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Supporting Information

Hemin catalyzed biomimetic oxidative phenol-indole [3+2] reactions in aqueous media

Yu Fu,[a] Qile Yu,[a] Yulong Zhang,[a] Zhonghong Gao,*[a] Yuzhou Wu,*[a] and Fangrui Zhong*[a,b]

[a]Key laboratory of Material Chemistry for Energy Conversion and Storage, Ministry of Education, Hubei Key Laboratory of Bioinorganic Chemistry & Materia Medica, School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology (HUST), 1037 Luoyu Road, Wuhan 430074, China.

[b]Shenzhen Huazhong University of Science and Technology Research Institute, Shenzhen 518000, China.

zhgao144@hust.edu.cn; wuyuzhou@hust.edu.cn; chemzfr@hust.edu.cn

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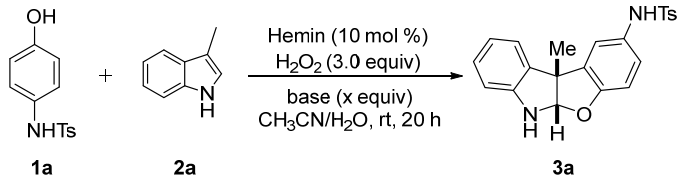
1. General Information

Chemicals and solvents were purchased from commercial suppliers and used as received unless noted. All products were purified by flash chromatography on silica gel. The chemical yields referred are isolated products. ^{1}H NMR and ^{13}C NMR spectra were recorded on 400 MHz or 600 MHz Bruker spectrometers. Chemical shifts of ^{1} H were reported in part per million relative to the $CDCl_3$ residual peak (δ 7.26). Chemical shifts of ^{13}C NMR were reported relative to $CDCl_3$ (δ 77.16). The used abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint.(quintet), m (multiplet), br (broad). Multiplets which arise from accidental equality of coupling constants of magnetically non-equivalent protons are marked as virtual (virt.). Infrared spectra were recorded on a Perkin Elmer FT-IR Spectrum. High resolution mass spectra (HRMS) data were measured on a APCI-micro TOF. Reactions were monitored by TLC analysis using silica gel 60 Å F-254 thin layer plates and compounds were visualized with a UV light at 254 nm or 365 nm. Flash column chromatography was performed on silica gel 60Å, 10-40μm.

2. Reaction condition optimizations

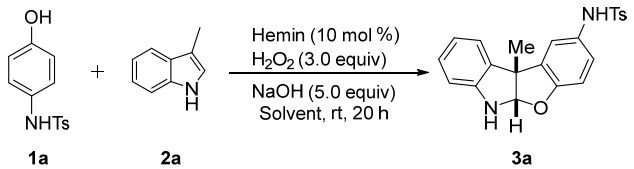
Table S1. The effect of different Bases



Entry[a]	Base	x	Yield(%)[b]
1	KOH	5.0	68
2	NaOH	5.0	91
3	Na_2CO_3	5.0	<10%
4	$NaHCO_3$	5.0	trace
5	K_2CO_3	5.0	Trace
6	Na_2HPO_4	5.0	Trace
7	NaOH	3.0	32
8	NaOH	8.0	66

[a]Reactions were performed with **1a** (0.25 mmol), hemin (0.01 mmol), **2a** (0.1 mmol), base and H_2O_2 (3.0 equiv) in CH_3CN/H_2O (v/v = 1:10, 7.0 mL) under air. [b]Isolated yields.

2.2 Table S2. Solvent screening



Entry[a]	Solvent	Yield(%)[b]
1	H_2O	36
2	H_2O/DMF (10:1)	Trace
3	H_2O/THF (10:1)	35
4	H_2O/DMSO (10:1)	71
5	H_2O/EtOH (10:1)	68
6	H_2O/Acetone (10:1)	52
7	H_2O/CH_3CN (10:1)	91
8	H_2O/MeOH (10:1)	42
9	PBS (pH 12.0)/CH_3CN (10:1)	21

[a]Reactions were performed with **1a** (0.25 mmol), hemin (0.01 mmol), **2a** (0.1 mmol), NaOH (0.5 mmol) and H_2O_2 (0.3 mmol) in solvent (7.0 mL) under air. [b]Isolated yields.

3. General Procedures

3.1. General Procedure 1

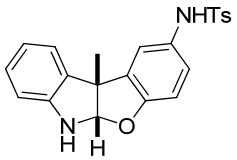
Indole **2** (0.1 mmol) was added into a solution of hemin (10 mol%), NaOH (0.5 mmol) and aminophenol **1** (0.25 mmol) in H_2O/MeCN (7.0 mL, v/v = 10/1), followed by the addition of H_2O_2 (30%, 34 μL) in one portion. The mixture was stirred at room temperature for 20 hours and then was quenched with saturated $Na_2S_2O_3$ solution (3 mL). The mixture was extracted with CH_2Cl_2 (3×15 mL). The combined organic layer was concentrated in vacuo to give a crude product, which was purified purified by chromatography on silica gel (eluent: Hexane/EtOAc, 100:1 to 5:1) to afford benzofuroindoline **3**.

3.2. General Procedure 2

Indole **2** (0.1 mmol) was added into a solution of hemin (10 mol%), NaOH (0.5 mmol) and aminophenol **1** (0.25 mmol) in H_2O/MeCN (7.0 mL, v/v = 1/1), followed by the addition of H_2O_2 (30%, 34 μL) in one portion. The mixture was stirred at room temperature for 20 hours and then was quenched with saturated $Na_2S_2O_3$ solution (3 mL). The mixture was extracted with CH_2Cl_2 (3×15 mL). The combined organic layer was concentrated in vacuo to give a crude product, which was purified purified by chromatography on silica gel (eluent: Hexane/EtOAc, 100:1 to 5:1) to afford benzofuroindoline **3**.

4. Analytical data of all products

4-Methyl-*N*-((5a*RS*,10b*SR*)-10b-methyl-6,10b-dihydro-5aH-benzofuro[2,3-b]indol-3-yl)benzenesulfonamide (3a)

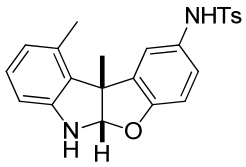


3a

Compound **3a** was synthesized following the General procedure 1.
A white solid, 1.40 g, 90% yield.
TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.52 (m, 2H), 7.26-7.17 (m, 2H), 7.08 (dd, *J* = 7.6, 1.6 Hz, 3H), 6.80 (td, *J* = 7.5, 0.8 Hz, 1H), 6.69 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.23 (s, 1H), 6.08 (d, *J* = 1.9 Hz, 1H), 5.02 (s, 1H), 2.41 (s, 3H), 1.63 (s, 3H).

The spectra data are matched with those reported[1].

_N_-((5a_RS_,10b_SR_)-10,10b-Dimethyl-6,10b-dihydro-5a_H_-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3b)

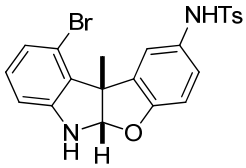


3b

Compound **3b** was synthesized following the General procedure 1.
A white solid, 30.5 mg, 75% yield.
TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.50 (m, 2H), 7.23-7.17 (m, 2H), 7.15 (d, *J* = 2.2 Hz, 1H), 6.95 (s, 1H), 6.90 (d, *J* = 7.9 Hz, 1H), 6.69-6.57 (m, 3H), 6.17 (s, 1H), 6.07 (d, *J* = 2.7 Hz, 1H), 4.90 (s, 1H), 2.40 (s, 3H), 2.29 (s, 3H), 1.63 (s, 3H).

The spectra data are matched with those reported[1].

_N_-((5a_RS_,10b_SR_)-10-Bromo-10b-methyl-6,10b-dihydro-5a_H_-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3c)



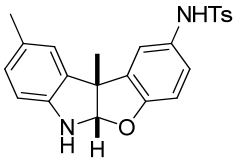
3c

Compound **3c** was synthesized following the General procedure 1.
A white solid, 36.8 mg, 78% yield.
TLC: R_f = 0.65 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.55 (m, 2H), 7.26-7.23 (m, 2H), 7.07-6.99 (m, 3H), 6.81-6.75 (m, 1H), 6.64 (d, *J* = 8.3 Hz, 1H), 6.62 (d, *J* = 8.3 Hz, 1H), 6.22 (s, 1H), 6.06 (d, *J* = 2.4 Hz,

1H), 5.01 (s, 1H), 2.41 (s, 3H), 1.62 (s, 3H).

The spectra data are matched with those reported[1].

***N*-((5a*RS*,10b*SR*)-9,10b-Dimethyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3d)**

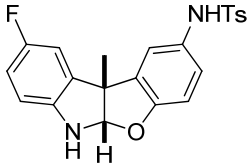


3d

Compound **3d** was synthesized following the General procedure 1.
A white solid, 28.4 mg, 70% yield.
TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.50 (m, 2H), 7.23-7.17 (m, 2H), 7.17-7.12 (m, 1H), 6.97-6.94 (m, 1H), 6.94-6.87 (m, 1H), 6.69-6.57 (m, 3H), 6.20-6.14 (m, 1H), 6.09-6.05 (m, 1H), 4.95-4.86 (m, 1H), 2.40 (s, 3H), 2.29 (s, 3H), 1.63 (s, 3H).

The spectra data are matched with those reported[1].

***N*-((5a*SR*,10b*RS*)-9-Fluoro-10b-methyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b] indol-3-yl)-4-methylbenzenesulfonamide (3e)**

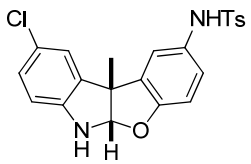


3e

Compound **3e** was synthesized following the General procedure 1.
A white solid, 29.1 mg, 71% yield.
TLC: R_f = 0.65 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.53 (m, 2H), 7.28-7.20 (m, 2H), 7.19-7.13 (m, 2H), 7.01 (d, *J* = 2.3 Hz, 1H), 6.75 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.62 (d, *J* = 8.5 Hz, 1H), 6.56-6.51 (m, 1H), 6.25 (s, 1H), 6.03 (d, *J* = 2.3 Hz, 1H), 5.00 (s, 1H), 2.39 (s, 3H), 1.59 (s, 3H).

The spectra data are matched with those reported[1].

***N*-((5a*SR*,10b*RS*)-9-Chloro-10b-methyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3f)**

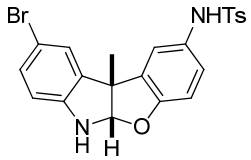


3f

Compound **3f** was synthesized following the General procedure 1.
A white solid, 29.0 mg, 68% yield.
TLC: R_f = 0.68 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64-7.53 (m, 2H), 7.29-7.18 (m, 2H), 7.08-6.99 (m, 3H), 6.79 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.63 (d, *J* = 8.3 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 1H) 6.40 (s, 1H), 6.06 (d, *J* = 2.4 Hz, 1H), 5.03 (d, *J* = 1.7 Hz, 1H), 2.41 (s, 3H), 1.61 (s, 3H).

The spectra data are matched with those reported[1].

_N_-((5a_SR_,10b_RS_)-9-Bromo-10b-methyl-6,10b-dihydro-5a_H_-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3g)

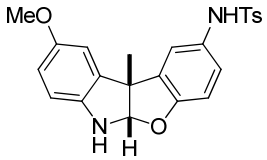


3g

Compound **3g** was synthesized following the General procedure 1.
A white solid, 33.9 mg, 72% yield.
TLC: R_f = 0.67 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.52 (m, 2H), 7.28-7.19 (m, 2H), 6.96 (d, *J* = 2.3 Hz, 1H), 6.80 (ddd, *J* = 15.1, 8.7, 2.5 Hz, 2H), 6.71 (dd, *J* = 8.1, 2.6 Hz, 1H), 6.65 (d, *J* = 8.5 Hz, 1H), 6.60 (dd, *J* = 8.5, 4.2 Hz, 1H), 6.41 (s, 1H), 6.07 (d, *J* = 2.6 Hz, 1H), 4.93 (d, *J* = 2.1 Hz, 1H), 2.41 (s, 3H), 1.60 (s, 3H).

The spectra data are matched with those reported[1].

_N_-((5a_RS_,10b_SR_)-9-Methoxy-10b-methyl-6,10b-dihydro-5a_H_-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3h)

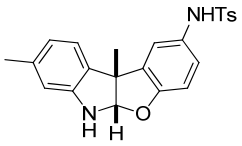


3h

Compound **3h** was synthesized following the General procedure 1.
A white solid, 35.9 mg, 85% yield.
TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.46 (m, 2H), 7.24-7.15 (m, 2H), 7.05 (d, *J* = 2.3 Hz, 1H), 6.72-6.55 (m, 5H), 6.14 (s, 1H), 6.04 (d, *J* = 2.8 Hz, 1H), 4.79 (d, *J* = 2.3 Hz, 1H), 3.75 (s, 3H), 2.38 (s, 3H), 1.60 (s, 3H).

The spectra data are matched with those reported[1].

_N_-((5a_RS_,10b_SR_)-8,10b-Dimethyl-6,10b-dihydro-5a_H_-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3i)



3i

Compound **3i** was synthesized following the General procedure 1.

A white solid, 32.5 mg, 80% yield.

TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]

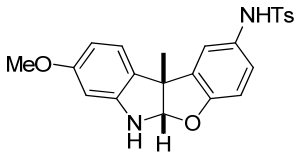
IR: 3399, 3258, 2924, 2850, 1485, 1160 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.51 (m, 2H), 7.28-7.19 (m, 2H), 7.05 (d, *J* = 2.3 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.72-6.57 (m, 3H), 6.52 (s, 1H), 6.18 (s, 1H), 6.06 (d, *J* = 2.0 Hz, 1H), 4.96 (s, 1H), 2.41 (s, 3H), 2.28 (s, 3H), 1.61 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 146.9, 143.6, 138.4, 135.8, 134.2, 130.2, 129.5, 129.0, 127.4, 125.0, 122.3, 120.7, 119.9, 110.2, 109.8, 105.2, 55.7, 23.9, 21.6, 21.5.

