Synthesis of Azomethine Imines Using an Intramolecular Alkyne Hydrohydrazination Approach

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Supporting Information

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Difficult Substrates - Further Calibration on the Scope of this Reactivity

Advantages of bis(trifluoromethyl)benzohydrazides. As discussed in the manuscript, the use of bis(trifluoromethyl)benzoyl group proved crucial to isolate the desired dipole and to minimize byproduct formation. This section of the supporting information supports this statement. In analogy to our communication on intramolecular alkene hydroamination, the three hydrazides shown below were synthesized and tested. We encountered two related challenges during our efforts. First, hydroamination attempts indicated the formation of a mixture of products (^{1}H NMR analysis). The desired azomethine imines appeared to be formed with all three hydrazides (representative spectra are provided in the Appendix), but attempts to isolate these products failed in the hand of two co-authors. Similarly, attempts to isolate and identify the byproduct(s) formed under these conditions failed. In contrast, in reactions of bis(trifluoromethyl)benzohydrazides byproduct formation was minimized and the azomethine imines could be readily isolated and purified using silica gel chromatography.

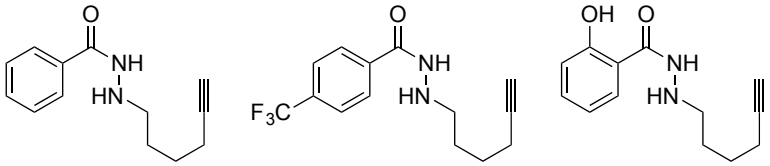
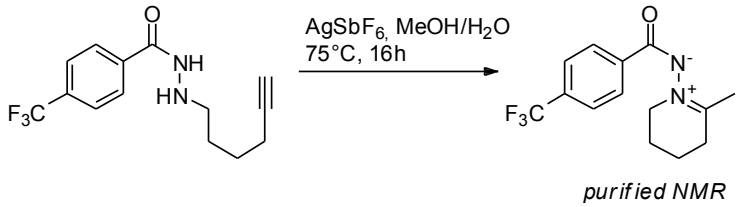


Figure S1. Other benzoic hydrazides tested to access azomethine imines

To confirm that the mixtures described above were not due to an equilibrium between the azomethine imines and a tautomer (e.g. the neutral ene hydrazide), we independently synthesized the desired product using silver catalysis (see equation below). The transformation below likely involves hydration of the triple bond[1] followed by condensation to form the desired azomethine imine: To a solution of *N*'-(hex-5-ynyl)-4-(trifluoromethyl)-benzohydrazide (0.076 g, 0.27 mmol) in MeOH/H_2O (10:1, 0.6 mL) was added $AgSbF_6$ (0.092 g, 0.027 mmol).

[1] Thuong, M. B. T.; Mann, A.; Wagner, A. *Chem. Commun.* **2012**, *48*, 434.

The reaction mixture was stirred overnight at 75°C. The crude mixture was then concentrated under vacuum and purified by column chromatography (2% MeOH in CH_2Cl_2). This approach allowed us to obtain a relatively pure sample of the desired azomethine imine. This suggests that byproduct formation competes with the desired hydroamination reaction under the typical thermolysis conditions for the substrates presented in Figure S1.



Other substrates prepared. Other hydroaminations were attempted. For example the two substrates below were synthesized and subjected to the reaction conditions. All starting material reacted, but little to no hydroamination was observed. Only a 4% yield of the desired product was isolated for the formation of the 7-membered azomethine imine.

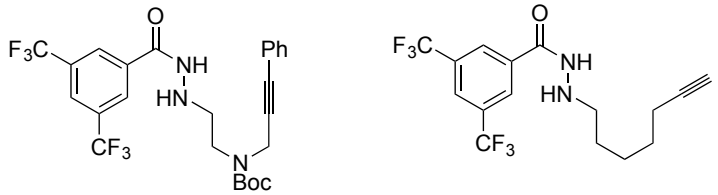


Figure S2. Other substrates tested to access azomethine imines

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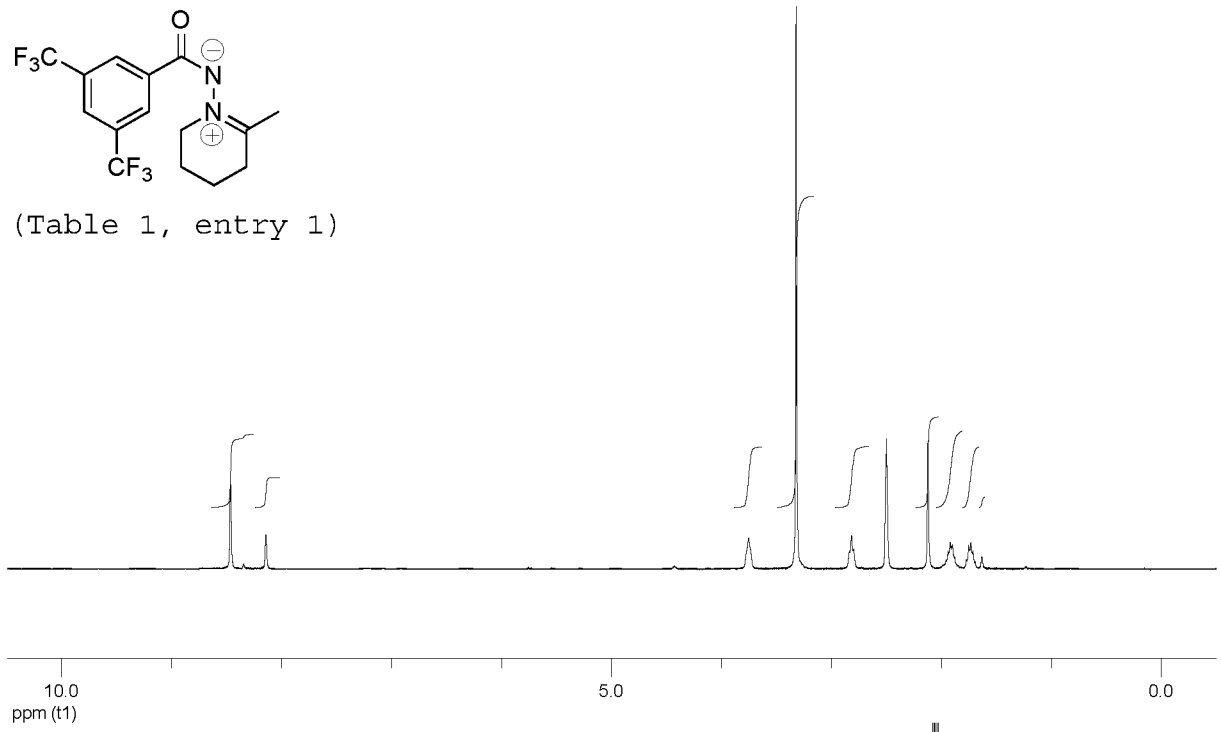

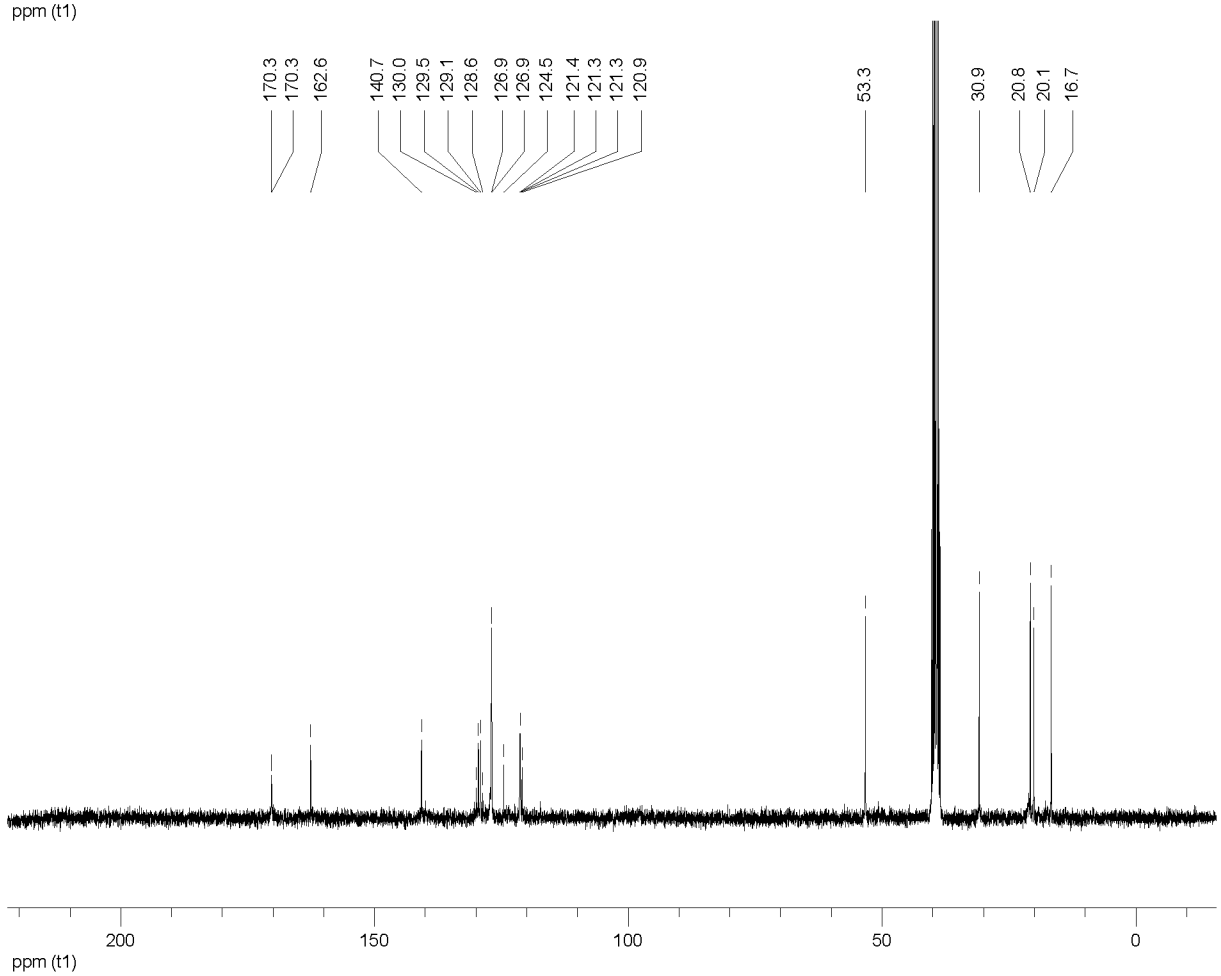

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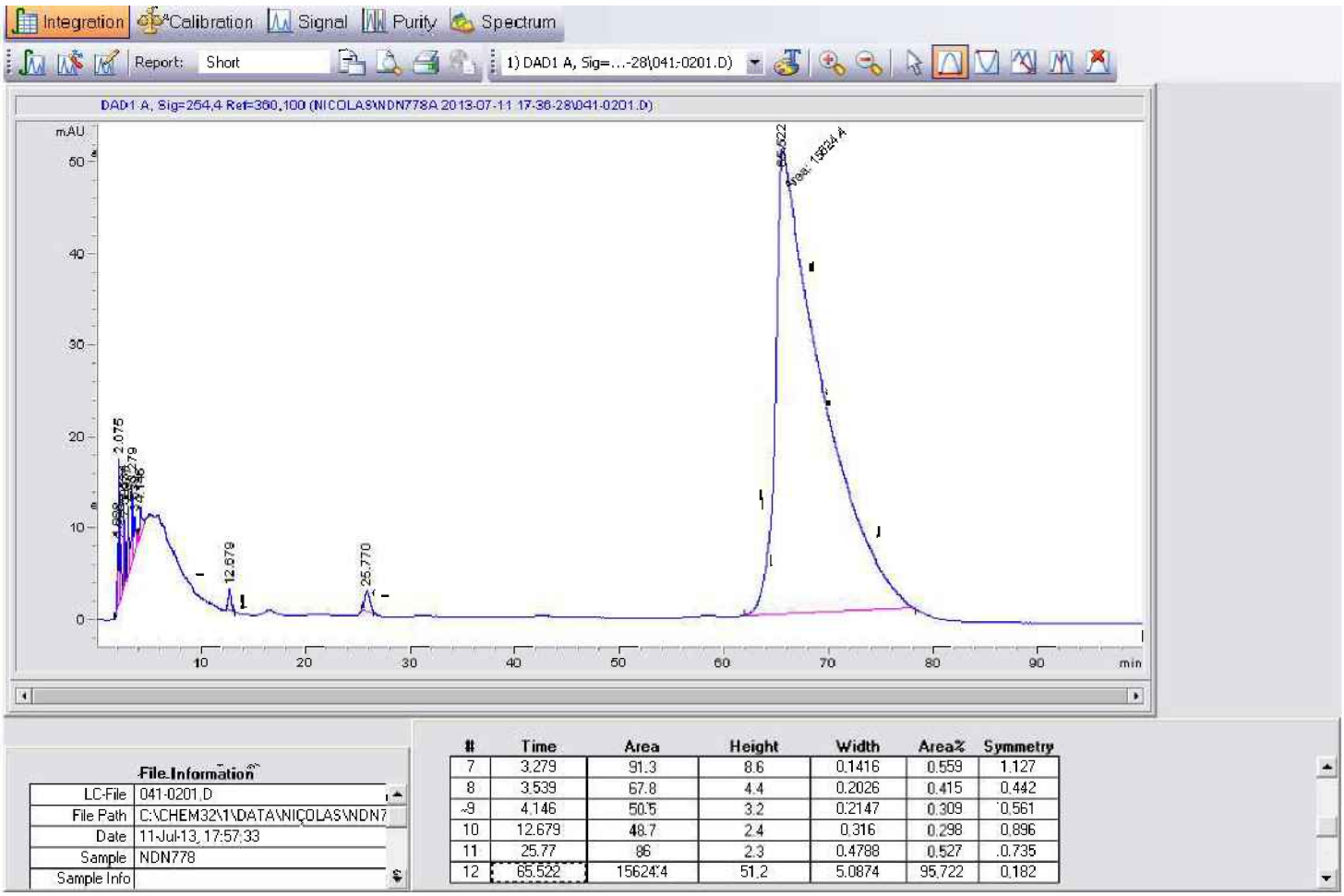
HPLC: Zorbax Rx-SIL, iPrOH/hexane = 10/90, 1 mL/min,254 nm, t = 65.5 min



#	Time	Area	Height	Width	Area%	Symmetry
7	3.279	91.3	8.6	0.1416	0.559	1.127
8	3.539	67.8	4.4	0.2026	0.415	0.442
9	4.146	50.5	3.2	0.2147	0.309	0.561
10	12.679	48.7	2.4	0.316	0.298	0.896
11	25.77	86	2.3	0.4788	0.527	0.735
12	65.522	15624.4	51.2	5.0874	95.722	0.182

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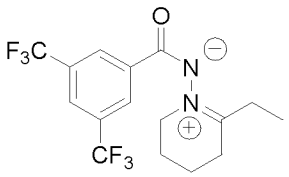

