SUPPORTING INFORMATION

for

Catalyst-free ambient temperature synthesis of isoquinoline-fused benzimidazoles from 2-alkynylbenzaldehydes via alkyne hydroamination

by Manisha Mishra,[a] Dylan Twardy,[b] Clifford Ellstrom,[a] Kraig A. Wheeler,[c] Roman Dembinski[b] and Béla Török*[a]

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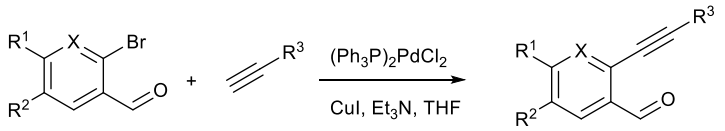
Content:

Synthesis of substituted aldehydes 4:



4

	R^1	R^2	R^3	X
4a	H	H	Ph	C
4b	O-CH_2-O		Ph	C
4c	H	F	Ph	C
4d	F	OMe	Ph	C
4e	H	H	cyclopropyl	C
4f	H	H	$SiMe_3$	C
4g	H	H	Ph	N

Scheme SI 1. Synthesis of substituted alkynylbenzaldehyde derivatives[1]

General procedure for the synthesis of substituted aldehydes 4[1]:
A Schlenk flask (25 mL) equipped with a septum was charged with a 2-bromo-benzaldehyde (1.0 equiv), triethylamine (2.0 equiv), alkyne (1.2-1.4 equiv), and THF (7 mL). Nitrogen was purged through the solution via syringe needle for at least 15 min. Another Schlenk flask (25 mL), equipped with a reflux condenser, was charged with *trans*-dichlorobis(triphenylphosphine)palladium(II) (0.03 equiv), and copper iodide (0.05 equiv). The flask was evacuated and refilled with nitrogen, and the solution containing 2-bromo-benzaldehyde was added via syringe. The reaction mixture was stirred (magnetic stir bar) and heated at 70-80^{o}C (50^{o}C for **4g**) for 12 h. The solvent was removed by rotary evaporator and oil pump vacuum. Silica gel column chromatography (2 × 15 cm; hexanes/ethyl acetate 5-10%) gave usually colorless fractions. For **4d**, recrystallization from ethyl acetate gave crystals that were used for analysis. The spectral data of 2-(phenylethynyl)benzaldehyde (**4a**),[2,3] 6-(phenylethynyl)benzo[*d*][1,3]dioxole-5-carbaldehyde (or 6-phenylethynylpiperonal) (**4b**),[4] 5-fluoro-2-(phenylethynyl)benzaldehyde (**4c**)[5] 2-(cyclopropylethynyl)benzaldehyde (**4e**),[6] 2-(phenylethynyl)nicotinaldehyde (**4g**),[6] were in agreement with those reported in literature.

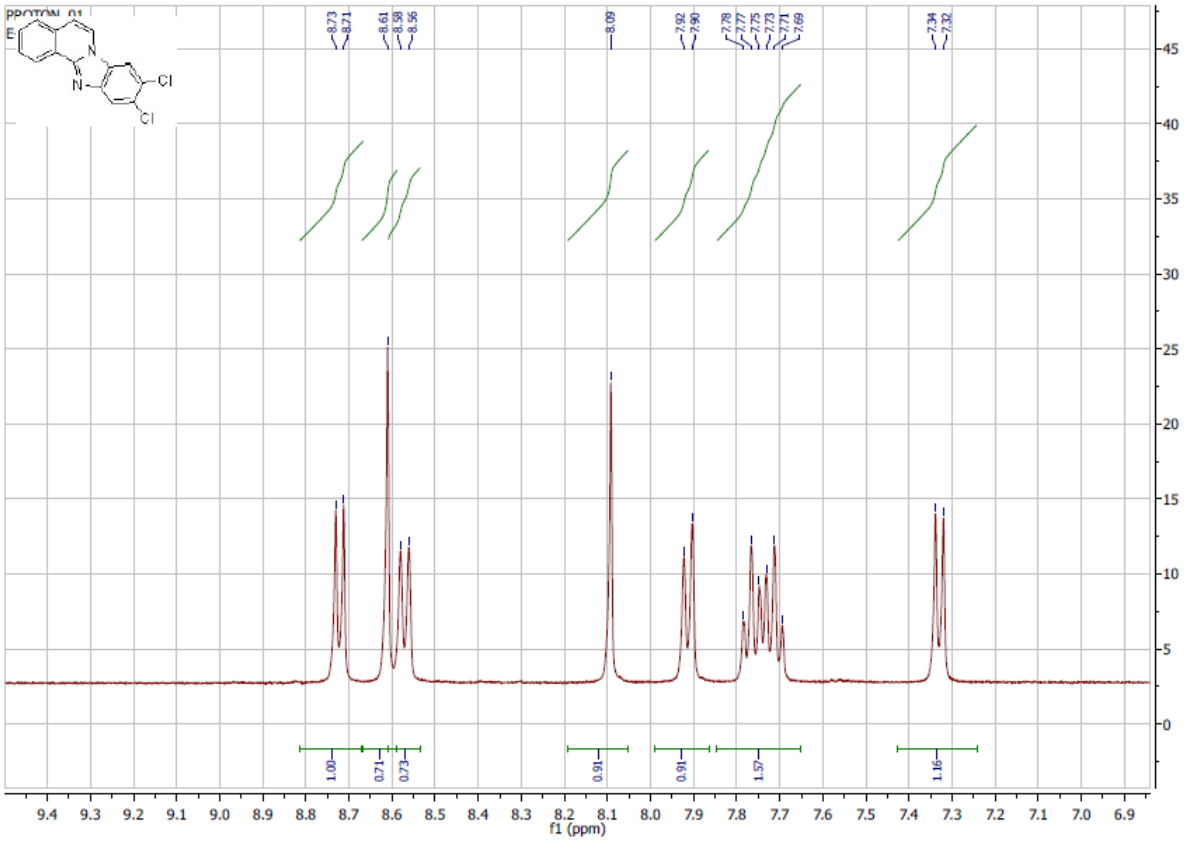
5-Fluoro-4-methoxy-2-(phenylethynyl)benzaldehyde (**4d**): yield: 45%; colorless solid, mp: 121-125 °C; ^{1}H NMR: ($CDCl_3$, 400 MHz): δ(ppm) = 3.97 (3H, s), 7.35 (1H, d, *J* = 11.0 Hz), 7.37-7.41 (3H, m), 7.51 (1H, part of d, second line obscured), 7.53-7.57 (2H, m), 10.54 (1H, s). ^{13}C NMR: ($CDCl_3$, 100 MHz): δ(ppm) = 56.51, 83.73 (d, J = 2.8 Hz), 95.98, 111.00 (d, J = 3.8 Hz), 120.38 (d, J = 20.5 Hz), 121.01 (d, J = 9.6 Hz), 122.33, 128.72(2C), 129.28, 131.78(2C), 133.26 (d, J = 2.9 Hz), 148.89 (d, J = 11.4 Hz), 155.71 (d, J = 258.1 Hz), 190.39. IR (ν, cm^{-1}): 3369, 3081, 3020, 2973, 2939, 2852, 2760, 2393, 2213, 2081, 1782, 1692, 1610, 1566; HRMS: (ESI-TOF) $[M + H]^+$ calcd for $C_{16}H_{12}FO_2$ 255.0816, found 255.0817.

References for the synthesis and characterization of compounds **4**:

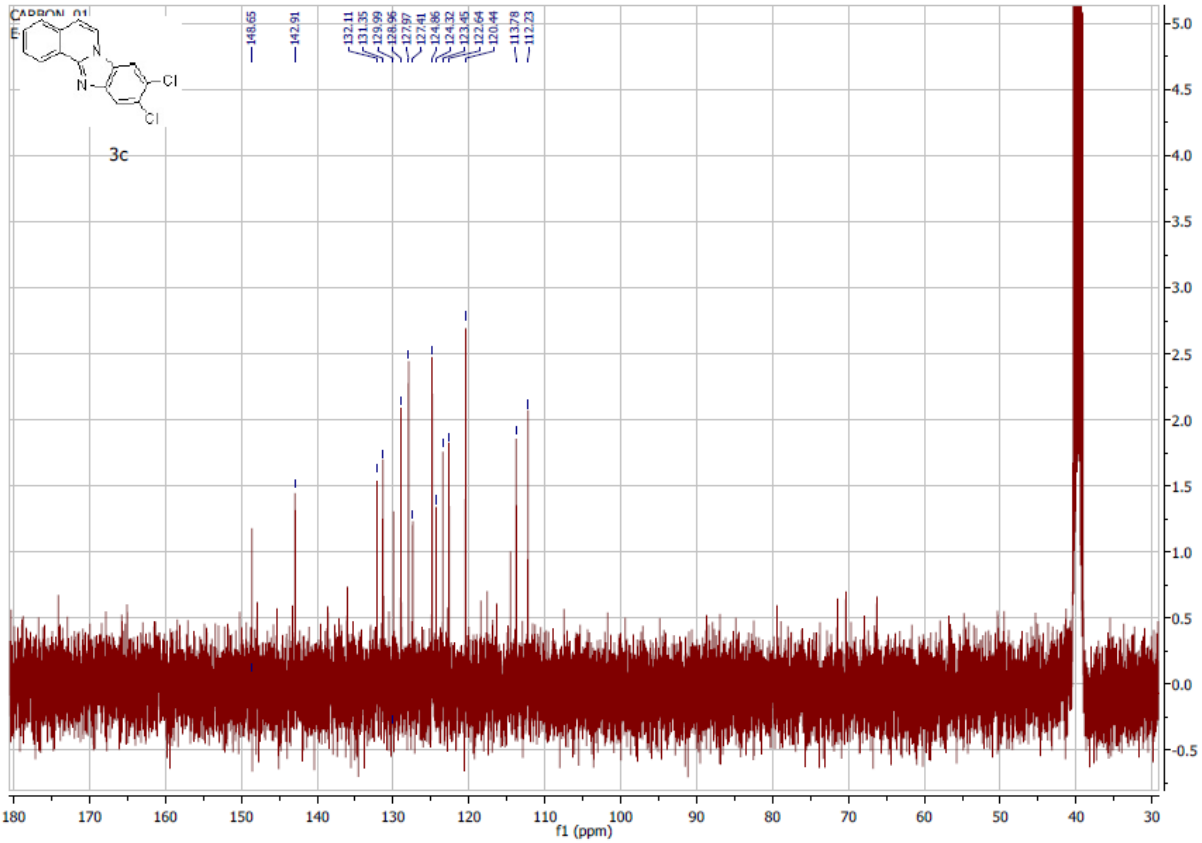
[1] S. Zhu, H. Huang, Z. Zhang, T. Ma, H. Jiang, *J. Org. Chem.*, 2014, **79**, 6113.
[2] G. Dyker, W. Stirner and G. Henkel, *Eur. J. Org. Chem.*, 2000, 1433.
[3] K. R. Roesch, R. C. Larock, *J. Org. Chem.*, 2002, **67**, 86.
[4] I. Cikotiene, R. Buksnaitiene, R. Sazinas, *Tetrahedron*, 2011, **67**, 706.
[5] Z. Chai, Z. Xie, X. Liu, G. Zhao, J. Wang, *J. Org. Chem.*, 2008, **73**, 2947.
[6] J. Park, S. Bhilare, S. Youn, *Org. Lett.*, 2011, **13**, 2228.

^{1}H and ^{13}C NMR spectra of compounds 3 and 5

^{1}H NMR of **3c**



^{13}C NMR of **3c**



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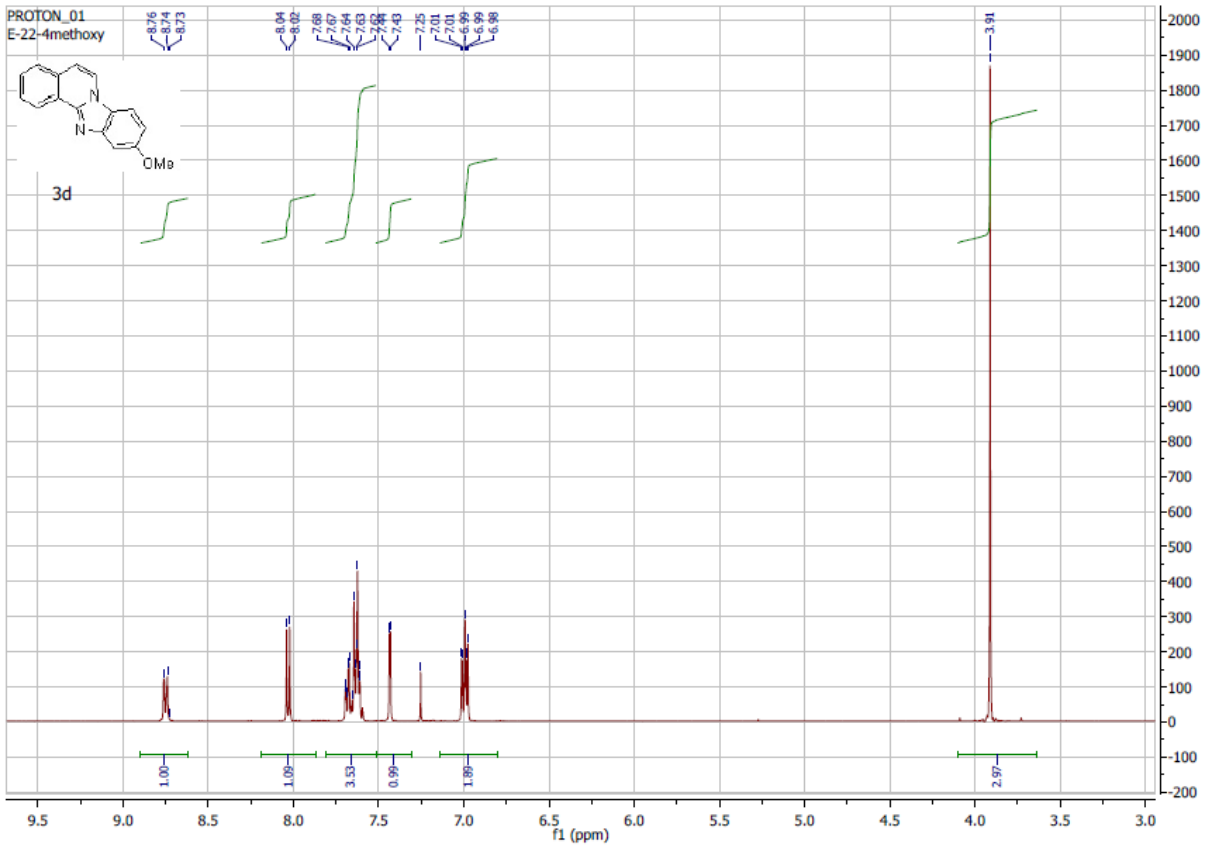

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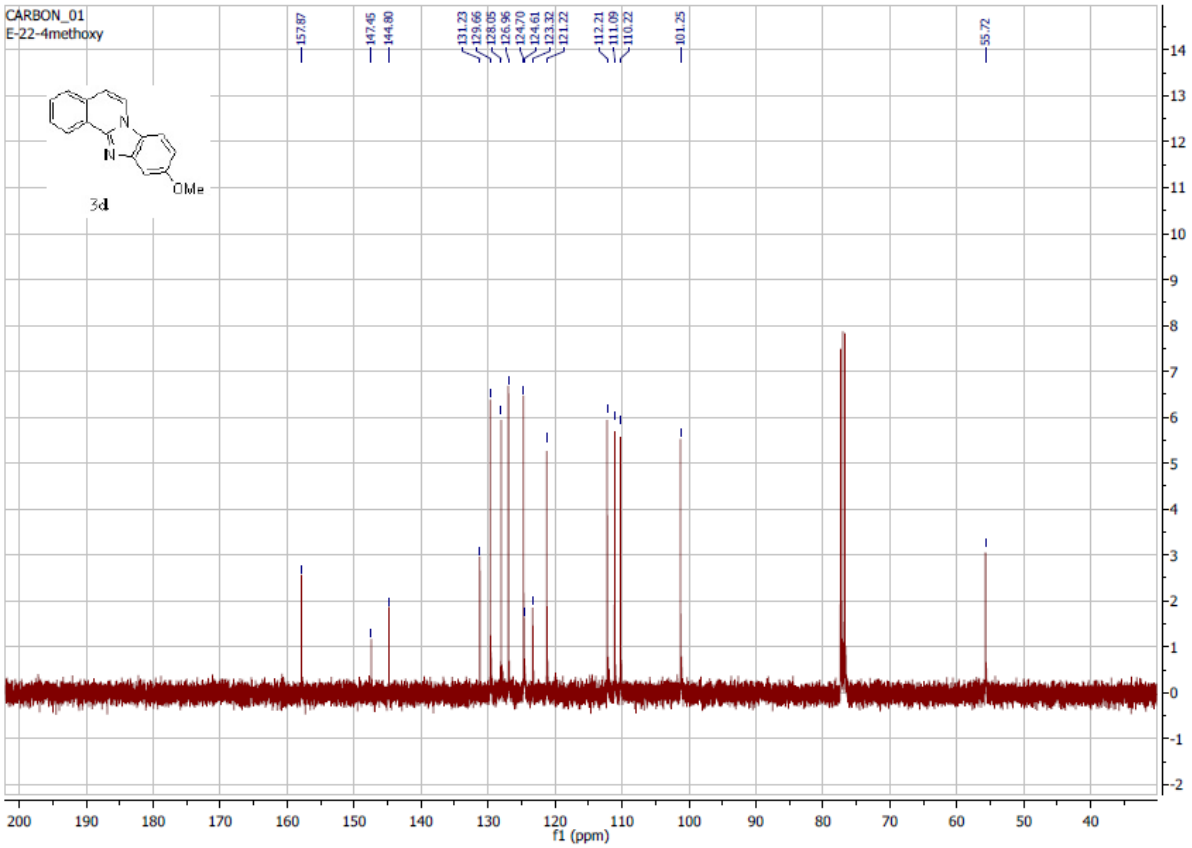

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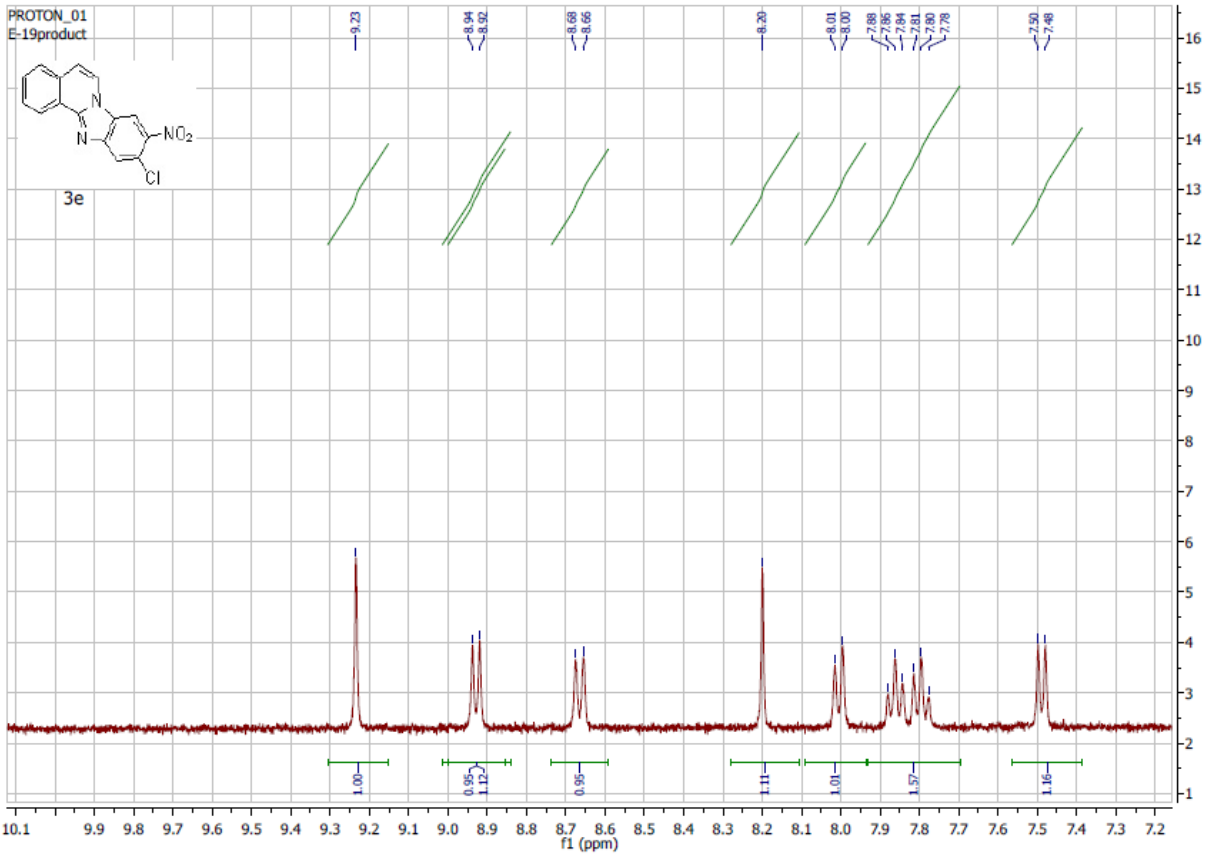

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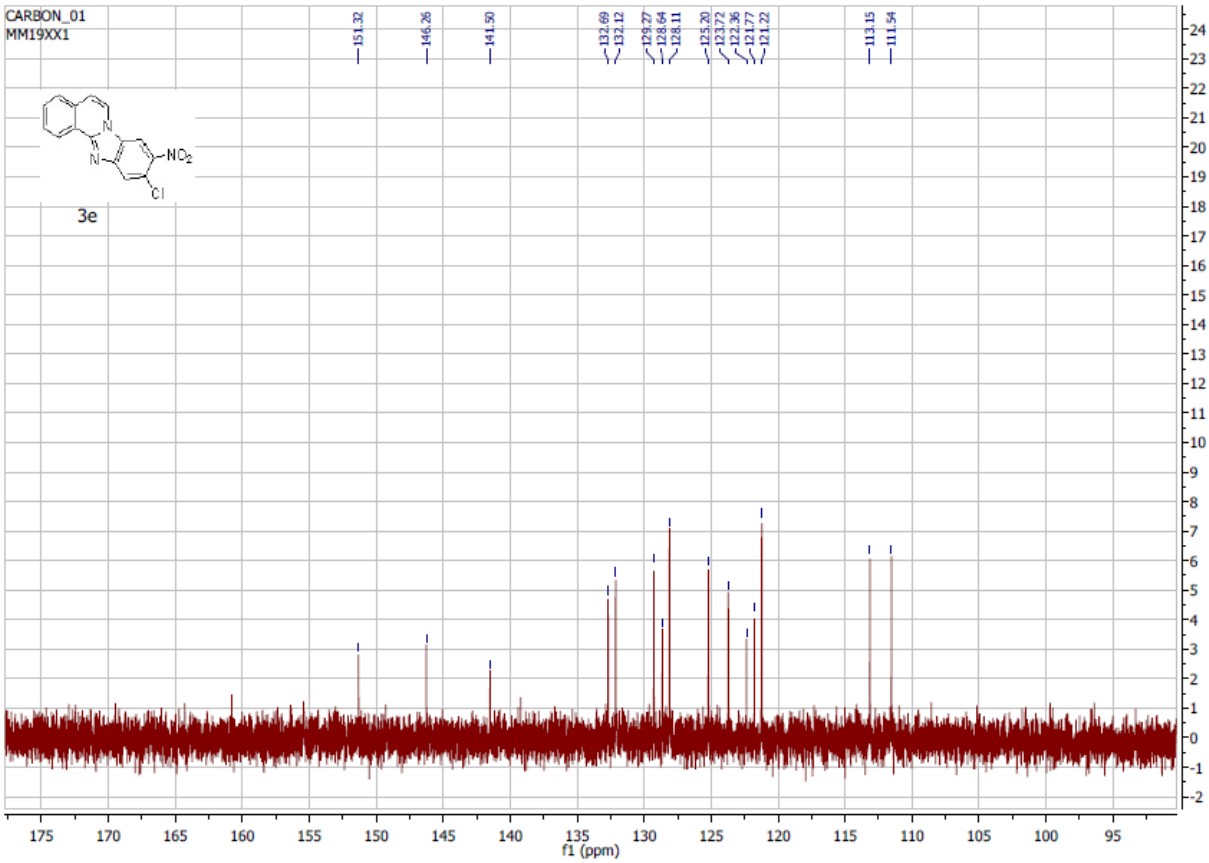

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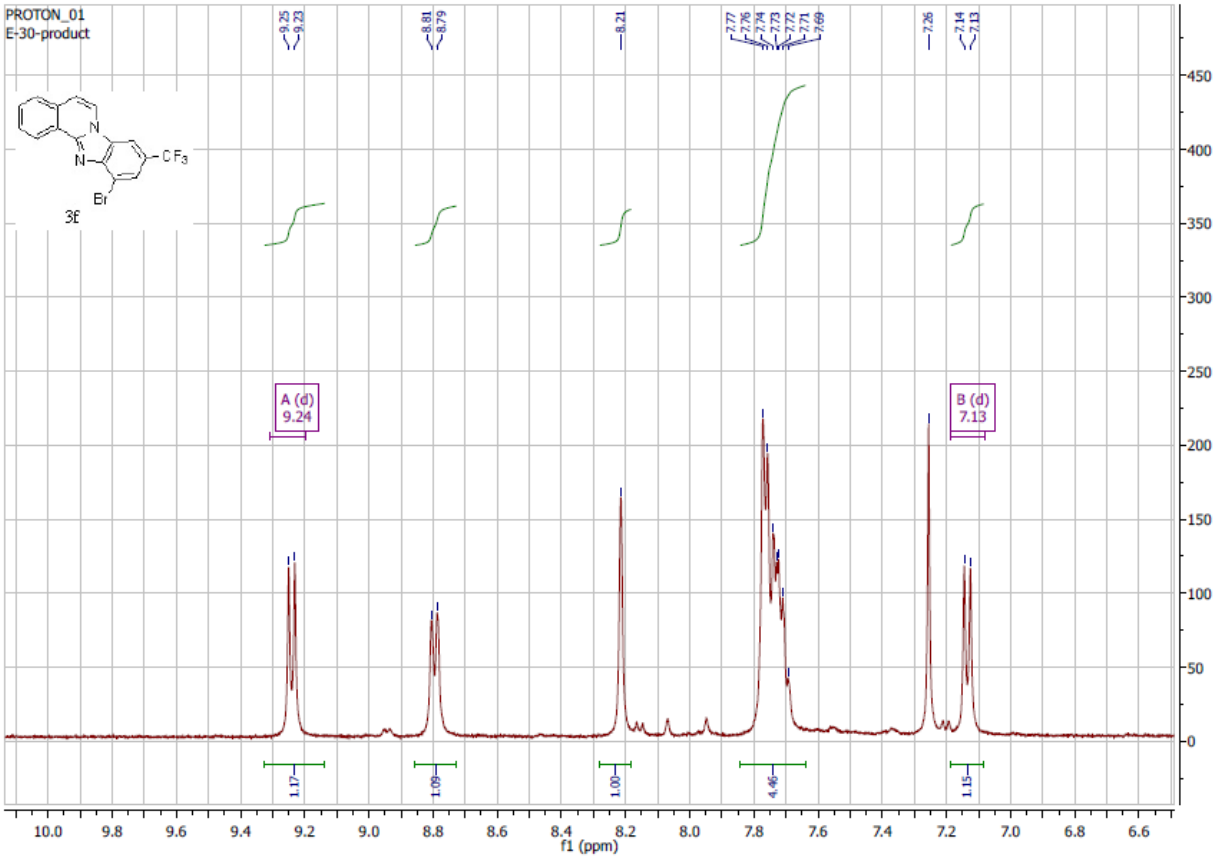

