A Copper-Catalyzed Arylation of Tryptamines for the Synthesis of Pyrroloindolines

Madeleine E. Kieffer, Kangway V. Chuang, Sarah E. Reisman*

The Warren and Katharine Schlinger Laboratory of Chemistry and Chemical Engineering Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125 reisman@caltech.edu

Supporting Information 1 (Experimental Procedures):

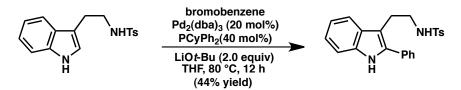
Table of Contents

1.	General considerations	S3
2.	Optimization of reaction parameters	S4
3.	Synthesis of N-tosyl tryptamine derivatives	S 6
4.	Synthesis of N-tosyl-N'-alkyl tryptamine derivatives	S 9
5.	Synthesis of Diaryliodonium tetrafluoroborates	S10
6.	Synthesis of N-tosyl pyrroloindolines	S12
7.	Reaction scalability and catalyst efficiency: large scale reaction	S21

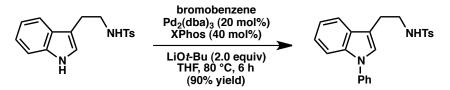
1. General Considerations. Unless otherwise stated, reactions were performed under a nitrogen atmosphere using freshly dried solvents. Tetrahydrofuran (THF), methylene chloride (CH₂Cl₂), acetonitrile (MeCN), dimethylformamide (DMF), and toluene (PhMe) were dried by passing through activated alumina columns. Triethylamine (Et₃N) was distilled over calcium hydride prior to use. Unless otherwise stated, chemicals and reagents were used as received. All reactions were monitored by thin-layer chromatography using EMD/Merck silica gel 60 F254 pre-coated plates (0.25 mm) and were visualized by UV, p-anisaldehyde, or KMnO₄ staining. Reaction samples were analyzed on an Agilent 1290 Series LC/MS using an Eclipse Plus C18 column (RRHD 1.8 μ m, 2.1 x 50 mm, 11,072 plates). Flash column chromatography was performed either as described by Still et al.¹ using silica gel (partical size 0.032-0.063) purchased from Silicycle or using pre-packaged RediSep[®]Rf columns on a CombiFlash Rf system (Teledyne ISCO Inc.). Alumina was purchased from Sigma-Aldrich (Aluminum oxide, ~150 mesh, 58Å pore size, activated, basic, Brockmann I) and deactivated with 3% v/w H2O (30.0 mL / 970 g). ¹H and ¹³C NMR spectra were recorded on a Varian 400 MR (at 400 MHz and 101 MHz, respectively), a Varian Inova 500 (at 500 MHz and 126 MHz, respectively), or a Varian Inova 600 (at 600 MHz and 150 MHz, respectively), and are reported relative to internal CHCl₃ (¹H, δ = 7.26) or DMSO (¹H, δ = 2.50), and CDCl₃ (¹³C, $\delta = 77.0$), or DMSO (¹³C, $\delta = 40.0$). Data for ¹H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicity and qualifier abbreviations are as follows: s =singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm⁻¹). HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), or mixed (MM) ionization mode.

2. Optimization of Reaction Parameters

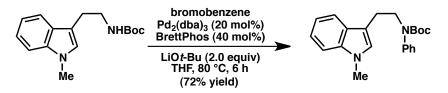
A. Palladium-Catalyzed Reaction Screens



To a flame-dried vial in the glove box was charged PCyPh₂ (11 mg, 0.04 mmol), Pd₂(dba)₃ (11 mg, 0.02 mmol), N-tosyltryptamine (31 mg, 0.1 mmol), bromobenzene (51 μ L, 0.5 mmol), LiOtBu (16 mg, 0.2 mmol) and THF (1 mL). The vial was sealed and heated to 80 °C for 12 hours. The reaction mixture was filtered through a plug of silica and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (20% EtoAc in hexanes) to afford 2-phenyl tryptamine **17** (16.9 mg, 0.04 mmol, 44%). ¹H NMR (CDCl₃, 500 MHz) δ 8.11 (s, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.52 – 7.42 (m, 5H), 7.40 (ddd, *J* = 4.1, 1.5, 1.5 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.20 (dd, *J* = 16.1, 7.8 Hz, 3H), 7.09 (dd, *J* = 7.8, 7.2 Hz, 1H), 4.35 (t, *J* = 5.8 Hz, 1H), 3.28 (dd, *J* = 13.3, 6.8 Hz, 2H), 3.08 (dd, *J* = 7.1, 7.1 Hz, 2H), 2.40 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 143.2, 136.7, 135.8, 132.5, 129.6, 129.0, 128.5, 128.10, 128.09, 127.0, 122.6, 120.0, 118.8, 110.9, 108.3, 43.2, 25.0, 21.5;HRMS (MM) calc'd for [M+H]⁺ 391.1475, found 391.1491.



To a flame-dried vial in the glove box was charged XPhos (19 mg, 0.04 mmol), Pd₂(dba)₃ (11 mg, 0.02 mmol), N-tosyltryptamine (31 mg, 0.1 mmol), bromobenzene (51 μ L, 0.5 mmol), LiOtBu (16 mg, 0.2 mmol) and THF (1 mL). The vial was sealed and heated to 80 °C for 6 hours. The reaction mixture was filtered through a plug of silica and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (20% EtoAc in hexanes) to afford N-phenyl tryptamine **16** (35.2 mg, 0.09 mmol, 90%). ¹H NMR (CDCl₃, 500 MHz) δ 7.70 – 7.65 (m, 2H), 7.57 – 7.43 (m, 6H), 7.39 – 7.32 (m, 1H), 7.23 (dd, *J* = 11.6, 4.5 Hz, 3H), 7.16 – 7.10 (m, 1H), 7.09 (s, 1H), 4.54 (t, *J* = 6.1 Hz, 1H), 3.34 (q, *J* = 6.6 Hz, 2H), 2.99 (t, *J* = 6.7 Hz, 2H), 2.38 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 143.3, 139.4, 136.8, 136.1, 129.6, 128.3, 127.0, 126.4, 126.2, 124.1, 122.7, 120.1, 118.8, 112.7, 110.7, 43.1, 25.4, 21.5. HRMS (MM) calc'd for [M+H]⁺ 391.1475, found 391.1470.



To a flame-dried vial in the glove box was charged BrettPhos (6.4 mg, 0.012 mmol), Pd₂(dba)₃ (3.5 mg, 0.006 mmol), *N*-Boc-*N'*-methyltryptamine (8 mg, 0.1 mmol), bromobenzene (16 μ L, 0.15 mmol), LiOtBu (4.8 mg, 0.06 mmol) and THF (1 mL). The vial was sealed and heated to 80 °C for 6 hours. The reaction mixture was filtered through a plug of silica and concentrated *in vacuo*. The crude residue was purified by silica gel flash chromatography (20% EtoAc in hexanes) to afford N-phenyl tryptamine **15** (28.0 mg, 0.02 mmol, 72%). ¹H NMR (CDCl₃, 500 MHz) δ 7.54 (d, *J* = 7.9 Hz, 1H), 7.34 (dd, *J* = 10.7, 4.9 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.24 – 7.18 (m, 4H), 7.07 (ddd, *J* = 7.9, 7.0, 1.0 Hz, 1H), 6.85 (s, 1H), 3.97 – 3.87 (m, 2H), 3.72 (s, 3H), 3.06 – 2.95 (m, 2H), 1.42 (s, 10H). ¹³C NMR (CDCl₃, 126 MHz) 148.4, 143.5, 139.4, 136.4, 135.6, 132.6, 131.9, 129.6, 128.5, 127.2, 127.1, 127.0, 125.7, 124.3, 119.2, 109.4, 84.4, 62.1, 47.4, 37.9, 21.4, 20.8. FTIR (NaCl, thin film): 3056, 3027, 2949, 2891, 2827, 1762, 1605, 1491, 1347, 1160, 1092, 1022. HRMS (MM) calc'd for [M+H]⁺ 409.1381, found 409.1363.

B. Copper-Catalyzed Reaction Screen

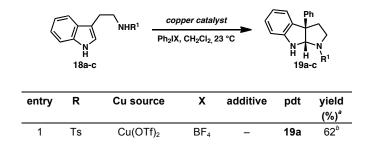
General Procedure – To a flame-dried, 1-dram vial was charged the appropriate tryptamine (0.10 mmol), 4,4'di-*tert*-butylbiphenyl, diaryl iodonium salt (0.11 mmol), copper catalyst (0.010 mmol), and additive (0.10 mmol, if applicable). Anhydrous CH_2Cl_2 (1.0 mL) was then added and the reaction stirred under inert atmosphere and monitored by UHPLC-MS for optimal yield.

The following response factors relative to an internal standard of 4,4'-di-*tert*-butylbiphenyl were measured and calculated based on three runs of varied concentration at $\lambda = 254$ nm:

N-Tosyltryptamine **18a** (Starting Material): Response Factor = 0.117

N-Tosylpyrroloindoline **19a** (Product): Response Factor = 0.253

UHPLC samples were analyzed at $\lambda = 254$ nm and yields calculated based on the above factors.

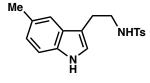


2	Ts	-	BF_4	-	19a	0
3	Boc	Cu(OTf) ₂	BF_4	-	19b	<5
4	Ac	Cu(OTf) ₂	BF_4	-	19c	<5
5	Ts	(CuOTf) ₂ •PhMe	BF_4	-	19a	64
6	Ts	Cul	BF_4	-	19a	0
7	Ts	Cu(MeCN)PF ₆	BF_4	-	19a	0
8	Ts	Cu(OAc) ₂	BF_4	-	19a	64
9	Ts	Cu(OTf) ₂	PF_6	-	19a	28
10	Ts	Cu(OTf)₂	OTf	_	19a	32
11	Ts	Cu(OTf) ₂	CI	-	19a	0
12	Ts	Cu(OTf) ₂	BF_4	dtbpy	19a	<5
13	Ts	Cu(OTf) ₂	BF_4	NaHCO ₃	19a	55
14	Ts	Cu(OTf) ₂	BF_4	AcOH	19a	62
15	Ts	Cu(OTf) ₂	BF₄	_°	19a	65

[a] Determined by HPLC versus an internal standard. [b] Isolated yield. [c] [Ph-I-Mes]BF4 was employed as the electrophile

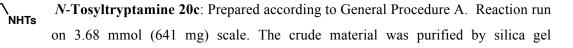
3. Preparation of *N*-tosyltryptamine derivatives (20a – 20j):

General Procedure A – To a solution of tryptamine (1.00 equiv) in CH_2Cl_2 (0.1 M) was added Et_3N (1.50 equiv). The solution was cooled to 0 °C in an ice bath and *p*-toluenesulfonyl chloride (1.01 equiv) added in one portion as solid against a positive steam of nitrogen. The solution was stirred for 15 minutes, then the ice bath removed and allowed to warm up to ambient temperature (20 to 25 °C) and stirred for an additional 4 hours. The reaction was then quenched with 1 N aq. HCl (equal volume to CH_2Cl_2 used) and the organic layer separated and washed with another portion of 1N aq. HCl. The combined aqueous layers were then combined and back extracted with CH_2Cl_2 (20 mL), then the organic layers combined, dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting crude residue was purified by flash chromatography (SiO₂) to afford *N*-tosyltryptamine as a white or off-white solid.



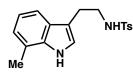
N-Tosyltryptamine 20b: Prepared according to General Procedure A. Reaction run on 6.40 mmol (1.30 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford 20b as a white, amorphous solid (1.58 g, 4.81 mmol, 75 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.98

(s, 1H), 7.67 - 7.60 (m, 2H), 7.25 - 7.19 (m, 3H), 7.17 (dd, J = 1.5, 0.7 Hz, 1H), 7.01 (dd, J = 8.3, 1.6 Hz, 1H), 6.92 (d, J = 2.3 Hz, 1H), 4.46 (t, J = 6.0 Hz, 1H), 3.26 (q, J = 6.5 Hz, 2H), 2.89 (dd, J = 6.9, 6.3 Hz, 2H), 2.41 (s, 3H), 2.40 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) 143.2, 136.7, 134.7, 129.6, 128.7, 127.0, 127.0, 123.8, 122.7, 118.1, 110.9, 110.9, 42.9, 25.4, 21.5, 21.4; FTIR (NaCl, thin film): 3401, 3290, 3042, 2919, 2864, 1597, 1423, 1320, 1303, 1157, 1093. HRMS (MM) calc'd for [M+H]⁺ 329.1318, found 329.1316.



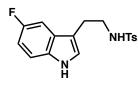
chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **20c** as a white, amorphous solid (940 mg, 2.87 mmol, 78 % yield).

¹H NMR (CDCl₃, 500 MHz) δ 7.94 (s, 1H), 7.67 – 7.59 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 6.92 – 6.86 (m, 2H), 4.46 (t, *J* = 6.1 Hz, 1H), 3.25 (q, *J* = 6.5 Hz, 2H), 2.90 (t, *J* = 6.6 Hz, 2H), 2.45 (s, 3H), 2.40 (s, 3H). ¹³C NMR (CDCl₃, 126 MHz) δ 143.2, 136.8, 136.7, 132.1, 129.6, 127.0, 124.7, 121.9, 121.3, 118.1, 111.3, 111.2, 43.0, 25.5, 21.6, 21.5. FTIR (NaCl, thin film): 3401, 3280, 2913, 2859, 1456, 1404, 1320, 1301, 1157, 1093. HRMS (MM) calc'd for [M+H]⁺ 329.1318, found 329.1307.



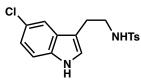
N-Tosyltryptamine 20d: Prepared according to General Procedure A. Reaction run on 3.84 mmol (669 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford 20d as a white, amorphous solid

(1.02g, 3.11 mmol, 81 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 8.27 (s, 1H), 7.90 (d, J = 8.2 Hz, 2H), 7.57 – 7.50 (m, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.24 (dd, J = 9.7, 2.0 Hz, 3H), 4.75 (t, J = 6.1 Hz, 1H), 3.53 (q, J = 6.5 Hz, 2H), 3.18 (t, J = 6.6 Hz, 2H), 2.73 (s, 3H), 2.66 (s, 3H); ¹³C NMR (126 MHz, cdcl₃) δ 143.3, 136.7, 136.0, 129.6, 127.0, 126.3, 122.7, 122.3, 120.5, 119.7, 116.2, 112.0, 43.0, 25.6, 21.5, 16.61 FTIR (NaCl, thin film): 3400, 3275, 3047, 2908, 2849, 1436, 1320, 1303, 1157, 1093, 1063. HRMS (MM) calc'd for [M+H]⁺ 329.1318, found 329.1307.

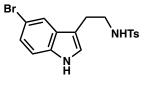


N-Tosyltryptamine 20e: Prepared according to General Procedure A. Reaction run on 3.43 mmol (610 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford 20e as an off-white, amorphous solid (940 mg, 2.83 mmol, 82 % yield). ¹H NMR (CDCl₃, 500 MHz) & 8.12 (s, 1H), 7.64

 $-7.60 \text{ (m, 2H)}, 7.28 - 7.24 \text{ (m, 1H)}, 7.22 \text{ (dd, } J = 8.5, 0.6 \text{ Hz}, 2\text{H}), 7.02 \text{ (d, } J = 2.4 \text{ Hz}, 1\text{H}), 6.99 - 6.89 \text{ (m, 2H)}, 4.45 \text{ (t, } J = 6.0 \text{ Hz}, 1\text{H}), 3.24 \text{ (q, } J = 6.6 \text{ Hz}, 2\text{H}), 2.87 \text{ (dd, } J = 6.8, 6.4 \text{ Hz}, 2\text{H}), 2.40 \text{ (s, 3H)}; {}^{13}\text{C}$ NMR (126 MHz, CDCl₃) δ 157.6 (d, $J_{\text{C-F}} = 233.8 \text{ Hz}$), 143.5, 136.4, 132.8, 129.6, 127.1 (d, $J_{\text{C-F}} = 10.0 \text{ Hz}$), 127.0, 124.4, 111.9 (d, $J_{\text{C-F}} = 8.8 \text{ Hz}$), 111.6 (d, $J_{\text{C-F}} = 5.0 \text{ Hz}$), 110.6 (d, $J_{\text{C-F}} = 26.3 \text{ Hz}$), 103.4 (d, $J_{\text{C-F}} = 22.5 \text{ Hz}$), 42.71, 25.32, 21.47; FTIR (NaCl, thin film): 3392, 3275, 2933, 2864, 1486, 1457, 1319, 1301, 1157, 1093 cm⁻¹. HRMS (MM) calc'd for [M+H]⁺ 333.1068, found 333.1058.

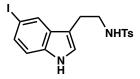


N-Tosyltryptamine 20f: Prepared according to General Procedure A. Reaction run on 3.34 mmol (650 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford 20f as an offwhite, amorphous solid (1.08 g, 3.10 mmol, 92 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 8.18 (s, 1H), 7.65 – 7.57 (m, 2H), 7.28 (d, *J* = 2.0 Hz, 1H), 7.24 (d, *J* = 0.5 Hz, 1H), 7.21 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.11 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 4.49 (t, *J* = 6.0 Hz, 1H), 3.23 (q, *J* = 6.6 Hz, 2H), 2.86 (td, *J* = 6.7, 0.6 Hz, 2H), 2.40 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 143.5, 136.4, 134.7, 129.7, 127.9, 126.9, 125.2, 124.1, 122.5, 117.9, 112.3, 111.2, 42.7, 25.2, 21.5; FTIR (NaCl, thin film): 3385, 3275, 2913, 2859, 1464, 1422, 1319, 1156, 1093 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 349.0772, found 349.0766.



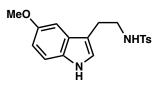
5-Bromo-*N***-Tosyltryptamine 20g**: Reaction run on 7.99 mmol (1.91 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **20g** as a white amorphous solid (2.63g, 6.69 mmol, 84% yield). ¹H NMR (CDCl₃, 500 MHz) δ 8.17 (s, 1H), 7.68 – 7.65 (m, 1H), 7.63 – 7.59 (m,

2H), 7.41 (dd, J = 8.5, 1.6 Hz, 1H), 7.23 (dd, J = 8.5, 0.6 Hz, 2H), 7.12 (dd, J = 8.5, 0.4 Hz, 1H), 6.95 (d, J = 2.3 Hz, 1H), 4.48 (t, J = 6.0 Hz, 1H), 3.23 (q, J = 6.5 Hz, 2H), 2.85 (t, J = 6.6 Hz, 2H), 2.41 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 143.5, 136.4, 135.4, 130.5, 129.7, 129.4, 127.3, 126.9, 123.5, 113.3, 110.9, 82.9, 42.8, 25.2, 21.6; FTIR (NaCl, thin film): 3376, 3290, 2922, 2864, 1598, 1460, 1420, 1320, 1157, 1093 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 393.0267, found 393.0260.



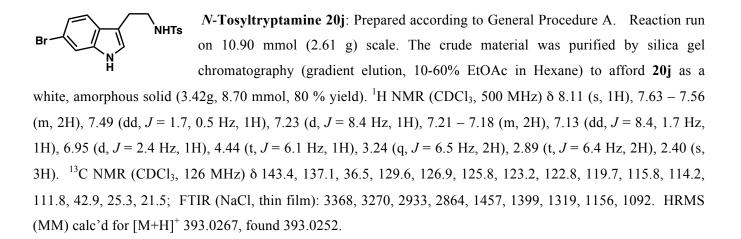
5-Iodo-*N***-tosyltryptamine 20h:** To a 50-mL Schlenk tube was charged 5-bromo-*N*-tosyltryptamine **20g** (858 mg, 2.18 mmol, 1.00 equiv), CuI (42.0 mg, 0.220 mmol, 0.10 equiv), and NaI (654 mg, 4.36 mmol, 2.00 equiv). The vessel was then evacuated and backfilled with N₂ three times, and *N*,*N*'-dimethylethylene diamine (47 μ L, 0.44 mmol,

0.20 equiv) and 1,4-dioxane (2.2 mL) added. The vessel was then sealed and heated to 100 °C for 23 hours, then cooled to room temperature, and quenched with concentrated aqueous NH₄OH (10 mL), then diluted with H₂O (30 mL). The mixture was then extracted with CH₂Cl₂ (3 x 30 mL), the organic layers combined, dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. Flash chromatography (gradient elution, 10-60% EtOAc in Hexanes) afforded 5-iodo-N-tosyltryptamine as a white solid (900 mg, 2.04 mmol, 94% yield). ¹H NMR (CDCl₃, 500 MHz) δ 8.27 (s, 1H), 7.63 – 7.57 (m, 2H), 7.44 (d, *J* = 1.8 Hz, 1H), 7.24 – 7.17 (m, 4H), 6.96 (d, *J* = 2.4 Hz, 1H), 4.62 (t, *J* = 6.0 Hz, 1H), 3.22 (q, *J* = 6.6 Hz, 2H), 2.83 (t, *J* = 6.6 Hz, 2H), 2.40 (s, 3H). ¹³C NMR (CDCl₃, 126 MHz) δ 143.5, 136.3, 134.9, 129.7, 128.5, 126.9, 124.9, 124.0, 120.9, 112.8, 112.6, 111.0, 42.7, 25.1, 21.5; FTIR (NaCl, thin film): 3391, 3290, 2928, 2854, 1598, 1456, 1417, 1319, 1288, 1157, 1093 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 441.0128, found 441.0130.



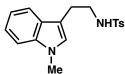
5-Methoxy-*N***-Tosyltryptamine 20i**: Prepared according to General Procedure A. Reaction run on 5.94 mmol (1.13 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 10-60% EtOAc in Hexane) to afford **20i** as a white amorphous solid (1.68g, 4.88 mmol, 82 % yield). ¹H NMR (CDCl₃, 500 MHz)

δ 7.98 (s, 1H), 7.64 – 7.58 (m, 2H), 7.24 (dd, J = 8.7, 0.5 Hz, 1H), 7.20 (d, J = 7.9 Hz, 2H), 6.95 (d, J = 2.3 Hz, 1H), 6.87 – 6.81 (m, 2H), 4.45 (t, J = 6.0 Hz, 1H), 3.80 (s, 3H), 3.25 (q, J = 6.5 Hz, 2H), 2.91 (t, J = 6.6 Hz, 2H), 2.40 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 154.0, 143.3, 136.6, 131.6, 129.6, 127.2, 127.0, 123.3, 112.5, 112.0, 111.2, 100.2, 55.8, 42.8, 25.4, 21.5; FTIR (NaCl, thin film): 3390, 3285, 2928, 2824, 1486, 1459, 1437, 1319, 1215, 1156, 1092 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 345.1267, found 345.1266.



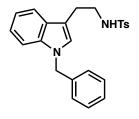
4. Preparation of *N*-tosyl-*N*'-alkyltryptamines (20k - 20l):

General procedure B – To a solution of *N*-tosyltryptamine (1.57 g, 5.00 mmol, 1.00 equiv) in DMF (17 mL) at 20 °C was added NaH (60% dispersion in mineral oil, 0.700 g, 17.5 mmol, 3.5 equiv) slowly, with vigorous stirring, and stirring continued at 20 °C. After 30 minutes, the solution was cooled to 0 °C in an ice bath, and the appropriate alkyl halide (5.00 mmol, 1.00 equiv) was added dropwise by syringe over three minutes. Stirring was continued at 0 °C for two hours, and the reaction allowed to warm to 20 °C and stirring continued for 13 hours. The reaction was then carefully quenched by the dropwise addition of saturated, aqueous ammonium chloride (10 mL), and the mixture diluted with EtOAc (100 mL), and washed with brine (2 x 50 mL). The organic layer was then dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. Flash chromatography (SiO₂) afforded *N*'-alkylated tryptamines as a white solid.



N-tosyl-*N*'-methyltryptamines 20k: Prepared according to General Procedure B. NHTs Reaction run on 5.00 mmol (1.57 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 20-40% EtOAc in Hexane) to afford 20k as a white, amorphous solid (1.18 g, 3.59 mmol, 72 % yield). ¹H NMR (CDCl₃, 500 MHz) & 7.64 (d, J = 8.3 Hz, 2H), 7.40 (d, J = 7.9 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.25 - 7.19 (m, 3H), 7.05 (dd, J = 7.4, 7.4 Hz, 1H), 6.82 (s, 1H), 6.82 (s, 1H), 7.10 Hz, 100 Hz, 14.41 (t, J = 6.0 Hz, 1H), 3.73 (s, 3H), 3.26 (q, J = 6.5 Hz, 2H), 2.92 (t, J = 6.6 Hz, 2H), 2.41 (s, 3H). ¹³C NMR (CDCl₃, 126 MHz) & 143.1, 143.1, 137.0, 136.8, 129.6, 129.5, 129.5, 129.5, 129.5, 129.5, 127.3, 127.2, 126.9, 121.7, 118.9, 118.9, 118.5, 109.9, 109.9, 109.3, 109.3, 43.2, 43.2, 32.6, 32.5, 25.3, 25.3, 21.5, 21.4, 14.1; FTIR

(NaCl, thin film):3292, 3051, 2929, 1616, 1473, 1325, 1158, 1093 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 329.1318, found 329.1314.

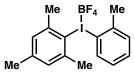


N-tosyl-N'-benzyltryptamines: Prepared according to General Procedure B. Reaction run on 5.00 mmol (1.57 g) scale. The crude material was purified by silica gel chromatography (gradient elution, 20-30% EtOAc in Hexane) to afford 201 as a white, amorphous solid (1.52 g, 3.76 mmol, 75 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.62 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 7.9 Hz, 1H), 7.33 – 7.22 (m, 4H), 7.21 – 7.13 (m, 3H), 7.12 –

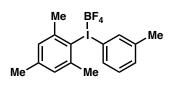
7.07 (m, 2H), 7.06 - 7.01 (m, 1H), 6.85 (s, 1H), 5.23 (s, 2H), 4.44 (t, J = 6.1 Hz, 1H), 3.27 (q, J = 6.6 Hz, 2H), 2.91 (t, J = 6.7 Hz, 2H), 2.38 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 143.2, 137.3, 136.8, 136.8, 129.6, 128.8, 127.7, 127.5, 127.0, 126.8, 126.5, 122.0, 119.3, 118.7, 110.7, 109.8, 49.9, 43.1, 25.5, 21.5; FTIR (NaCl, thin film): 3284, 3057, 3029, 2922, 1597, 1466, 1326, 1159, 1094, 1076 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 405.1557, found 405.1630.

5. Preparation of diaryliodonium tetrafluoroborates:

General Procedure C – To a solution of aryl iodide (1.00 equiv) in Ac₂O (0.5 M) was added mCPBA (1.50 equiv). After stirring 1 hour at 23 °C, the mixture was cooled to 0 °C and mesitylene (1.10 equiv) was added followed by dropwise addition of HBF₄ (50% aq solution, 2.00 equiv). The reaction continued stirring at 0 °C for 30 minutes, followed by 6 hours at 23 °C. The mixture was diluted with water, extracted with CH₂Cl₂, dried over MgSO₄, filtered and concentrated *in vacuo*. Crude reaction mixtures were dissolved in minimal CH₂Cl₂ and precipated with Et₂O to yield fine, white powders. The precipitate was filtered and dried overnight under high vacuum at 100 °C.

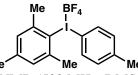


(2-Methylphenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate **(S-1)**: Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.18 g) scale. Trituration afforded **S-1** as a white powder (3.0 g, 7.1 mmol, 71 % yield). ¹H NMR (500 MHz, DMSO) δ 7.96 (d, J = 7.8 Hz, 1H), 7.56 – 7.54 (m, 2H), 7.29 – 7.23 (m, 1H), 7.21 (s, 2H), 2.56 (s, 6H), 2.56 (s, 3H), 2.29 (s, 3H). ¹³C NMR (DMSO, 125 MHz) δ 143.5, 142.1, 141.2, 137.2, 132.9, 132.4, 130.4, 129.8, 122.3, 119.1, 26.6, 24.9, 21.0. FTIR (NaCl, thin film): 1587, 1558, 1457, 1382, 1301, 1064, 1024. HRMS (MM) calc'd for [M]⁺ 337.0448, found 337.0443.



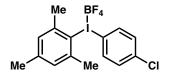
(3-Methylphenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate (S-2): Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.18 g) scale. Trituration afforded S-2 as a white powder (3.9 g, 9.2 mmol, 92 % yield). ¹H NMR (500 MHz, DMSO) δ 7.85 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* =

7.6 Hz, 1H), 7.38 (t, J = 7.8 Hz, 1H), 7.22 (s, 2H), 2.60 (s, 6H), 2.32 (s, 3H), 2.29 (s, 3H); ¹³C NMR (DMSO, 126 MHz) δ 143.5, 142.45, 142.1, 135.1, 133.0, 132.2, 132.0, 130.3, 122.9, 114.8, 26.8, 21.2, 21.0. FTIR (NaCl, thin film): 2913, 1595, 1558, 1452, 1301, 1063, 1024 cm⁻¹; HRMS (MM) calc'd for [M]⁺ 337.0448, found 337.0443.



(4-Methylphenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate (S-3): Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.18 g) scale. Trituration afforded S-3 as a white powder (3.4 g, 8.2 mmol, 80 % yield).

¹H NMR (500 MHz, DMSO) δ 7.90 – 7.84 (m, 2H), 7.31 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.20 (s, 2H), 2.60 (s, 6H), 2.33 (s, 3H), 2.29 (s, 3H). ¹³C NMR (DMSO, 125 MHz) δ 143.5, 142.7, 141.9, 135.0, 133.0, 130.2, 123.2, 111.4, 26.8, 21.7, 21.0. FTIR (NaCl, thin film): 1586, 1451, 1381, 1064, 1024. HRMS (MM) calc'd for [M]⁺ 337.0448, found 447.0446.

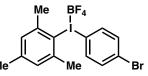


(4-Chlorophenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate (S-5): Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.39 g) scale. Trituration afforded S-5 as a white powder (1.92 g, 4.3 mmol, 44 % yield). ¹H NMR (500 MHz, DMSO) δ 7.99 – 7.93 (m, 2H), 7.60 – 7.55 (m, 2H), 7.23 (d, J = 0.5 Hz, 2H), 2.59 (s, 6H), 2.30 (s, 3H); ¹³C NMR (DMSO, 125 MHz) δ 143.7, 142.1, 137.5, 136.7, 132.3, 130.3, 123.3, 112.8, 26.77, 21.02; FTIR (NaCl, thin film): 1469, 1380, 1301, 1064, 1027 cm⁻¹; HRMS (MM) calc'd for [M-BF₄]⁺ 356.9901, found 356.9895.

