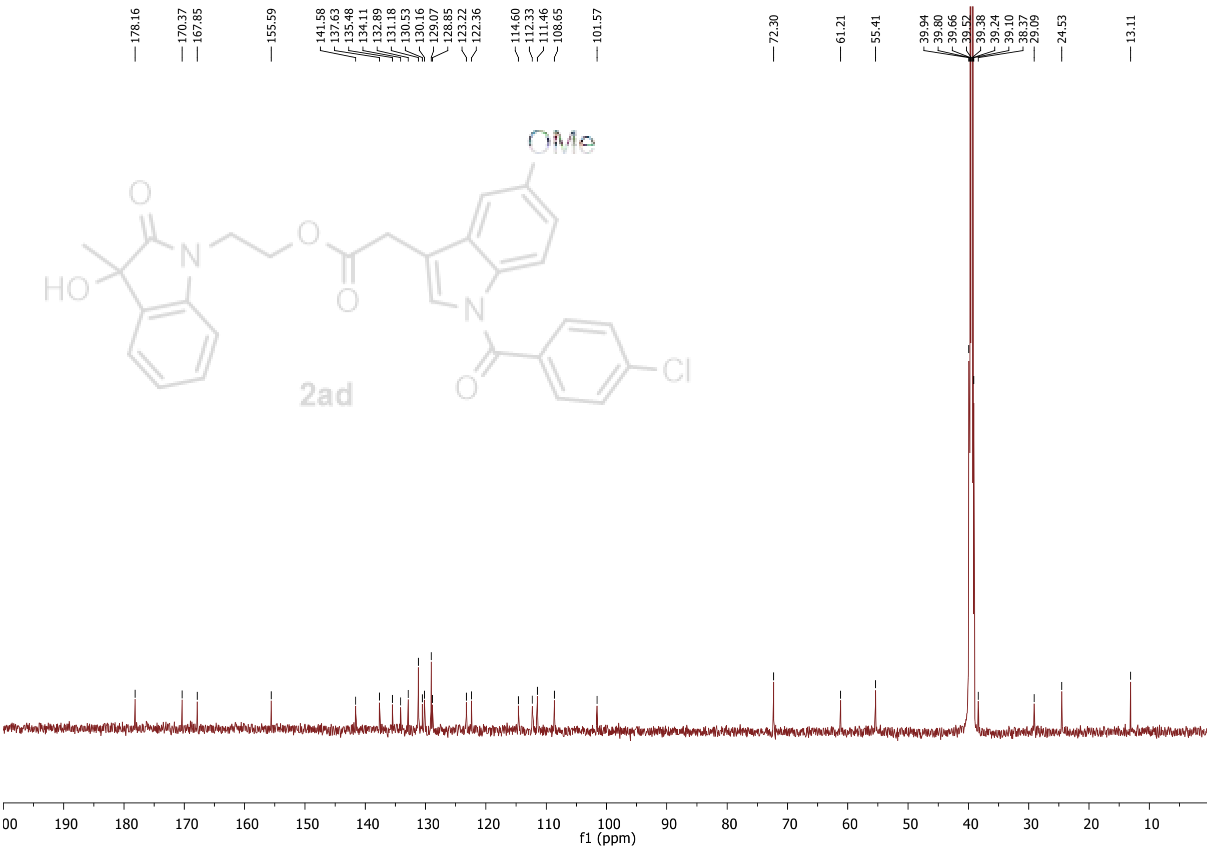
NMR of compound (**2ac**)



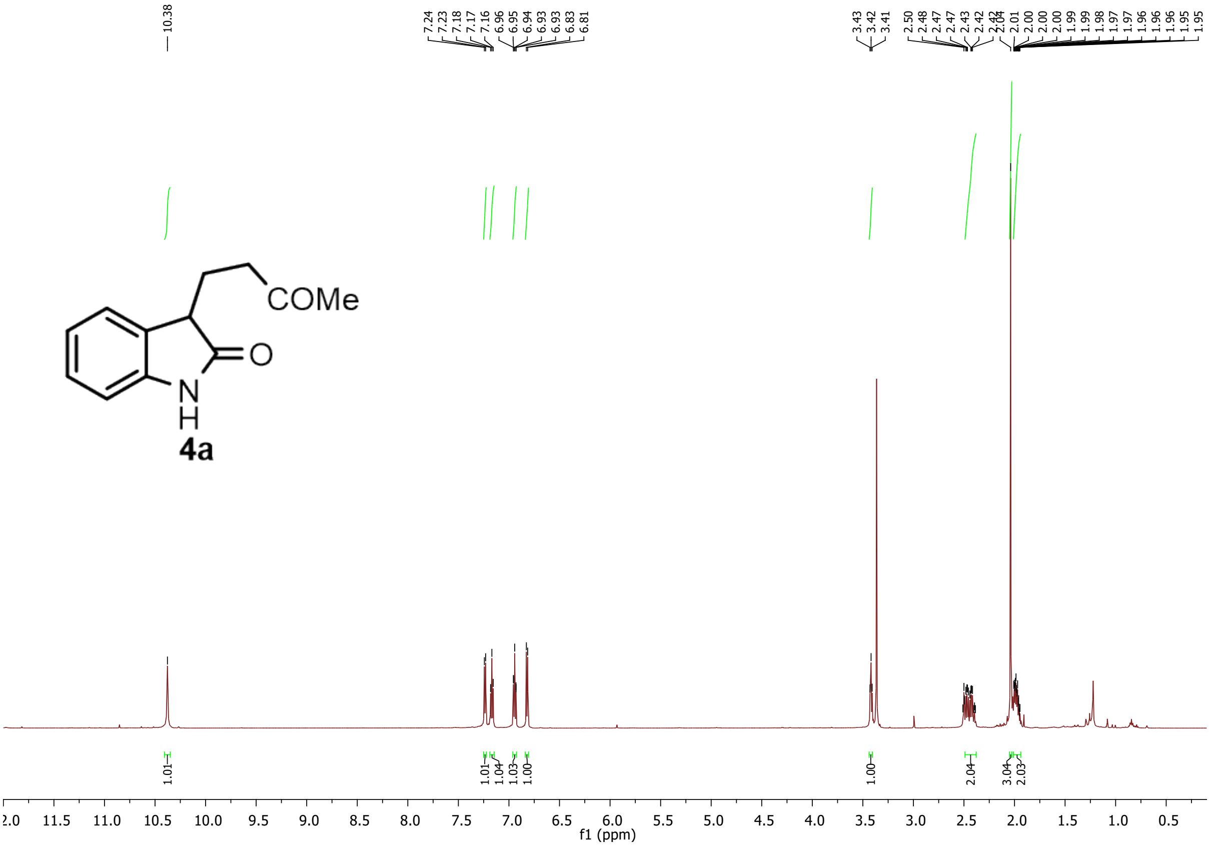