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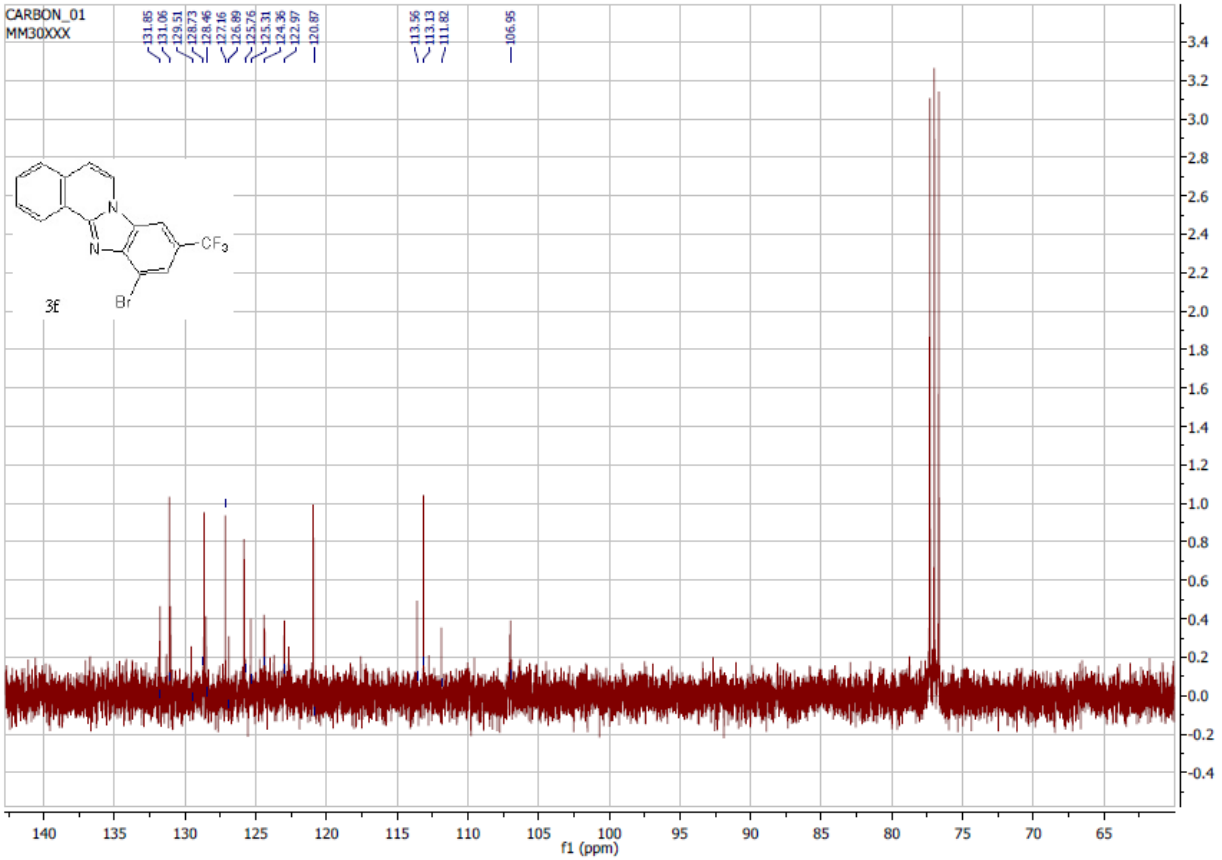

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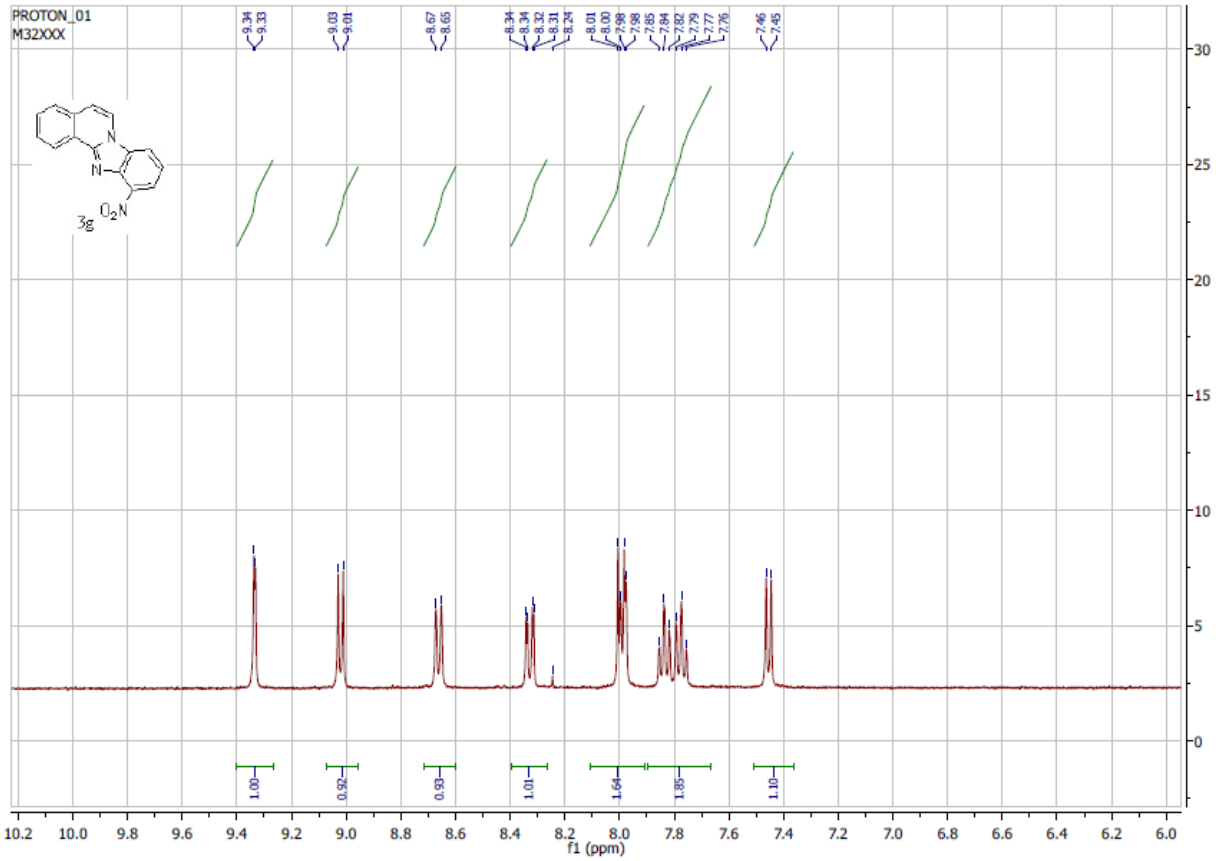

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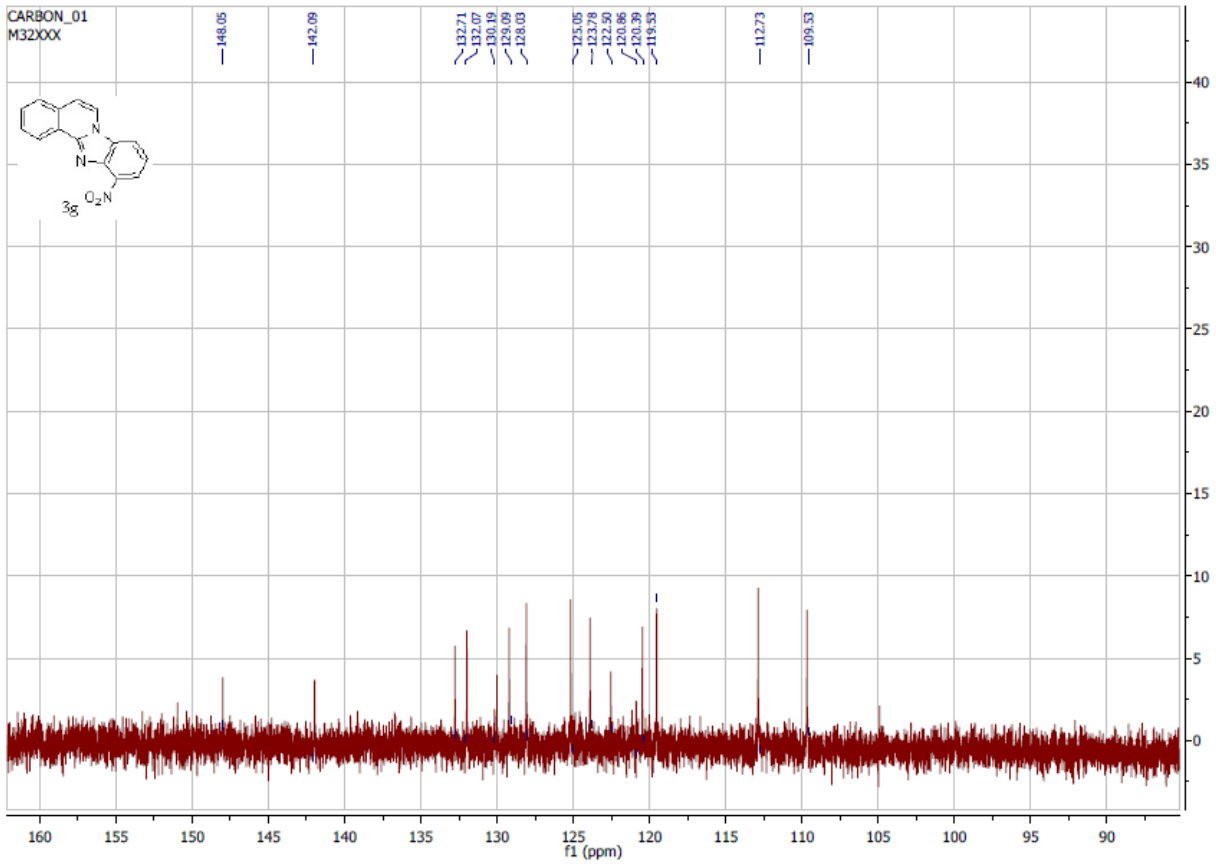

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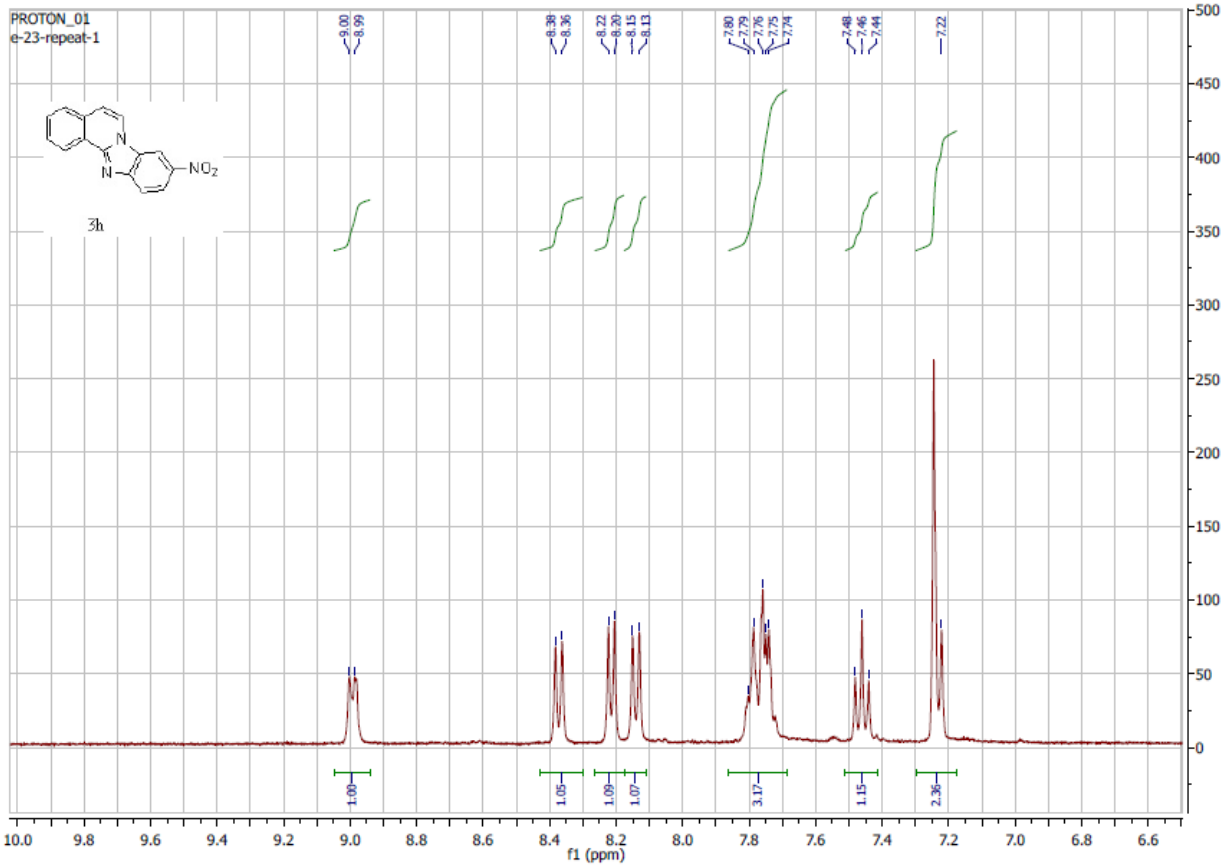

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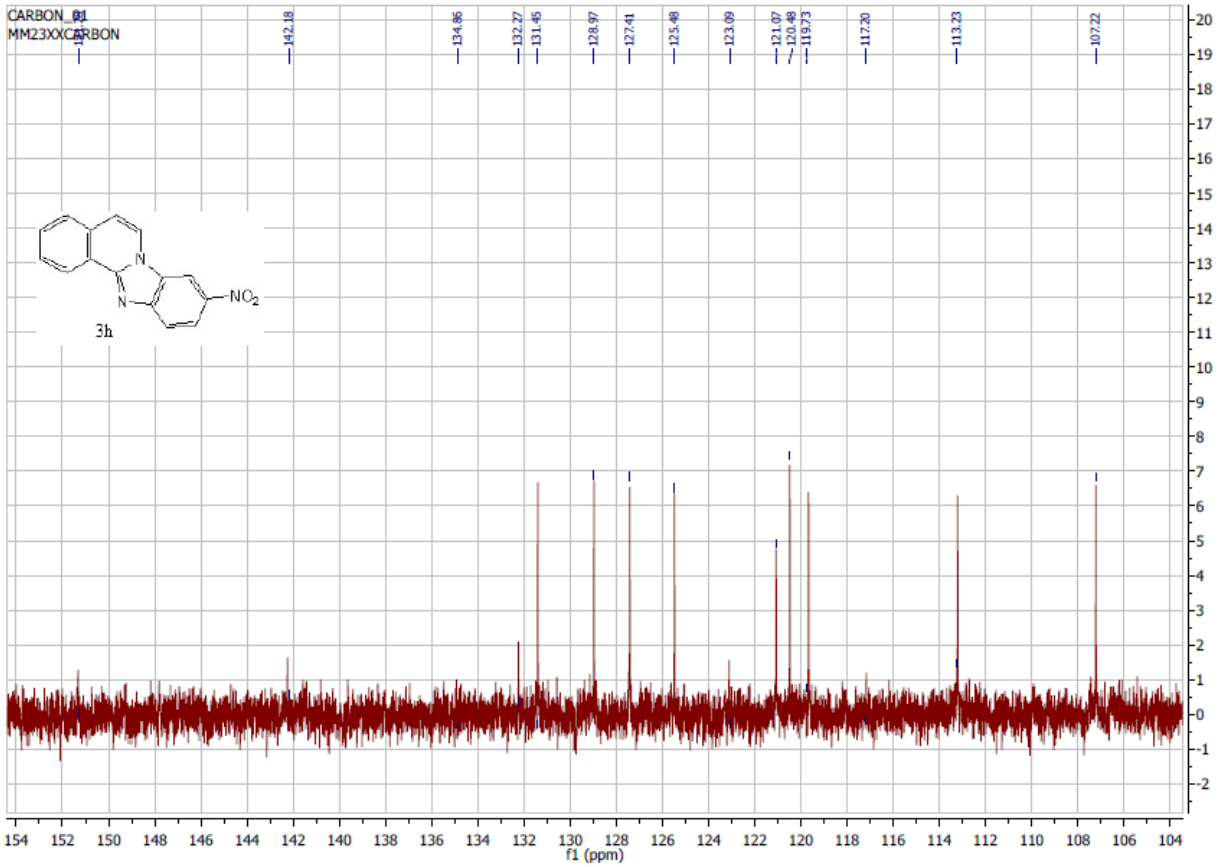

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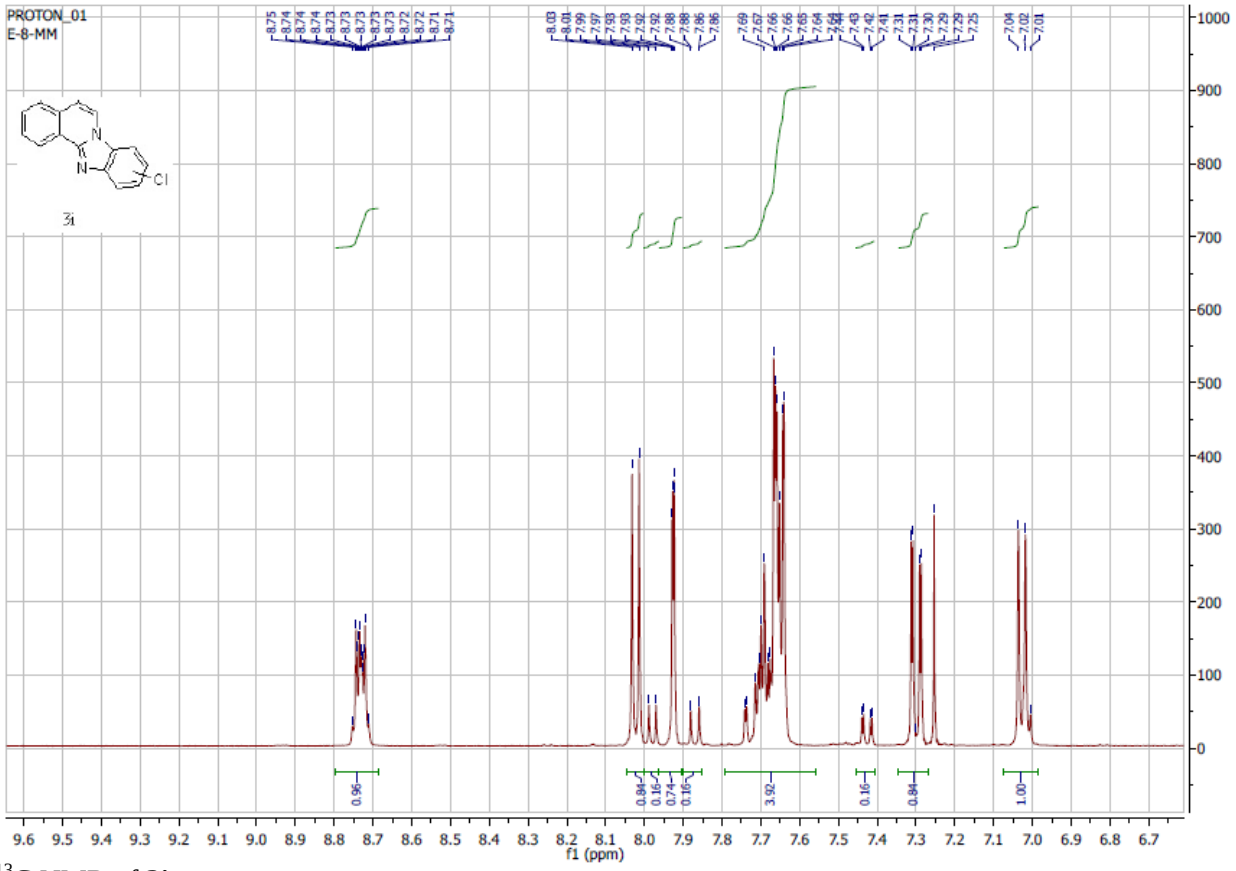

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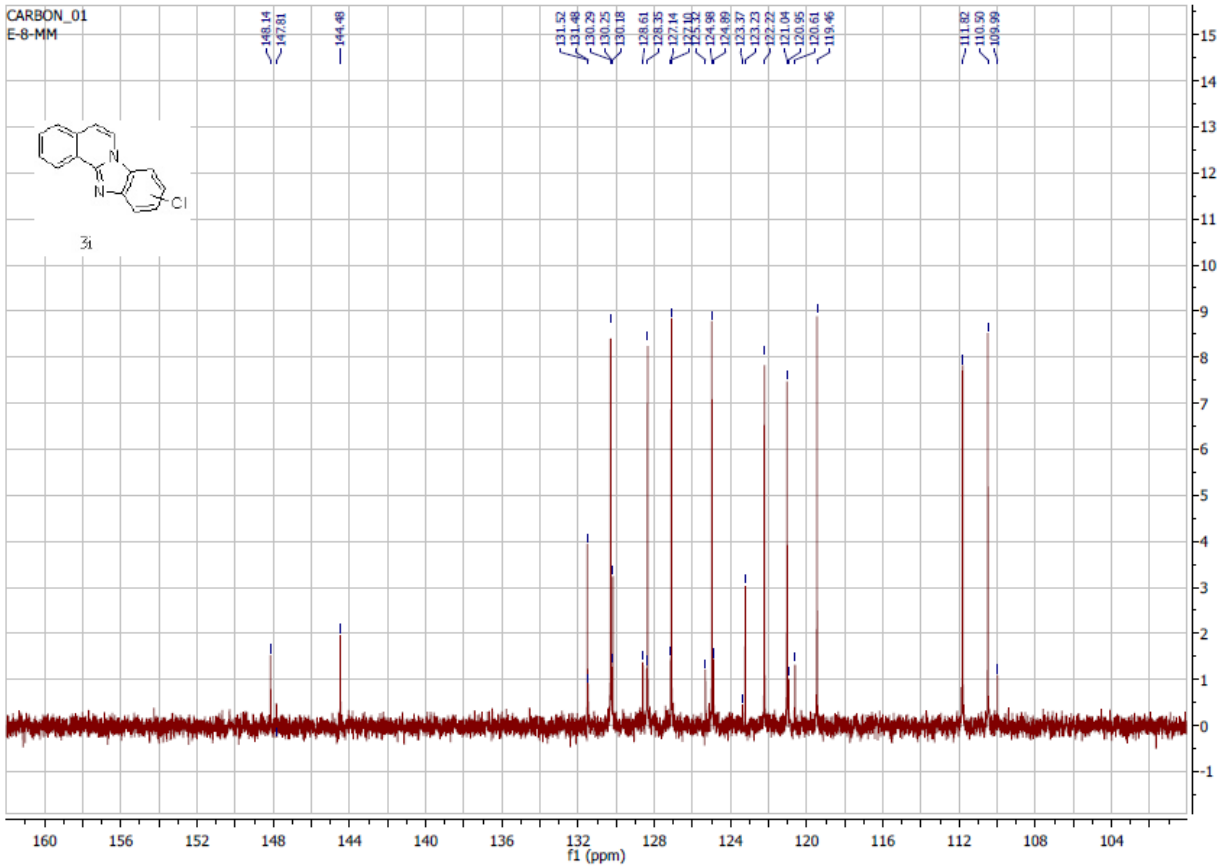

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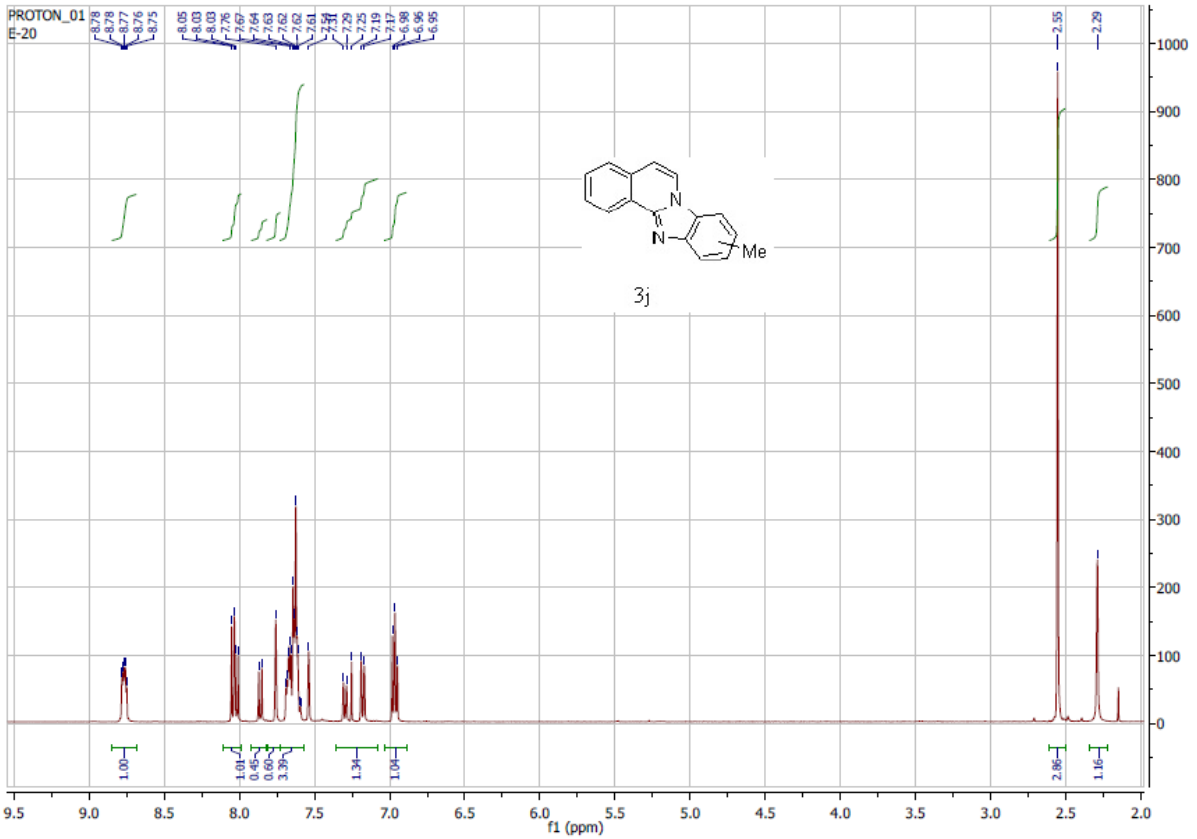