(4-Bromophenyl)(2,4,6-trimethylphenyl)iodonium

tetrafluoroborate

(S-6):



Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.83 g) scale. Trituration afforded **S-6** as a white powder (2.67 g, 5.5 mmol, 55 % yield). ¹H NMR (500 MHz, DMSO) δ 7.91 – 7.86 (m, 2H), 7.73 – 7.68 (m, 2H), 7.23 (d, J = 0.5 Hz, 2H), 2.59 (s, 6H), 2.30 (s, 3H). ¹³C NMR (DMSO, 126 MHz) δ 143.8, 142.1, 136.8, 135.2, 130.3, 126.3, 123.2, 113.5, 26.8, 21.0; FTIR (NaCl, thin film): 1085, 1469, 1388, 1303, 1064 1024 cm⁻¹; HRMS (MM) calc'd for $[M-BF_4]^+$ 400.9396, found 400.9392.

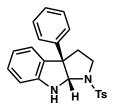
(4-iodophenyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate (S-7): Prepared BF_4 Me according to General Procedure C. Reaction run on 5.0 mmol (1.24 g) scale. Trituration afforded S-7 as a white powder (1.59 g, 3.0 mmol, 30 % yield). ¹H NMR (500 MHz, DMSO) δ 7.88 – 7.82 (m, 2H), 7.73 – 7.69 (m, 2H), 7.22 (s, 2H), 2.58 (s, 6H), 2.30 (s, 3H); ¹³C NMR (DMSO, 125 MHz) & 143.71, 142.06, 140.93, 136.50, 130.31, 123.13, 114.38, 100.25, 26.77, 21.02; FTIR

(NaCl, thin film): 1464, 1380, 1303, 1064, 1024, 984 cm⁻¹; HRMS (MM) calc'd for [M-BF₄]⁺ 448.9258, found 448.9248.

Me BF_4 (4-ethoxycarbonyl)(2,4,6-trimethylphenyl)iodonium tetrafluoroborate (S-8): Prepared according to General Procedure C. Reaction run on 10.0 mmol (2.76 g) scale. Trituration afforded S-8 as a white powder (2.20 g, 4.6 mmol, 46 % yield). CO₂Et Me ¹H NMR (500 MHz, DMSO) δ 8.11 – 8.05 (m, 2H), 8.02 – 7.96 (m, 2H), 7.24 (d, J = 0.5 Hz, 2H), 4.32 (q, J = 7.1) Hz, 2H), 2.59 (s, 6H), 2.30 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H); ¹³C NMR (DMSO, 125 MHz) δ 165.03, 143.8, 142.2, 135.2, 133.1, 132.4, 130.4, 123.2, 119.8, 62.0, 26.8, 21.0, 14.5; FTIR (NaCl, thin film): 2984, 1719, 1583, 1449, 1395, 1365, 1277, 1064, 1024 cm⁻¹; HRMS (MM) calc'd for [M–BF₄]⁺ 395.0502, found 395.0493.

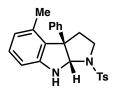
5. Preparation of *N*-tosylpyrroloindolines (19, 21-22):

General Procedure D – To a flame-dried flask was charged the appropriate *N*-tosyltryptamine derivative (0.300 mmol, 1.0 equiv), the appropriate iodonium (0.330 mmol, 1.1 equiv), Cu(OAc)₂ or Cu(OTf)₂ (0.030 mmol or 0.060 mmol, 0.10 equiv or 0.20 mmol) and CH₂Cl₂ (3.0 mL). The reaction was stirred for the time indicated, at which point the reaction was diluted with CH_2Cl_2 (10 mL), and quenched with saturated aq. NaHCO₃ (15 mL). The organic layer was separated and washed with additional NaHCO₃ (2 x 15 mL) and the resulting aqueous layers were then combined and back extracted with CH_2Cl_2 (15 mL). The organic layers were combined, dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. The crude residue was purified by flash chromatography (SiO₂ or basic alumina) to afford the *N*-tosylpyrroloindoline as a white or off-white solid.



Pyrroloindoline 19a: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 4 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in hexanes) to afford **19a** as a white, amorphous solid (72.6 mg, 0.19 mmol, 62 % yield).

¹H NMR (CDCl₃, 500 MHz) δ 7.76 – 7.71 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.25 – 7.15 (m, 3H), 7.14 – 7.09 (m, 3H), 7.00 (ddd, *J* = 7.4, 1.1, 0.5 Hz, 1H), 6.80 – 6.74 (m, 1H), 6.70 (dd, *J* = 7.8, 0.6 Hz, 1H), 5.43 (s, 1H), 4.91 (s, 1H), 3.65 (ddd, *J* = 10.6, 7.8, 1.4 Hz, 1H), 3.25 (td, *J* = 11.0, 5.6 Hz, 1H), 2.48 (ddd, *J* = 12.4, 5.6, 1.0 Hz, 1H), 2.44 (s, 3H), 2.34 (ddd, *J* = 12.4, 11.3, 7.9 Hz, 1H). ¹³C NMR (CDCl₃, 126 MHz) δ 148.8, 143.6, 143.0, 136.3, 131.4, 129.8, 128.8, 128.6, 127.0, 127.0, 125.7, 123.9, 119.6, 110.1, 85.6, 61.8, 48.1, 37.3, 21.5. FTIR (NaCl, thin film): 3366, 2978, 2878, 1610, 1595, 1491, 1466, 1332, 1318, 1303, 1159, 1094. HRMS (MM) calc'd for [M+H]⁺ 391.1475, found 391.1473.



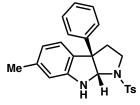
Pyrroloindoline 21a: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **21a** as a white foam (99.4 mg, 0.25 mmol, 82 % yield).

¹H NMR (CDCl₃, 500 MHz) δ 7.78 – 7.70 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.24 – 7.15 (m, 3H), 7.12 – 7.08 (m, 2H), 6.95 (dd, *J* = 6.5, 0.8 Hz, 1H), 6.89 – 6.82 (m, 1H), 6.72 (dd, *J* = 7.4, 7.4 Hz, 1H), 5.47 (s, 1H), 4.70 (s, 1H), 3.67 (ddd, *J* = 10.5, 7.8, 1.5 Hz, 1H), 3.24 (ddd, *J* = 10.9, 10.9, 5.6 Hz, 1H), 2.47 (ddd, *J* = 12.4, 5.6, 1.1 Hz, 1H), 2.44 (s, 3H), 2.35 (ddd, *J* = 12.4, 11.2, 7.8 Hz, 1H), 2.16 (s, 3H). ¹³C NMR (CDCl₃, 126 MHz) δ 147.4, 143.6, 143.1, 136.5, 130.8, 129.8, 129.7, 128.6, 126.98, 126.94, 125.7, 121.4, 119.7, 119.5, 85.5, 62.2, 48.2, 37.6, 21.5, 16.7. FTIR (NaCl, thin film): 3351, 3059, 2892, 1595, 1447, 1332, 1153, 1089. HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1629.

Pyrroloindoline 21b: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material

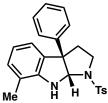
was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **21b** as a white, amorphous solid (76.6 mg, 0.19 mmol, 63 % yield).

¹H NMR (CDCl₃, 500 MHz) δ 7.73 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.25 - 7.16 (m, 3H), 7.15 - 7.10 (m, 2H), 6.91 (dd, J = 7.9, 1.0 Hz, 1H), 6.79 (d, J = 0.4 Hz, 1H), 6.61 (d, J = 7.9 Hz, 1H), 5.41 (s, 1H), 3.64 (ddd, J = 7.9 Hz, 1H), 5.41 (s, 1H), 3.64 (ddd, J = 7.9 Hz, 1H), 5.41 (s, 1H), 5.41 (s, 1H), 3.64 (ddd, J = 7.9 Hz, 1H), 5.41 (s, 1H), 5.41J = 10.5, 7.8, 1.3 Hz, 1H), 3.25 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.38 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.50 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 11.0, 11.0, 5.6 (m, 2H), 2.50 (m, 2H), 12.3, 11.3, 7.9 Hz, 1H), 2.22 (s, 3H). ¹³C NMR (CDCl₃, 126 MHz) & 146.4, 143.5, 143.1, 136.3, 131.7, 129.8, 129.2, 129.0, 128.6, 126.97, 126.95, 125.7, 124.4, 110.1, 85.9, 61.8, 48.1, 37.1, 21.5, 20.9. FTIR (NaCl, thin film): 3385, 2922, 1617, 1597, 1496, 1448, 1340, 1159, 1093. HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1644.



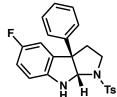
Pyrroloindoline 21c: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford 21c as a white foam (61.0 mg, 0.15 mmol, 50 % yield).

¹H NMR (CDCl₃, 500 MHz) δ 7.77 – 7.70 (m, 2H), 7.30 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.25 -7.14 (m, 3H), 7.13 - 7.07 (m, 2H), 6.88 (d, J = 7.6 Hz, 1H), 6.59 (ddd, J = 7.6, 1.4, 0.7 Hz, 1H), 6.55 - 6.51 (m, 2H), 6.55 (m, 2H), 6.551H), 5.41 (s, 1H), 4.83 (s, 1H), 3.64 (ddd, J = 10.6, 7.8, 1.4 Hz, 1H), 3.27 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.41 (m, 1H), 2.44 (s, 3H), 2.31 (ddd, J = 7.9, 6.9, 5.7 Hz, 1H), 2.28 (s, 3H). ¹³C NMR (CDCl₃, 126 MHz) δ 149.0, 143.6, 143.2, 138.8, 136.4, 129.8, 128.6, 128.6, 127.0, 126.9, 125.7, 123.6, 120.4, 111.0, 85.9, 61.6, 48.2, 37.3, 21.5, 21.5. FTIR (NaCl, thin film): 3353, 2889, 1595, 1490, 1448, 1331, 1307, 1159, 1119, 1092. HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1609.



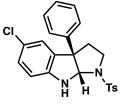
Pyrroloindoline 21d: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 6 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford 21d as a white, crystalline solid (69.2 mg, 0.17 mmol, 57% yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.81 – 7.70 (m, 2H), . Ts 7.30 (d, J = 7.9 Hz, 2H), 7.25 - 7.15 (m, 3H), 7.13 - 7.07 (m, 2H), 6.95 (d, J = 7.4 Hz, 1H), 6.86 (d, J = 7.1 Hz, 1H), 6.72 (dd, J = 7.4, 7.4 Hz, 1H), 5.47 (s, 1H), 4.70 (s, 1H), 3.67 (ddd, J = 10.5, 7.8, 1.4 Hz, 1H), 3.24 (ddd, J = 10.5, 1.4 Hz, 1H), 3.4 Hz, 1H, 1 10.9, 10.9, 5.6 Hz, 1H), 2.47 (ddd, J = 12.4, 5.6, 1.1 Hz, 1H), 2.44 (s, 3H), 2.35 (ddd, J = 12.4, 11.2, 7.8 Hz, 1H), 2.16 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 147.4, 143.6, 143.1, 136.5, 130.8, 129.8, 129.7, 128.6, 127.0, 126.9, 125.7, 121.4, 119.7, 119.5, 85.5, 62.2, 48.2, 37.6, 21.5, 16.7; FTIR (NaCl, thin film): 3350, 2892, 1594, 1490,

1465, 1448, 1331, 1319, 1305, 1243, 1151, 1109, 1089 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1590.



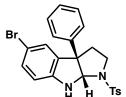
Pyrroloindoline 21e: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 24 hours. Reaction run on 0.30 mmol (99.7 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **21e** as a white, crystalline solid (80.1 mg, 0.20 mmol, 65 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.73 (d, *J* = 8.3 Hz,

2H), 7.30 (d, J = 8.0 Hz, 2H), 7.26 – 7.17 (m, 3H), 7.15 – 7.08 (m, 2H), 6.82 (ddd, J = 8.9, 8.9, 2.6 Hz, 1H), 6.71 (dd, J = 8.2, 2.6 Hz, 1H), 6.63 (dd, J = 8.5, 4.2 Hz, 1H), 5.43 (s, 1H), 3.65 (ddd, J = 10.5, 7.8, 1.4 Hz, 1H), 3.27 (ddd, J = 10.9, 10.9, 5.7 Hz, 1H), 2.48 – 2.39 (m, 1H), 2.44 (s, 3H), 2.33 (ddd, J = 12.5, 11.2, 7.9 Hz, 1H). ¹³C NMR (CDCl₃, 126 MHz) δ 157.4 (d, $J_{C-F} = 235.0$ Hz), 144.7, 143.7, 142.3, 136.1, 133.3 (d, $J_{C-F} = 7.5$ Hz), 129.9, 128.7, 127.3, 127.0, 125.6, 115.2 (d, $J_{C-F} = 22.5$ Hz), 111.2 (d, $J_{C-F} = 23.8$ Hz), 110.8 (d, $J_{C-F} = 7.5$ Hz), 86.2, 62.0, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3365, 2891, 1996, 1593, 1488, 1448, 1329, 1306, 1154, 1091. HRMS (MM) calc'd for [M+H]⁺ 409.1381, found 409.1375.



Pyrroloindoline 21f: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (105 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **21f** as a white, crystalline solid (81.7 mg, 0.19 mmol, 64 % yield).

¹H NMR (CDCl₃, 500 MHz) δ 7.74 – 7.69 (m, 2H), 7.29 (dd, *J* = 8.5, 0.6 Hz, 2H), 7.27 – 7.19 (m, 3H), 7.13 – 7.09 (m, 2H), 7.06 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.93 (d, *J* = 2.1 Hz, 1H), 6.62 (d, *J* = 8.3 Hz, 1H), 5.44 (s, 1H), 4.95 (s, 1H), 3.64 (ddd, *J* = 10.6, 7.8, 1.5 Hz, 1H), 3.27 (ddd, *J* = 11.0, 11.0, 5.6 Hz, 1H), 2.50 – 2.40 (m, 1H), 2.43 (s, 3H), 2.33 (ddd, *J* = 12.5, 11.2, 7.9 Hz, 1H). ¹³C NMR (CDCl₃, 126 MHz) δ 147.3, 143.8, 142.3, 136.1, 133.6, 129.9, 128.8, 128.7, 127.3, 126.9, 125.5, 124.1, 111.0, 85.8, 61.8, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3386, 3059, 2971, 1598, 1481, 1447, 1336, 1258, 1158, 1090 1037. HRMS (MM) calc'd for [M+H]⁺ 425.1085, found 425.1083.

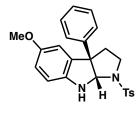


Pyrroloindoline 21g: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 24 hours. Reaction run on 0.30 mmol (118.0 g) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **21g** as a white, crystalline solid (82.1 mg, 0.18 mmol, 58 % yield). ¹H NMR (CDCl₃, 500 MHz) δ

7.75 - 7.69 (m, 2H), 7.29 (dd, J = 8.5, 0.6 Hz, 2H), 7.27 - 7.18 (m, 4H), 7.10 (dd, J = 8.1, 1.5 Hz, 2H), 7.06 (d, J = 2.0 Hz, 1H), 6.58 (d, J = 8.3 Hz, 1H), 5.43 (s, 1H), 4.96 (s, 1H), 3.64 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 10.7 Hz, 10.7 Hz), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 10.7 Hz), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz, 10.7 Hz), 3.27 (ddd, J = 10.7, 7.8, 1.5 Hz), 3.27 Hz), 3.27 Hz)

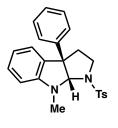
J = 11.0, 11.0, 5.6 Hz, 1H), 2.48 – 2.44 (m, 1H), 2.43 (s, 3H), 2.33 (ddd, J = 8.2, 6.4, 4.8 Hz, 1H). ¹³C NMR (CDCl₃, 126 MHz) 147.8, 143.8, 142.3, 136.1, 134.1, 131.5, 129.9, 128.7, 127.3, 126.9, 126.9, 125.5, 111.5, 111.1, 85.7, 61.8, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3386, 3059, 2971, 1598, 1477, 1336, 1258, 1093, 1037. HRMS (MM) calc'd for [M+H]⁺ 469.0580, found 469.0578.

Pyrroloindoline 21h: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 24 hours. Reaction run on 0.30 mmol (132.1 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **21h** as a white, amorphous solid (92.6 mg, 0.19 mmol, 62 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.33 (dd, *J* = 8.2, 1.8 Hz, 1H), 7.25 (d, *J* = 7.9 Hz, 2H), 7.23 – 7.15 (m, 4H), 7.08 – 7.03 (m, 2H), 6.45 (d, *J* = 8.3 Hz, 1H), 5.38 (d, *J* = 6.8 Hz, 1H), 4.93 (s, 1H), 3.59 (ddd, *J* = 10.6, 7.8, 1.5 Hz, 1H), 3.23 (ddd, *J* = 10.9, 10.9, 5.6 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.39 (s, 3H), 2.28 (ddd, *J* = 12.5, 11.2, 7.8 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) δ 148.4, 143.6, 142.4, 137.4, 136.1, 134.6, 132.6, 129.9, 128.7, 127.3, 126.9, 125.5, 112.2, 85.5, 80.3, 61.6, 48.0, 37.0, 21.5. FTIR (NaCl, thin film): 3385, 3057, 2968, 1597, 1476, 1446, 1420, 1334, 1260, 1159, 1093 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 517.0441, found 517.0436.



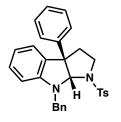
Pyrroloindoline 21i: Prepared according to General Procedure D using 10 mol% $Cu(OAc)_2$ for 6 hours. Reaction run on 0.30 mmol (103.3 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **21i** as a white, amorphous solid (72.6 mg, 0.19 mmol, 62 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.76 – 7.70 (m, 2H), 7.30 (d, J = 7.9 Hz, 2H), 7.25 – 7.15 (m, 3H), 7.15 – 7.08 (m, 2H),

6.69 (dd, J = 8.5, 2.5 Hz, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.60 (d, J = 2.5 Hz, 1H), 5.40 (s, 1H), 4.71 (s, 1H), 3.71 (s, 3H), 3.65 (ddd, J = 10.5, 7.8, 1.3 Hz, 1H), 3.25 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.44 (m, 1H), 2.43 (s, 3H), 2.32 (ddd, J = 12.4, 11.3, 7.9 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) 153.9, 143.6, 142.7, 142.6, 136.3, 133.0, 129.8, 128.6, 127.1, 127.0, 125.7, 113.6, 110.8, 110.6, 86.3, 62.1, 55.8, 48.1, 37.0, 21.5; FTIR (NaCl, thin film): 3380, 3057, 3025, 2947, 2832, 1598, 1492, 1336, 1159, 1093, 1035; HRMS (MM) calc'd for [M+H]⁺ 421.1580, found 421.1577.



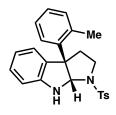
Pyrroloindoline 21k: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 24 hours. Reaction run on 0.30 mmol (98.5 mg) scale. The crude material was purified on basic alumina (gradient elution, 20 - 25% THF in Hexane) to afford **21k** as a white, solid (65.1 mg, 0.16 mmol, 54% yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.71 – 7.65 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.20 – 7.17 (m, 3H), 7.17 – 7.13 (m, 1H), 6.96 – 6.89 (m, 2H), 6.85 (dd, J

= 7.3, 1.1 Hz, 1H), 6.67 (ddd, J = 7.4, 7.4, 0.8 Hz, 1H), 6.50 (d, J = 7.9 Hz, 1H), 5.53 (s, 1H), 3.76 (ddd, J = 12.1, 7.0, 1.0 Hz, 1H), 3.13 (ddd, J = 11.9, 11.9, 5.2 Hz, 1H), 3.06 (s, 3H), 2.44 (s, 3H), 2.21 (ddd, J = 12.2, 5.0, 1.2 Hz, 1H), 2.05 (ddd, J = 12.0, 12.0, 7.1 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) 150.5, 143.6, 143.0, 136.5, 132.2, 129.7, 128.8, 128.4, 127.2, 126.7, 125.9, 123.62, 117.8, 106.2, 91.9, 61.1, 48.8, 38.0, 31.2, 21.5; FTIR (NaCl, thin film): 3056, 3027, 2949, 2891, 2827, 1762, 1605, 1491, 1347, 1160, 1092, 1022 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1600.



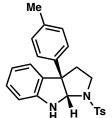
Pyrroloindoline 211: Prepared according to General Procedure D using 10 mol% Cu(OAc)₂ for 24 hours. Reaction run on 0.30 mmol (121 mg) scale. The crude material was purified on basic alumina (gradient elution, 20 - 25% THF in Hexane) to afford **211** as a white foam (83.4 mg, 0.17 mmol, 58% yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.64 – 7.52 (m, 2H), 7.41 – 7.36 (m, 2H), 7.36 – 7.30 (m, 2H), 7.29 – 7.24 (m, 1H), 7.19 – 7.12 (m, 5H), 7.09 – 7.02 (m, 1H),

 $6.89 - 6.81 \text{ (m, 3H)}, 6.64 \text{ (ddd, } J = 7.4, 7.4, 0.9 \text{ Hz}, 1\text{H}), 6.42 \text{ (d, } J = 7.8 \text{ Hz}, 1\text{H}), 5.69 \text{ (s, 1H)}, 4.89 \text{ (d, } J = 16.4 \text{ Hz}, 1\text{H}), 3.82 \text{ (dd, } J = 12.5, 6.8 \text{ Hz}, 1\text{H}), 3.25 \text{ (ddd, } J = 12.2, 12.2, 5.1 \text{ Hz}, 1\text{H}), 2.41 \text{ (s, 3H)}, 2.24 \text{ (dd, } J = 11.9, 4.7 \text{ Hz}, 1\text{H}), 2.06 \text{ (ddd, } J = 12.1, 12.1, 7.2 \text{ Hz}, 1\text{H}); ¹³C NMR (CDCl₃, 126 MHz) & 149.7, 143.6, 143.5, 138.5, 136.4, 132.2, 129.7, 128.7, 128.4, 128.4, 127.3, 127.2, 126.9, 126.7, 125.8, 123.9, 117.9, 106.5, 90.7, 61.3, 48.5, 48.1, 38.2, 21.5; FTIR (NaCl, thin film): 3062, 3027, 2898, 1604, 1493, 1346, 1158, 1089 \text{ cm}^{-1}; HRMS (MM) \text{ calc'd for } [M+H]^+ 481.1944, found 481.1947.$



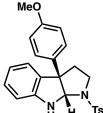
Pyrroloindoline 22a: Prepared according to General Procedure D using 20 mol% Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale with the symmetric di-*o*-tolyliodonium tetrafluoroborate. The crude material was purified by silica gel chromatography (gradient elution, 20% EtOAc in Hexane) to afford **22a** as a white, amorphous solid (60.6 mg, 0.15 mmol, 50 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.69 –

7.63 (m, 2H), 7.20 (d, J = 7.9 Hz, 2H), 7.14 – 7.04 (m, 4H), 7.03 – 6.98 (m, 1H), 6.92 (dd, J = 7.4, 0.8 Hz, 1H), 6.76 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 6.65 (d, J = 7.8 Hz, 1H), 5.67 (s, 1H), 4.94 (s, 1H), 3.59 (ddd, J = 10.1, 7.7, 4.0 Hz, 1H), 3.36 (ddd, J = 10.1, 8.6, 6.6 Hz, 1H), 2.69 (ddd, J = 12.9, 7.9, 7.9 Hz, 1H), 2.40 (s, 3H), 2.39 – 2.34 (m, 1H), 2.03 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 148.4, 143.5, 139.4, 136.4, 135.6, 132.6, 131.9, 129.6, 128.5, 127.2, 127.1, 127.0, 125.7, 124.3, 119.2, 109.4, 84.4, 62.1, 47.4, 37.9, 21.4, 20.8; FTIR (NaCl, thin film): 3390, 3057, 2975, 2883, 1606, 1485, 1338, 1158 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1633.



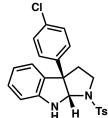
Pvrroloindoline 22b: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 20% EtOAc in Hexane) to afford 22b as a white, amorphous solid (90.0 mg, 0.22 mmol, 74 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.76 –

4.7, 4.0 Hz, 2H), 6.99 (ddd, J = 3.8, 3.8, 1.6 Hz, 3H), 6.77 (ddd, J = 7.4, 1.0 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.39 (s, 1H), 3.64 (ddd, J = 10.6, 7.8, 1.4 Hz, 1H), 3.25 (ddd, J = 10.9, 10.9, 5.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.44 (s, 3H), 2.37 – 2.29 (m, 1H), 2.28 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 148.7, 143.6, 140.0, 136.7, 136.31, 131.6, 129.8, 129.2, 128.7, 127.0, 125.6, 123.8, 120.0, 110.1, 85.7, 61.5, 48.1, 37.3, 21.5, 20.9; FTIR (NaCl, thin film): 3395, 3052, 3022, 2913, 1607, 1465, 1336, 1159, 1094, 1035 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1624.



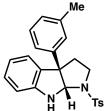
Pyrroloindoline 22c: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 4 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 6:3:1 Hexanes:CH₂Cl₂:Acetone) to afford 22c as a white foam (88.1 mg, 0.21 mmol, 70 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.75 – 7.70 (m, 2H), 7.30 (dd, J = 8.5, 0.6 Hz, 2H), 7.11 (ddd, J = 7.9, 7.4, 1.3 Hz, 1H), 7.04 – 6.96 (m, ĥ Ъ́тs 3H), 6.80 - 6.72 (m, 3H), 6.71 - 6.67 (m, 1H), 5.36 (s, 1H), 4.89 (br s, 1H), 3.74 (s, 3H), 3.63 (ddd, J = 10.6, 7.8, 10.6) 1.5 Hz, 1H), 3.23 (td, J = 10.9, 5.6 Hz, 1H), 2.47 – 2.40 (m, 1H), 3.2.44 (s, 3H) 2.32 (ddd, J = 12.4, 11.2, 7.8 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) δ 158.5, 148.77, 143.6, 136.3, 135.0, 131.7, 129.8, 128.7, 127.0, 126.8, 123.8, 119.6, 113.9, 110.1, 85.8, 61.2, 55.2, 48.2, 37.3, 21.5; FTIR (NaCl, thin film): 3390, 3047, 2953, 2834, 1608, 1512, 1483, 1466, 1336, 1251, 1183, 1159, 1094 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 421.1580, found

421.1580.



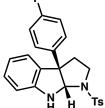
Pyrroloindoline 22d: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford 22d as a white, amorphous solid (86.5 mg, 0.20 mmol, 68 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.76 - 7.69 (m, 2H), 7.30 (dd, J = 8.5, 0.6 Hz, 2H), 7.21 – 7.15 (m, 2H), 7.15 – 7.09 (m, 1H), 7.06 – 7.00 (m, 2H),

6.95 (ddd, J = 7.4, 1.2, 0.5 Hz, 1H), 6.77 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (dd, J = 4.5, 4.0 Hz, 1H), 5.37 (s, 3.51 Hz)1H), 4.91 (br s, 1H), 3.65 (ddd, J = 10.7, 7.8, 1.5 Hz, 1H), 3.24 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.44 (s, 3H), 2.28 (ddd, J = 12.4, 11.2, 7.8 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) δ 148.7, 143.7, 141.5, 136.2, 132.9, 131.0, 129.9, 129.0, 128.7, 127.1, 126.9, 123.7, 119.7, 110.2, 85.6, 61.3, 48.1, 37.1, 21.5; FTIR (NaCl, thin film): 3386, 3051, 2970, 2893, 1607, 1493, 1466, 1483, 1399, 1336, 1159, 1093 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 425.1085, found 425.1077.



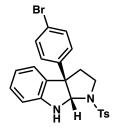
Pyrroloindoline 22e: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 20% EtOAc in Hexane) to afford **22e** as a white, amorphous solid (75.2 mg, 0.19 mmol, 63% yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.77 – 7.72 (m, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.14 – 7.08 (m, 2H), 7.02 – 6.97 (m, 2H), 6.92 – 6.86 (m,

2H), 6.77 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.42 (s, 1H), 3.66 (ddd, J = 10.6, 7.8, 1.4 Hz, 1H), 3.25 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.45 (m, 1H), 2.44 (s, 3H), 2.32 (ddd, J = 12.5, 11.4, 7.9 Hz, 1H), 2.25 (s, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 148.8, 143.6, 143.0, 138.2, 136.4, 131.4, 129.9, 128.7, 128.4, 127.8, 127.0, 126.3, 124.0, 122.8, 119.6, 110.1, 85.7, 61.8, 48.2, 37.6, 21.5, 21.5; FTIR (NaCl, thin film): 3390, 2047, 2970, 1607, 1483, 1466, 1340, 1159, 1094 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 405.1631, found 405.1626.



Pyrroloindoline 22f: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford 22f as a white, amorphous solid (80.3 mg, 0.20 mmol, 66 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.77 – 7.70 (m, 2H), **s** 7.30 (dd, J = 8.5, 0.6 Hz, 2H), 7.16 – 7.09 (m, 1H), 7.09 – 7.04 (m, 2H), 6.97 (ddd, J = 7.4,

1.2, 0.5 Hz, 1H), 6.93 – 6.86 (m, 2H), 6.78 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.38 (s, 1H), 3.66 (ddd, J = 10.6, 7.8, 1.4 Hz, 1H), 3.24 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.42 (m, 1H), 2.44 (s, 3H), 2.30 (ddd, J = 12.4, 11.2, 7.8 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) δ 161.6 (d, $J_{C-F} = 245.0$ Hz), 148.7, 143.7, 138.7, 138.7, 136.2, 131.3, 129.8, 128.9, 127.3 (d, $J_{C-F} = 7.5$ Hz), 126.9, 123.7, 119.7, 115.3 (d, $J_{C-F} = 20.0$ Hz), 110.2, 109.9, 85.7, 61.2, 48.1, 37.3, 21.5; FTIR (NaCl, thin film): 3391, 3051, 2970, 2892, 1607, 1510, 1483, 1466, 1400, 1336, 1233, 1160, 1095 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 409.1381, found 409.1363.



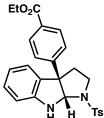
Pyrroloindoline 22g: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexane) to afford **22g** as a white, amorphous solid (83.4 mg, 0.19 mmol, 59 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.76 – 7.69 (m, 2H), 7.36 – 7.28 (m, 4H), 7.12 (ddd, *J* = 7.7, 7.7,

1.2 Hz, 1H), 7.00 – 6.92 (m, 3H), 6.77 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.37 (s, 1H), 4.91

(s, 1H), 3.65 (ddd, J = 10.7, 7.8, 1.4 Hz, 1H), 3.24 (ddd, J = 10.9, 10.9, 5.6 Hz, 1H), 2.49 – 2.40 (m, 1H), 2.44 (s, 3H), 2.27 (ddd, J = 12.4, 11.2, 7.9 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) δ 148.6, 143.7, 142.0, 136.1, 131.6, 130.9, 129.9, 129.0, 127.5, 126.9, 123.71, 121.0, 119.7, 110.2, 85.5, 61.4, 48.1, 37.0, 21.5; FTIR (NaCl, thin film): 3391, 3051, 2970, 2892, 1608, 1597, 1484, 1466, 1396, 1336, 1159, 1095 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 469.0580, found 469.0553.