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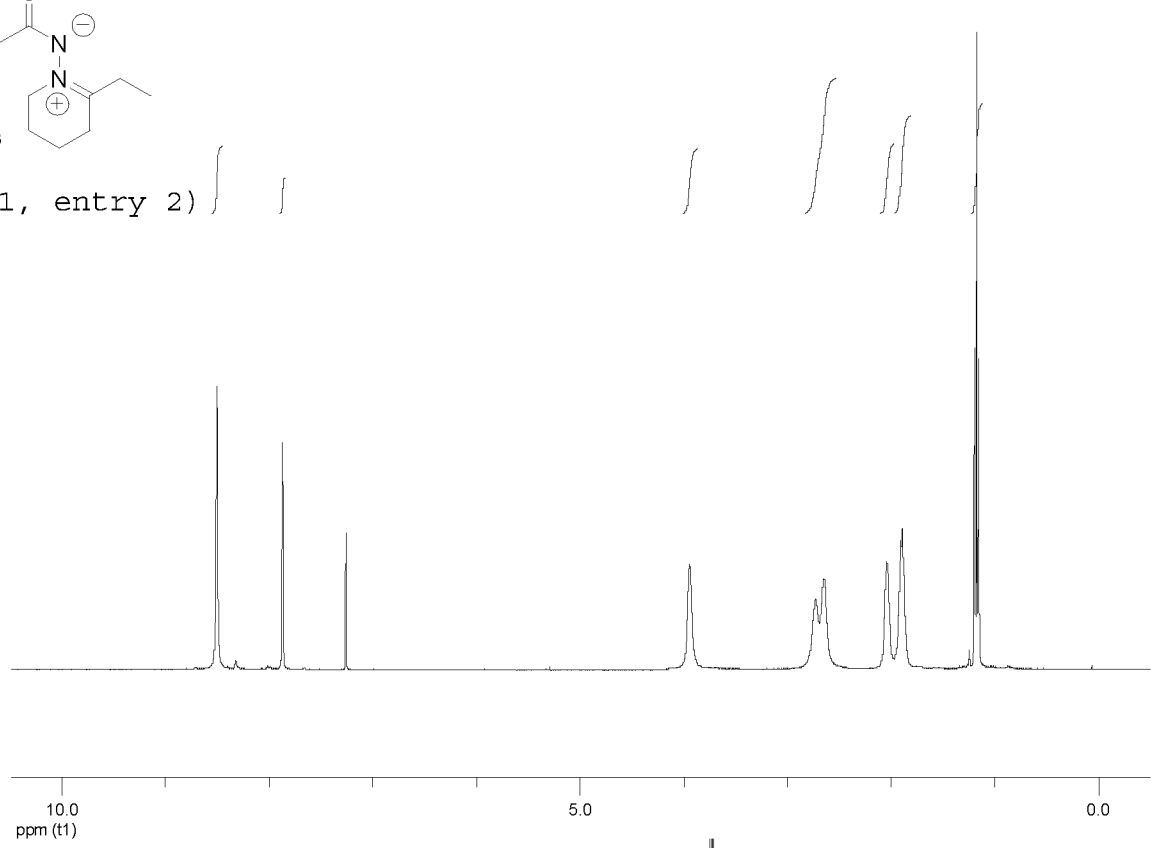

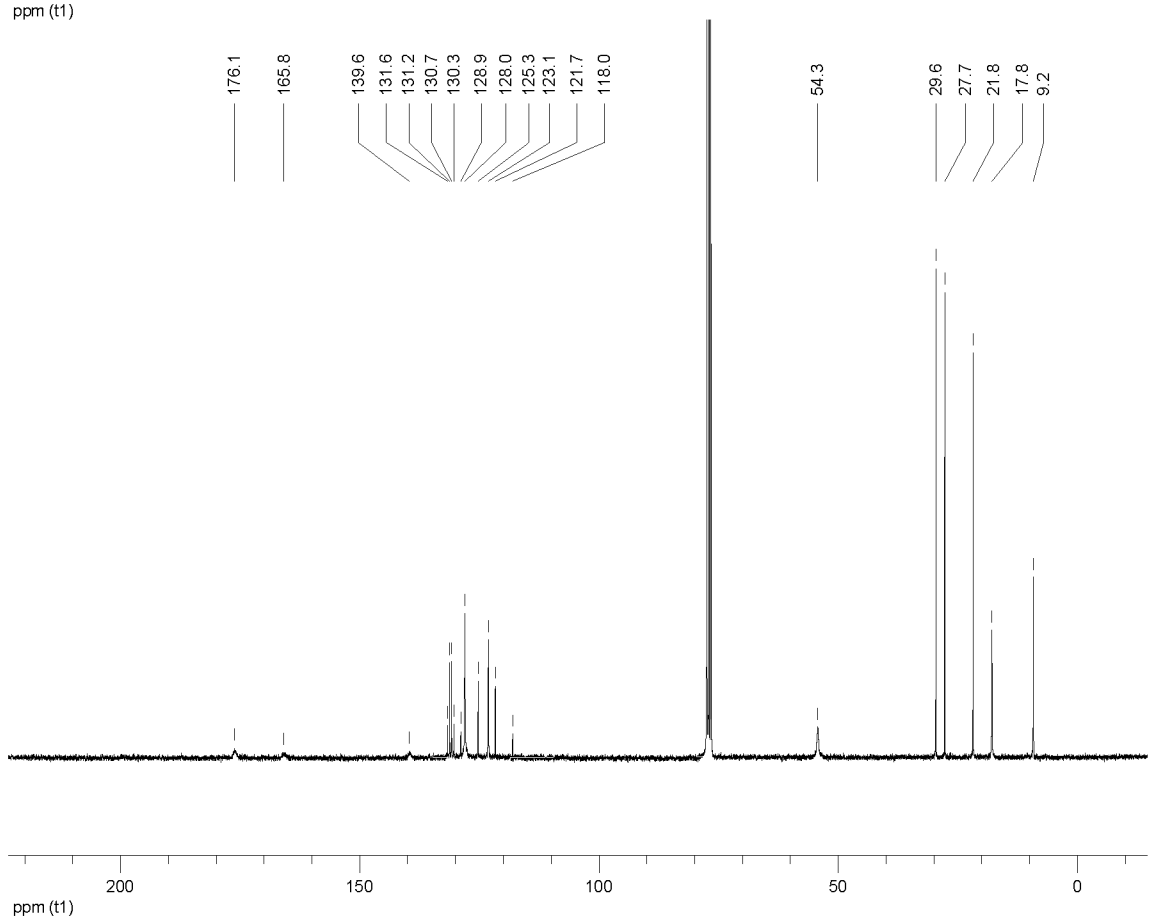

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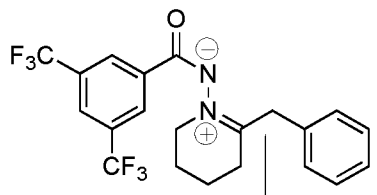

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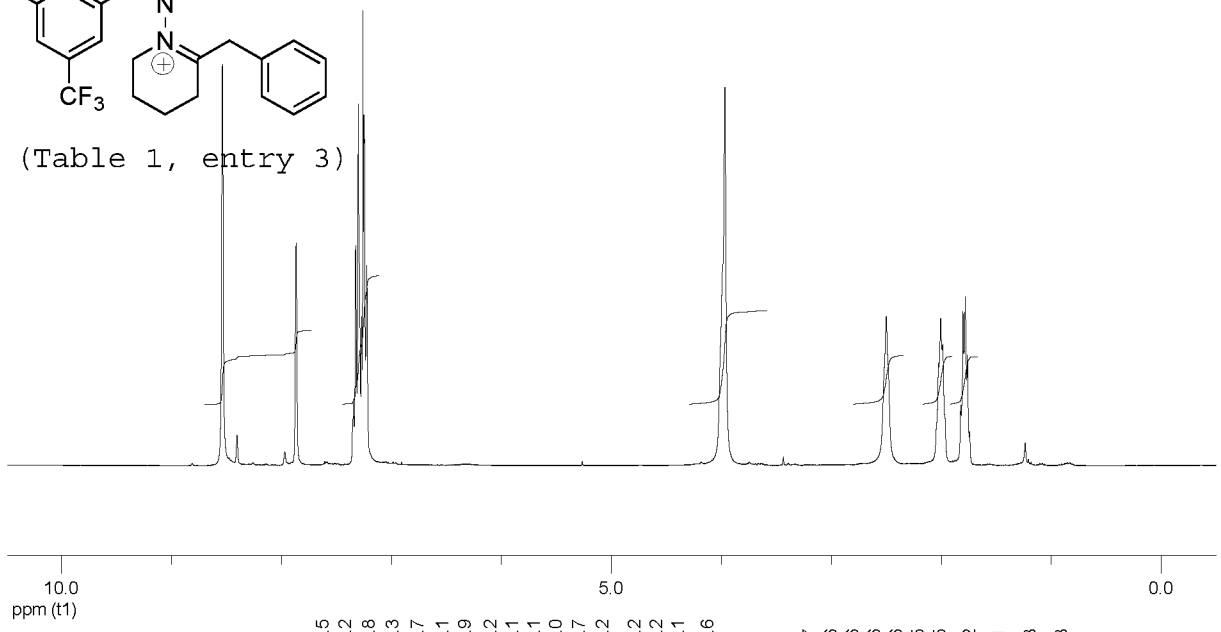
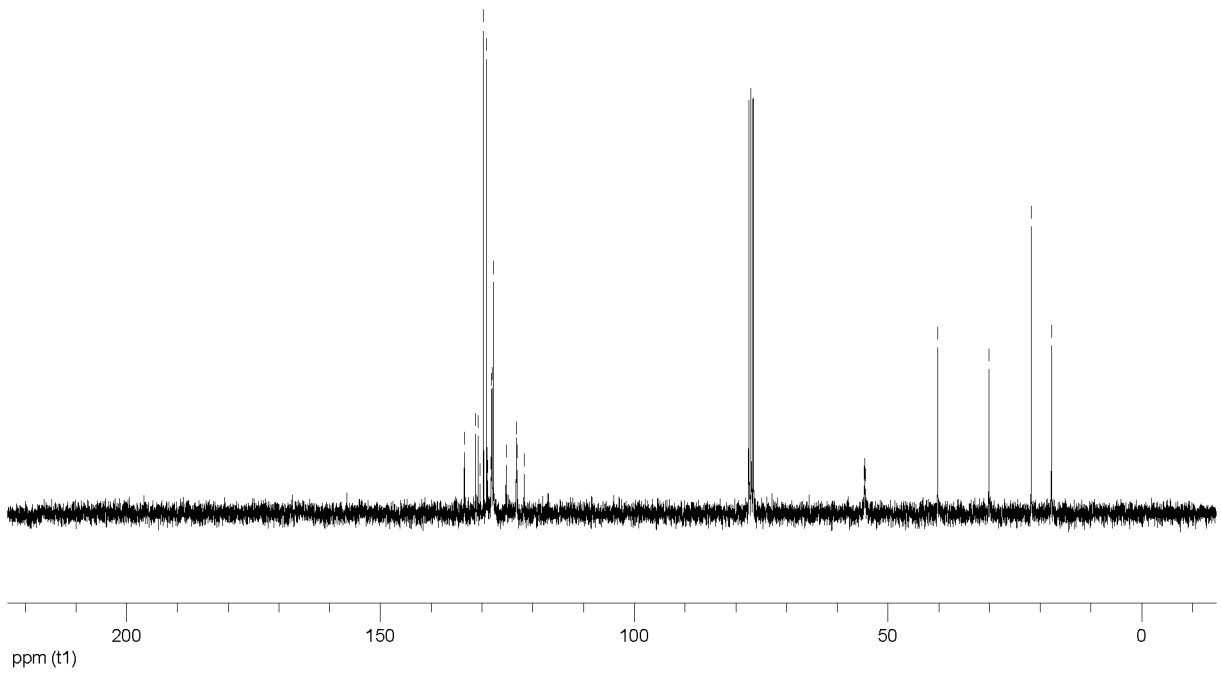


133.5 131.2 130.8 130.3 129.7 129.1 128.9 128.2 128.1 128.1 128.0 127.7 125.2 123.2 123.2 123.1 121.6

54.7 54.6 54.6 54.6 54.6 54.5 54.5 40.2 30.1 21.8 17.8



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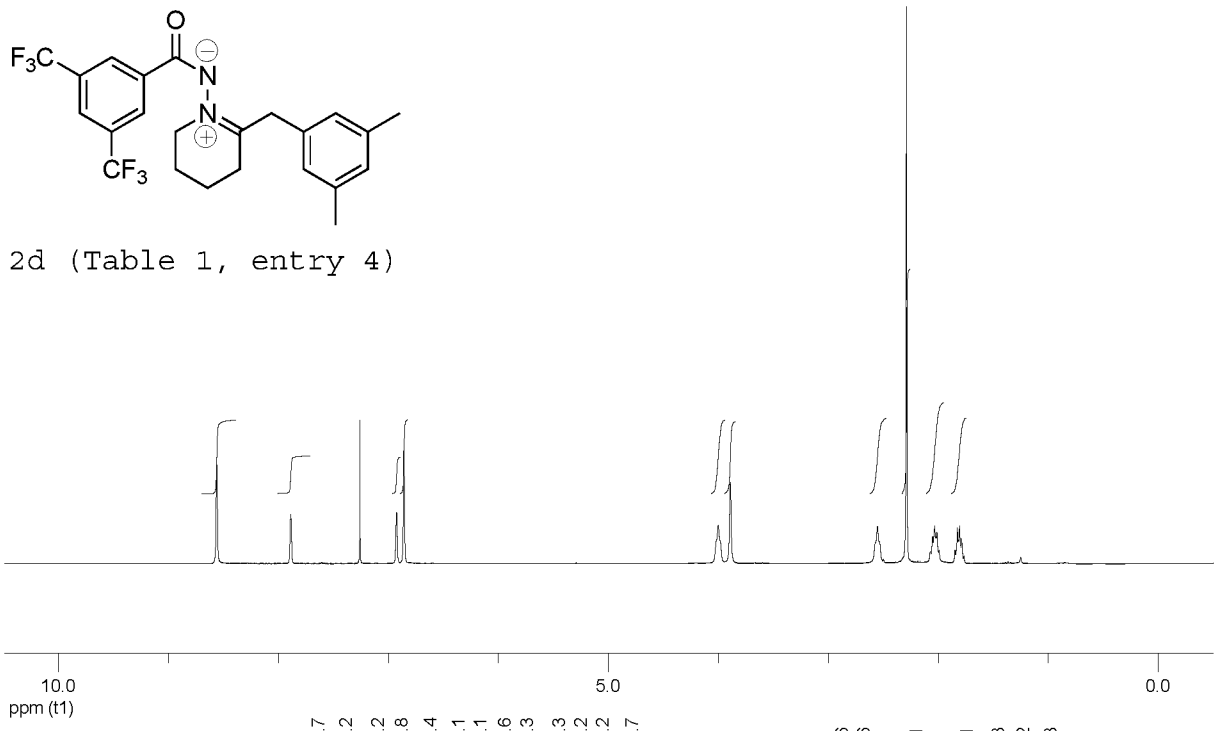