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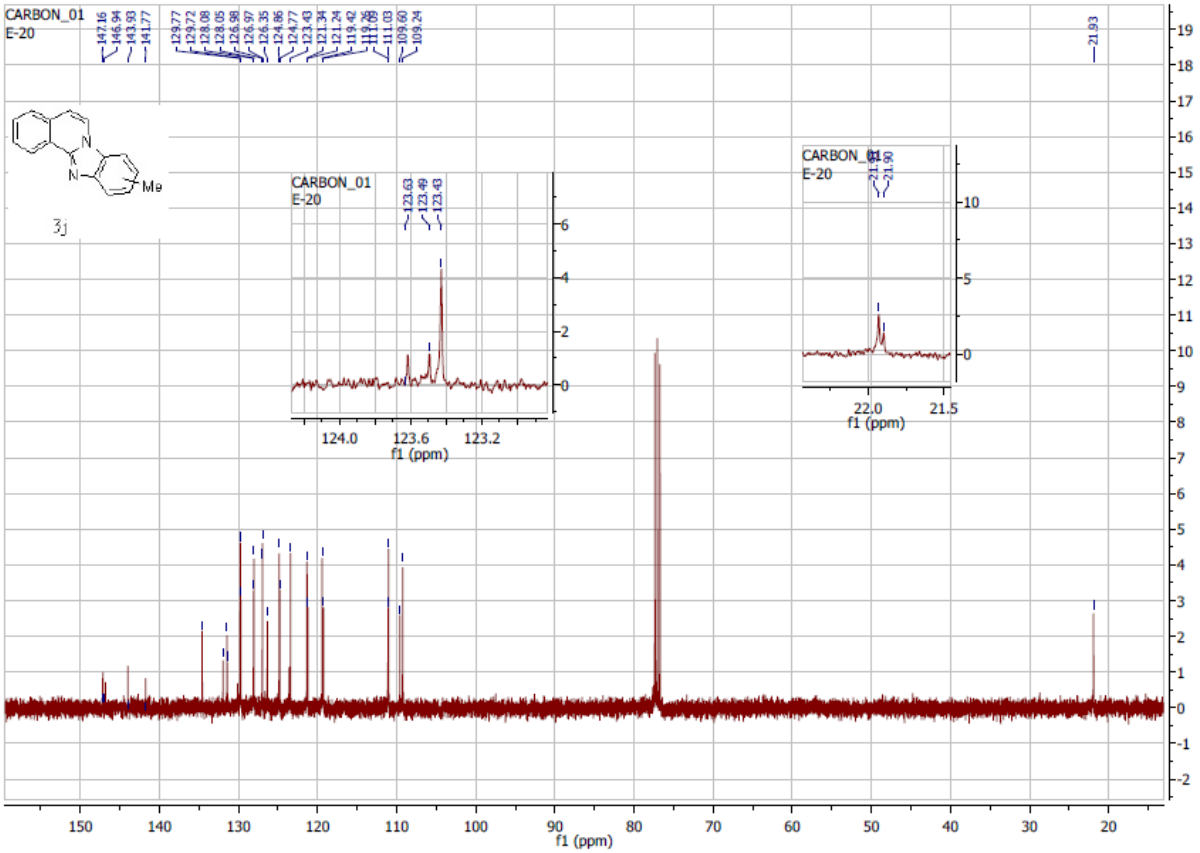

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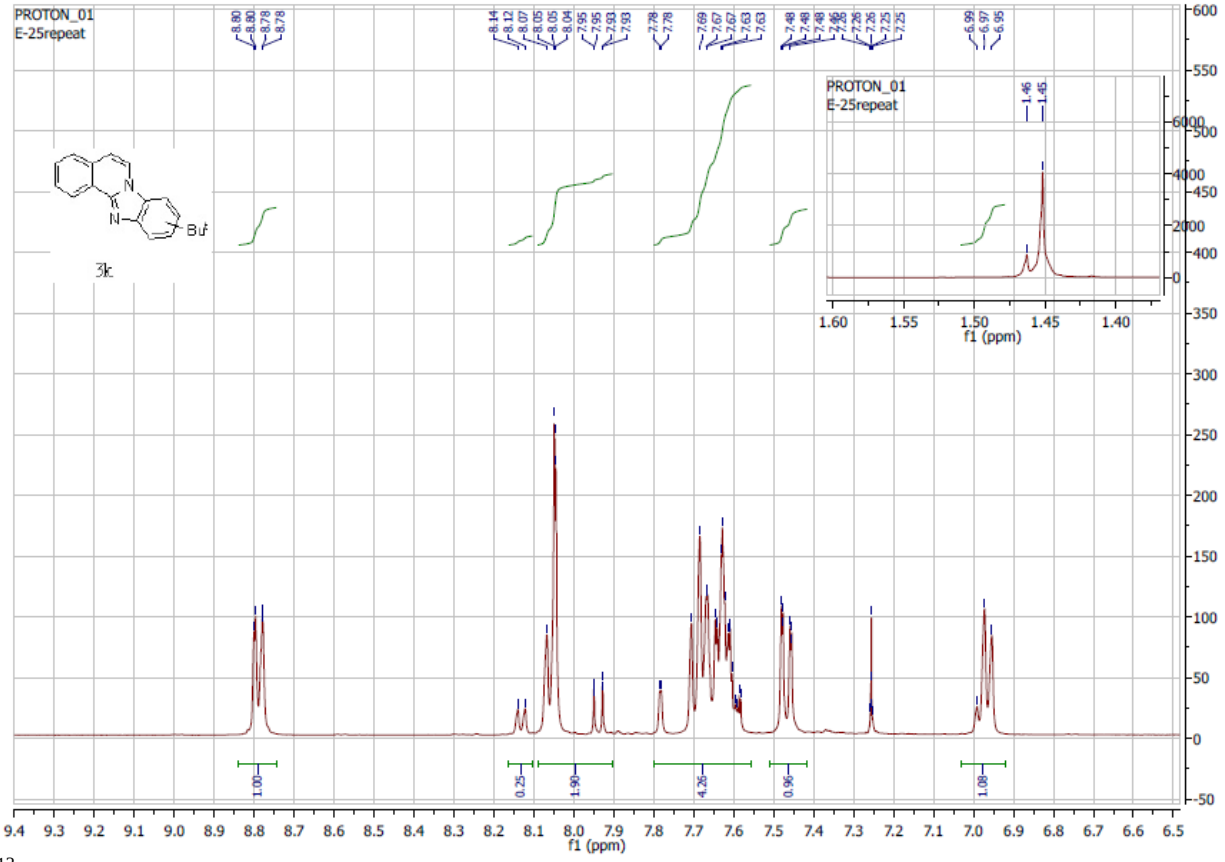

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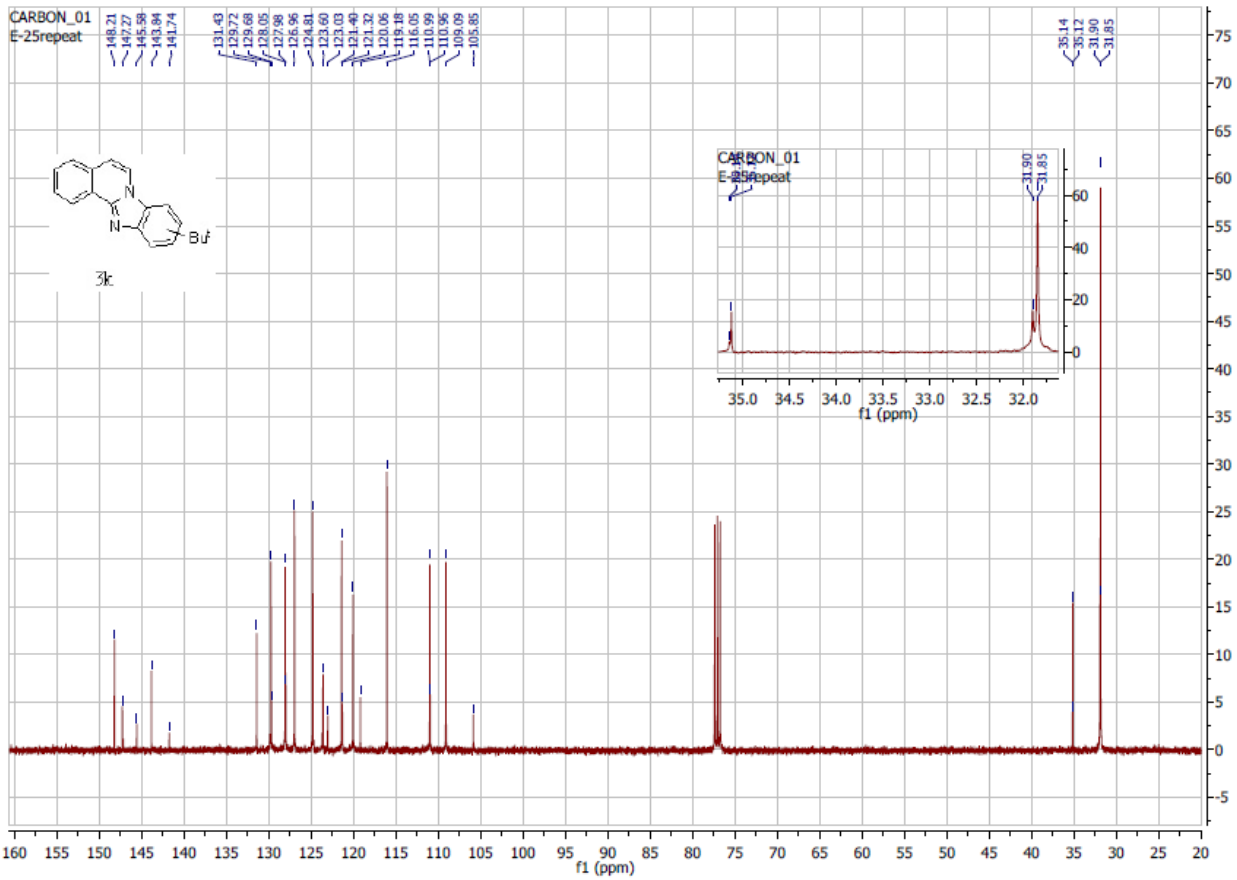

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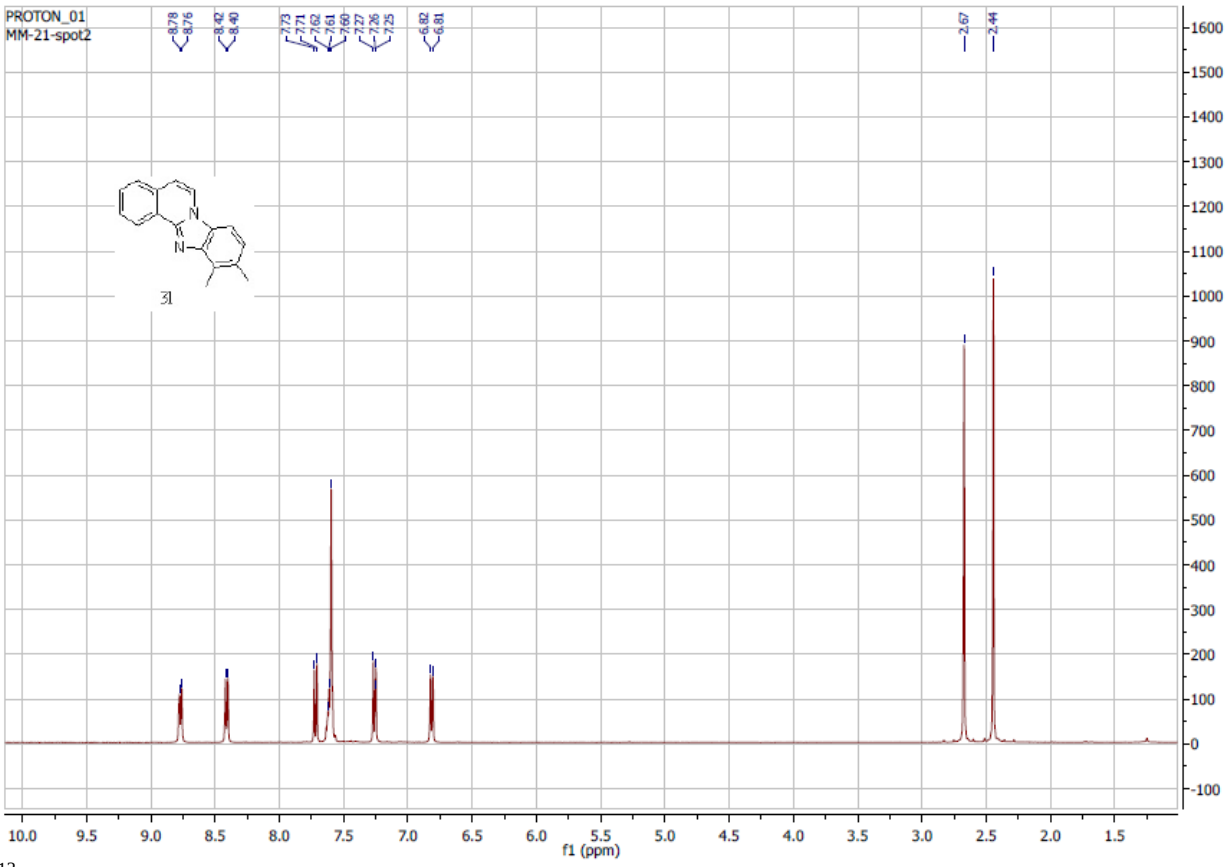

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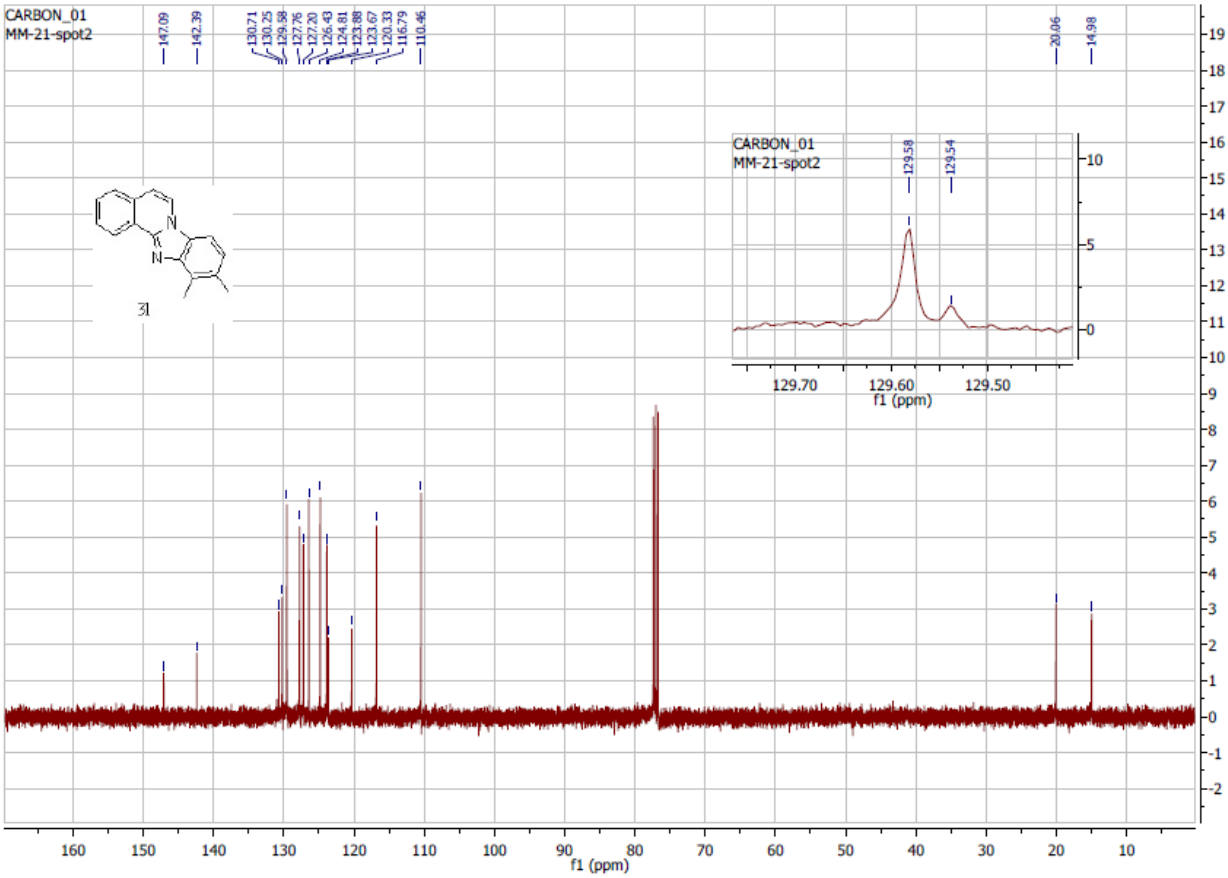

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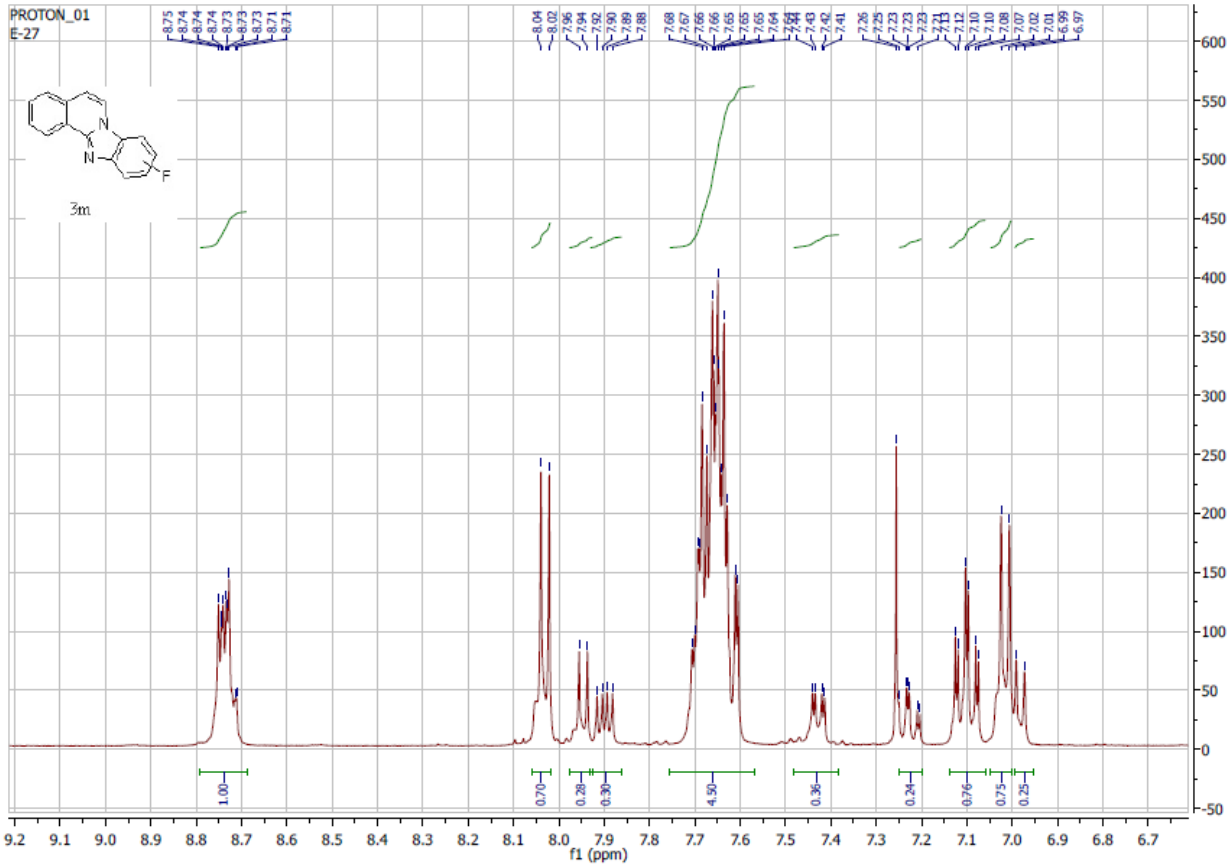

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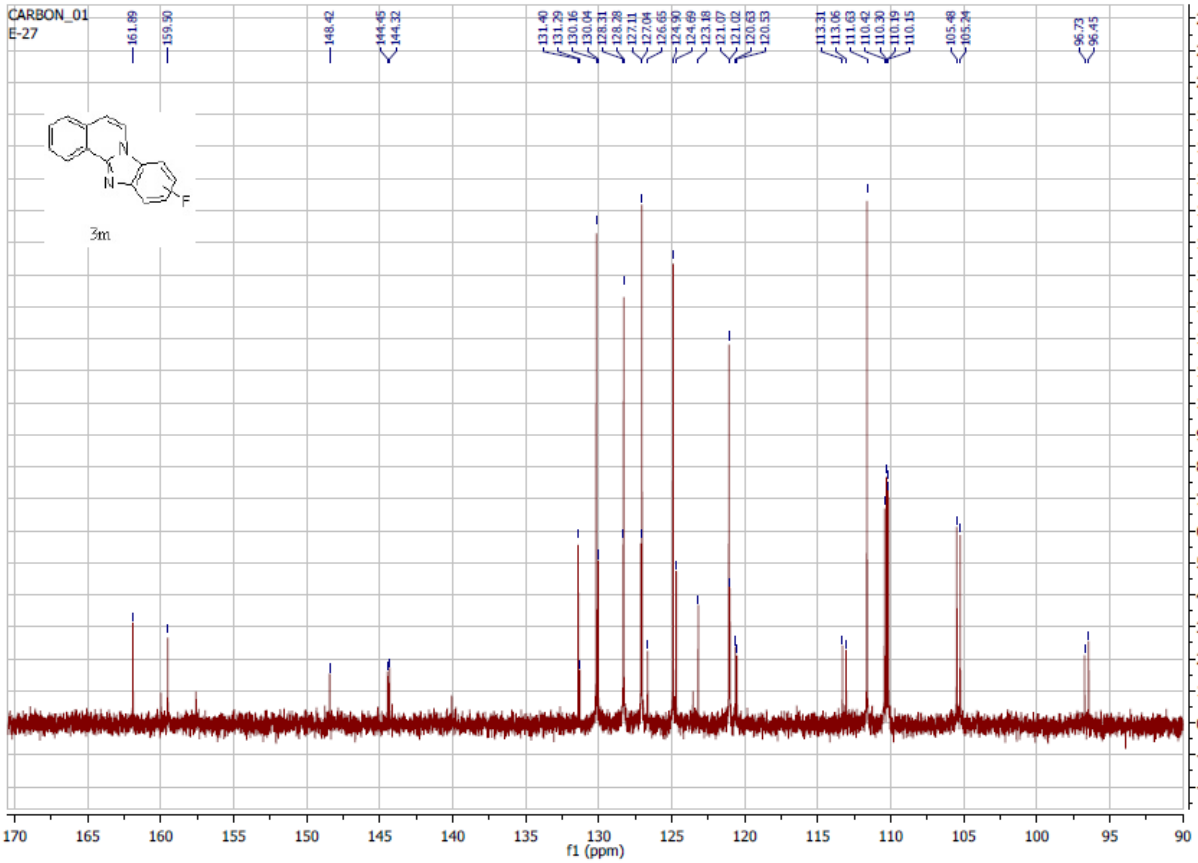

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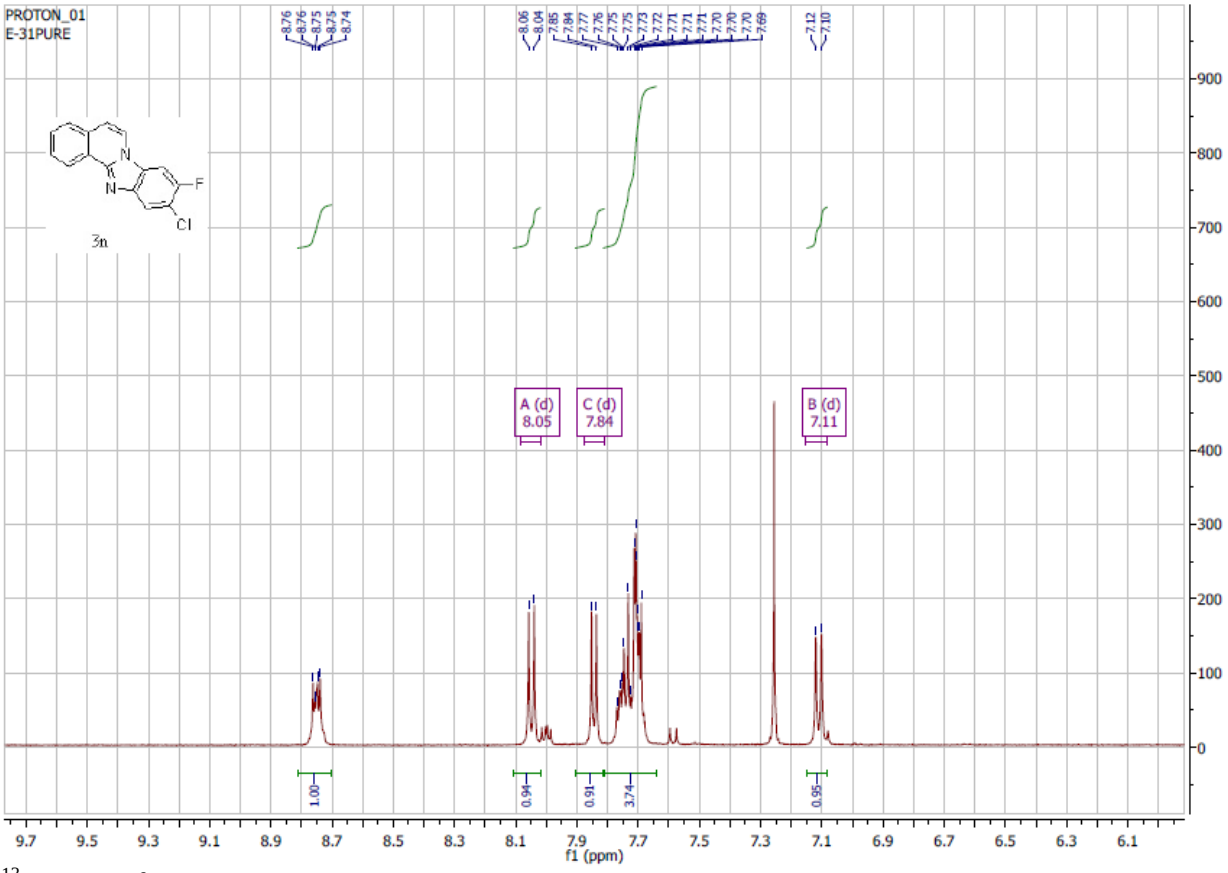