Pyrroloindoline 22h: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94 mg) scale. The crude material was purified on basic alumina (gradient elution, 40% THF in Hexanes) to afford 22h as a white, amorphous solid (95.8 mg, 0.19 mmol, 62 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.75 – 7.69 (m, 2H),
Ts 7.55 – 7.51 (m, 2H), 7.30 (d, J = 7.9 Hz, 2H), 7.12 (ddd, J = 7.7, 7.7, 1.2 Hz, 1H), 6.96 – 6.92

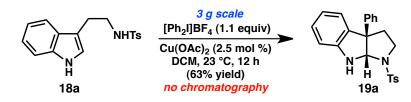
h Ts 7.55 – 7.51 (m, 2H), 7.30 (d, J = 7.9 Hz, 2H), 7.12 (ddd, J = 7.7, 7.7, 1.2 Hz, 1H), 6.96 – 6.92 (m, 1H), 6.88 – 6.83 (m, 2H), 6.76 (ddd, J = 7.4, 7.4, 1.0 Hz, 1H), 6.70 (d, J = 7.8 Hz, 1H), 5.35 (s, 1H), 3.64 (ddd, J = 10.7, 7.8, 1.4 Hz, 1H), 3.24 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.49 – 2.39 (m, 1H), 2.44 (s, 3H), 2.26 (ddd, J = 12.4, 11.2, 7.9 Hz, 1H); ¹³C NMR (CDCl₃, 126 MHz) δ 148.7, 143.8, 142.8, 137.6, 136.2, 130.9, 129.9, 129.0, 127.7, 126.9, 123.7, 119.8, 110.3, 92.5, 85.5, 61.5, 48.1, 36.9, 21.6; FTIR (NaCl, thin film): 3390, 3047, 2948, 2878, 1612, 1486, 1336, 1158, 1005 cm⁻¹; HRMS (MM) calc'd for [M+H]⁺ 517.0441, found 517.0424.



Pyrroloindoline 22i: Prepared according to General Procedure D using 20 mol % Cu(OTf)₂ for 12 hours. Reaction run on 0.30 mmol (94.0 mg) scale. The crude material was purified by silica gel chromatography (gradient elution, 6:3:1 Hexanes:DCM:Acetone) to afford **22i** as a colorless oil (78.2 mg, 0.17 mmol, 56 % yield). ¹H NMR (CDCl₃, 500 MHz) δ 7.91 – 7.85

N H Ts (m, 2H), 7.75 – 7.69 (m, 2H), 7.29 (dd, J = 8.5, 0.6 Hz, 2H), 7.21 – 7.15 (m, 2H), 7.14 – 7.08 (m, 1H), 6.96 (ddd, J = 7.4, 1.2, 0.5 Hz, 1H), 6.76 (ddd, J = 7.5, 7.5, 1.0 Hz, 1H), 6.71 (dd, J = 7.2, 0.7 Hz, 1H), 5.43 (s, 1H), 4.92 (s, 1H), 4.34 (q, J = 7.1 Hz, 2H), 3.66 (ddd, J = 10.7, 7.8, 1.4 Hz, 1H), 3.26 (ddd, J = 11.0, 11.0, 5.6 Hz, 1H), 2.49 (ddd, J = 12.3, 5.5, 1.0 Hz, 1H), 2.43 (s, 3H), 2.31 (ddd, J = 12.4, 11.3, 7.9 Hz, 1H), 1.36 (t, J = 7.1 Hz, 3H); ¹³C NMR (CDCl₃, 126 MHz) δ 166.1, 148.7, 148.0, 143.8, 136.2, 130.9, 129.9, 129.9, 129.7, 129.0, 126.9, 125.63, 123.8, 119.7, 110.2, 85.4, 61.8, 60.9, 48.1, 37.1, 21.5, 14.3; FTIR (NaCl, thin film): 3387, 3052, 2979, 2895, 1713, 1610, 1483, 1467, 1343, 1278, 1160, 1110 cm⁻¹. HRMS (MM) calc'd for [M+H]⁺ 463.1686, found 463.1666.

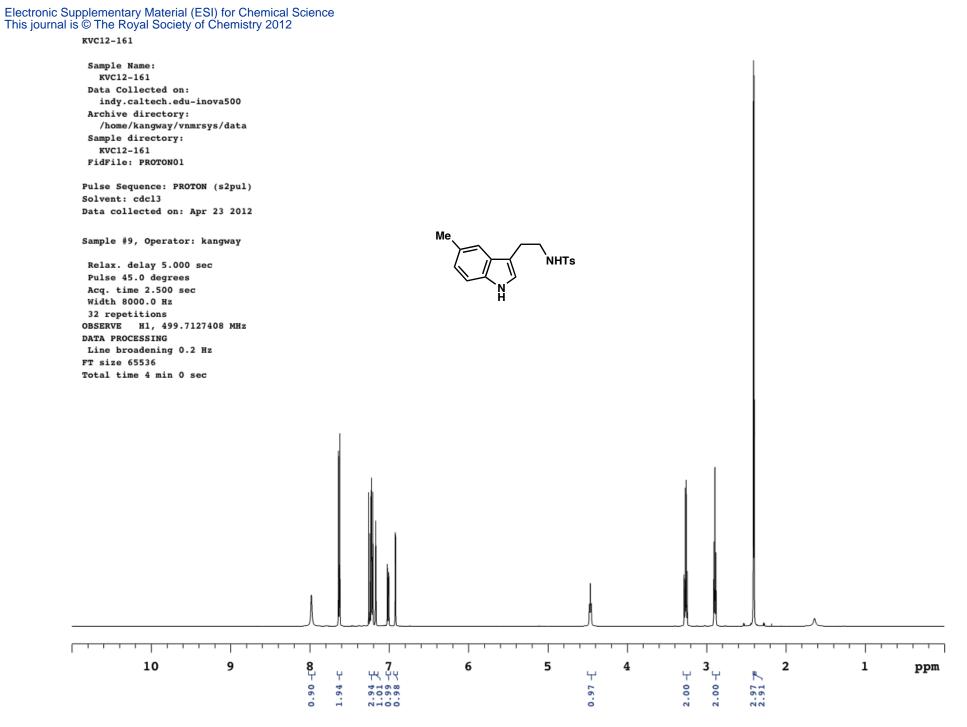
6. Catalyst Efficiency and Scalability



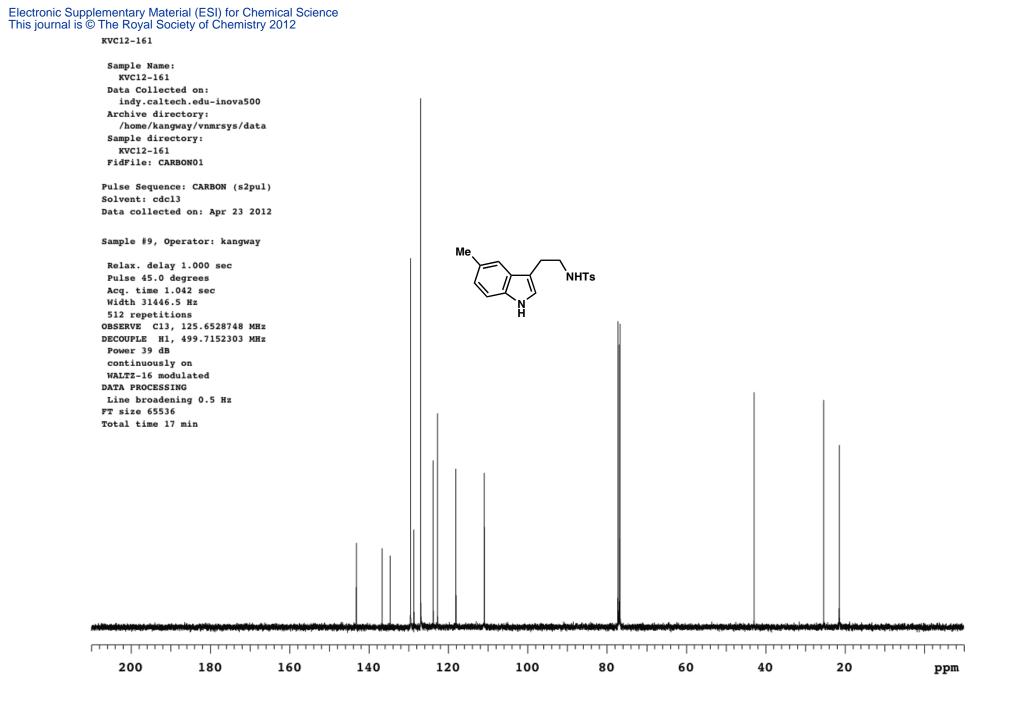
To a flame-dried, 100 mL flask was charged *N*-tosyltryptamine (3.15 g, 10.0 mmol, 1.0 equiv), Ph_2IBF_4 (4.04 g, 11.0 mmol, 1.1 equiv) and $Cu(OAc)_2$ (45.4 mg, 0.25 mmol, 0.025 equiv). The dissolved in 50 mL CH_2Cl_2 and allowed to stir at room temperature for 12 hours at which point the reaction was diluted with CH_2Cl_2 (100 mL), washed with saturated aqueous NaHCO₃ (2 x 50 mL) and the resulting aqueous layers were then combined and back extracted with CH_2Cl_2 (50 mL). The organic layers were combined, dried over anhydrous Na₂SO₄, filtered, and concentrated *in vacuo*. The resultant yellow solid was dissolved in 50 mL CH_2Cl_2 , 100 mL Et_2O and 200 mL hexanes to afford a light yellow powder. The powder was filtered and dried under vacuum to give **19a** (2.55g, 6.5 mmol, 65% yield).

References

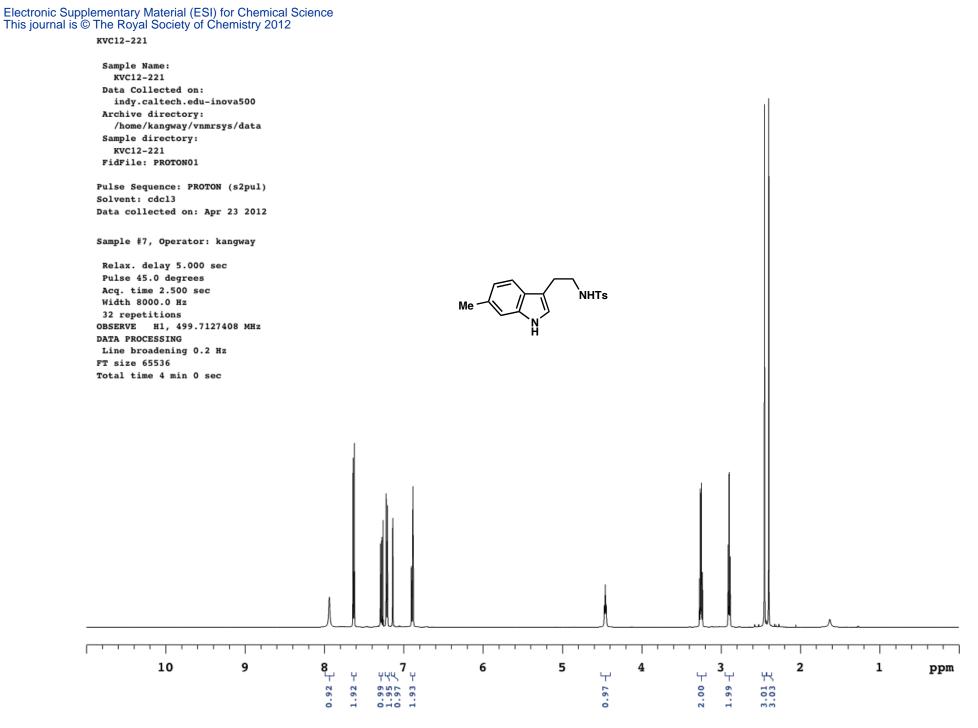
¹ Still, W. C., Kahn, M. & Mitra, A. Rapid chromatographic technique for preparative separations with moderate resolution. *J. Org. Chem.* **43**, 2923-2925 (1978).



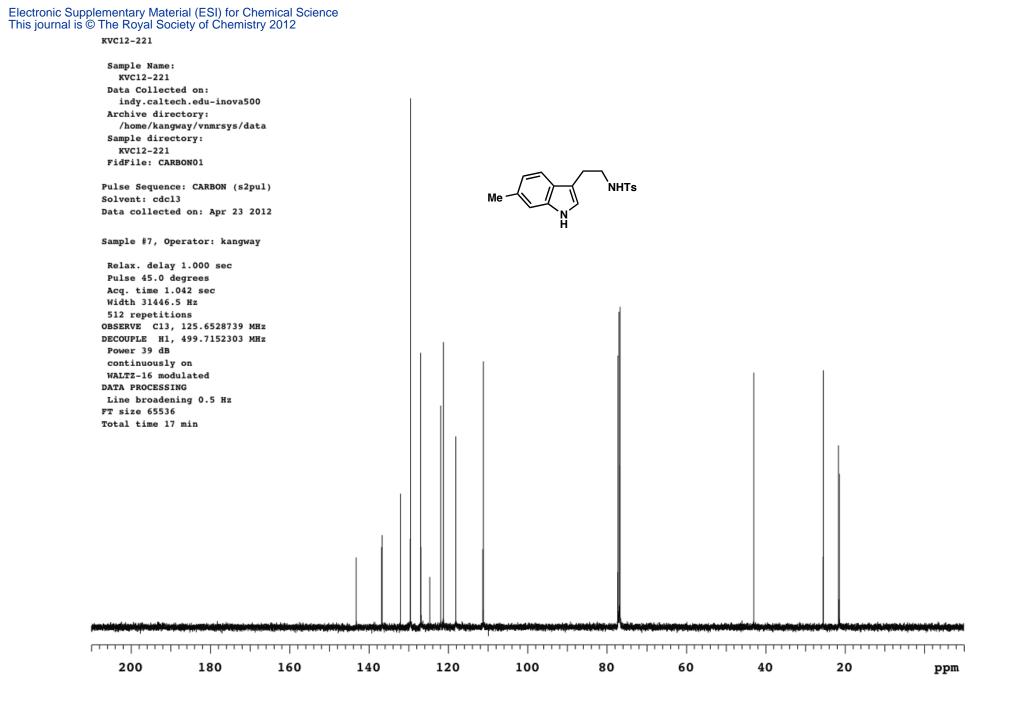
A second to the Safety of the second s



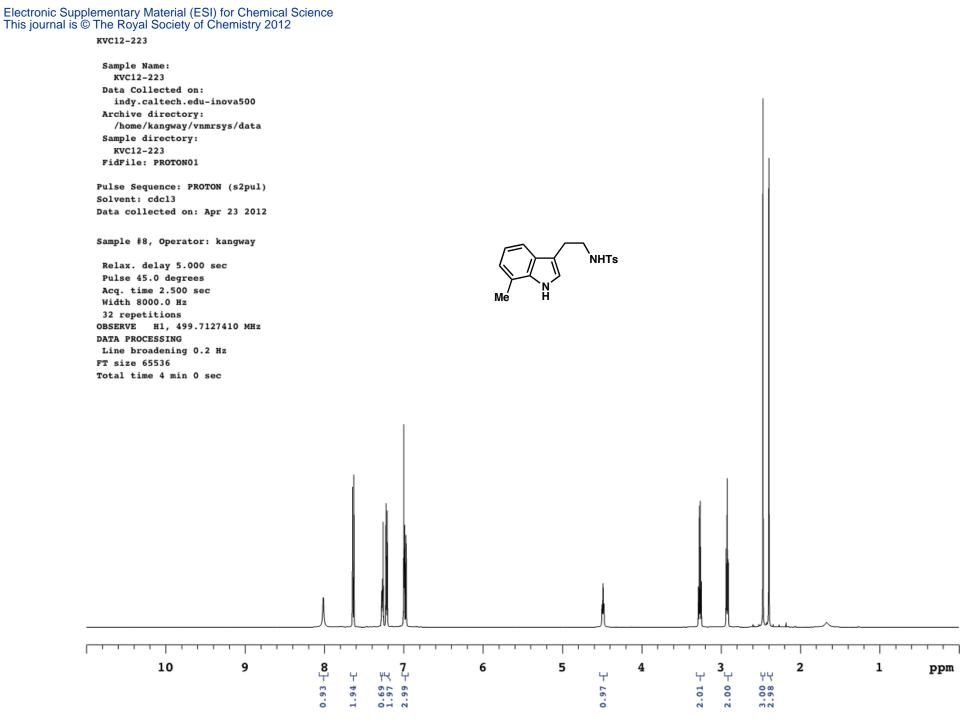
Storada Saturation



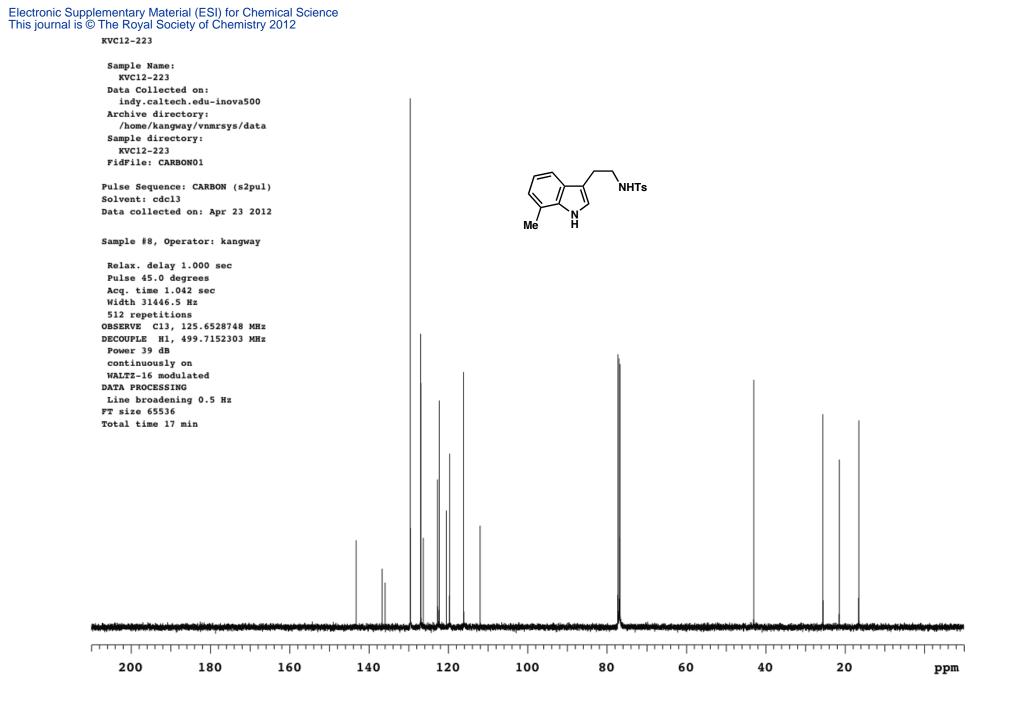
Steers between the second



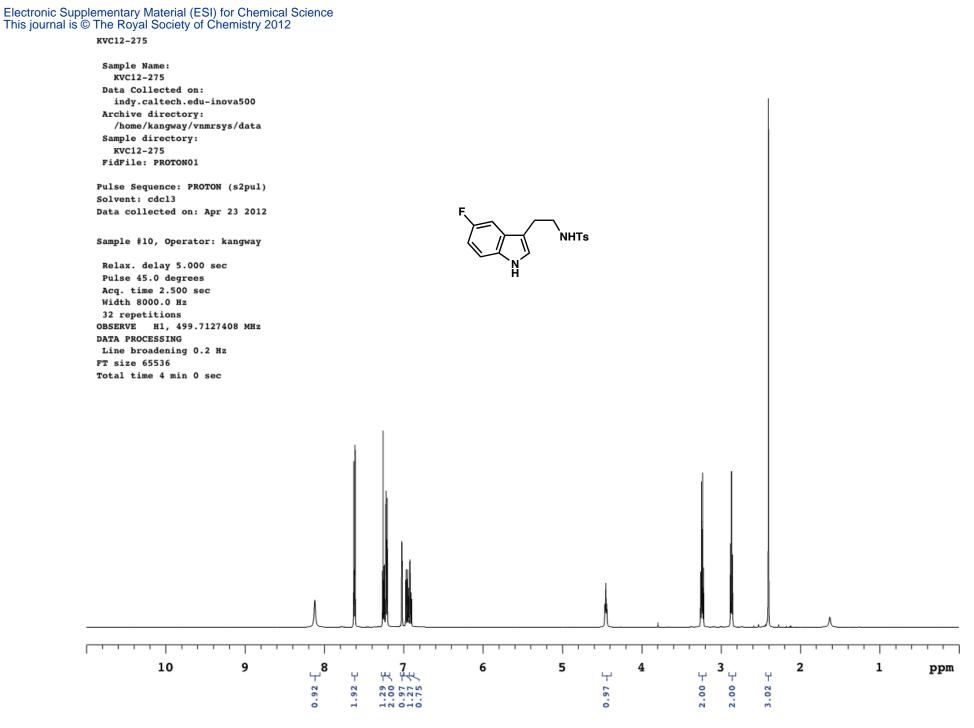
Storador - Saturation



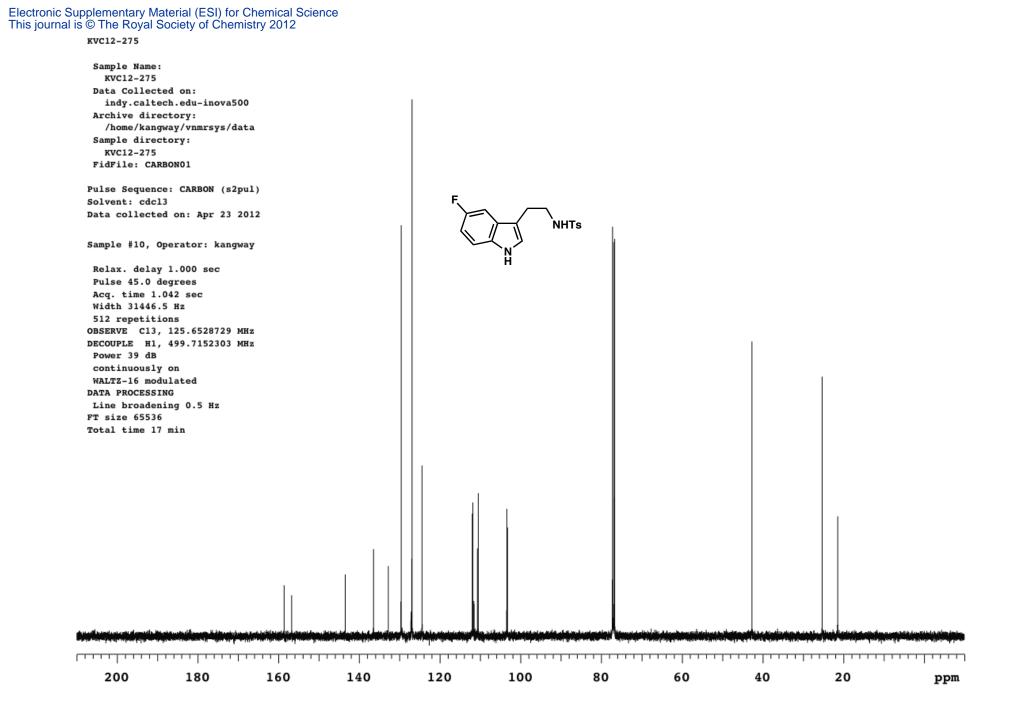
March 1997 - Set and a Set in the



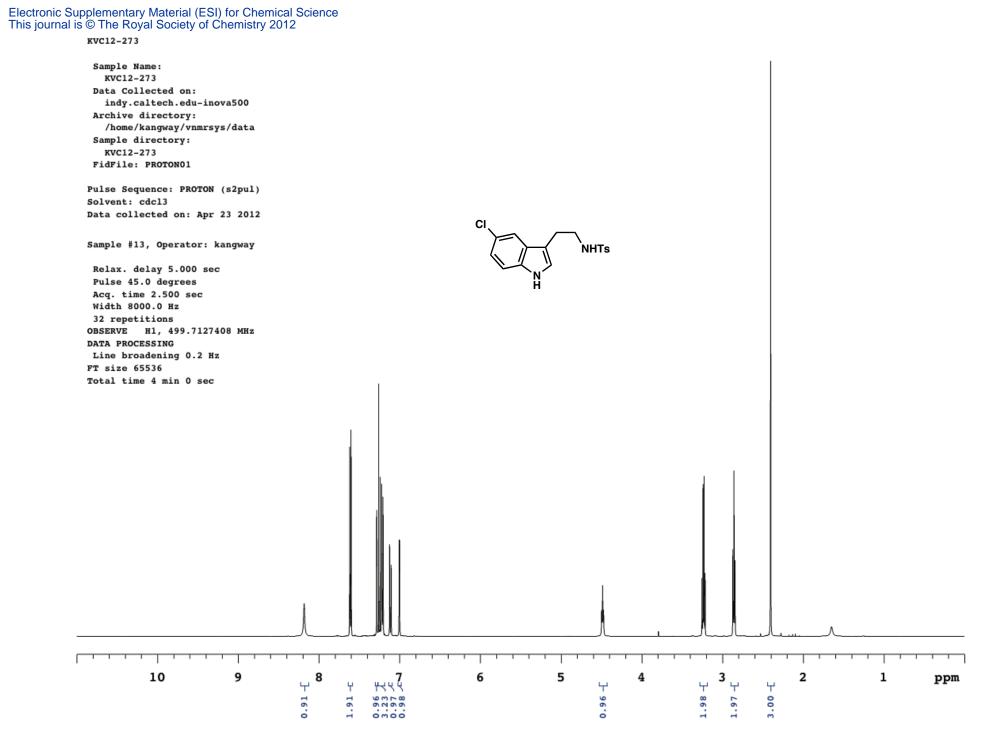
24.85 million 284.5



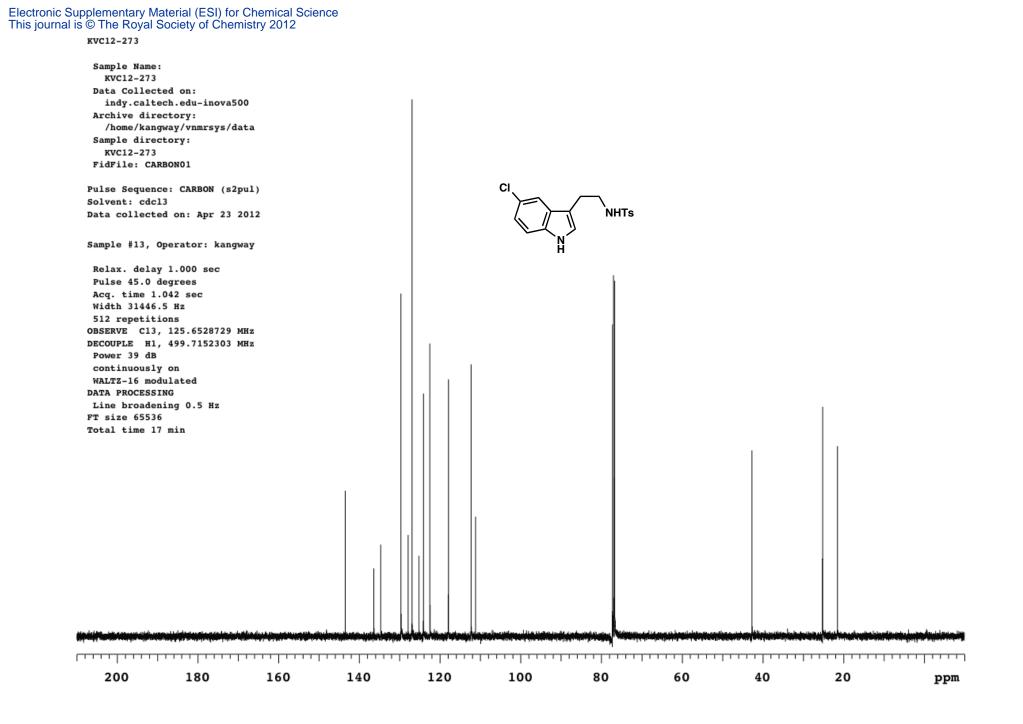
· 같은 이 아이는 것을 같은 것이 아이는 것을 같은 것을 하는 것을 수 있다.