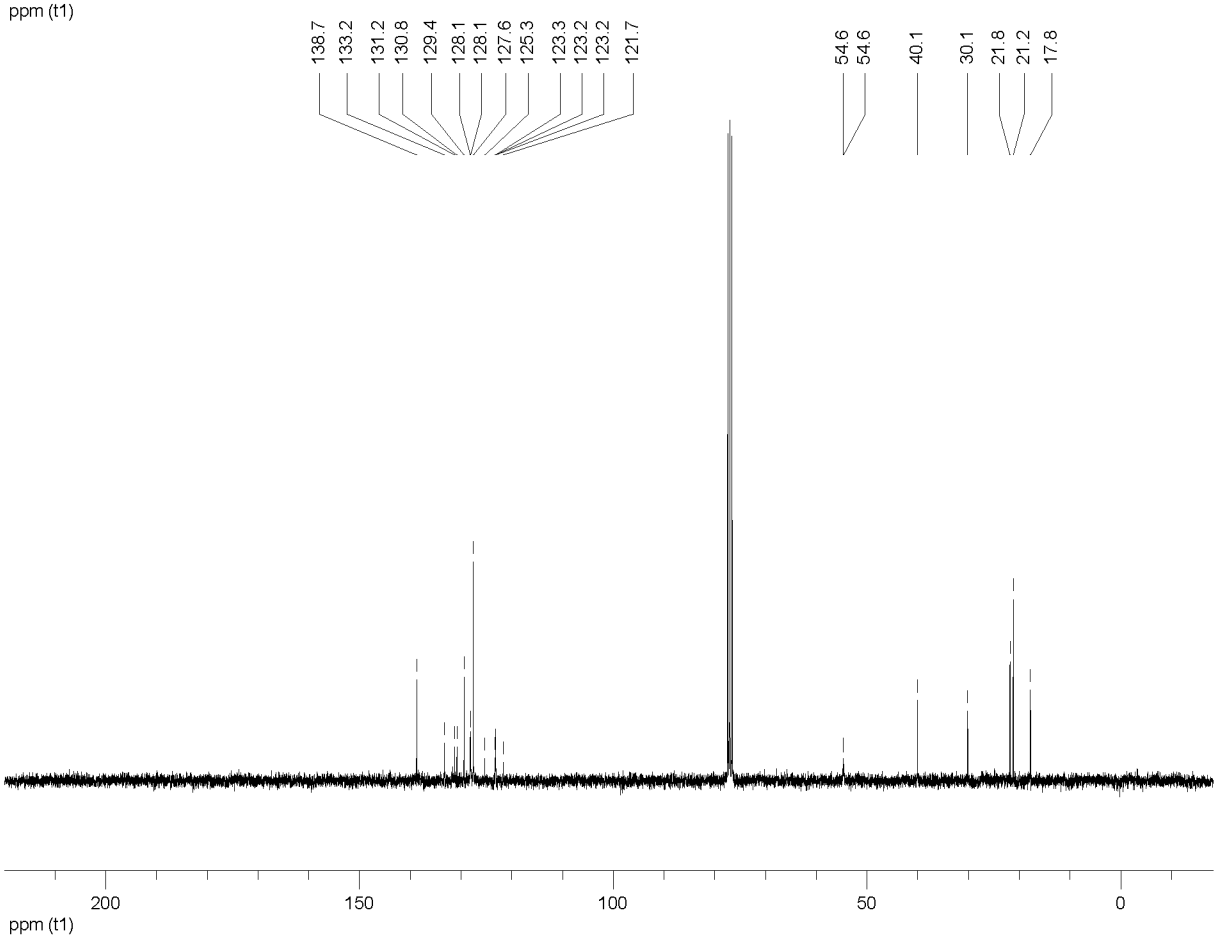

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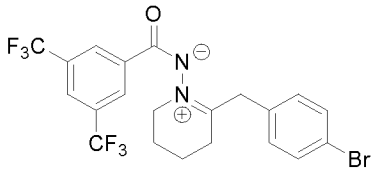

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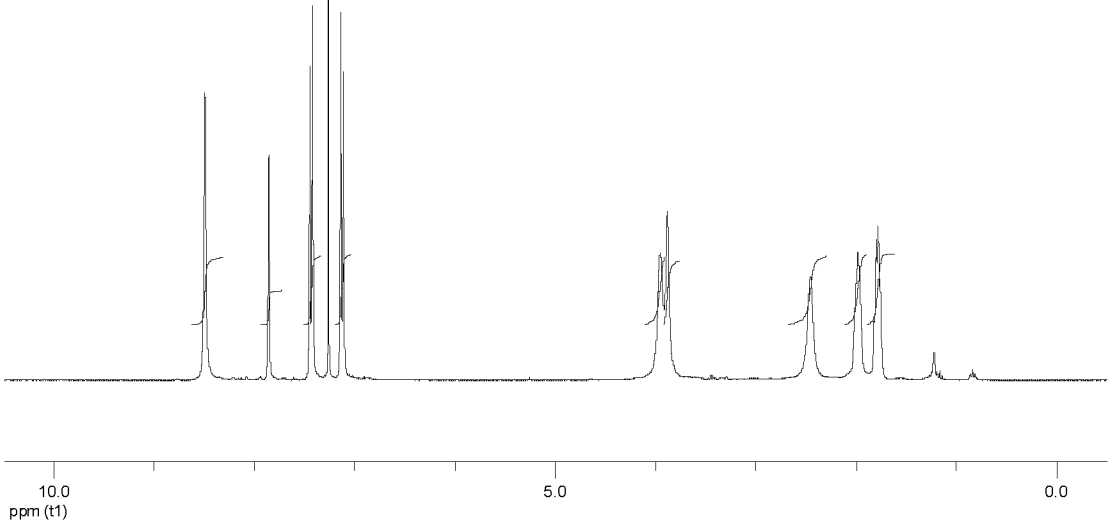

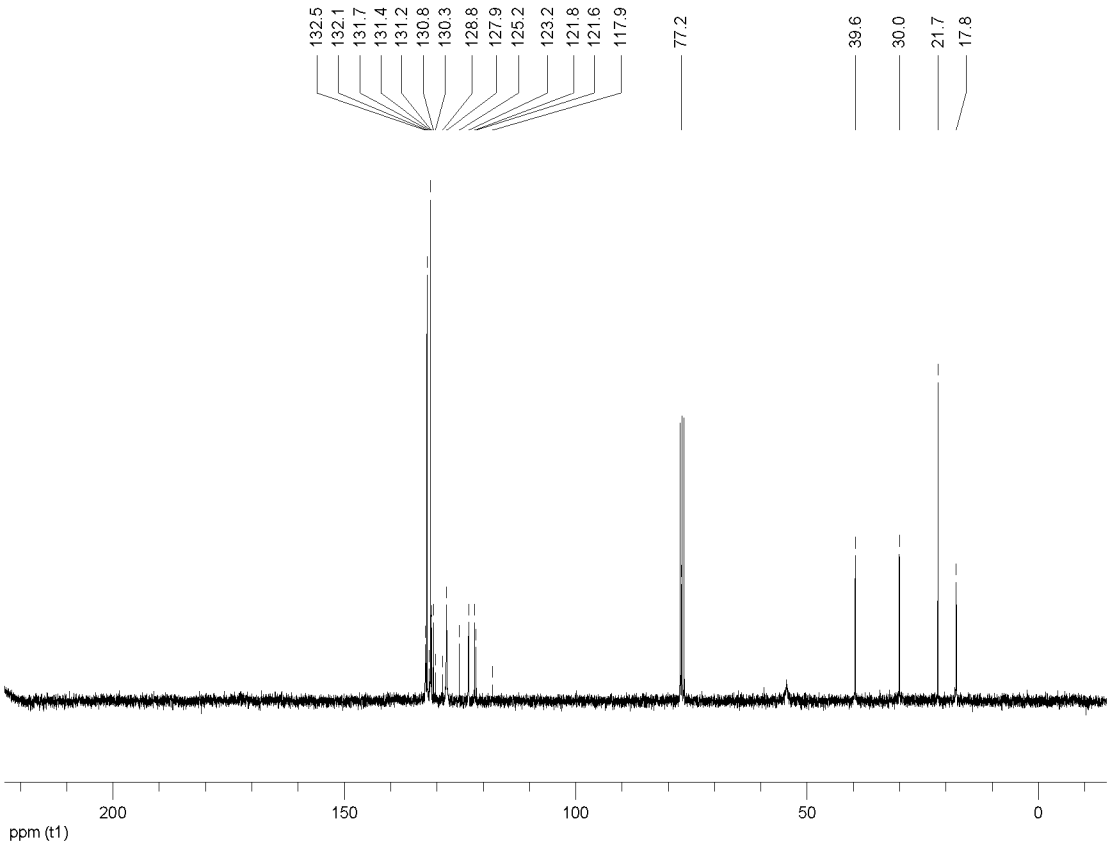

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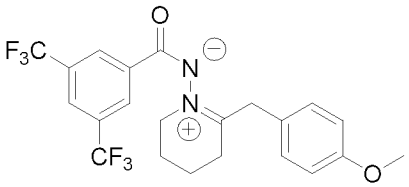

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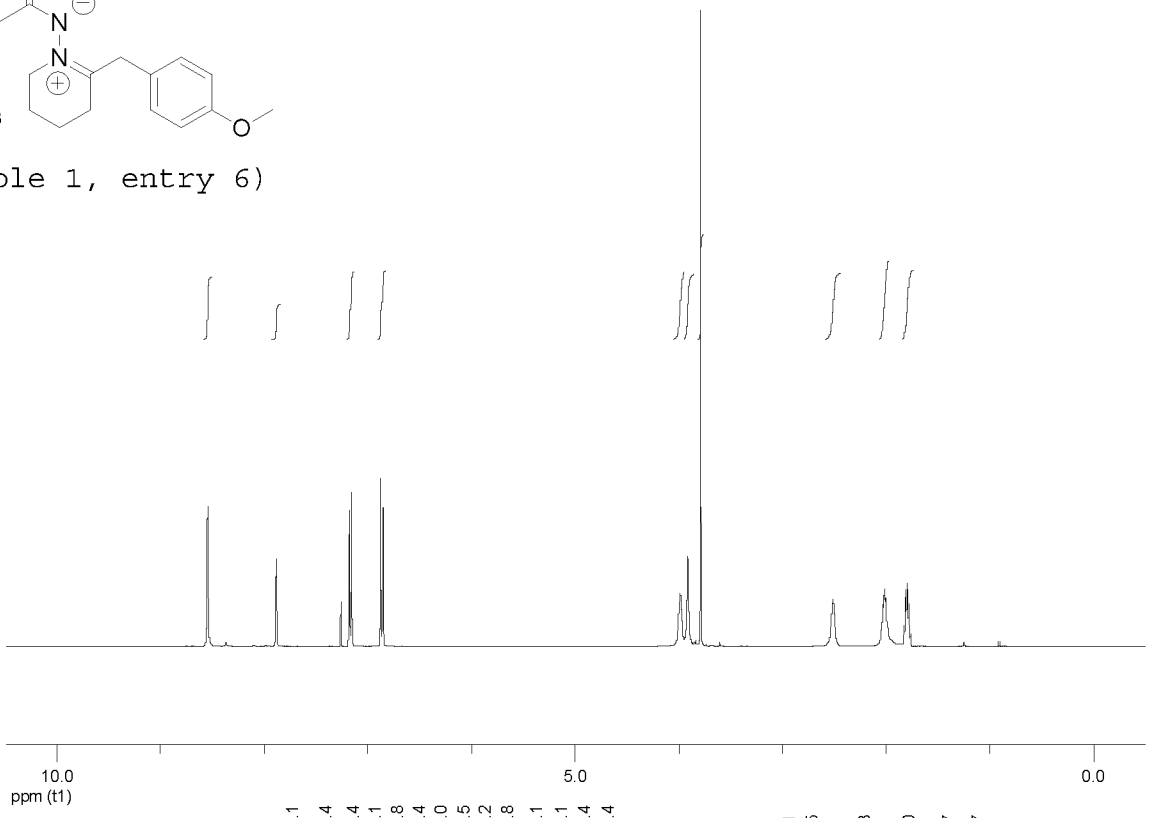

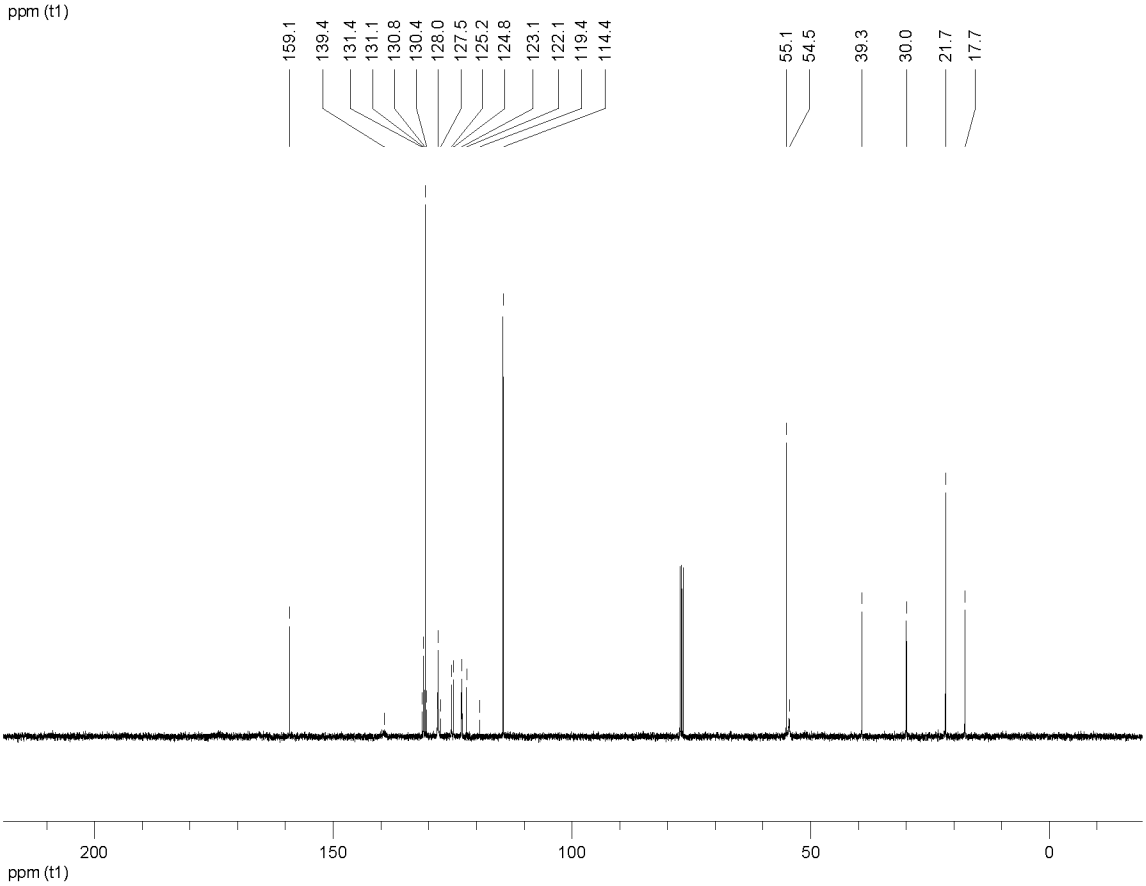

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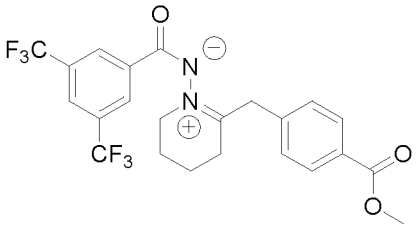

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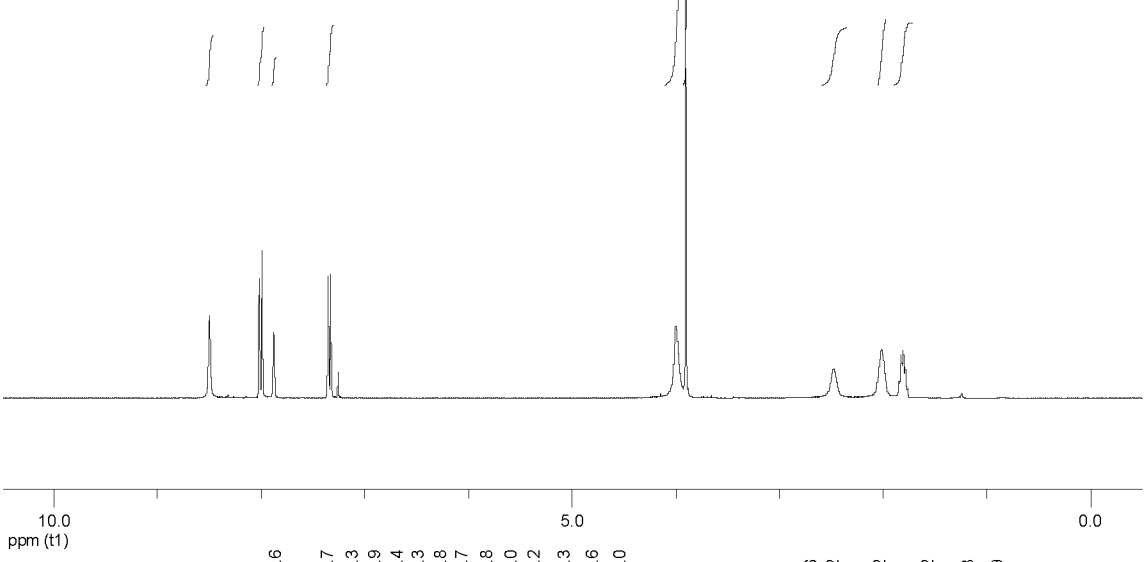