HRMS (ESI): $C_{23}H_{22}N_2O_3SNa$ $[M+Na]^+$: calcd: 429.1208; found: 429.1210

N-((5a*RS*,10b*SR*)-8-Methoxy-10b-methyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3j)



3j

Compound **3j** was synthesized following the General procedure 1.

A white solid, 33.8 mg, 80% yield.

TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]

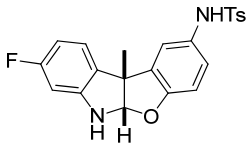
IR: 3399, 3258, 2925, 2853, 1486, 1159 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.48 (m, 2H), 7.21-7.12 (m, 2H), 7.02 (d, *J* = 2.2 Hz, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.65 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.31 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.24 (d, *J* = 2.2 Hz, 1H), 6.14 (s, 1H), 6.04 (d, *J* = 2.2 Hz, 1H), 4.98 (s, 1H), 3.74 (s, 3H), 2.39 (s, 3H), 1.59 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 157.1, 148.0, 143.6, 135.8, 134.3, 129.5, 129.0, 127.4, 125.4, 124.9, 122.9, 119.9, 109.8, 105.4, 104.9, 96.0, 55.4, 55.4, 24.0, 21.6.

HRMS (ESI): $C_{23}H_{22}N_2O_4SNa$ $[M+Na]^+$: calcd: 445.1156; found: 445.1154

N-((5a*SR*,10b*RS*)-8-Fluoro-10b-methyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3k)



3k

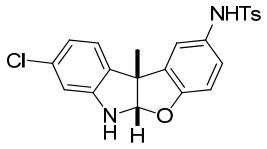
Compound **3k** was synthesized following the General procedure 1.

A white solid, 30.0 mg, 73% yield.

TLC: R_f = 0.65 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.59 (m, 2H), 7.26-7.18 (m, 2H), 7.06 (d, *J* = 2.2 Hz, 1H), 6.97 (dd, *J* = 8.2, 5.4 Hz, 1H), 6.70 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 6.46 (ddd, *J* = 9.3, 8.3, 2.3 Hz, 1H), 6.37 (dd, *J* = 9.5, 2.3 Hz, 1H), 6.31 (s, 1H), 6.08 (d, *J* = 2.3 Hz, 1H), 5.09 (s, 1H), 2.41 (s, 3H), 1.62 (s, 3H).

The spectra data are matched with those reported[1].

N-((5a*SR*,10b*RS*)-8-Chloro-10b-methyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3l)

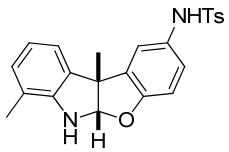


3l

Compound **3l** was synthesized following the General procedure 1.
A white solid, 30.7 mg, 72% yield.
TLC: R_f = 0.65 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.48 (m, 2H), 7.25-7.16 (m, 2H), 7.05 (d, *J* = 2.3 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.77-6.60 (m, 4H), 6.26 (s, 1H), 6.07 (d, *J* = 2.3 Hz, 1H), 5.07 (s, 1H), 2.41 (s, 3H), 1.62 (s, 3H).

The spectra data are matched with those reported[1].

N-((5a*RS*,10b*SR*)-7,10b-Dimethyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3m)

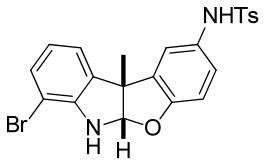


3m

Compound **3m** was synthesized following the General procedure 1.
A white solid, 33.3 mg, 82% yield.
TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.49 (m, 2H), 7.24-7.12 (m, 2H), 7.03 (d, *J* = 2.3 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 2H), 6.75-6.65 (m, 2H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.25 (s, 1H), 6.08 (d, *J* = 2.1 Hz, 1H), 4.84 (s, 1H), 2.38 (s, 3H), 2.17 (s, 3H), 1.60 (s, 3H).

The spectra data are matched with those reported[1].

N-((5a*SR*,10b*RS*)-7-Bromo-10b-methyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3n)

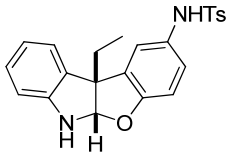


3n

Compound **3n** was synthesized following the General procedure 1.
A white solid, 37.7 mg, 80% yield.
TLC: R_f = 0.65 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.49 (m, 2H), 7.23 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.20-7.14 (m, 2H), 7.09 (d, *J* = 2.1 Hz, 1H), 7.03 (d, *J* = 7.3 Hz, 1H), 6.72-6.65 (m, 3H), 6.18 (s, 1H), 6.10 (d, *J* = 2.2 Hz, 1H), 5.25 (s, 1H), 2.40 (s, 3H), 1.65 (s, 3H).

The spectra data are matched with those reported[1].

N-((5a*SR*,10b*RS*)-10b-Ethyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3o)

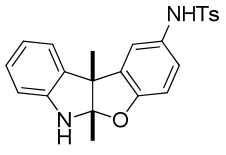


3o

Compound **3o** was synthesized following the General procedure 2.
A white solid, 25.6 mg, 63% yield.
TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.49 (m, 2H), 7.24-7.16 (m, 2H), 7.12-7.03 (m, 2H), 7.01 (d, *J* = 2.3 Hz, 1H), 6.80 (td, *J* = 7.5, 0.9 Hz, 1H), 6.74-6.65 (m, 2H), 6.62 (d, *J* = 8.4 Hz, 1H), 6.24-6.14 (m, 2H), 5.00 (d, *J* = 2.1 Hz, 1H), 2.40 (s, 3H), 2.03 (dd, *J* = 11.9, 7.4 Hz, 2H), 1.60 (s, 3H), 0.80 (t, *J* = 7.4 Hz, 3H).

The spectra data are matched with those reported[1].

N-((5a*RS*,10b*SR*)-5a,10b-Dimethyl-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-2-yl)-4-methylbenzenesulfonamide (3p)

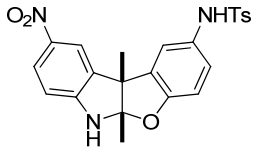


3p

Compound **3p** was synthesized following the General procedure 2.
A white solid, 26.4 mg, 65% yield.
TLC: R_f = 0.72 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59-7.48 (m, 2H), 7.25-7.17 (m, 2H), 7.11-7.04 (m, 2H), 7.03 (d, *J* = 2.3 Hz, 1H), 7.00 (d, *J* = 7.0 Hz, 1H), 6.79 (dd, *J* = 7.5, 0.9 Hz, 1H), 6.72-6.61 (m, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 6.27 (s, 1H), 4.82 (s, 1H), 2.41 (s, 3H), 1.66 (s, 3H), 1.53 (s, 3H).

The spectra data are matched with those reported[1].

***N*-((5a*RS*,10b*SR*)-5a,10b-Dimethyl-9-nitro-6,10b-dihydro-5a*H*-benzofuro[2,3-b]indol-2-yl)-4-methylbenzenesulfonamide (3q)**

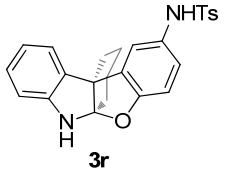


3q

Compound **3q** was synthesized following the General procedure 2.
A white solid, 23.9 mg, 53% yield.
TLC: R_f = 0.72 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.91 (d, *J* = 2.2 Hz, 1H), 7.64-7.56 (m, 2H), 7.26-7.16 (m, 2H), 6.97 (d, *J* = 2.3 Hz, 1H), 6.89 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.65 (d, *J* = 8.5 Hz, 1H), 6.58 (d, *J* = 8.7 Hz, 1H), 6.40 (s, 1H), 5.43 (s, 1H), 2.39 (s, 3H), 1.71 (s, 3H), 1.58 (s, 3H).

The spectra data are matched with those reported[1].

***N*-((5aSR,10bSR)-5,6-Dihydro-5a,10b-butanoindeno[2,1-b]indol-9-yl)-4-methylbenzenesulfonamide (3r)**

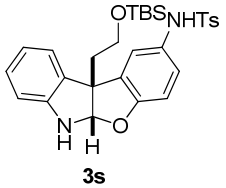


3r

Compound **3r** was synthesized following the General procedure 2.
A white solid, 18.2 mg, 42% yield.
TLC: R_f = 0.6 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.51 (m, 2H), 7.26-7.17 (m, 2H), 7.12-7.01 (m, 2H), 6.87 (d, *J* = 6.7 Hz, 1H), 6.82-6.68 (m, 3H), 6.56 (d, *J* = 8.4 Hz, 1H), 6.20 (s, 1H), 4.80 (s, 1H), 2.42 (s, 3H), 2.40-2.31 (m, 1H), 2.31-2.20 (m, 1H), 1.87-1.81 (m, 1H), 1.73-1.61 (m, 2H), 1.58-1.51 (m, 2H), 1.21-1.19 (m, 1H).

The spectra data are matched with those reported[1].

***N*-((5a*SR*,10b*RS*)-10b-(2-((Tert-butyldimethylsilyl)oxy)ethyl)-6,10bdihydro-5a*H* benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide(3s)**

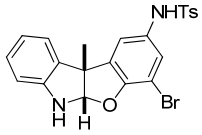


3s

Compound **3s** was synthesized following the General procedure 2.
A white solid, 24.2 mg, 45% yield.
TLC: R_f = 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.58 (m, 2H), 7.26-7.18 (m, 2H), 7.12-7.01 (m, 3H), 6.83-6.72 (m, 1H), 6.74-6.53 (m, 4H), 6.18 (s, 1H), 4.95 (d, *J* = 2.7 Hz, 1H), 3.56 (t, *J* = 6.0 Hz, 2H), 2.40 (s, 3H), 2.24 (t, *J* = 6.0 Hz, 2H), 0.85 (s, 9H), -0.08 (d, *J* = 3.0 Hz, 6H).

The spectra data are matched with those reported[1].

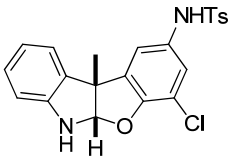
_N_-((5a_SR_,10b_RS_)-4-Bromo-10b-methyl-6,10b-dihydro-5a_H_-benzofuro[2,3-b]indol-3-yl)-4-methylbenzenesulfonamide (3t)



3t

Compound **3t** was synthesized following the General procedure 1.
A white solid, 30.7 mg, 65% yield.
TLC: R_f = 0.65 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
IR: 3311, 3061, 2921, 2851, 1454, 1160 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.51 (m, 2H), 7.28-7.19 (m, 2H), 7.12 (td, *J* = 7.7, 1.2 Hz, 1H), 7.05 (d, *J* = 5.3 Hz, 2H), 6.89 (d, *J* = 2.1 Hz, 1H), 6.81 (td, *J* = 7.5, 0.9 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.33 (s, 1H), 6.16 (d, *J* = 2.2 Hz, 1H), 5.14 (s, 1H), 2.42 (s, 3H), 1.64 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7, 146.4, 143.9, 135.5, 134.8, 132.2, 130.2, 129.7, 128.5, 127.4, 127.2, 122.5, 120.1, 118.4, 109.4, 105.3, 102.2, 57.0, 23.7, 21.6.
HRMS (ESI): $C_{22}H_{19}BrN_2O_3SNa$ $[M+Na]^+$: calcd: 493.0158; found: 493.0158

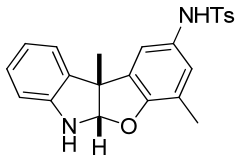
_N_-((5a_SR_,10b_RS_)-4-Chloro-10b-methyl-6,10b-dihydro-5aH-benzofuro[2,3-b]indol-2-yl)-4-methylbenzenesulfonamide(3u)



3u

Compound **3u** was synthesized following the General procedure 1.
A white solid, 25.6 mg, 60% yield.
TLC: R_f = 0.65 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]
IR: 3312, 3110, 2922, 2852, 1457, 1158 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.52 (m, 2H), 7.28-7.16 (m, 2H), 7.12 (td, *J* = 7.7, 1.2 Hz, 1H), 7.03 (dd, *J* = 12.5, 4.6 Hz, 2H), 6.79 (dd, *J* = 16.1, 1.5 Hz, 2H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.39 (s, 1H), 6.16 (d, *J* = 2.2 Hz, 1H), 5.15 (s, 1H), 2.42 (s, 3H), 1.64 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.2, 146.4, 143.9, 135.5, 135.2, 132.2, 129.9, 129.6, 128.5, 127.4, 124.5, 122.5, 120.1, 117.7, 114.8, 109.4, 105.5, 56.8, 23.6, 21.6.
HRMS (ESI): $C_{22}H_{19}ClN_2O_3SNa$ $[M+Na]^+$: calcd: 449.0667; found: 449.0669

***N*-((5a*SR*,10b*RS*)-4,10b-Dimethyl-6,10b-dihydro-5aH-benzofuro[2,3-b]indol-2-yl)-4-methylbenzenesulfonamide(3v)**



3v

Compound **3v** was synthesized following the General procedure 1.

A white solid, 31.3 mg, 77% yield.

TLC: R_f= 0.7 (DCM/MeOH = 100/1, v/v). [UV, $KMnO_4$]

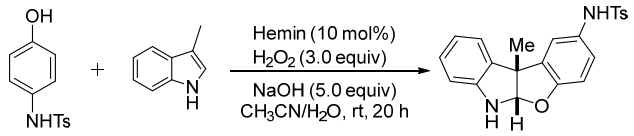
IR: 3314, 3101, 2921, 2852, 1471, 1157 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.53 (m, 2H), 7.28-7.19 (m, 2H), 7.07 (td, *J* = 7.7, 1.2 Hz, 1H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.80 (ddd, *J* = 8.9, 8.3, 1.6 Hz, 2H), 6.69 (d, *J* = 7.8 Hz, 1H), 6.60 (d, *J* = 1.7 Hz, 1H), 6.12 (s, 1H), 6.06 (d, *J* = 2.5 Hz, 1H), 5.02 (s, 1H), 2.42 (s, 3H), 2.11 (s, 3H), 1.60 (s,3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 146.7, 143.5, 135.9, 133.1, 132.9, 129.4, 128.8, 128.2, 127.4, 126.3, 122.6, 120.3, 119.8, 116.9, 109.3, 104.5, 56.2, 24.0, 21.6, 15.3.

