Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Bioinspired radical cyclization of tryptamines: synthesis of peroxypyrroloindolenines as potential anti-cancer agents

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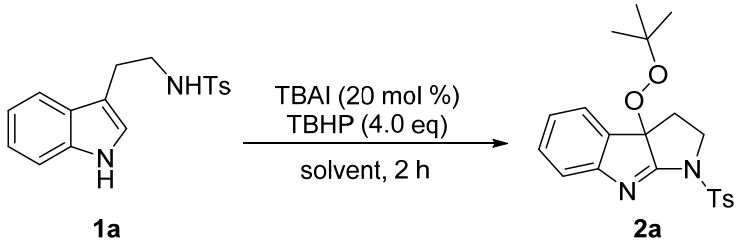
(A) General Information

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 NMR 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) or CD_3OD (δ 49.00). The used abbreviations are as follows: s (singlet), d (doublet), t (triplet), quart. (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.*). High resolution mass spectra (HRMS) data were measured on a ESI-microTOF Ⅱ. Melting points were measured on a SGW® X-4B and are not corrected. 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. Further visualization was achieved by staining with iodine, or $KMnO_4$ followed by heating on a hot plate. Flash column chromatography was performed on silica gel 60 Å, 10–40 μm.
N-tosyl tryptamine derivatives prepared according to known literature procedures.[1,2]

(B) Reaction Condition Optimizations

Table S1 solvent screening [a]



1a **2a**

entry	solvent	temp (^{o}C)	yield[b] (%)
1	CH_3CN	reflux	45
2	1,4-dioxane	90	78

[1] Muratore, M. E.; Holloway, C. A.; Pilling, A. W.; Storer, R. I.; Trevitt, G.; Dixon, D. J. *J. Am. Chem. Soc.* **2009**, *131*, 10796.
[2] Kieffer, M. E.; Chuang, K. V.; Reisman, S. E. *Chem. Sci.* **2012**, *3*, 3170.

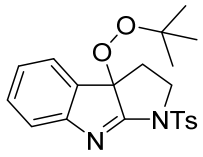
3	DCE	reflux	24
4	Toluene	90	34
5	THF	reflux	40
6	EtOAc	reflux	61
7	H_2O	90	0

[a]Reactions were performed with **1a** (0.2 mmol), TBAI (20 mol%), and TBHP (4.0 eq) in solvent (4.0 ml) for 2 hours. [b]Isolated yield.

(C) Representative Procedures and Analytical Data of the Desired Products

General procedure: A 50 mL round bottom flask was charged with TBAI (14.8 mg, 20 mol %), tryptamine substrates **1** (0.2 mmol, 1.0 eq) and 1,4-dioxane (4.0 mL), then TBHP (70% in wa-ter, 114.4 μL, 0.8 mmol, 4.0 eq) was added. The reaction mixture was heat to 90 °C for 2 h before cooled down to room temperature. Saturated aqueous $Na_2S_2O_3$ (10 mL) solution was slowly introduced and the resulting mixture was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (eluent: Hexane/EtOAc, 30:1 to 10:0) to afford perox-ypyrroloindolenine **2**.

3a-(*tert*-Butylperoxy)-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2a



2a

Compound **2a** was synthesized following the *general procedure.*

A white solid, 64.1 mg, 80% yield.

m.p.: 131 – 133 °C.

TLC: R_f = 0.67 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

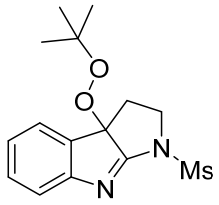
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 7.95 (m, 2H), 7.39 – 7.19 (m, 5H), 7.00 (*virt.* td, $J \cong 7.4$, 1.1 Hz, 1H), 4.49 (*virt.* td, $J \cong 10.4$, 5.1 Hz, 1H), 4.14 – 4.05 (m, 1H), 2.47 (*virt.* dd, $J \cong 13.7$, 5.1 Hz, 1H), 2.39 (s, 3H), 1.81 (ddd, J = 13.7, 10.4, 8.3 Hz, 1H), 1.04 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 159.4, 145.0, 134.7, 133.0, 130.6, 129.8, 128.1, 124.2, 123.7, 119.8, 93.4, 80.7, 55.8, 29.7, 26.2, 21.7.

IR (KBr/cm^{-1}) 3068.5, 2978.9, 2928.8, 1632.6, 1601.1, 1366.3, 1169.7, 751.9.

HRMS (ESI): $C_{21}H_{25}N_2O_4S$ [$(M+H)^+$]: calcd.: 401.1530; found: 401.1534.

3a-(*tert*-Butylperoxy)-1-(methylsulfonyl)-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2b



2b

Compound **2b** was synthesized following the *general procedure.*

A white solid, 44.1 mg, 68% yield.

m.p.: 165 – 170 ^{o}C.

TLC: R_f = 0.28 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

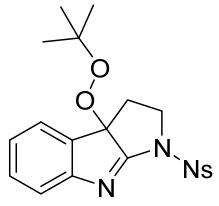
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 3H), 7.14 – 7.00 (m, 1H), 4.56 (*virt.* td, J ≅ 10.1, 5.0 Hz, 1H), 4.33 – 4.20 (m, 1H), 3.28 (s, 3H), 2.62 (*virt.* dd, J ≅ 13.6, 5.0 Hz, 1H), 2.13 (*virt.* dt, J ≅ 13.6, 10.1 Hz, 1H), 1.09 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.4, 159.0, 132.9, 130.7, 124.4, 124.1, 119.7, 93.4, 80.9, 56.2, 38.9, 30.3, 26.3.

IR (ATR/cm^{-1}) 2977.3, 2926.7, 1636.2, 1601.7, 1455.4, 1360.0, 1265.3, 1164.2, 1100.5, 998.4, 965.1, 874.3, 764.3.

HRMS (ESI): $C_{15}H_{20}N_2NaO_4S$ [$(M+Na)^+$]: calcd.: 347.1036; found: 347.1037.

3a-(*tert*-Butylperoxy)-1-((4-nitrophenyl)sulfonyl)-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2c



2c

Compound **2c** was synthesized following the *general procedure.*

A white solid, 47.5 mg, 55% yield.

m.p.: 166 – 170 ^{o}C.

TLC: R_f = 0.71 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

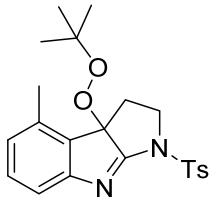
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.36 (m, 4H), 7.37 – 7.30 (m, 3H), 7.05 (t, J = 7.2 Hz, 1H), 4.57 (*virt.* td, J ≅ 11.2, 5.2 Hz, 1H), 4.21 – 4.12 (m, 1H), 2.51 (*virt.* dd, J ≅ 11.2, 5.2 Hz, 1H), 1.94 – 1.82 (m, 1H), 1.03 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.5, 158.8, 150.9, 143.2, 132.8, 130.8, 129.5, 124.4, 124.4, 124.4, 120.1, 93.1, 80.9, 56.3, 29.6, 26.2.

IR (ATR/cm^{-1}) 3105.8, 2981.2, 2930.3, 1636.1, 1602.8, 1533.1, 1371.7, 1262.8, 1175.1, 1095.7, 999.7, 857.2, 741.1, 623.3, 564.1.

HRMS (ESI): $C_{20}H_{21}N_3NaO_6S$ [$(M+Na)^+$]: calcd.: 454.1043; found: 454.1045.

3a-(*tert*-Butylperoxy)-4-methyl-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2d



2d

Compound **2d** was synthesized following the *general procedure.*

A white solid, 42.3 mg, 51% yield.

m.p.: 163 – 168 ^{o}C.

TLC: R_f = 0.66 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

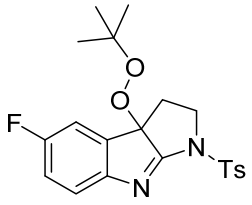
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.03 (m, 2H), 7.32 – 7.30 (m, 2H), 7.18 – 7.17 (m, 2H), 6.86 – 6.74 (m, 1H), 4.52 (*virt.* td, $J \cong$ 10.1, 5.2 Hz, 1H), 4.12 (*virt.* t, $J \cong$ 10.1 Hz, 1H), 2.50 – 2.42 (m, 1H), 2.41 (s, 3H), 2.26 (s, 3H), 1.96 – 1.84 (m, 1H), 1.04 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2, 159.4, 145.0, 135.0, 134.9, 130.9, 130.6, 129.8, 128.1, 125.5, 117.3, 93.3, 80.6, 56.0, 29.6, 26.2, 21.7, 18.0.

IR (ATR/cm^{-1}) 3049.4, 2981.0, 2924.7, 1628.9, 1594.5, 1432.6, 1361.3, 1240.0, 1171.1, 1090.5, 1050.6, 991.4, 910.6, 809.5, 669.2, 569.8.

HRMS (ESI): $C_{22}H_{26}N_2NaO_4S$ [$(M+Na)^+$]: calcd.: 437.1505; found: 437.1509.

3a-(*tert*-Butylperoxy)-5-fluoro-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2e



2e

Compound **2e** was synthesized following the *general procedure.*

A white solid, 57.7 mg, 67% yield.

m.p.: 148 – 153 ^{o}C.

TLC: R_f = 0.57 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

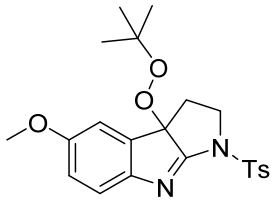
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 2H), 7.37 – 7.27 (m, 3H), 7.04 – 6.92 (m, 2H), 4.47 (m, 1H), 4.15 – 4.06 (m, 1H), 2.51 – 2.44 (m, 1H), 2.42 (s, 3H), 1.90 – 1.77 (m, 1H), 1.05 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 159.9 (d, J = 243.2 Hz), 155.0, 145.1, 134.7, 134.5 (d, J = 8.5 Hz), 129.9, 128.1, 120.2 (d, J = 8.3 Hz), 116.5 (d, J = 23.2 Hz), 112.4 (d, J = 25.2 Hz), 93.7 – 92.9 (m), 80.9, 55.6, 29.7, 26.2, 21.7.

IR (ATR/cm^{-1}) 2978.6, 2930.0, 1604.0, 1479.0, 1366.4, 1285.7, 1172.7, 1143.4, 1095.5, 1002.5, 813.0, 675.7, 581.7, 548.3.

HRMS (ESI): $C_{21}H_{23}FN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 441.1255; found: 441.1259.

3a-(*tert*-Butylperoxy)-5-methoxy-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2f



2f

Compound **2f** was synthesized following the *general procedure.*

A white solid, 51.1 mg, 61% yield.

m.p.: 147 – 150 ^{o}C.

TLC: R_f = 0.47 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

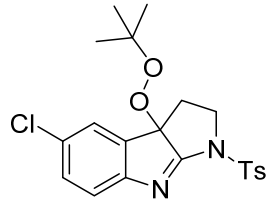
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 2H), 7.32 – 7.30 (m, 2H), 7.26 (d, *J* = 8.3 Hz, 1H), 6.90 (s, 1H), 6.80 (d, *J* = 8.3 Hz, 1H), 4.51 – 4.39 (m, 1H), 4.08 (*virt*. t, *J* ≅ 9.2 Hz, 1H), 3.77 (s, 3H), 2.45 (*virt*. dd, *J* ≅ 13.4, 5.1 Hz, 1H), 2.41 (s, 3H), 1.85 – 1.77 (m, 1H), 1.06 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 156.7, 152.4, 144.9, 134.8, 134.3, 129.8, 128.0, 119.9, 114.1, 112.0, 93.4, 80.7, 55.8, 55.5, 29.6, 26.2, 21.7.

IR (ATR/cm^{-1}) 2958.3, 2926.9, 1634.2, 1468.1, 1367.3, 1264.7, 1170.8, 1095.9, 1017.4, 926.1, 816.8, 668.9, 574.0, 548.0.

HRMS (ESI): $C_{22}H_{26}N_2NaO_5S$ [$(M+Na)^+$]: calcd.: 453.1455; found: 453.1455.

3a-(*tert*-butylperoxy)-5-chloro-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2g



2g

Compound **2g** was synthesized following the *general procedure.*

A white solid, 61.7 mg, 71% yield.

m.p.: 147.9 – 155.1^{o}C.

TLC: R_f = 0.72 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

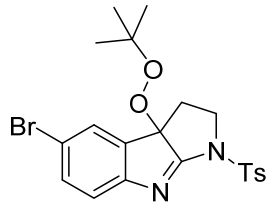
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.26 (m, 3H), 4.48 (*virt*. td, *J* ≅ 10.2, 5.1 Hz, 1H), 4.11 (*virt*. t, *J* ≅ 9.1 Hz, 1H), 2.48– 2.43 (m, 1H), 2.42 (s, 3H), 1.87 – 1.79 (m, 1H), 1.05 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 157.7, 145.1, 134.5, 134.4, 130.3, 129.8, 129.1, 127.9, 124.6, 120.4, 93.2, 80.9, 55.6, 29.6, 26.1, 21.6.

IR (ATR/cm^{-1}) 2980.6, 2928.5, 1632.5, 1596.6, 1448.5, 1367.7, 1254.6, 1172.1, 1095.4, 915.6, 817.7, 673.9, 580.5, 547.3.

HRMS (ESI): $C_{21}H_{23}{}^{35}ClN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 457.0959; found: 457.0961.

5-Bromo-3a-(*tert*-butylperoxy)-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2h



2h

Compound **2h** was synthesized following the *general procedure.*

A white solid, 74.8 mg, 78% yield.

m.p.: 159 – 165 ^{o}C.

TLC: R_f = 0.65 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 8.01 (m, 2H), 7.48 – 7.37 (m, 2H), 7.34 – 7.32 (m, 2H), 7.22 (d, *J* = 7.7 Hz, 1H), 4.48 (*virt*. td, *J* ≅ 10.4, 5.2 Hz, 1H), 4.11 (*virt*. t, *J* ≅ 9.2 Hz, 1H), 2.48 – 4.46 (m, 1H), 2.41 (s, 3H), 1.88 – 1.78 (m, 1H), 1.05 (s, 9H).

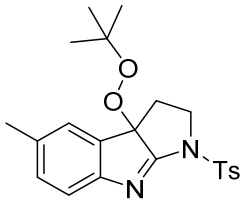
^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 158.3, 145.2, 134.9, 134.6, 133.4, 129.9, 128.0, 127.5, 121.1, 116.8, 93.3, 81.0, 55.8, 29.7, 26.2, 21.7.

IR (ATR/cm^{-1}) 2979.6, 2927.5, 1632.5, 1596.8, 1442.8, 1368.7, 1254.4, 1171.1, 1095.4, 915.2, 818.8, 673.8, 581.6, 547.7.

HRMS (ESI): $C_{21}H_{23}{}^{79}BrN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 501.0454; found: 501.0454.

HRMS (ESI): $C_{21}H_{23}{}^{81}BrN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 503.0433; found: 503.0437.

3a-(*tert*-Butylperoxy)-5-methyl-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2i



2i

Compound **2i** was synthesized following the *general procedure.*

A white solid, 60.5 mg, 73% yield.

m.p.: 143 – 146 ^{o}C.