Second the second second second



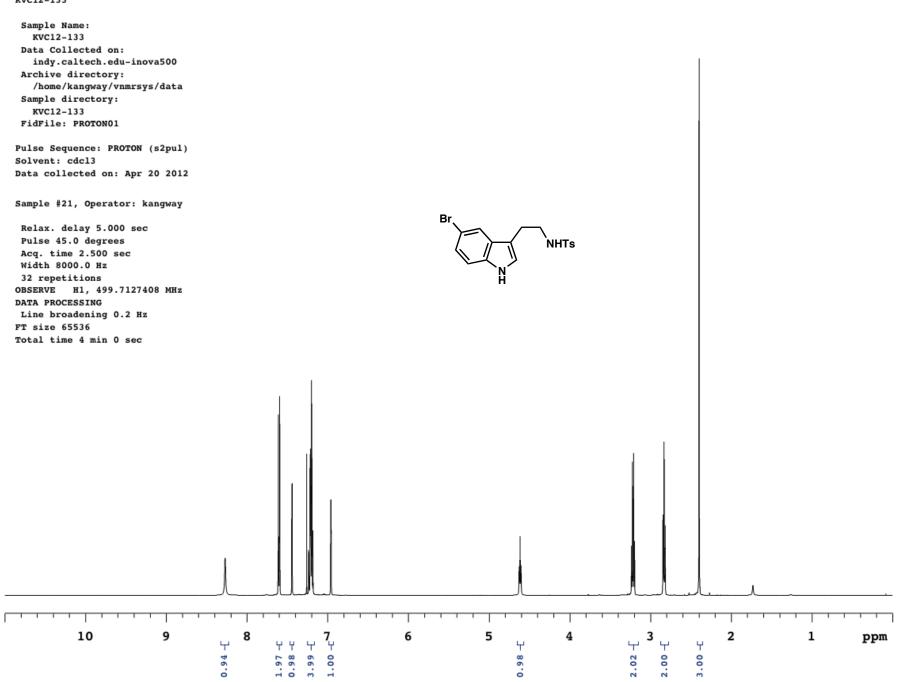
Alexandream Saturation in the



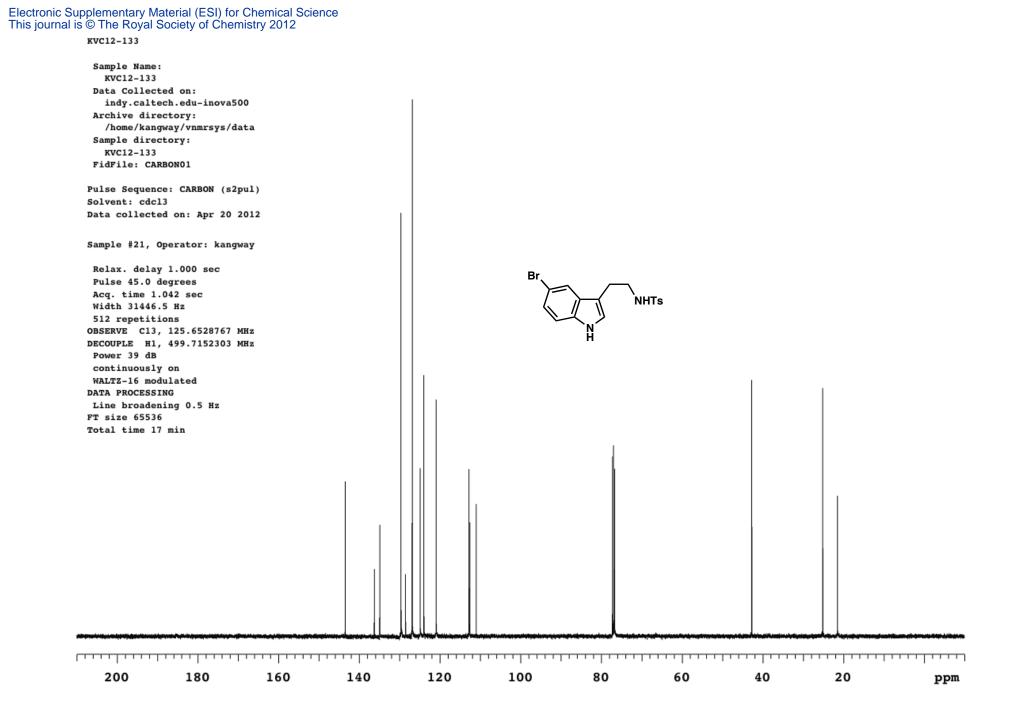
Market and the second sec

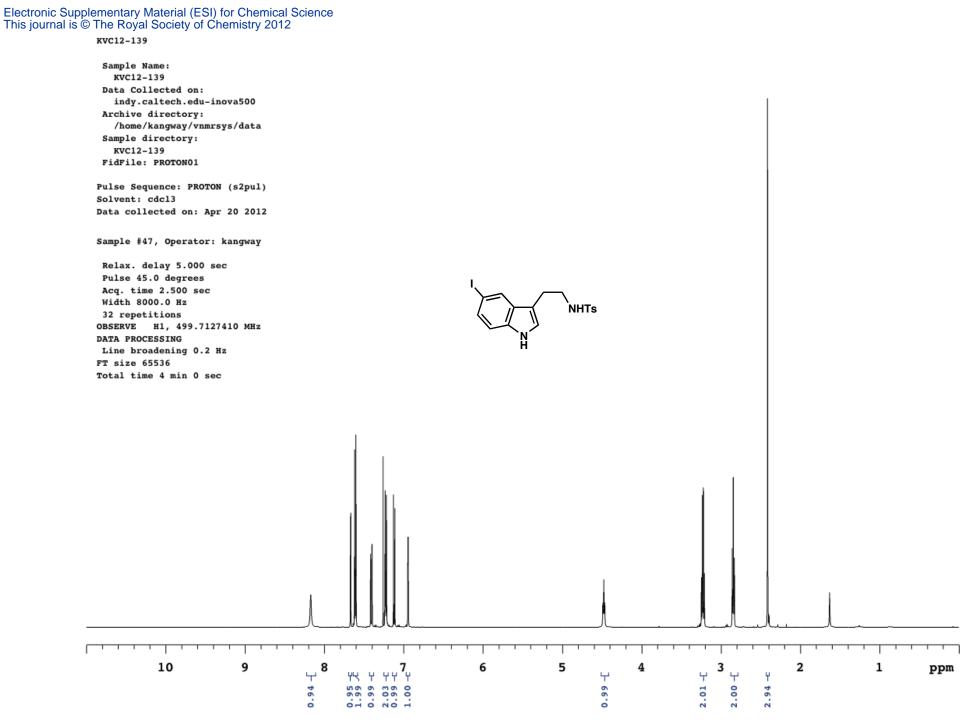
Electronic Supplementary Material (ESI) for Chemical Science This journal is © The Royal Society of Chemistry 2012

KVC12-133

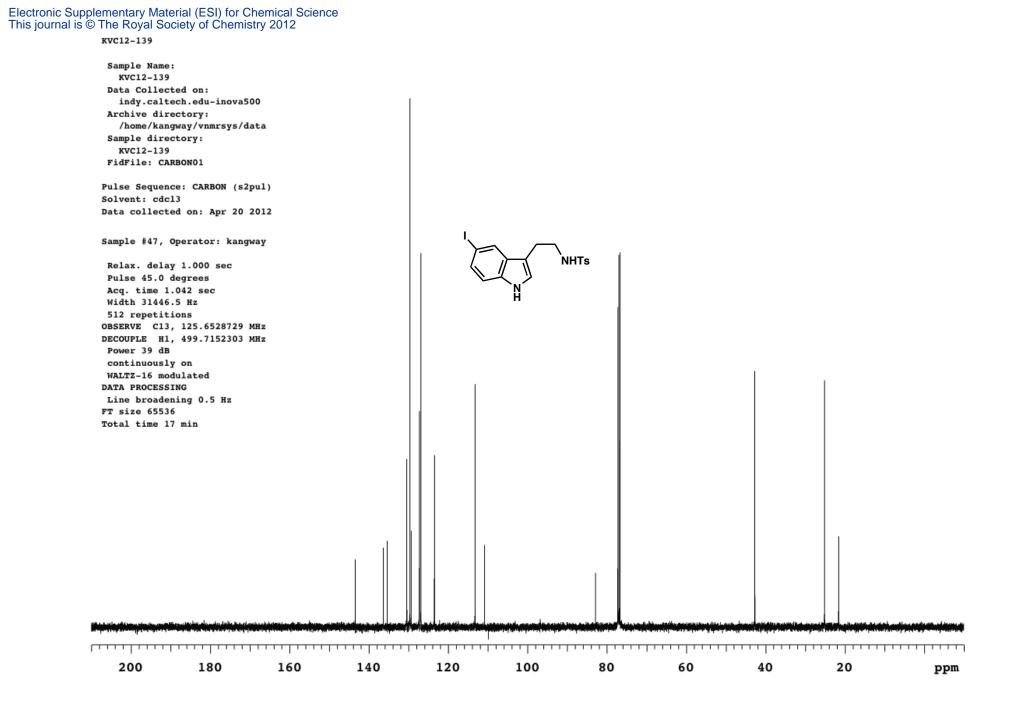


Sheet and the State area and

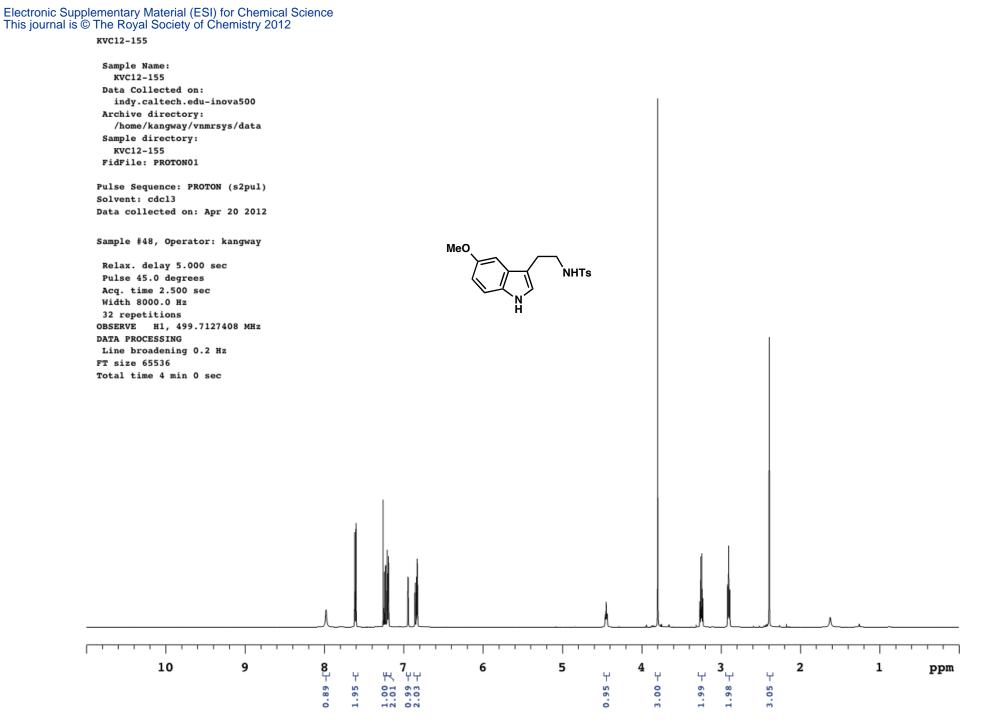




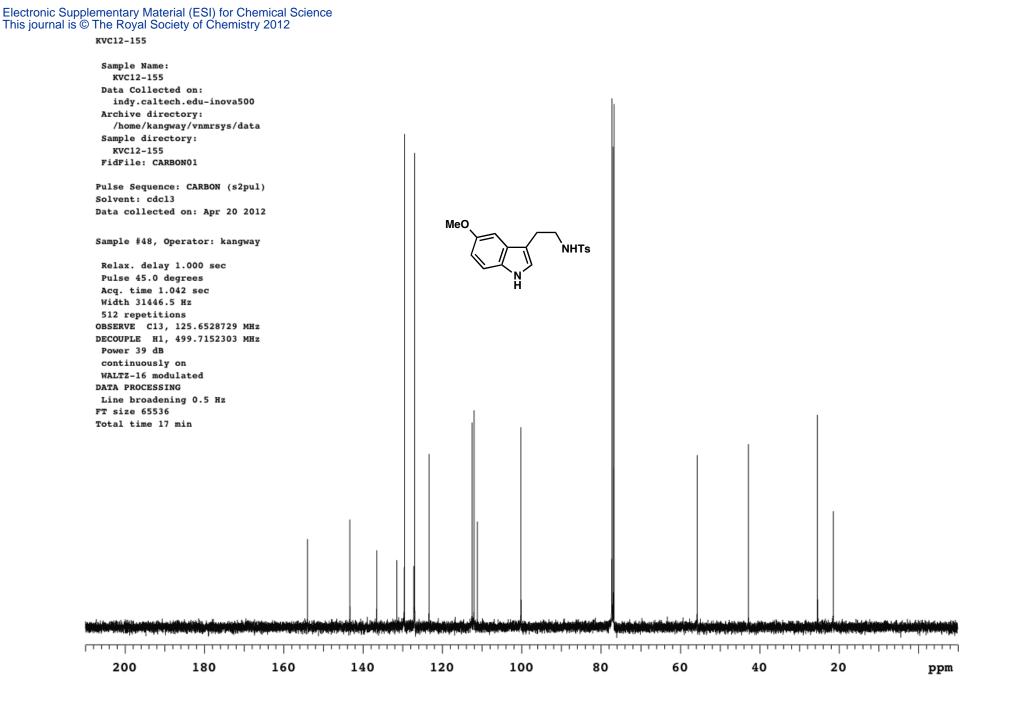
Storage States and a set of



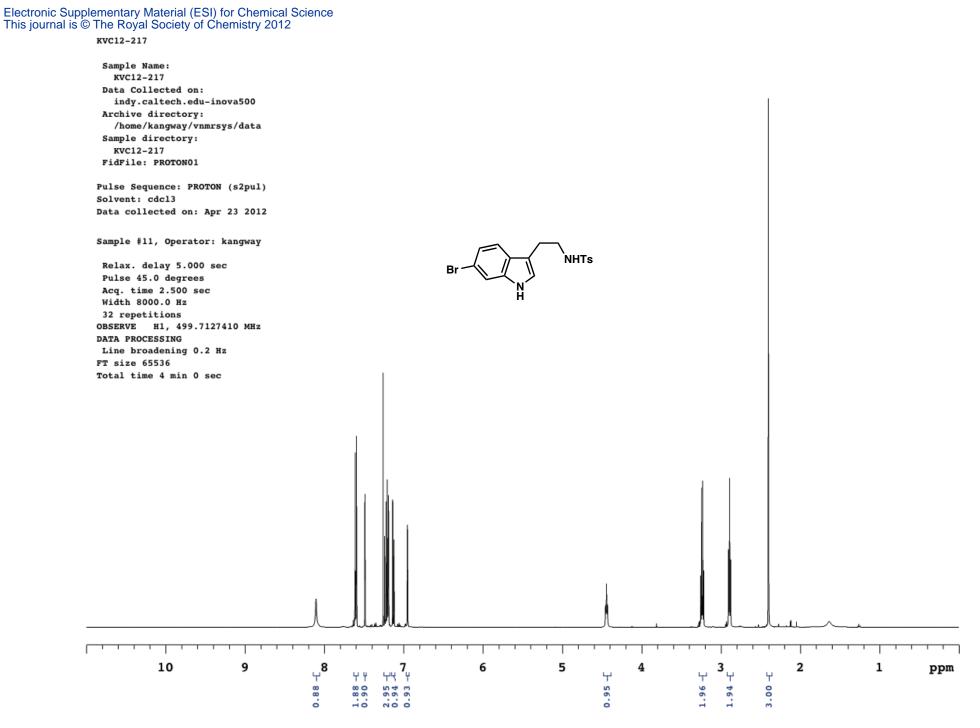
A state of the second sec



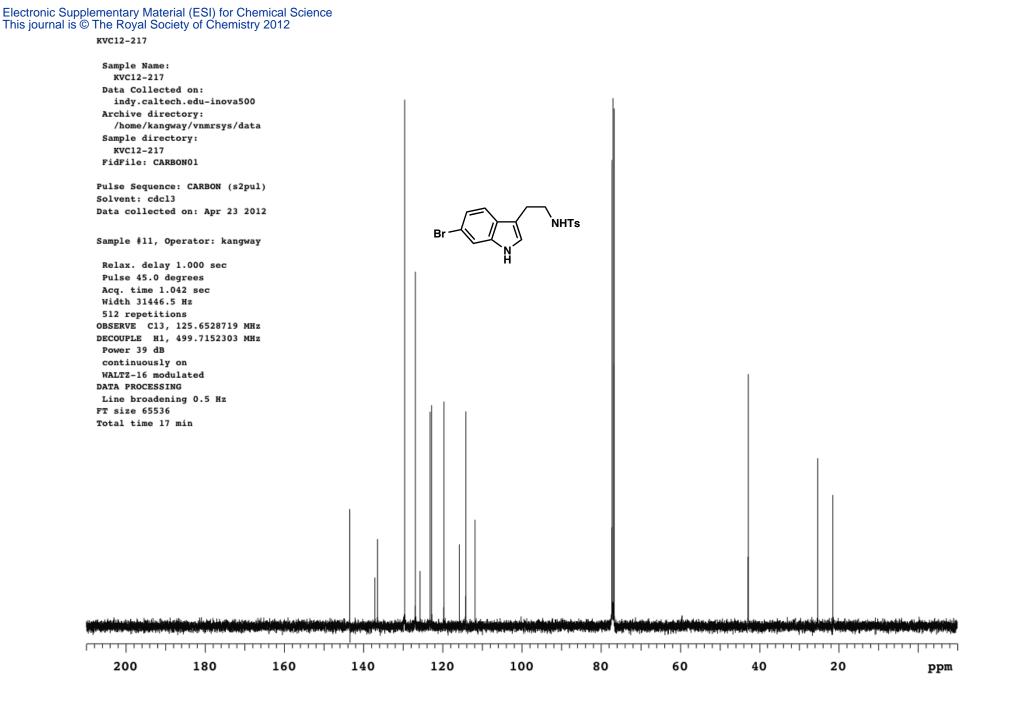
Maximum Set of Set of the Set of



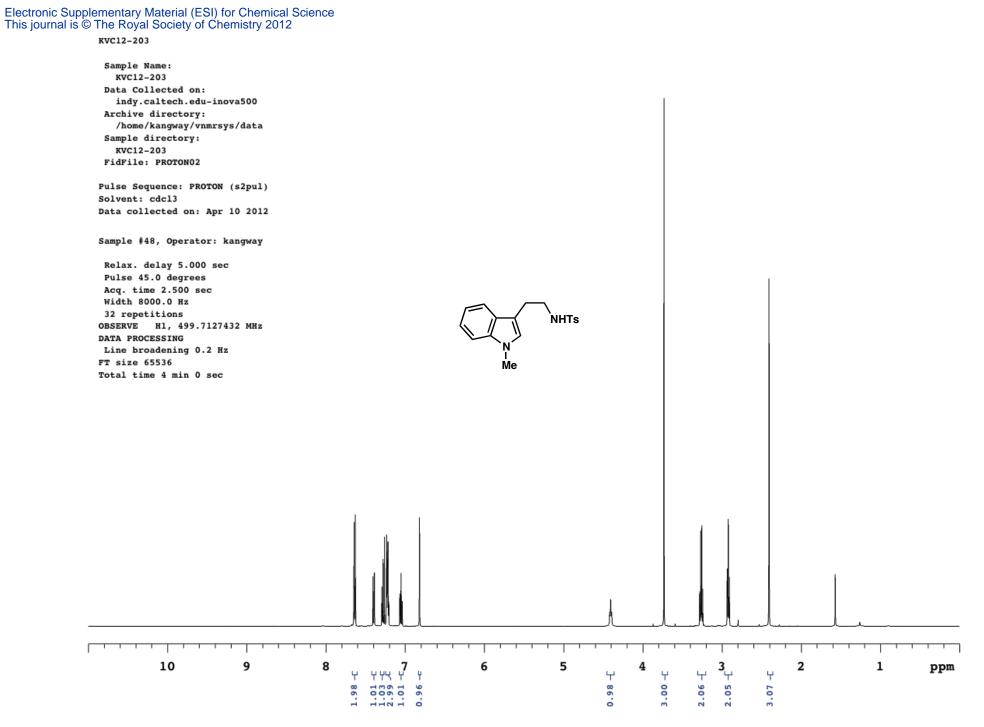
신유도 아이는 이 동생 나가 들어야 한다.