HRMS (ESI): $C_{23}H_{22}N_2O_3SNa$ $[M+Na]^+$: calcd: 429.1217; found: 429.1207

5. Scale-up Experiment

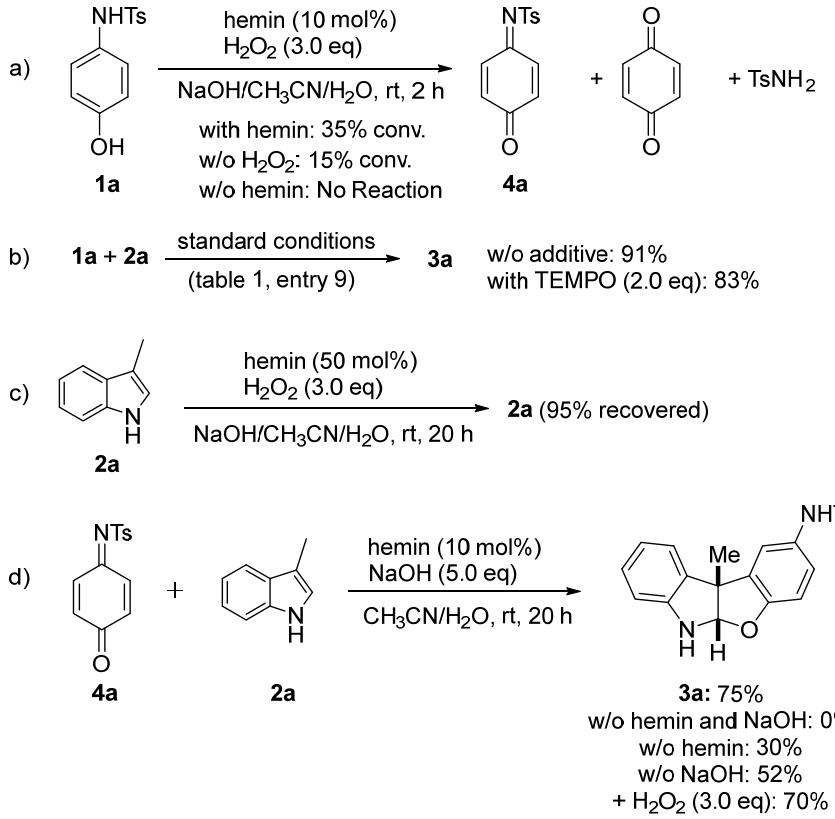


1a **2a** **3a** (1.41 gram, 90%)

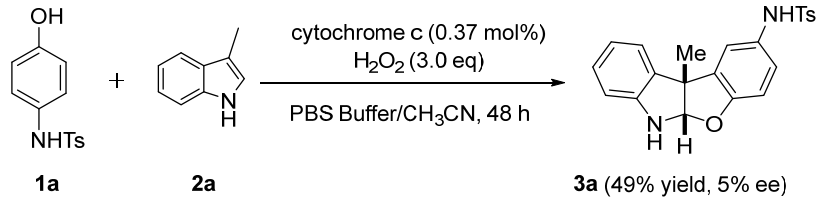
3-Methyl indole **2a** (4.0 mmol, 524.8 mg) was added into aqueous solution (H_2O/MeCN=10/1, 110 mL) of 10 mol% hemin (0.5 mg, 260.8 mg), NaOH (20 mmol, 800 mg) and N-(4-Hydroxyphenyl)-p-toluenesulphonamide **1a** (10 mmol, 2.632 g), followed by adding H_2O_2 (30%, 1.2 mL) in one portion. The mixture was stirred at room temperature for 20 hours and then was quenched with saturated $Na_2S_2O_3$ solution (50 mL). Then, the mixture was extracted with CH_2Cl_2 (3 × 80 mL). The combined organic layer was concentrated in vacuo to give a crude product, which was purified purified by chromatography on silica gel (eluent: Hexane/EtOAc, 100:1 to 5:1) to afford benzofuroindoline **3a** (1.41 g, 90%).

When the protocol was repeated with 2 mol% of hemin under otherwise identical conditions, product **3a** was isolated in 65% yield (1.02 g).

6. Mechanistic studies



7. Catalytic reaction with cytochrome c

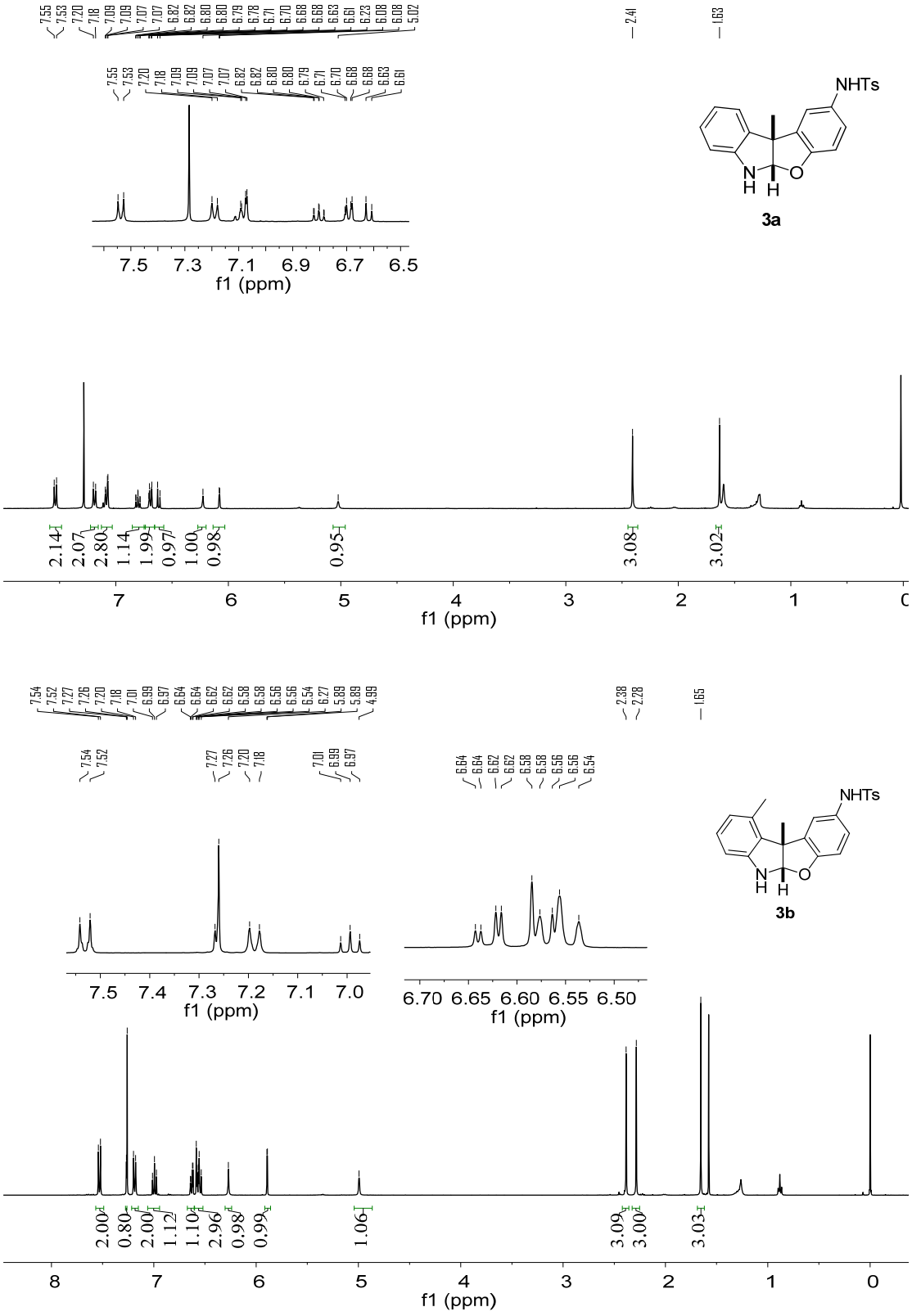


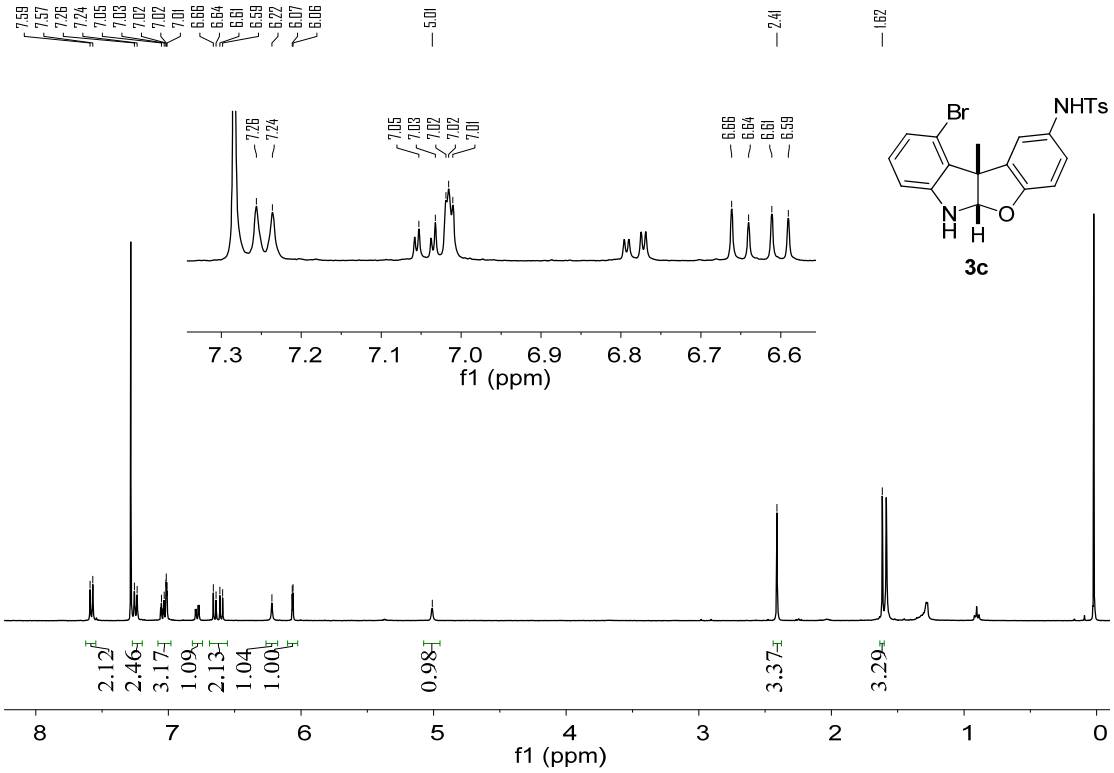
Indole **2a** (0.05 mmol, 6.6 mg) was added into a solution of cytochrome c (0.37 mol%, 2.2 mg), and aminophenol **1a** (0.1 mmol, 26.3 mg) in PBS buffer (pH 7.4)/MeCN (4.4 mL, v/v = 10/1), followed by the addition of H_2O_2 (30%, 17 μL) in one portion. The mixture was stirred at room temperature for 48 hours and then was quenched with saturated $Na_2S_2O_3$ solution (3 mL). The mixture was extracted with CH_2Cl_2 (3×5 mL). The combined organic layer was concentrated in vacuo to give a crude product, which was purified purified by chromatography on silica gel (eluent: Hexane/EtOAc, 100:1 to 5:1) to afford benzofuroindoline **3a** (9.6 mg, 49% yield). HPLC condition: Chiralpak IC-H, *n*-Hexane/*i*PrOH = 70/30, 1.0 mL/min, t_1 = 10.3 min, t_2 = 14.9 min. The ee value was 5%.