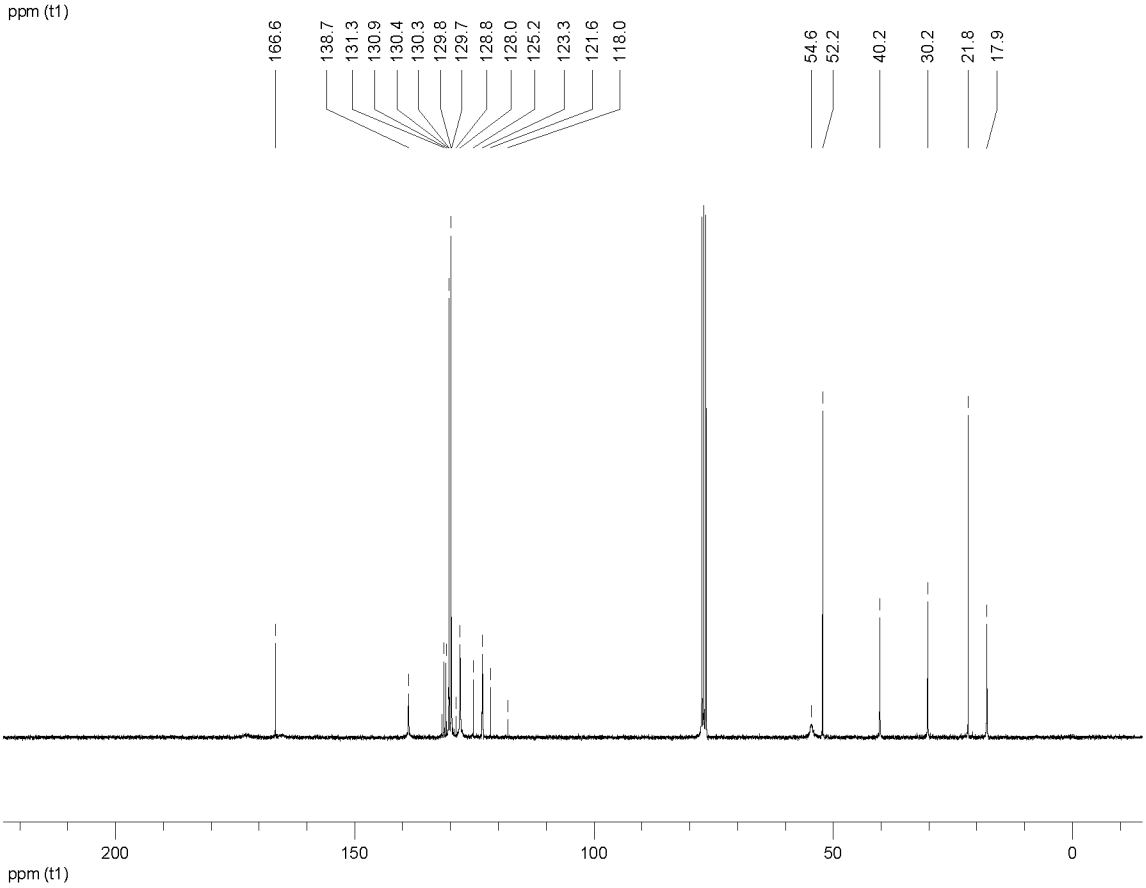

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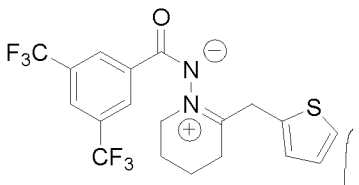

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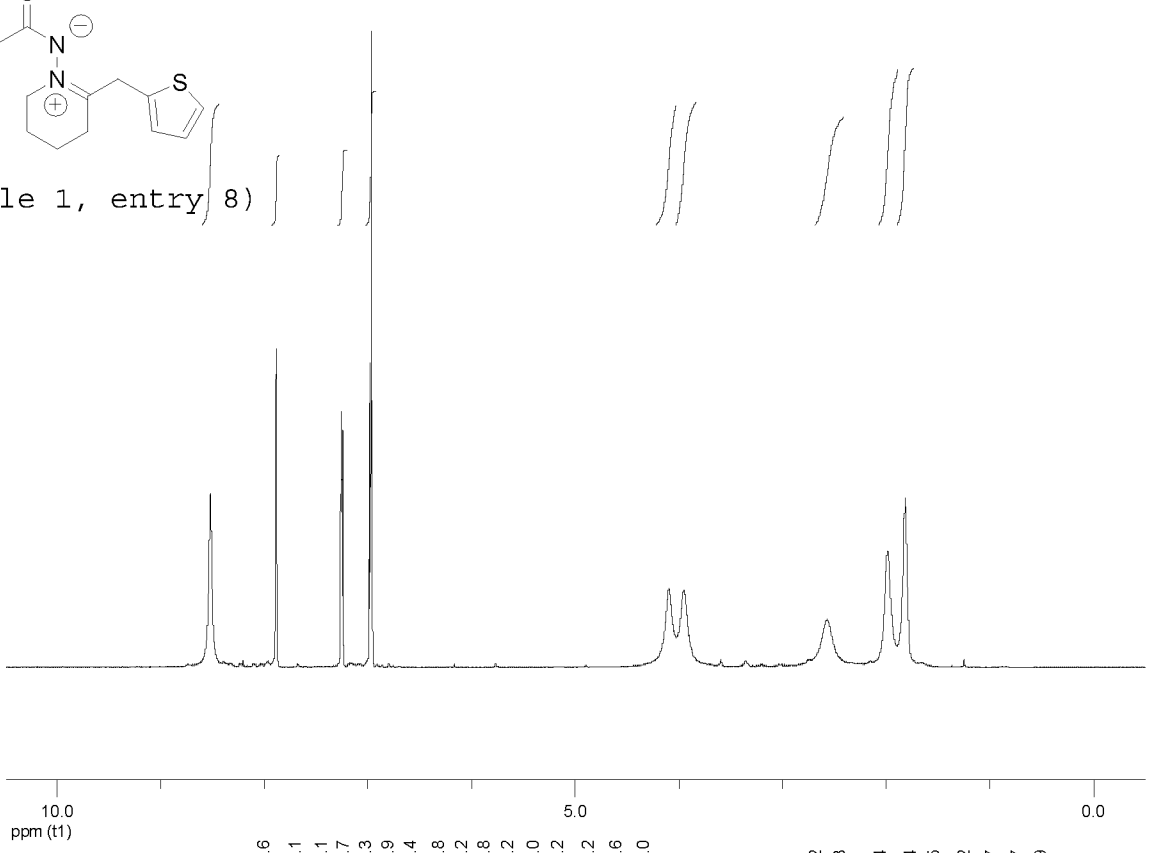

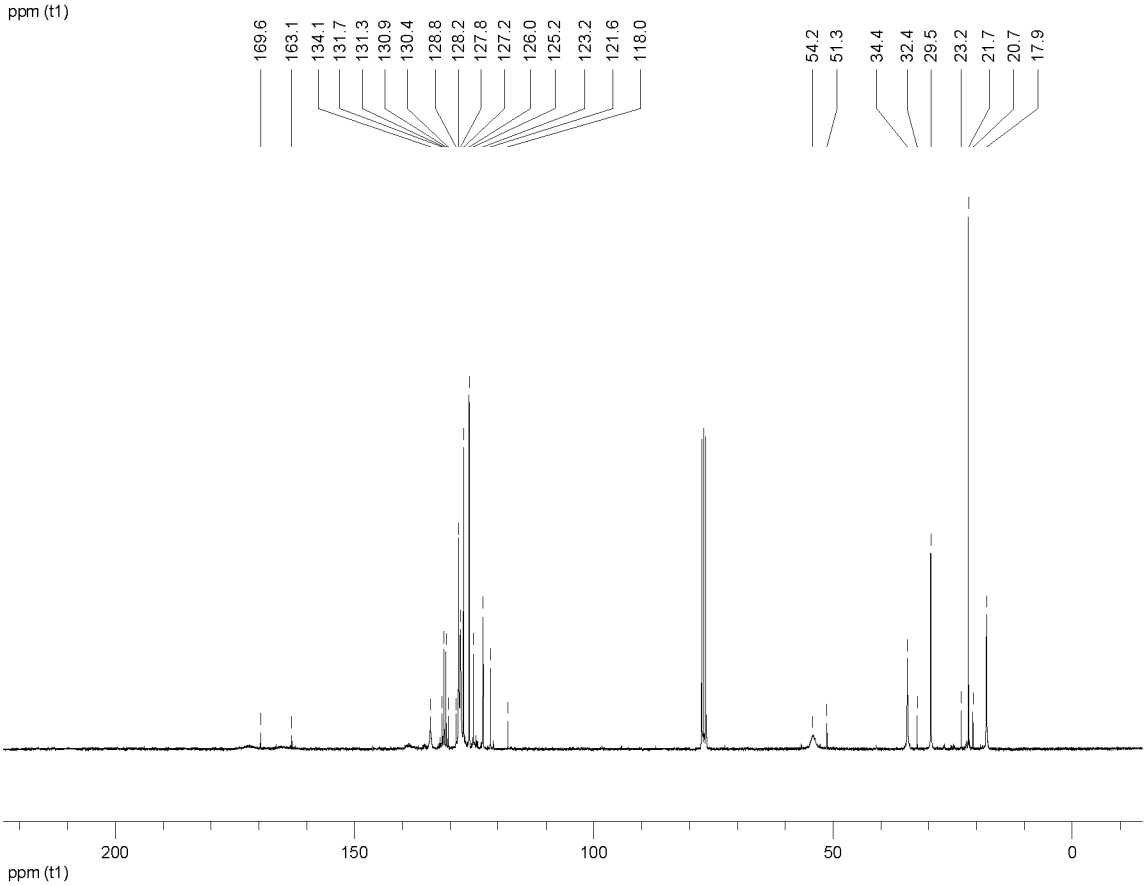

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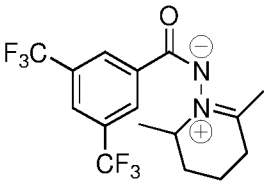

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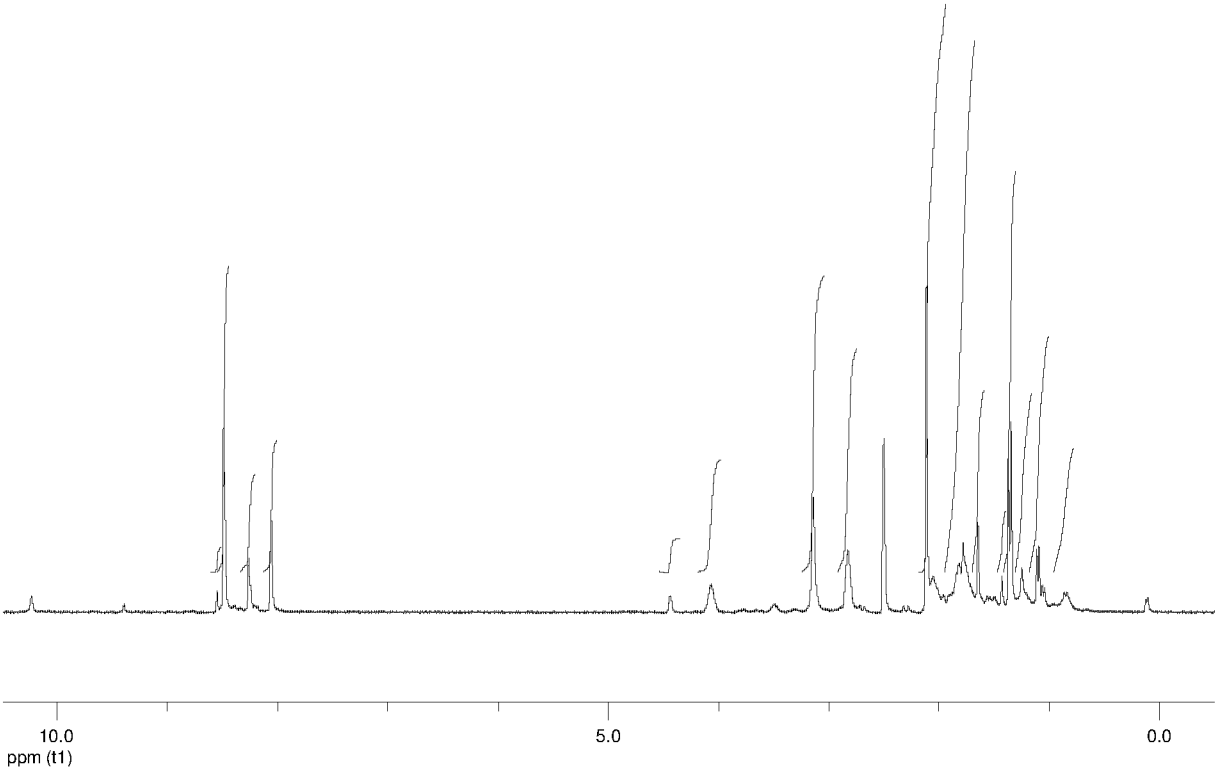