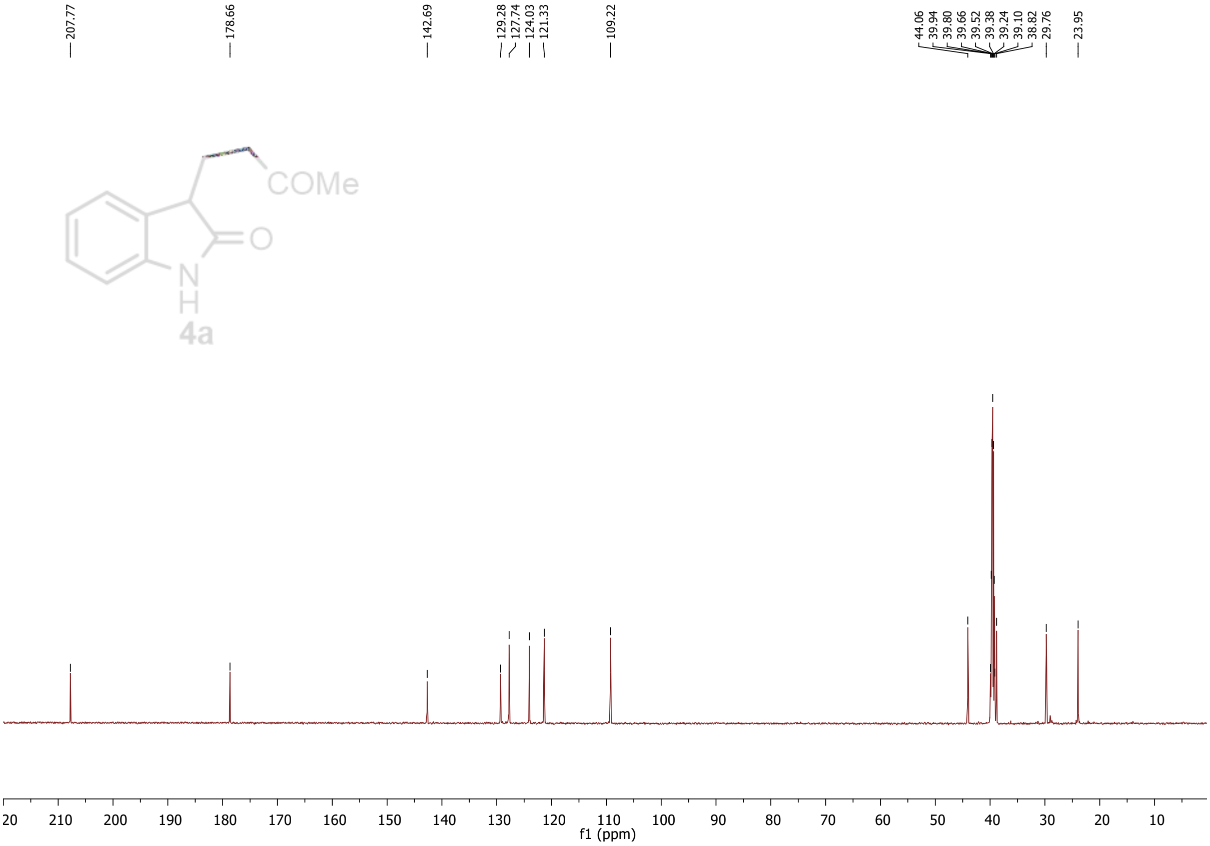
NMR of compound (**2ad**)



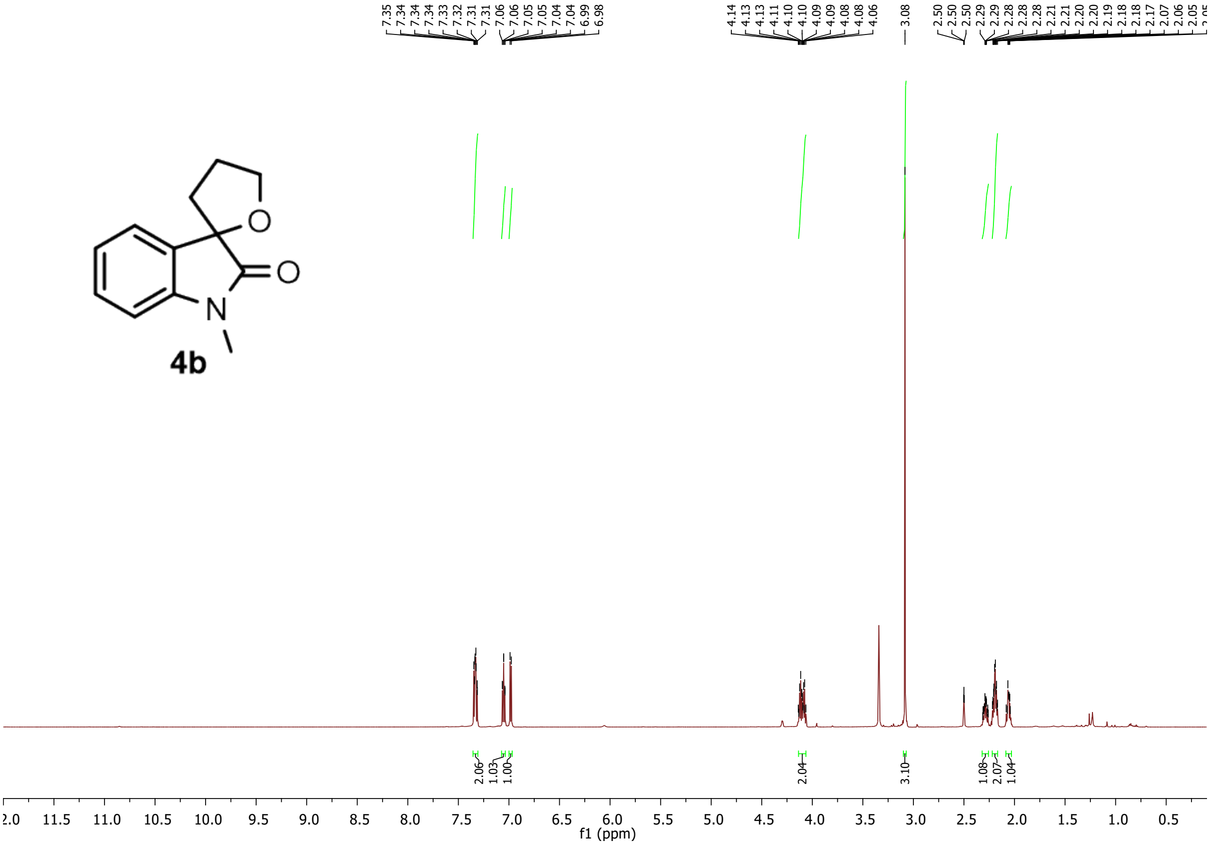