TLC: R_f = 0.41 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

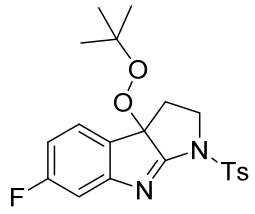
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 8.01 (m, 2H), 7.30 – 7.26 (m, 3H), 6.90 (s, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 4.53 – 4.39 (m, 1H), 4.08 (*virt*, t, *J* ≅ 9.1 Hz, 1H), 3.77 (s, 3H), 2.45 (*virt*. dd, *J* ≅ 13.9, 4.8 Hz, m, 1H), 2.40 (s, 3H), 1.86 – 1.75 (m, 1H), 1.06 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 156.7, 152.4, 144.9, 134.8, 134.3, 129.8, 128.0, 119.8, 114.1, 112.0, 93.3, 80.7, 55.8, 55.5, 29.6, 26.2, 21.7.

IR (ATR/cm^{-1}) 2980.5, 1634.1, 1468.3, 1367.4, 1264.6, 1170.9, 1095.8, 1017.0, 925.4, 816.4, 731.8, 668.6, 547.9.

HRMS (ESI): $C_{22}H_{26}N_2NaO_4S$ [$(M+Na)^+$]: calcd.: 437.1505; found: 437.1507.

3a-(*tert*-Butylperoxy)-6-fluoro-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2j



2j

Compound **2j** was synthesized following the *general procedure.*

A white solid, 52.7 mg, 63% yield.

m.p.: 146 – 149 ^{o}C.

TLC: R_f = 0.67 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

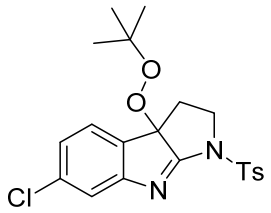
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 2H), 7.34 – 7.32 (m, 2H), 7.20 (s, 1H), 7.07 (d, *J* = 9.3 Hz, 1H), 6.69 (t, *J* = 8.7 Hz, 1H), 4.50 (*virt.* td, *J* ≅ 10.5, 10.1, 4.8 Hz, 1H), 4.12 (*virt.* t, *J* ≅ 9.1 Hz, 1H), 2.47 (s, 1H), 2.42 (s, 3H), 1.92 – 1.66 (m, 1H), 1.04 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.5, 164.6 (d, *J* = 246.9 Hz), 161.4 (d, *J* = 11.8 Hz), 145.3, 134.6, 129.9, 128.5 (d, *J* = 2.6 Hz), 128.1, 124.8 (d, *J* = 10.0 Hz), 109.8 (d, *J* = 22.9 Hz), 108.1 (d, *J* = 25.0 Hz), 92.8, 80.8, 55.9, 29.8, 26.2, 21.7.

IR (ATR/cm^{-1}) 2979.5, 2927.5, 1599.4, 1470.8, 1367.5, 1281.5, 1173.1, 1096.6, 1004.2, 904.3, 813.3, 674.9, 579.7, 547.4.

HRMS (ESI): $C_{21}H_{23}FN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 441.1255; found: 441.1259.

3a-(*tert*-Butylperoxy)-6-chloro-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2k



2k

Compound **2k** was synthesized following the *general procedure.*

A white solid, 65.3 mg, 75% yield.

m.p.: 148 – 154 ^{o}C.

TLC: R_f = 0.74 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

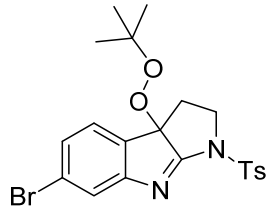
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 2H), 7.34 – 7.32 (m, 3H), 7.18 (d, *J* = 7.9 Hz, 1H), 6.99 (d, *J* = 7.3 Hz, 1H), 4.50 (*virt.* td, *J* ≅ 10.0, 5.0 Hz, 1H), 4.11 (*virt.* t, *J* ≅ 9.0 Hz, 1H), 2.51 – 2.44 (m, 1H), 2.42 (s, 3H), 1.88 – 1.76 (m, 1H), 1.05 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 160.7, 145.3, 136.2, 134.6, 131.3, 129.9, 128.1, 124.7, 123.6, 120.4, 93.0, 80.9, 55.9, 29.9, 26.2, 21.7.

IR (ATR/cm^{-1}) 2980.7, 2929.3, 1632.5, 1596.6, 1449.3, 1366.6, 1281.2, 1172.5, 1095.3, 1003.2, 870.3, 814.9, 673.9, 576.8, 547.3.

HRMS (ESI): $C_{21}H_{23}{}^{35}ClN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 457.0959; found: 457.0963.

6-Bromo-3a-(*tert*-butylperoxy)-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2l



2l

Compound **2l** was synthesized following the *general procedure.*

A white solid, 65.2 mg, 68% yield.

m.p.: 156 – 160 ^{o}C.

TLC: R_f = 0.71 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 8.01 (m, 2H), 7.49 (s, 1H), 7.34 – 7.32 (m, 2H), 7.17 – 7.13 (m, 2H), 4.51 (*virt.* td, *J* ≅ 10.1, 5.1 Hz, 1H), 4.11 (*virt.* t, *J* ≅ 8.9 Hz, 1H), 2.52 – 2.44 (m, 1H), 2.42 (s, 3H), 1.87 – 1.75 (m, 1H), 1.05 (s, 9H).

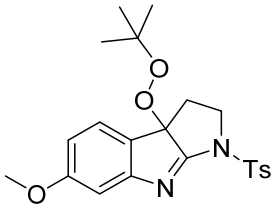
^{13}C NMR (101 MHz, $CDCl_3$) δ 175.0, 160.8, 145.3, 134.6, 131.8, 129.9, 128.1, 126.5, 125.1, 124.2, 123.2, 93.1, 81.0, 55.9, 29.8, 26.2, 21.7.

IR (ATR/cm^{-1}) 2981.5, 2928.4, 1632.9, 1595.9, 1447.8, 1365.5, 1282.1, 1171.1, 1097.9, 1003.4, 871.4, 815.5, 674.8, 577.2.

HRMS (ESI): $C_{21}H_{23}{}^{79}BrN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 501.0454; found: 501.0450.

HRMS (ESI): $C_{21}H_{23}{}^{81}BrN_2NaO_4S$ [$(M+Na)^+$]: calcd.: 503.0433; found: 503.0429.

3a-(*tert*-Butylperoxy)-6-methoxy-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2m



2m

Compound **2m** was synthesized following the *general procedure.*

A white solid, 63.7 mg, 74% yield.

m.p.: 165 – 168 ^{o}C.

TLC: R_f = 0.40 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

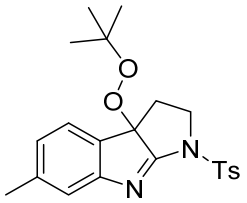
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.02 (m, 2H), 7.33 – 7.31 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.02 – 6.91 (m, 1H), 6.51 (d, *J* = 7.9 Hz, 1H), 4.48 (*virt.* td, *J* ≅ 10.1, 5.1 Hz, 1H), 4.09 (*virt.* t, *J* ≅ 9.2 Hz, 1H), 3.81 (s, 3H), 2.49 – 2.43 (m, 1H), 2.41 (s, 3H), 1.81 (*virt.* dt, *J* ≅ 13.3, 10.1 Hz, 1H), 1.05 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 175.1, 162.0, 161.3, 145.1, 134.8, 129.8, 128.1, 124.9, 124.6, 108.3, 106.7, 93.1, 80.7, 55.9, 55.5, 30.0, 26.3, 21.7.

IR (ATR/cm^{-1}) 2981.4, 2930.4, 1636.8, 1605.8, 1460.6, 1369.2, 1262.0, 1169.9, 1096.6, 929.7, 819.4, 733.1, 669.1, 592.2, 551.1.

HRMS (ESI): $C_{22}H_{26}N_2NaO_5S$ [$(M+Na)^+$]: calcd.: 453.1455; found: 453.1455.

3a-(*tert*-Butylperoxy)-6-methyl-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2n



2n

Compound **2n** was synthesized following the *general procedure.*

A white solid, 44.8 mg, 54% yield.

m.p.: 147 – 153 ^{o}C.

TLC: R_f = 0.73 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

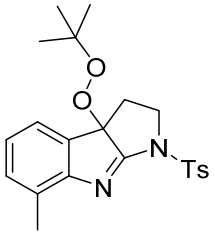
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.03 (m, 2H), 7.32 – 7.30 (m, 2H), 7.18 (s, 1H), 7.15 (d, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 7.1 Hz, 1H), 4.49 (*virt.* td, *J* ≅ 10.1, 5.2 Hz, 1H), 4.08 (*virt.* t, *J* ≅ 9.1 Hz, 1H), 2.46 (*virt.* dd, *J* ≅ 13.7, 4.9 Hz, 1H), 2.41 (s, 3H), 2.35 (s, 3H), 1.83 – 1.73 (m, 1H), 1.06 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.2, 159.6, 145.0, 140.9, 134.8, 130.0, 129.8, 128.1, 124.2, 123.9, 120.8, 93.2, 80.7, 55.9, 29.9, 26.3, 21.9, 21.7.

IR (ATR/cm^{-1}) 2979.8, 2927.0, 1604.0, 1456.3, 1364.8, 1262.8, 1172.0, 1094.6,1004.2, 814.5, 675.1, 578.1, 547.7.

HRMS (ESI): $C_{22}H_{26}N_2NaO_4S$ [$(M+Na)^+$]: calcd.: 437.1505; found: 437.1509.

3a-(*tert*-Butylperoxy)-7-methyl-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole 2o



2o

Compound **2o** was synthesized following the *general procedure.*

A white solid, 51.4 mg, 62% yield.

m.p.: 140 – 146 ^{o}C.

TLC: R_f = 0.82 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

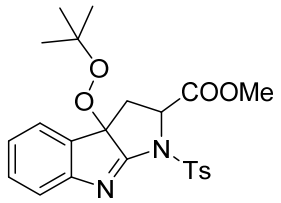
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 6.9 Hz, 2H), 6.91 (t, *J* = 6.9 Hz, 1H), 4.53 (*virt.* td, *J* ≅ 10.2, 5.2 Hz, 1H), 4.10 (*virt.* t, *J* ≅ 9.3 Hz, 1H), 2.48 (s, 3H), 2.40 (s, 3H), 1.79 – 1.70 (m, 1H), 1.67 (s, 1H), 1.09 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 157.3, 145.0, 134.5, 133.0, 132.1, 129.6, 129.2, 128.4, 123.5, 121.7, 93.4, 80.7, 67.2, 56.0, 26.3, 21.7, 16.8.

IR (ATR/cm^{-1}) 3053.8, 2977.8, 2926.4, 1632.3, 1599.5, 1459.3, 1367.8, 1276.1, 1170.5, 1095.8, 926.5, 759.2, 669.9, 588.5, 547.4.

HRMS (ESI): $C_{22}H_{26}N_2NaO_4S$ [$(M+Na)^+$]: calcd.: 437.1505; found: 437.1508.

Methyl 3a-(*tert*-butylperoxy)-1-tosyl-1,2,3,3a-tetrahydropyrrolo[2,3-b]indole-2-carboxylate 2p



2p

Compound **2p** was synthesized following the *general procedure.*

A white solid, 73.4 mg, 80% yield. The product contains a mixture of two inseparable diastereoisomers (1.5:1).

TLC: R_f = 0.55 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

Minor product:

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.11 (m, 2H), 7.36 (m, 5H), 7.04 (d, *J* = 8.1 Hz, 1H), 5.29 – 5.22 (m, 1H), 3.84 (s, 3H), 3.00 – 2.91 (m, 1H), 2.42 (s, 3H), 2.21 (m, 1H), 0.91 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 169.8, 159.7, 144.9, 136.0, 132.6, 130.9, 129.6, 128.7, 124.5, 124.2, 120.3, 92.2, 80.7, 68.8, 52.9, 32.6, 26.0, 21.7.

Major product:

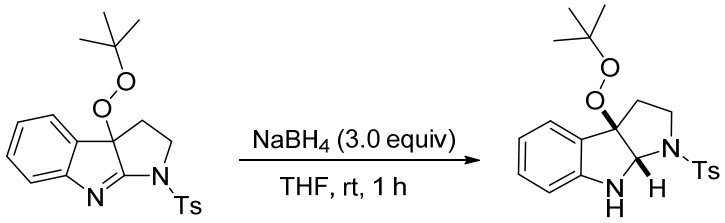
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.1 Hz, 3H), 7.33 – 7.21 (m, 7.5H), 6.99 (d, *J* = 8.1 Hz, 1.5H), 5.20 (m, 1.5H), 3.75 (s, 4.5H), 2.88 (m, 1.5H), 2.42 (s, 4.5H), 2.04 (m, 1.5H), 0.91 (s, 13.5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 170.0, 159.2, 145.2, 134.9, 132.7, 130.7, 129.6, 128.2, 124.4, 123.8, 119.9, 92.7, 80.7, 68.6, 52.9, 35.5, 26.1, 21.7.

IR (ATR/cm^{-1}) 3063.9, 2981.1, 1757.5, 1637.9, 1601.5, 1449.0, 1365.9, 1171.0, 1090.4, 912.6, 810.1, 733.5, 666.4, 571.0.

HRMS (ESI): $C_{23}H_{26}N_2NaO_6S$ [$(M+Na)^+$]: calcd.: 481.1404; found: 481.1407.

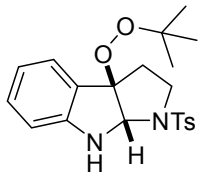
Reduction procedure:



2a **3a** (87%)

A 50 ml round bottom flask was charged with substrate **2a** (0.2 mmol, 1.0 equiv) and THF (8.0 mL), then $NaBH_4$ (3.0 equiv) was added portionwise at room temperature and the mixture was stirred until the starting material was disappeared and monitored by analysis TLC (1 h). Saturated aqueous NH_4Cl solution (20 mL) was added to the mixture carefully, extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (eluent: Hexane/EtOAc, 30:1 to 10:0) to afford peroxypyrroloindoline **3a**.

3a-(*tert*-Butylperoxy)-1-tosyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole 3a



3a

A white solid, 70.0 mg, 87% yield.

m.p.: 98 – 101 °C.

TLC: R_f = 0.71 (Hexane/EtOAc = 3:1) [UV, $KMnO_4$].

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.77 (m, 2H), 7.34 – 7.32 (m, 2H), 7.12 – 7.22 (m, 1H), 6.76 (*virt*. t, $J \cong 7.4$ Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 5.43 (d, J = 1.8 Hz, 1H), 4.91 (s, 1H), 3.38 (ddd, J = 10.0, 8.0, 5.0 Hz, 1H), 3.32 – 3.21 (m, 1H), 2.54 (*virt*. dt, $J \cong 12.5$, 8.0 Hz, 1H), 2.43 (s, 3H), 2.16 (ddd, J = 12.5, 6.8, 5.0 Hz, 1H), 1.06 (s, 9H).