Reference

1. Liao L, Shu C, Zhang M, et al. *Angew. Chem. Int. Ed.*, **2014**, *126*, 10639-10643.

8. NMR Spectra of Products

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7.24
7.05
7.03
7.02
7.02
7.01
6.66
6.64
6.61
6.59
6.22
6.07
6.06
5.01
2.41
1.62
Br
NHTs
N
H
H
O
3c
7.3
7.2
7.1
7.0
6.9
6.8
6.7
6.6
f1 (ppm)
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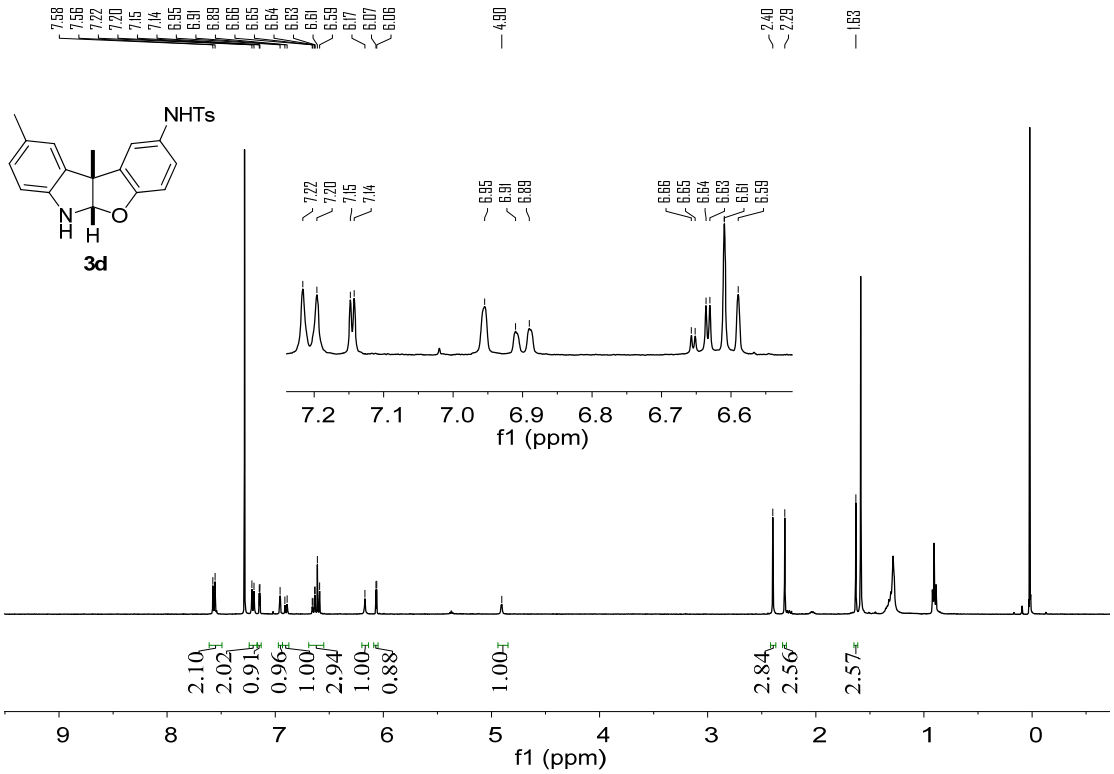
2.46
3.17
1.09
2.13
1.04
1.00
0.98
3.37
3.29
8
7
6
5
4
3
2
1
0
f1 (ppm)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6.61
6.59
6.17
6.07
6.06
4.90
2.40
2.29
1.63
NHTs
N
H
H
O
3d
7.2
7.1
7.0
6.9
6.8
6.7
6.6
f1 (ppm)
2.10
2.02
0.91
0.96
1.00
2.94
1.00
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1.00
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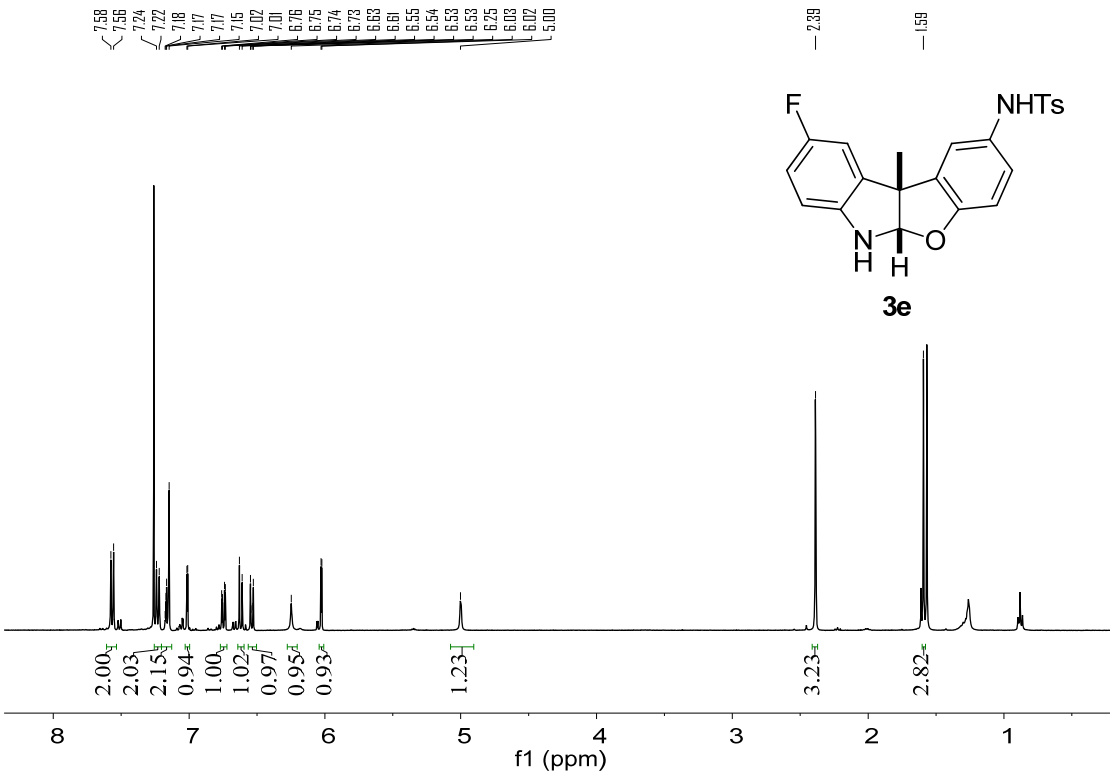
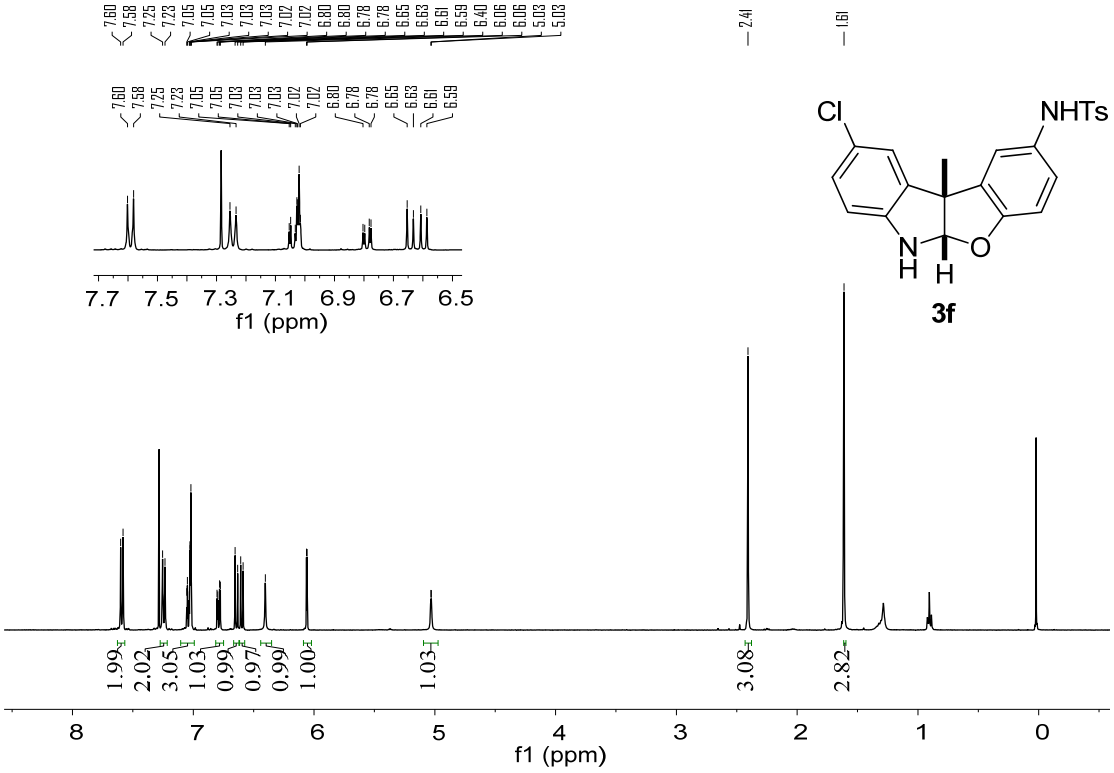
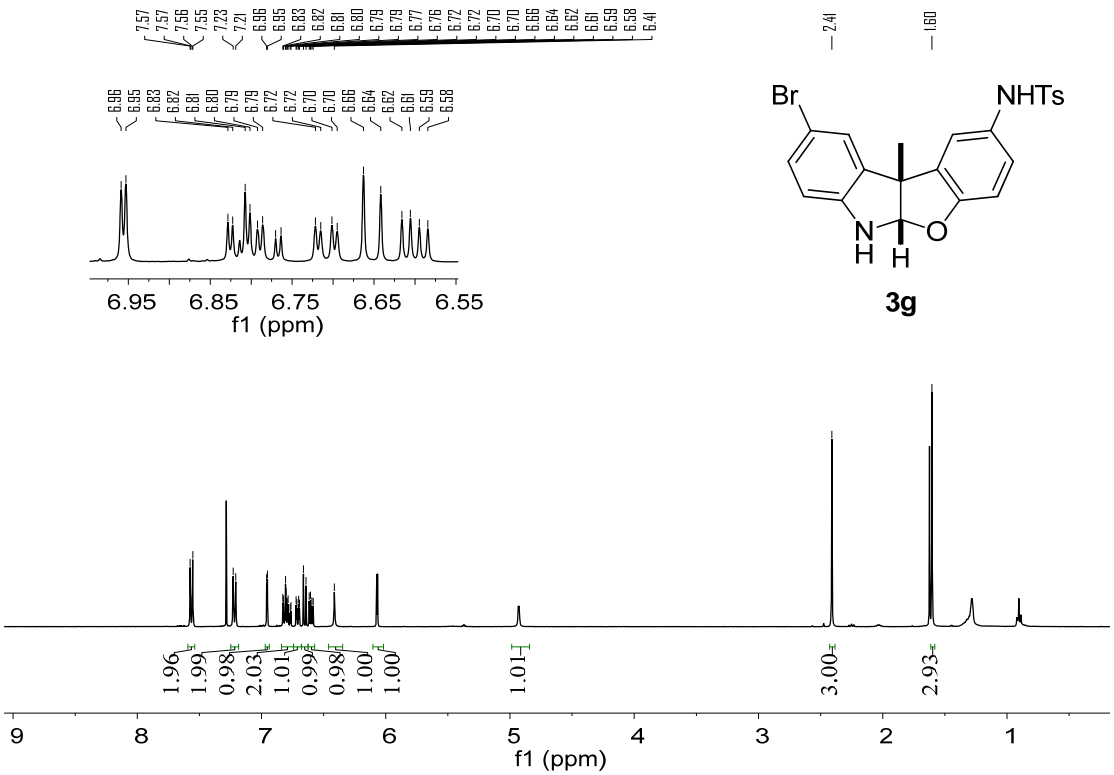
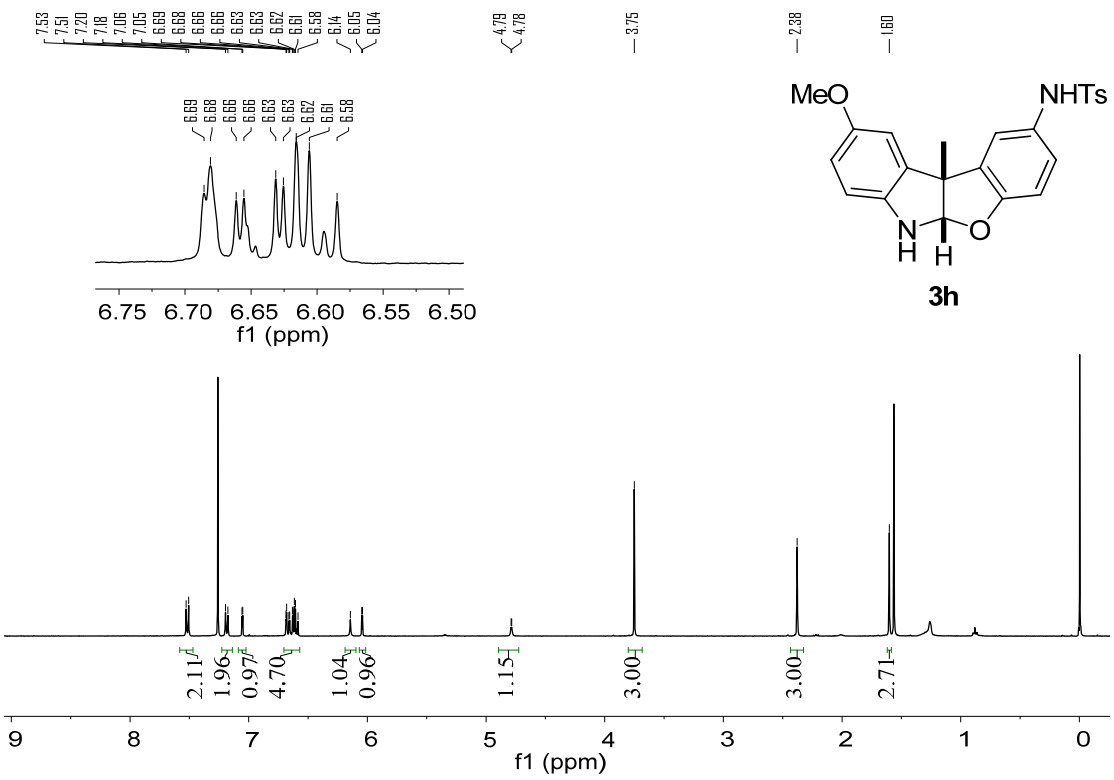
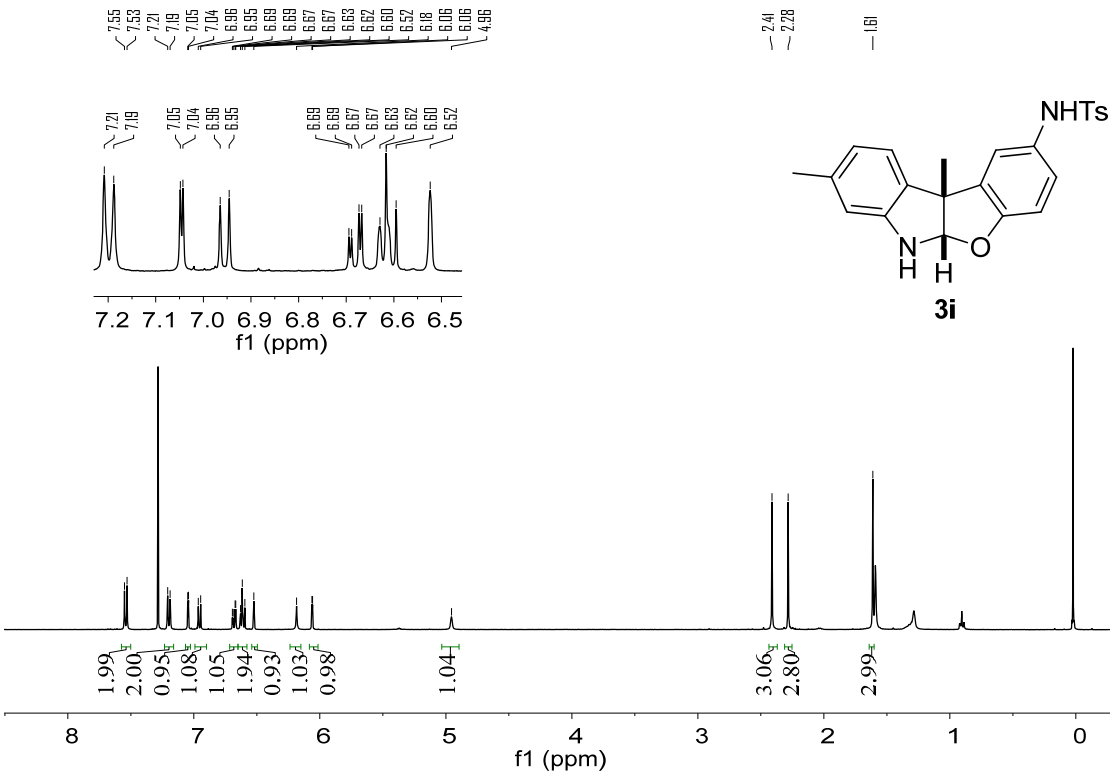
2.56
2.57
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