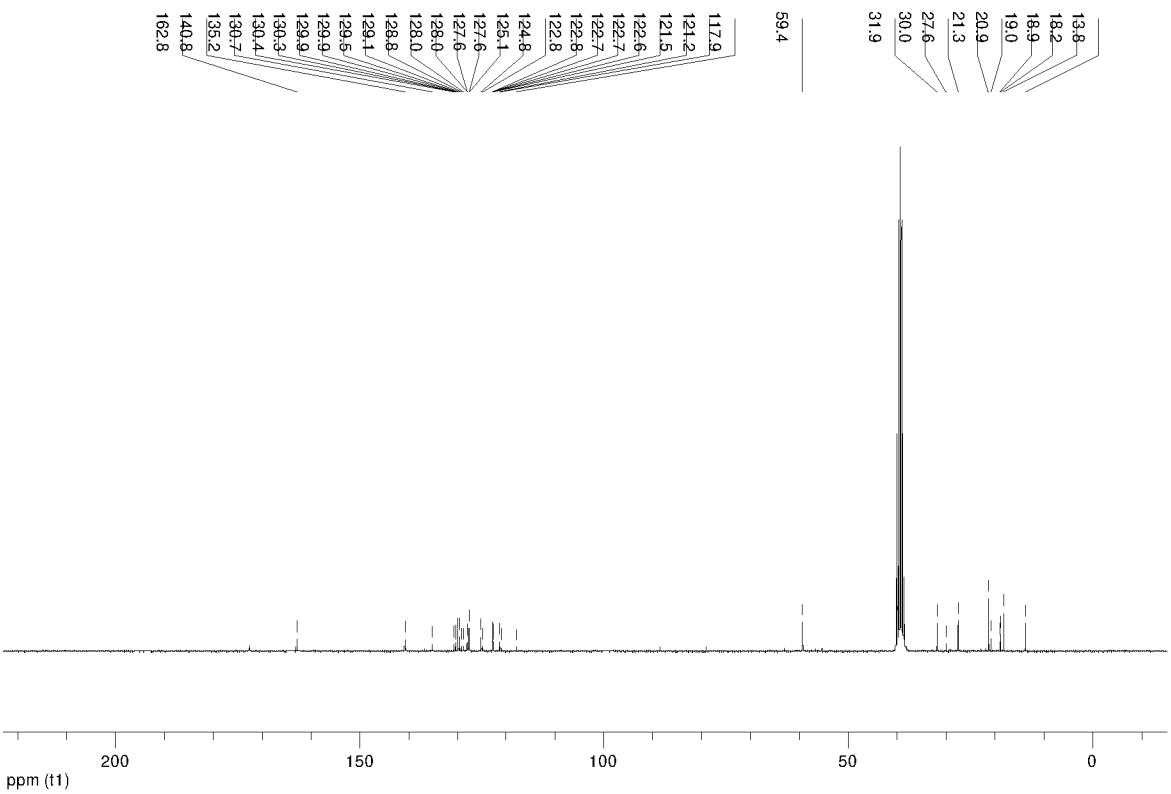

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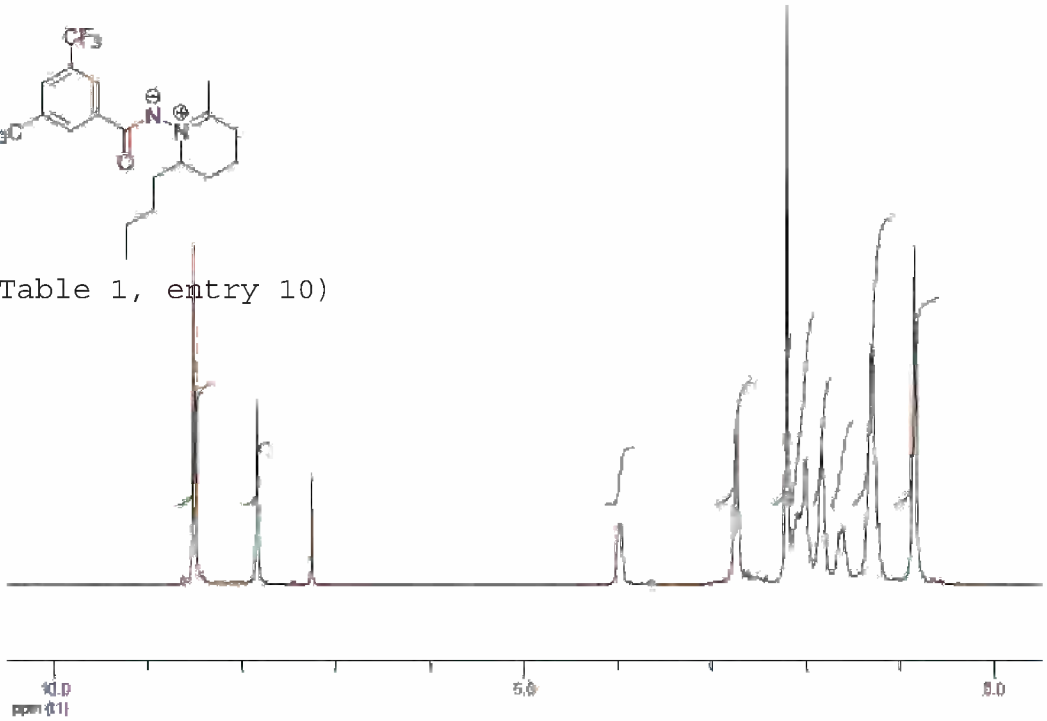

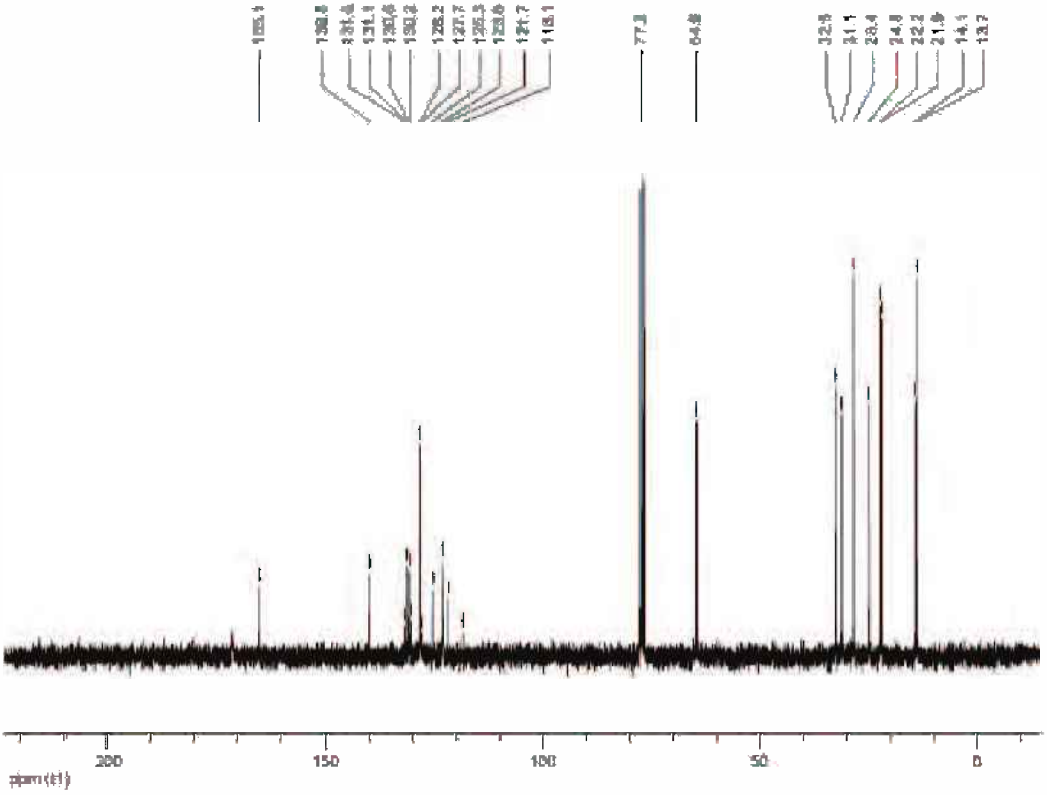

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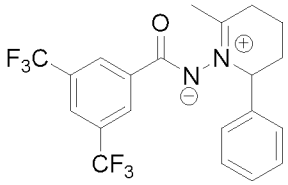

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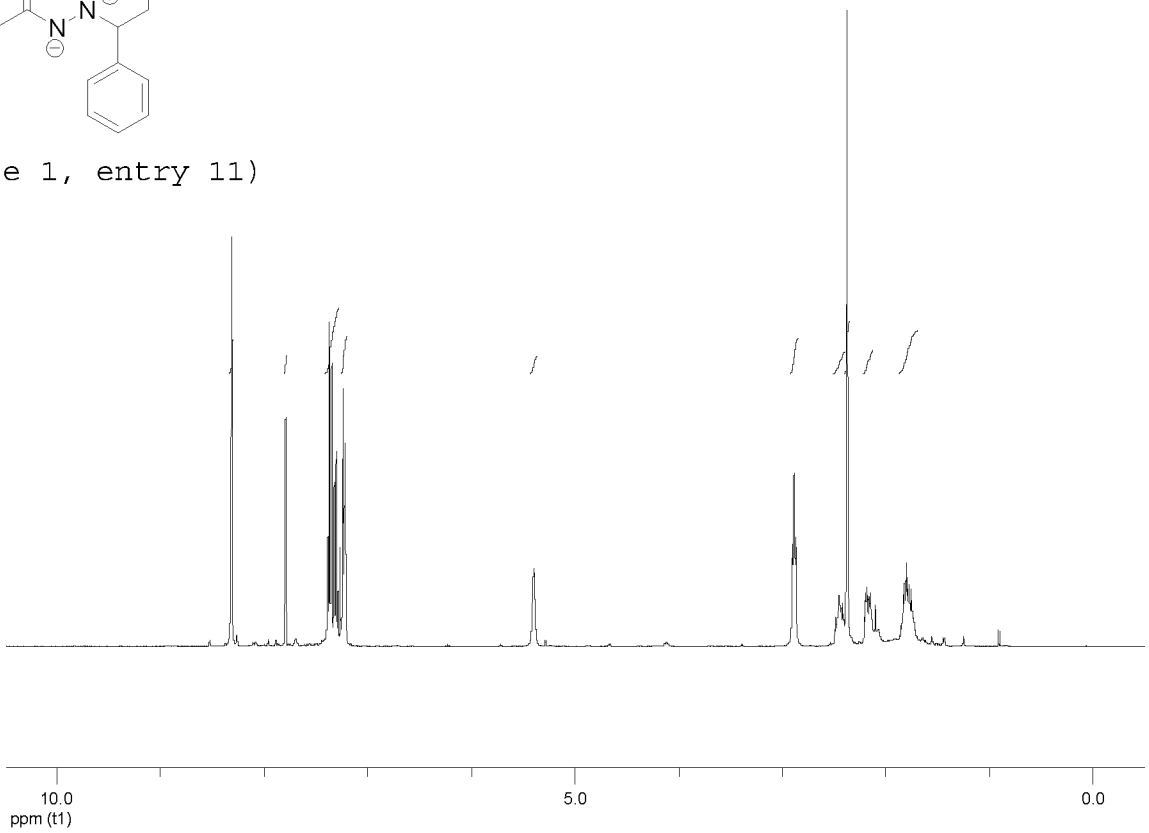

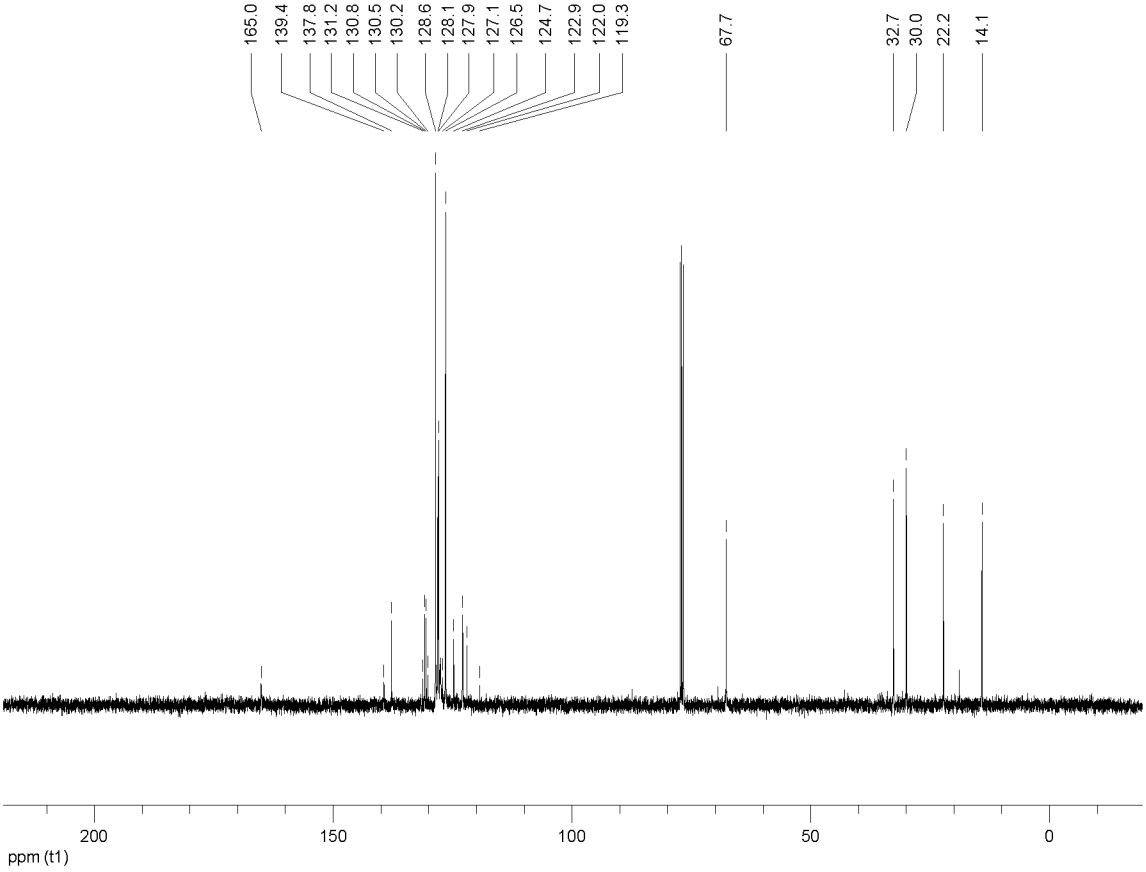

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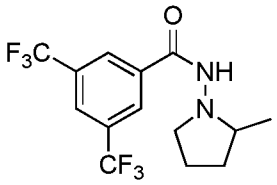

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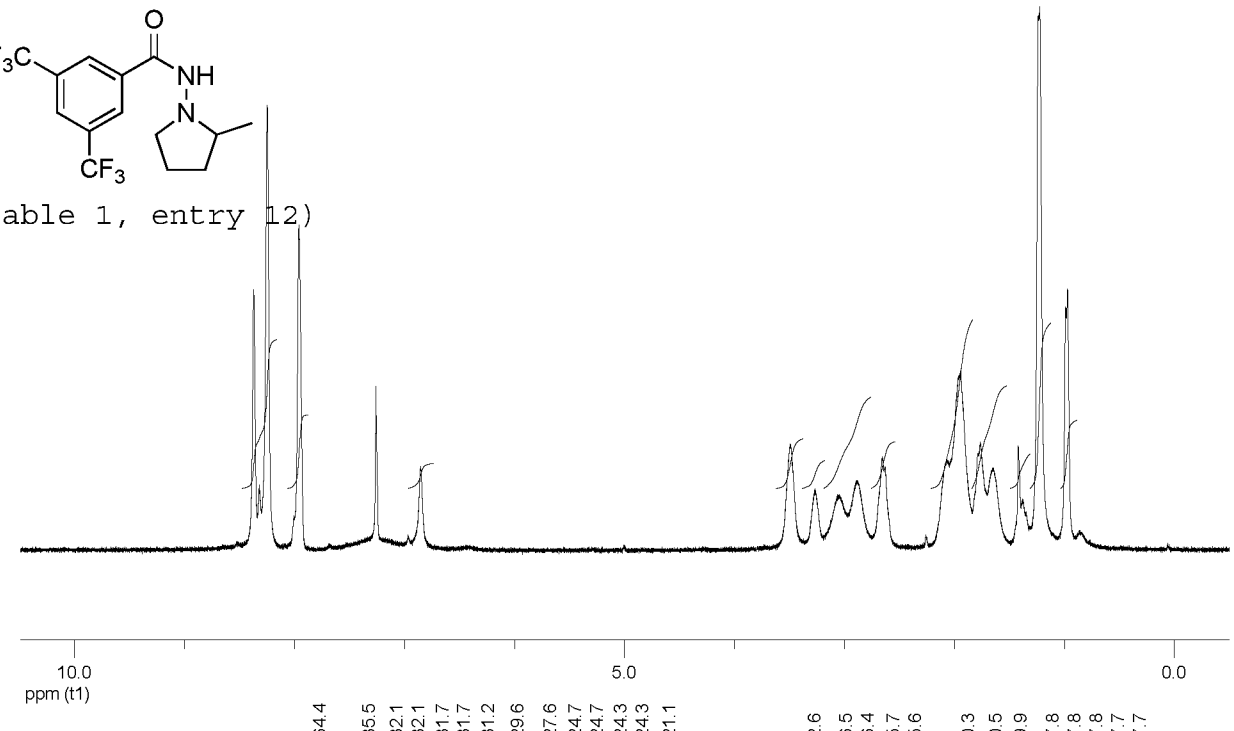