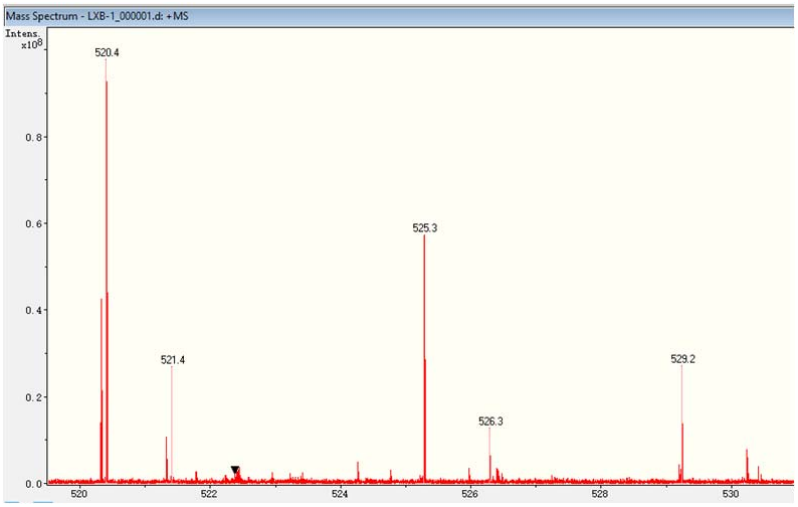
^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 143.8, 135.1, 130.9, 129.8, 127.7, 126.0, 124.8, 119.1, 110.3, 97.9, 80.1, 79.4, 47.4, 33.9, 26.5, 21.6.

IR (KBr/cm^{-1}) 3438.2, 3057.5, 2976.1, 2889.5, 1613.0, 1339.5, 1164.0, 754.1.

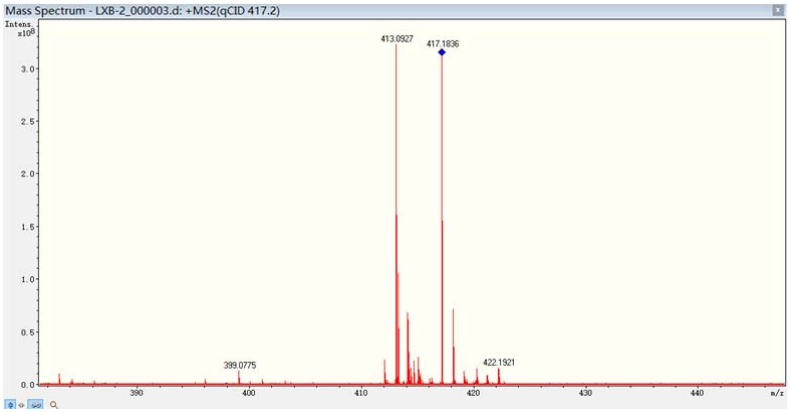
HRMS (ESI): C21H26N2NaO4S [$(M+Na)^+$]: calcd.: 425.1505; found: 425.1504.

(D) Mass Analysis of Reaction Mixtures

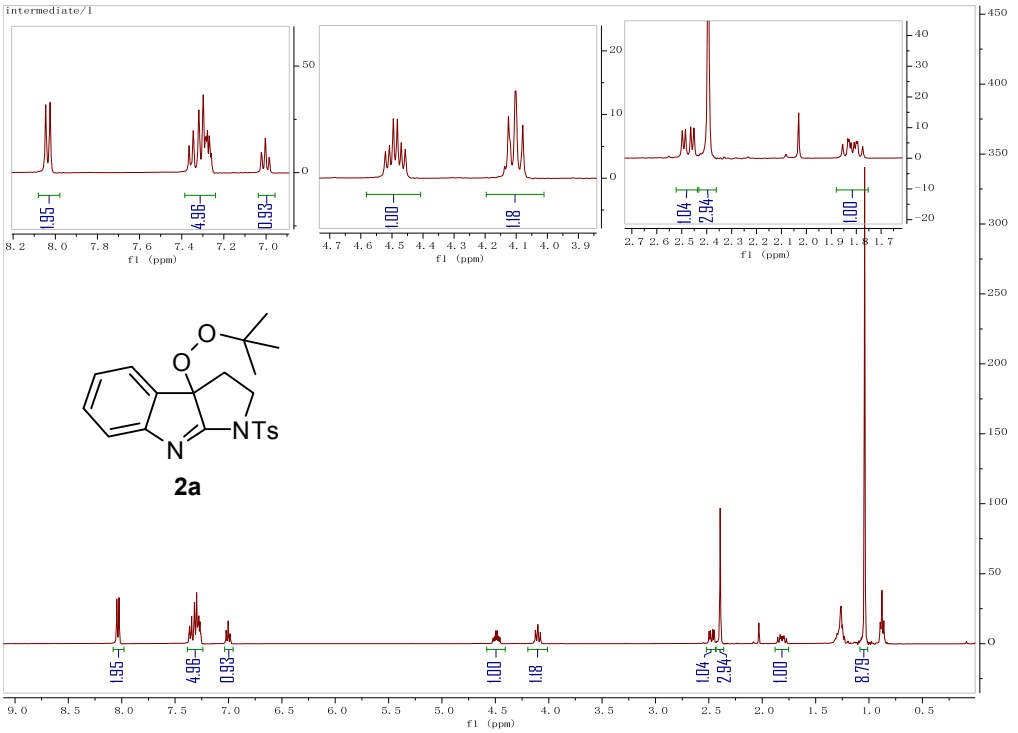
*MS analysis of reaction mixture of **1a***

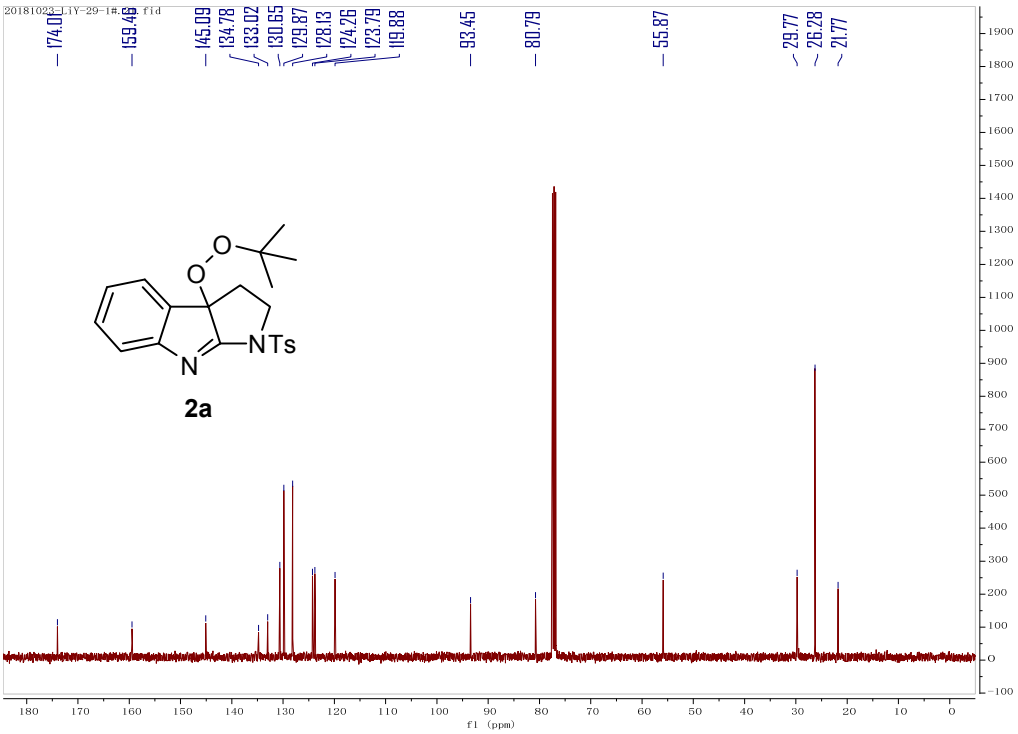


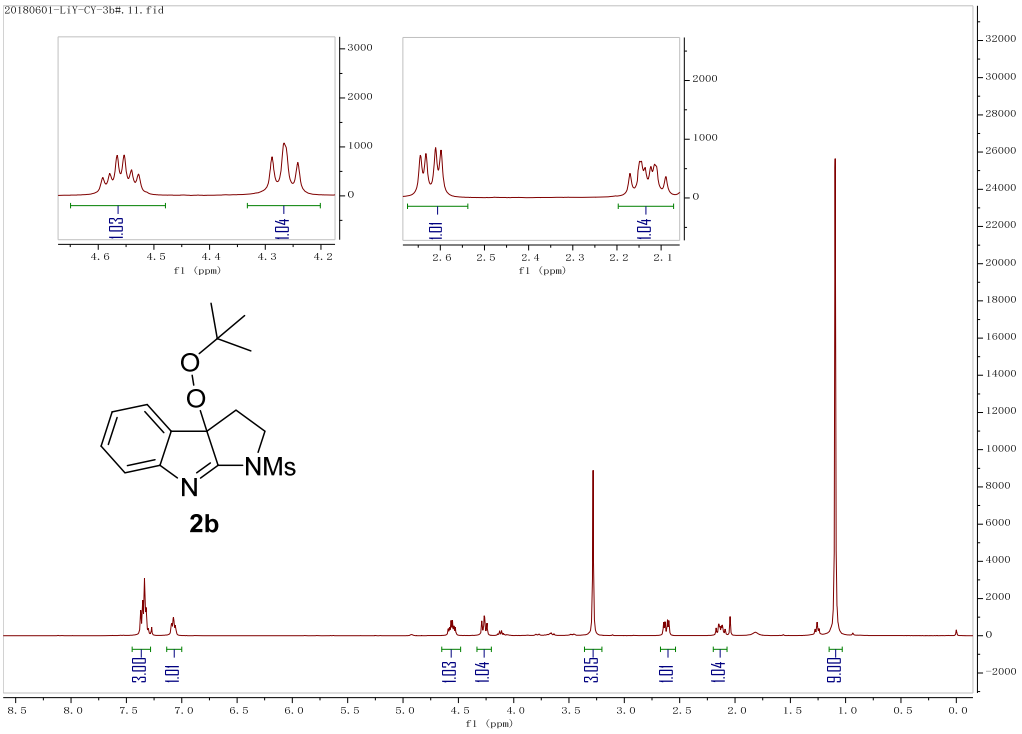
*MS analysis of reaction mixture of substrate **4***


Mass Spectrum - LXB-2_000003.d: +MS2(qCID 417.2)
Intens
x10^6
3.0
2.5
2.0
1.5
1.0
0.5
0.0
413.0927
417.1836
399.0775
422.1921
390
400
410
420
430
440
m/z

(E) ^{1}H and ^{13}C NMR Spectra Data of All Products



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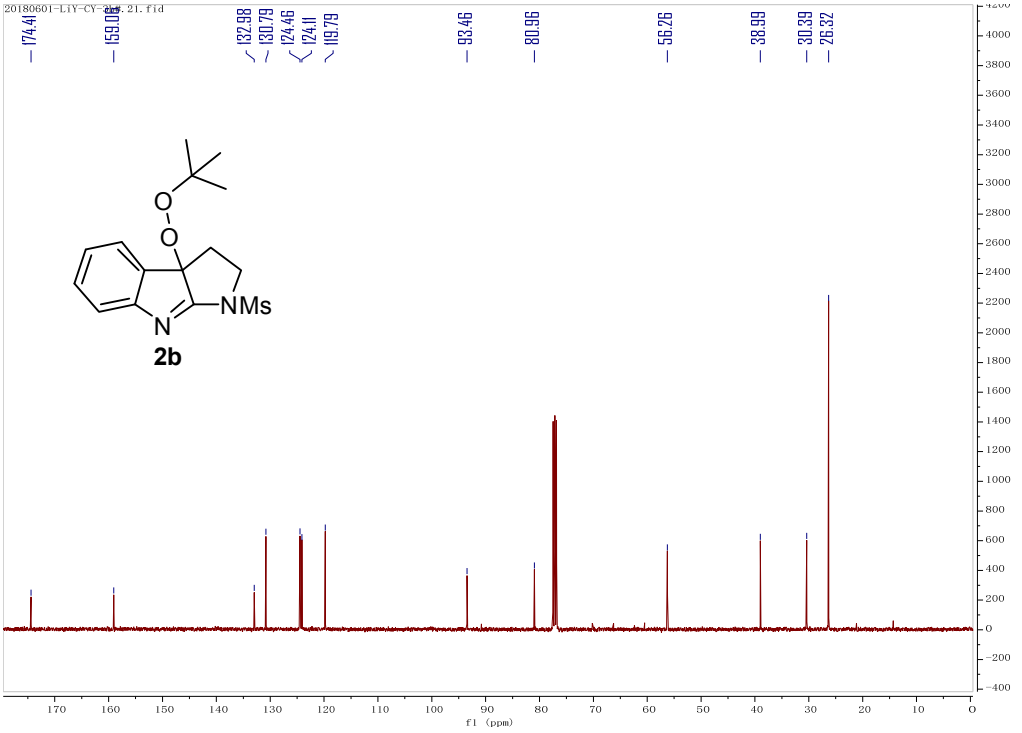
1.04
1.01
1.04
f1 (ppm)
O
O
NMs
N
2b
3.00
1.01
1.03
1.04
3.05
1.01
1.04
9.00
f1 (ppm)


20180601-LiY-CY-3b#.21.fid
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130.79
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124.11
119.79
93.46
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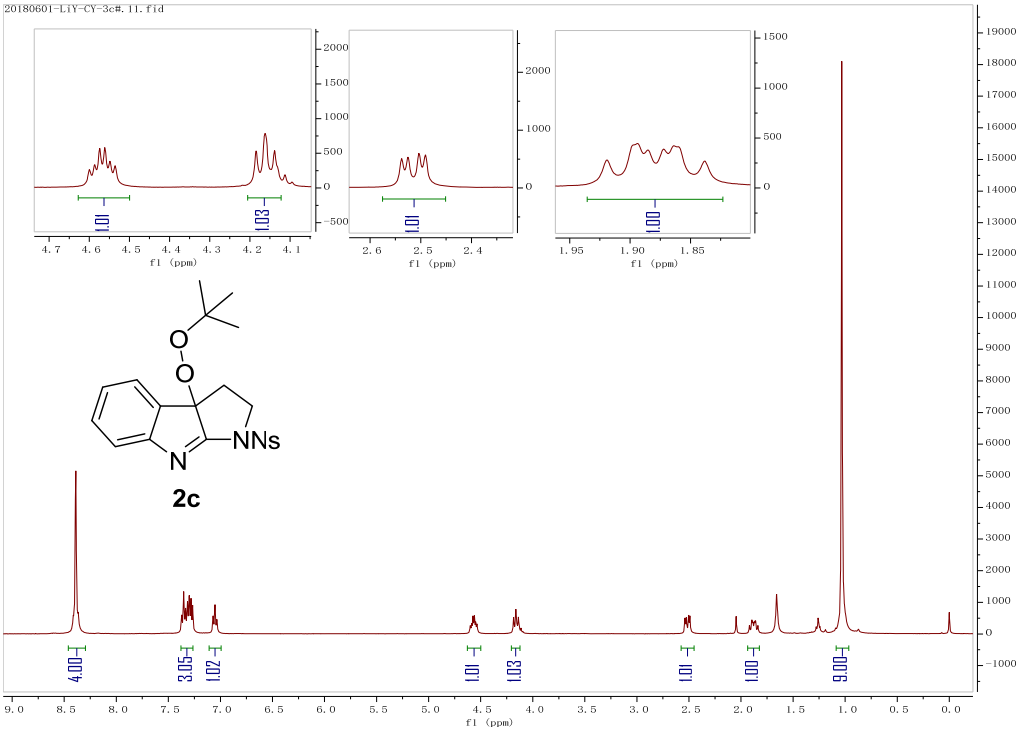
26.32
O
O
NMs
N
2b
f1 (ppm)