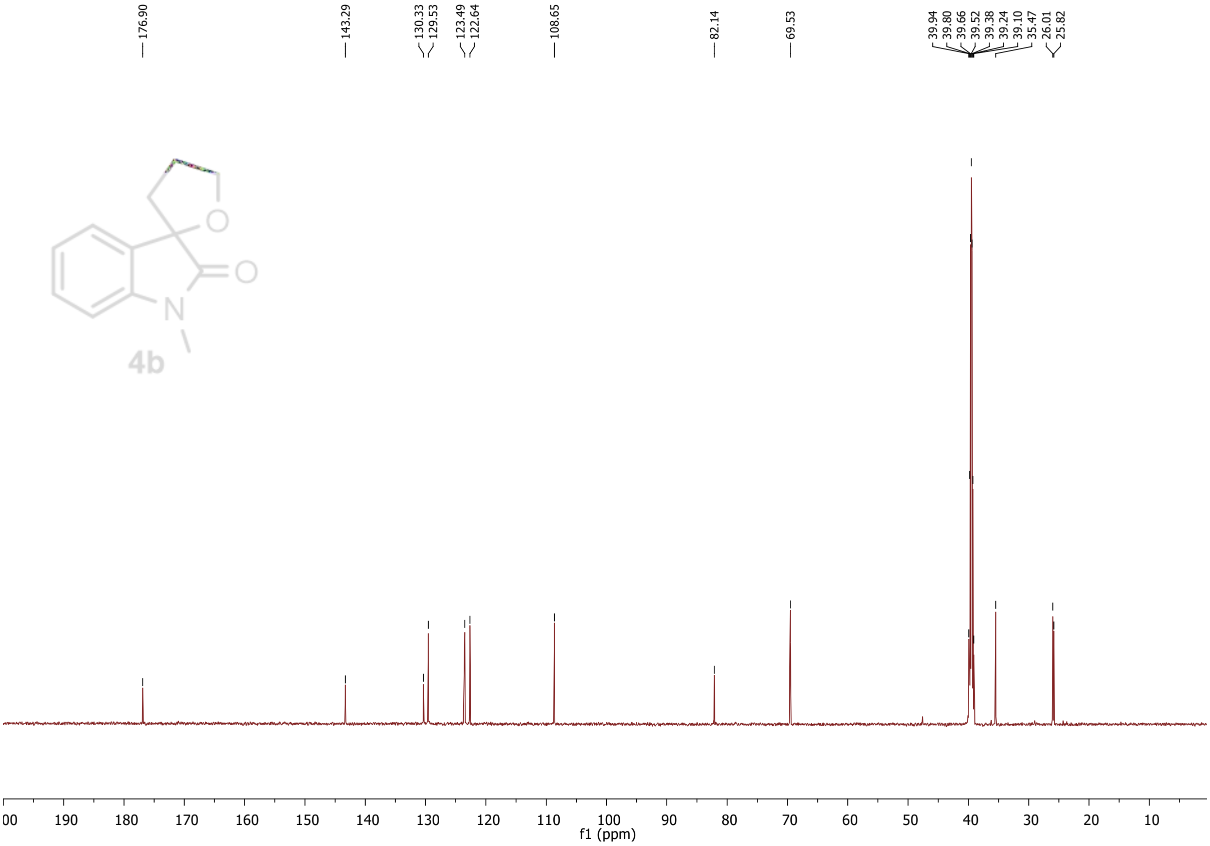
NMR of compound (**4a**)