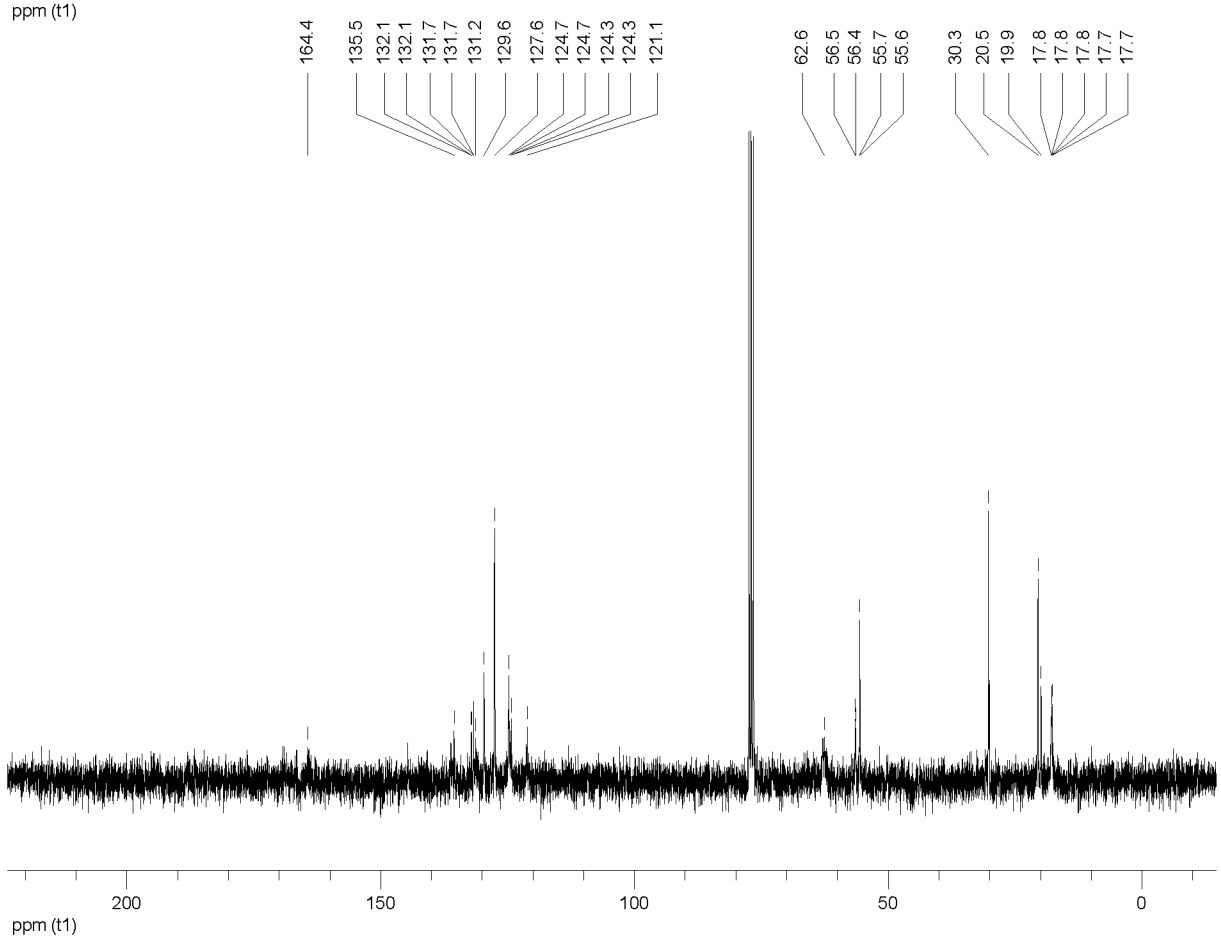

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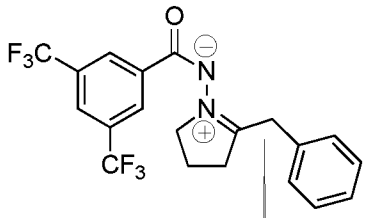

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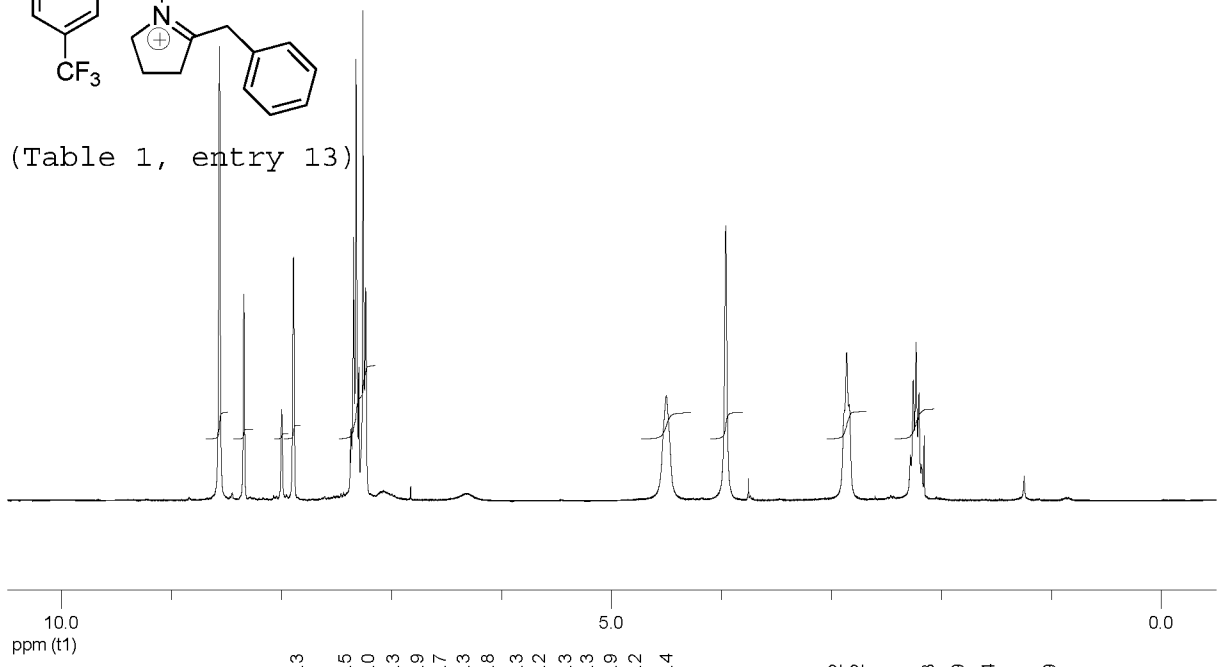

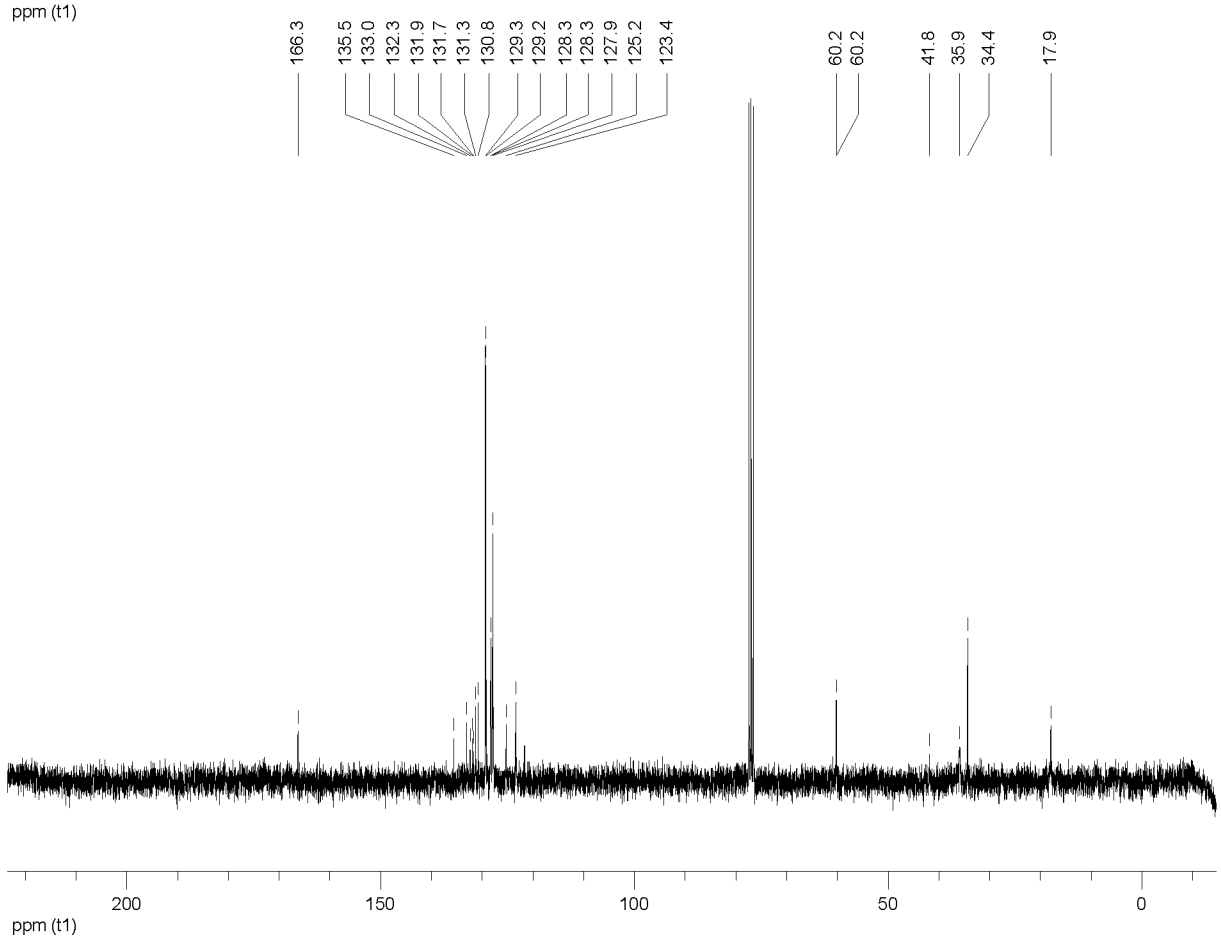

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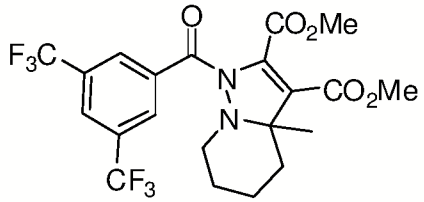

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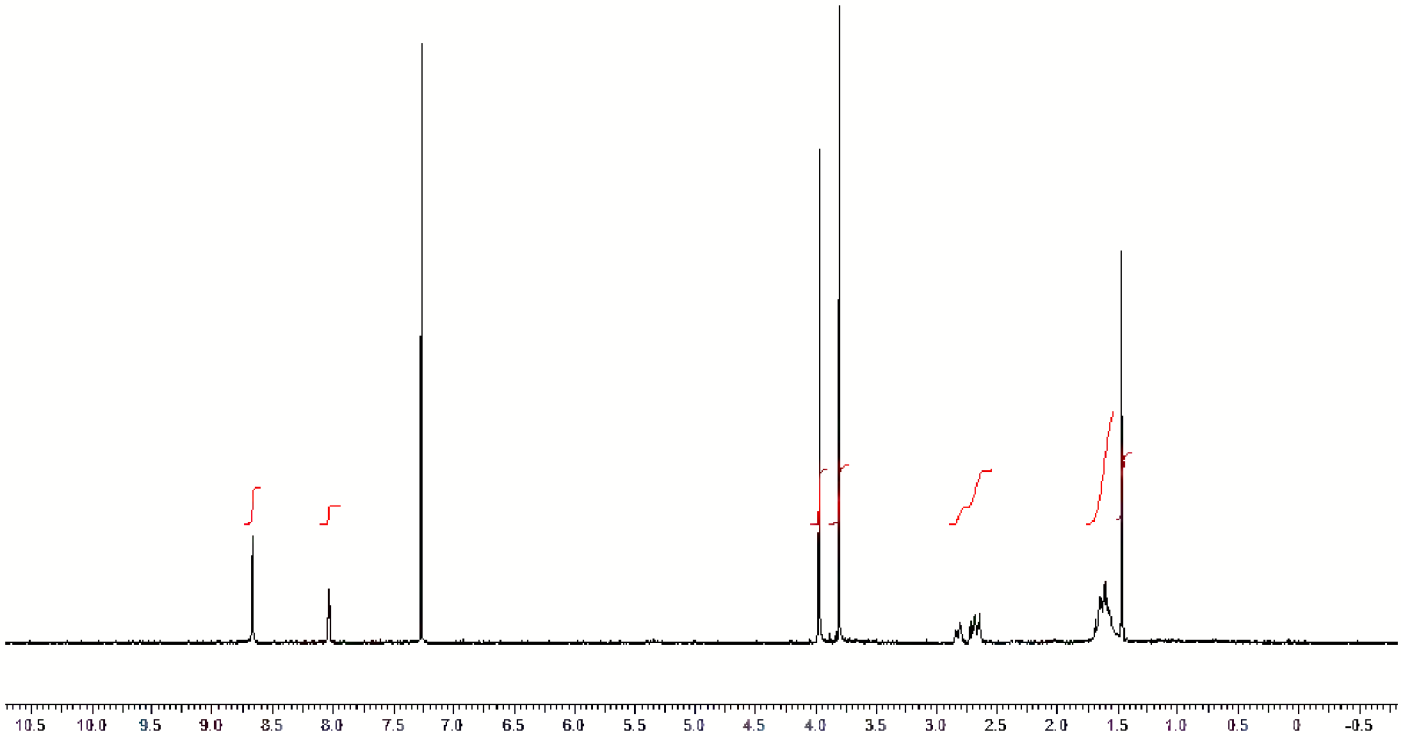

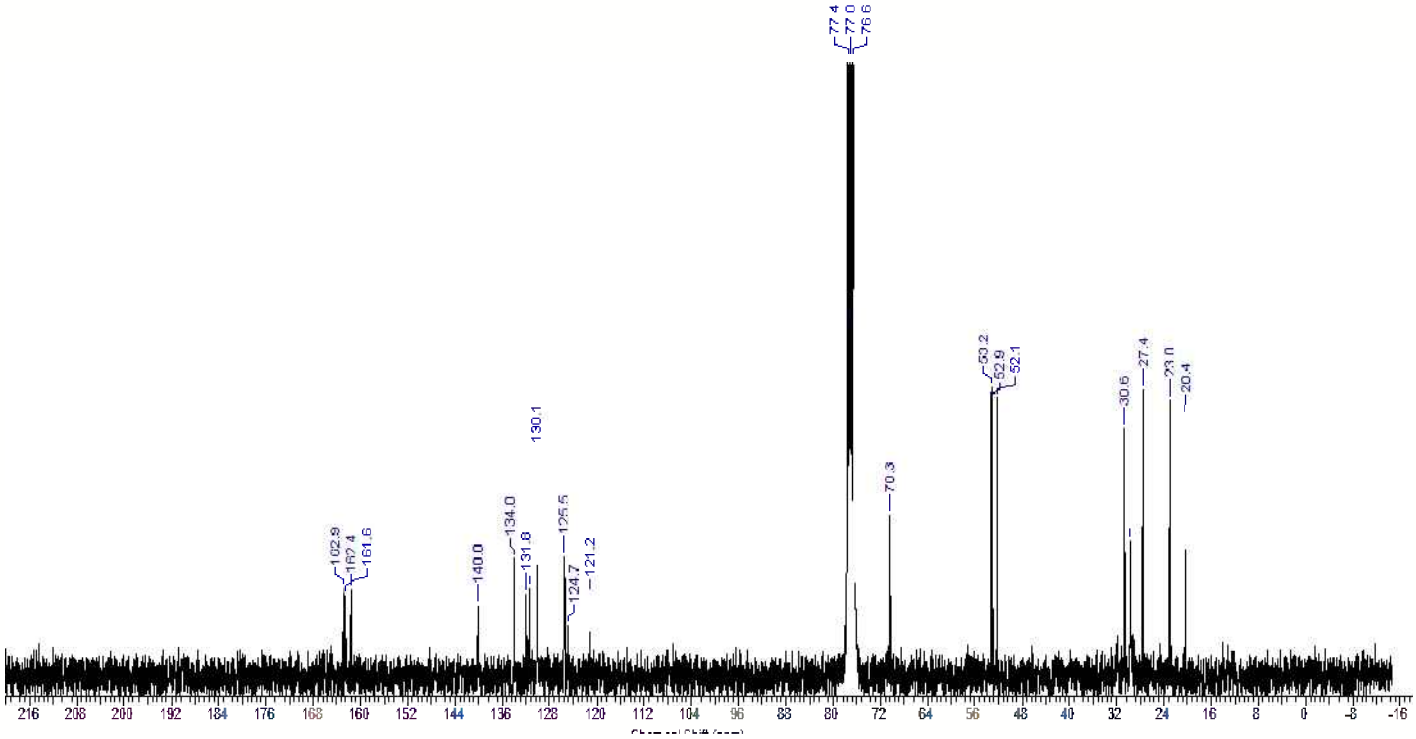

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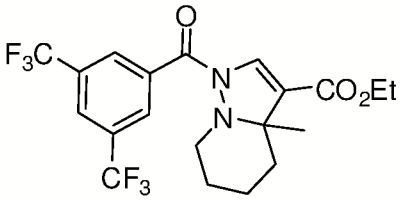