20180601-LIY-CY-3c#.11.fid
f1 (ppm)
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1.01
1.00
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O
NNs
N
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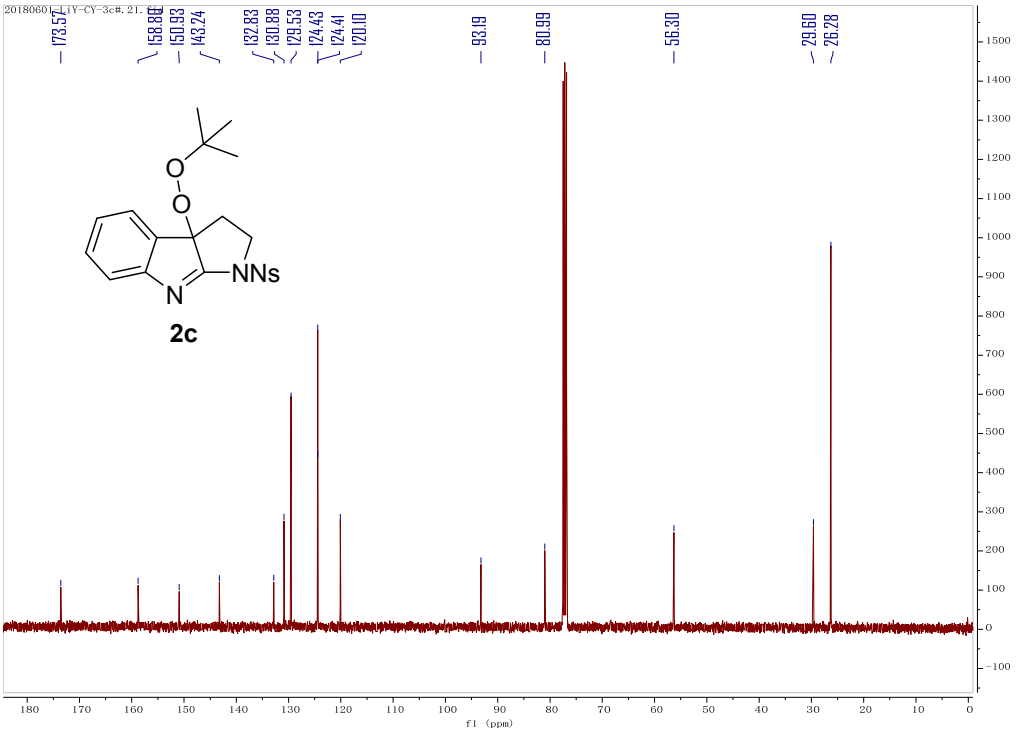
1.02
1.01
1.03
1.01
1.00
9.00


20180601-LIY-CY-3c#.21.
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158.86
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143.24
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130.88
129.53
124.43
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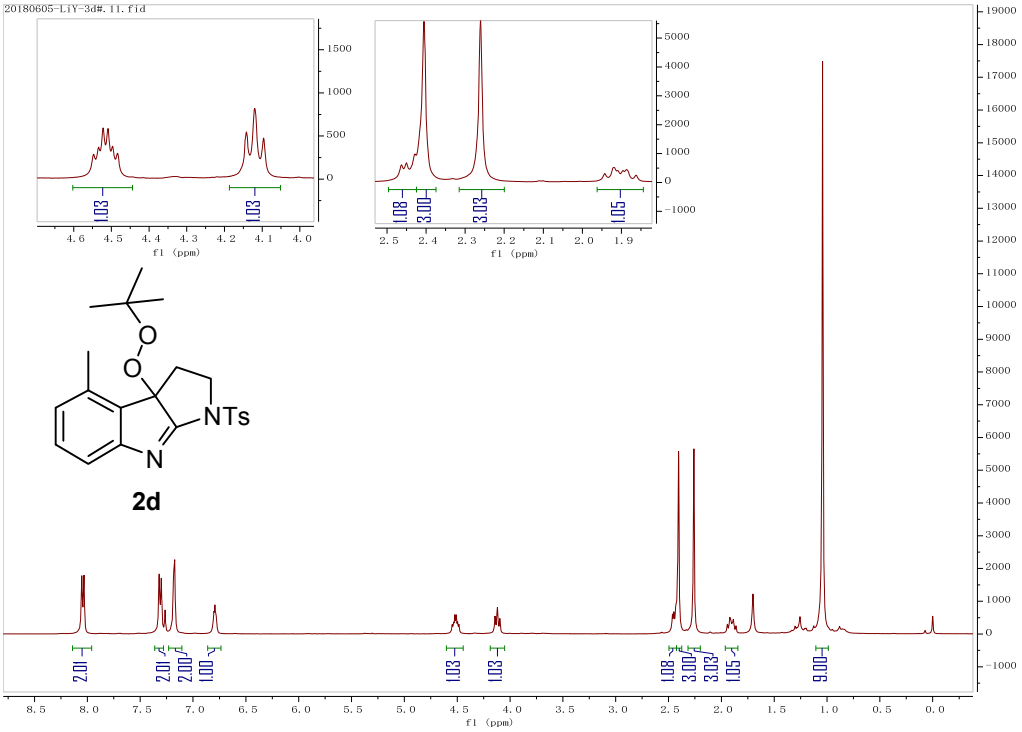
26.28
f1 (ppm)
O
O
NNs
N
2c


20180605-LiY-3d#. 11. fid
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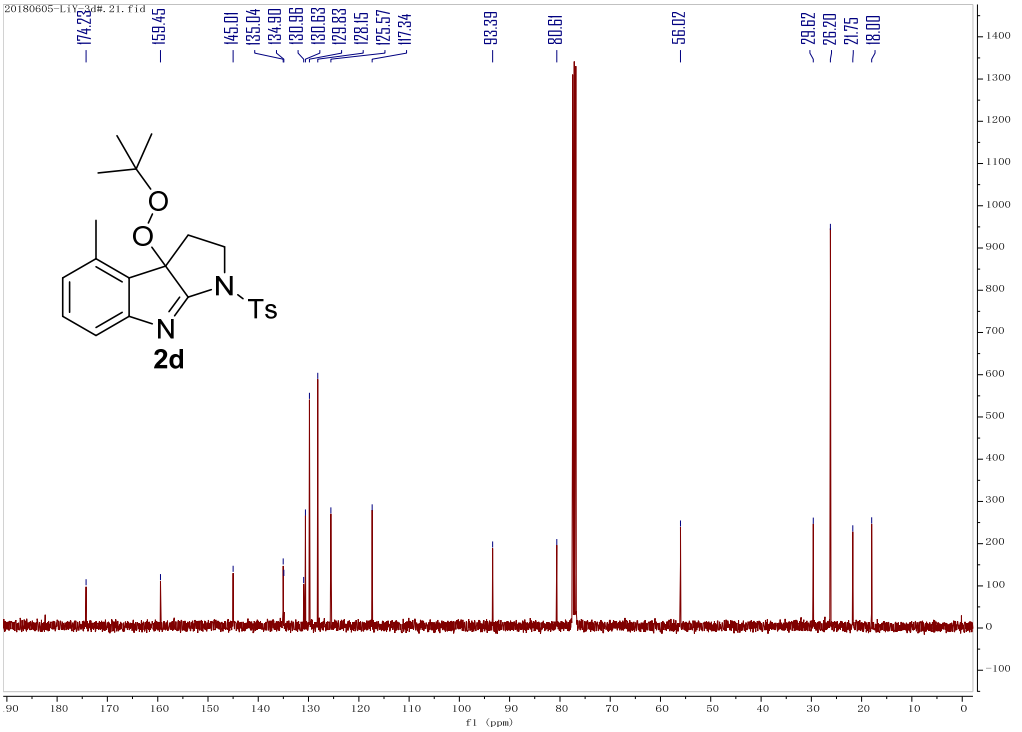
O
NTs
N
2d
f1 (ppm)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135.04
134.90
130.96
130.63
129.83
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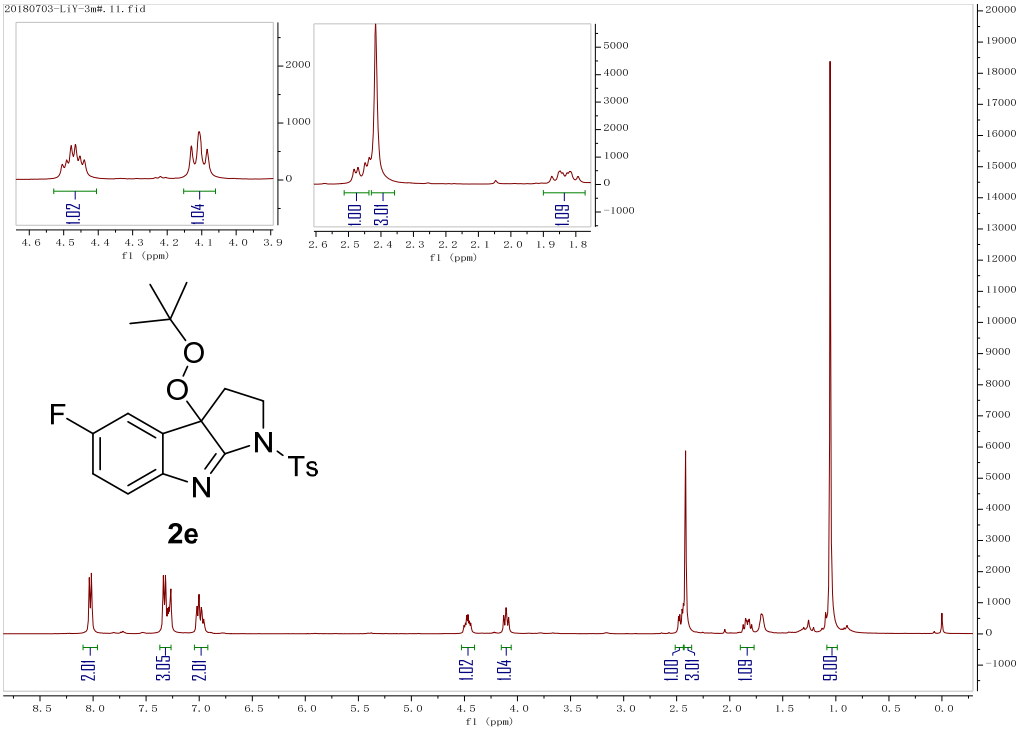
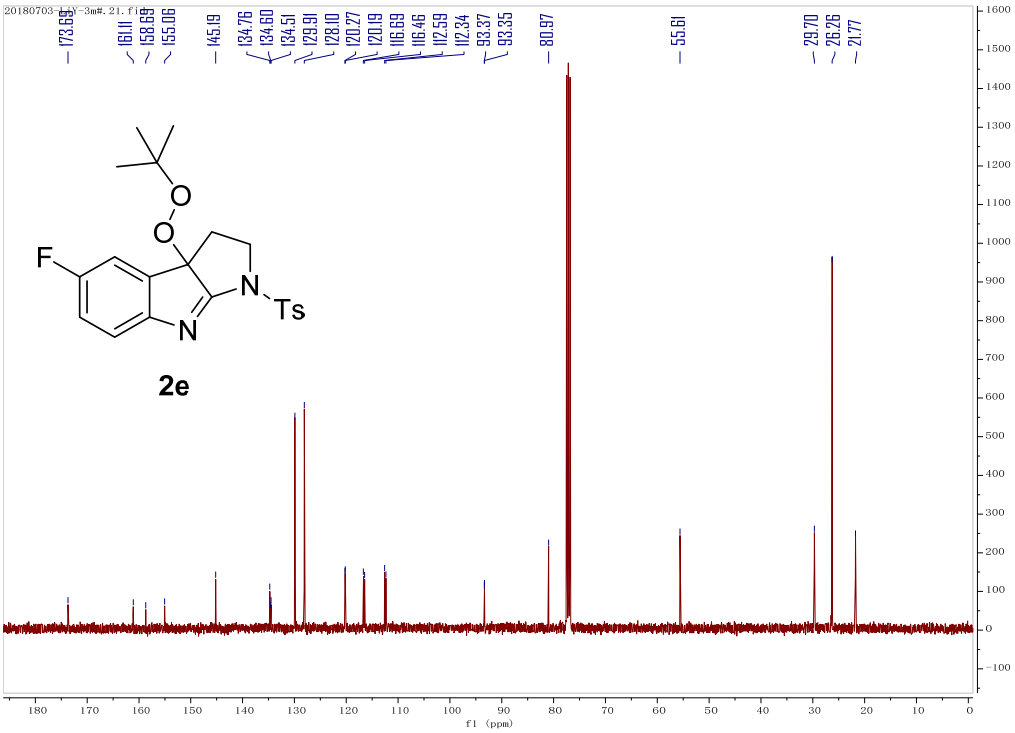
O
O
N
Ts
N
2d
f1 (ppm)


20180703-LiY-3m#.11.fid
O
O
F
N
Ts
N
2e
f1 (ppm)


20180703-LiY-3m#.21.fid
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161.11
158.69
155.06
145.19
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134.60
134.51
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116.46
112.59
112.34
93.37
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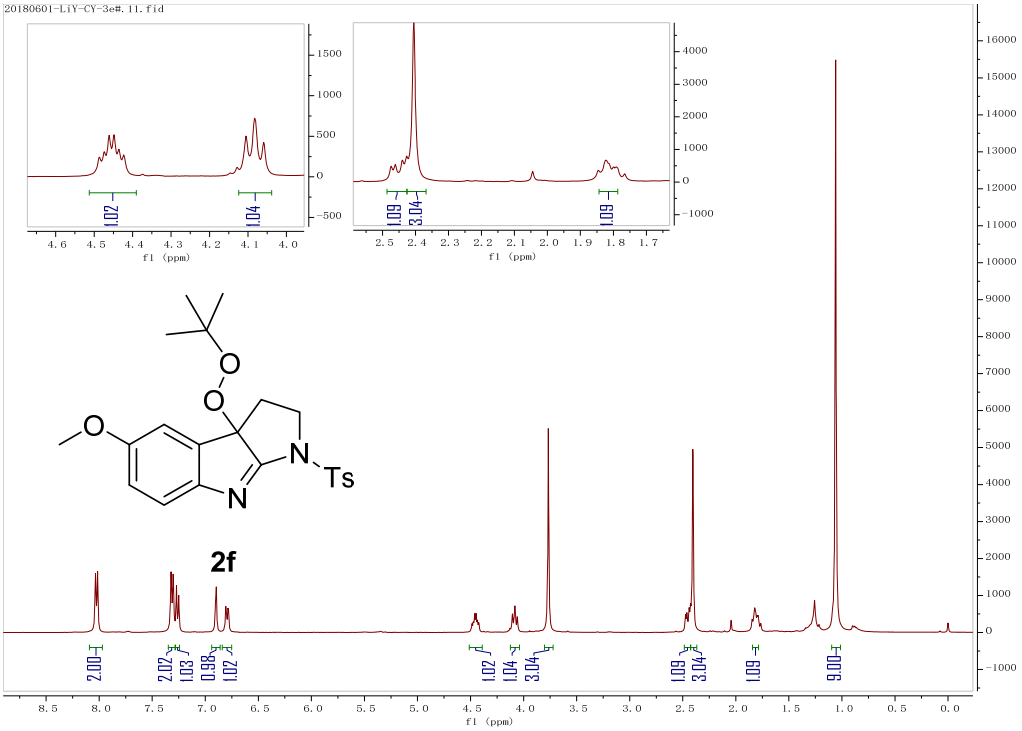
O
O
F
N
Ts
N
2e
f1 (ppm)