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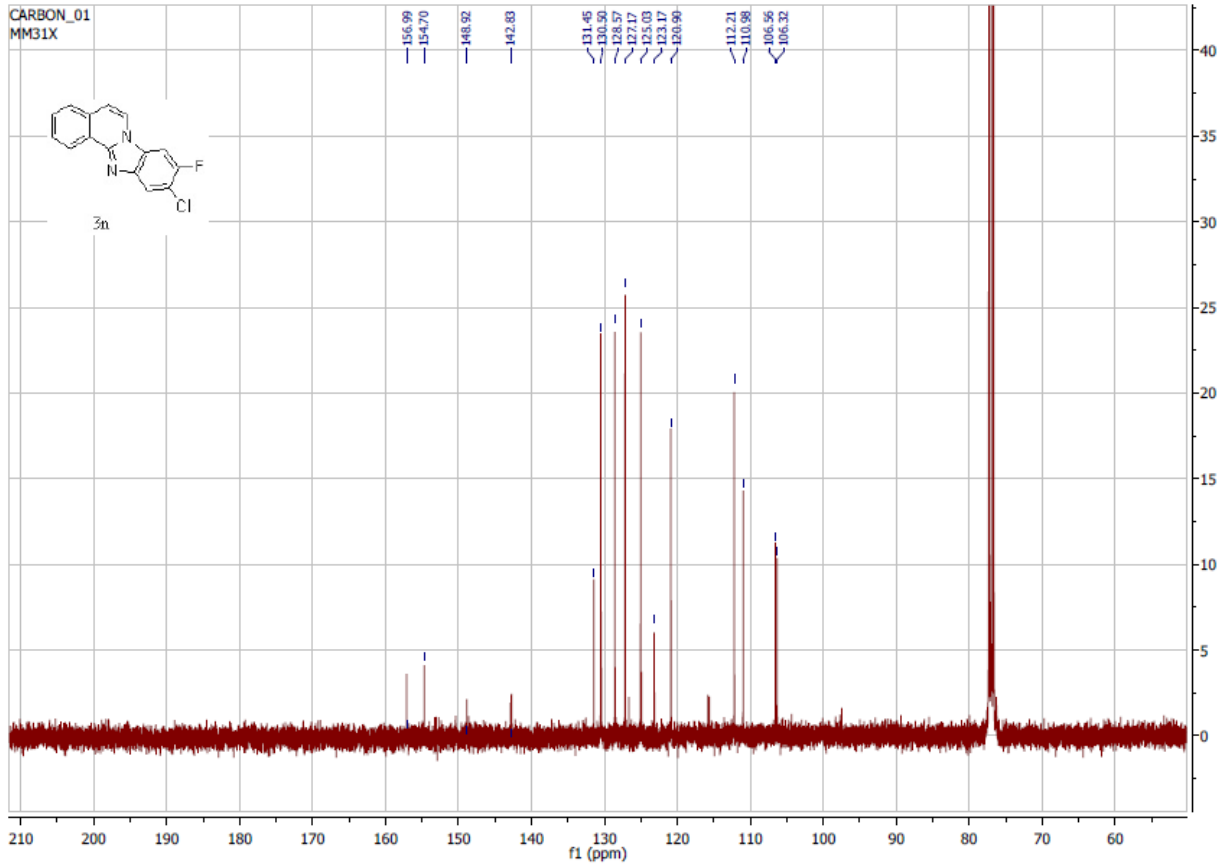

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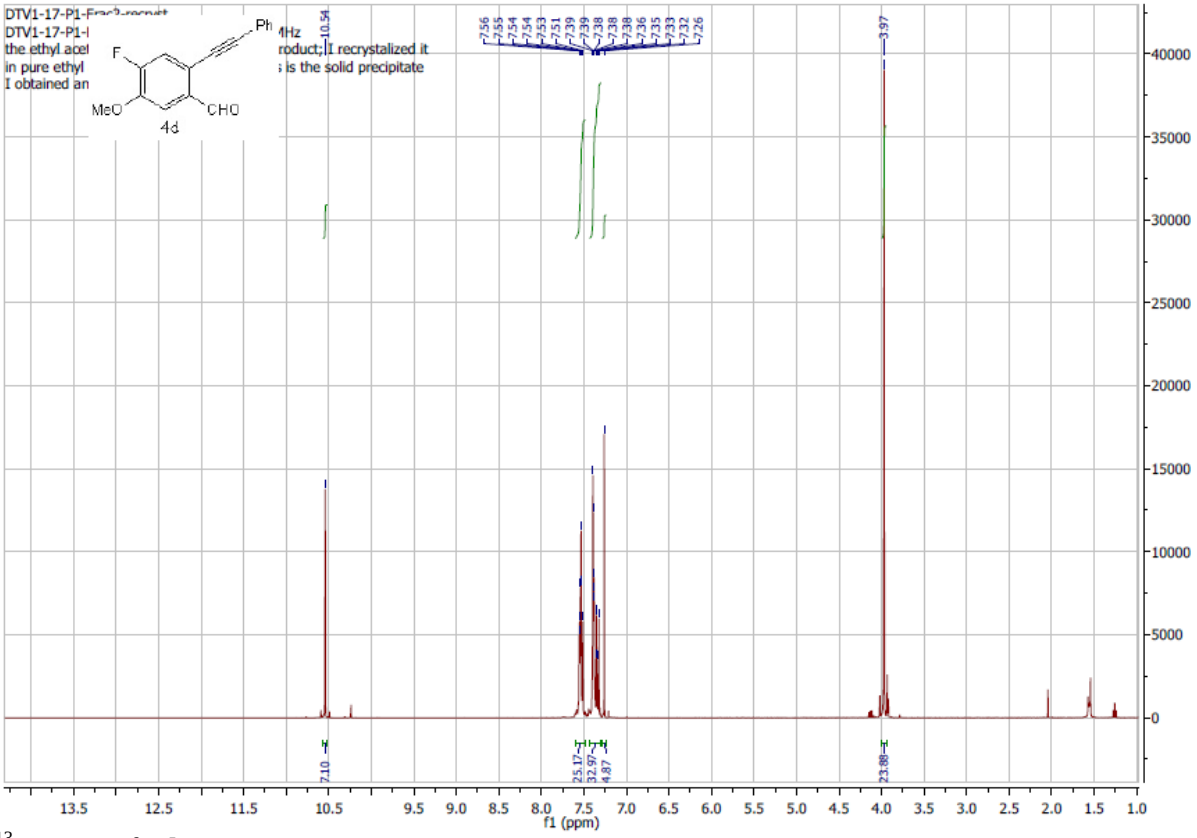

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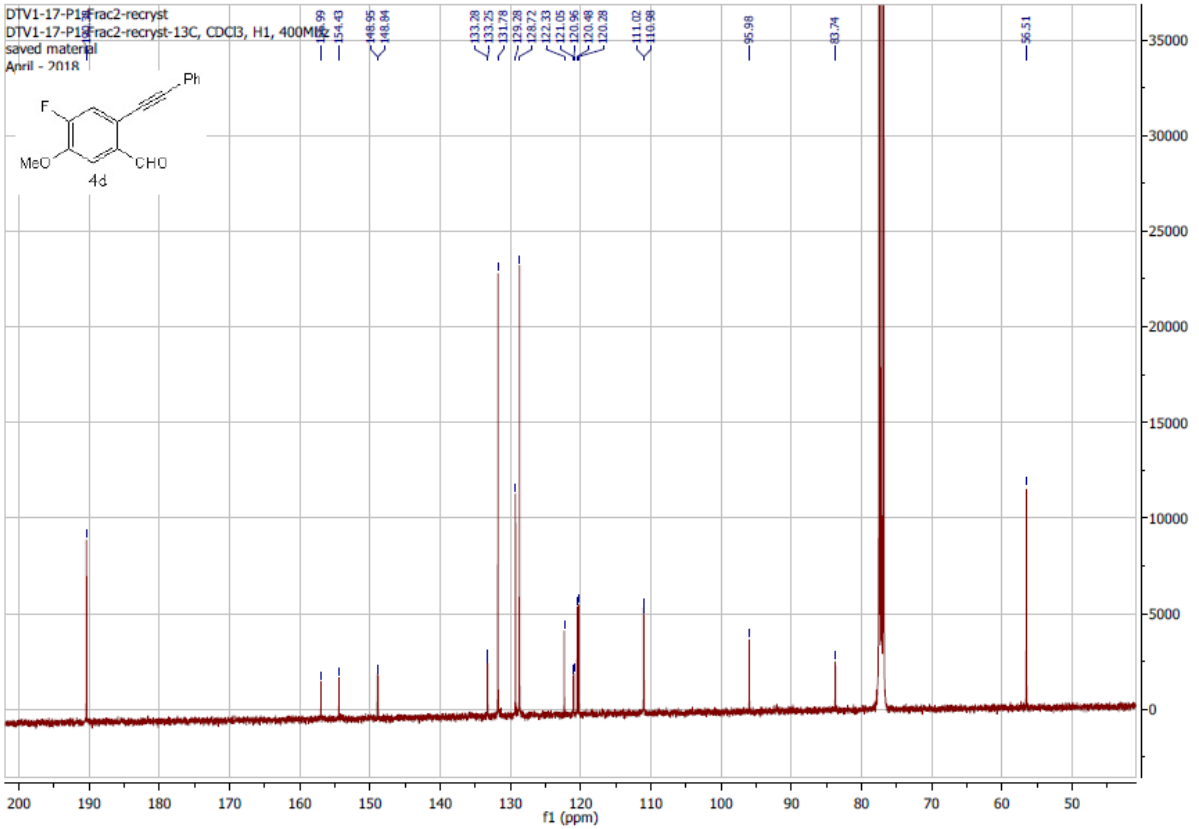

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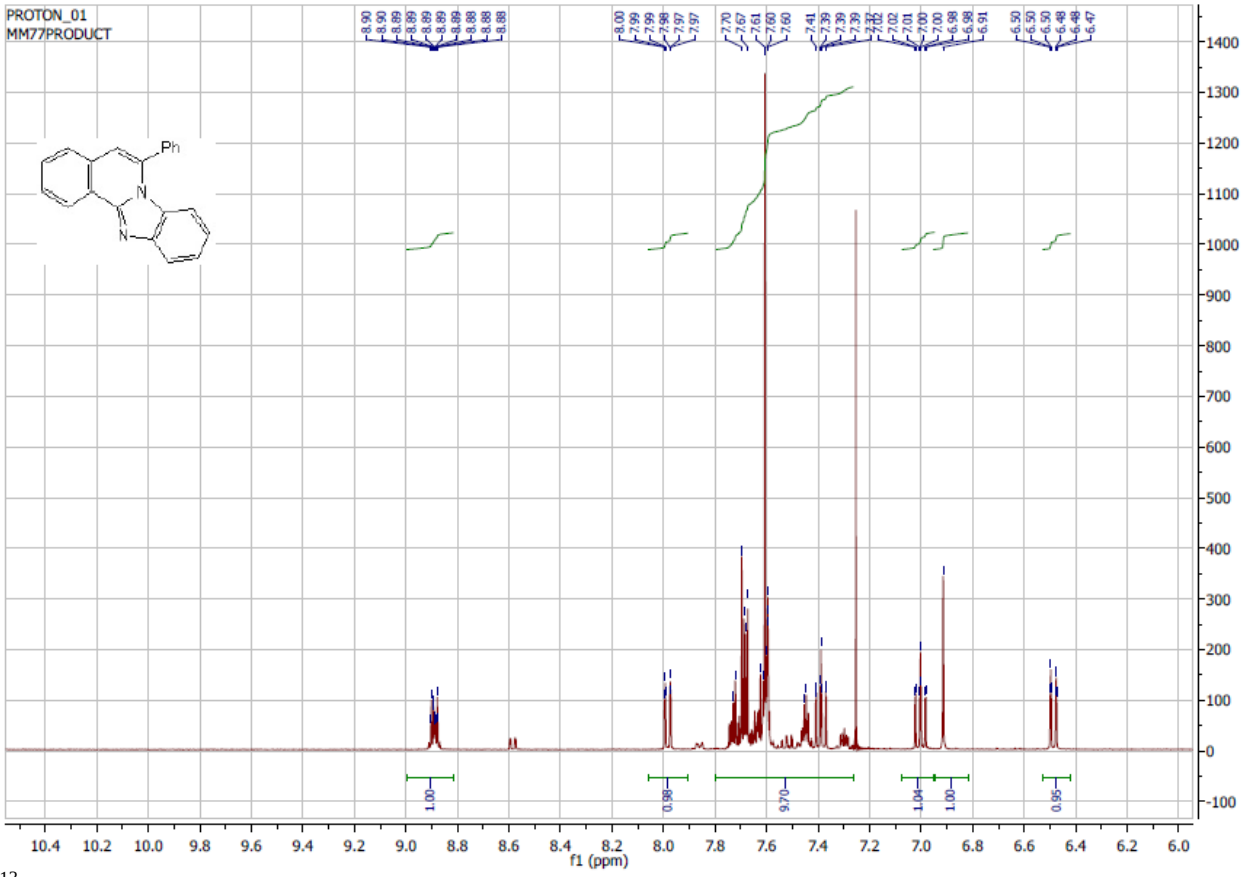

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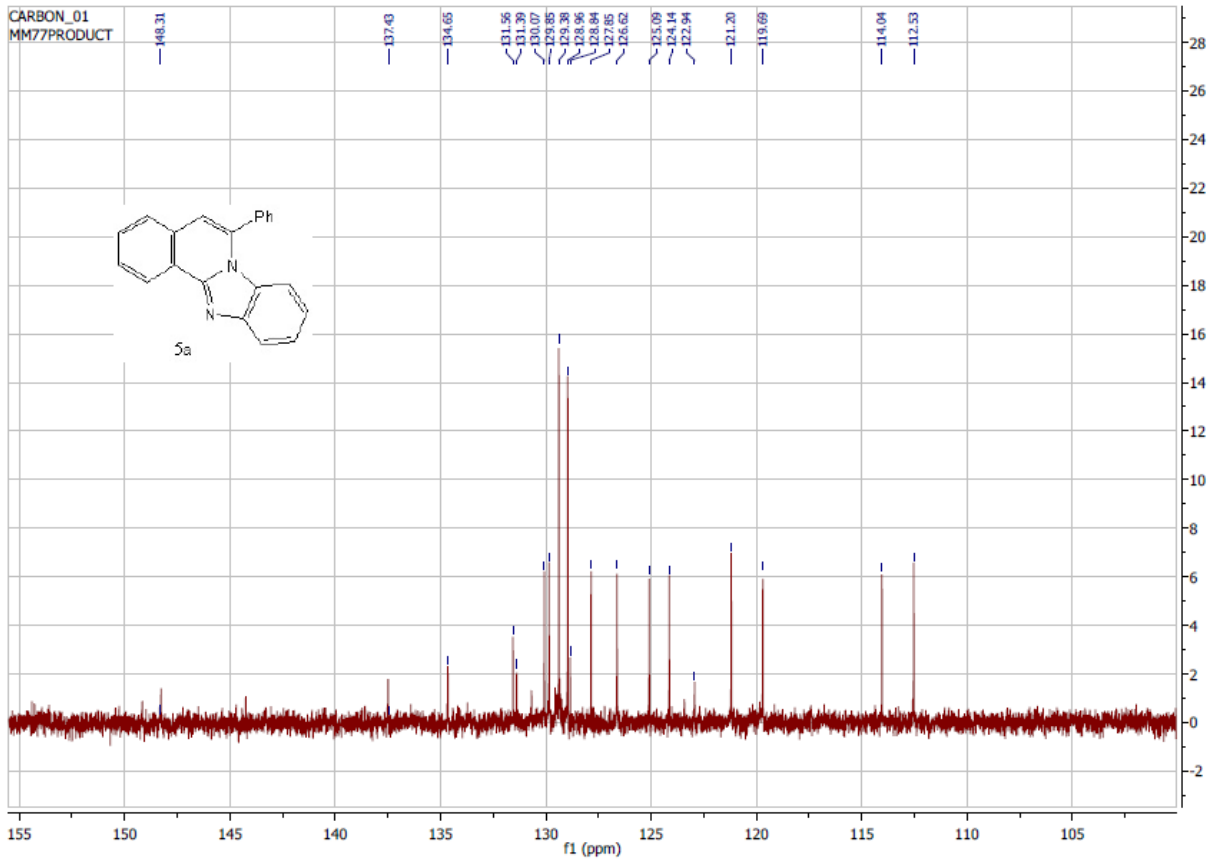

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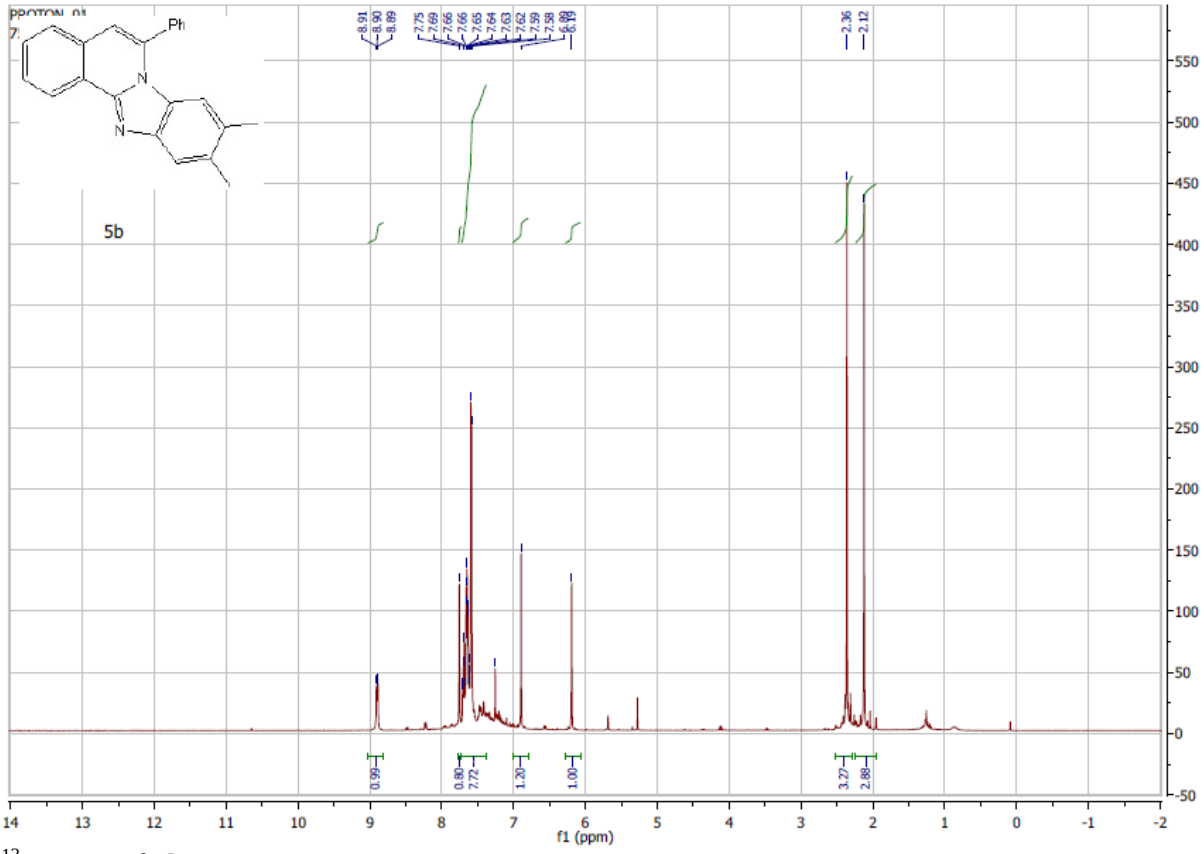

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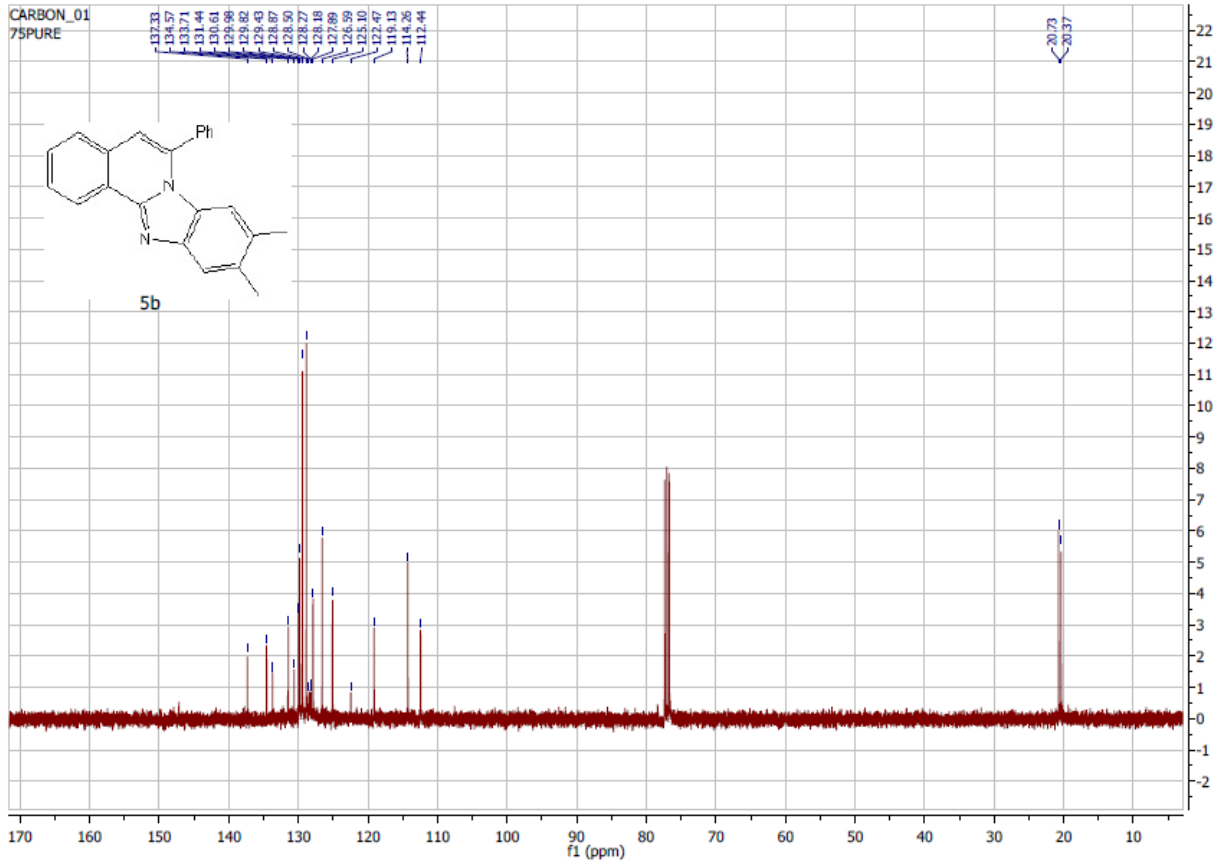

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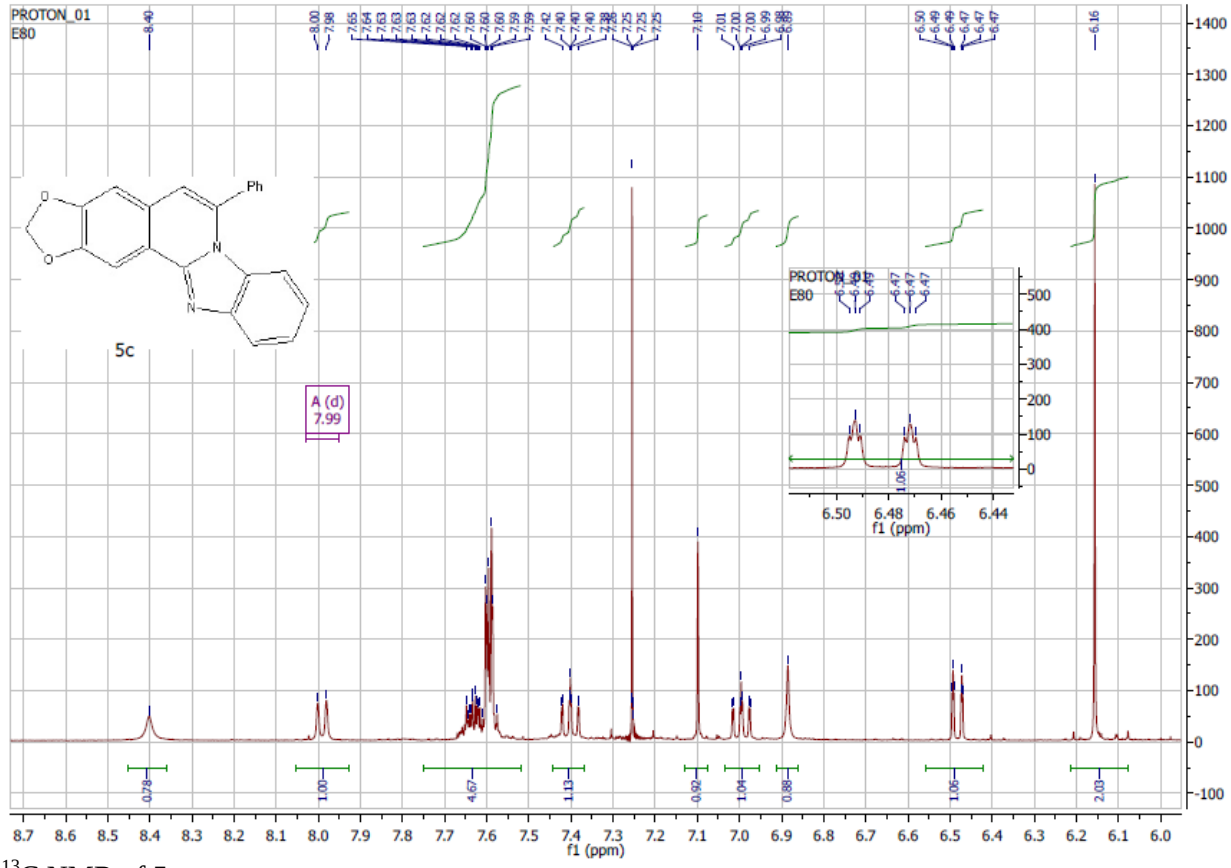