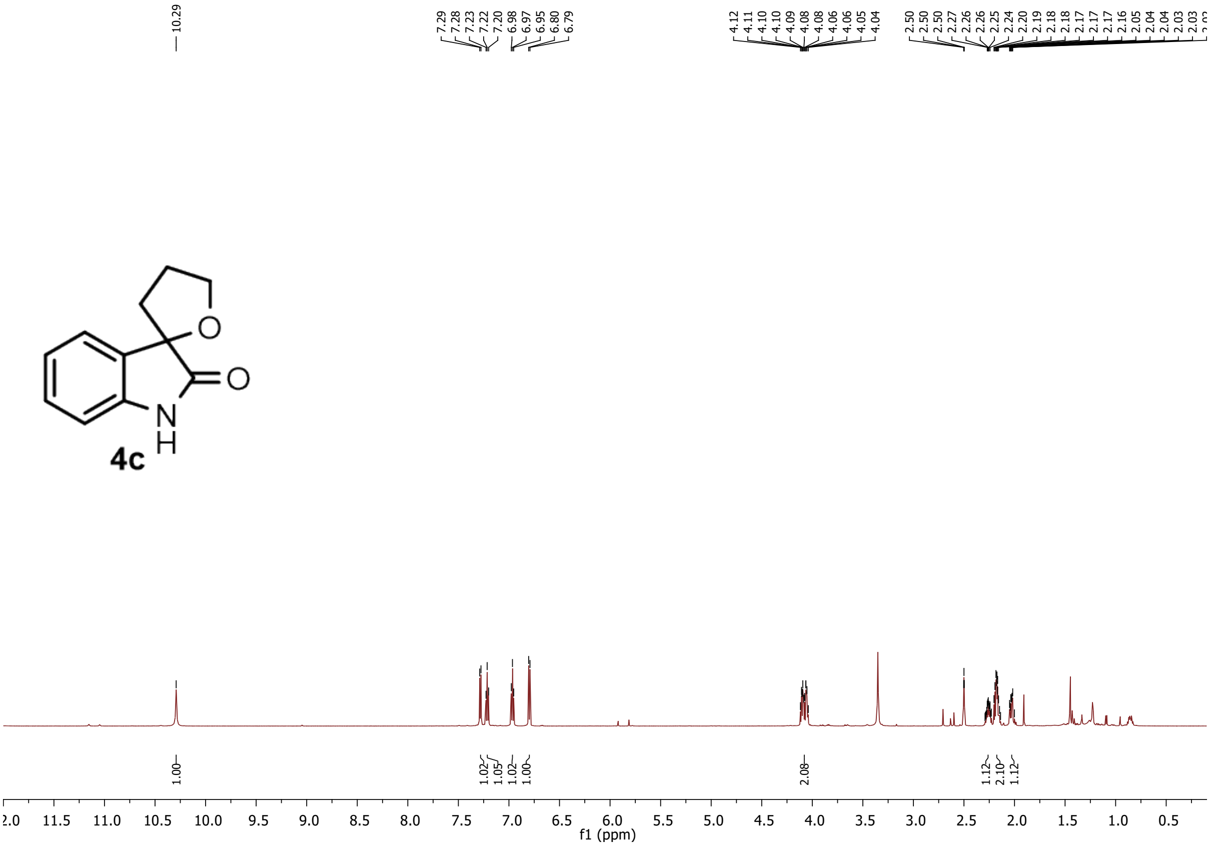


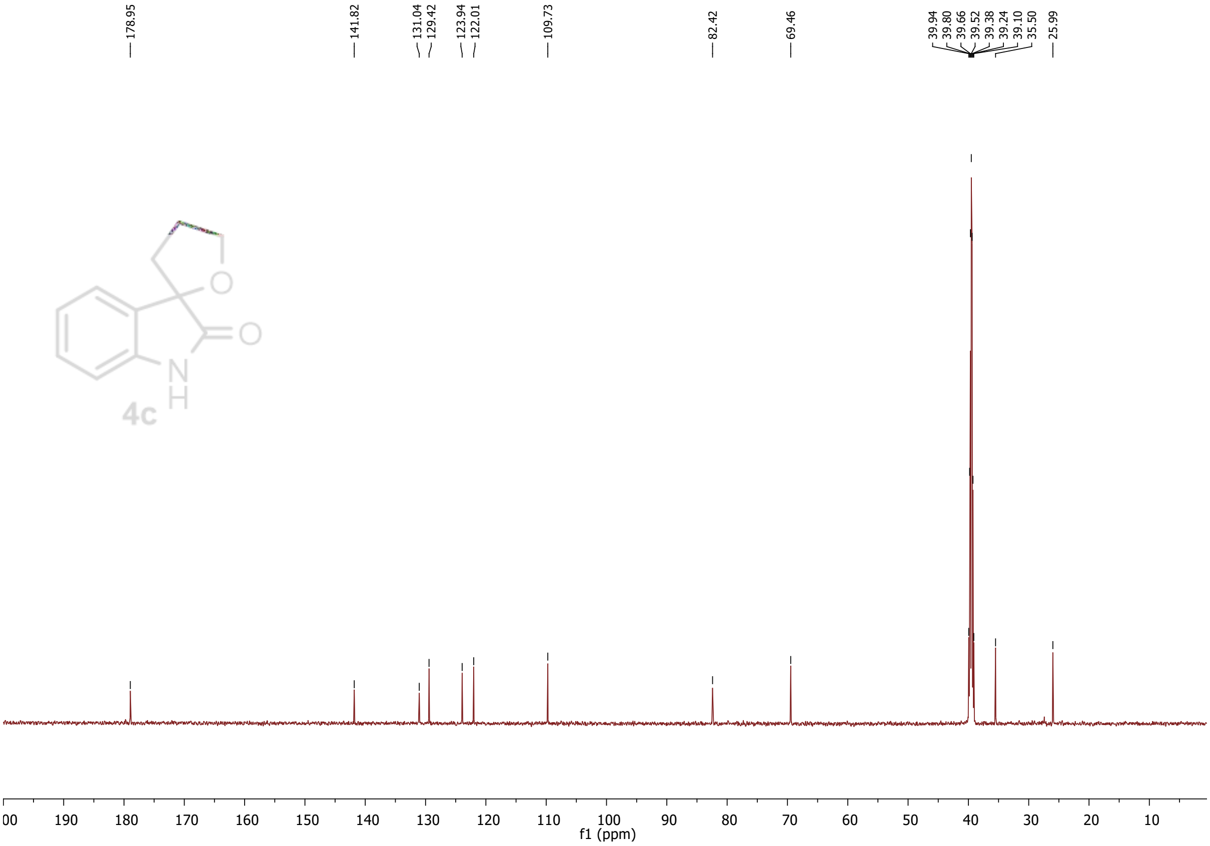
NMR of compound (**4b**)