20180601-LiY-CY-3e#.11.fid
f1 (ppm)
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1.09
3.04
1.09
O
O
O
N
Ts
N
2f
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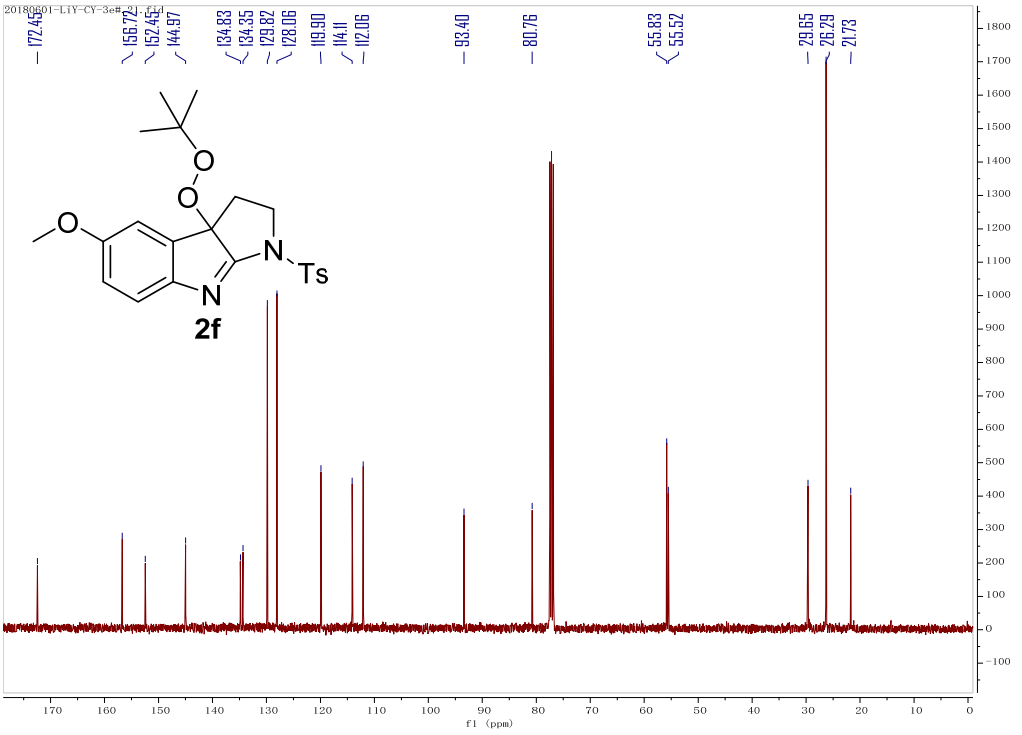
2.02
1.03
0.98
1.02
1.02
1.04
3.04
1.09
3.04
1.09
9.00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129.82
128.06
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114.11
112.06
93.40
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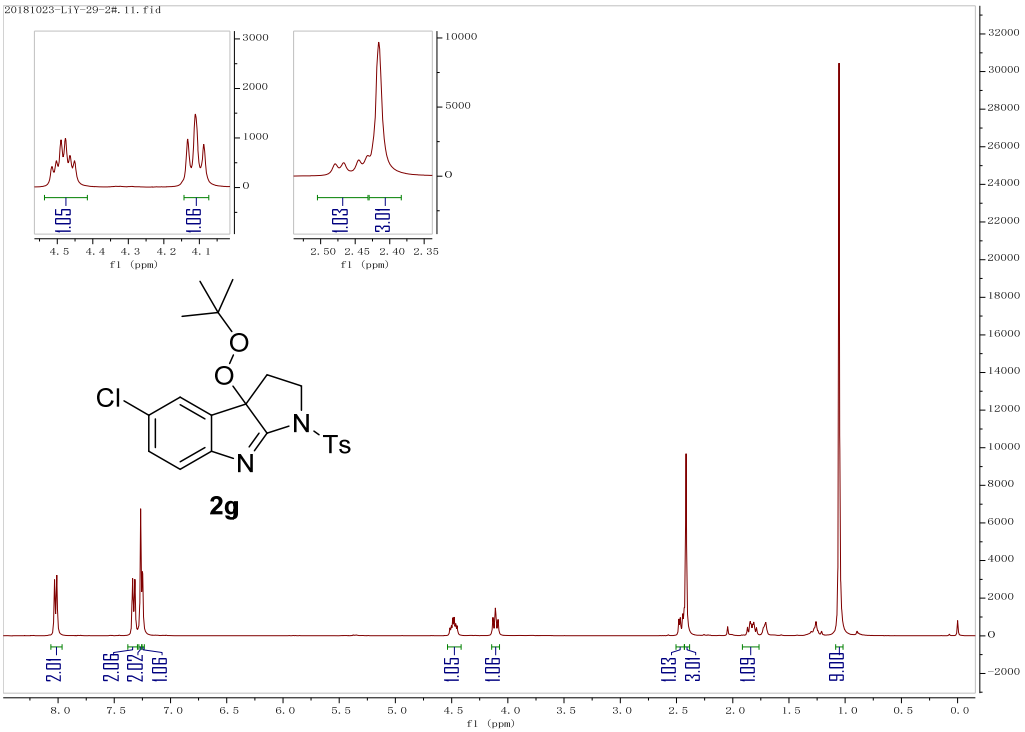
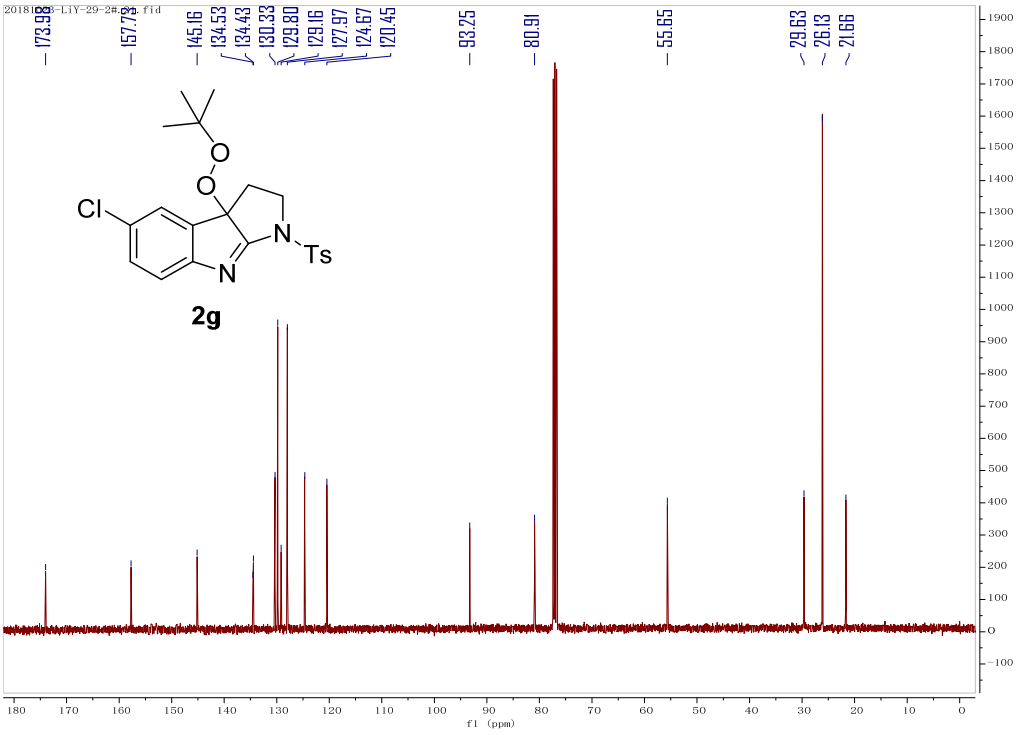
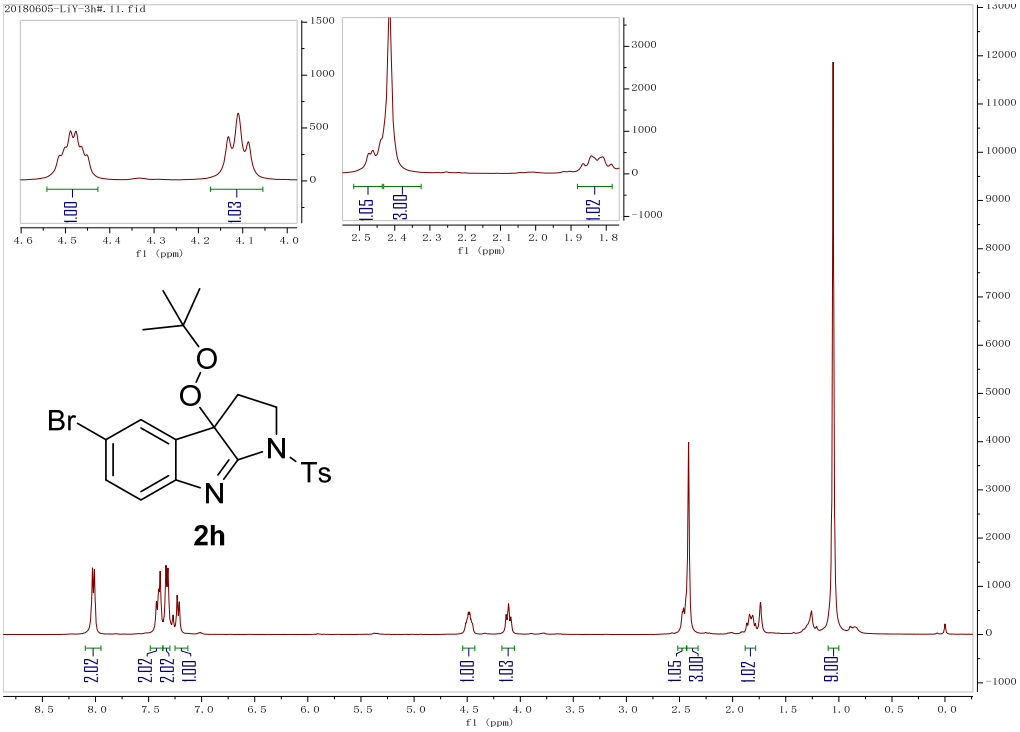
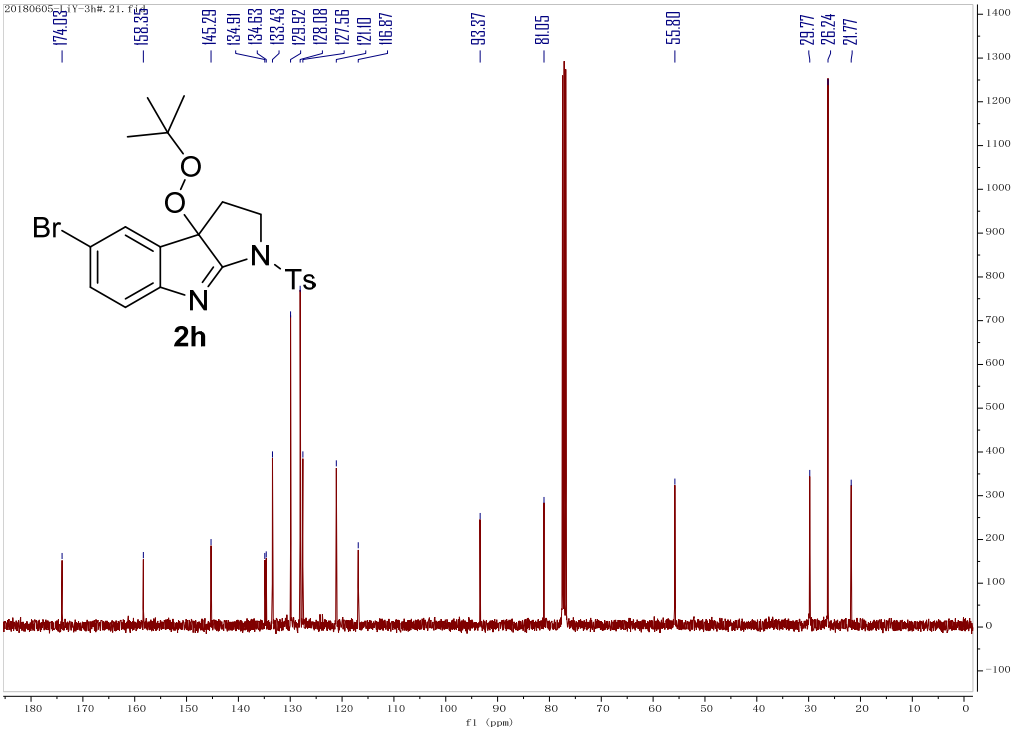
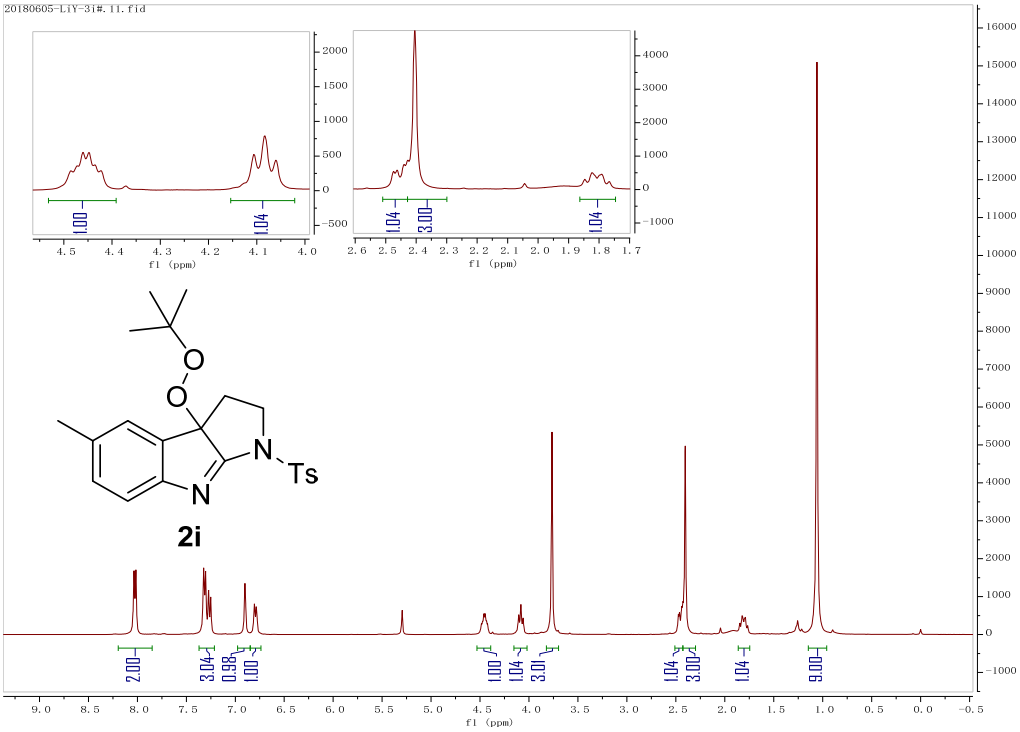
55.83
55.52
29.65
28.29
21.73
O
O
O
N
Ts
N
2f
f1 (ppm)