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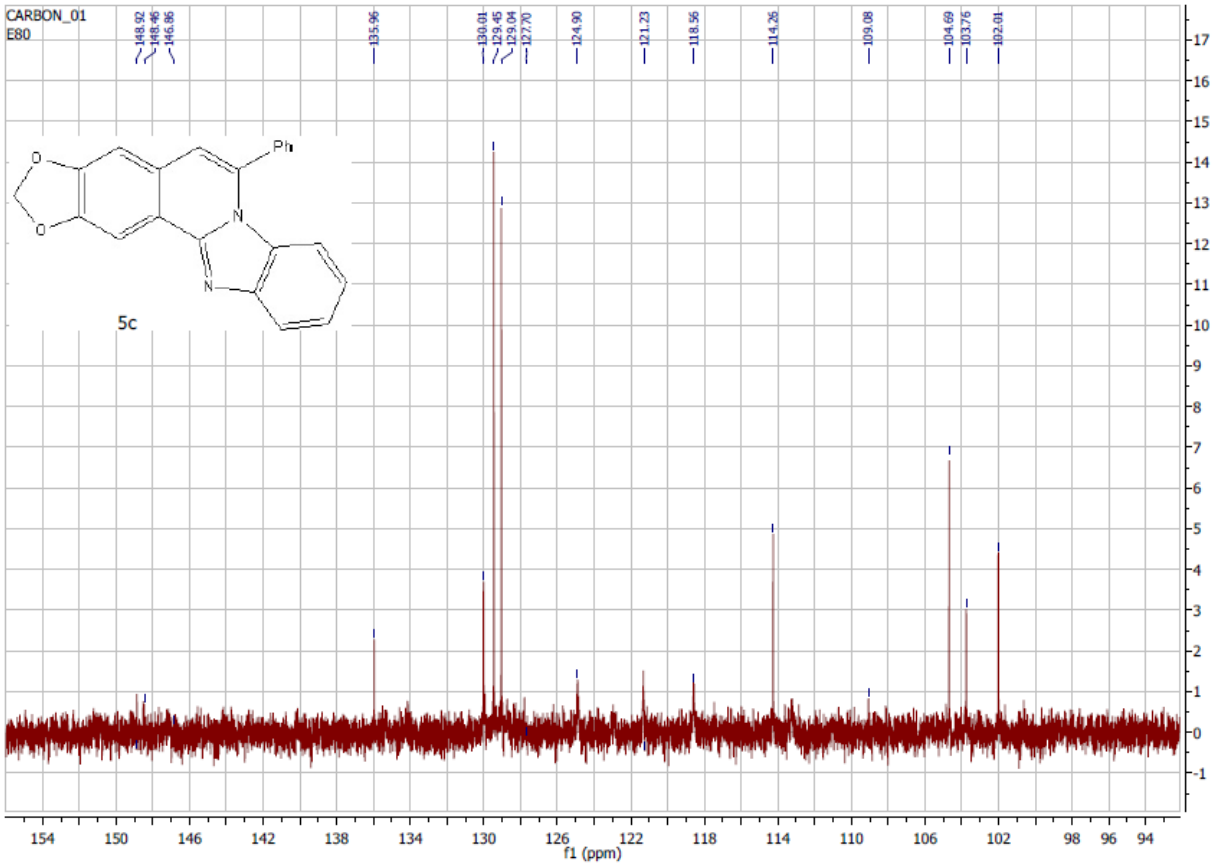

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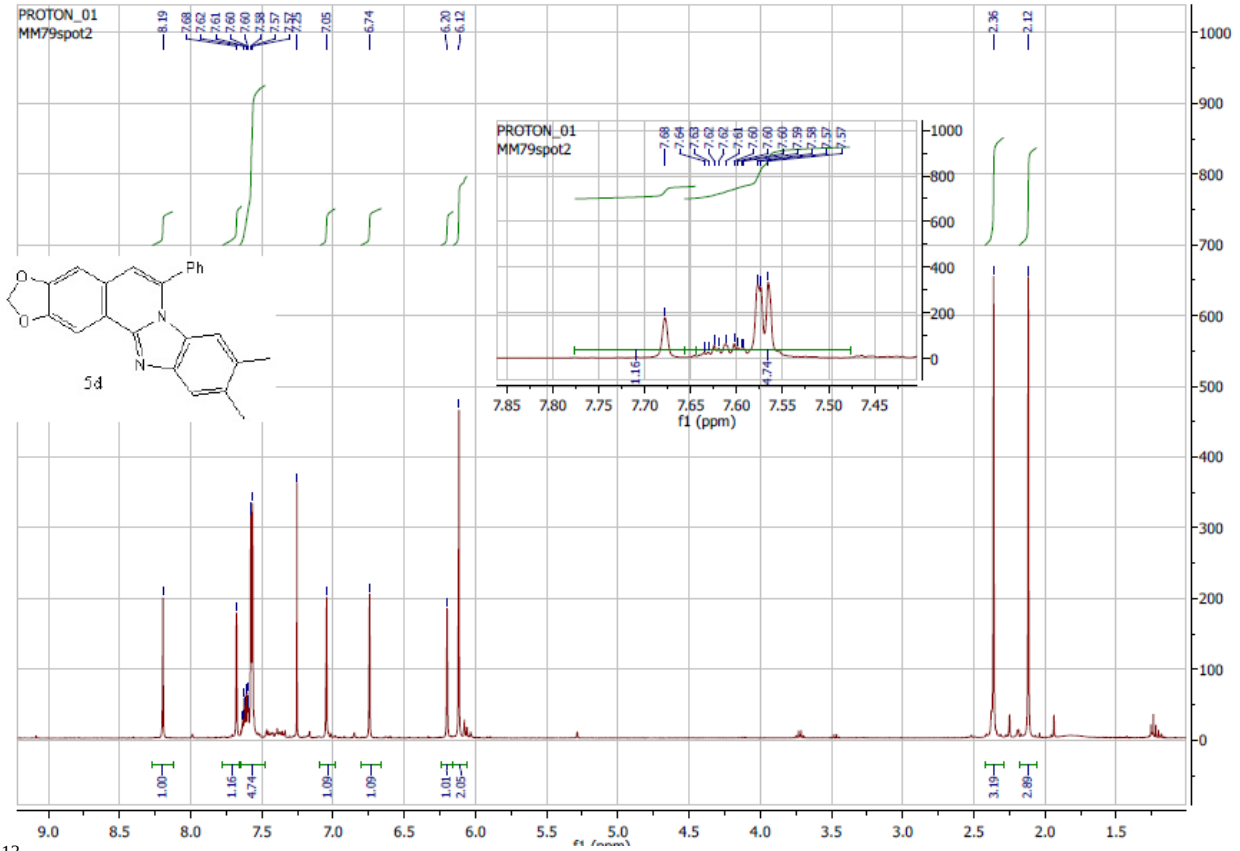

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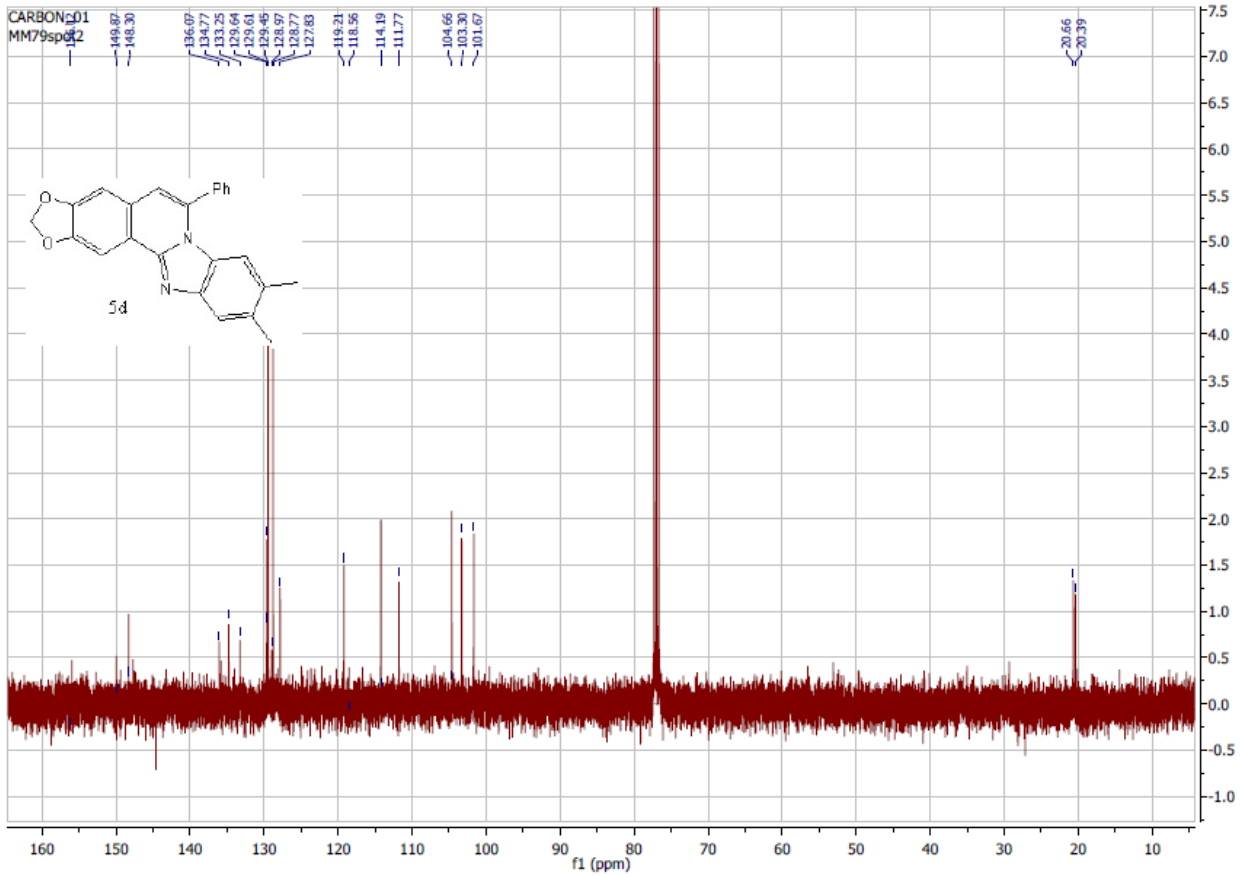

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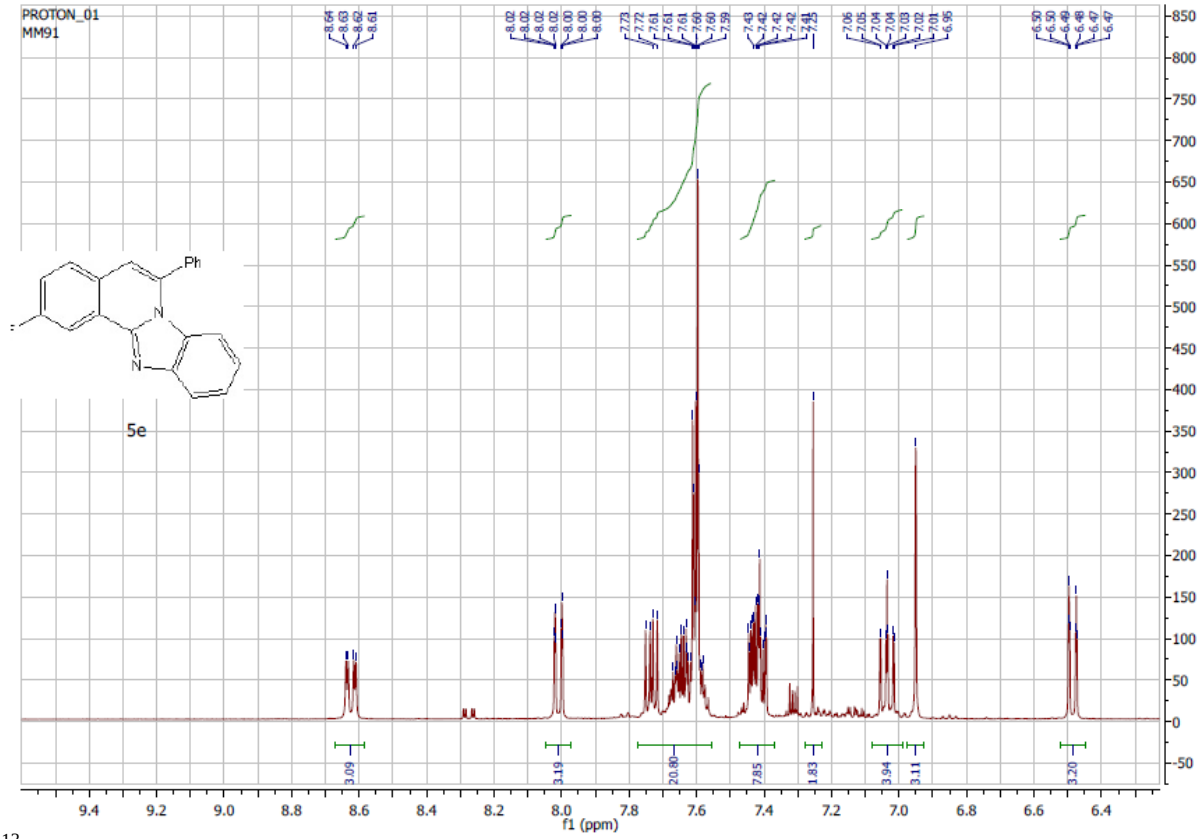

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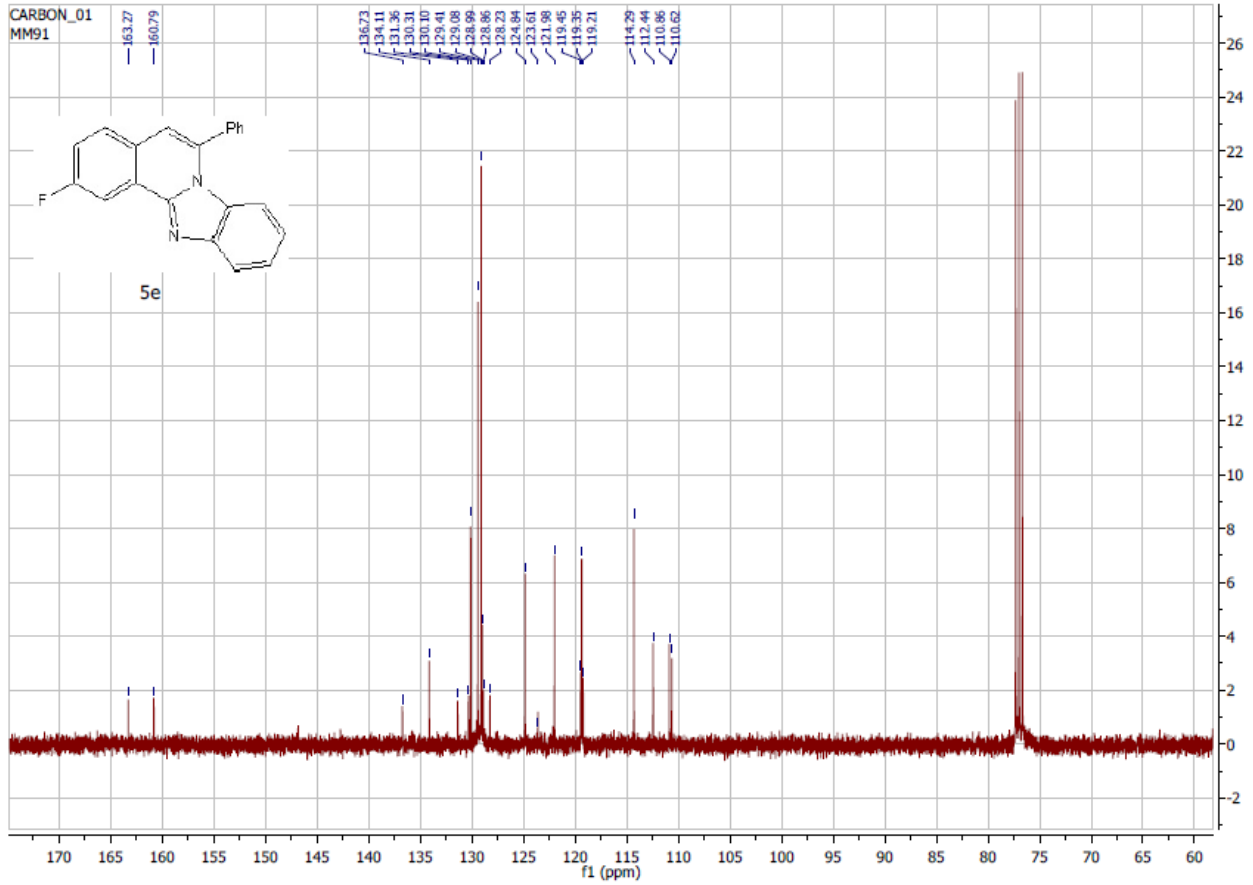

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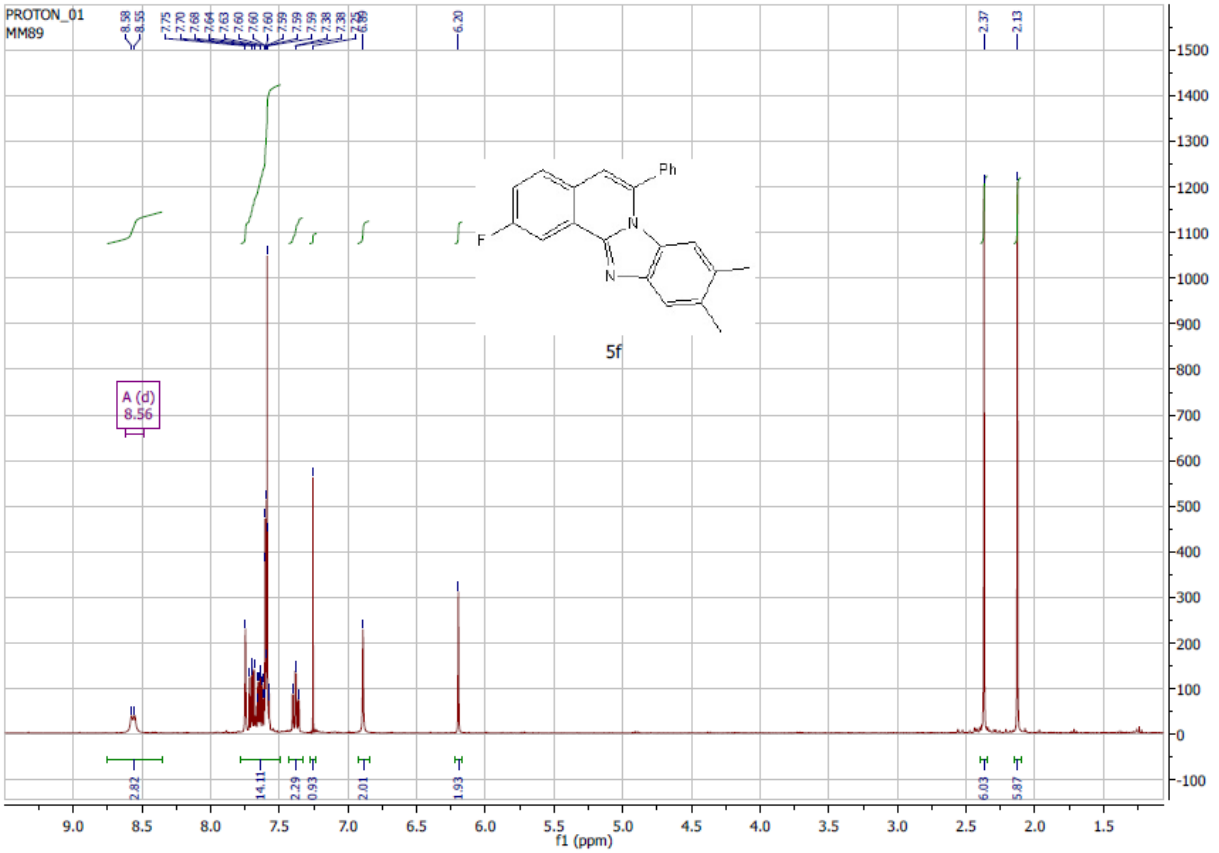

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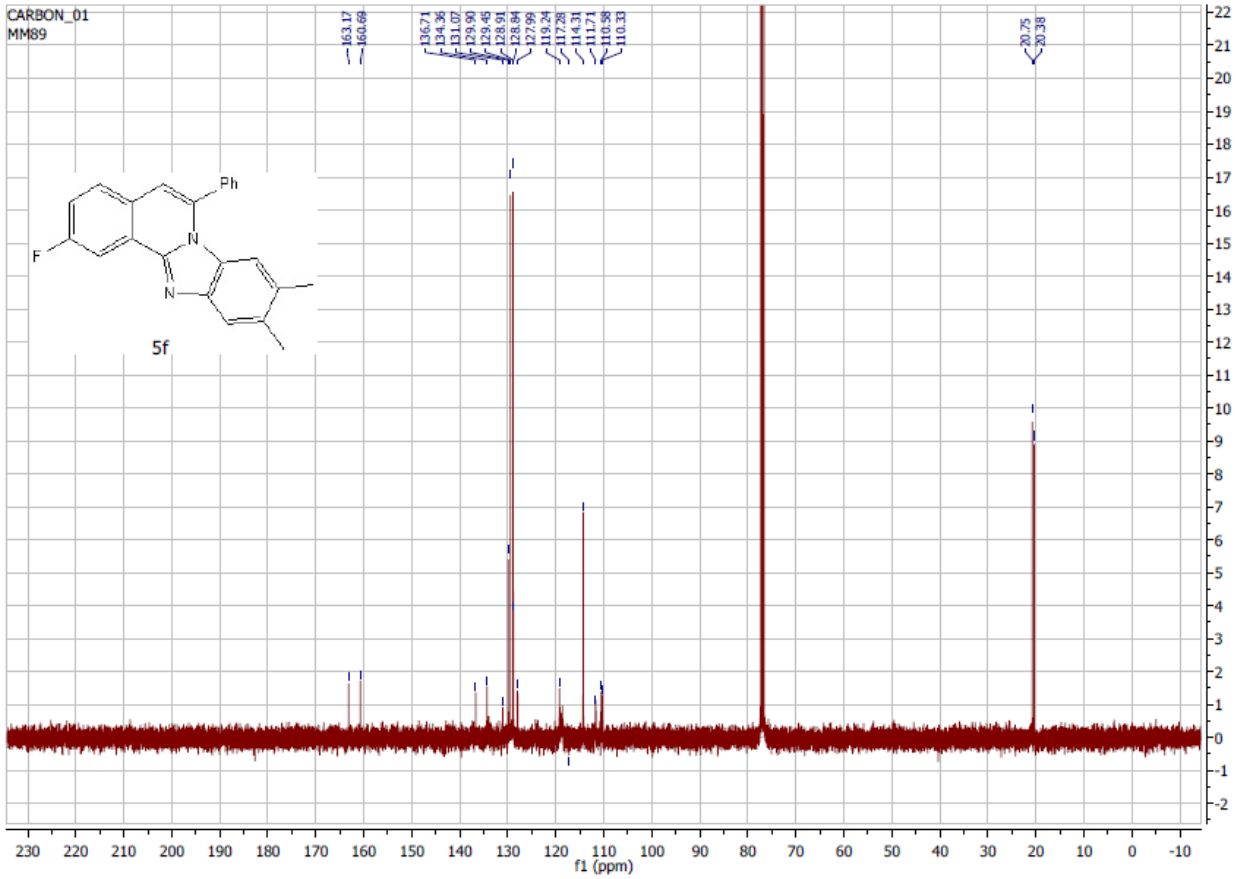

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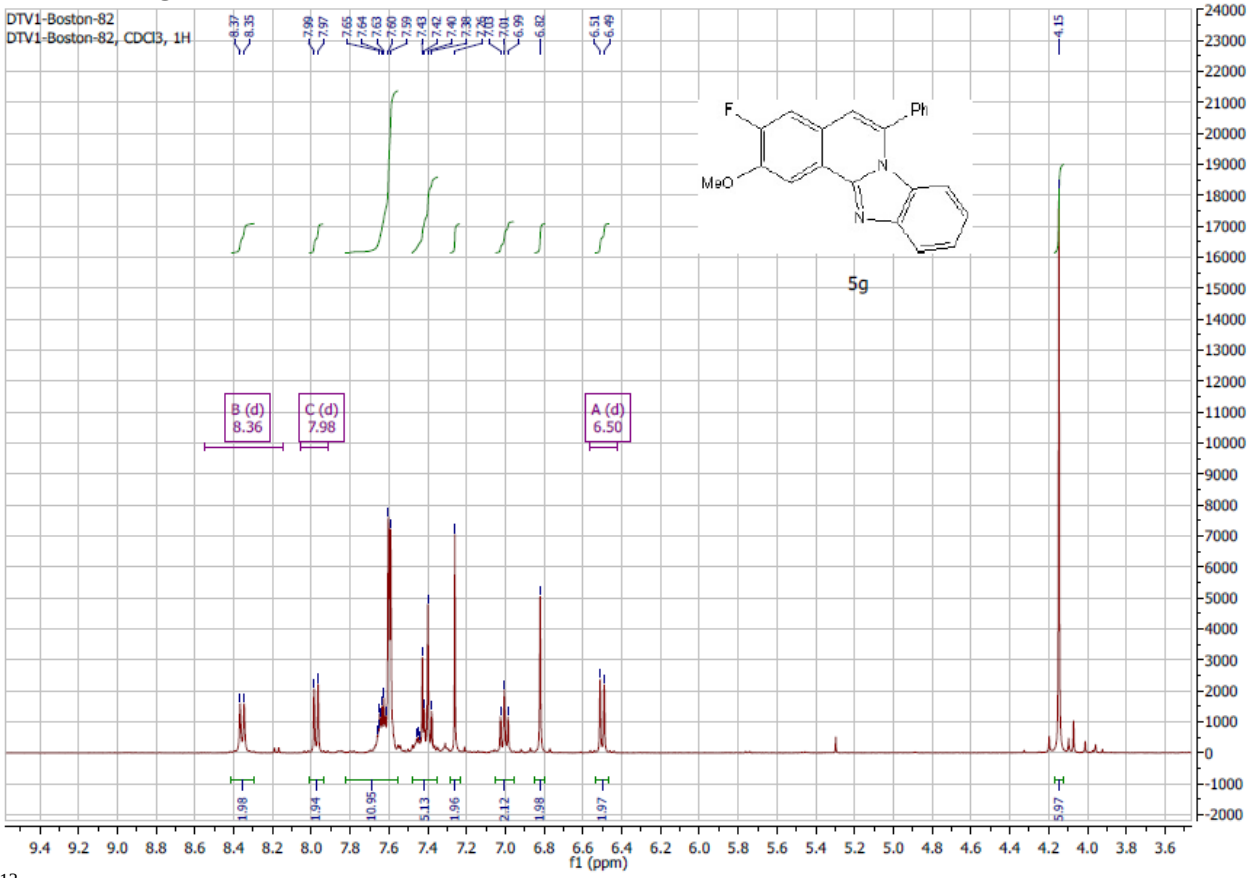