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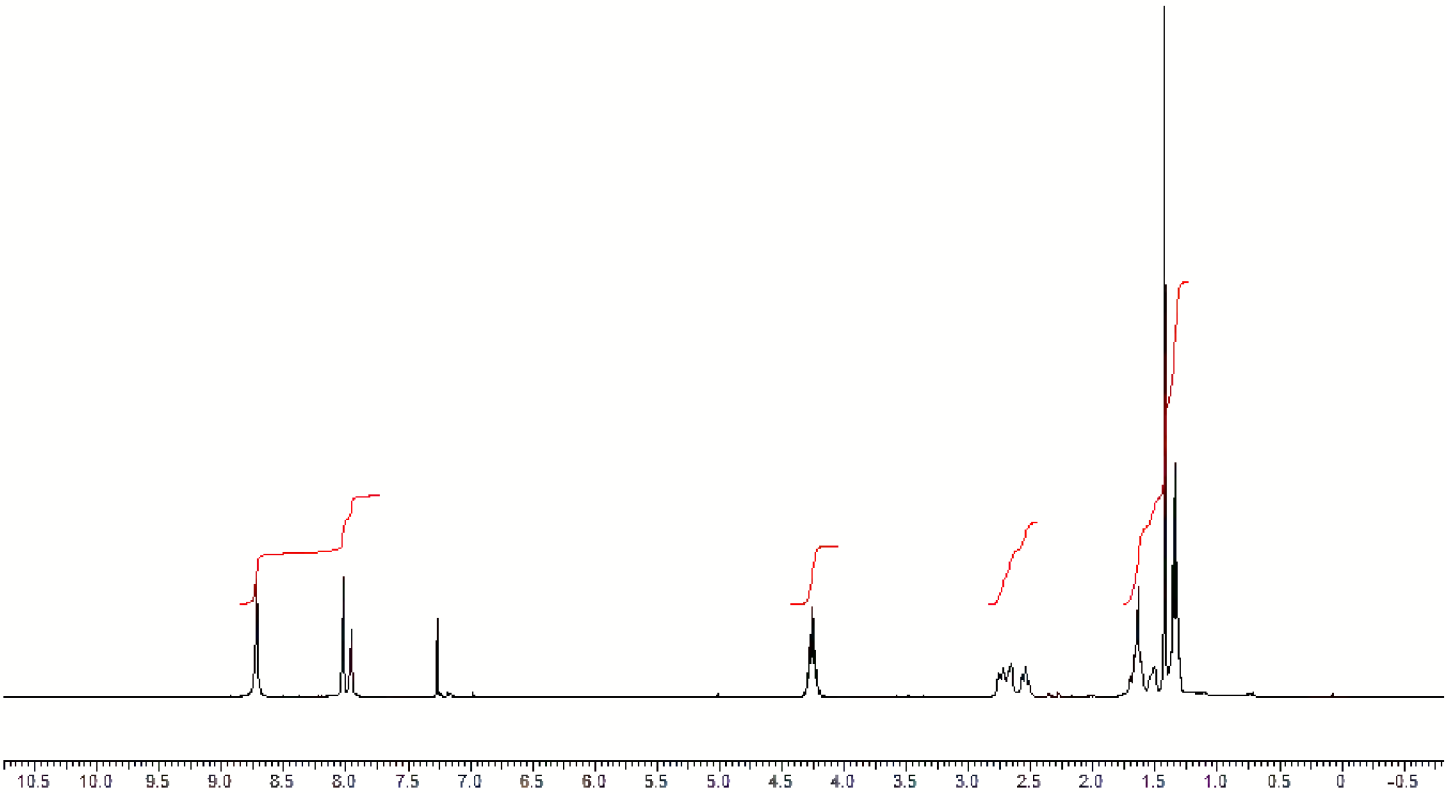

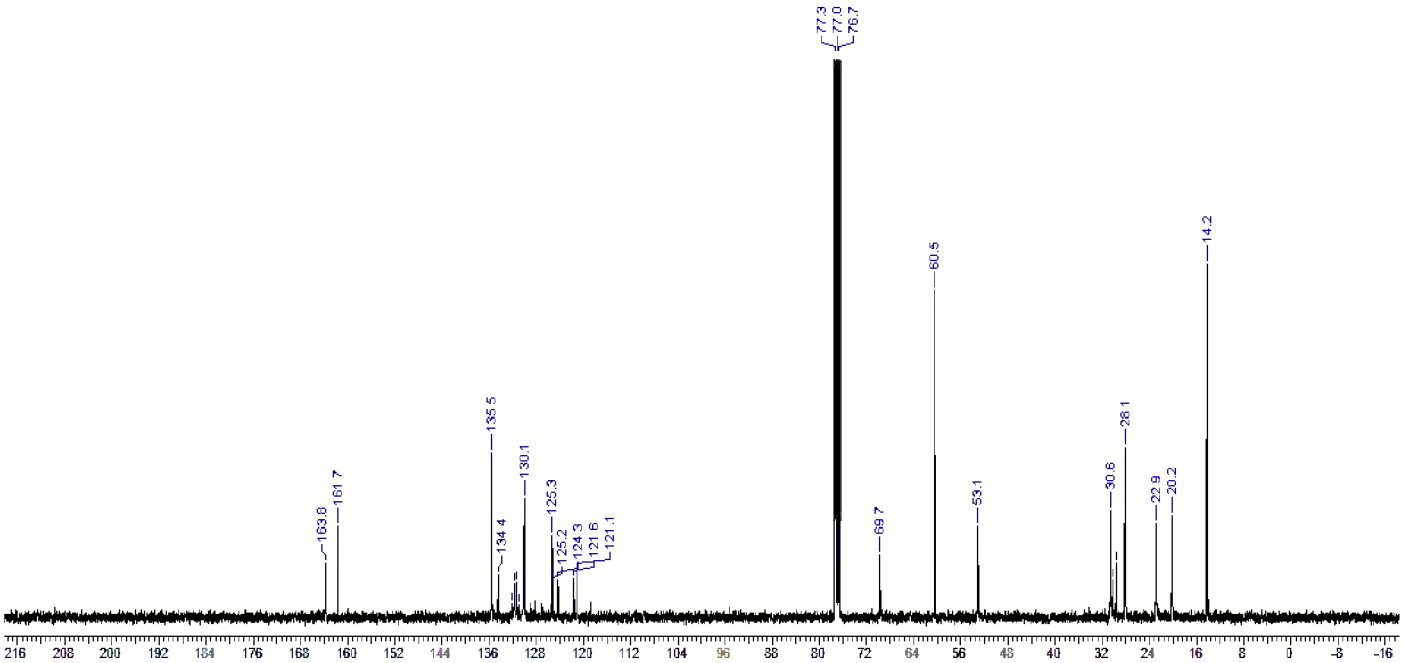

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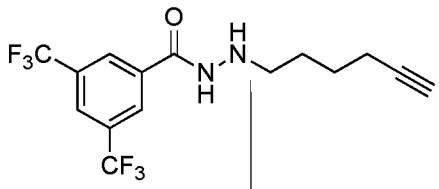

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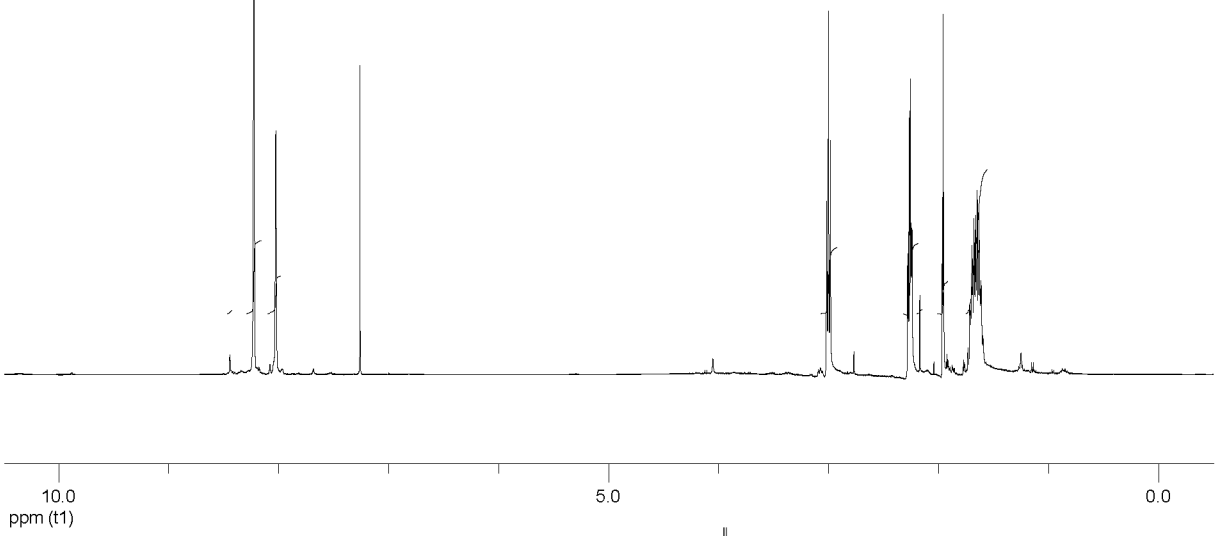
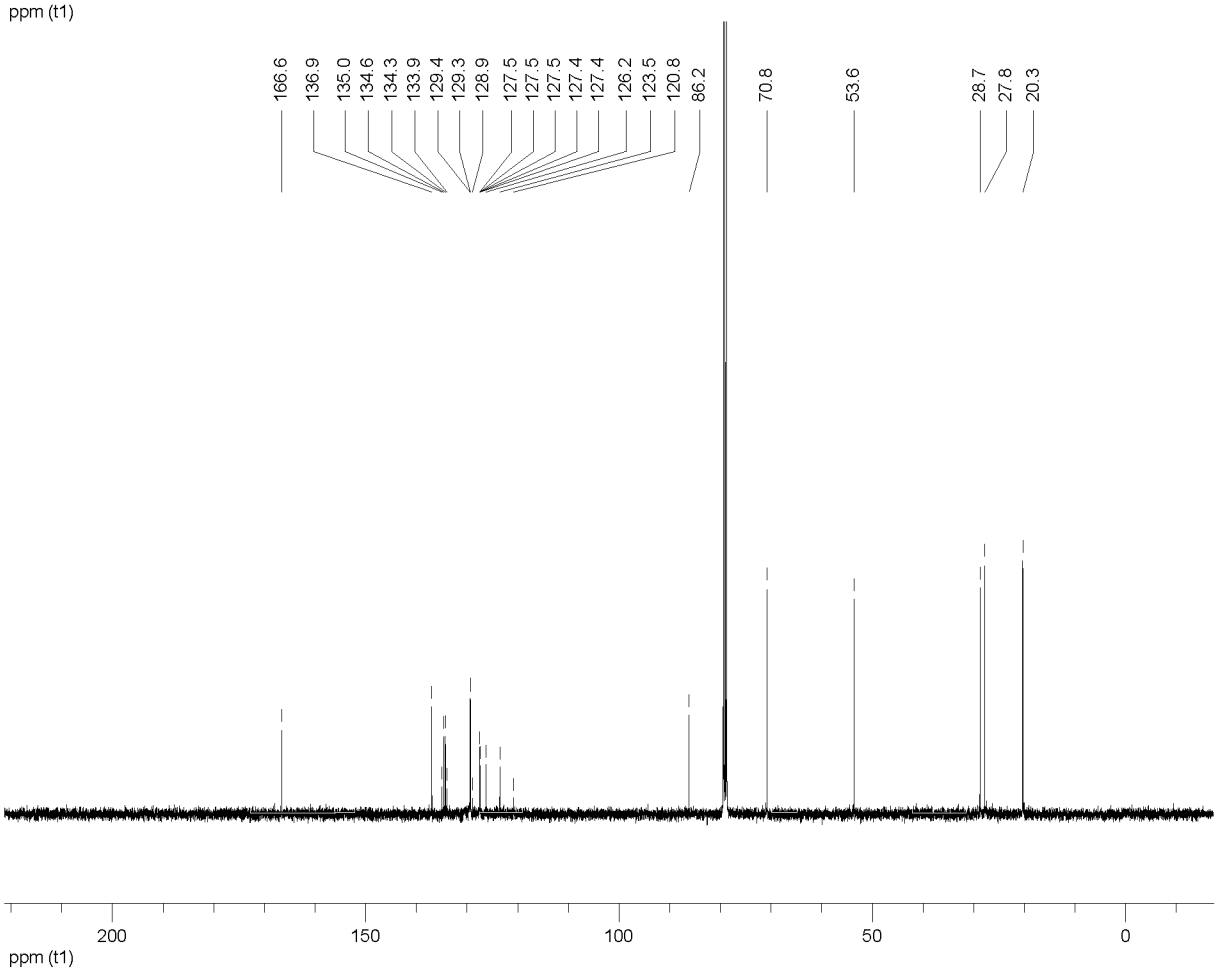
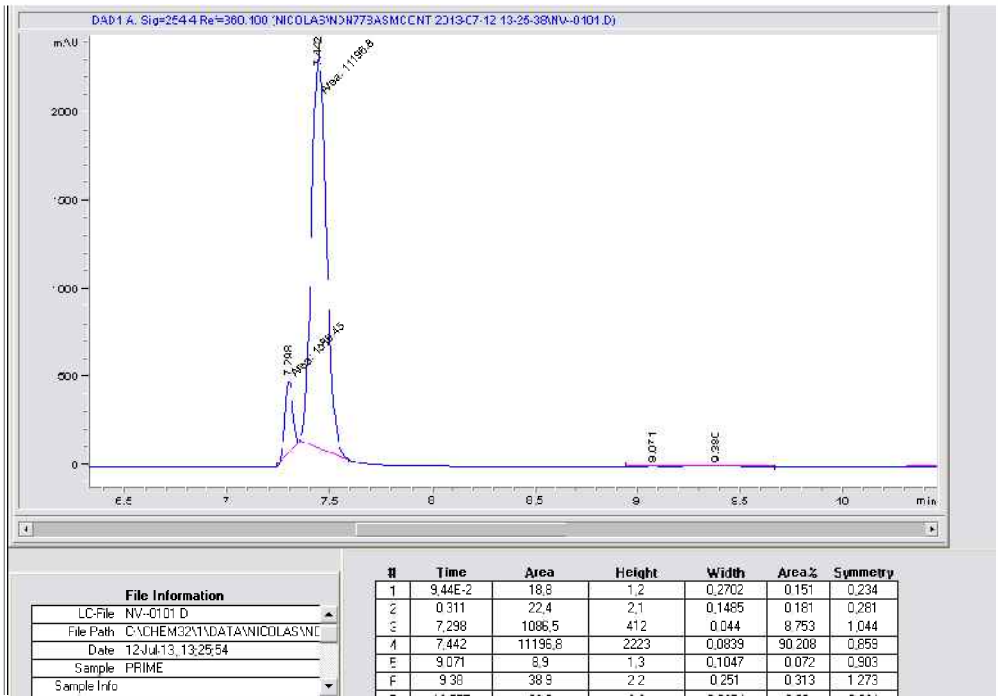