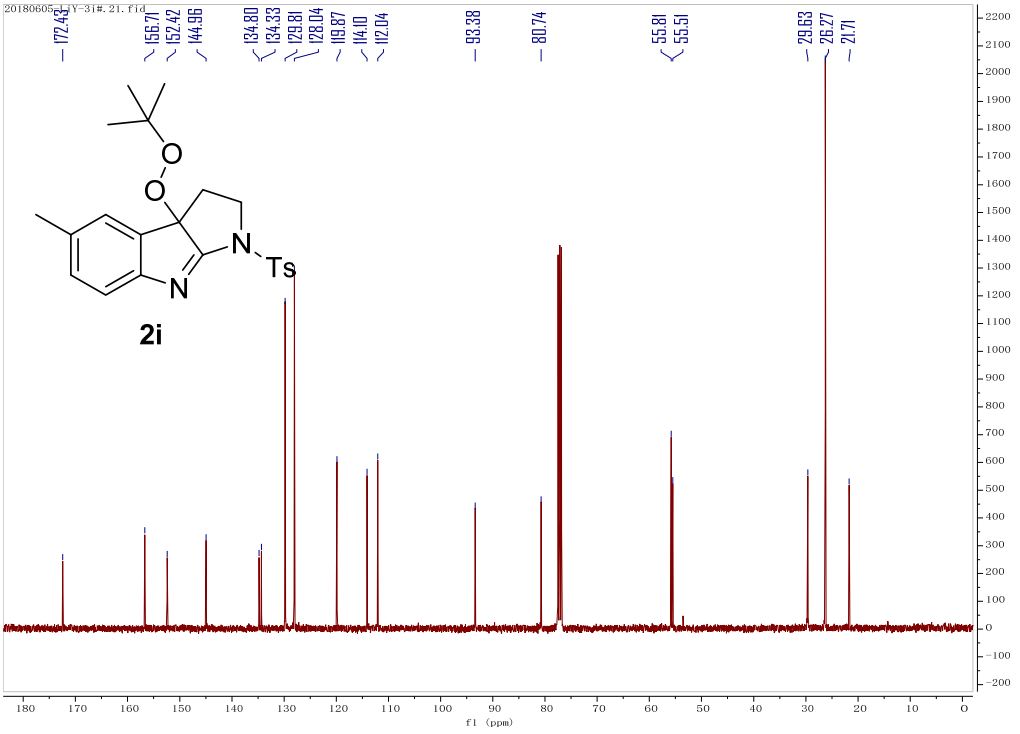

20181023-LiY-29-2#. 11. fid
Cl
O
O
N
Ts
N
2g
f1 (ppm)

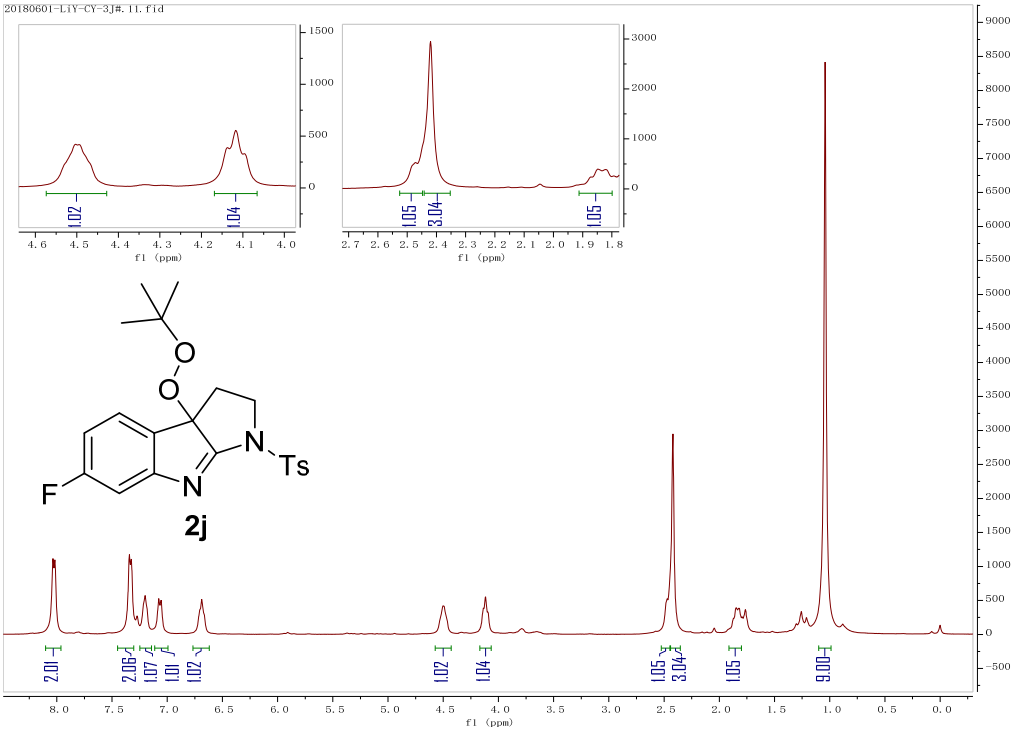

20181023-LiY-29-2#. 3. fid
173.98
157.79
145.16
134.53
134.43
130.33
129.80
129.16
127.97
124.67
120.45
93.25
80.91
55.65
29.63
26.13
21.66
Cl
O
O
N
Ts
N
2g
f1 (ppm)

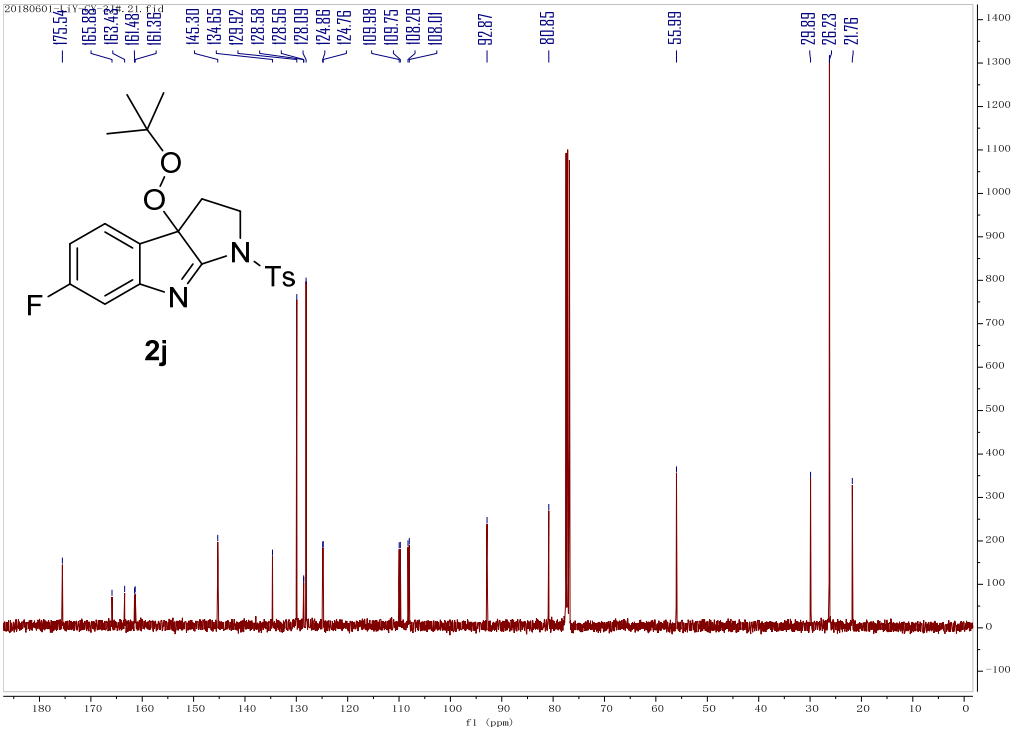

20180605-LiY-3h#. 11. fid
Br
O
O
N
Ts
N
2h
f1 (ppm)

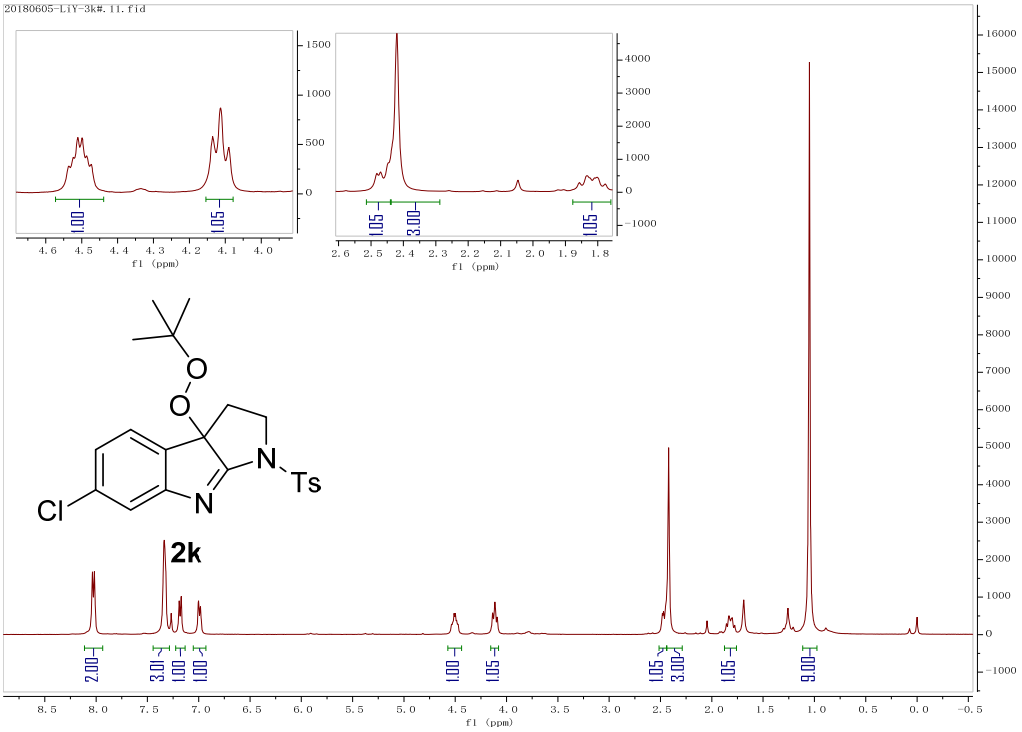

20180605-LiY-3h#. 21. fid
174.05
158.39
145.29
134.91
134.63
133.43
129.92
128.08
127.56
121.10
116.87
93.37
81.05
55.80
29.77
26.74
21.77
Br
O
O
N
Ts
N
2h
f1 (ppm)

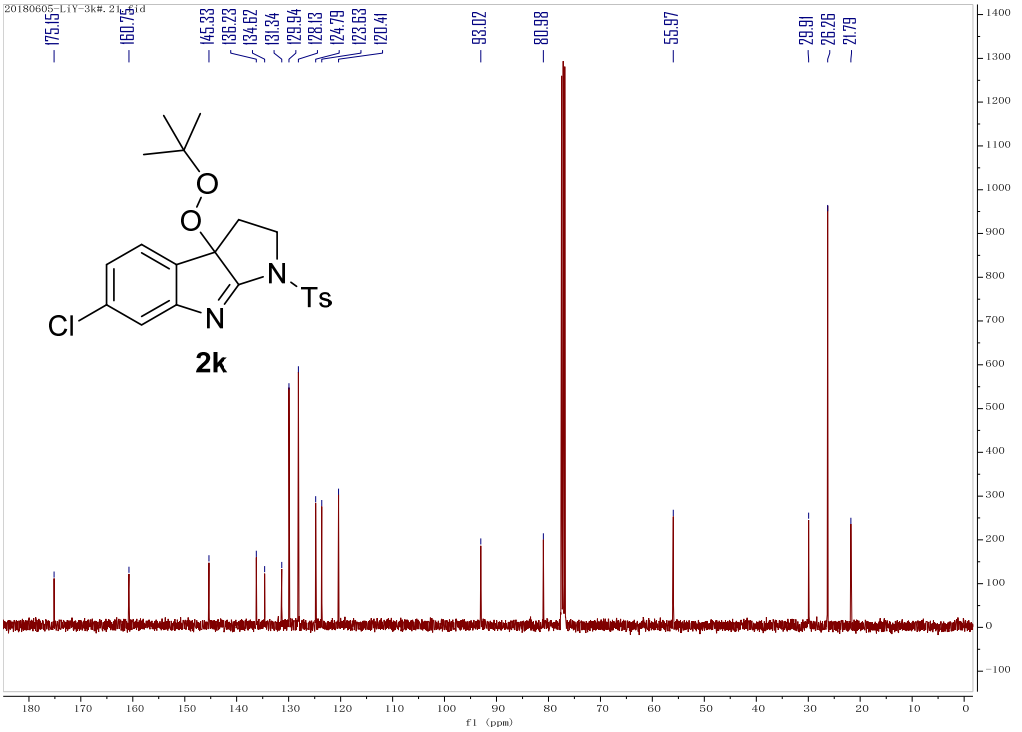

20180605-LiY-3i#.11.fid
2i
f1 (ppm)

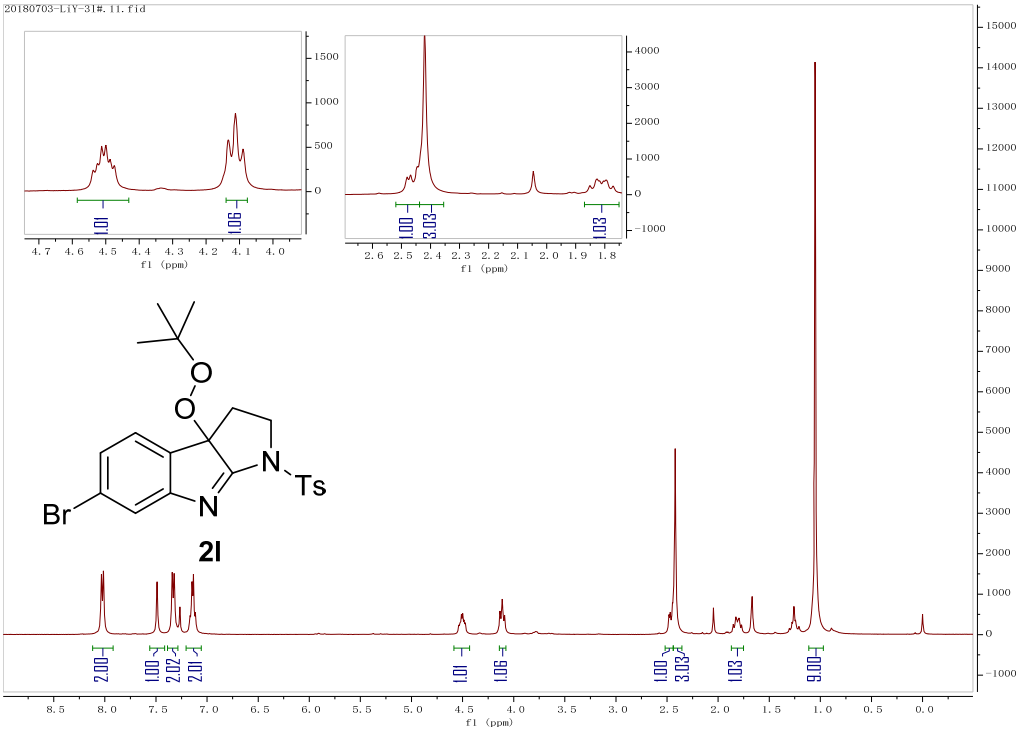

20180605-LiY-3i#.21.fid
172.48
156.71
152.42
144.96
134.80
134.33
129.81
128.04
119.87
114.10
112.04
93.38
80.74
55.81
55.51
29.63
26.27
21.71
2i
f1 (ppm)