F
NHTs
N
H
H
O
3e
f1 (ppm)


Cl
NHTs
N
H
H
O
3f
f1 (ppm)


Br
NHTs
N
H
O
H
3g
f1 (ppm)


MeO
NHTs
N
H
O
H
3h
f1 (ppm)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7.05
7.04
6.96
6.95
6.69
6.69
6.67
6.67
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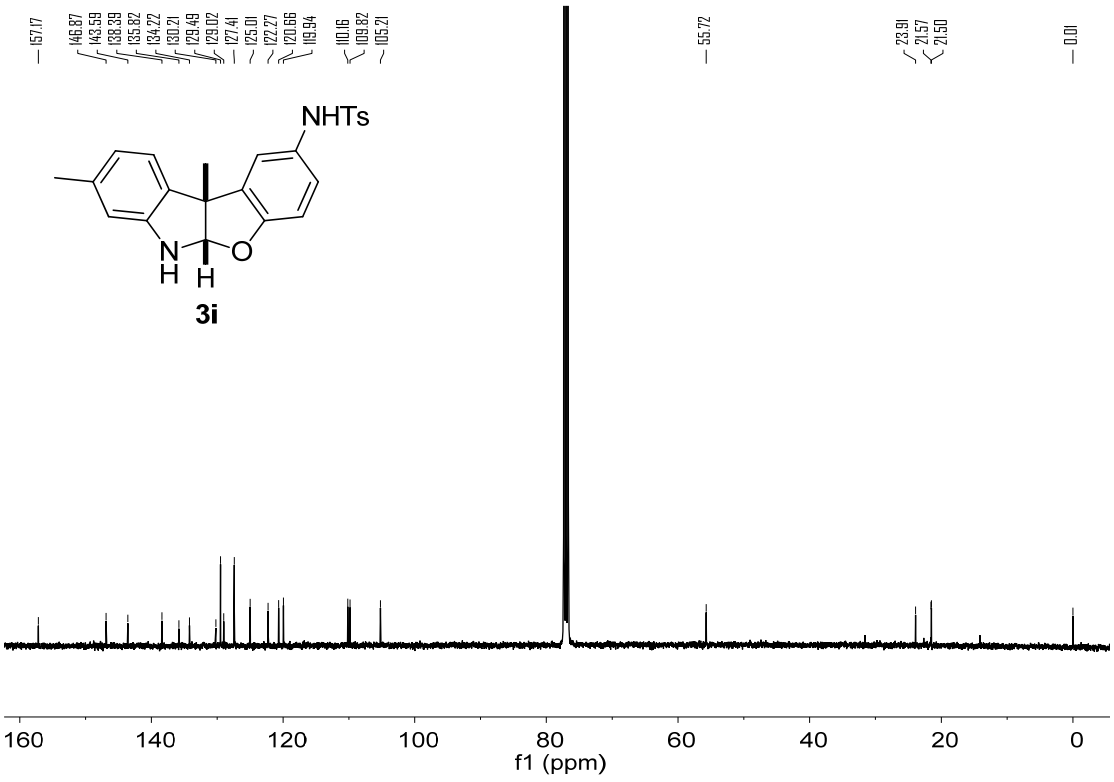
6.62
6.60
6.52
6.18
6.06
6.06
4.96
2.41
2.28
1.61
NHTs
N
H
H
O
3i
7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5
f1 (ppm)
1.99
2.00
0.95
1.08
1.05
1.94
0.93
1.03
0.98
1.04
3.06
2.80
2.99
8 7 6 5 4 3 2 1 0
f1 (ppm)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135.82
134.22
130.21
129.49
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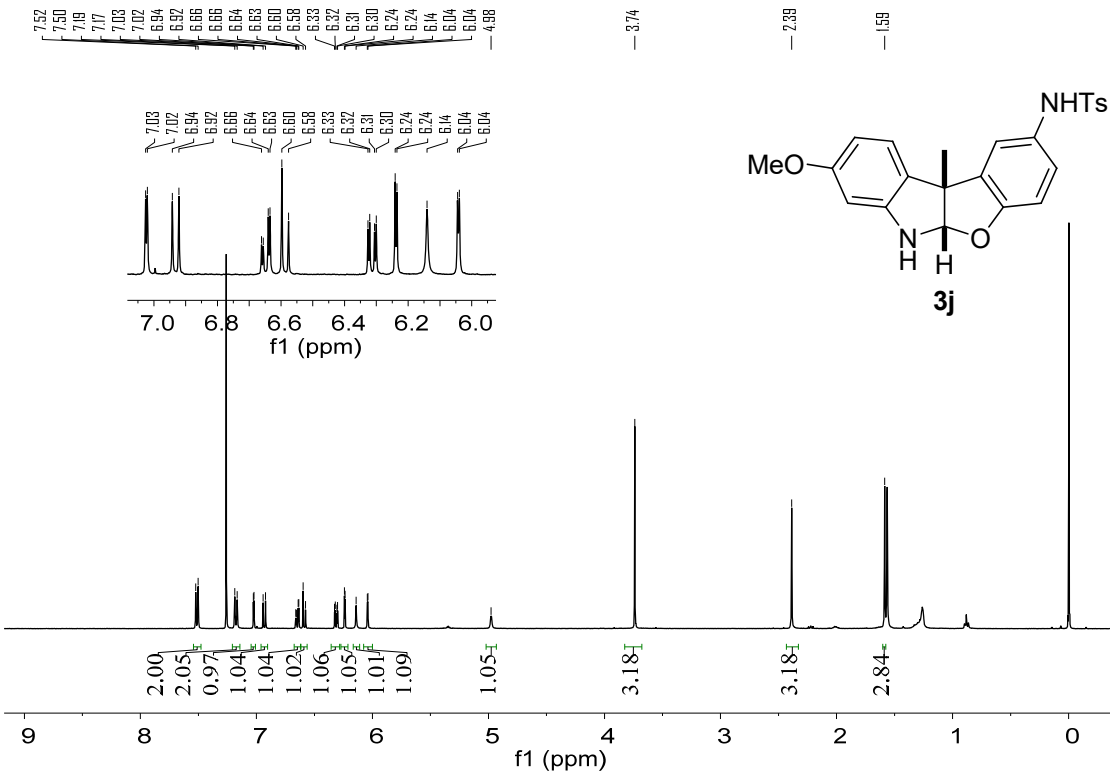
127.41
125.01
122.27
120.66
119.94
110.16
109.82
105.21
55.72
23.91
21.57
21.50
0.01
NHTs
N
H
H
O
3i
160 140 120 100 80 60 40 20 0
f1 (ppm)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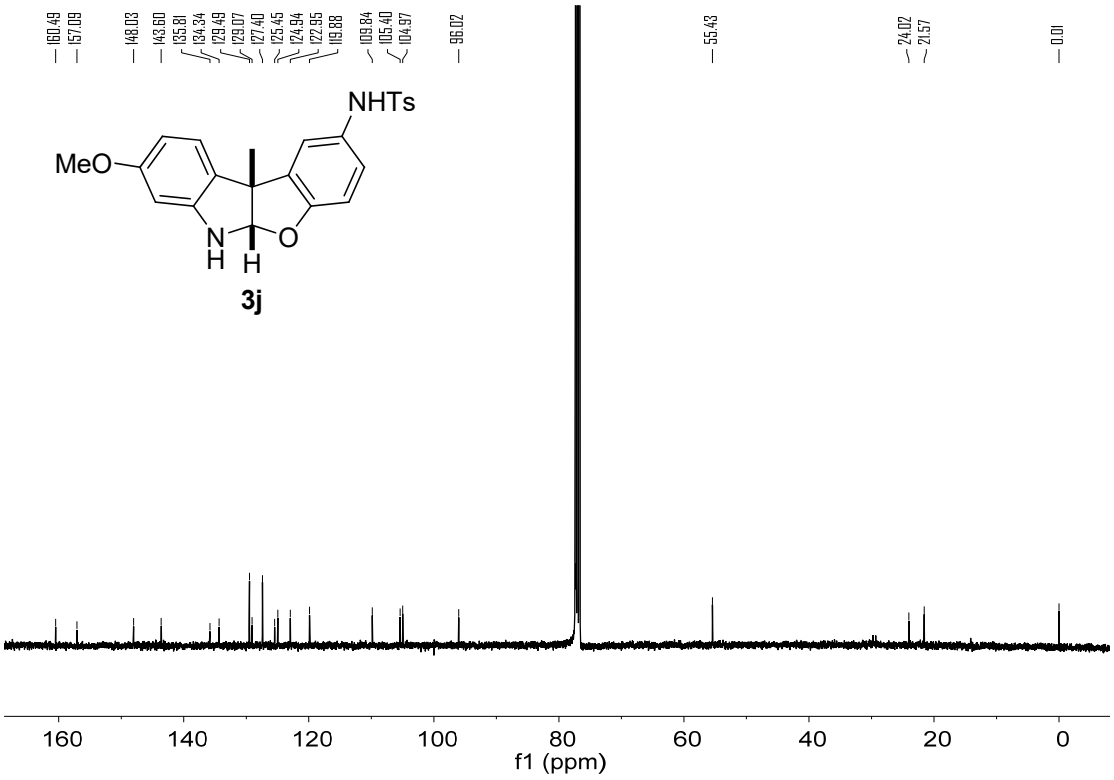
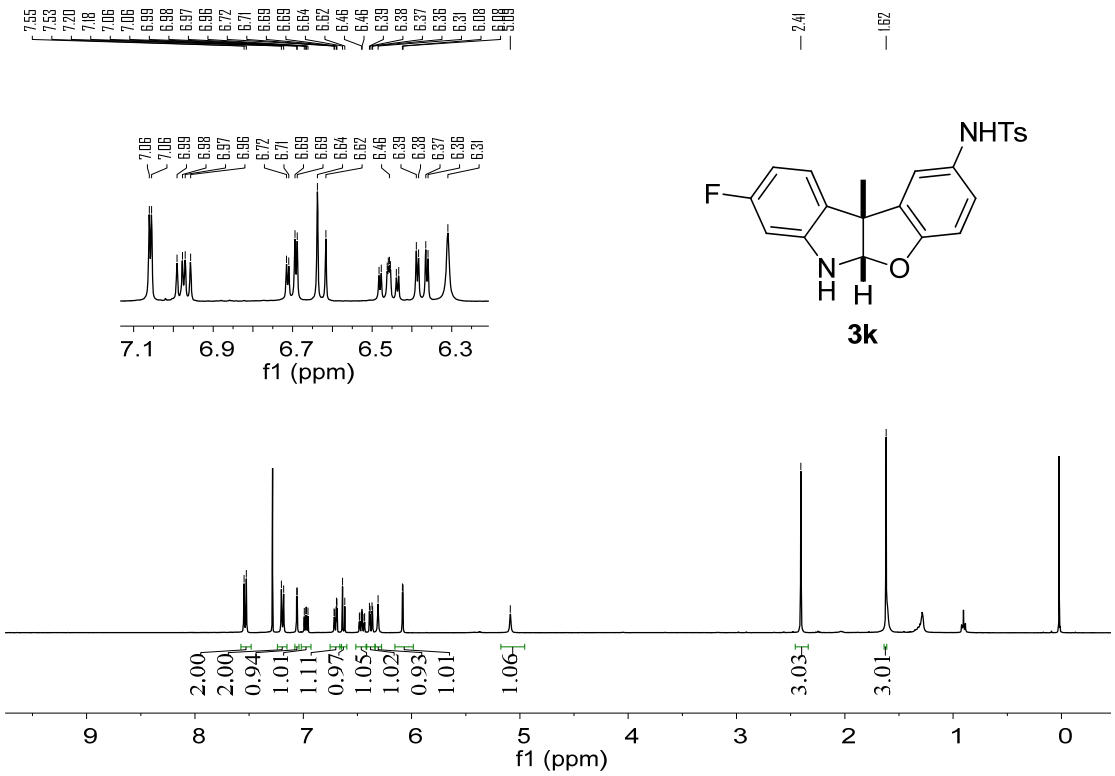
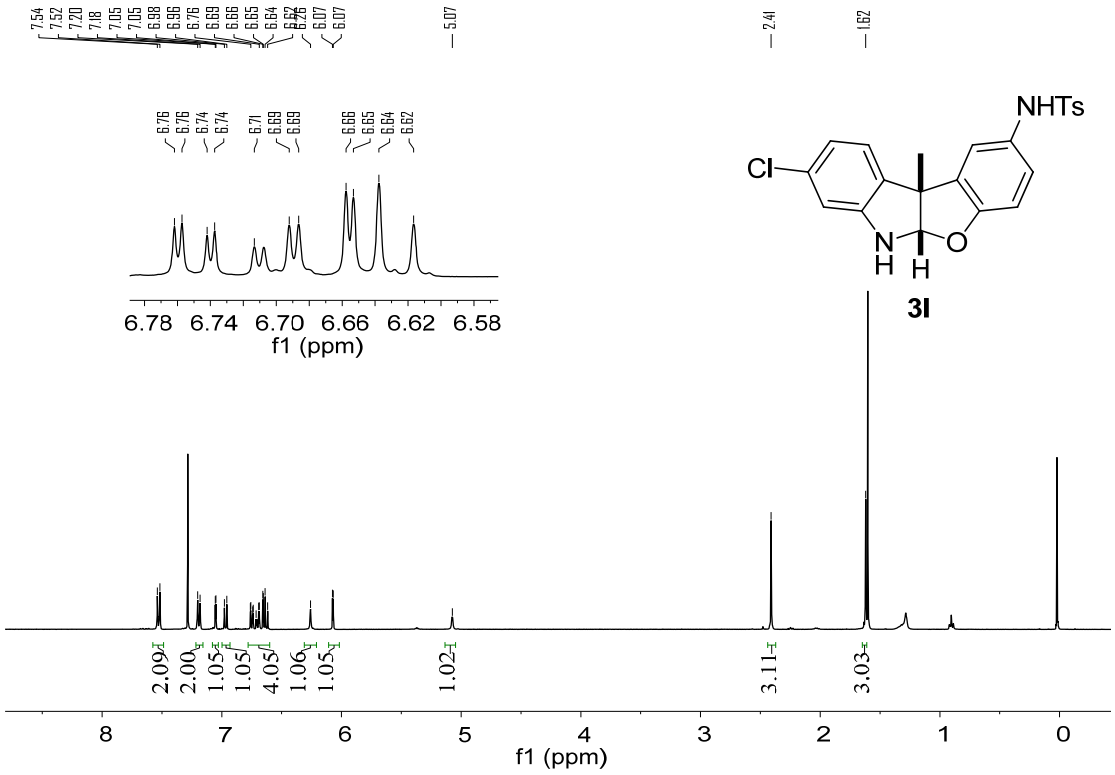
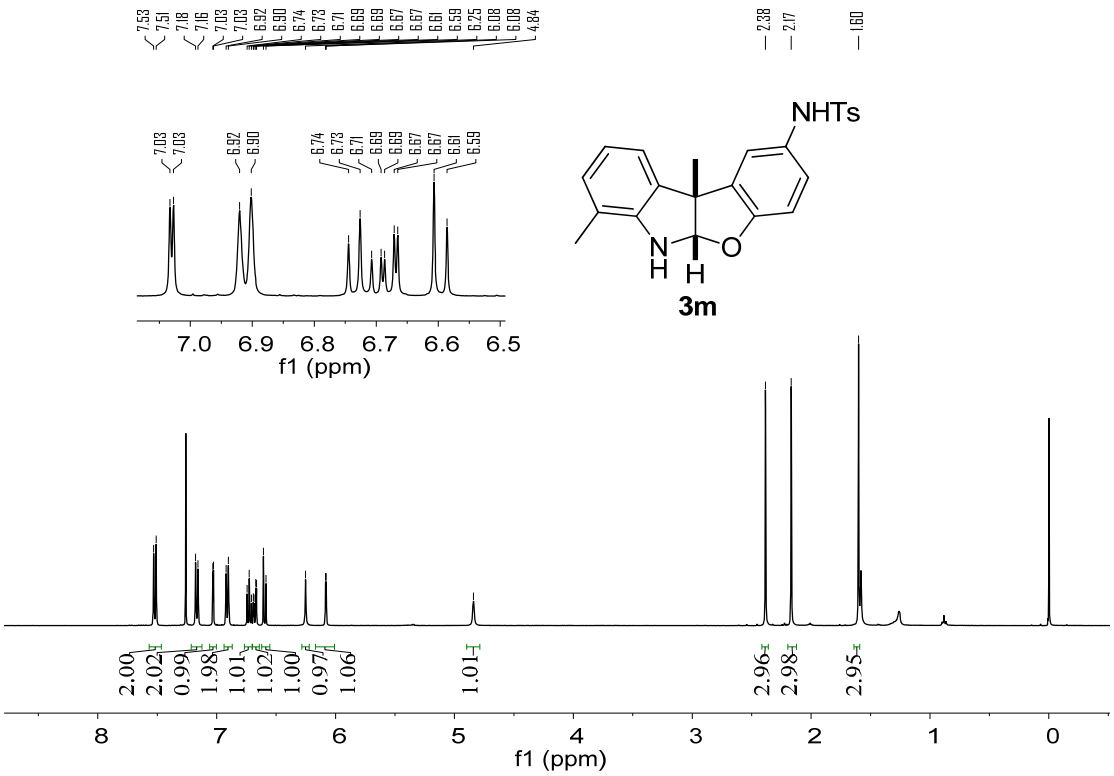
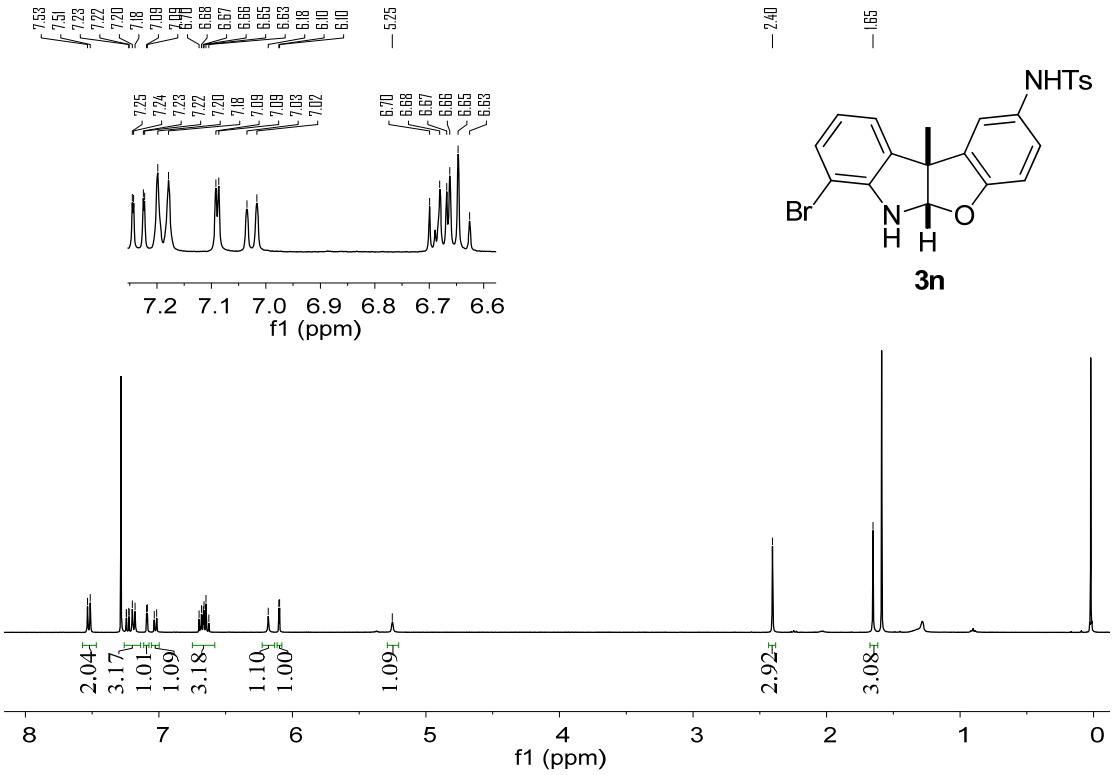
7.50
7.19
7.17
7.03
7.02
6.94
6.92
6.66
6.66
6.64
6.63
6.60
6.58
6.33
6.32
6.31
6.30
6.24
6.24
6.14
6.04
6.04
4.98
3.74
2.39
1.59
NHTs
MeO
N
H
H
O
3j
f1 (ppm)
2.00
2.05
0.97
1.04
1.04
1.02
1.06
1.05
1.01
1.09
1.05
3.18
3.18
2.84