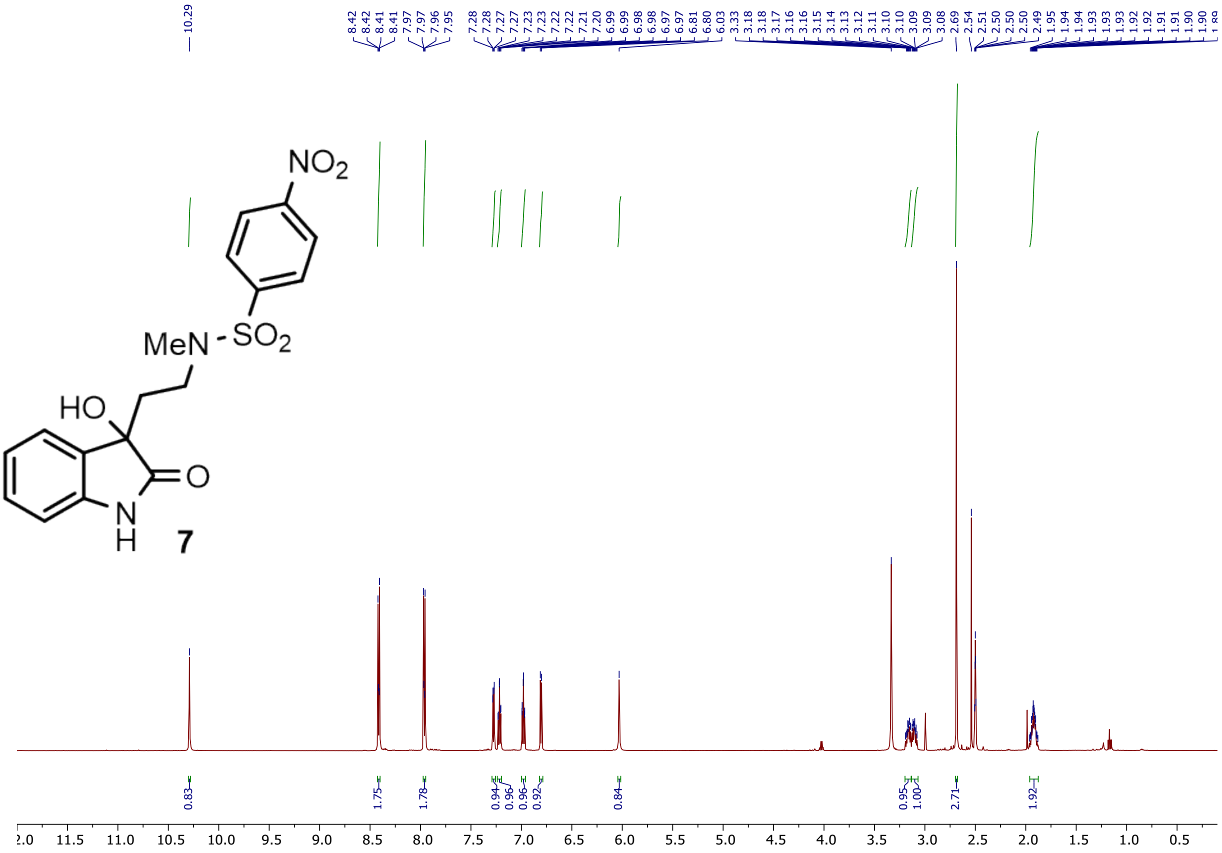


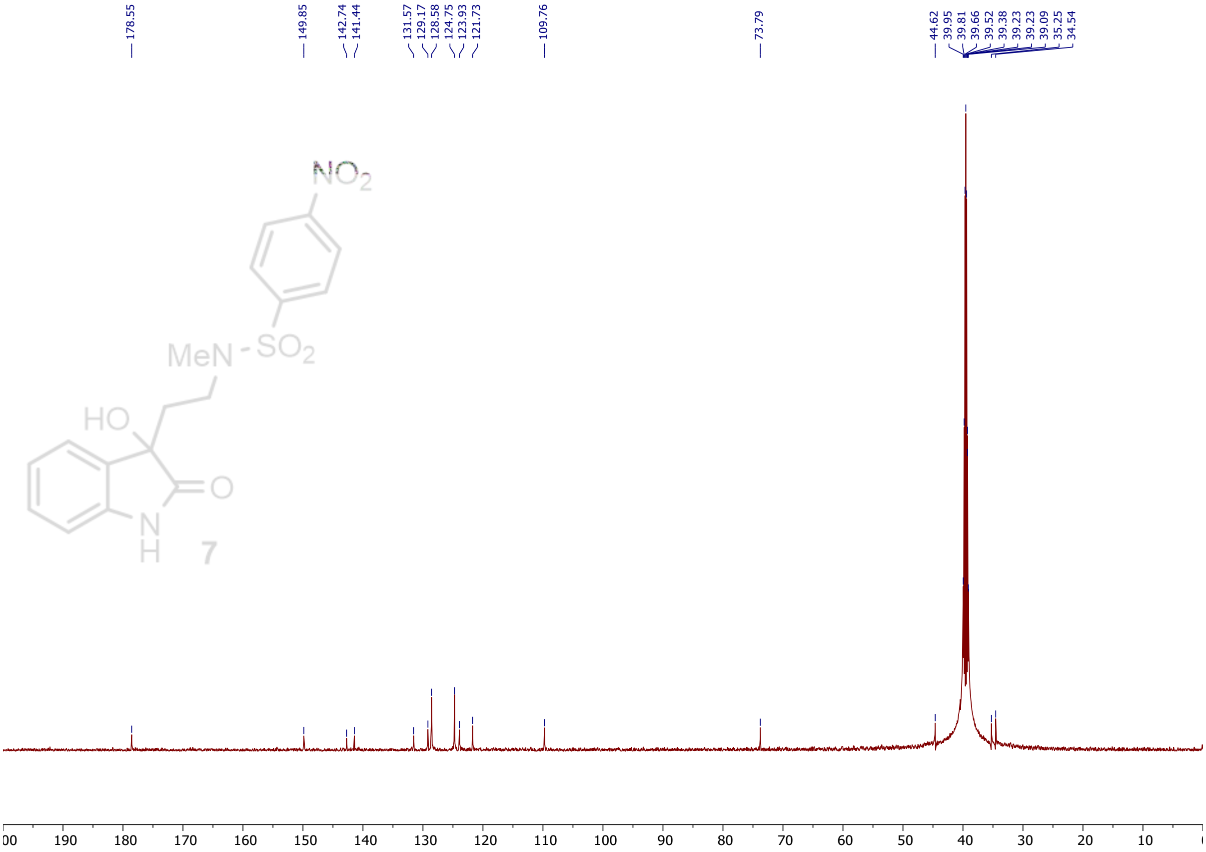
NMR of compound (**4c**)