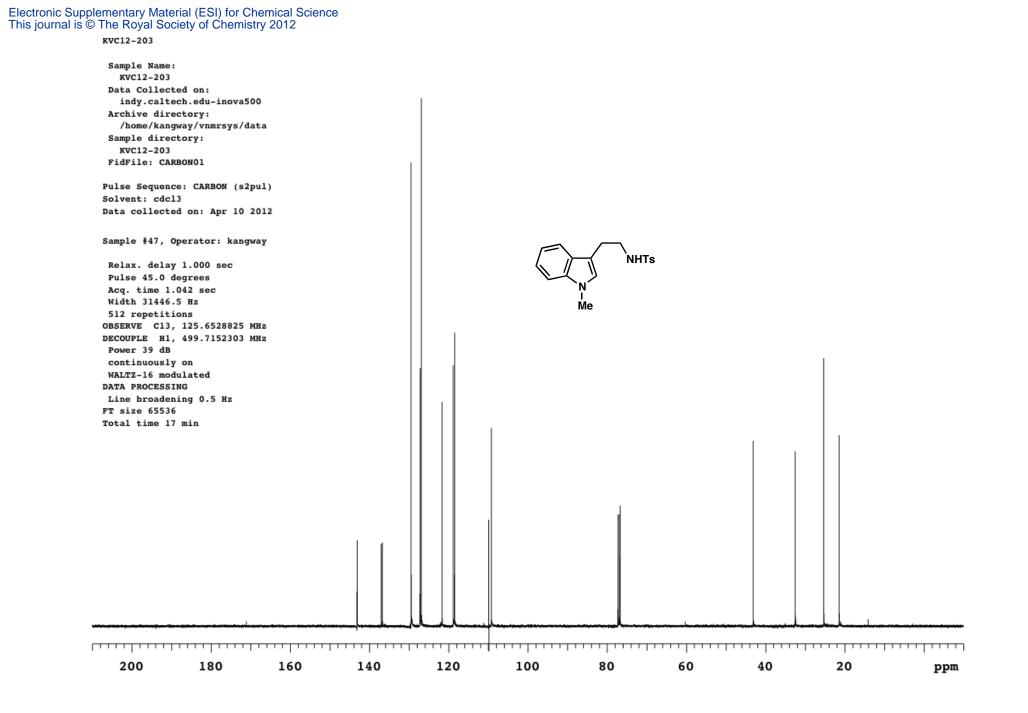
March 1997 - Set and a Set in



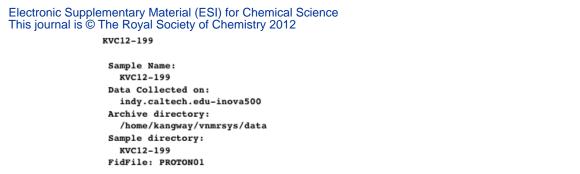
Alexandra Sutures Alexandre

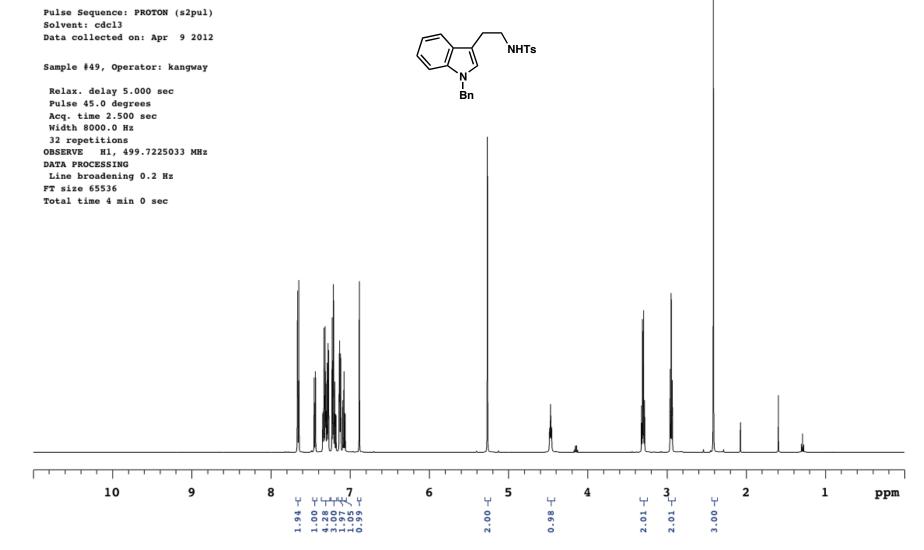


More and the Soft arrest in State

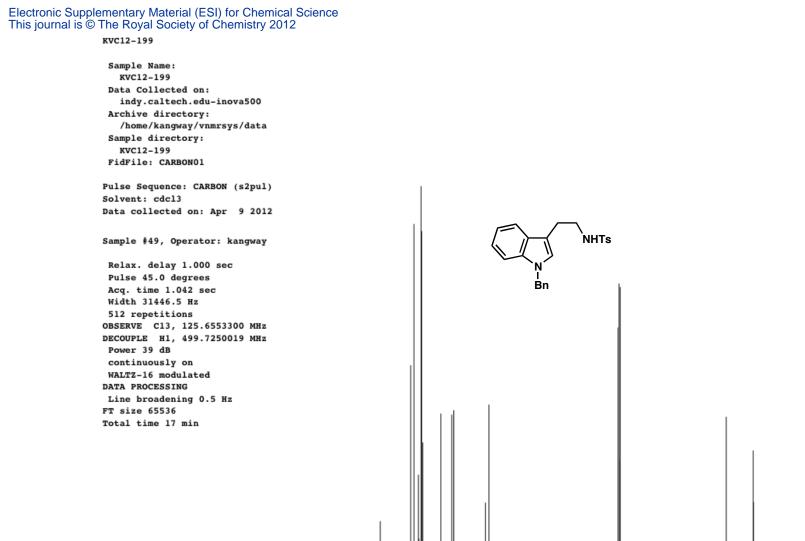


Selected to Select an explosion of the

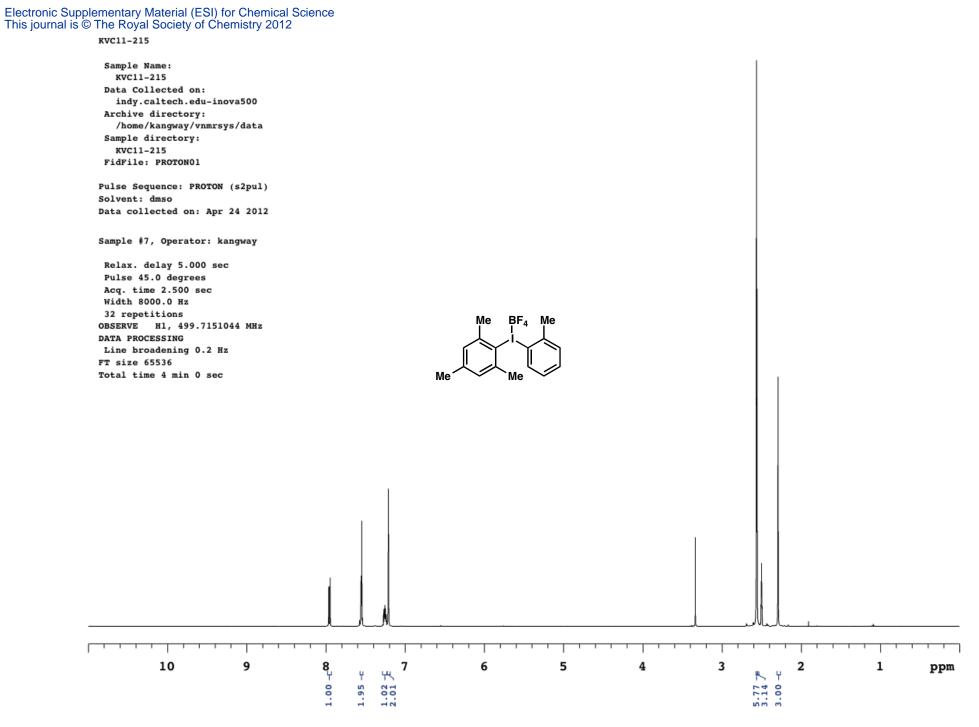




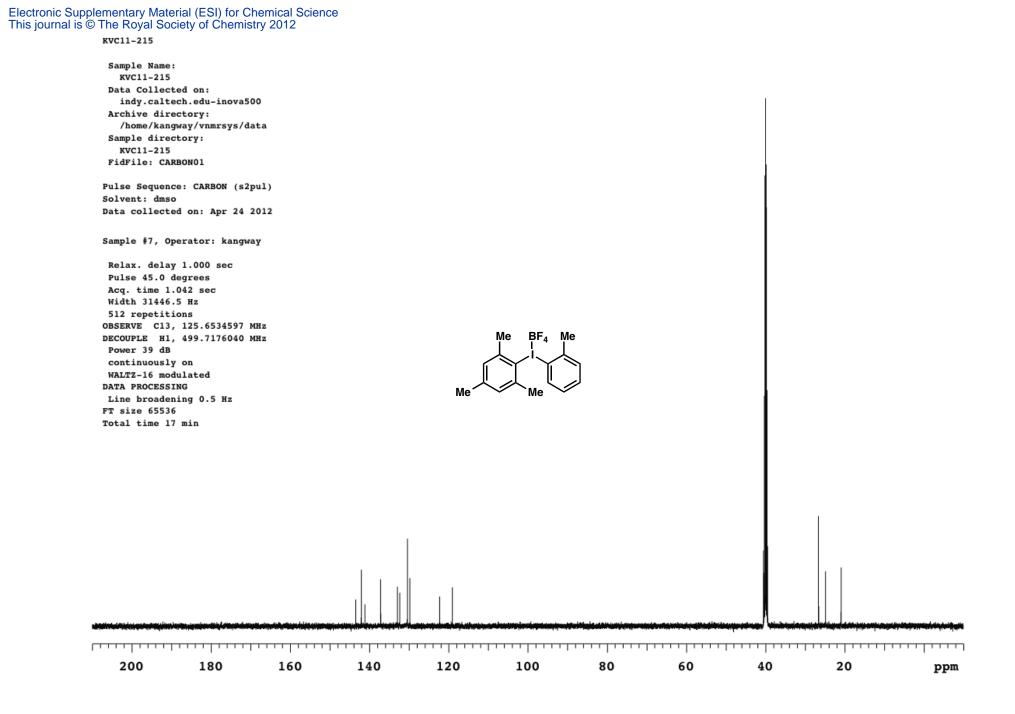
Storaction Set and shares



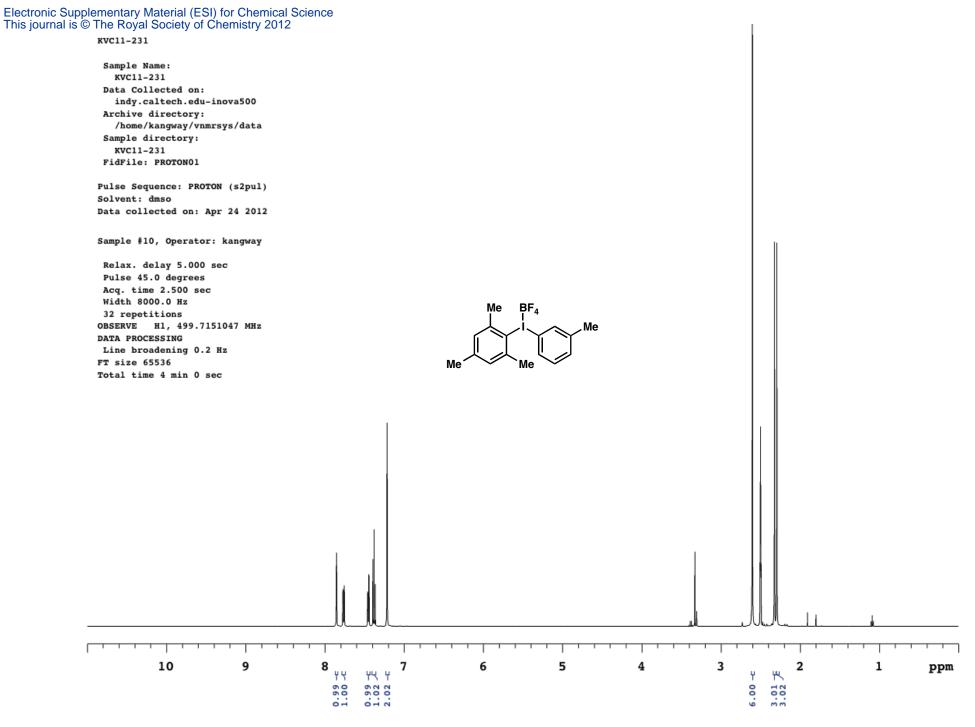
ppm



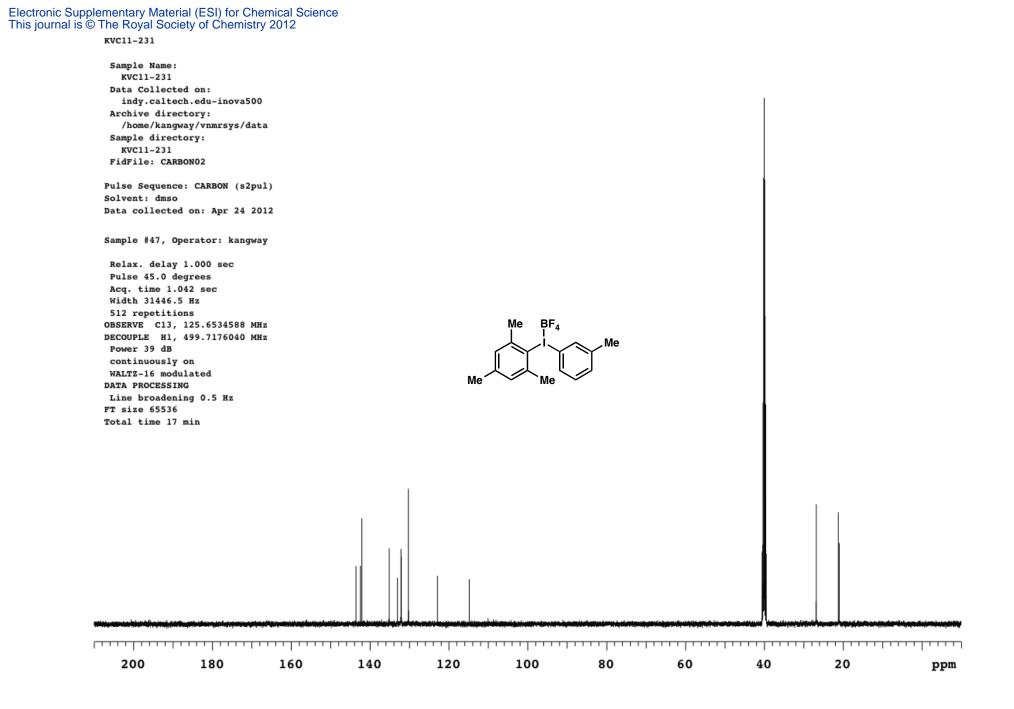
Algenzie Satures in Set



Selection and the Selection real Selection of the Selecti

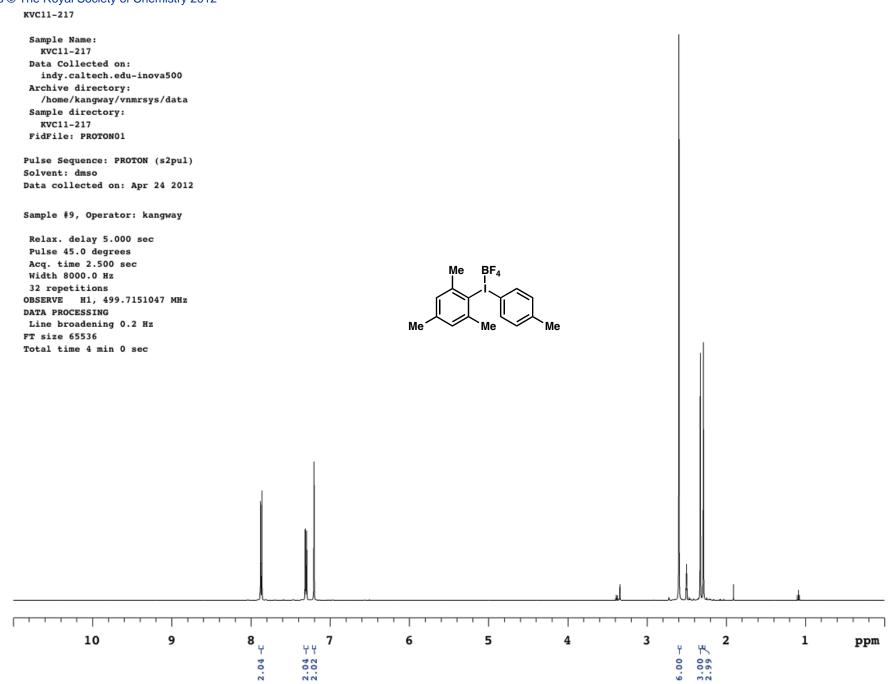


Alexandre Saturation Sector

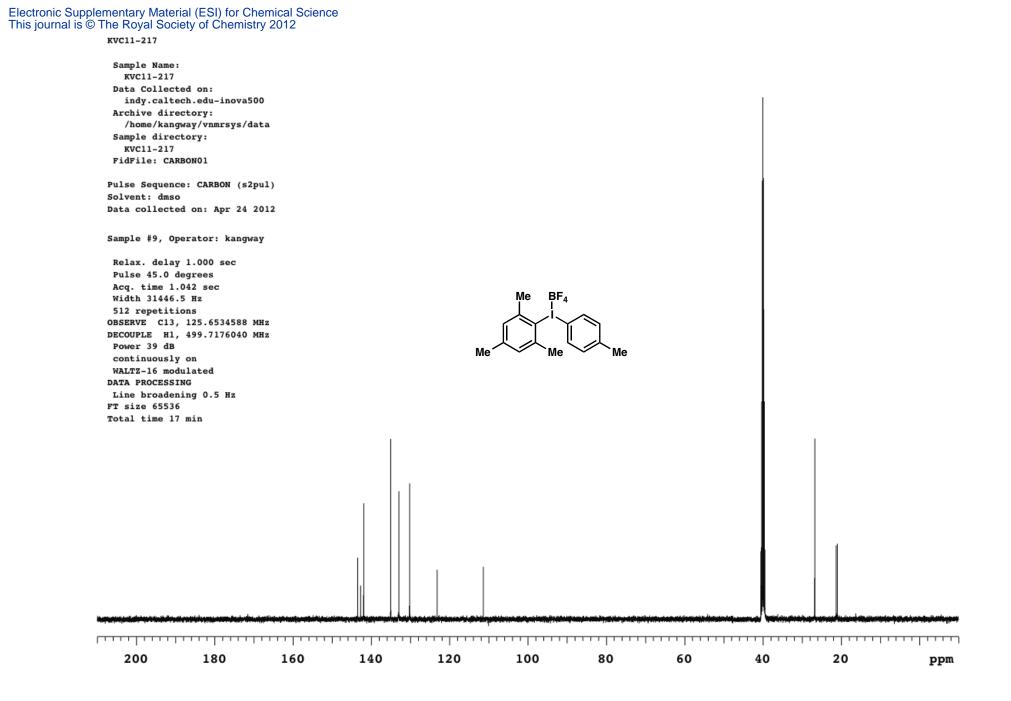


Alexandra tells a successful a

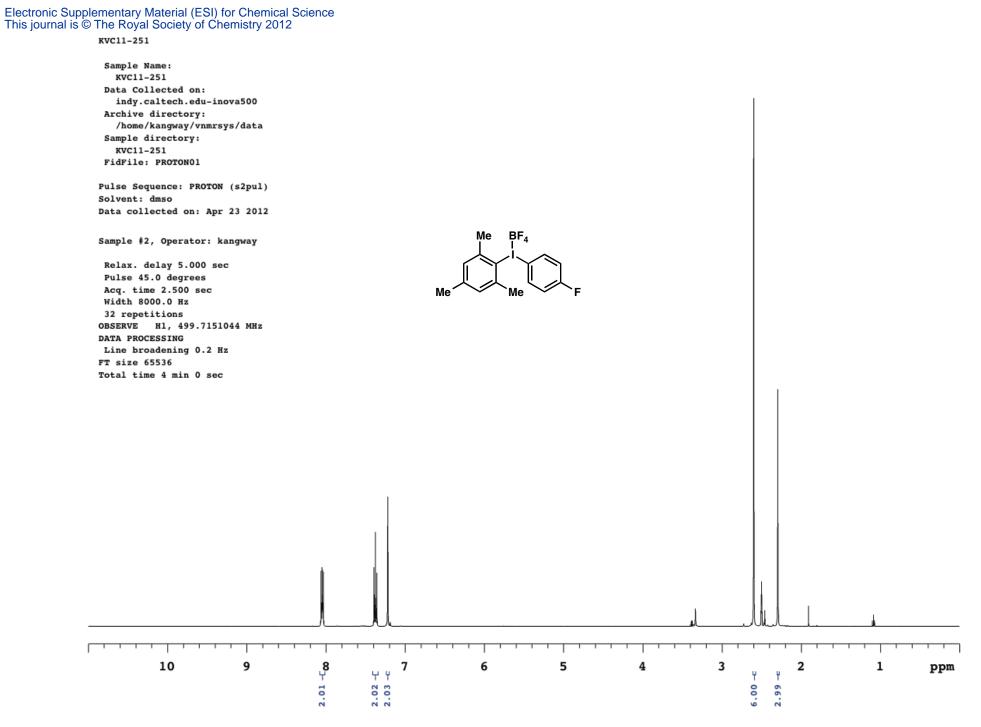




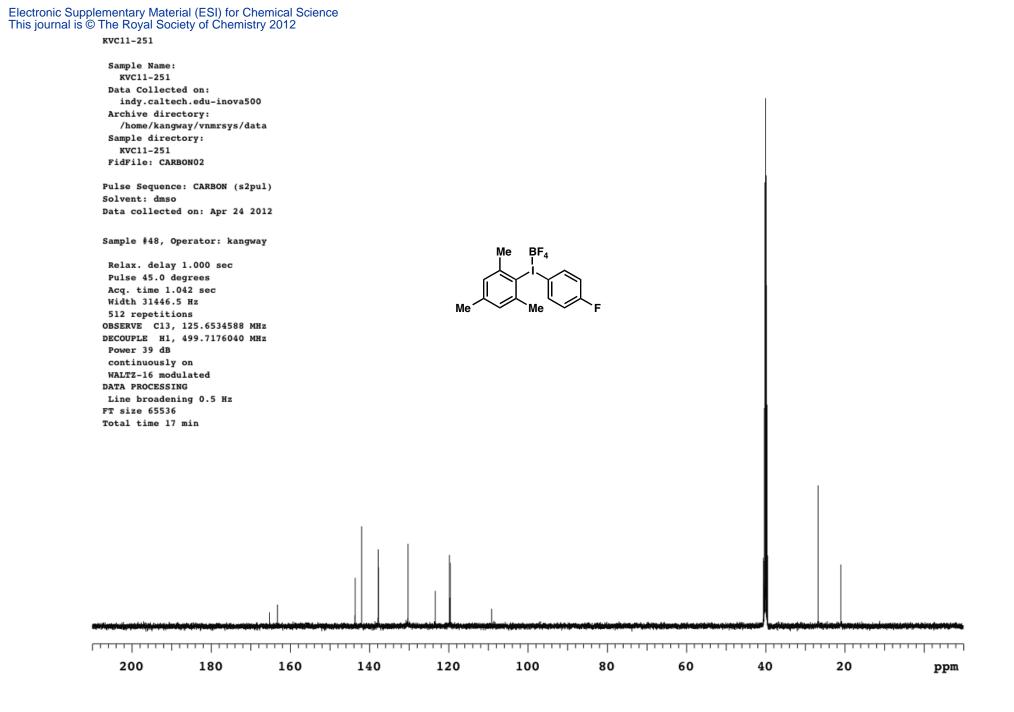
denter and the state of the second state of th



Maria a territori di Safti america M

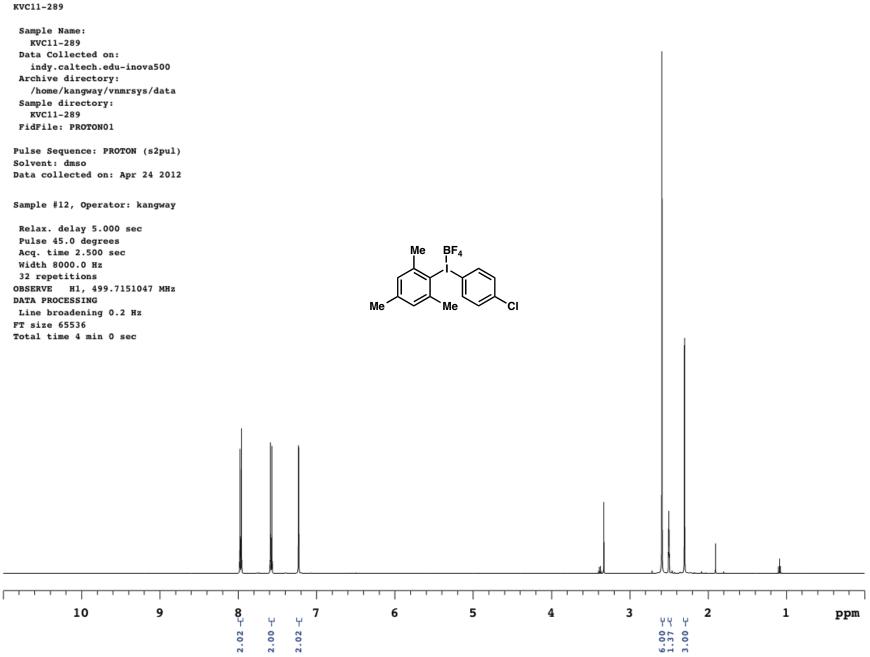


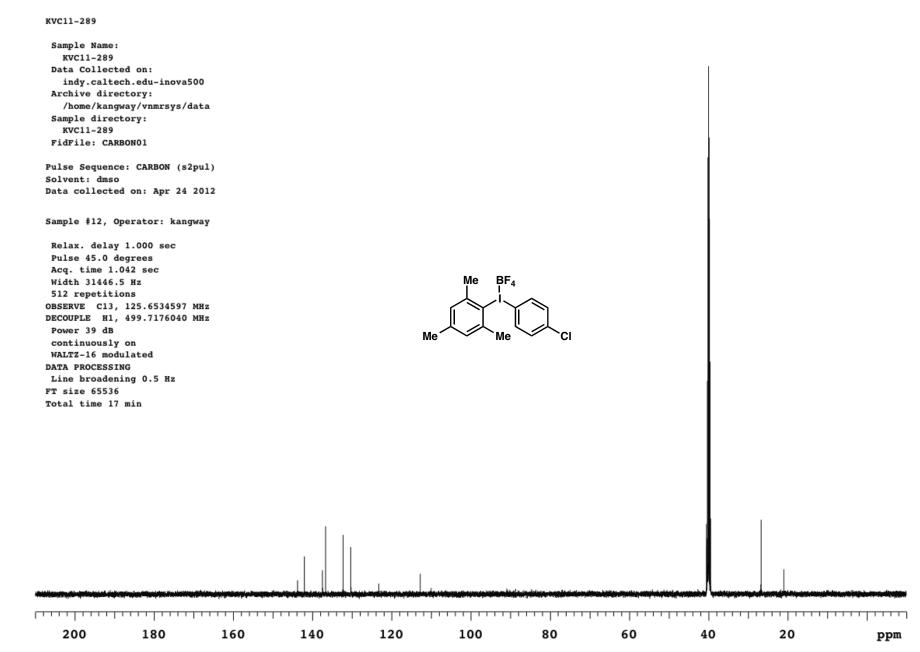
Storador - Saturation -



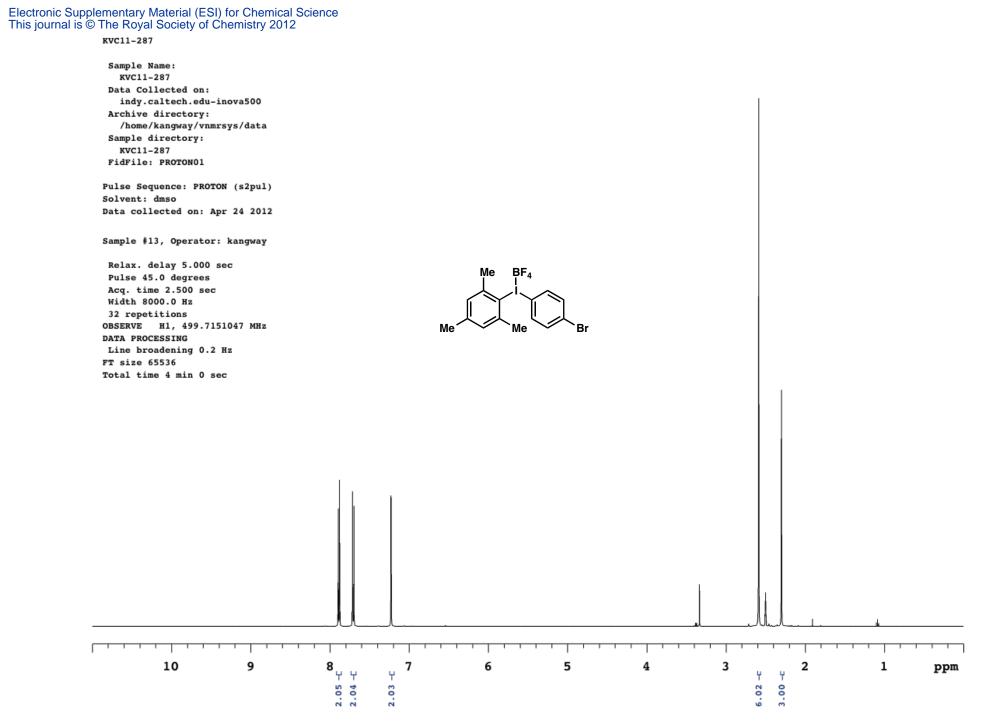
Substantia Set processes



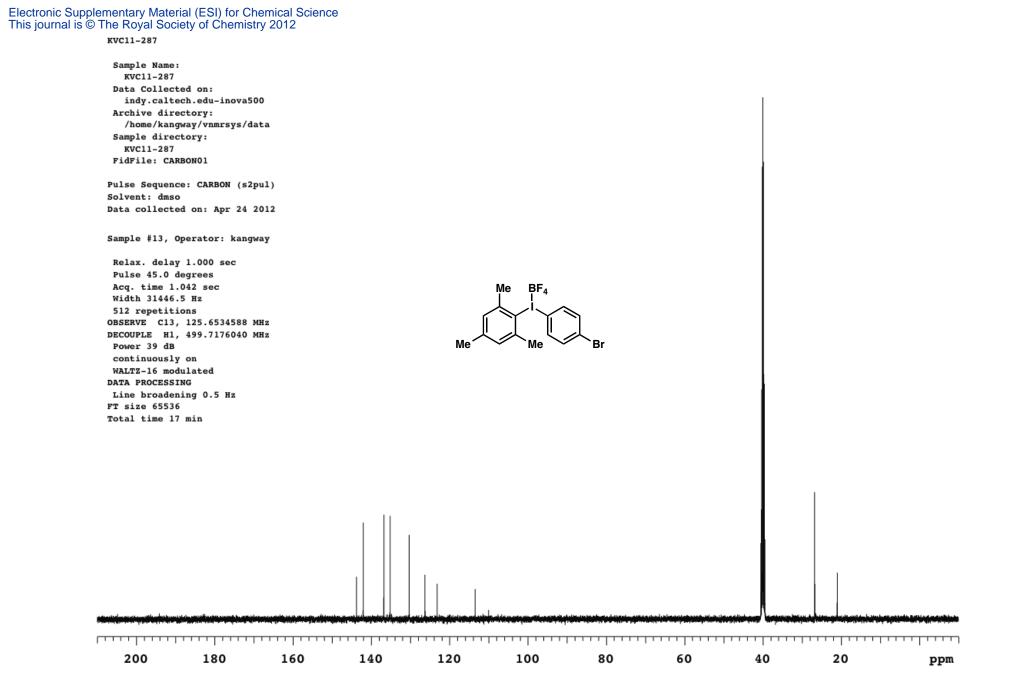




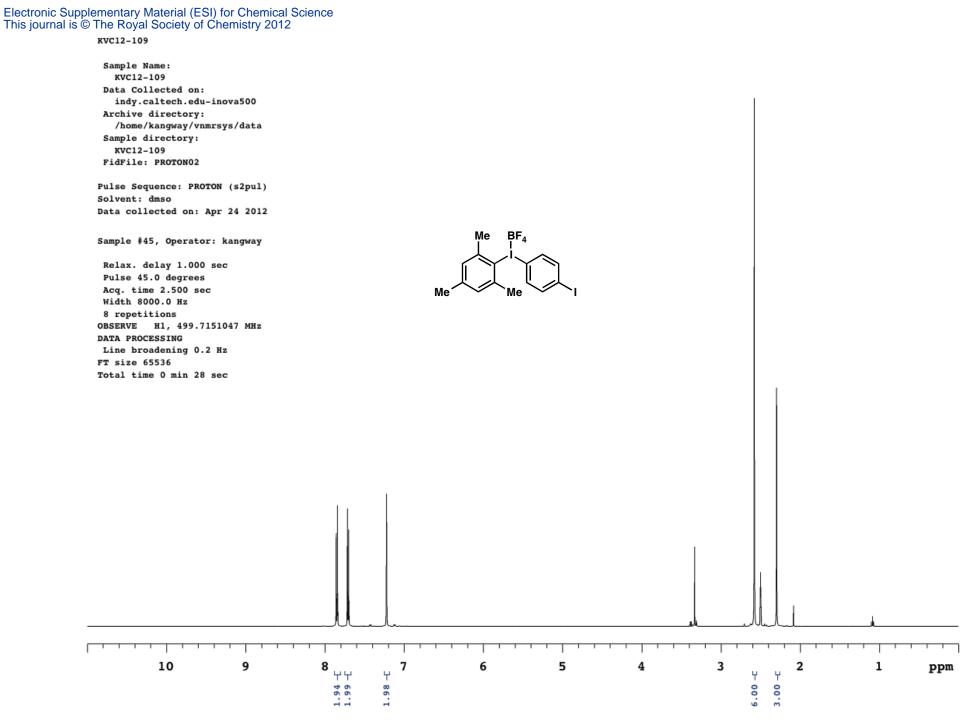
a fuere this is subcered.



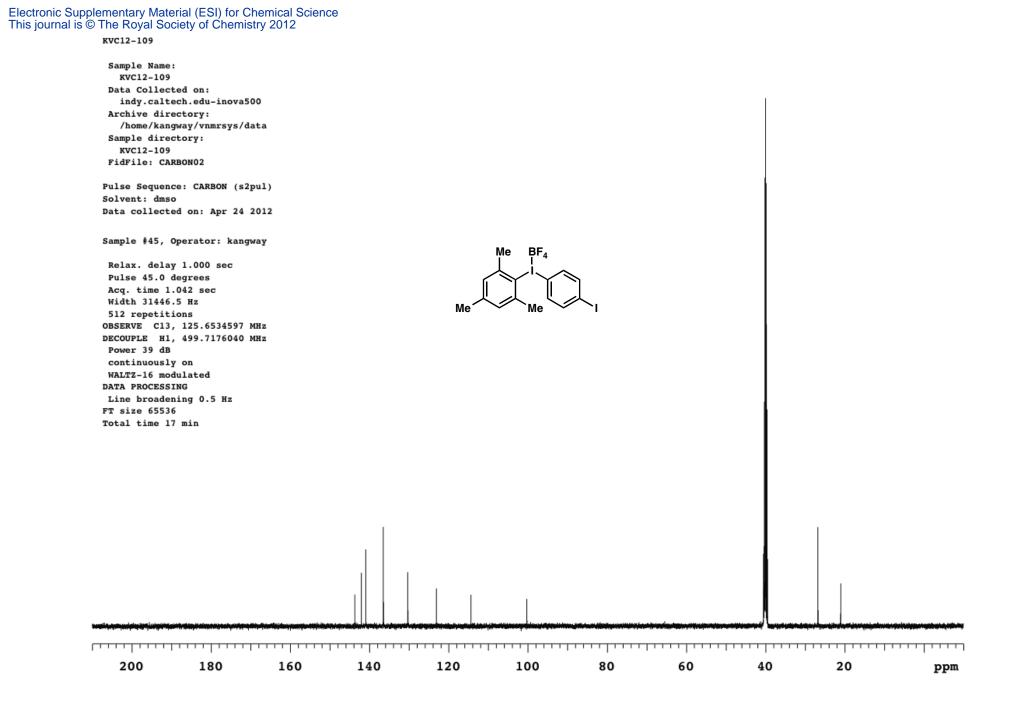
Algebra when a first service and the



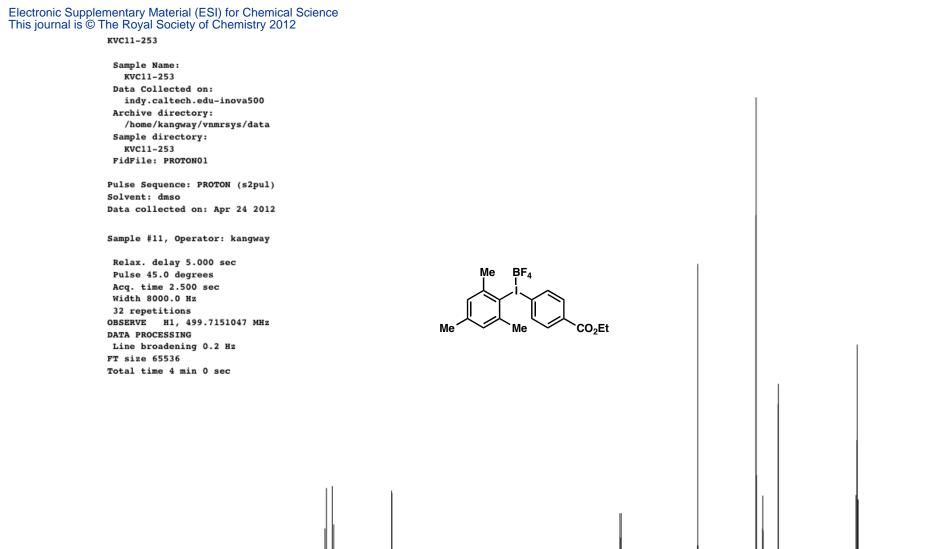
Street and a standard street and standard street and st