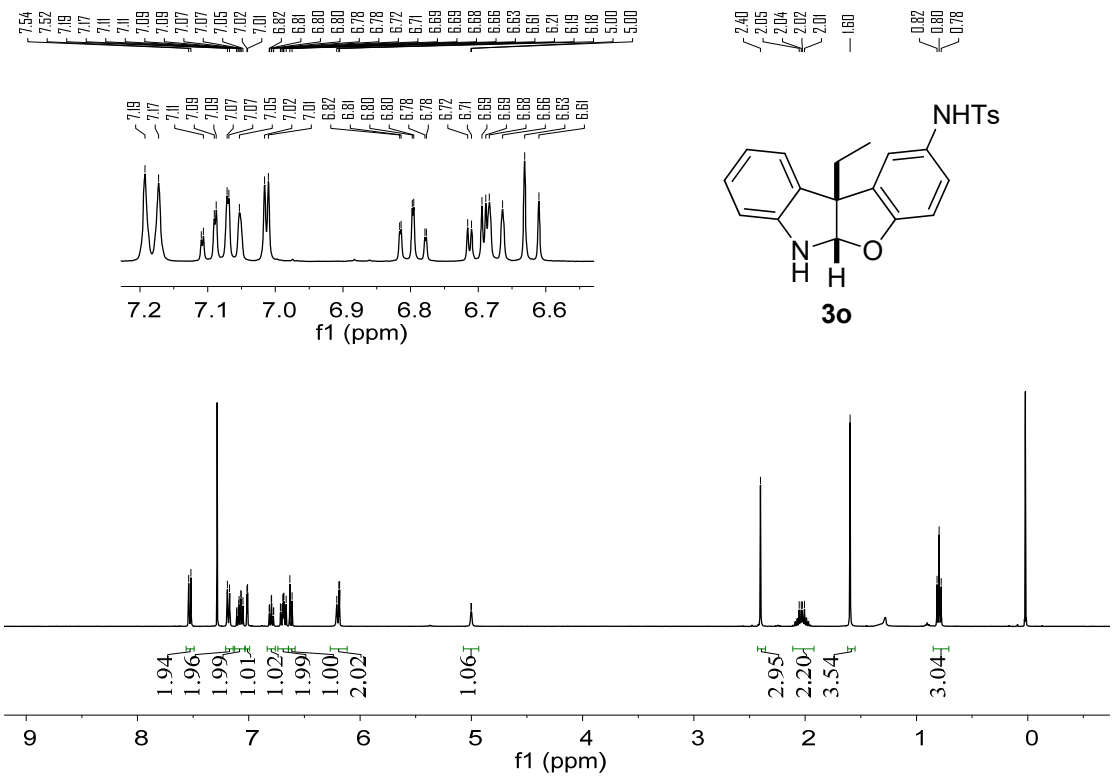

160.49
157.09
148.03
143.60
135.81
134.34
129.49
129.07
127.40
125.45
124.94
122.85
119.88
109.84
105.40
104.97
96.02
55.43
24.02
21.57
0.01
NHTs
MeO
N
H
H
O
3j
f1 (ppm)

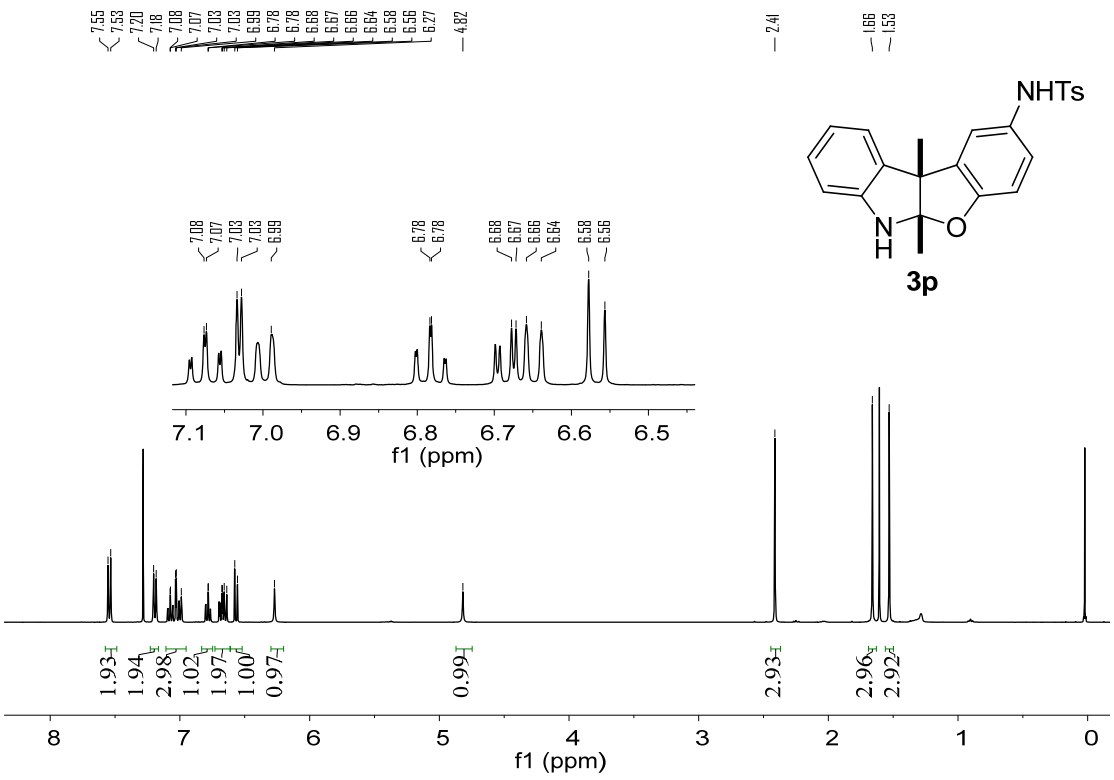

NHTs
F
N
H
H
O
3k
f1 (ppm)