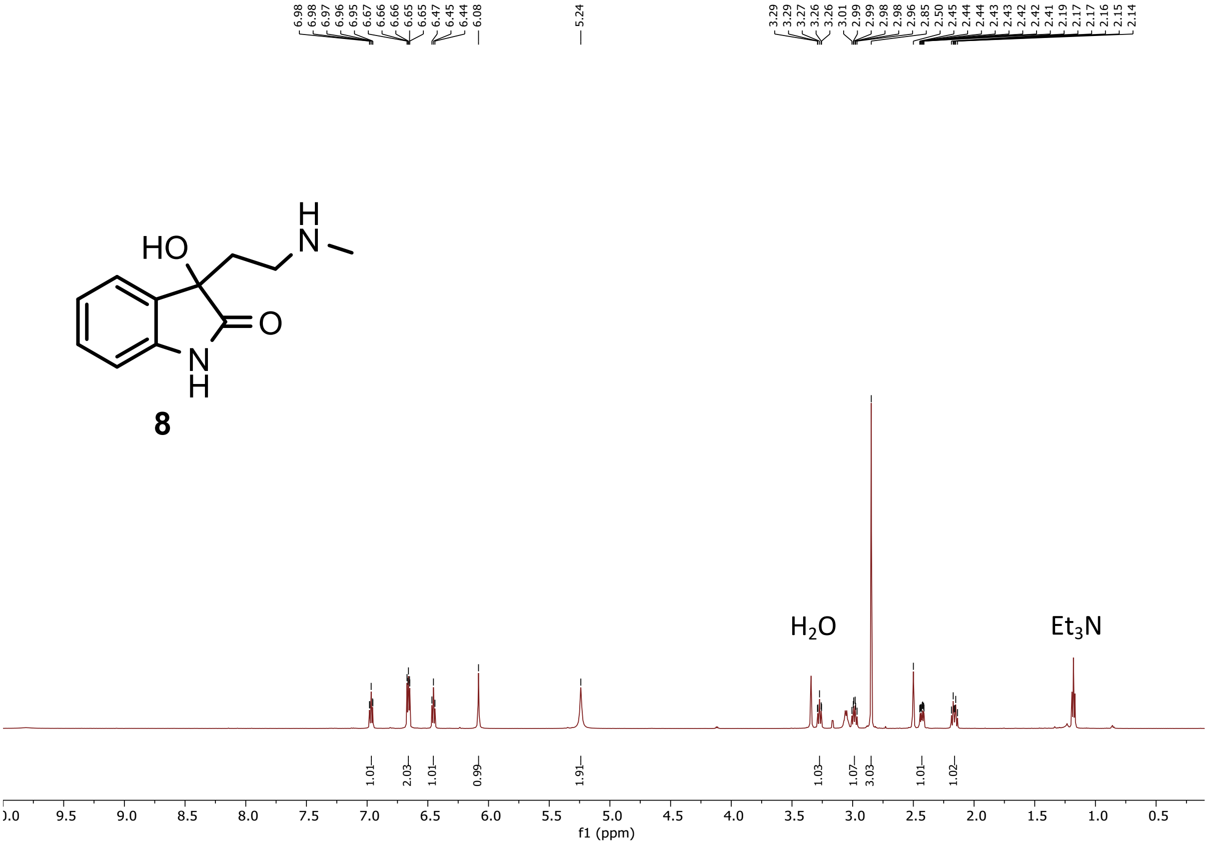


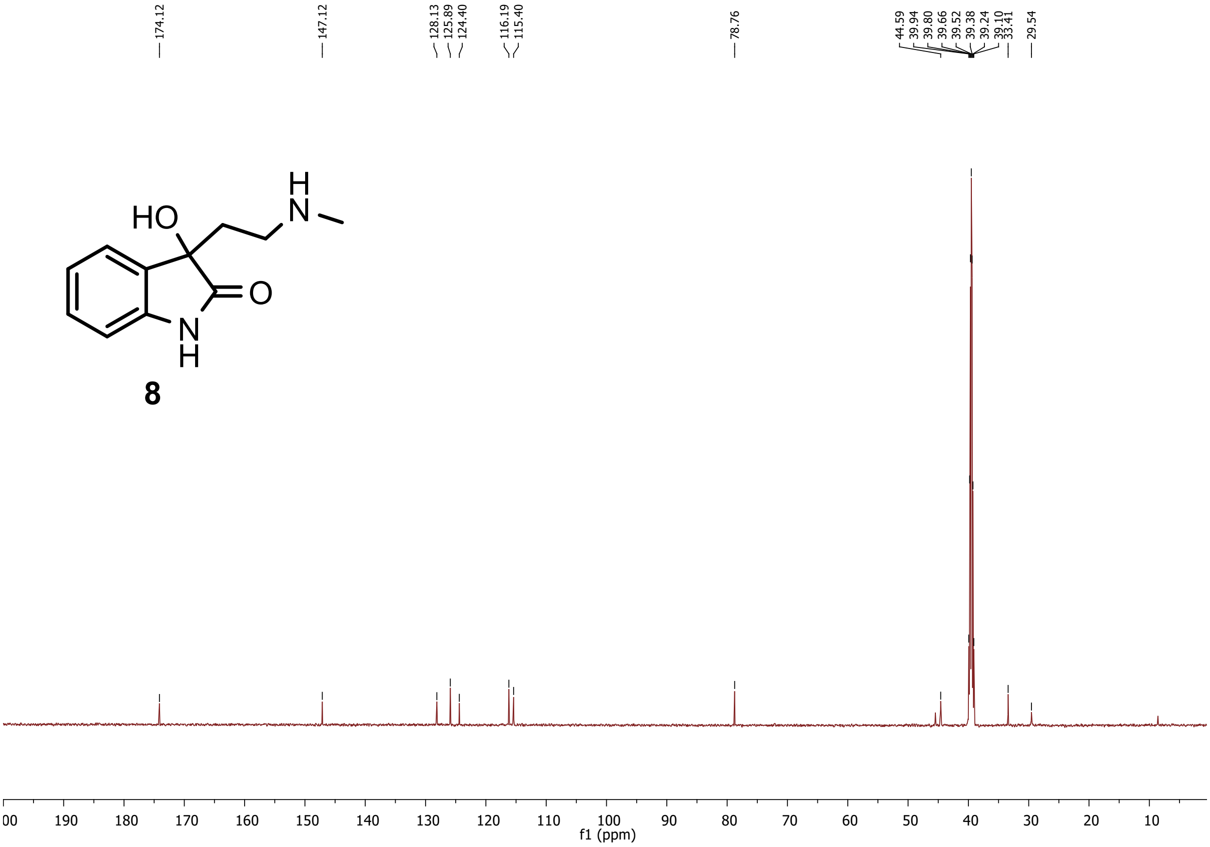
NMR of compound (**7**)