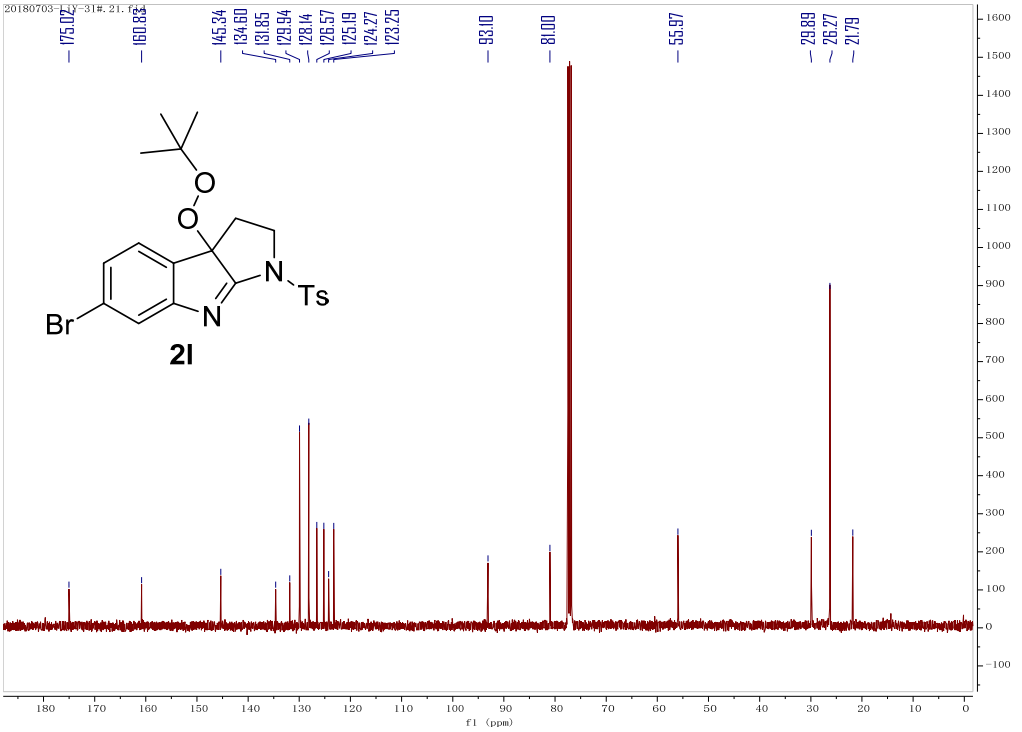

20180601-LIY-CY-3J#.11.fid
O
O
N
Ts
F
N
2j
f1 (ppm)

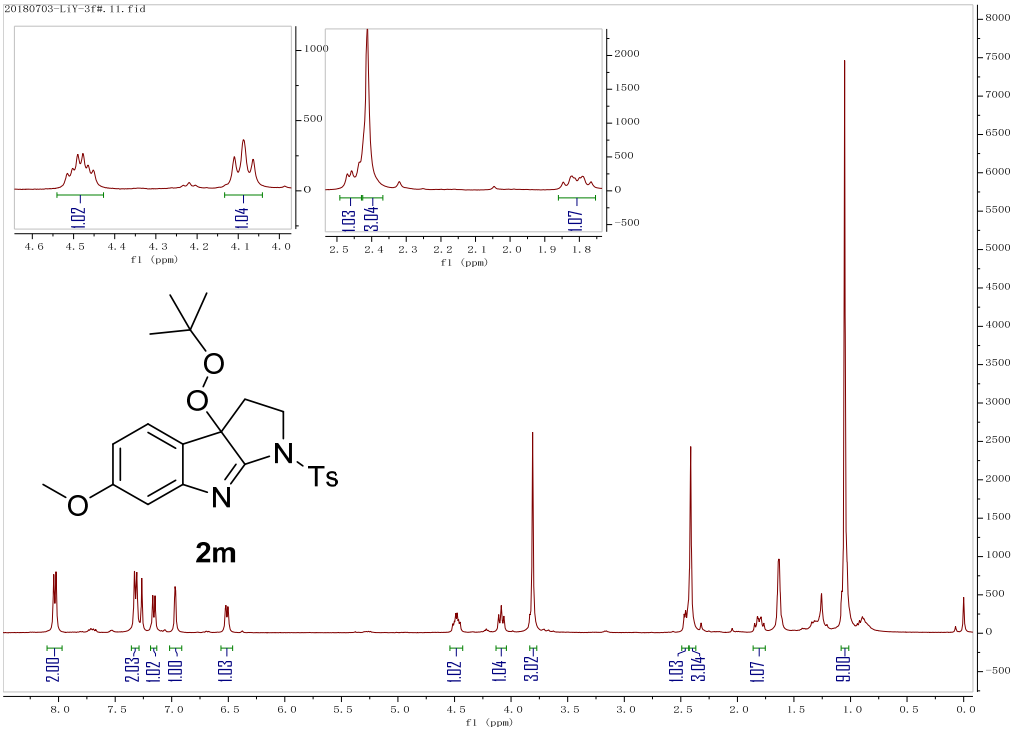

175.54
165.88
163.48
161.48
161.38
145.30
134.65
129.92
128.58
128.56
128.09
124.86
124.76
109.98
109.75
108.26
108.01
92.87
80.85
55.99
29.83
26.23
21.76
O
O
N
Ts
F
N
2j
f1 (ppm)

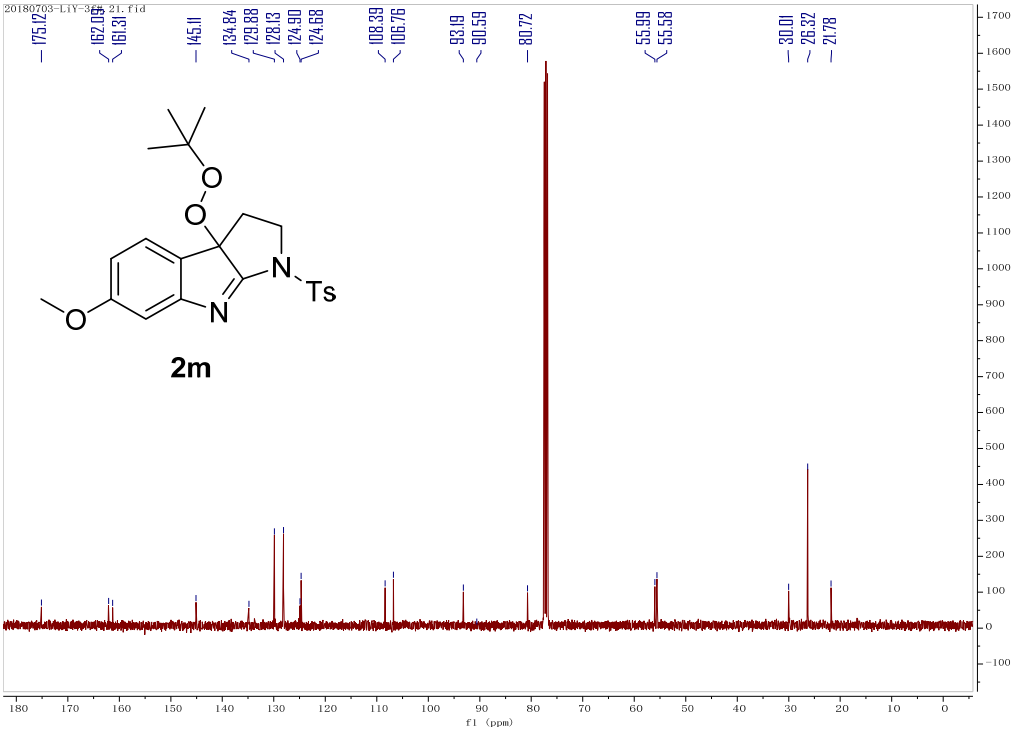

20180605-LiY-3k#. 11. fid
f1 (ppm)
O
O
N
Ts
Cl
N
2k

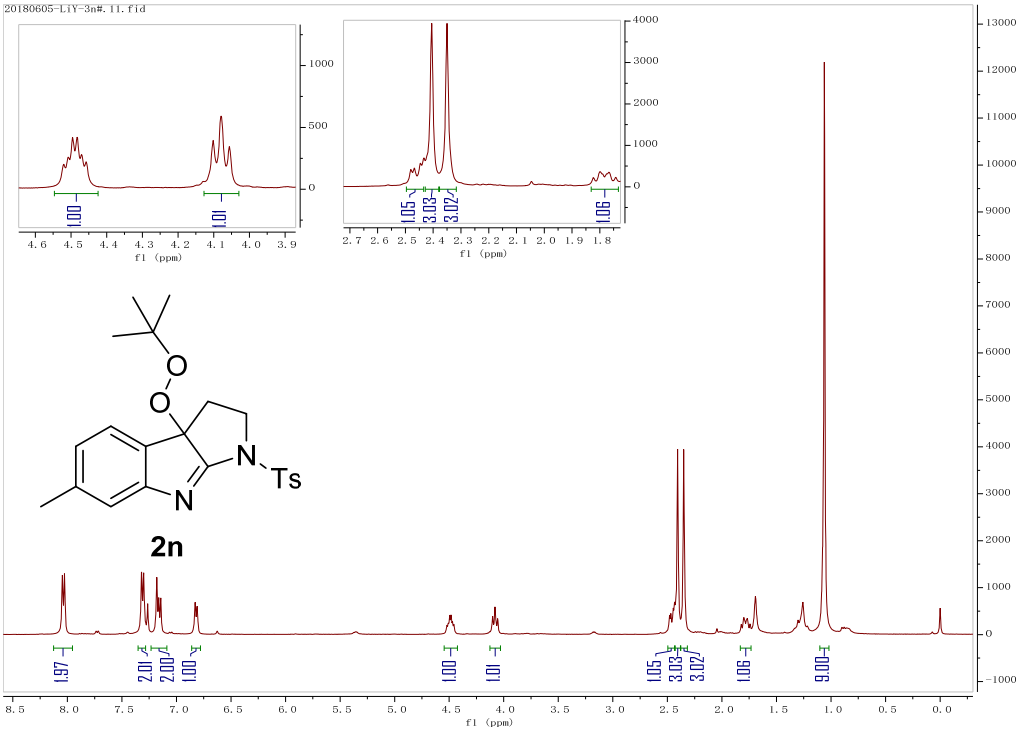

20180605-LiY-3k#. 21. fid
175.15
160.75
145.33
136.23
134.62
131.34
129.94
128.13
124.79
123.63
120.41
93.02
80.98
55.97
29.91
26.26
21.79
f1 (ppm)
O
O
N
Ts
Cl
N
2k

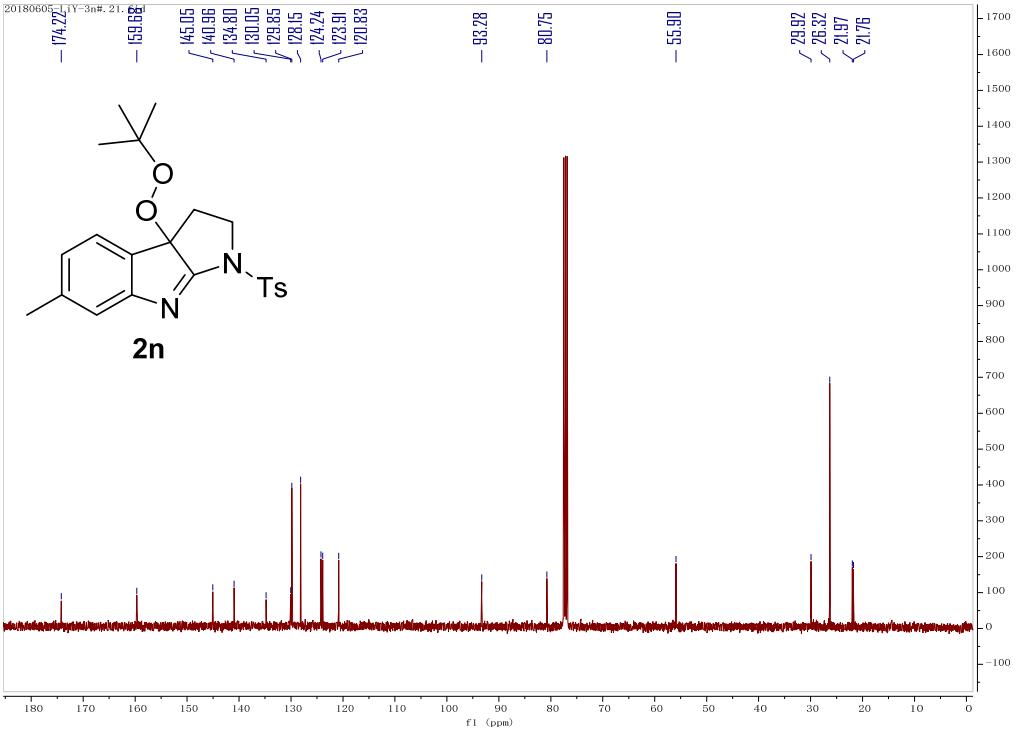

20180703-LiY-31#. 11. fid
Br
N
Ts
O
O
N
2l

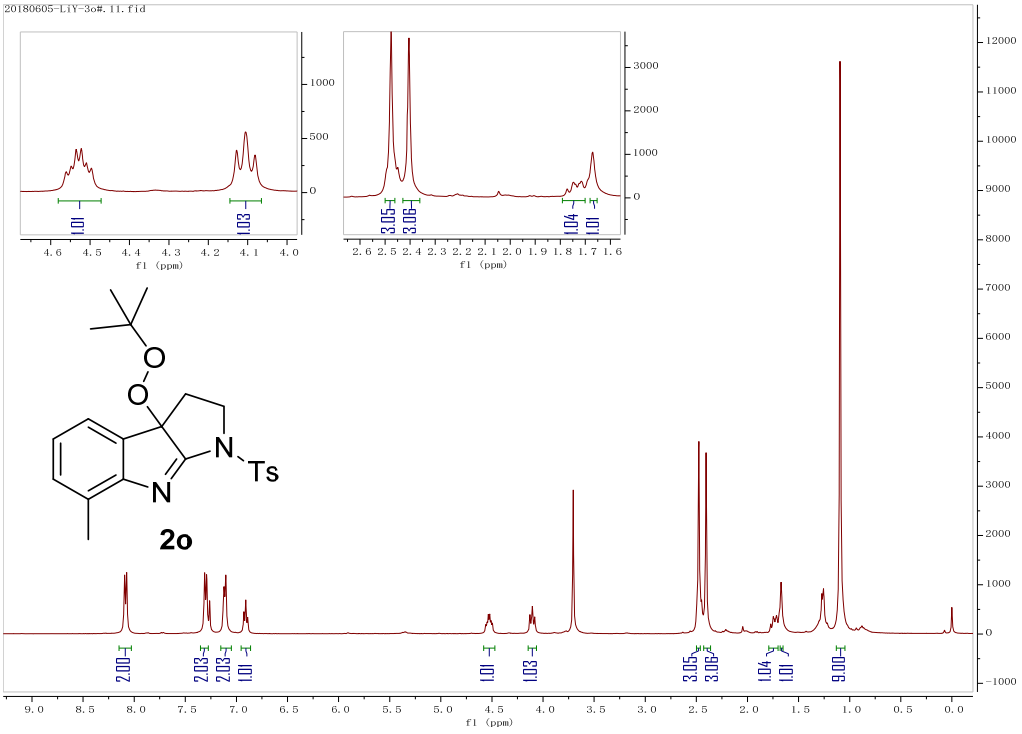

20180703-LiY-31#. 21. fid
175.02
160.83
145.34
134.60
131.85
129.94
128.14
126.57
125.19
124.27
123.25
93.10
81.00
55.97
29.83
26.27
21.79
Br
N
Ts
O
O
N
2l