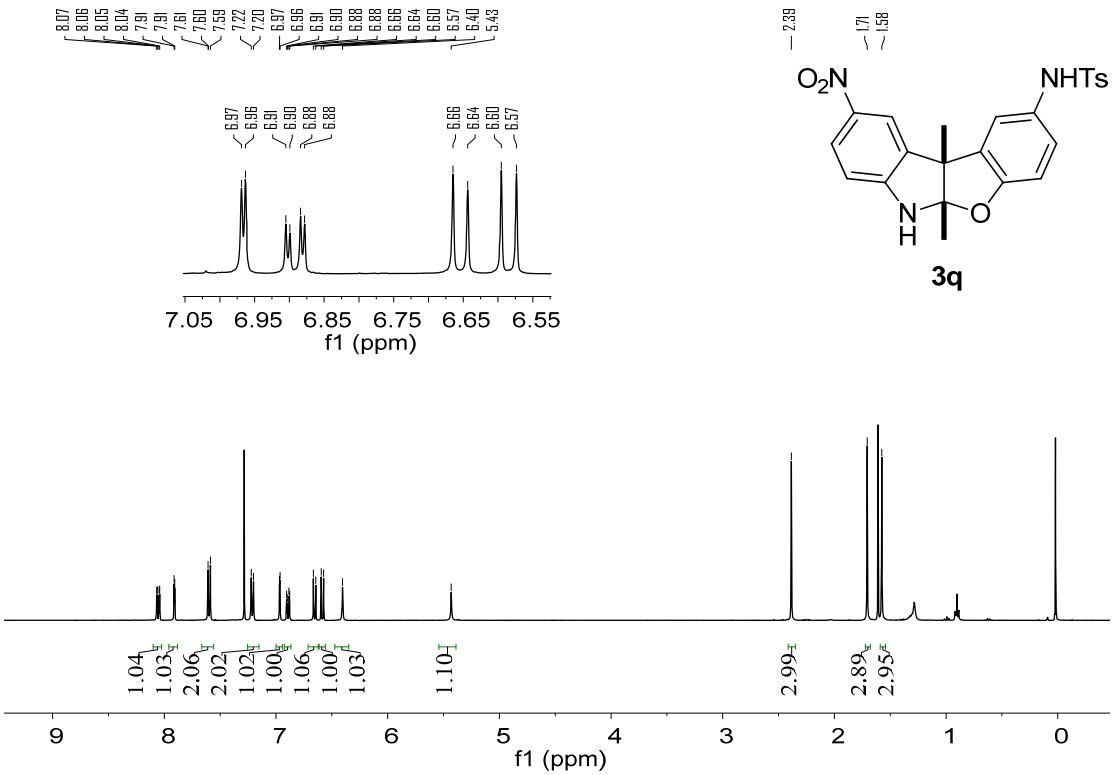

NHTs
Cl
N
H
H
O
3l
f1 (ppm)

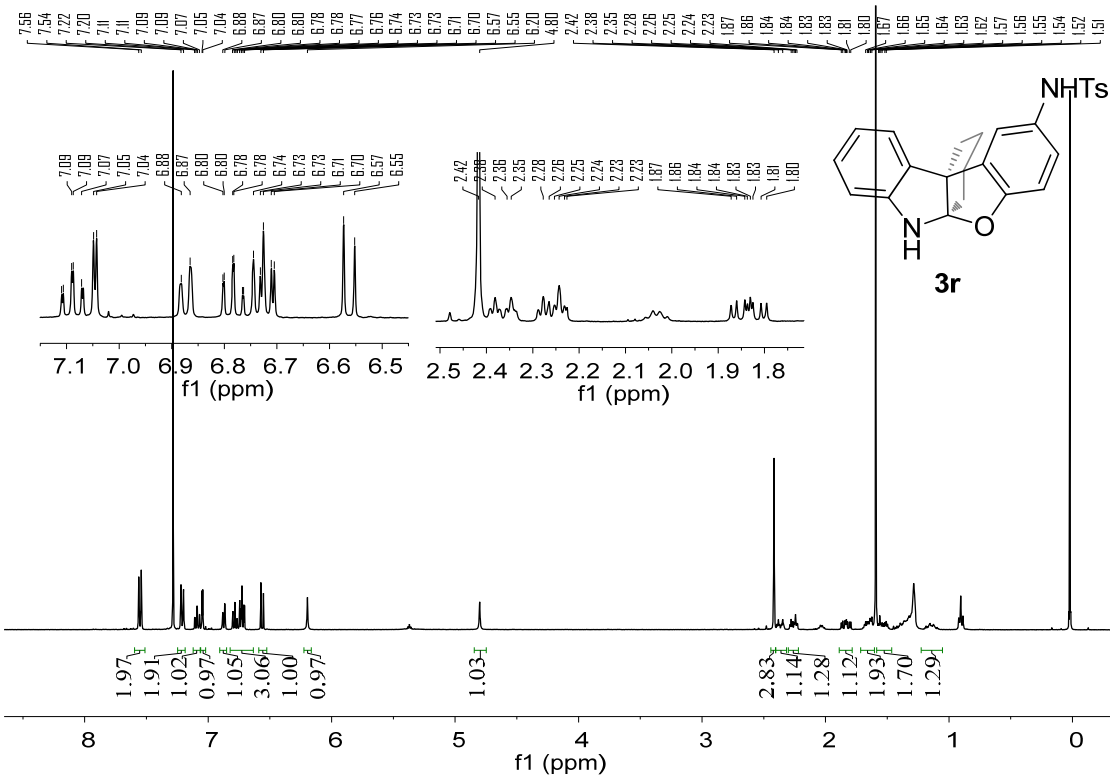

NHTs
N
H
H
O
3m
f1 (ppm)

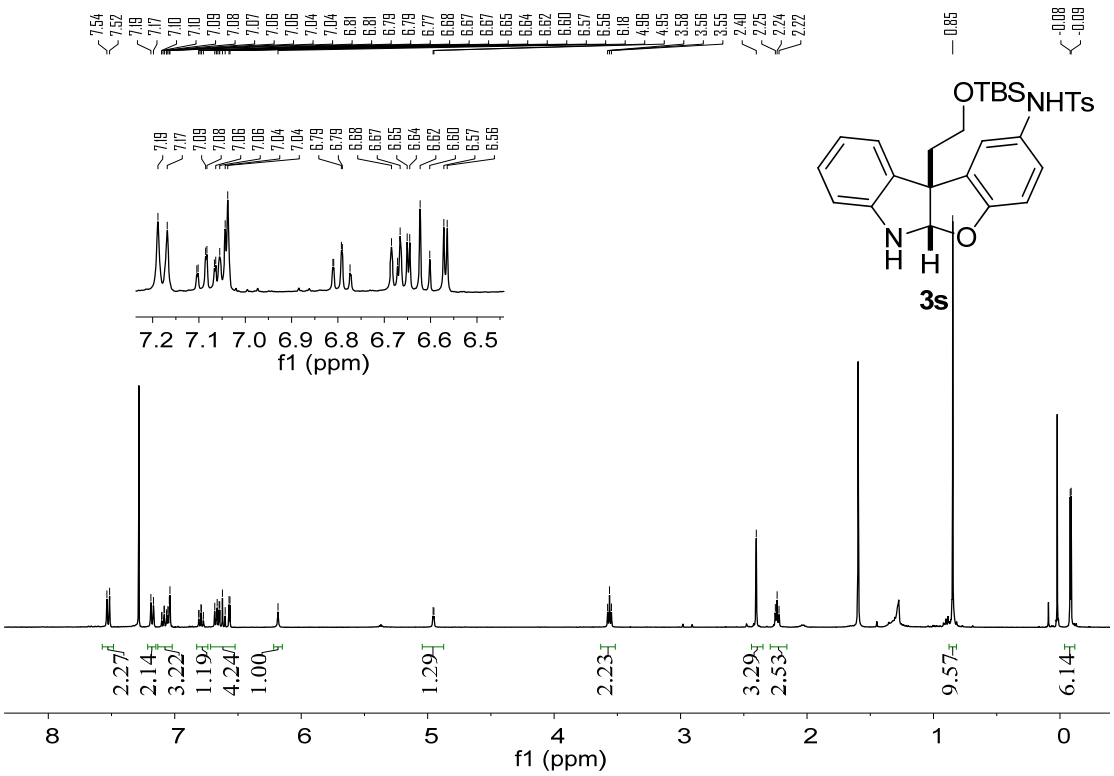

Br
NHTs
N
H
H
O
3n
f1 (ppm)

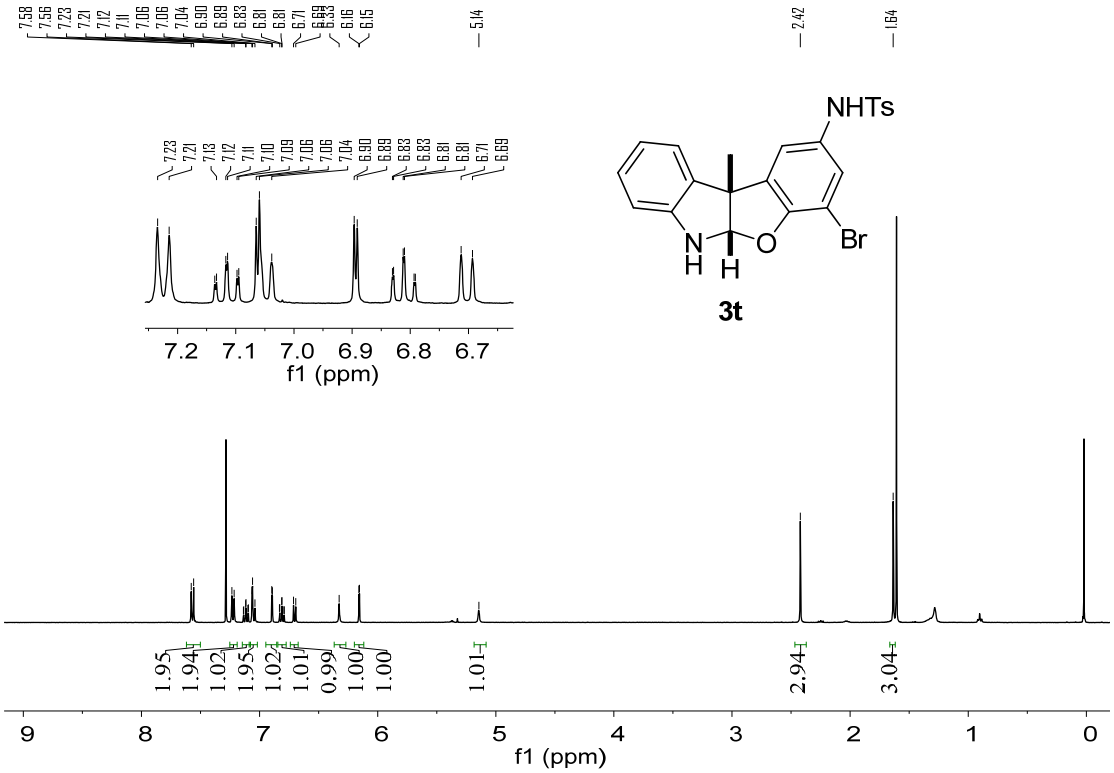

NHTs
N
H
O
H
3o
f1 (ppm)

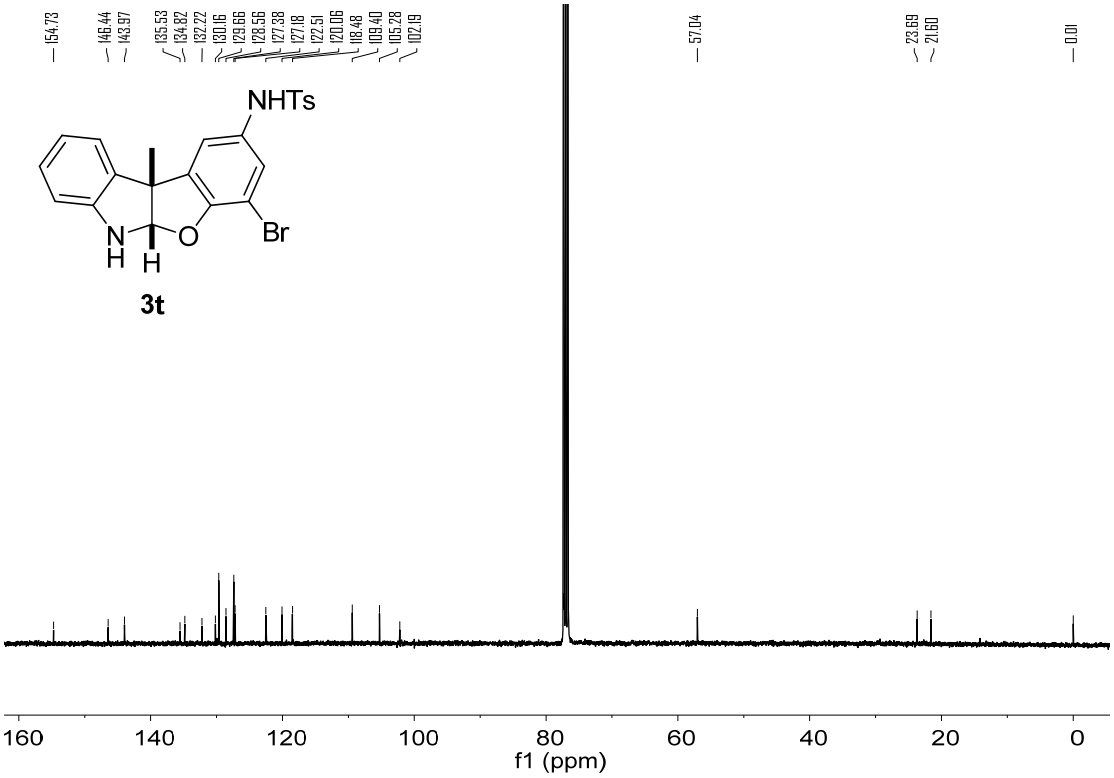

NHTs
N
H
O
3p
f1 (ppm)