Alexander's Soft areas for



sector with the sector state of the



10

2.04 Å

9

5

4

Ψ

2.07

3

2

¥

Y

6.07 3.00 1

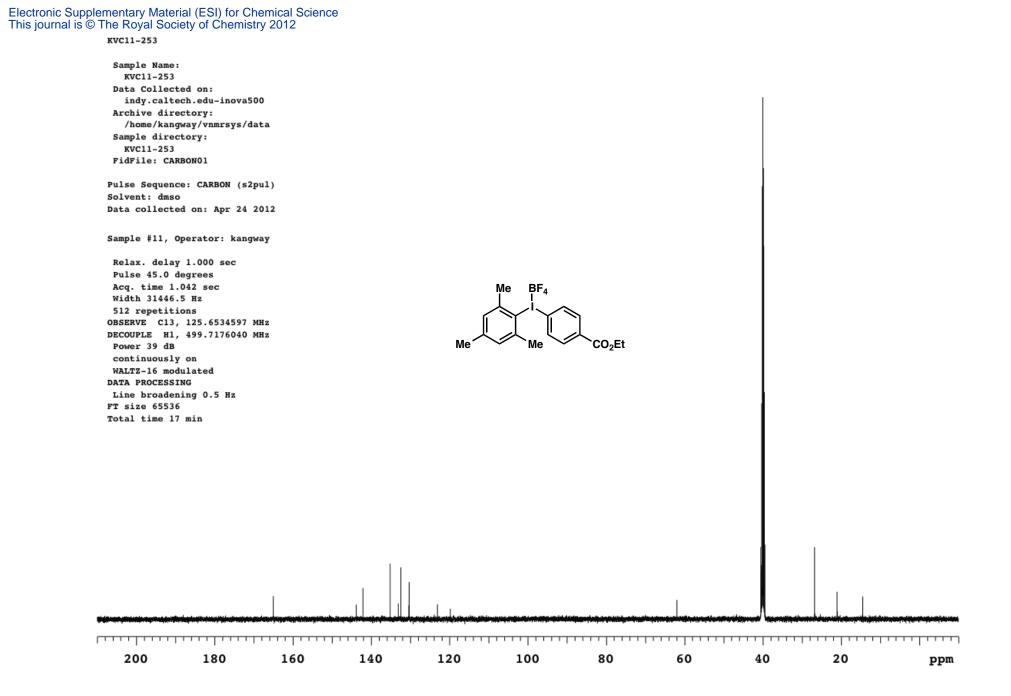
3.10 -{

ppm

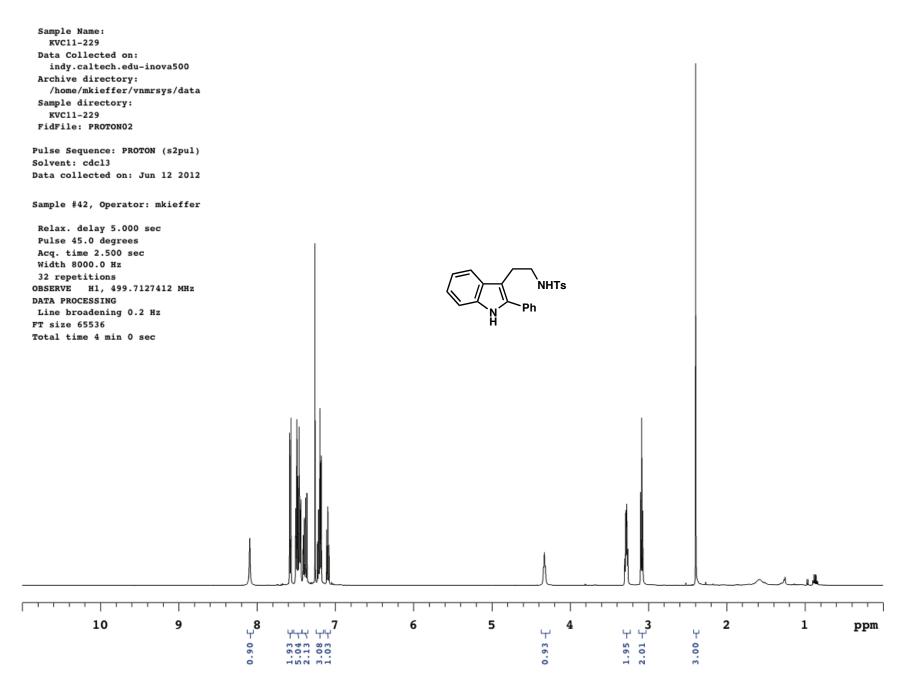
6

7

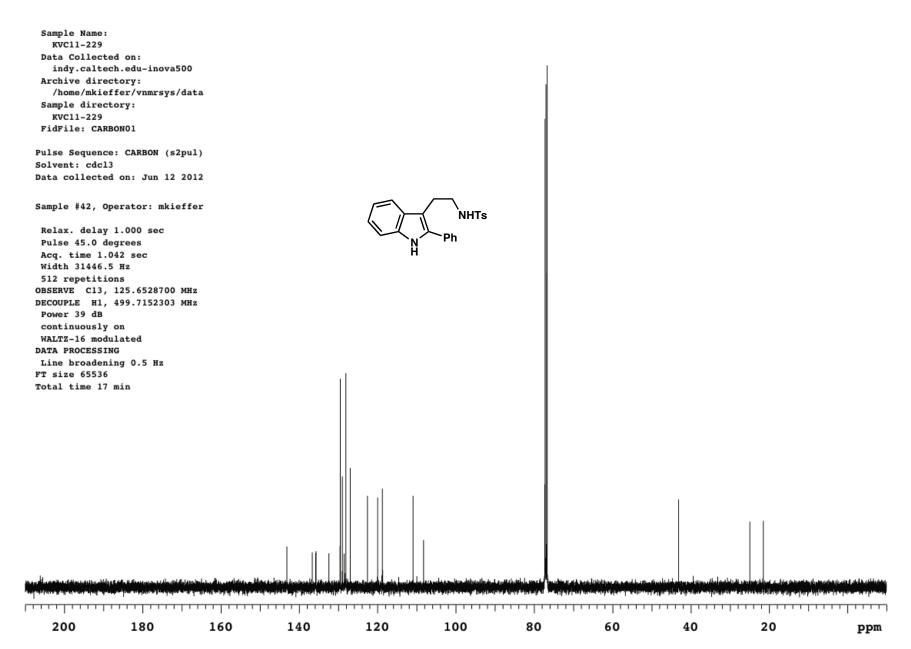
2.04 -



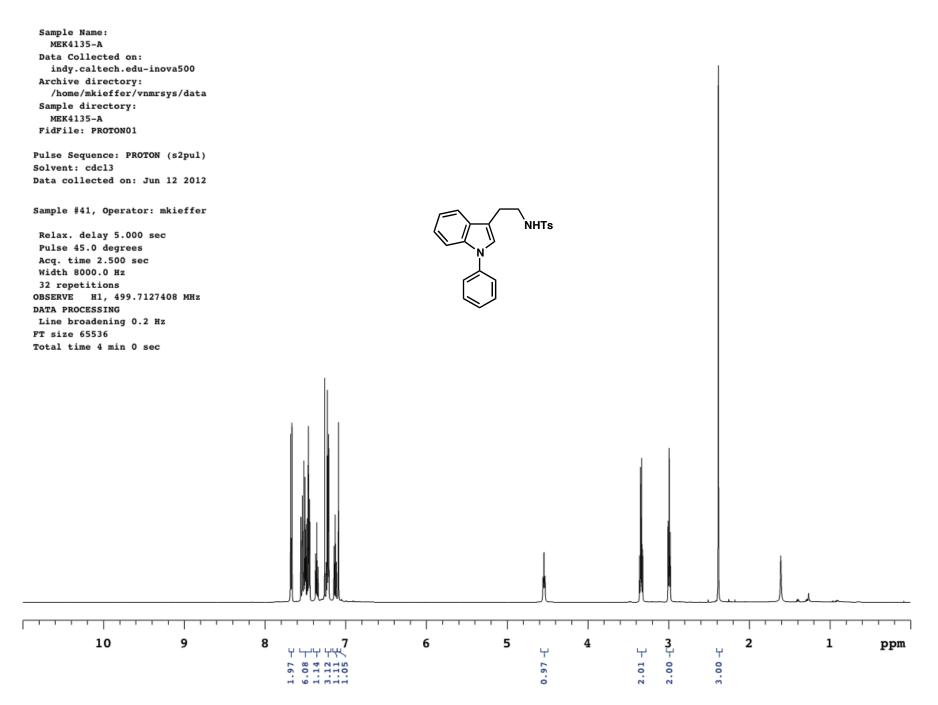
Alexandra Saturation



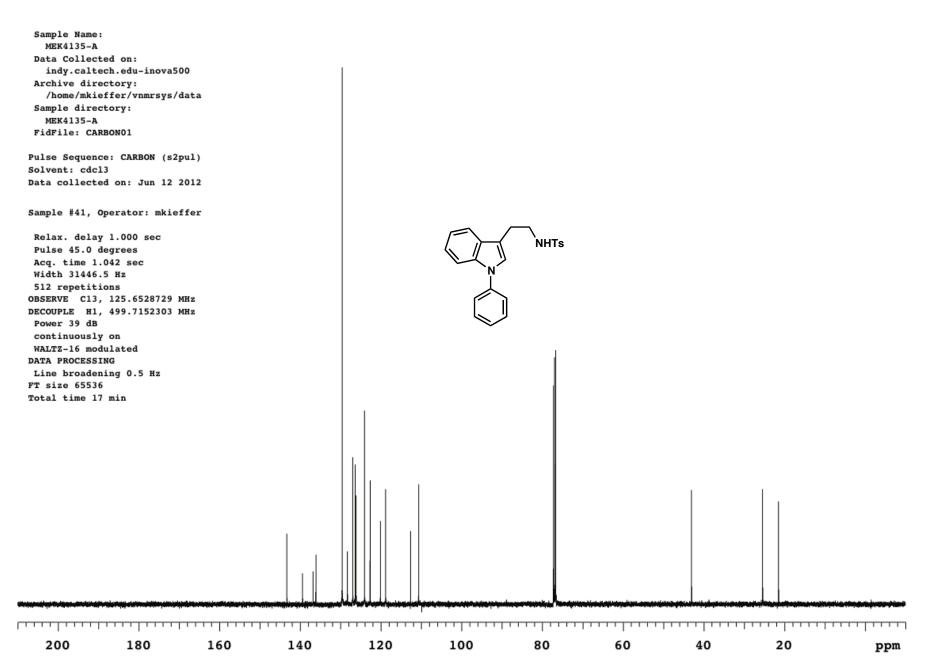
Content to Safe an early of the

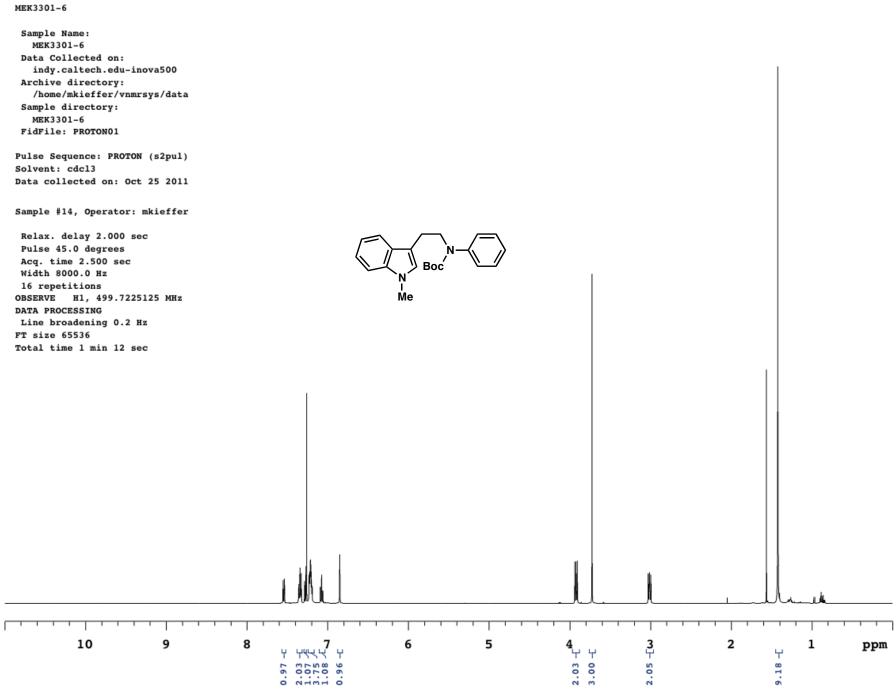


Maria a la compañía de la compañía d



Alexandra Saturation Sole





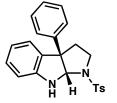
MEK4100

Sample Name: MEK4100 Data Collected on: indy.caltech.edu-inova500 Archive directory: /home/kangway/vnmrsys/data Sample directory: MEK4100 FidFile: PROTON01

Pulse Sequence: PROTON (s2pul) Solvent: cdcl3 Data collected on: Apr 18 2012

Sample #48, Operator: kangway

Relax. delay 5.000 sec Pulse 45.0 degrees Acq. time 2.500 sec Width 8000.0 Hz 32 repetitions OBSERVE H1, 499.7127408 MHz DATA PROCESSING Line broadening 0.2 Hz FT size 65536 Total time 4 min 0 sec





9

8

1.97 f

10

¥

0.98

6

44

0.99

0008

Nmmo

5₄

0.93

4

1.00 년

3

Ψ

1.02

2

 \mathcal{H}

1.06

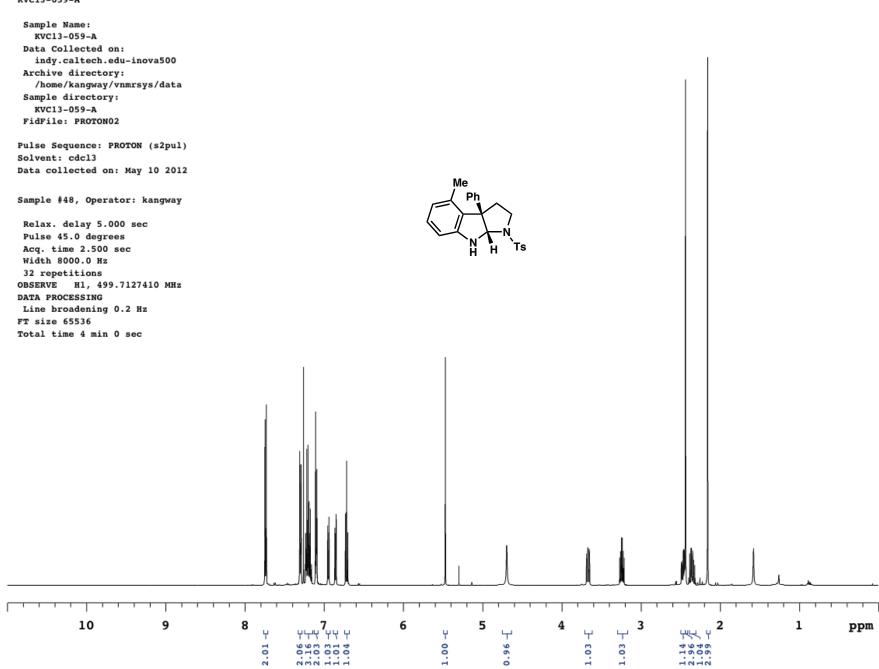
1

ppm

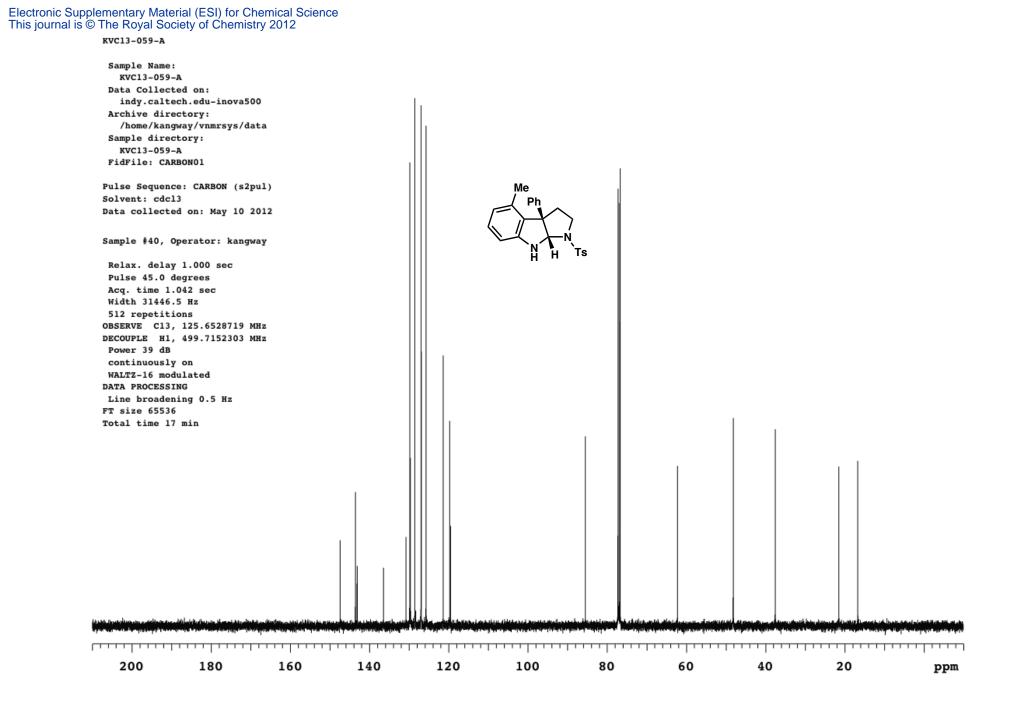
MEK4100 Sample Name: MEK4100 Data Collected on: indy.caltech.edu-inova500 Archive directory: /home/kangway/vnmrsys/data Sample directory: MEK4100 FidFile: CARBON01 Pulse Sequence: CARBON (s2pul) Solvent: cdcl3 Data collected on: Apr 18 2012 Sample #48, Operator: kangway Relax. delay 1.000 sec Pulse 45.0 degrees Acq. time 1.042 sec Width 31446.5 Hz 512 repetitions OBSERVE C13, 125.6528719 MHz DECOUPLE H1, 499.7152303 MHz Power 39 dB continuously on WALTZ-16 modulated DATA PROCESSING Line broadening 0.5 Hz FT size 65536 Total time 17 min ______ 200 180 160 140 120 100 80 60 20 40 ppm

A second second states are second so

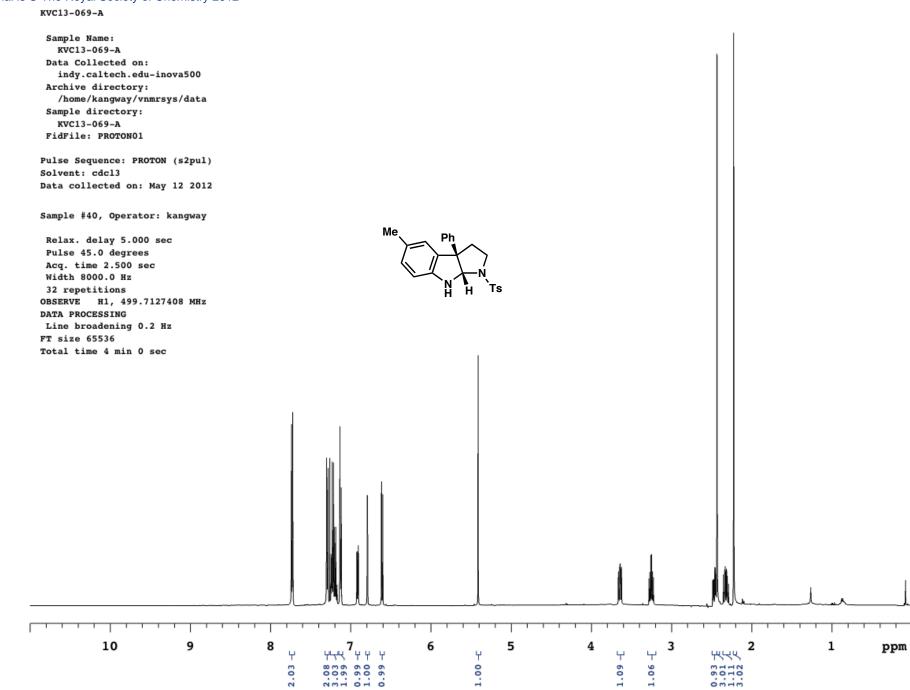




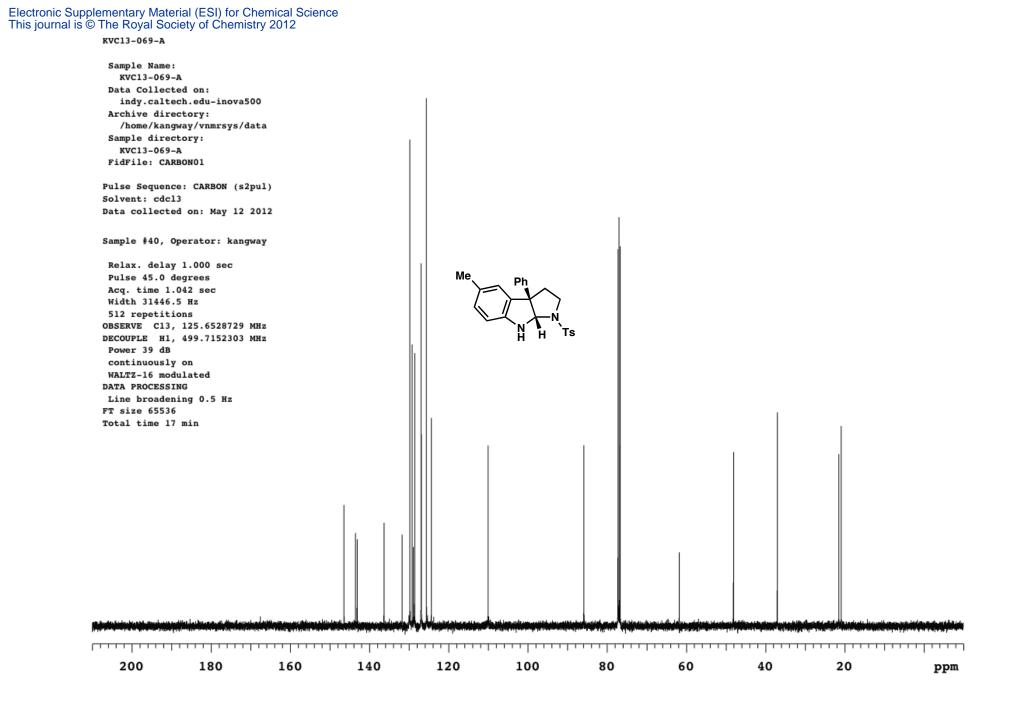
Sheering the Constraint and Solar



a fuere this is subcered.

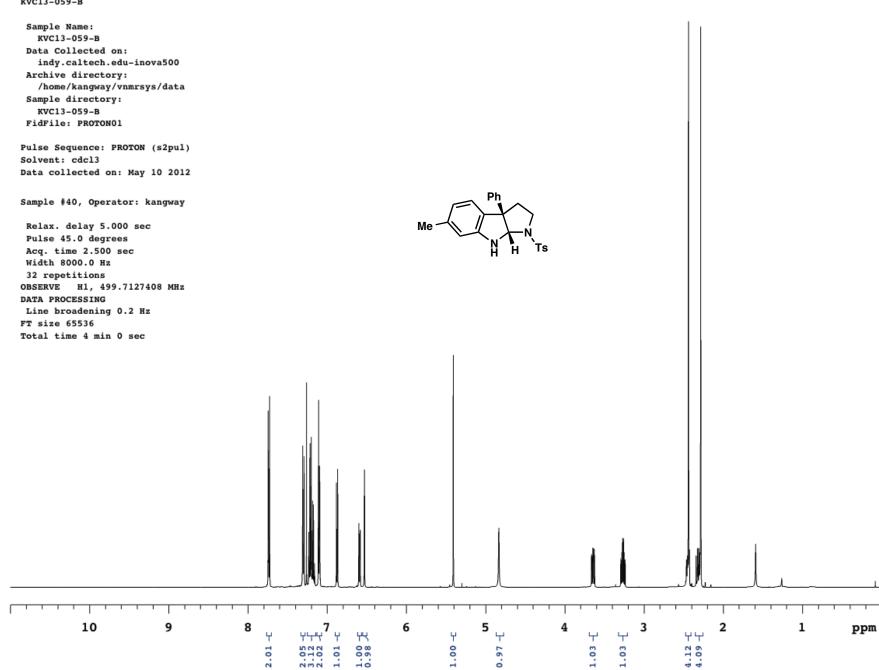


승규는 가슴을 다 가슴을 다 가지 않는 것이 있다.