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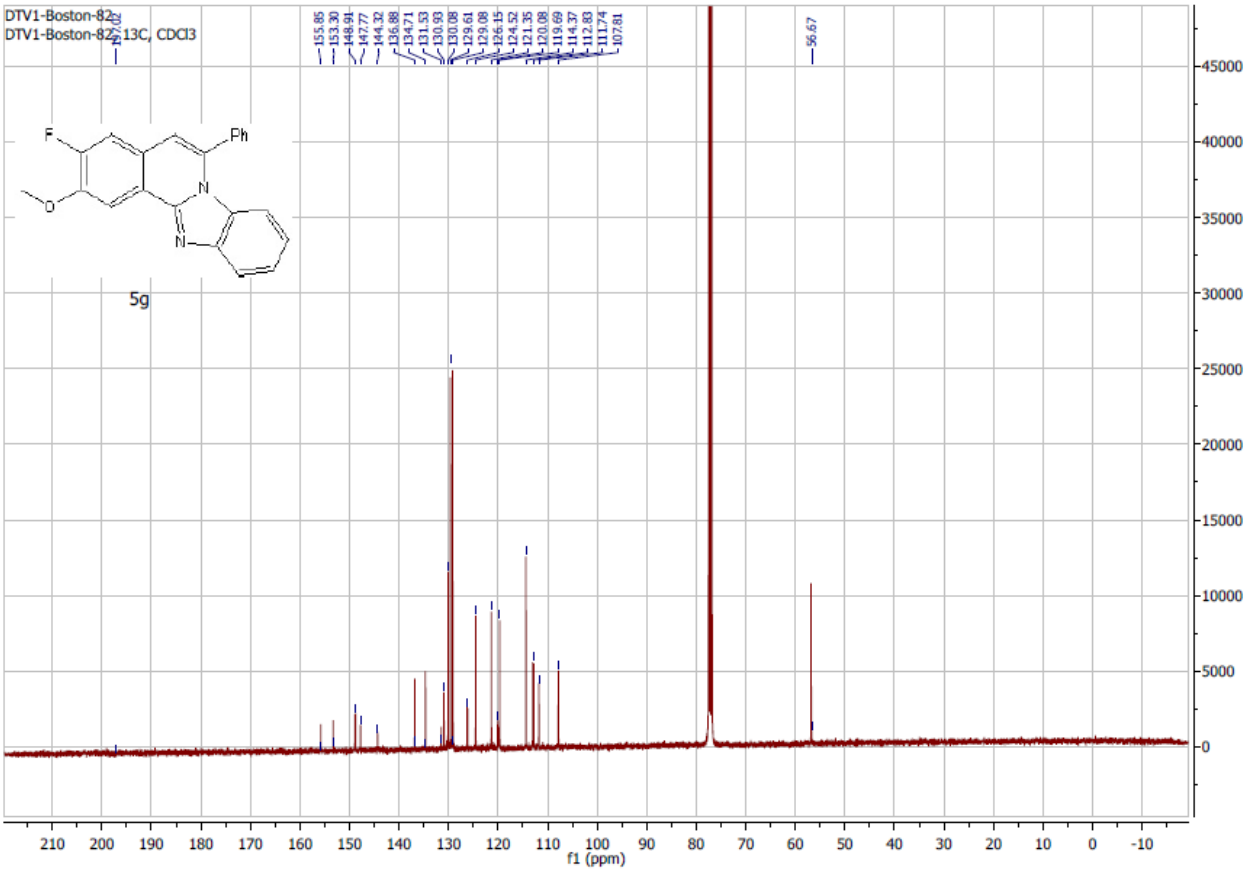

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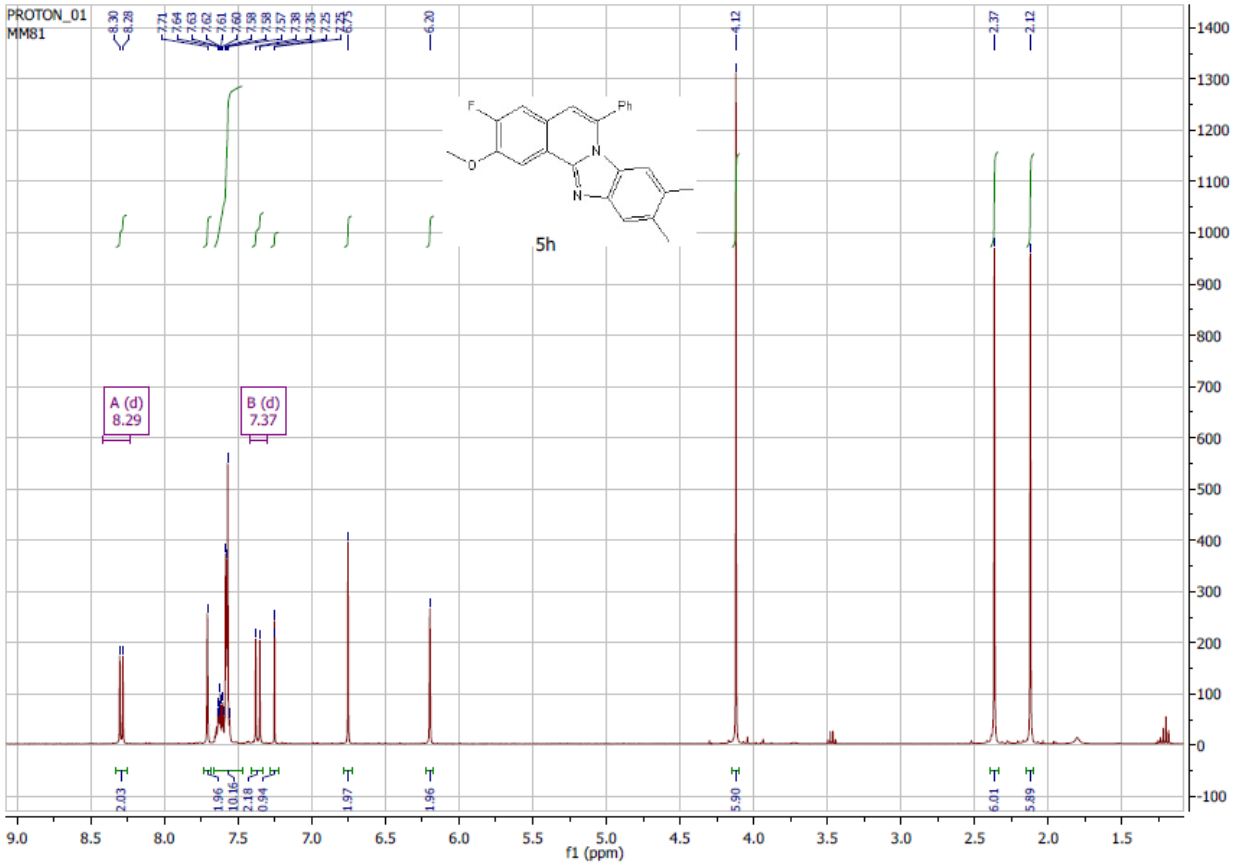

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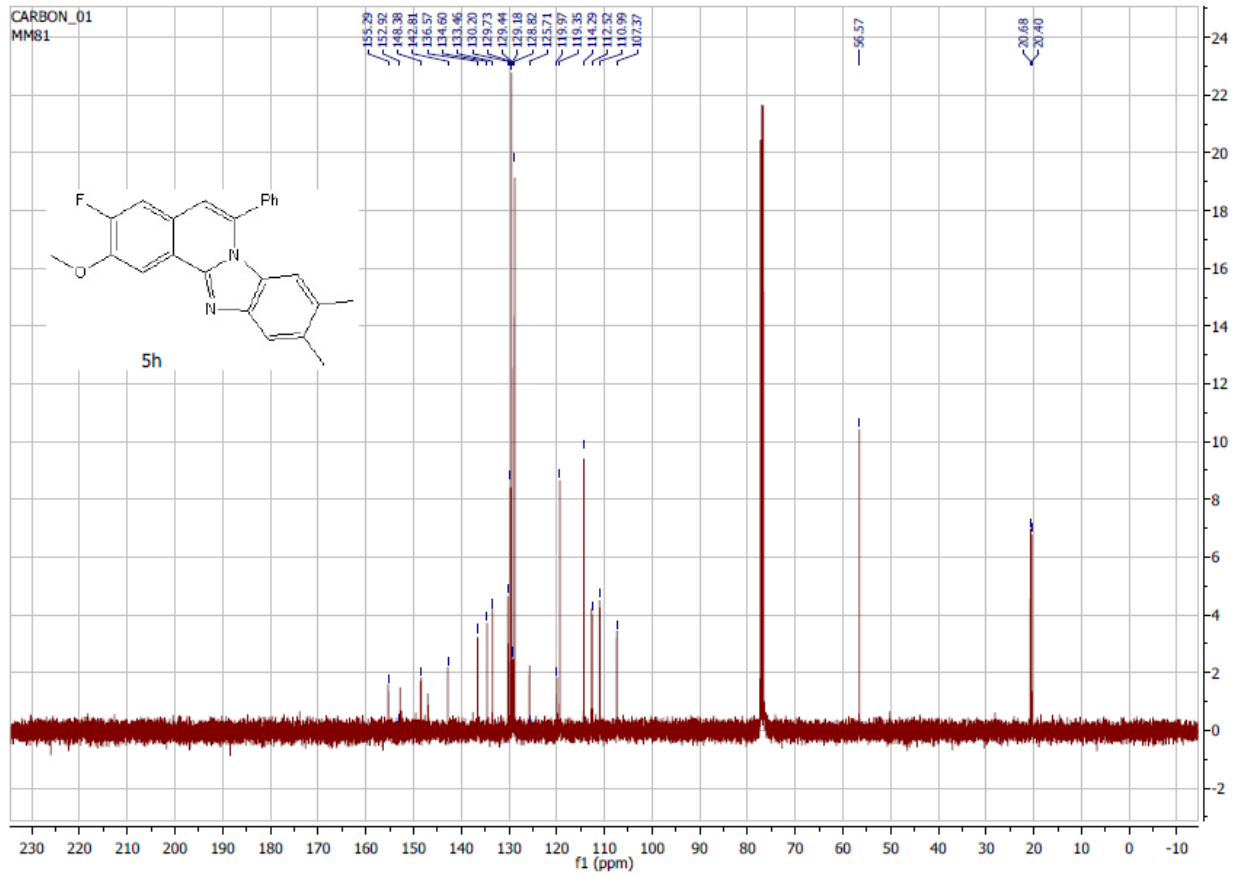
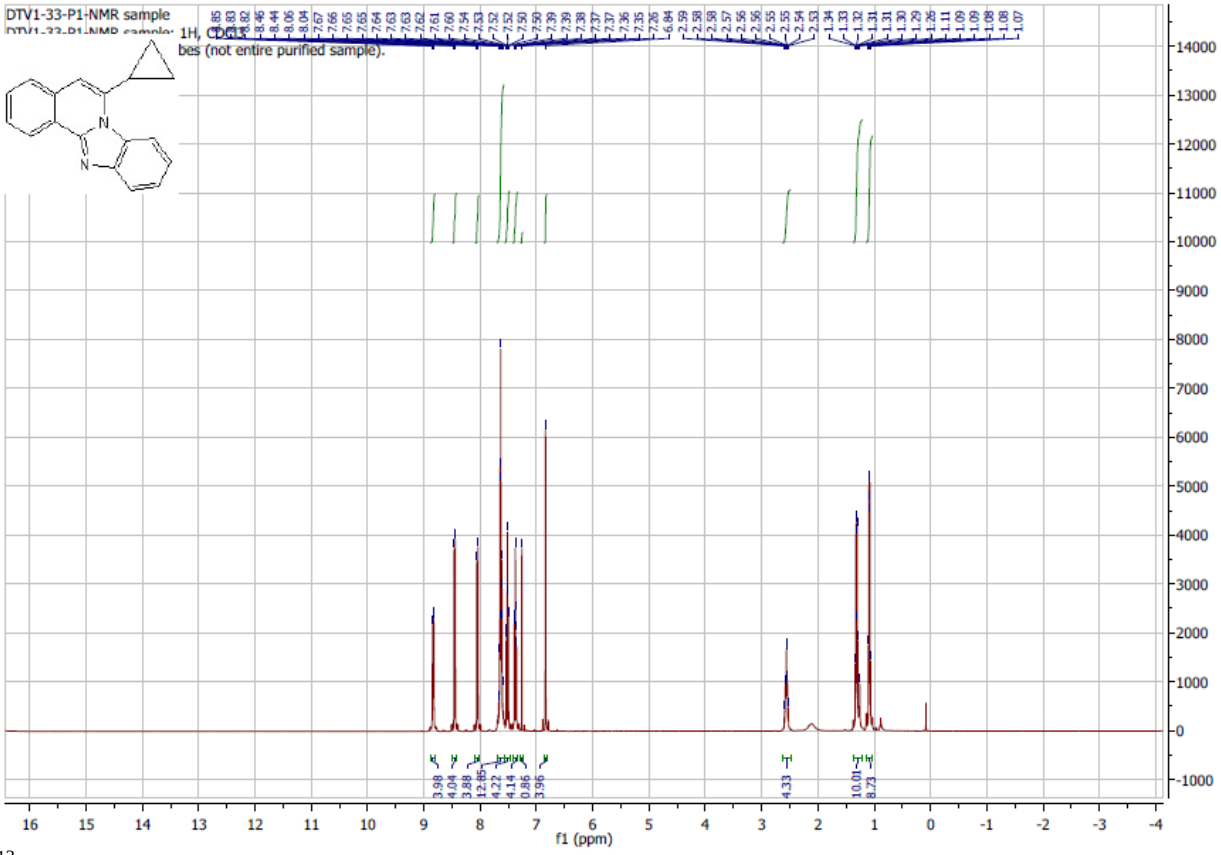


^{1}H NMR of **5i**



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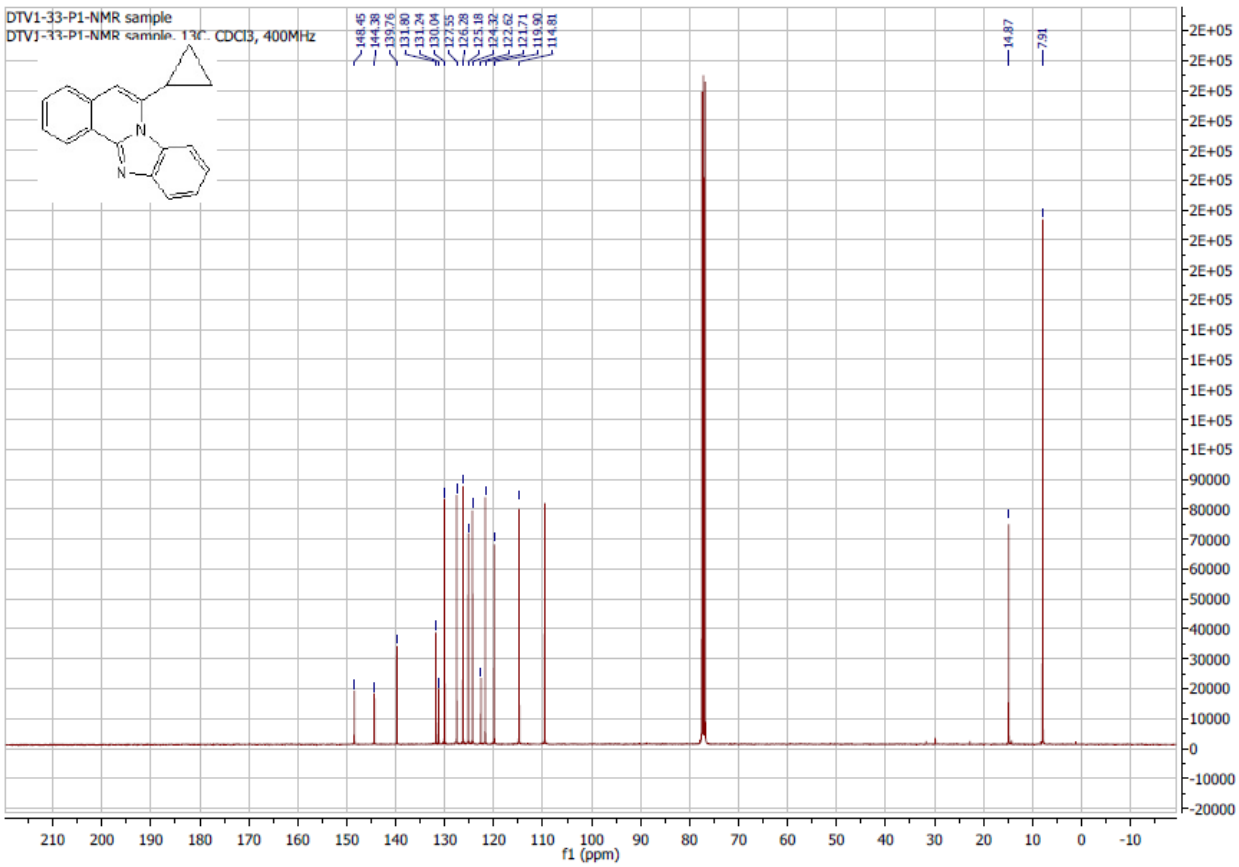
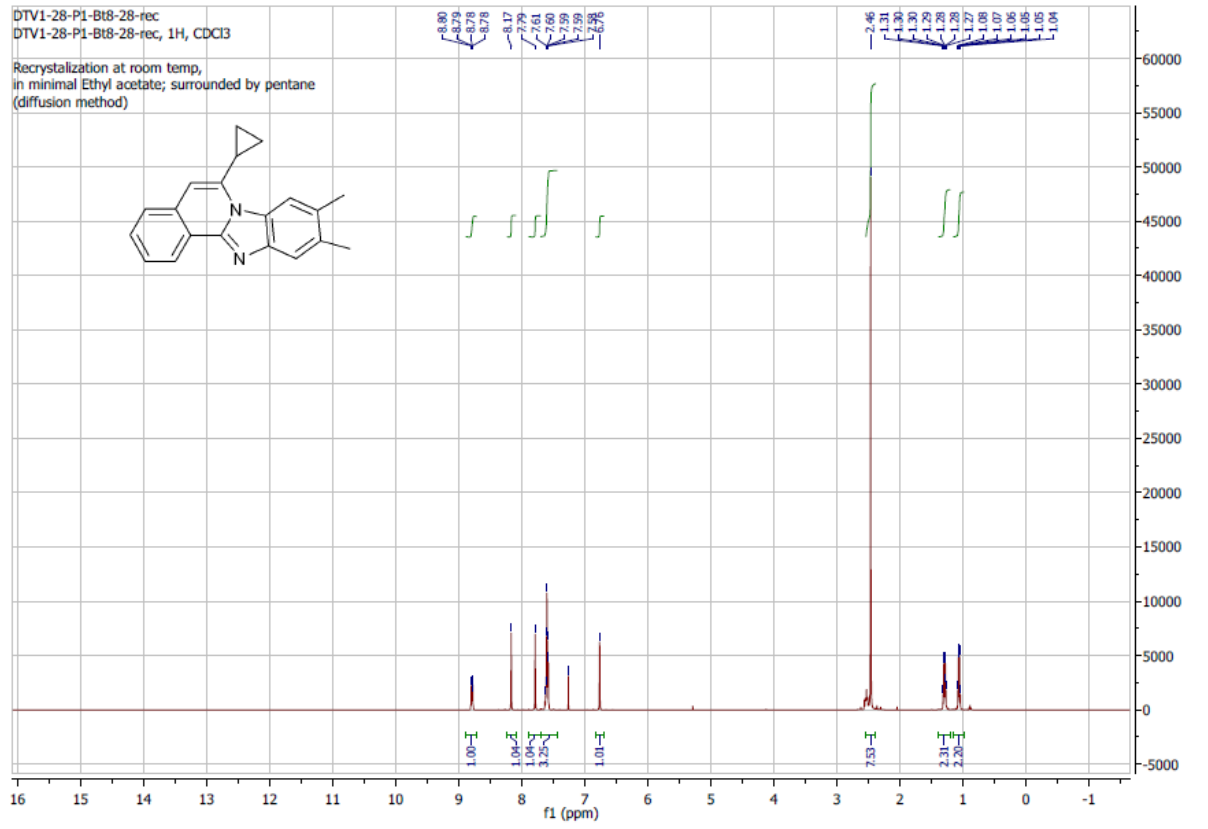
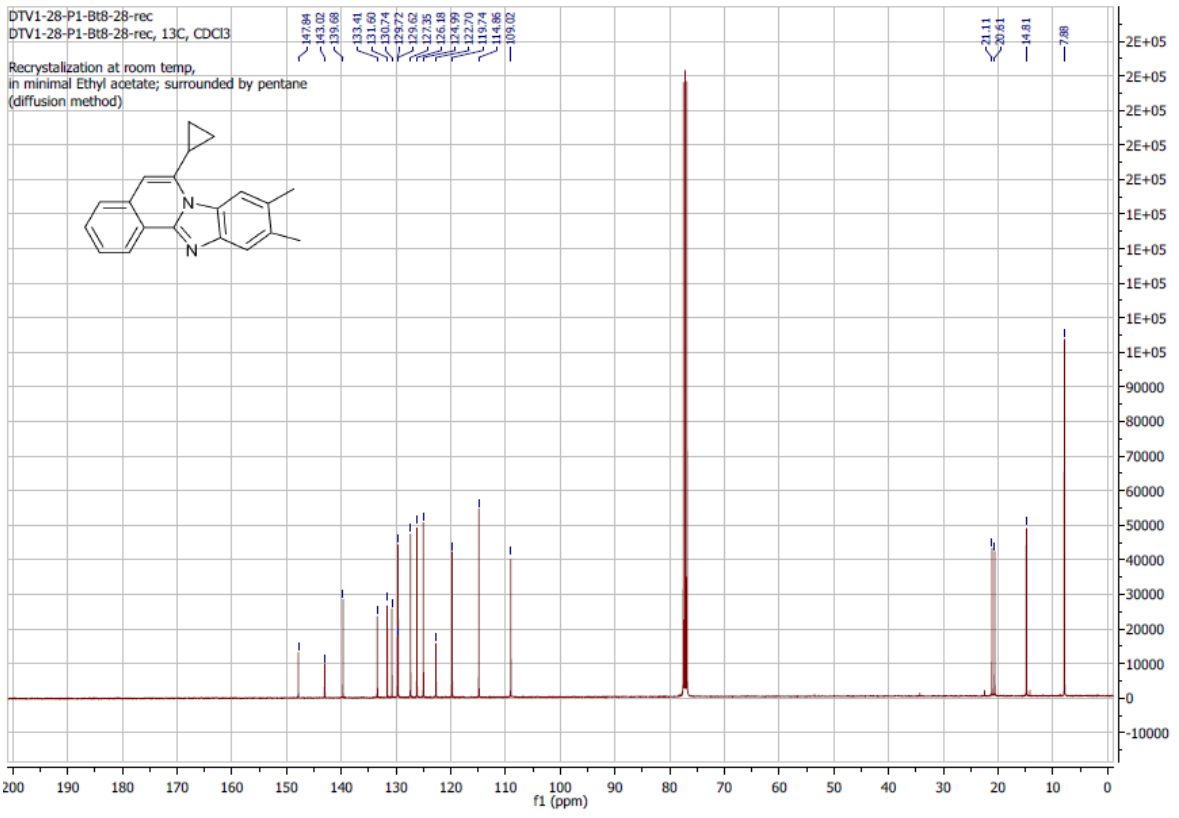