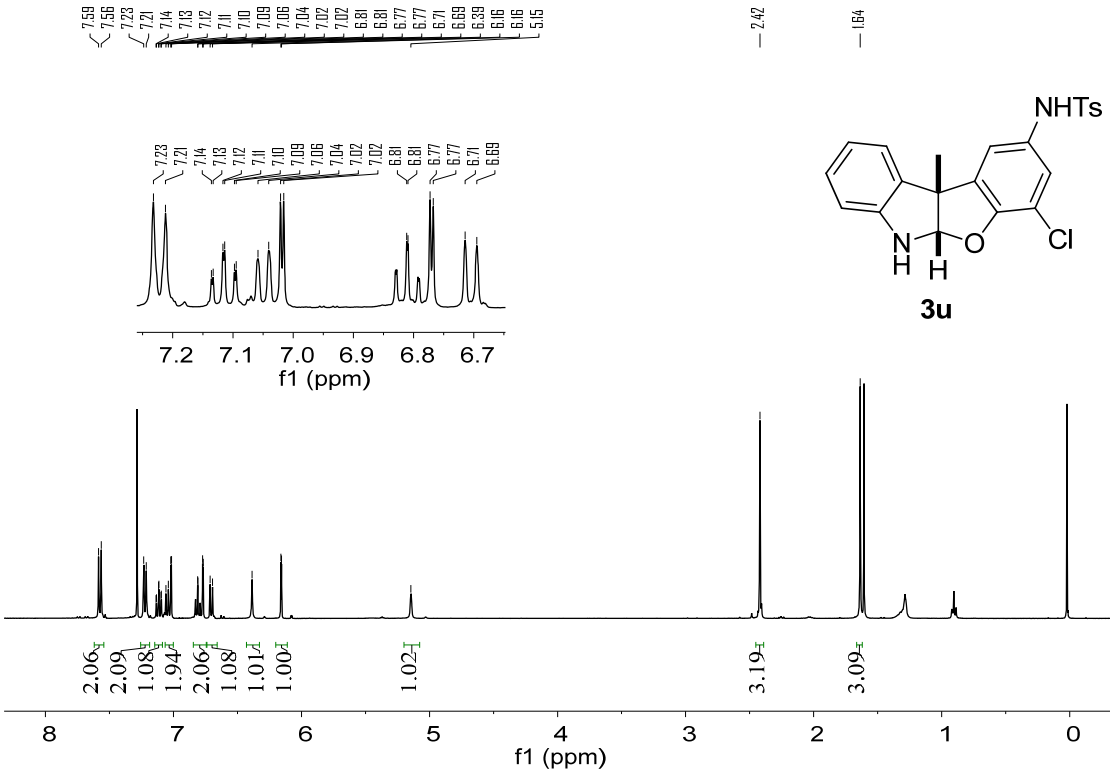

8.07 8.06 8.05 8.04 7.91 7.91 7.61 7.60 7.59 7.22 7.20 6.97 6.96 6.91 6.90 6.88 6.66 6.64 6.60 6.57 6.40 5.43
2.39 1.71 1.58
O2N
NHTs
N
H
O
3q
6.97 6.96 6.91 6.90 6.88 6.88 6.66 6.64 6.60 6.57
7.05 6.95 6.85 6.75 6.65 6.55
f1 (ppm)
1.04 1.03 2.06 2.02 1.02 1.00 1.06 1.00 1.03 1.10 2.99 2.89 2.95
9 8 7 6 5 4 3 2 1 0
f1 (ppm)

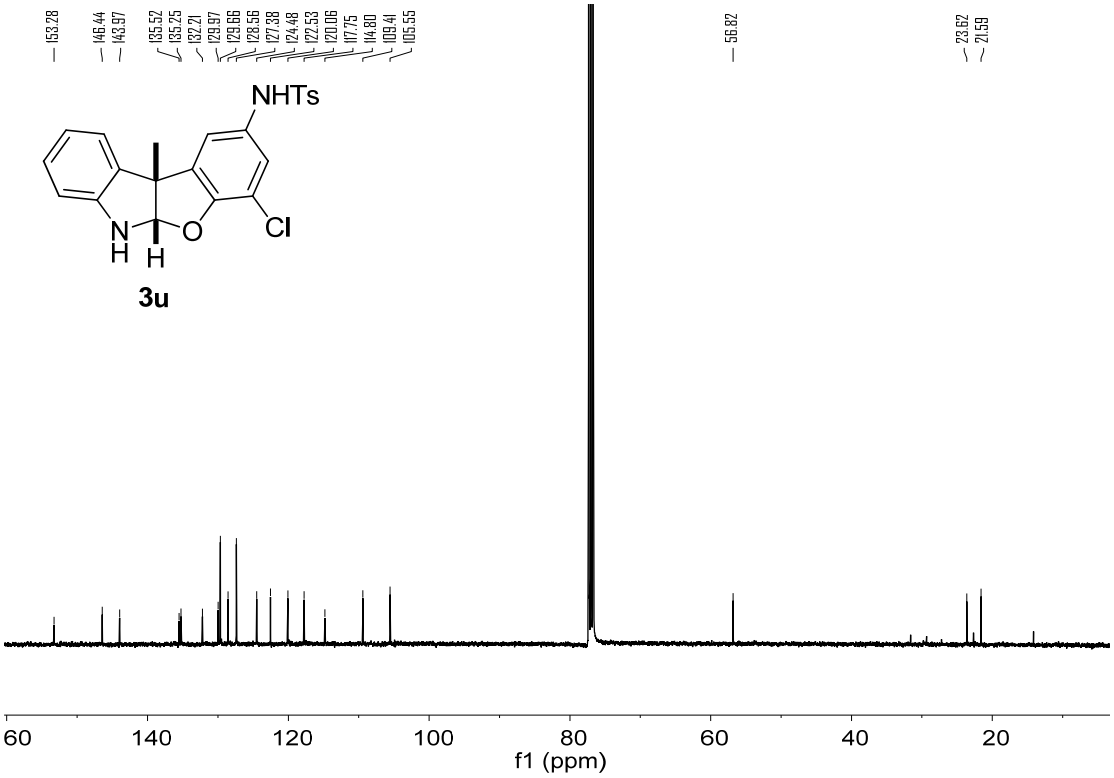

7.56 7.54 7.22 7.20 7.11 7.11 7.09 7.09 7.07 7.05 7.04 6.88 6.87 6.80 6.80 6.78 6.78 6.74 6.73 6.73 6.71 6.70 6.57 6.55 6.20 4.80 2.42 2.38 2.35 2.28 2.26 2.25 2.24 2.23 1.87 1.86 1.84 1.84 1.83 1.83 1.81 1.80 1.67 1.66 1.65 1.64 1.63 1.62 1.57 1.56 1.55 1.54 1.52 1.51
NHTs
N
H
O
3r
7.09 7.09 7.07 7.05 7.04 6.88 6.87 6.80 6.80 6.78 6.78 6.74 6.73 6.73 6.71 6.70 6.57 6.55
7.1 7.0 6.9 6.8 6.7 6.6 6.5
f1 (ppm)
2.42 2.38 2.36 2.35 2.28 2.26 2.25 2.24 2.23 2.23 1.87 1.86 1.84 1.84 1.83 1.83 1.81 1.80
2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8
f1 (ppm)
1.97 1.91 1.02 0.97 1.05 3.06 1.00 0.97 1.03 2.83 1.14 1.28 1.12 1.93 1.70 1.29
8 7 6 5 4 3 2 1 0
f1 (ppm)

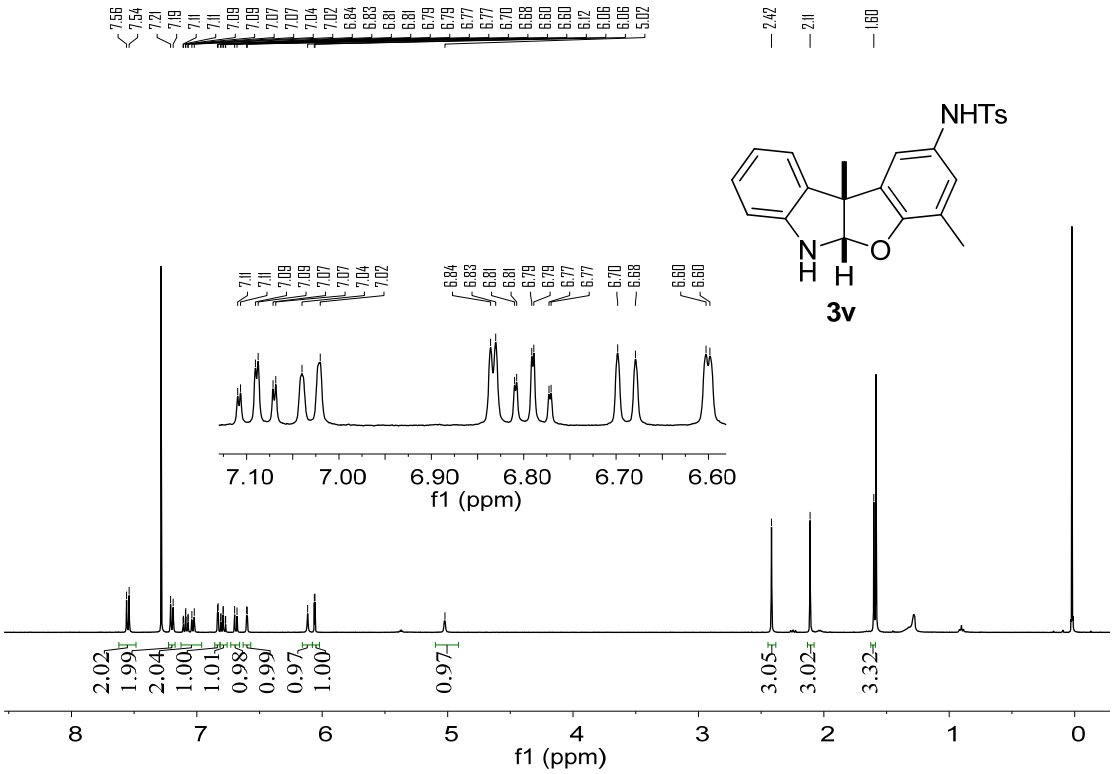

OTBSNHTs
N
H
H
O
3s
7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5
f1 (ppm)
8 7 6 5 4 3 2 1 0
f1 (ppm)

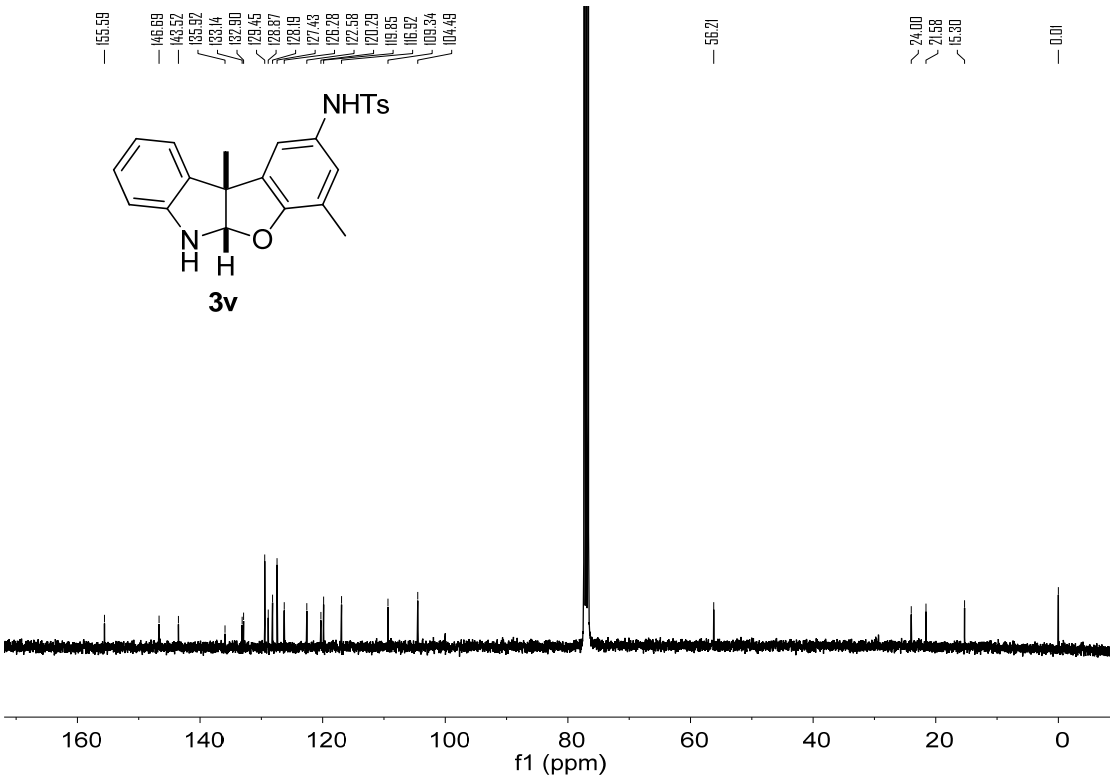

NHTs
N
H
H
O
Br
3t
7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
9 8 7 6 5 4 3 2 1 0
f1 (ppm)


154.73
146.44
143.97
135.53
134.82
132.22
130.16
129.66
128.56
127.38
127.18
122.51
120.06
118.48
109.40
105.28
102.19
57.04
23.69
21.60
0.01
NHTs
Br
N
H
O
H
3t
160
140
120
100
80
60
40
20
0
f1 (ppm)


7.59
7.56
7.23
7.21
7.14
7.13
7.12
7.11
7.10
7.09
7.06
7.04
7.02
7.02
6.81
6.81
6.77
6.77
6.71
6.69
6.33
6.16
6.16
5.15
2.42
1.64
NHTs
Cl
N
H
O
H
3u
7.2
7.1
7.0
6.9
6.8
6.7
f1 (ppm)
2.06
2.09
1.08
1.94
2.06
1.08
1.01
1.00
1.02
3.19
3.09
8
7
6
5
4
3
2
1
0
f1 (ppm)


153.28
146.44
143.97
135.52
135.25
132.21
129.97
129.66
128.56
127.38
124.48
122.53
120.06
117.75
114.80
109.41
105.55
56.82
23.62
21.59
NHTs
Cl
N
H
O
H
3u
60
140
120
100
80
60
40
20
f1 (ppm)


7.56
7.54
7.21
7.19
7.11
7.11
7.09
7.09
7.07
7.07
7.07
7.04
7.02
6.84
6.83
6.81
6.81
6.79
6.79
6.77
6.77
6.70
6.68
6.60
6.60
6.12
6.06
6.06
5.02
2.42
2.11
1.60
NHTs
N
H
O
3v
7.10
7.00
6.90
6.80
6.70
6.60
f1 (ppm)
2.02
1.99
2.04
1.00
1.01
0.98
0.99
0.97
1.00
0.97
3.05
3.02
3.32
8
7
6
5
4
3
2
1
0
f1 (ppm)


155.59
146.69
143.52
135.92
133.14
132.90
129.45
128.87
128.19
127.43
126.28
122.58
120.29
119.85
116.92
109.34
104.49
56.21
24.00
21.58
15.30
0.01
NHTs
N
H
H
O
3v
160
140
120
100
80
60
40
20
0
f1 (ppm)