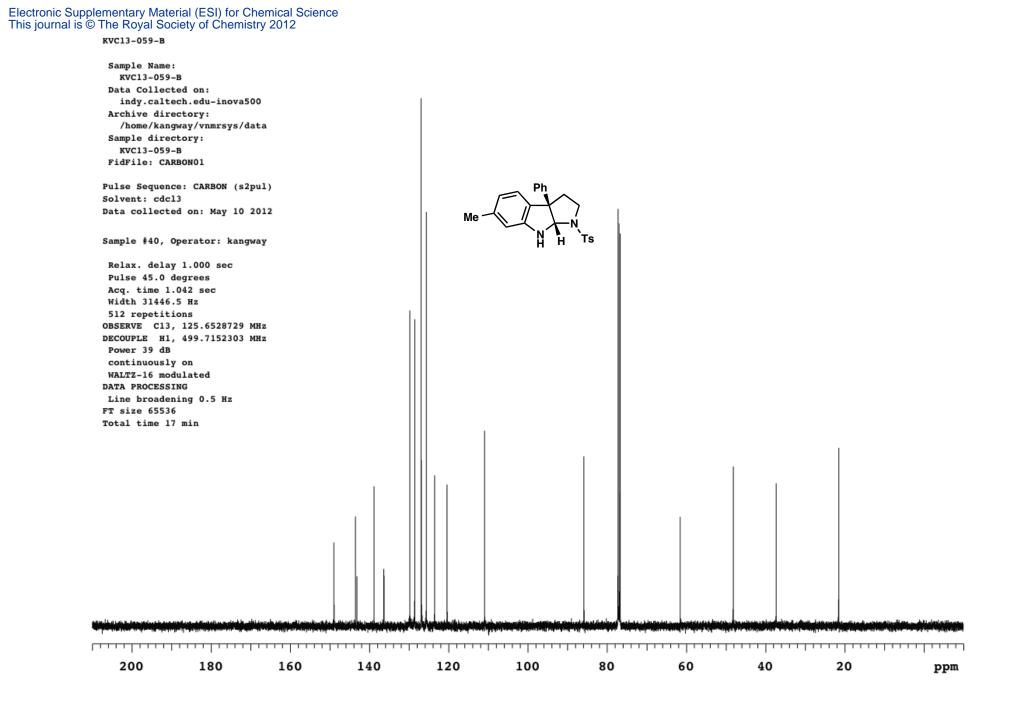


Sternals - Set and Ass



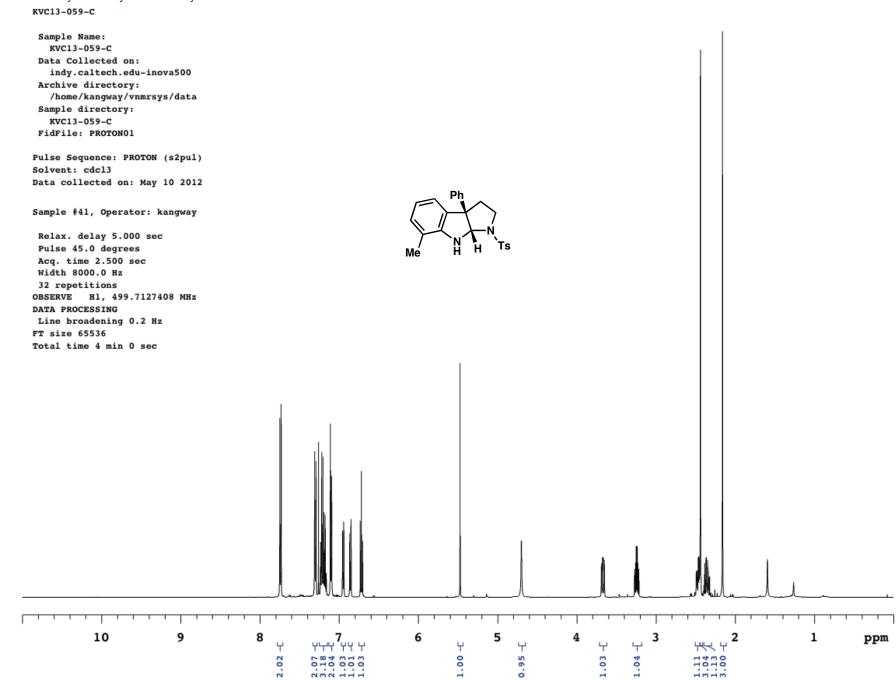


More part of Soft and soft in

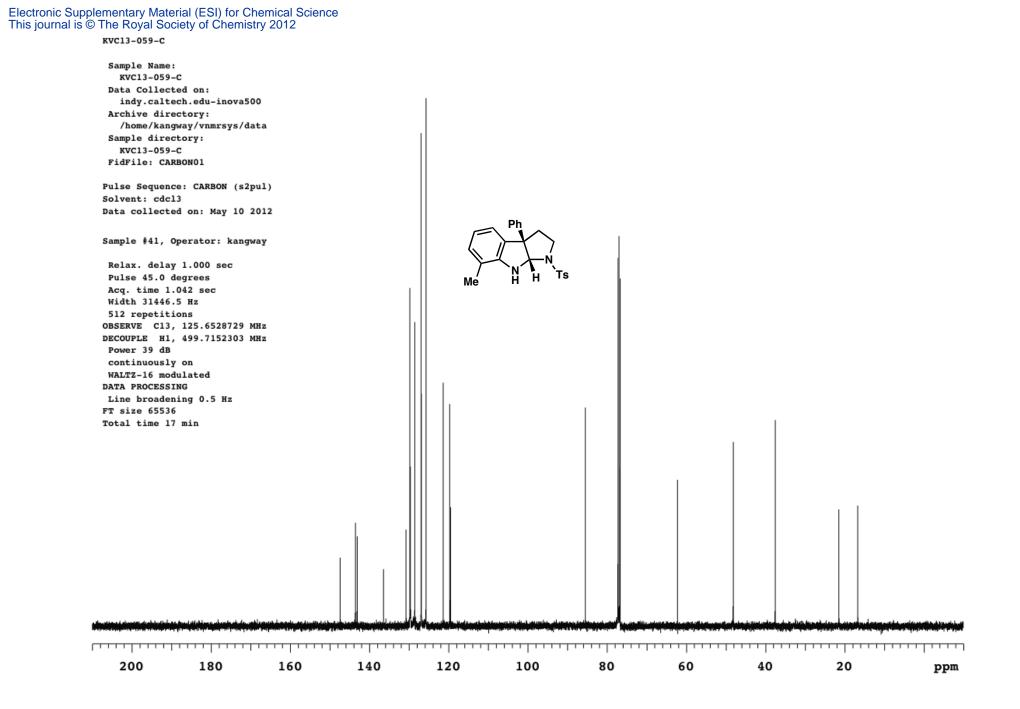


Alexandra Saturation Sector



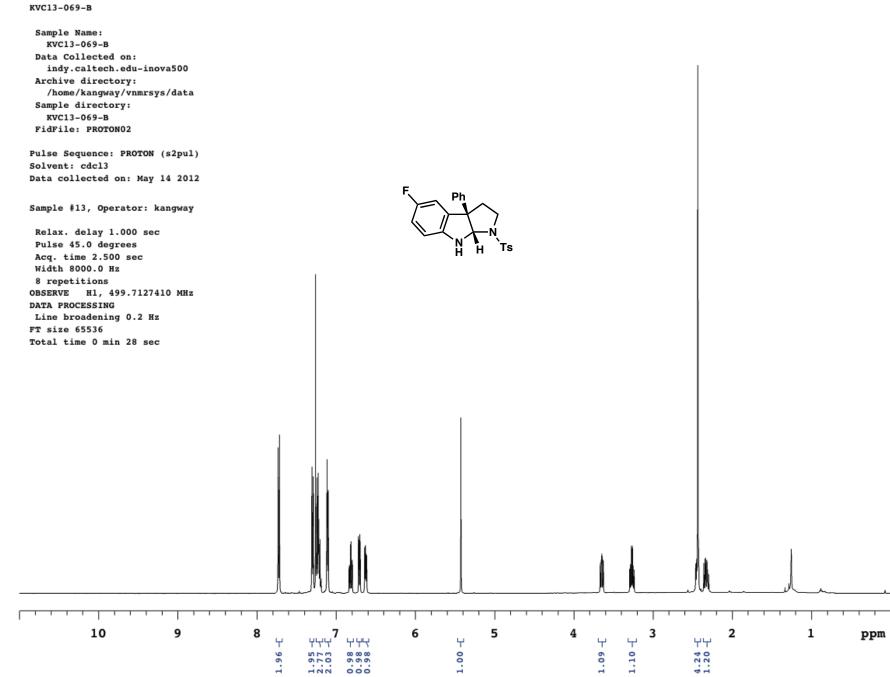


States and street State and such as

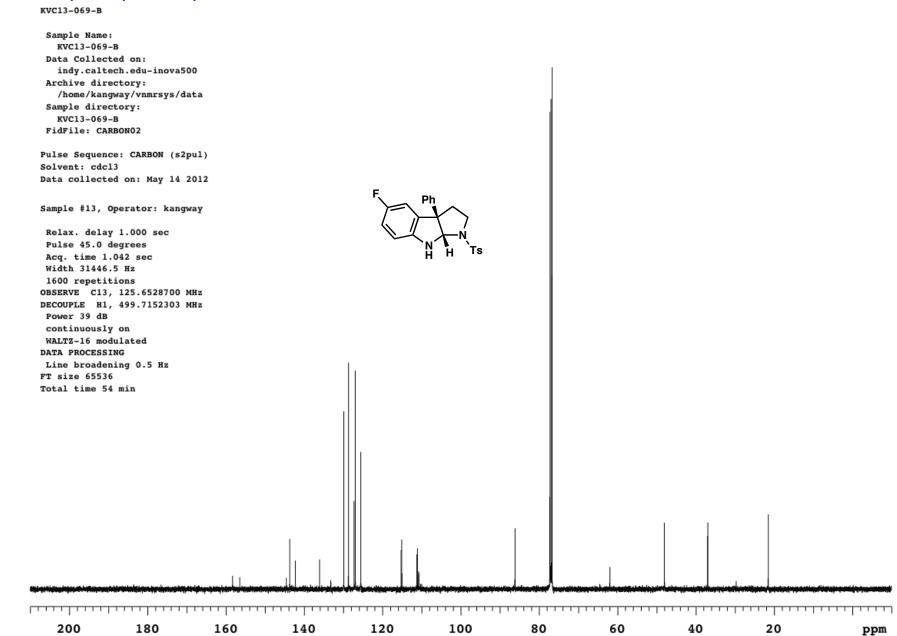


Alexandra Saturation

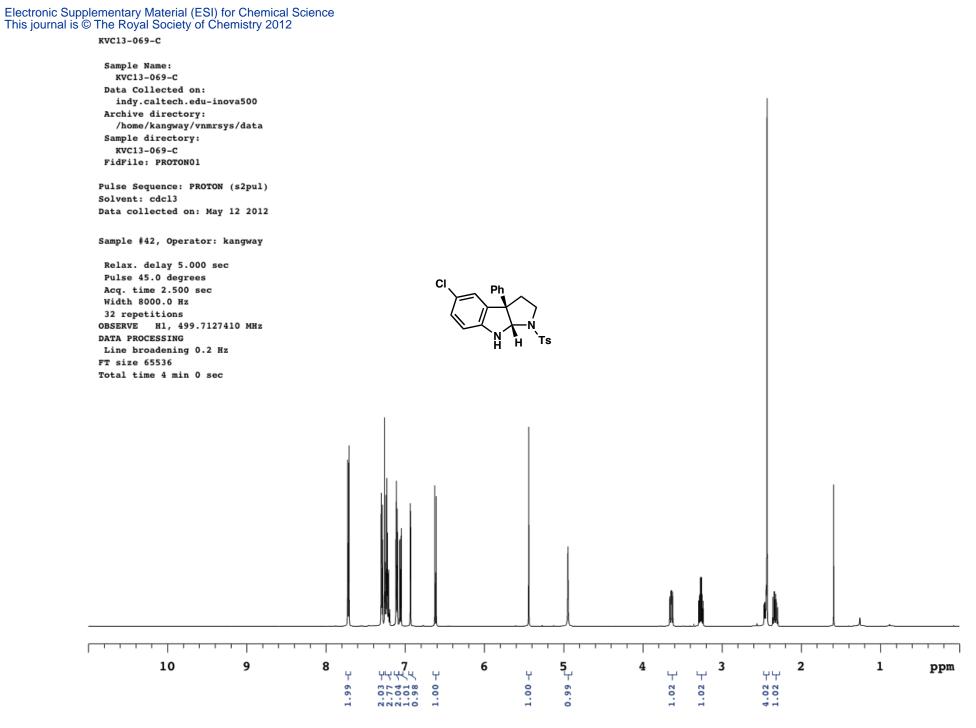




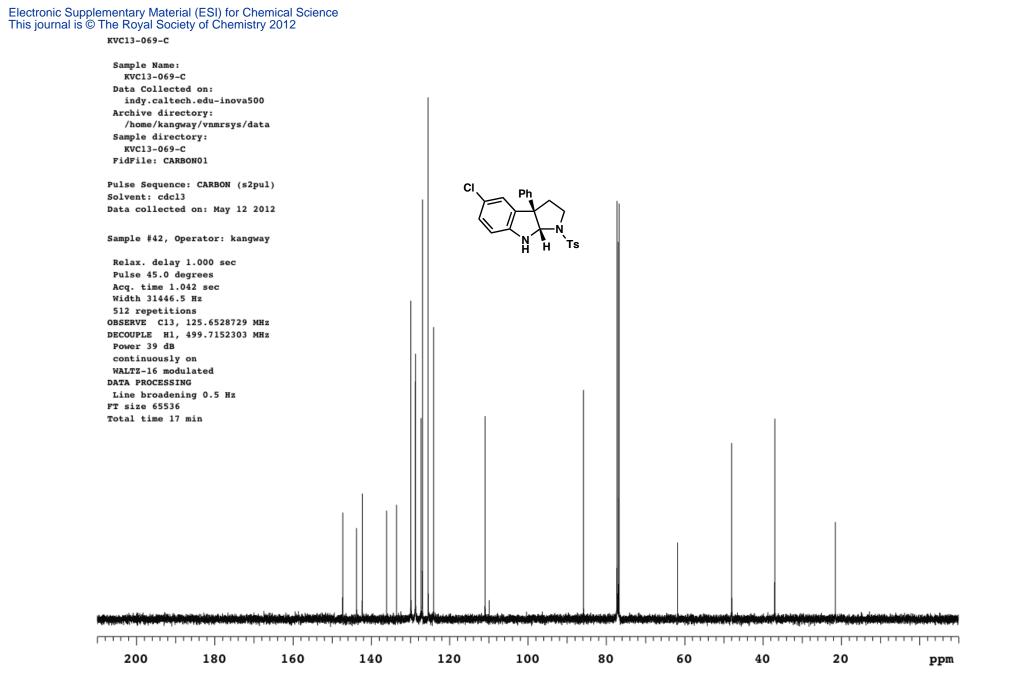
Storauter - Saturner at



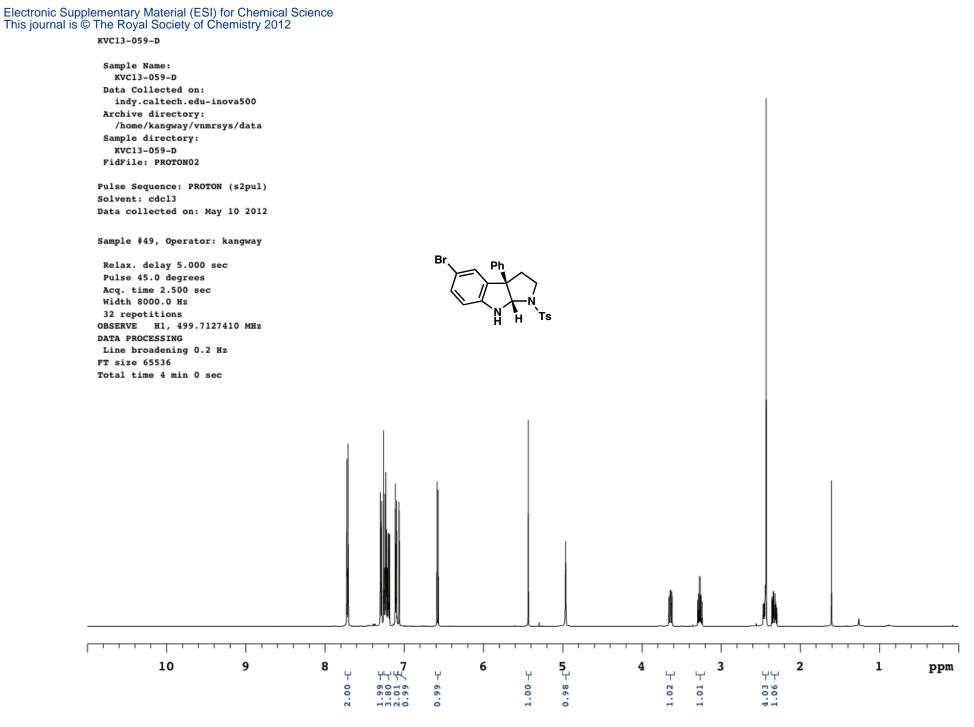
Selection of the South Area South



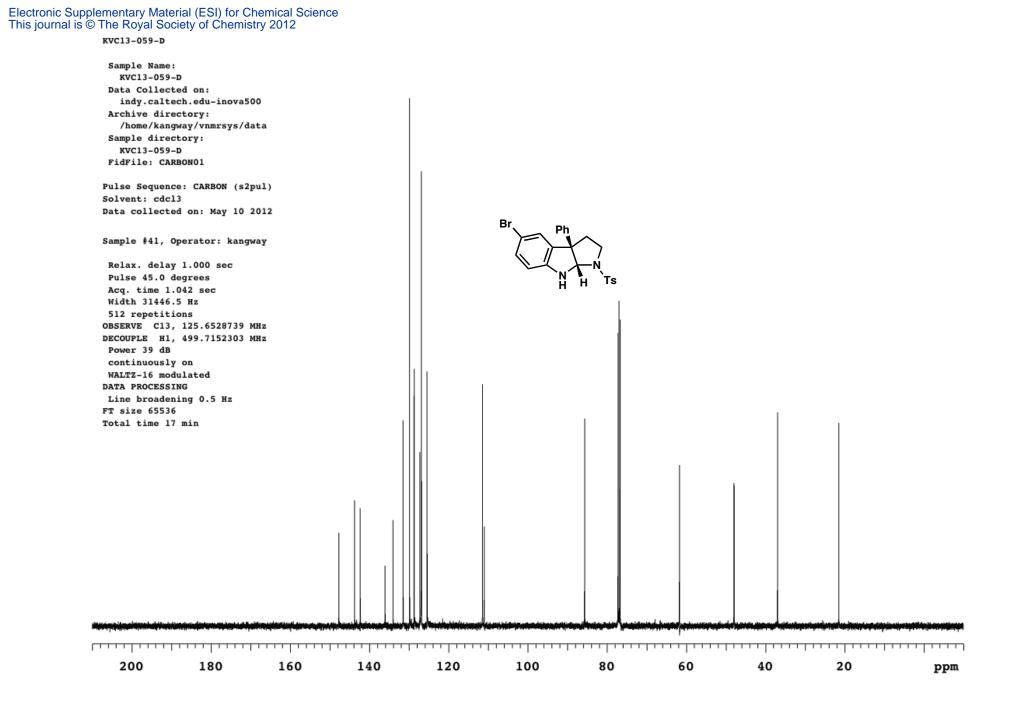
Show and the second second



Sternal and Safe and Add



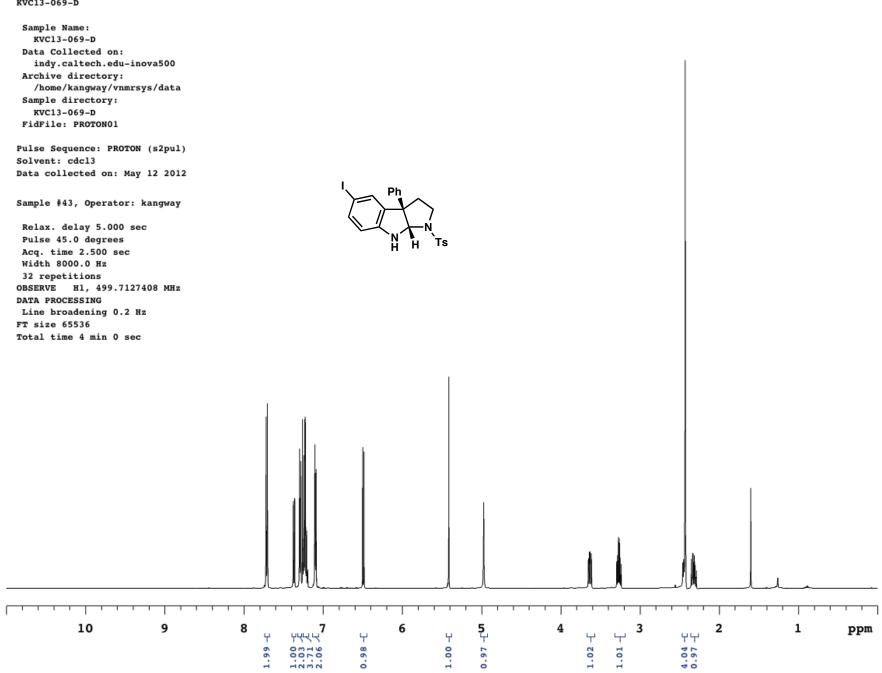
Storador - Saturation -

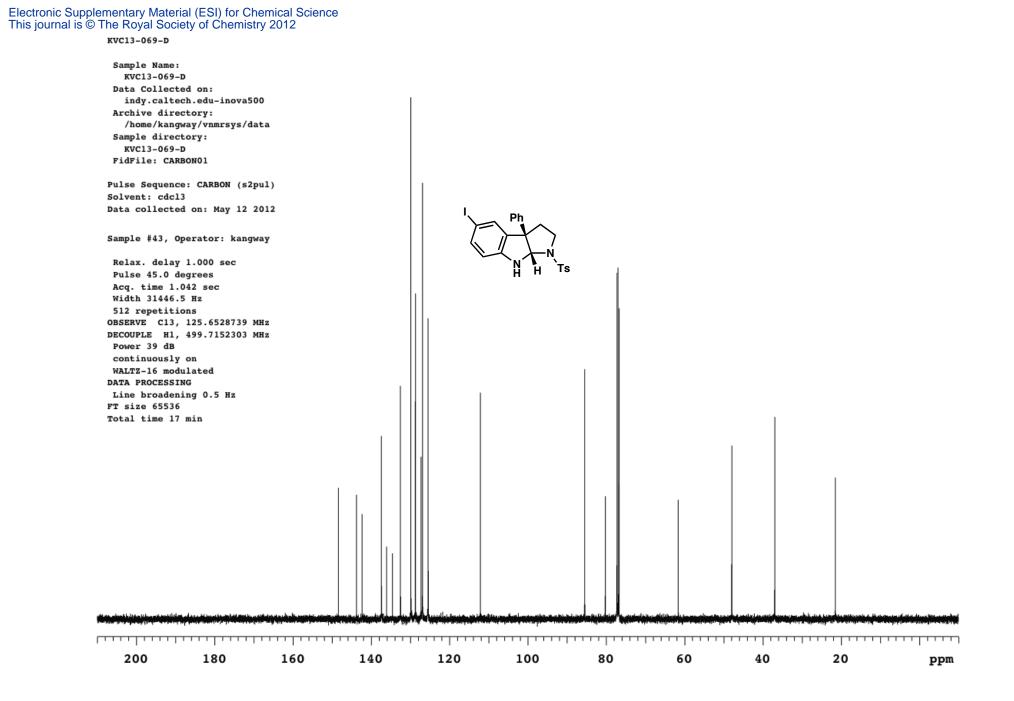


sector sector states and sectors and secto



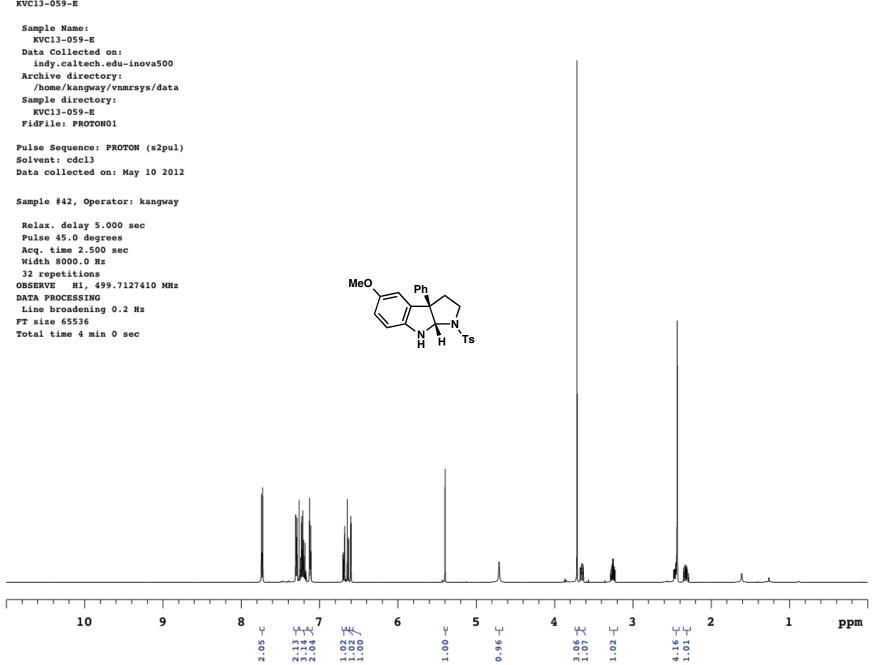


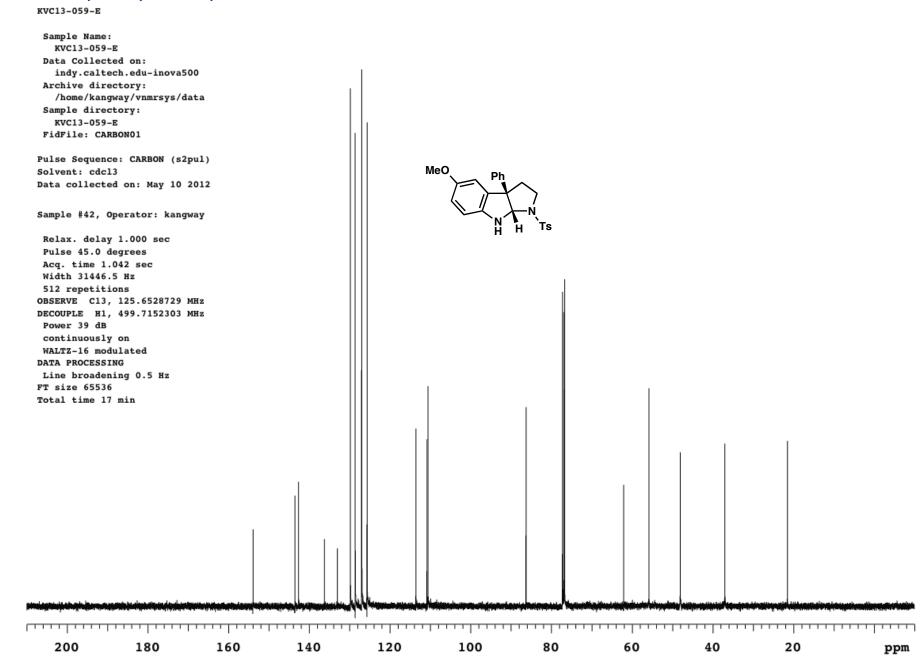




Plan a la constant de restant

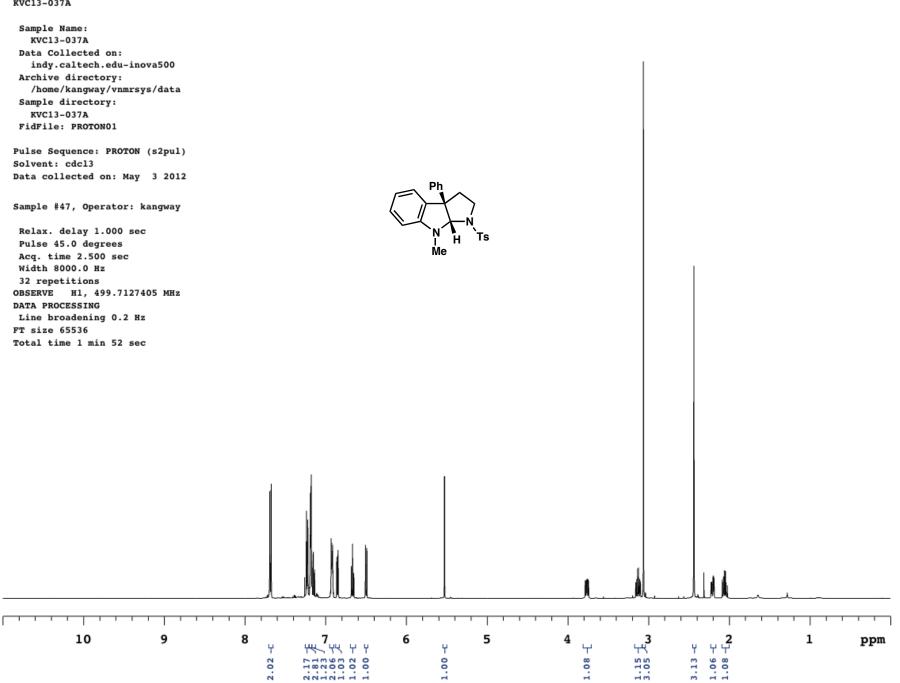


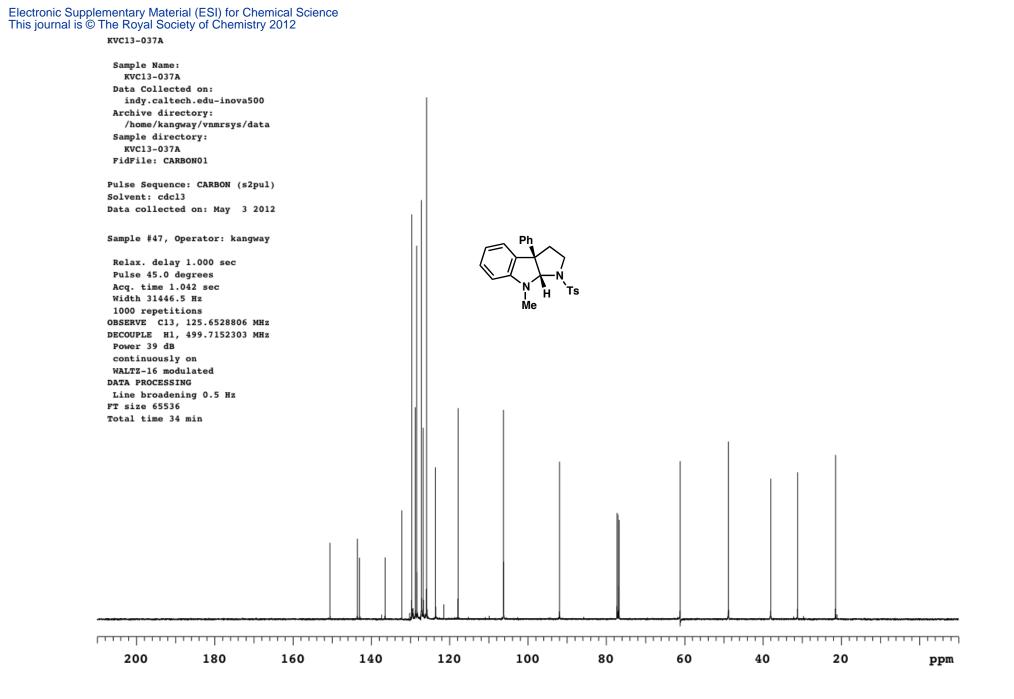




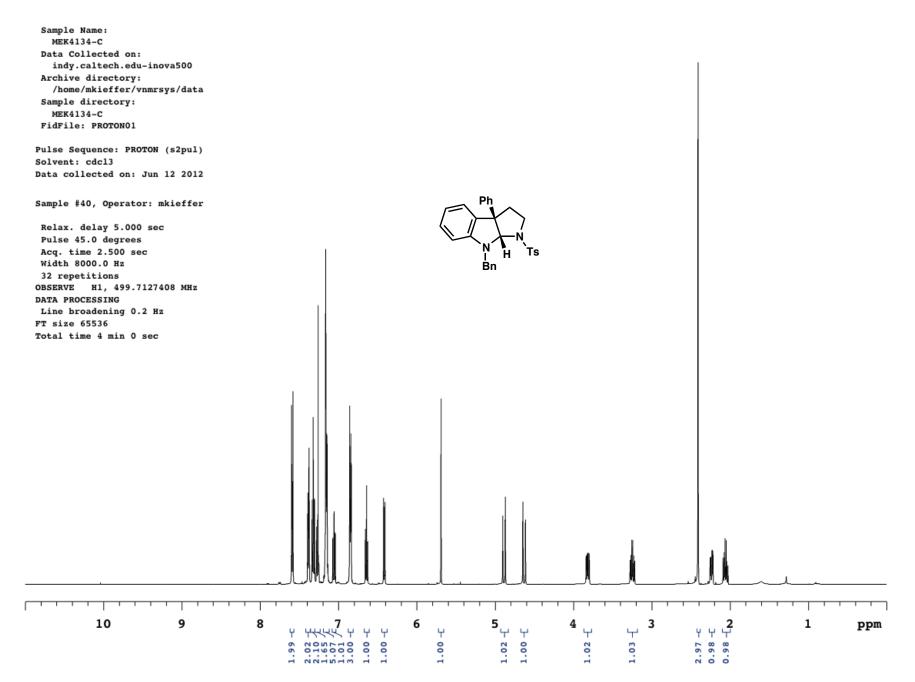
and the second states are a second states of the second states of the second states of the second states of the