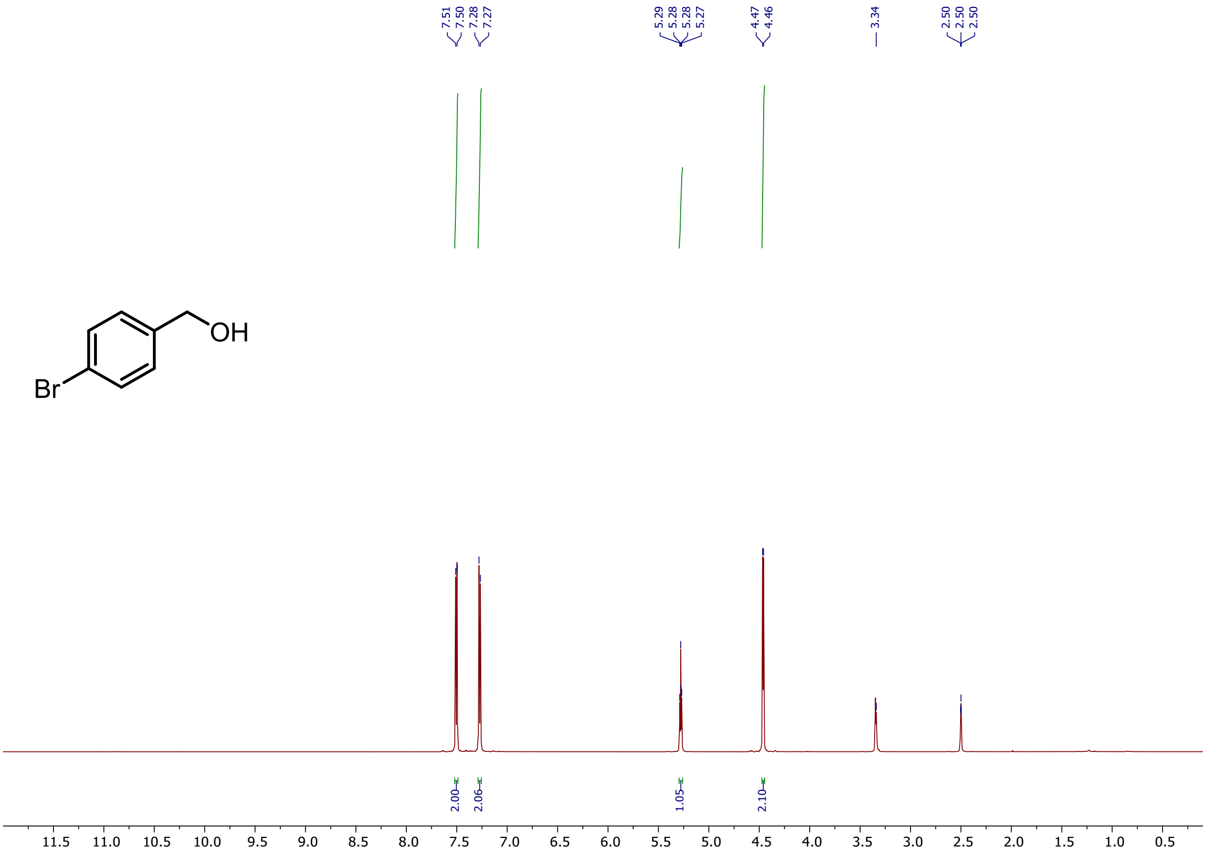


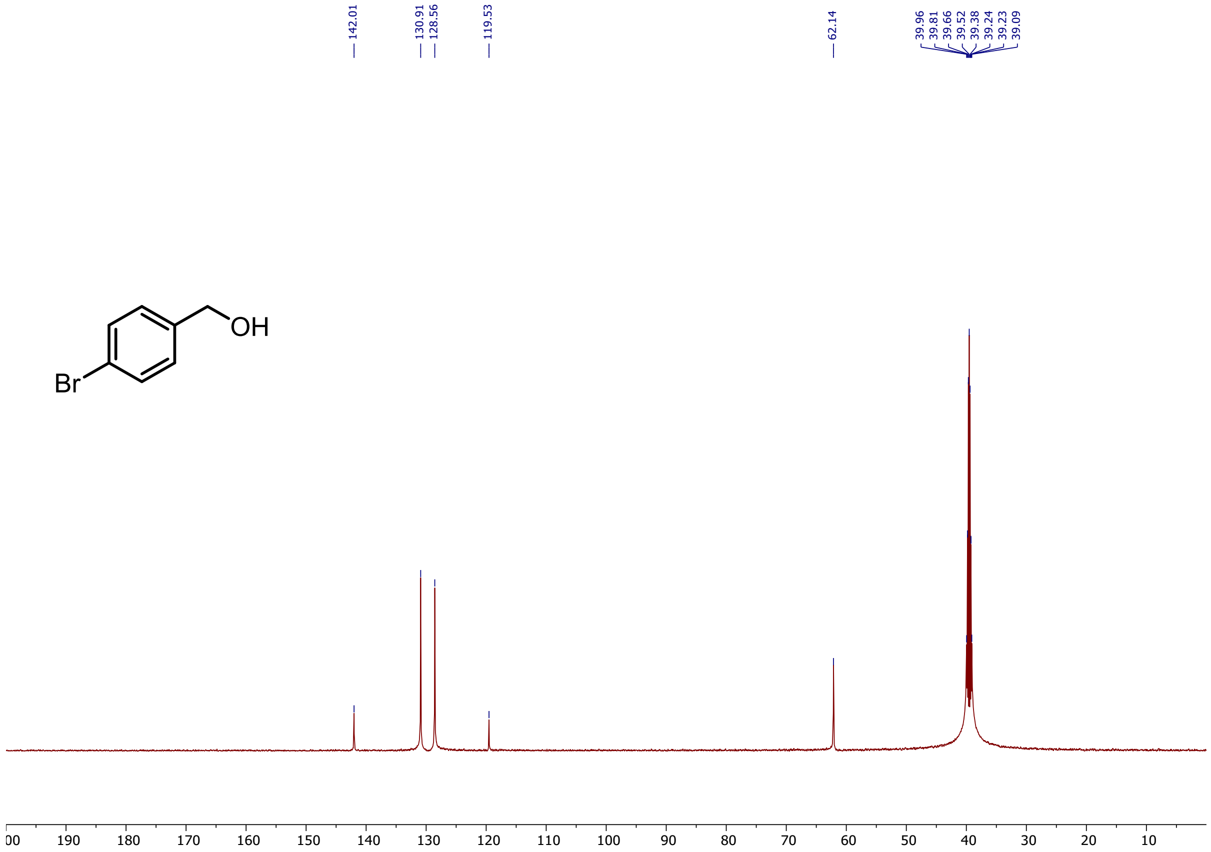
NMR of Compound **(8)**





NMR of (4-Bromophenyl)methanol





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