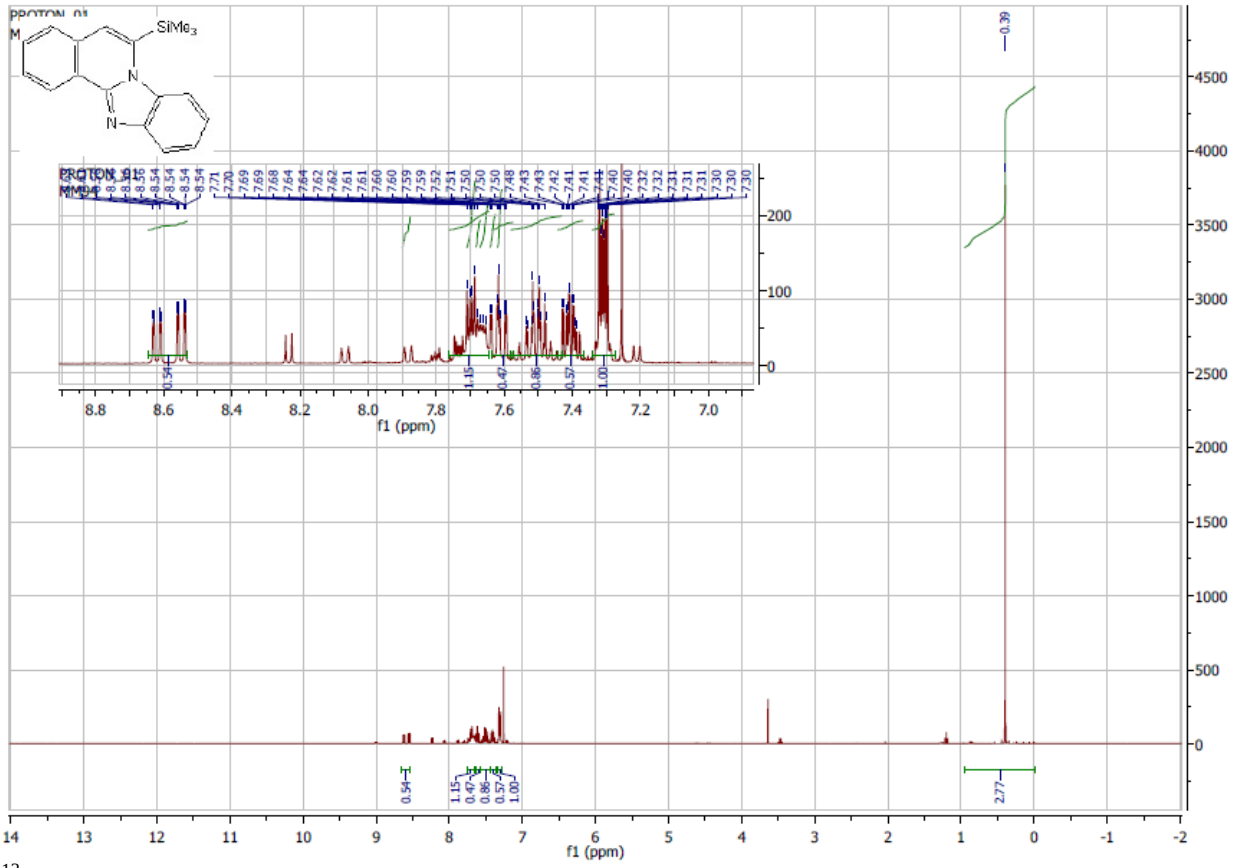
^{1}H NMR of **5i**



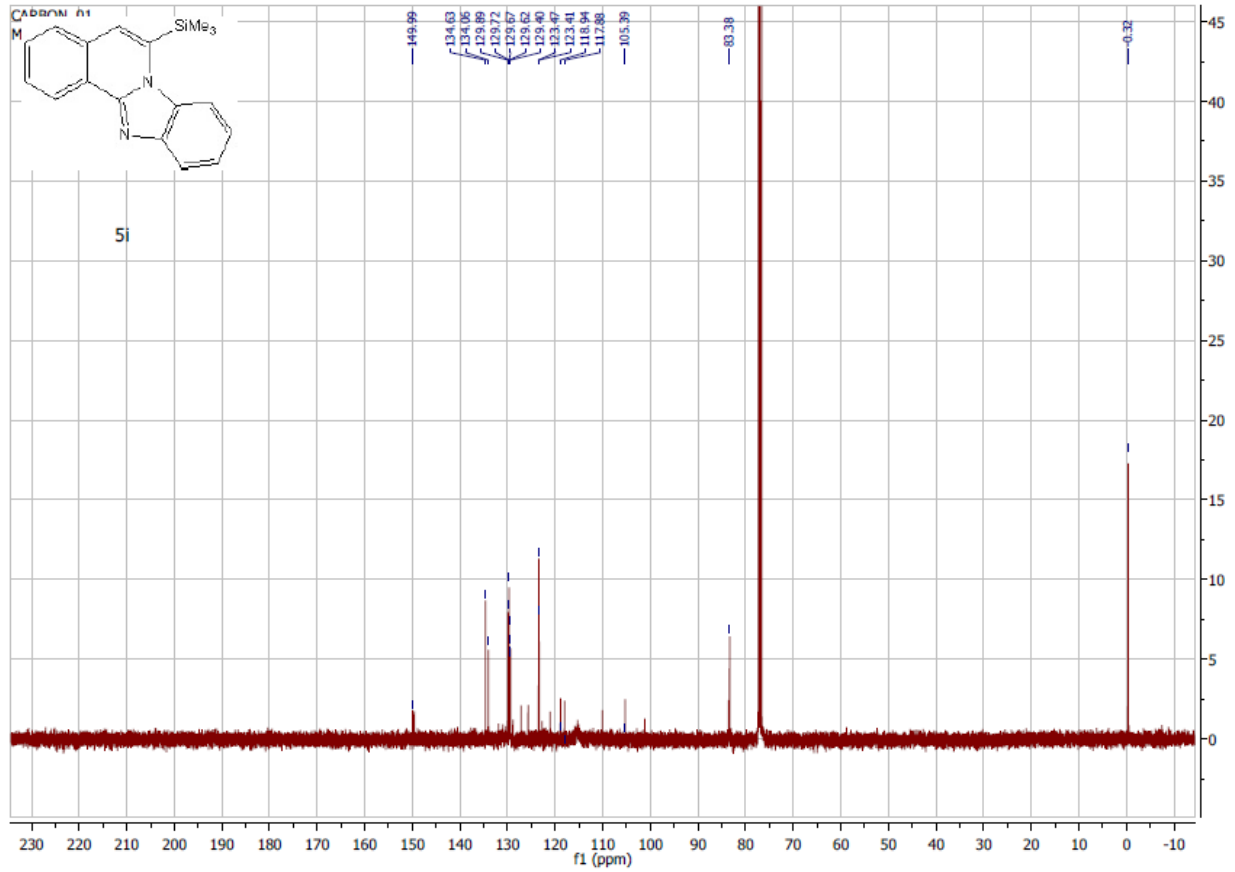
^{13}C NMR of **5i**



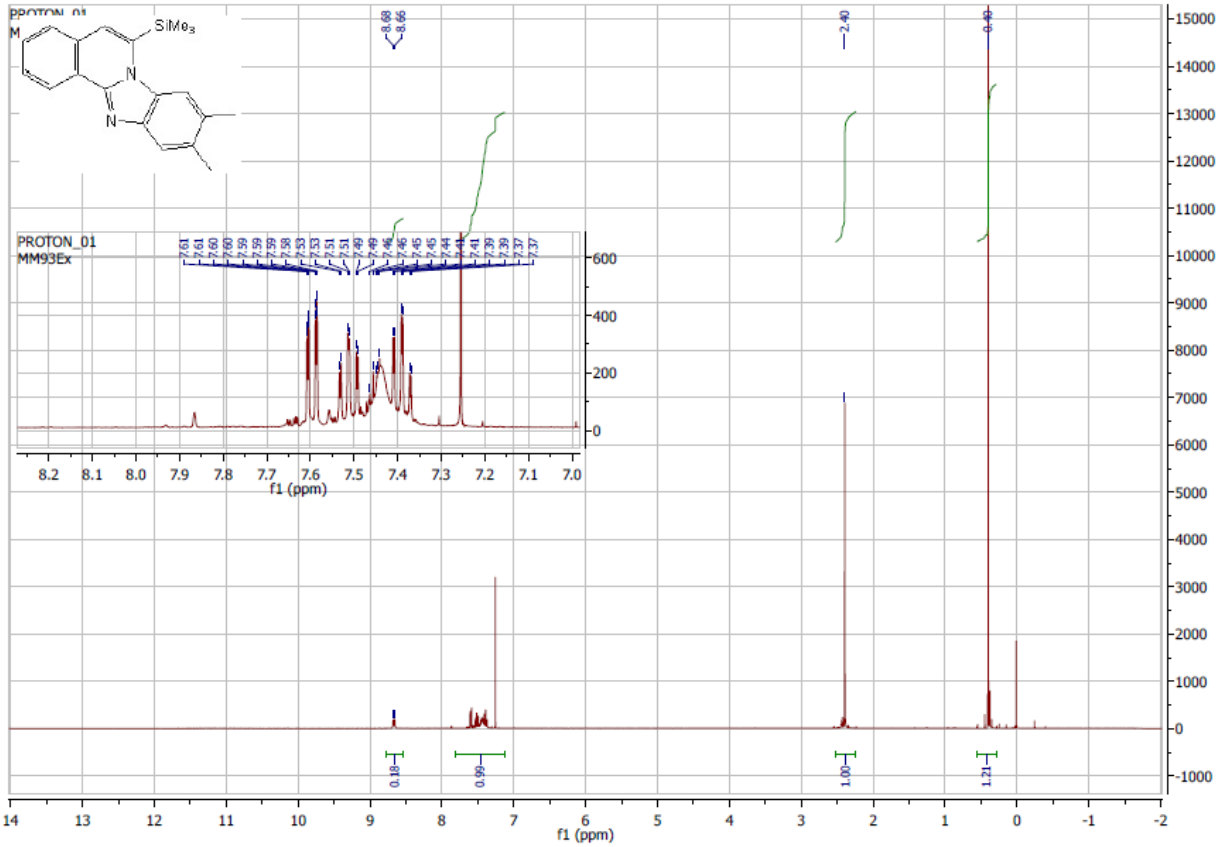
^{1}H NMR of **5k**



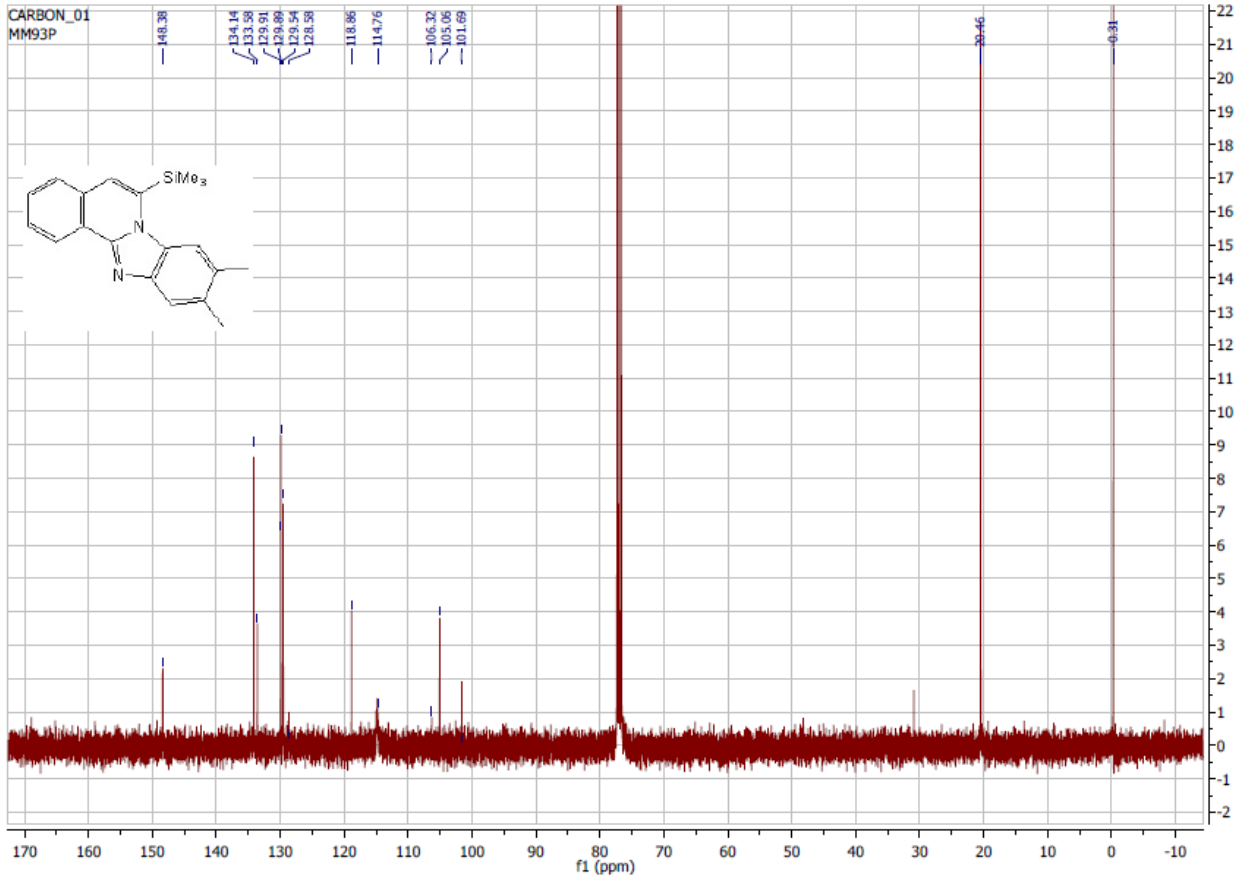
^{13}C NMR of **5k**



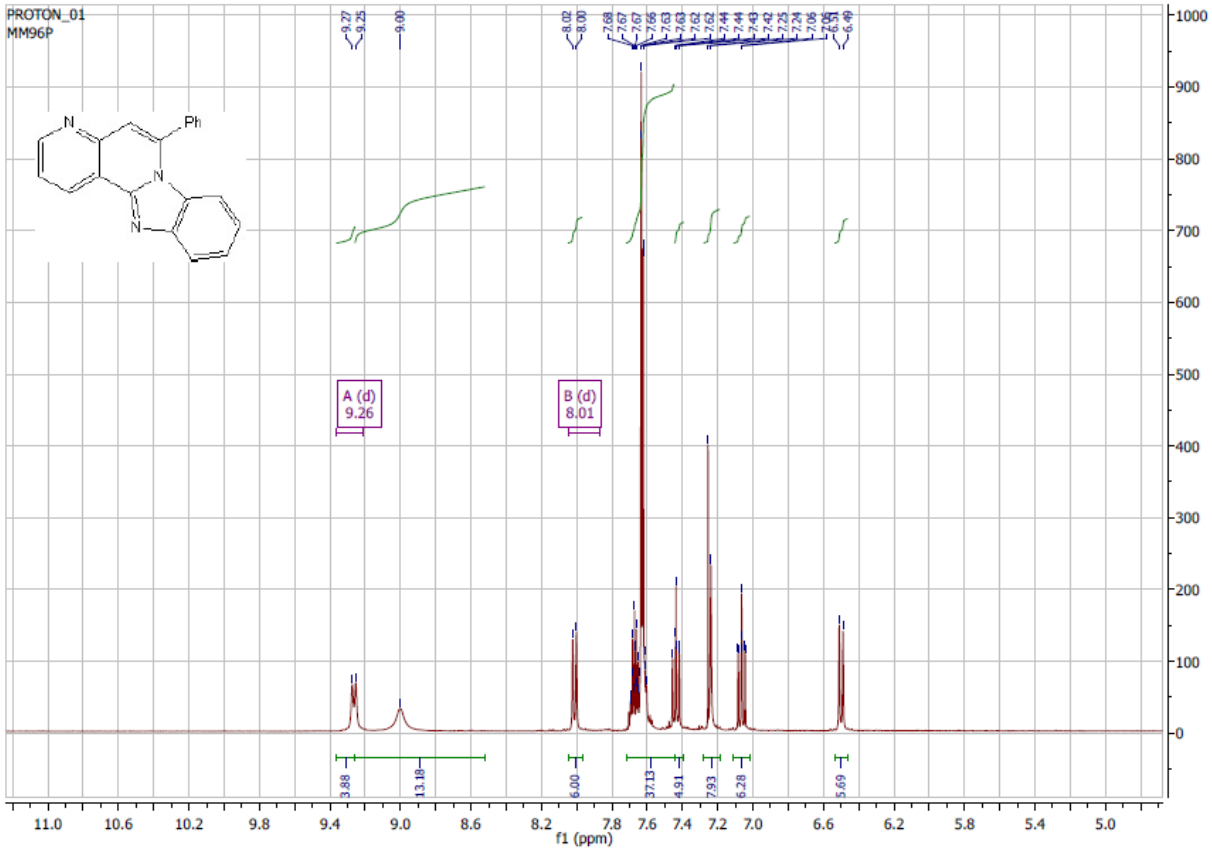
^{1}H NMR of **5l**



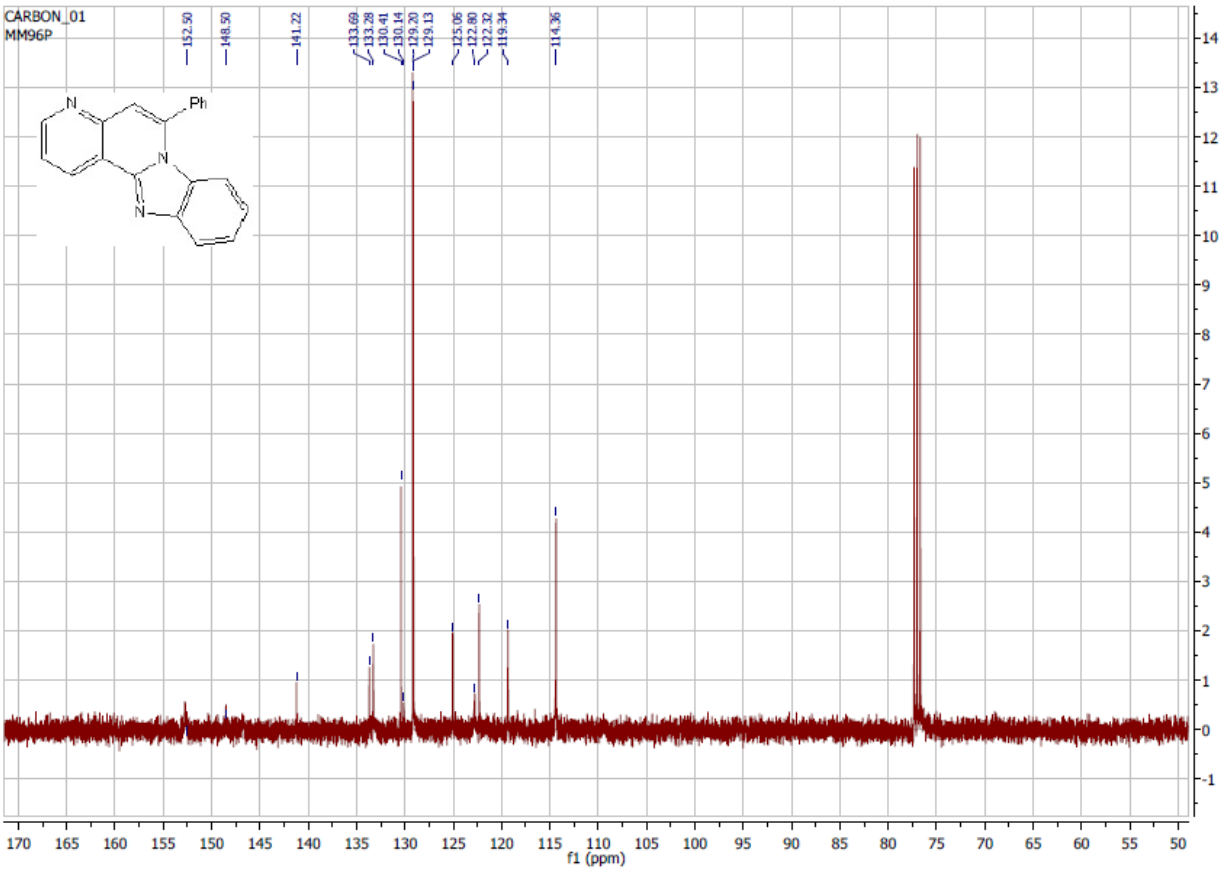
^{13}C NMR of **5l**



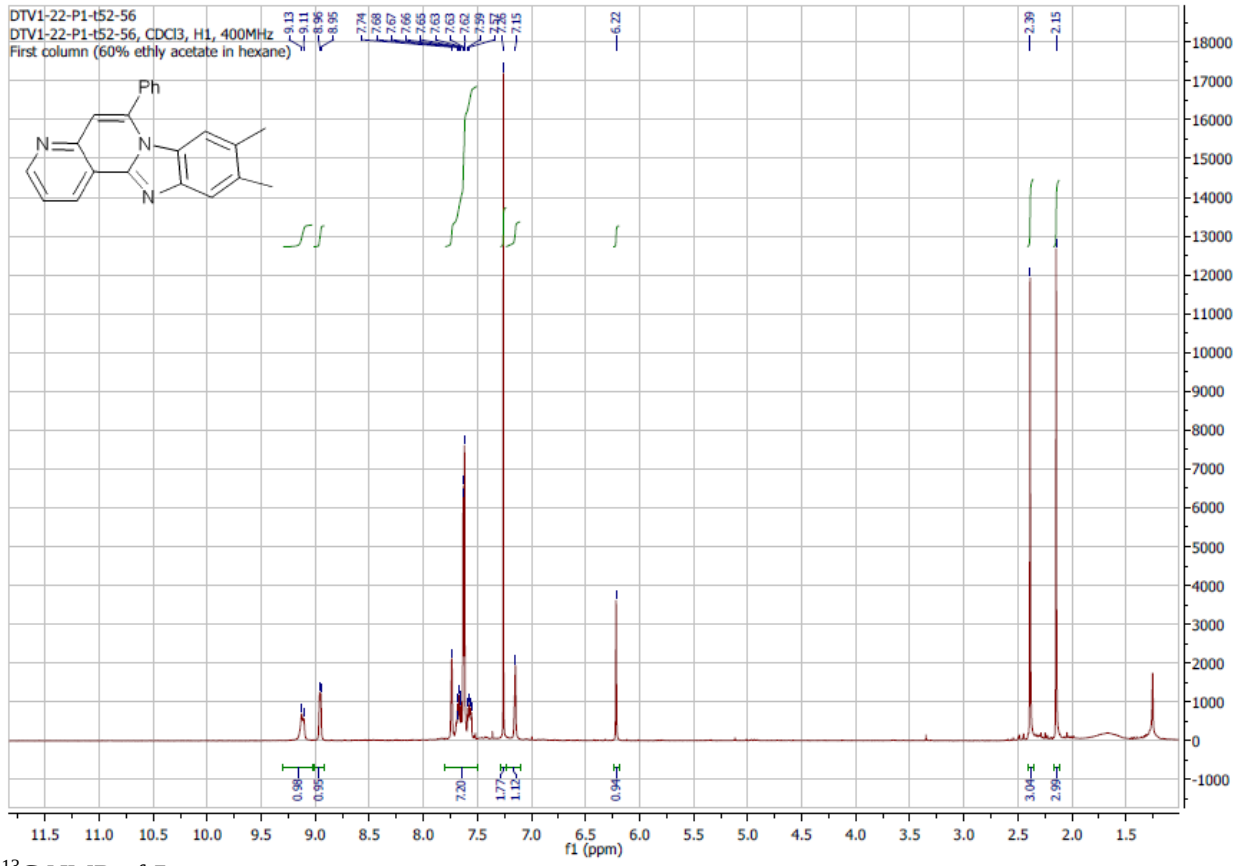
^{1}H NMR of **5m**



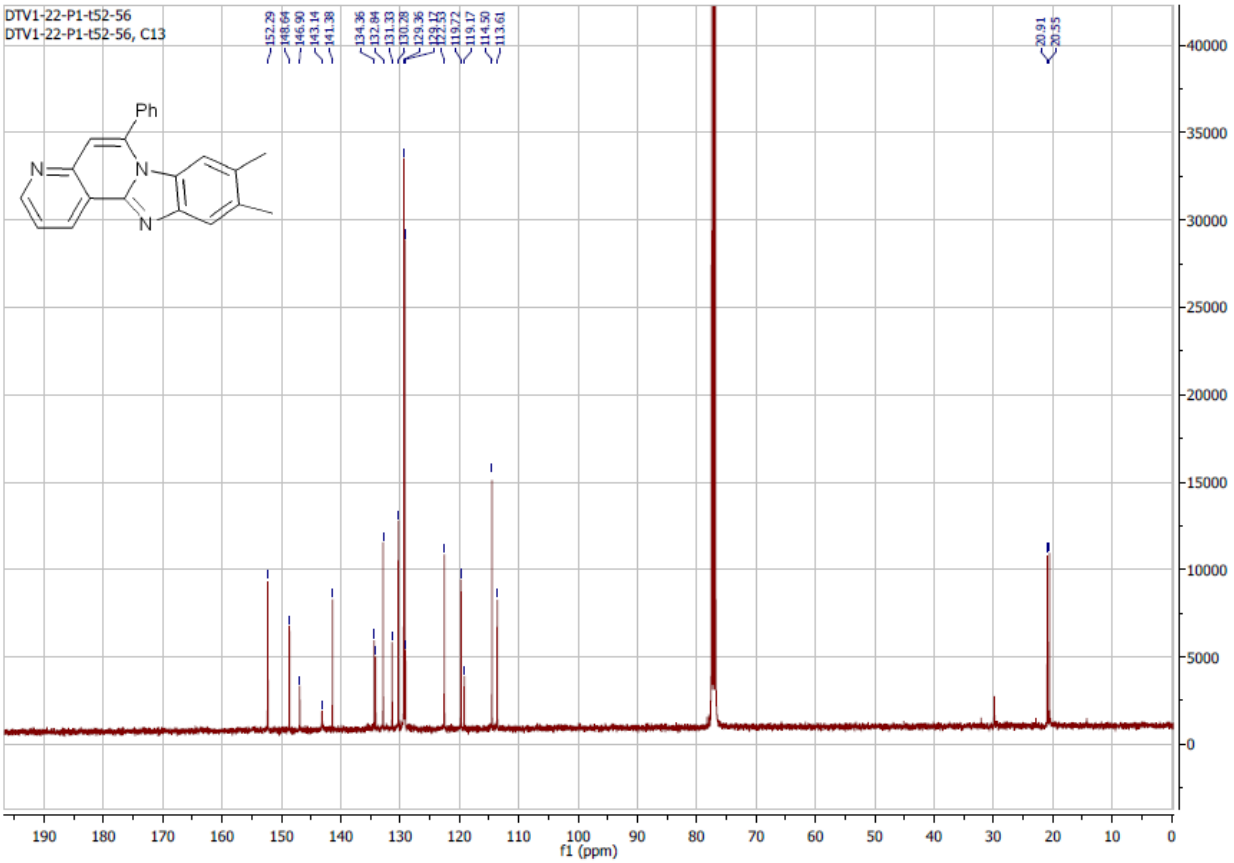
^{13}C NMR of **5m**



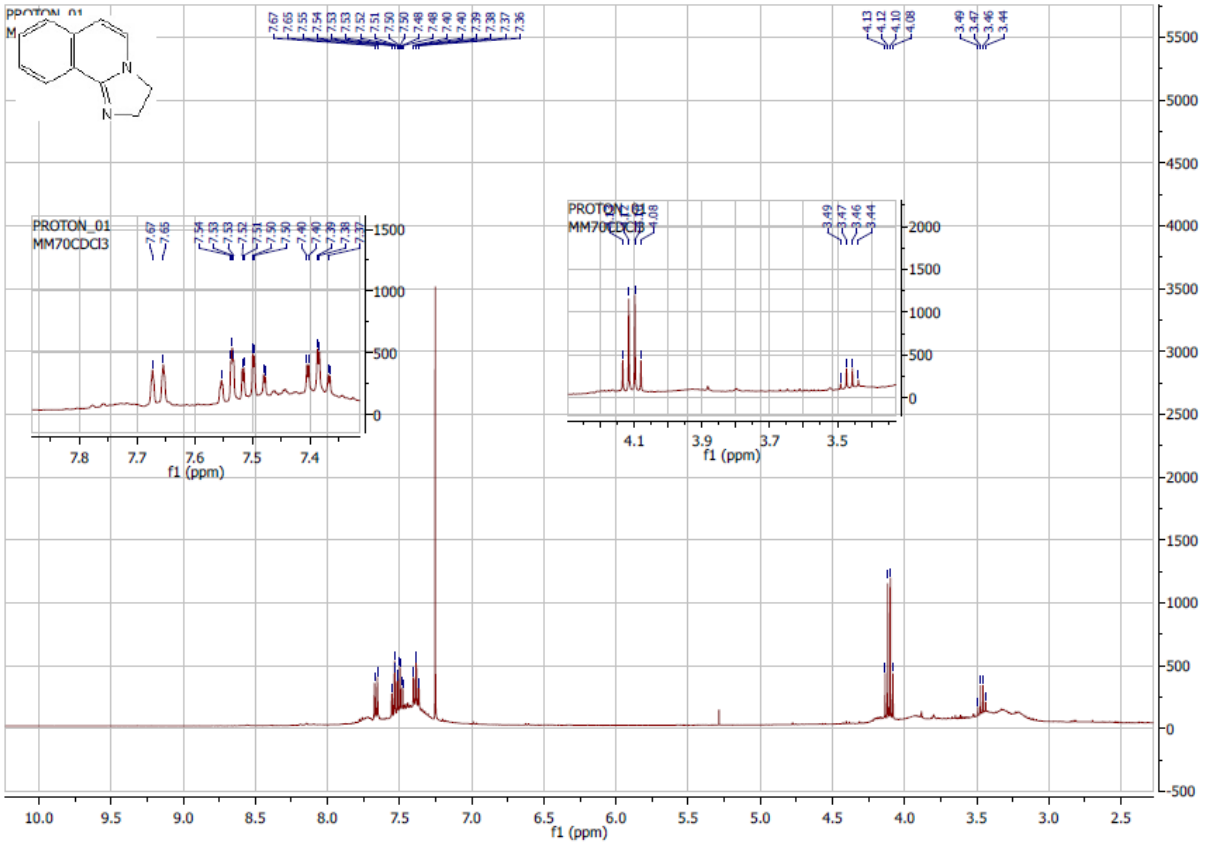
^{1}H NMR of **5n**