KVC13-037A

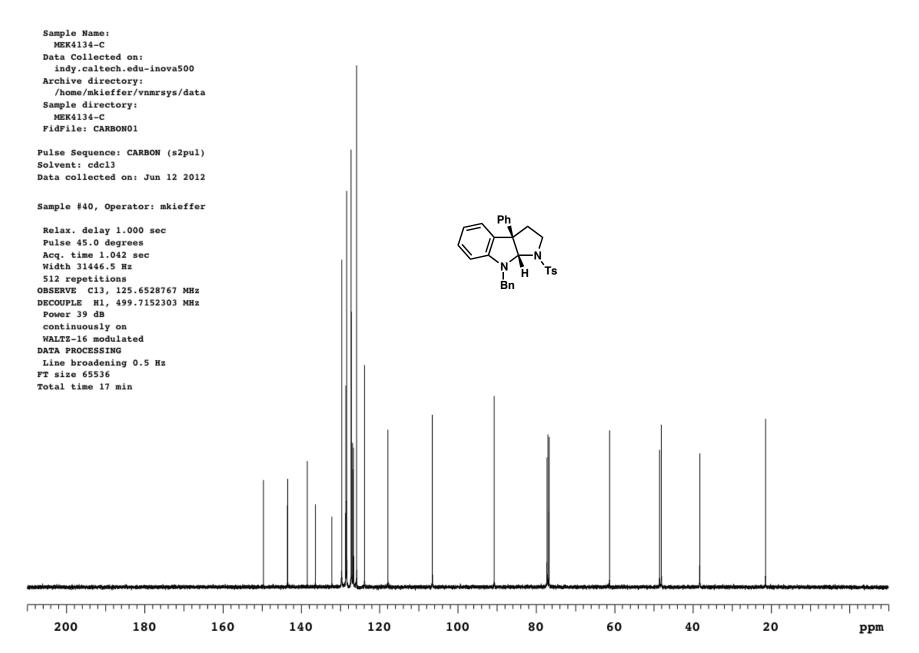




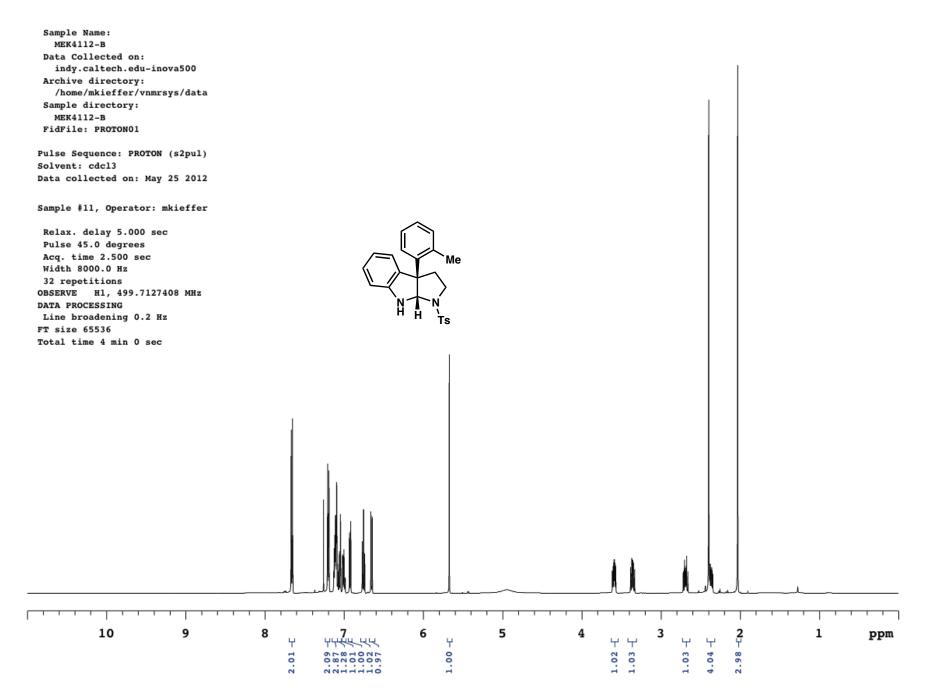
Marine States and States and States



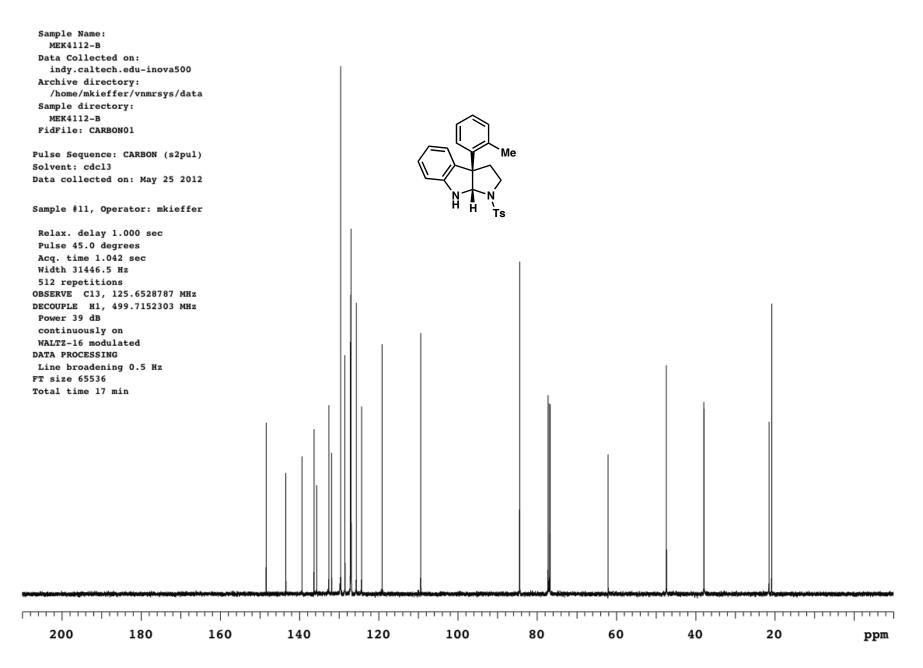
all sector field in the sector of the



Selection of the Selection of the

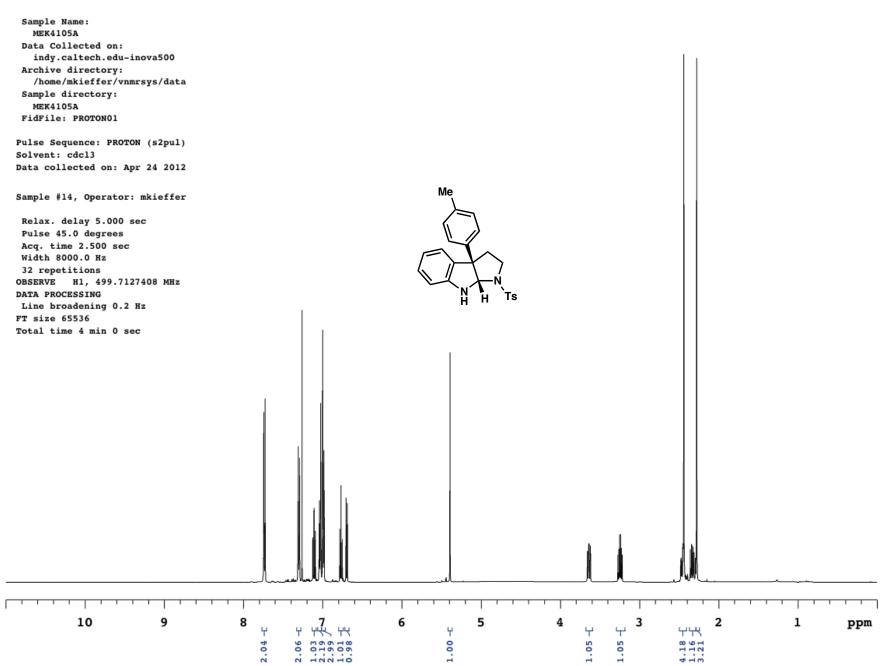


Storautor - Saturnation -

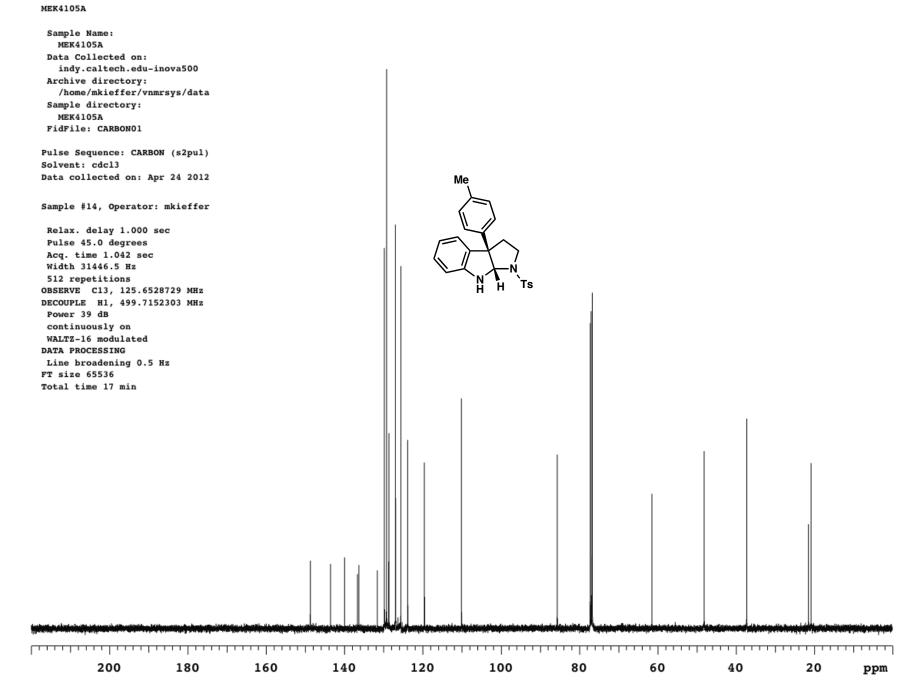


and a second second

MEK4105A

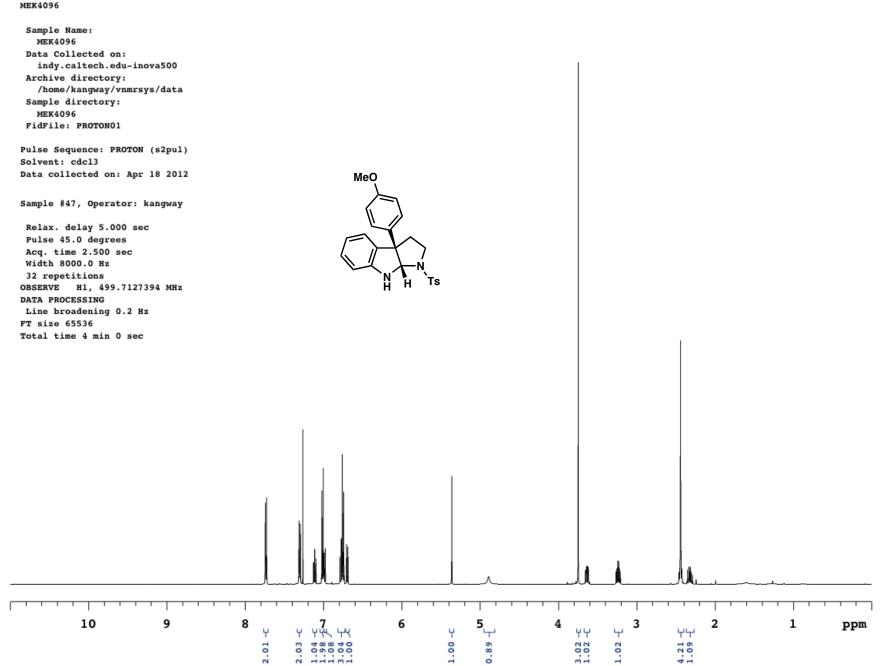


Sheet and the second se

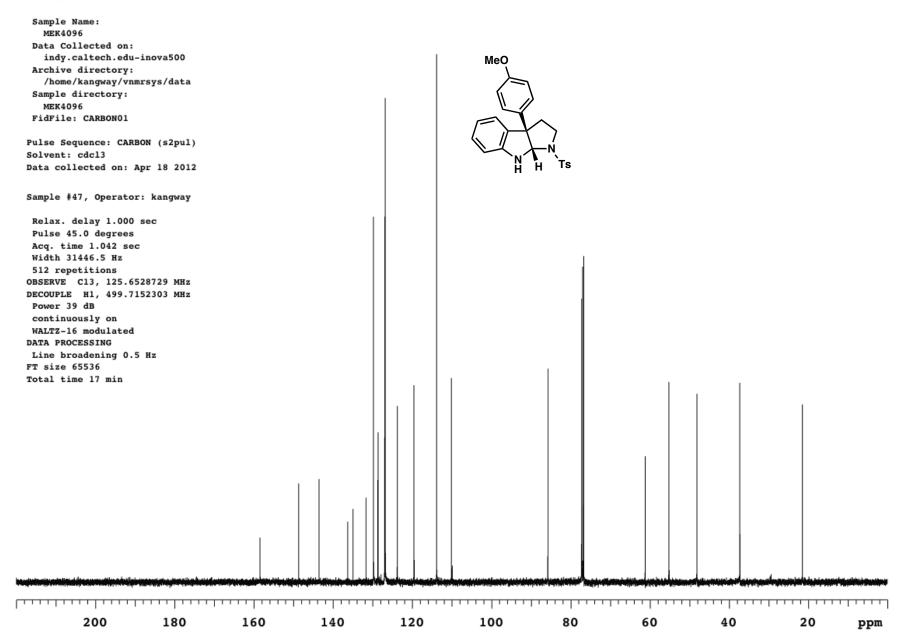


Content of Soft and soft of the

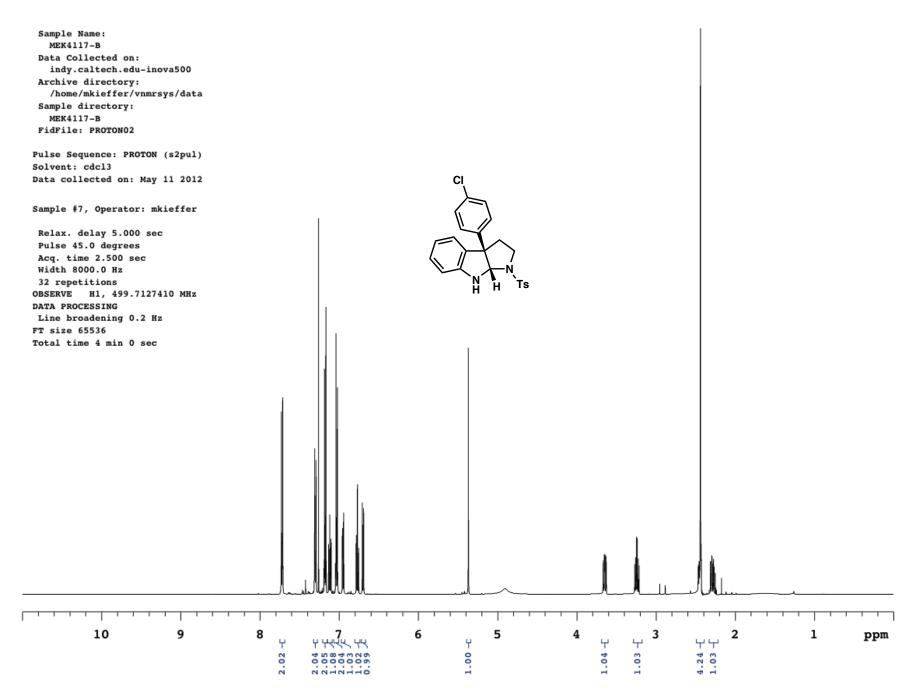




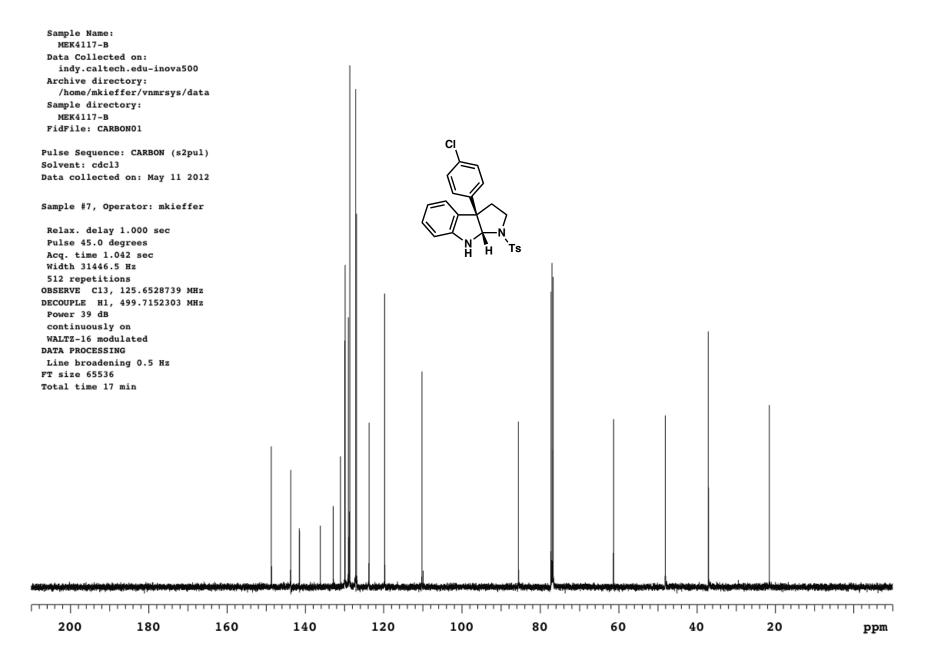
MEK4096



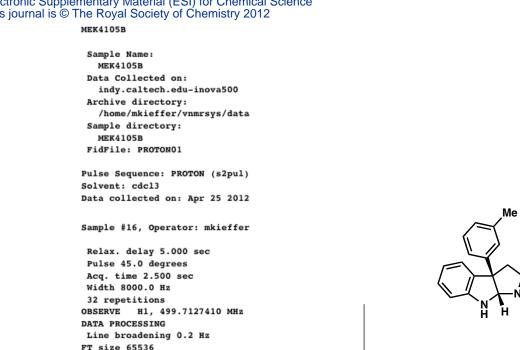
Show and the Safe arrest to the

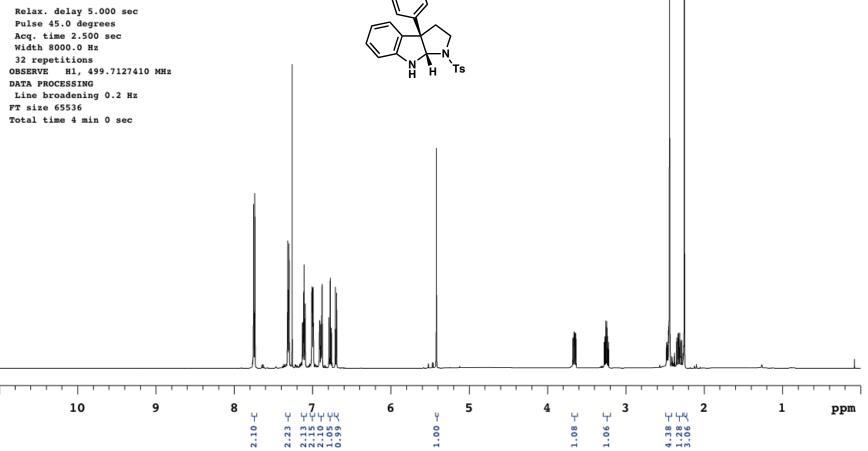


Storauter Saturnation 1

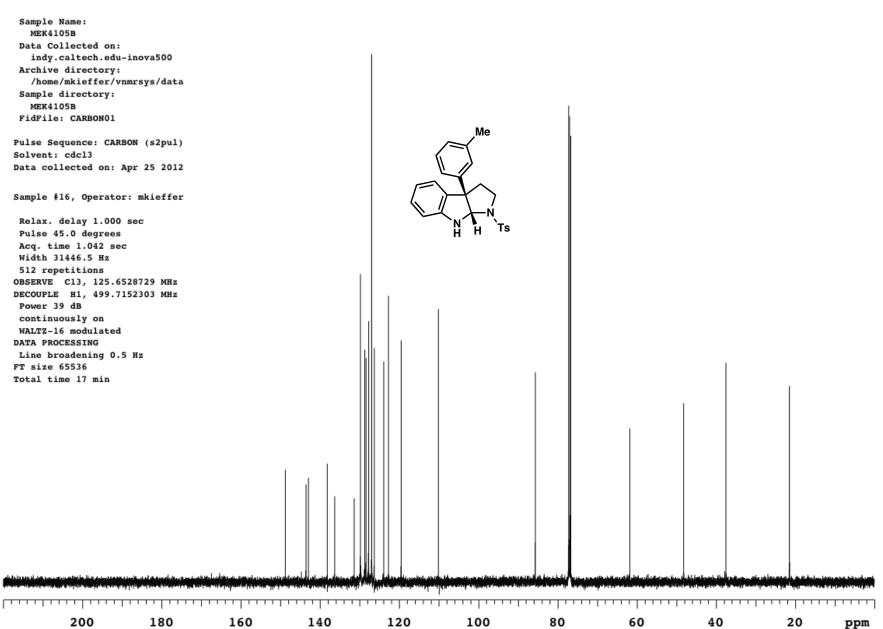


Selection of the Selection of the

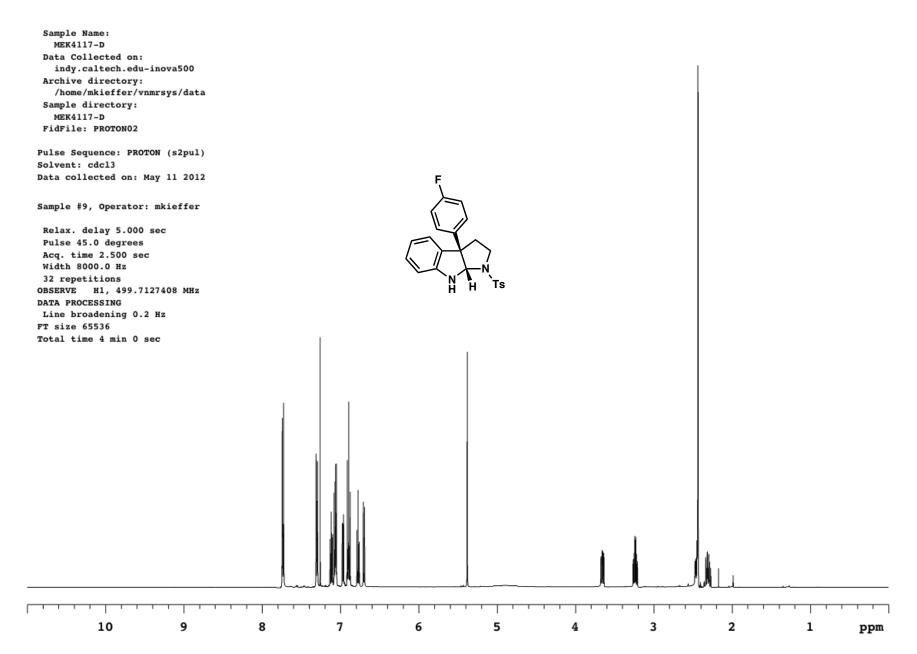




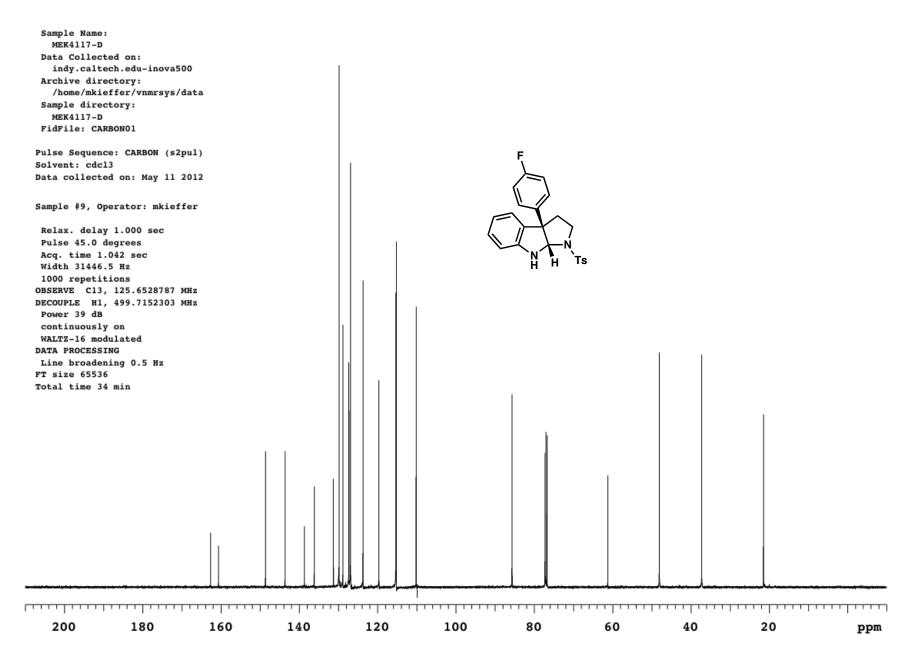




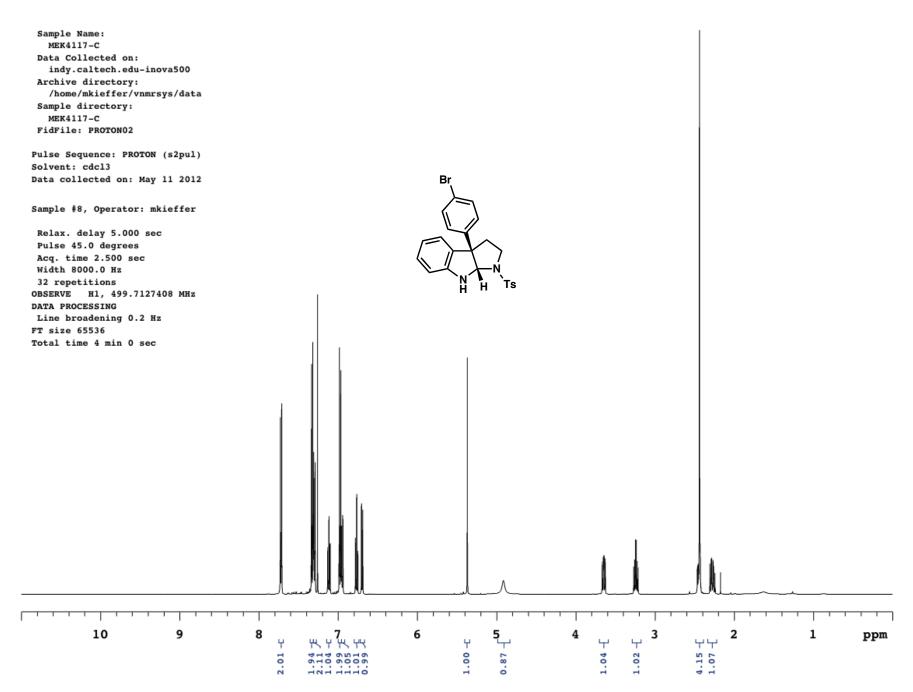
Storautics - Satures - Satures



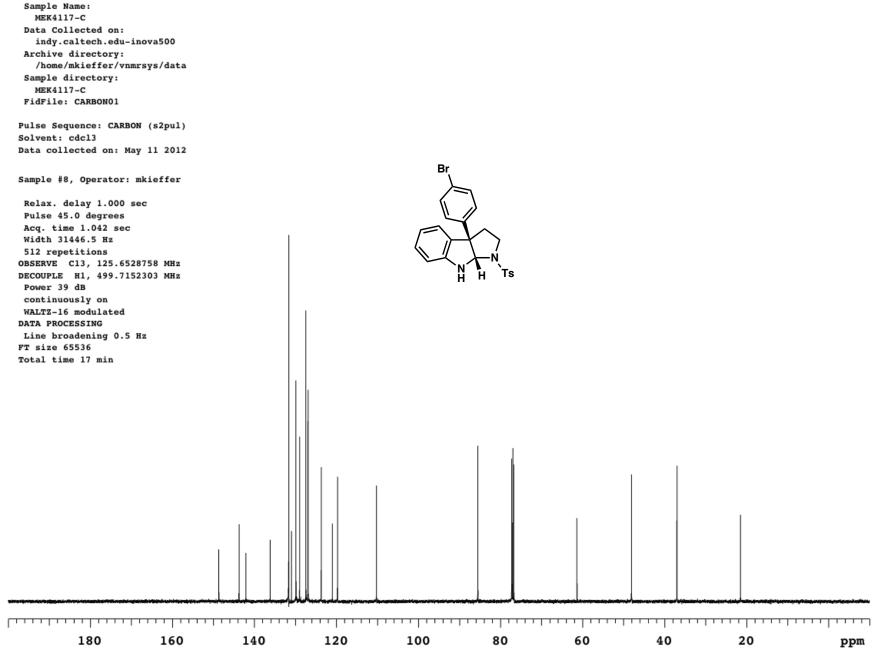
entre de la companya de la companya



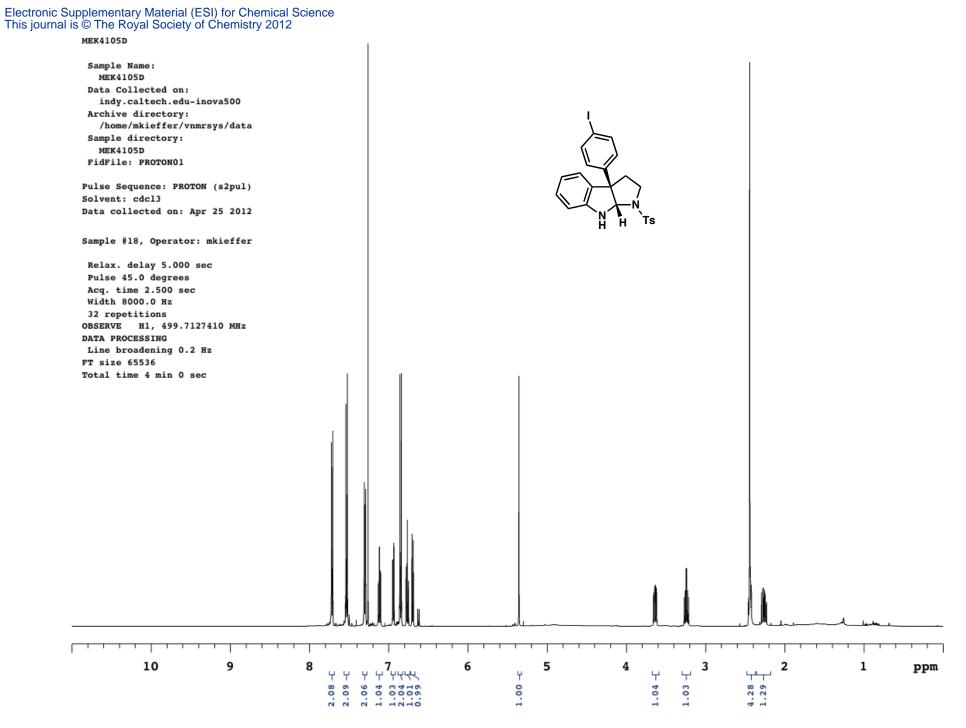
States and the Soft and soft and



Storactics - Satisfies as a

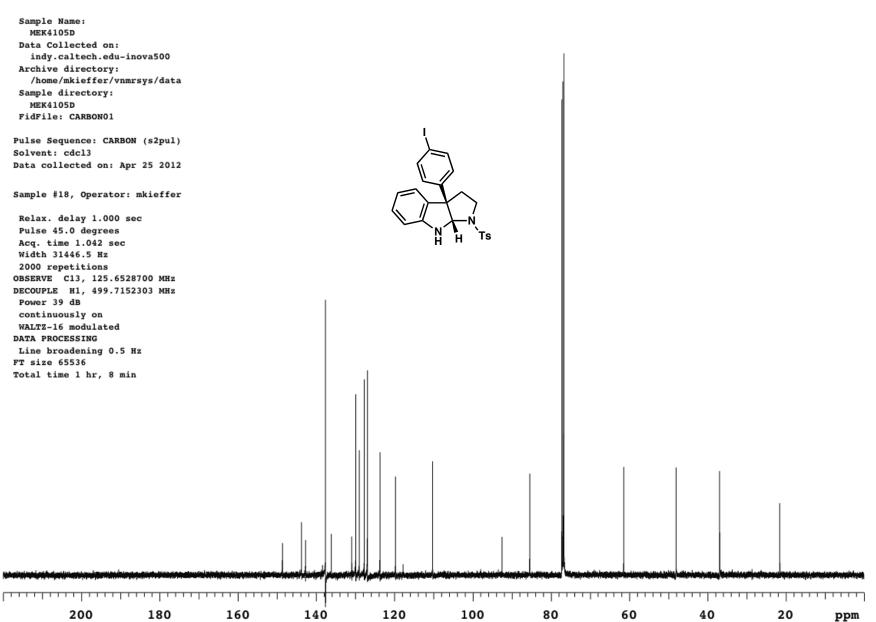


Contractor de Contractor de Contractor

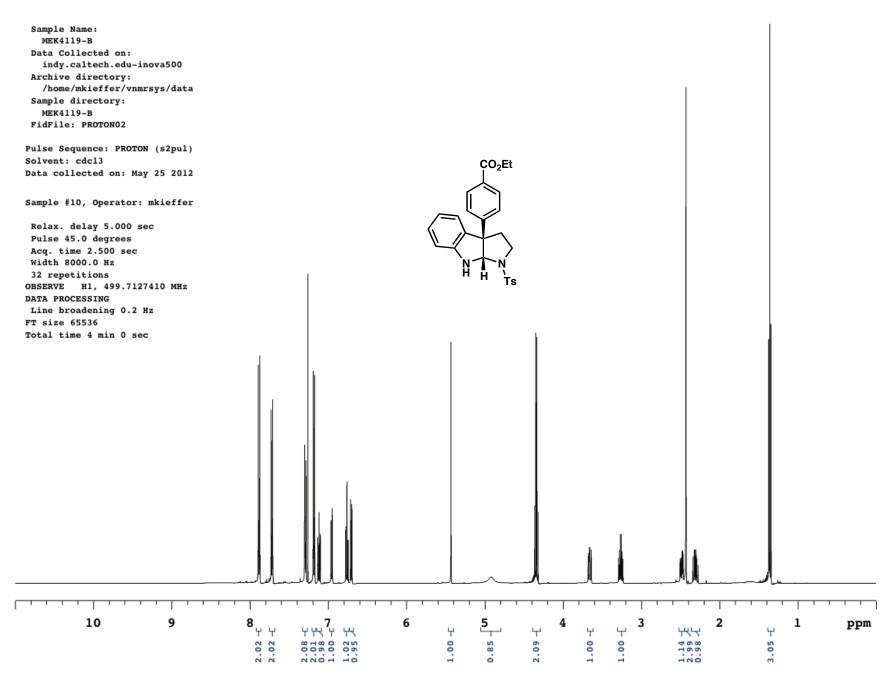


Sheet and the second seco

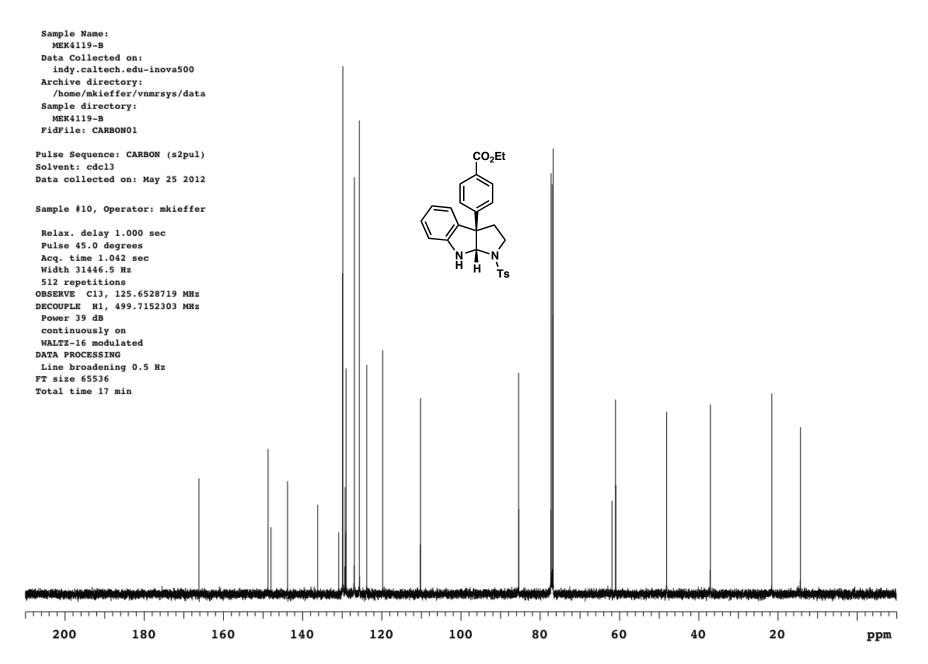




Set of set of the se



Alexandra Saturation Sector



sector sector sector sectors and se