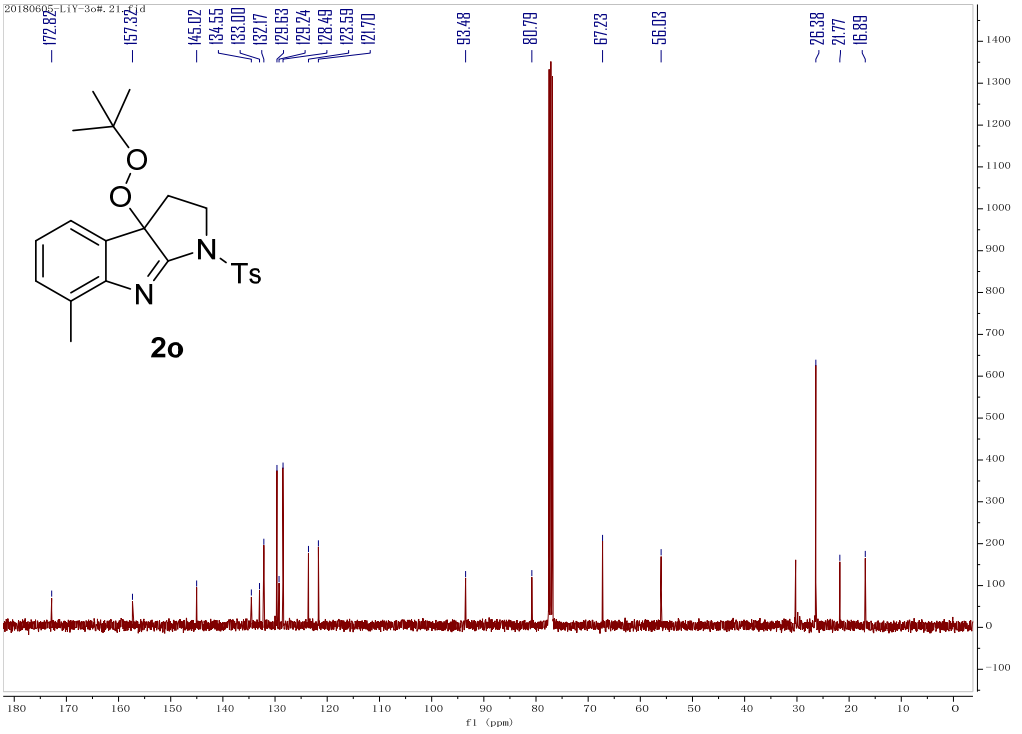

2m

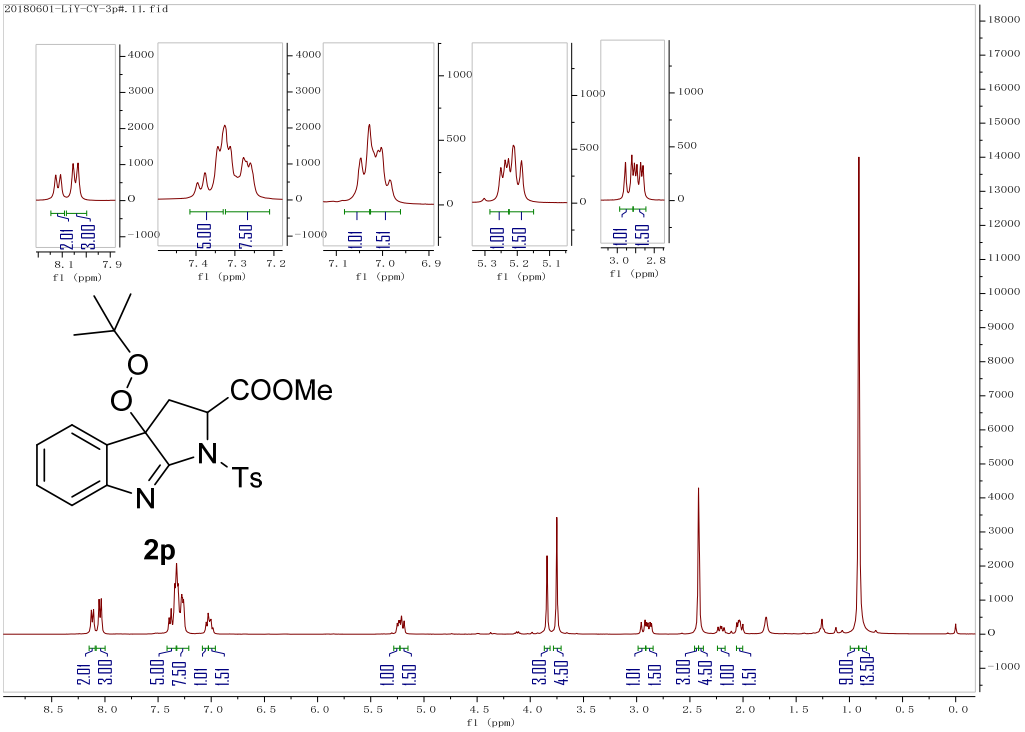

2m

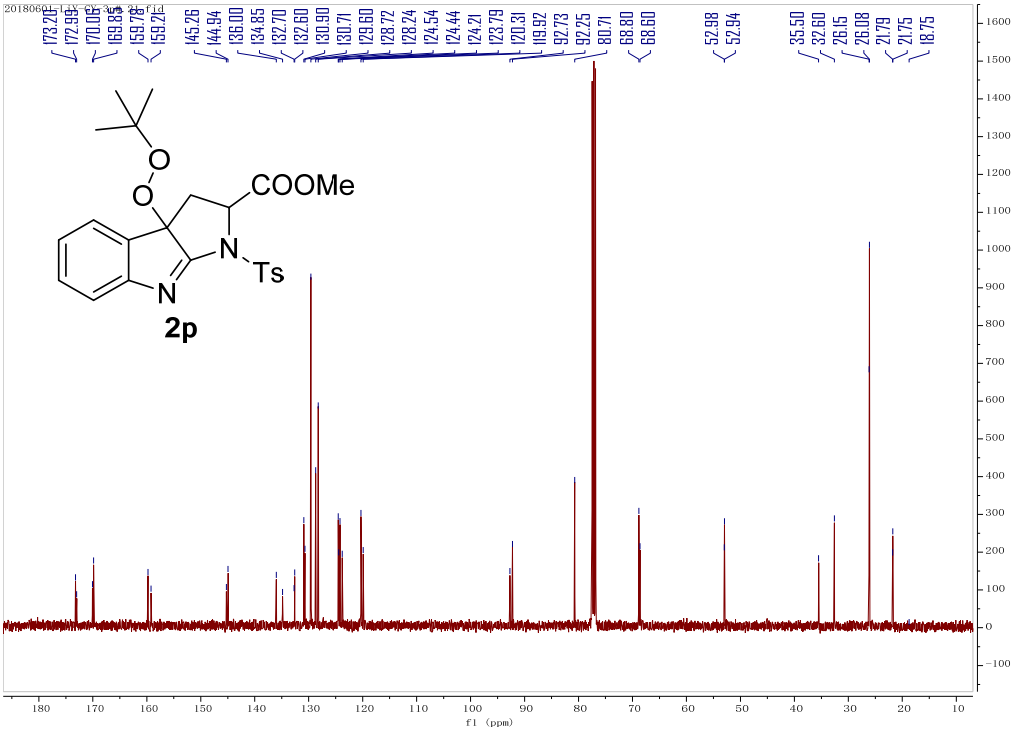

20180605-LiY-3n#. 11. fid
1.00
1.01
1.05
3.03
3.02
1.06
f1 (ppm)
O
O
N
Ts
N
2n
1.97
2.01
2.00
1.00
1.00
1.01
1.05
3.03
3.02
1.06
9.00
f1 (ppm)

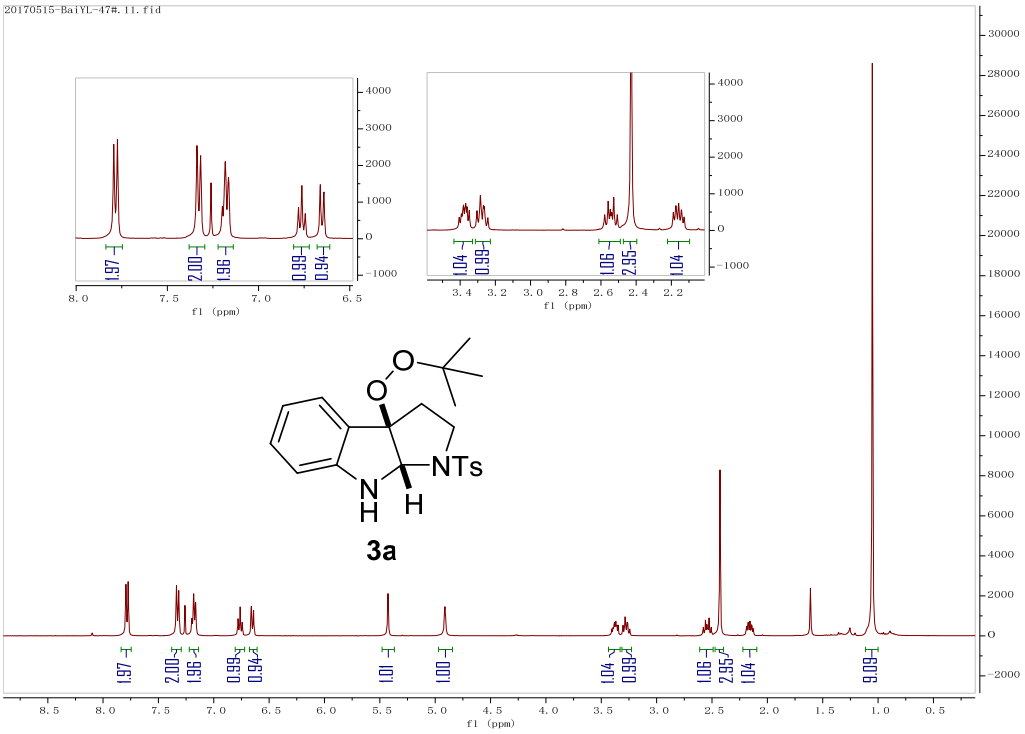

20180605-LiY-3n#. 21. fid
174.22
159.68
145.05
140.96
134.80
130.05
129.85
128.15
124.24
123.91
120.83
93.28
80.75
55.90
29.92
26.32
21.97
21.76
O
O
N
Ts
N
2n
f1 (ppm)

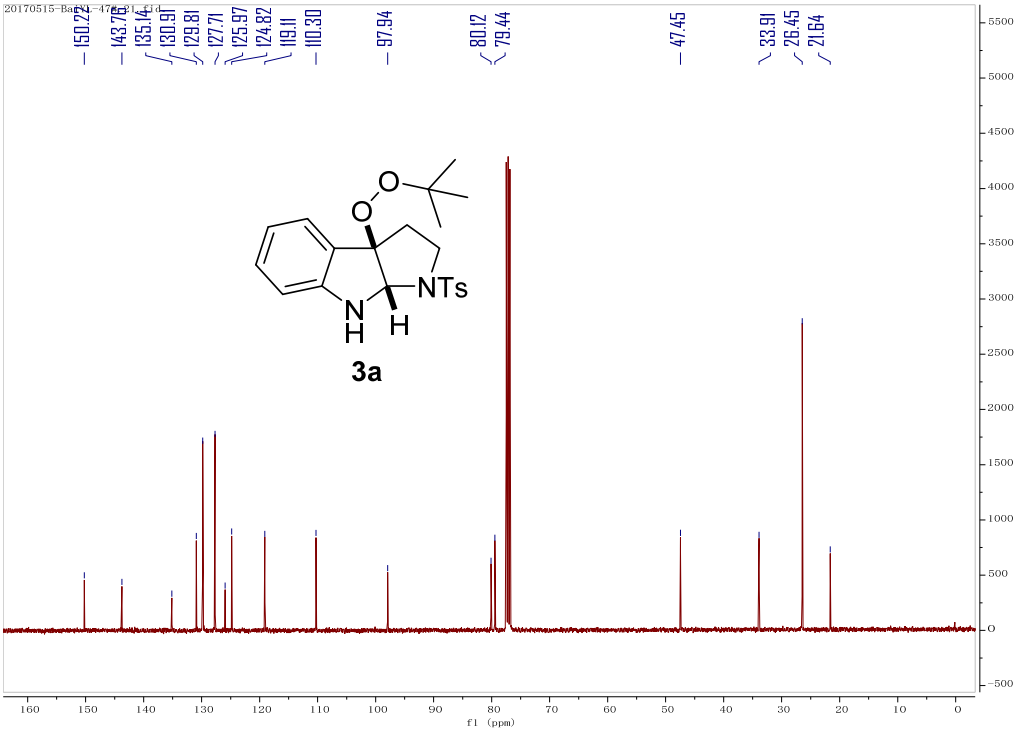

20180605-LiY-3o#. 11. fid
O
O
N
Ts
N
2o
f1 (ppm)


20180605-LiY-3o#. 21. fid
172.82
157.32
145.02
134.55
133.00
132.17
129.63
129.24
128.49
123.59
121.70
93.48
80.79
67.23
56.03
26.38
21.77
16.89
O
O
N
Ts
N
2o
f1 (ppm)


COOMe
Ts
2p


COOMe
Ts
2p


20170515-BaiYL-47#.11.fid
O
O
NTs
N
H
H
3a
1.97
2.00
1.96
0.99
0.94
1.01
1.00
1.04
0.99
1.06
2.95
1.04
9.09
f1 (ppm)


150.27
143.76
135.14
130.91
129.81
127.71
125.97
124.82
119.11
110.30
97.94
80.12
79.44
47.45
33.91
26.45
21.64
O
O
NTs
N
H
H
3a
f1 (ppm)