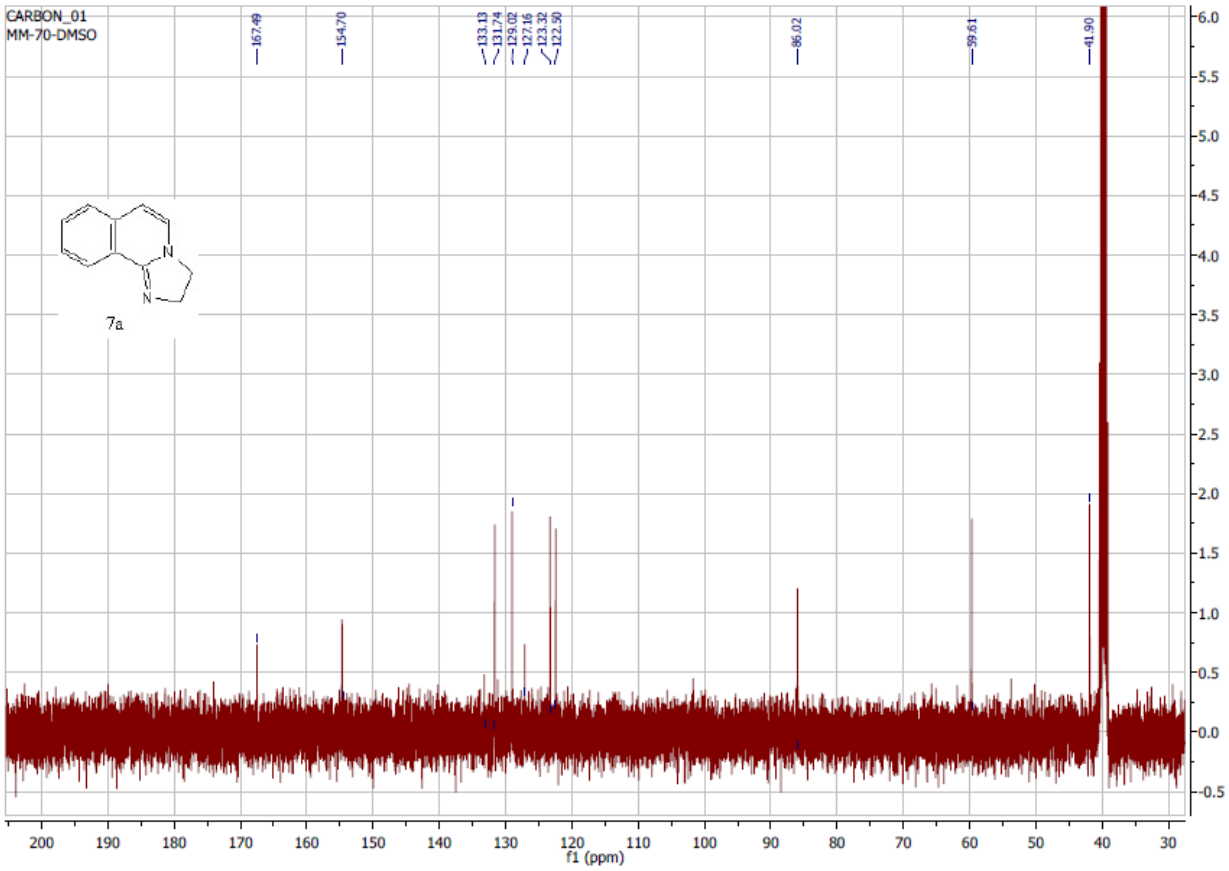
^{13}C NMR of **5n**



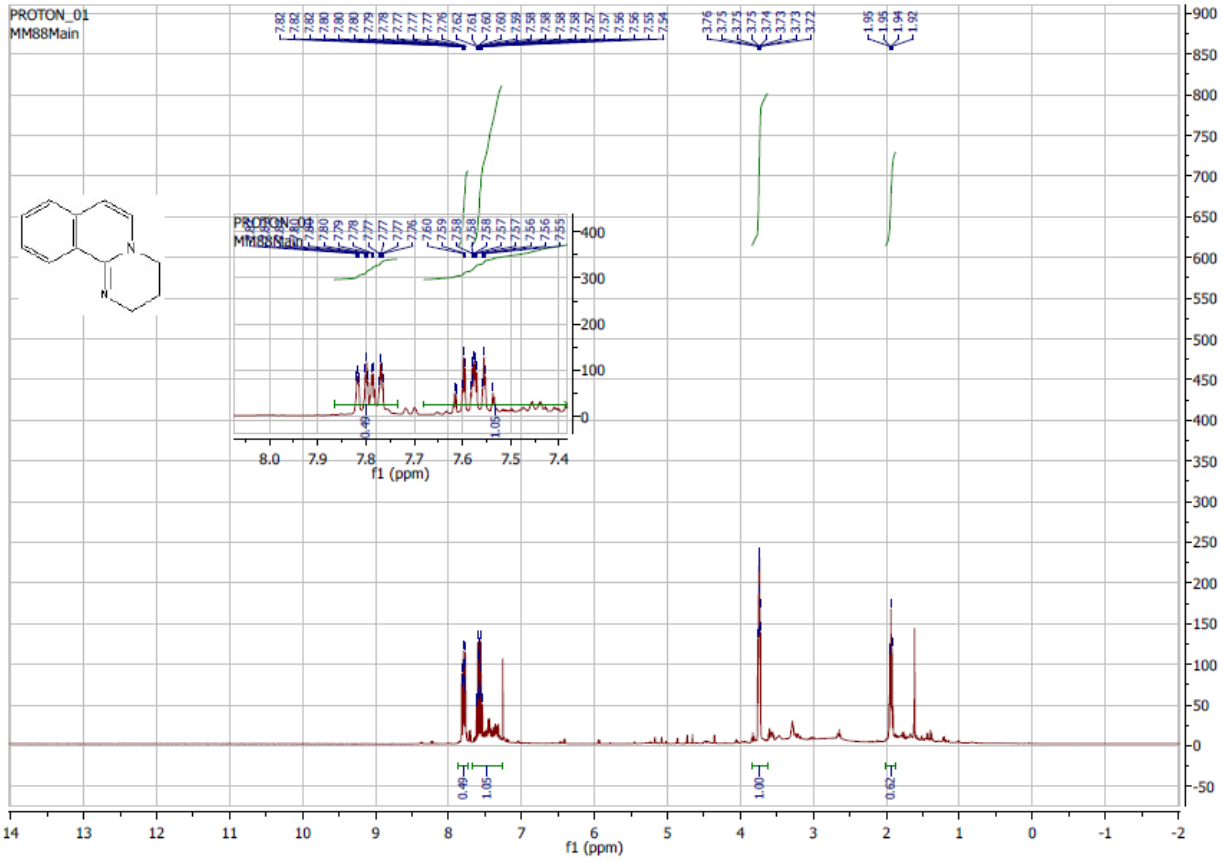
^{1}H NMR of **7a**



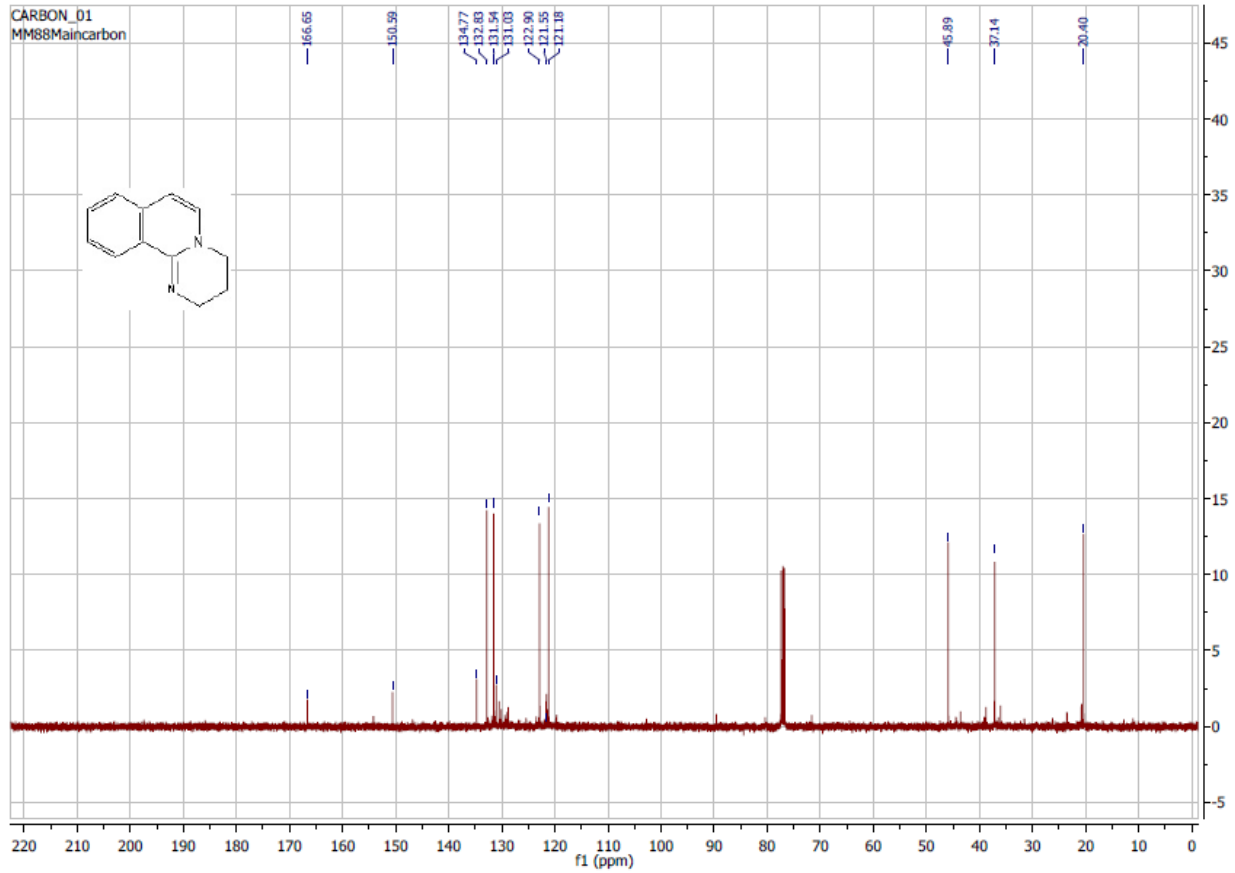
^{13}C NMR of **7a**



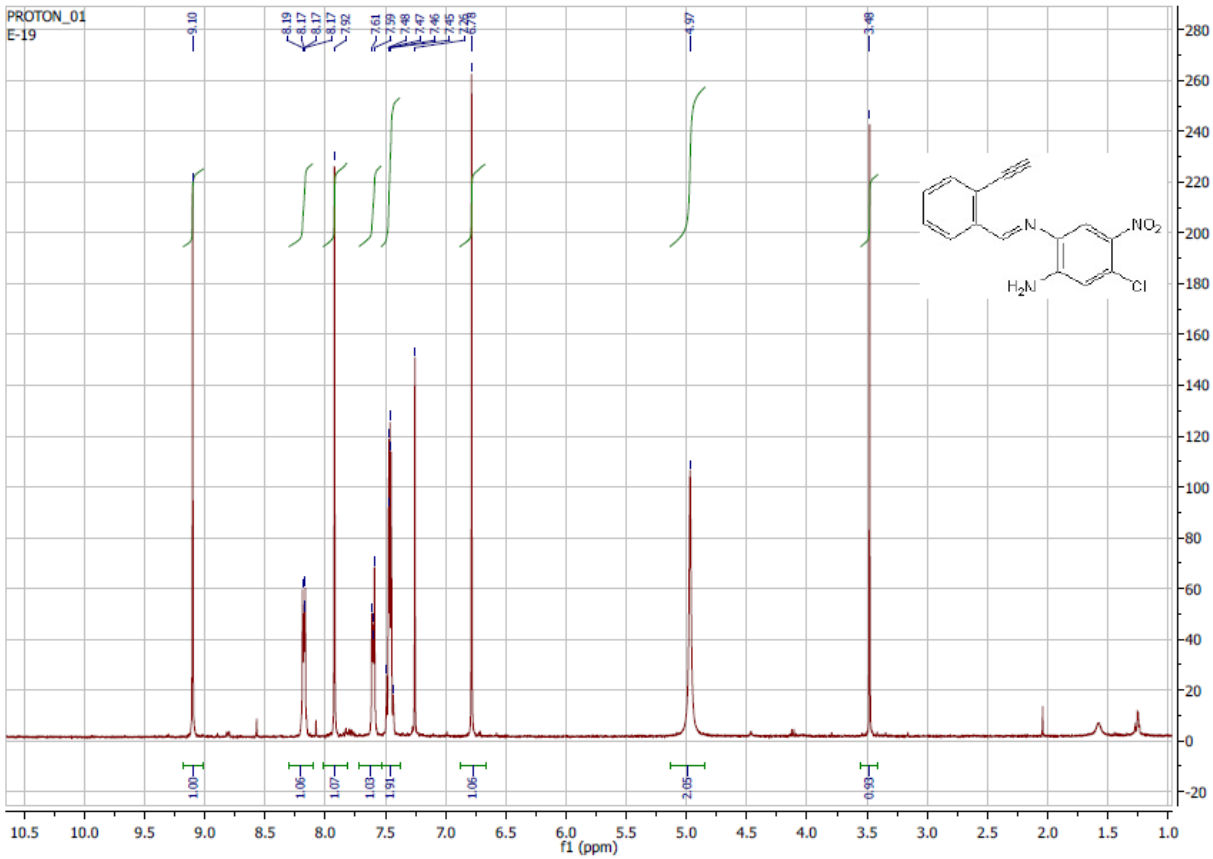
^{1}H NMR of **7b**



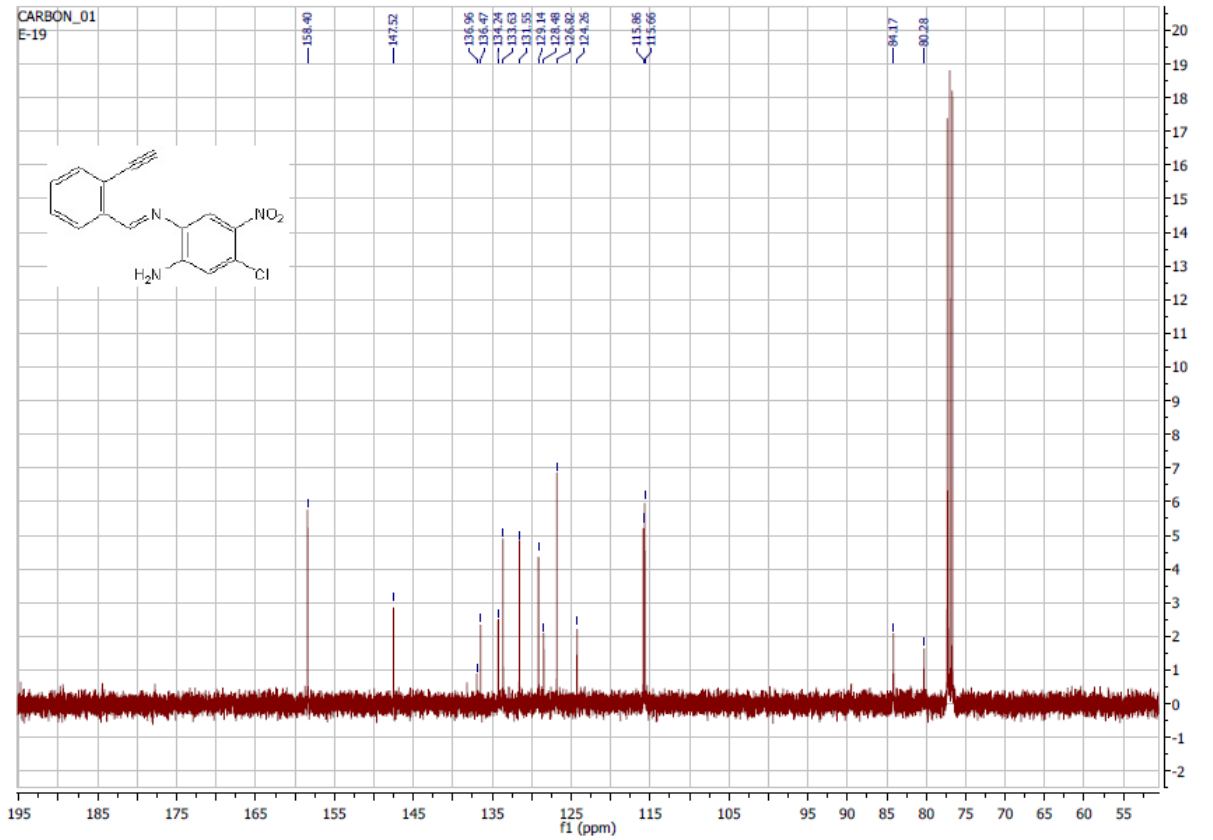
^{13}C NMR of **7b**



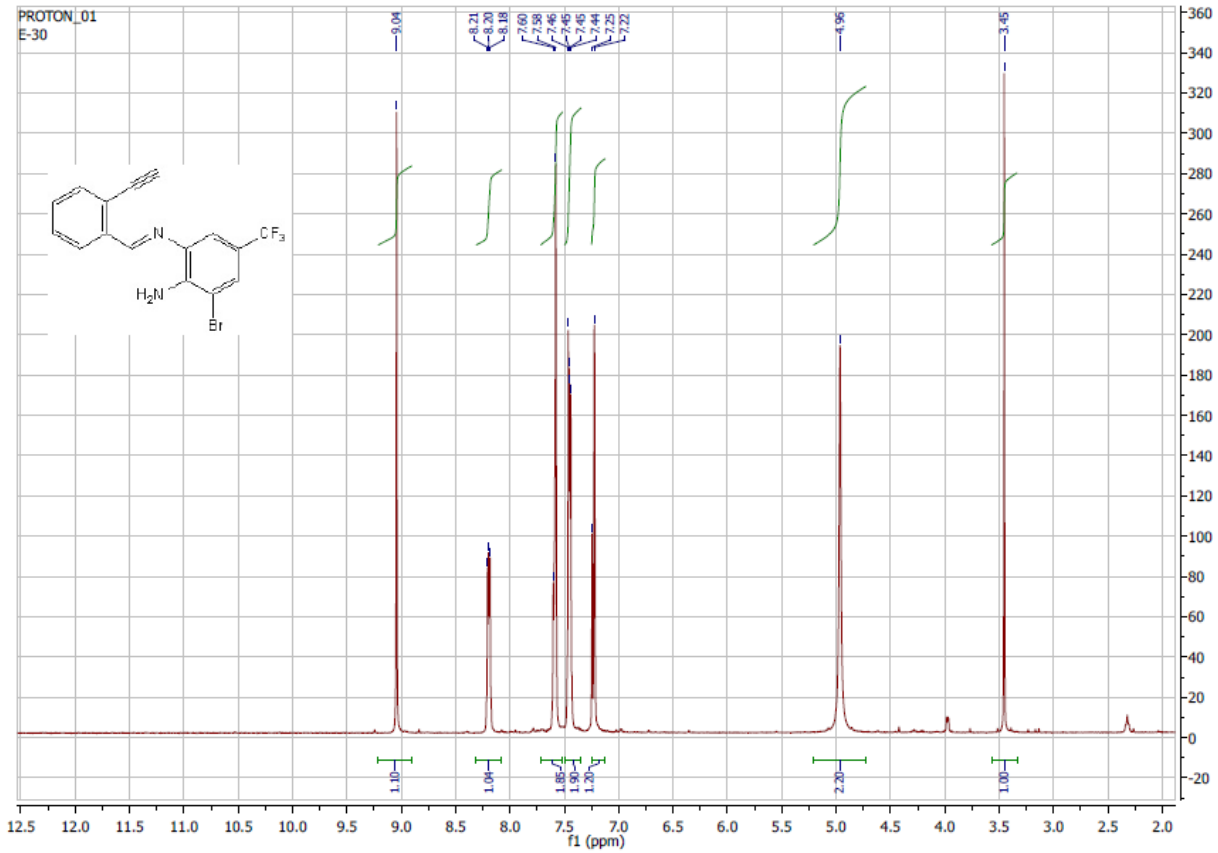
^{1}H NMR of **8e**



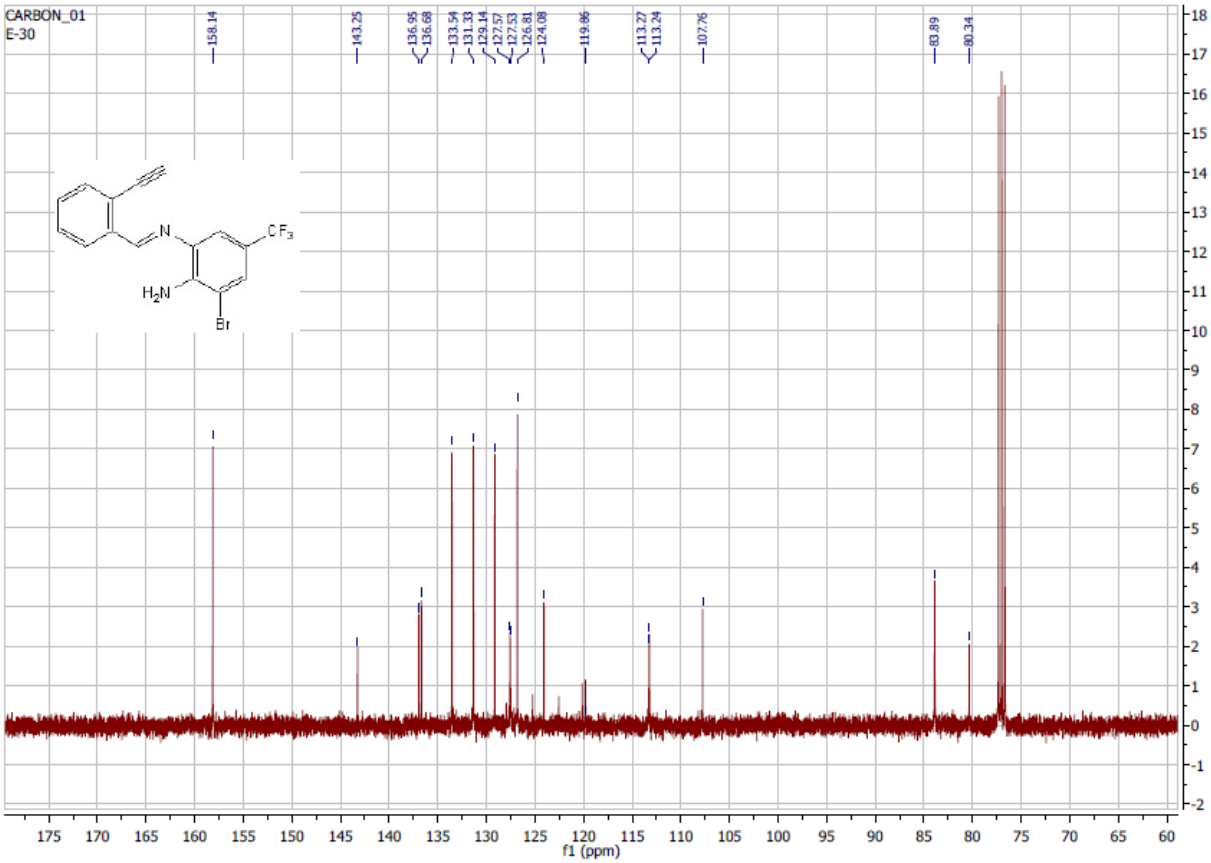
^{13}C NMR of **8e**



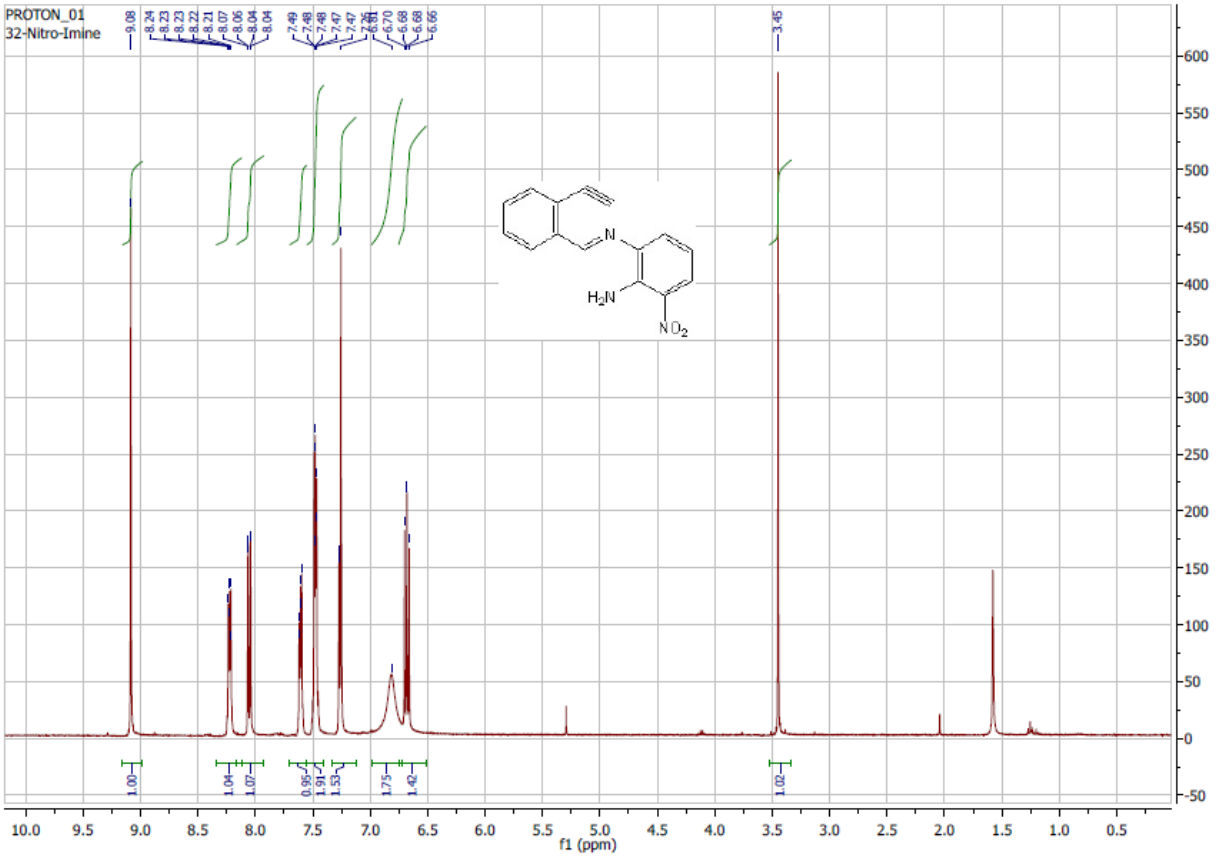
^{1}H NMR of **8f**



^{13}C NMR of **8f**



^{1}H NMR of **8g**



^{13}C NMR of **8g**