PDF compression, OCR, web optimization using a watermarked evaluation copy of CVISION PDFCompressor

HPLC: Zorbax Rx-SIL, iPrOH/hexane = 5/95, 1 mL/min, 254 nm, t = 7.4 min



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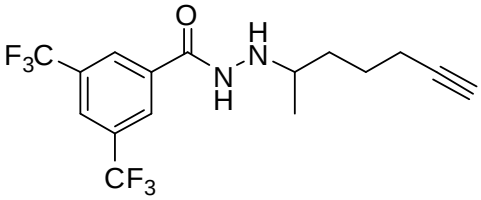
1	9.44E-2	18.8	1.2	0.2702	0.151	0.234
2	0.311	22.4	2.1	0.1485	0.181	0.281
3	7.298	1086.5	412	0.044	8.753	1.044
4	7.442	11196.8	2223	0.0839	90.208	0.859
5	9.071	8.9	1.3	0.1047	0.072	0.903
6	9.38	38.9	2.2	0.251	0.313	1.273

PDF compression, OCR, web optimization using a watermarked evaluation copy of CVISION PDFCompressor



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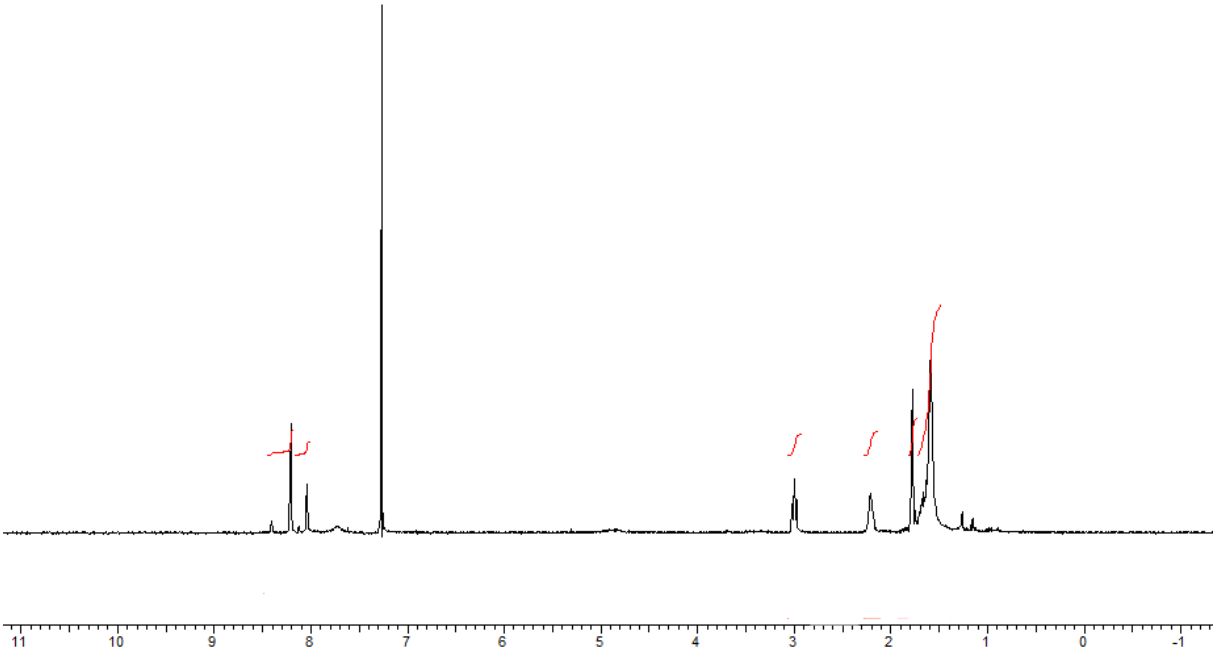

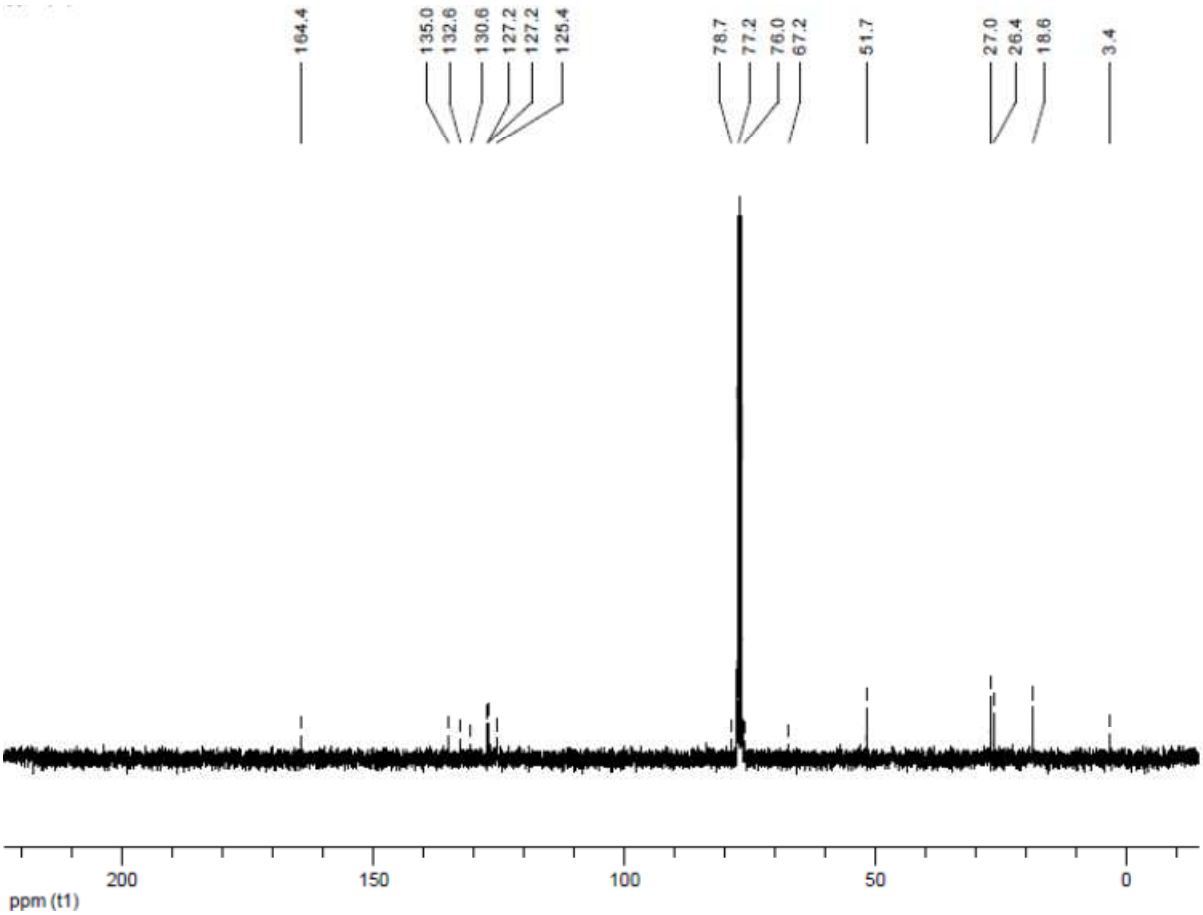

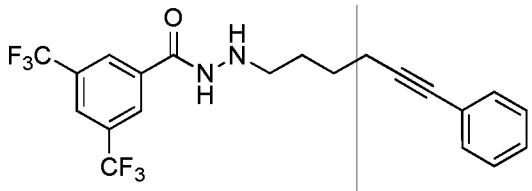

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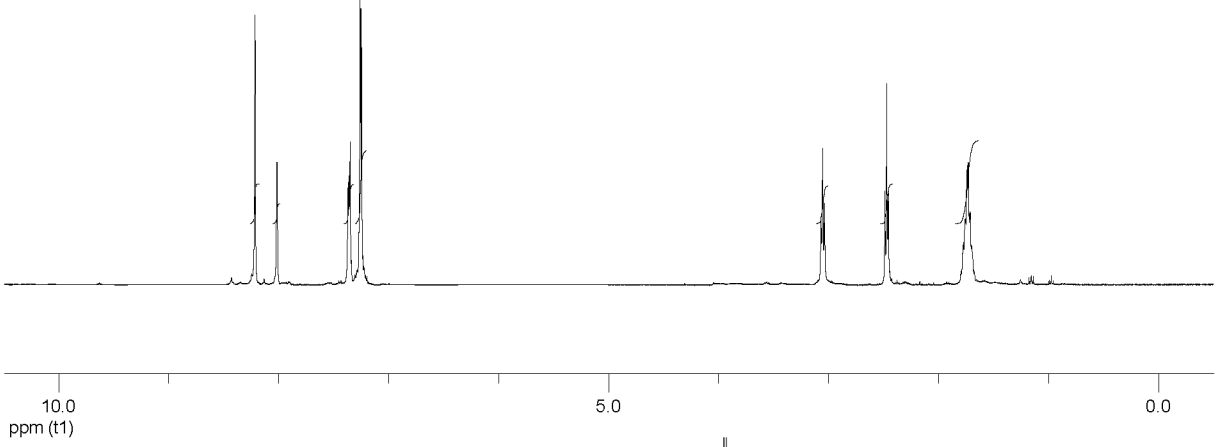
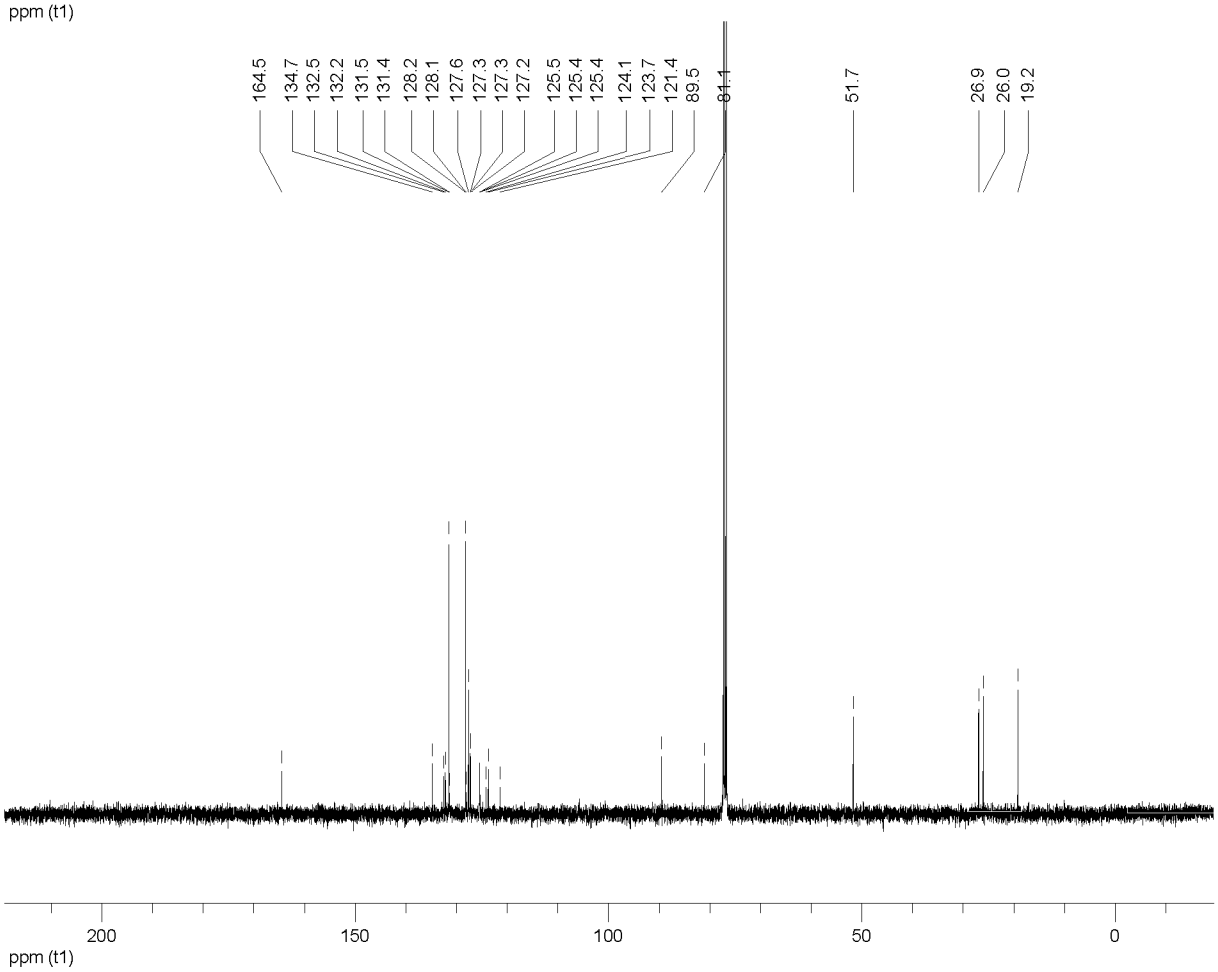
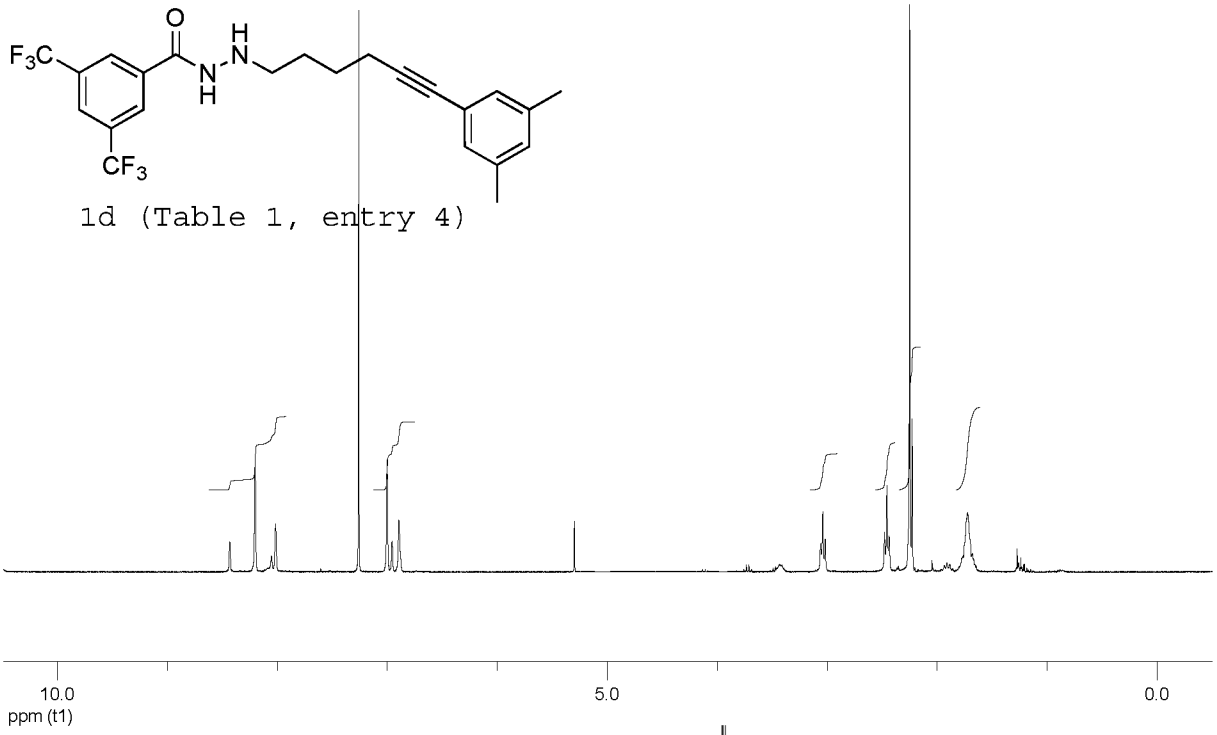
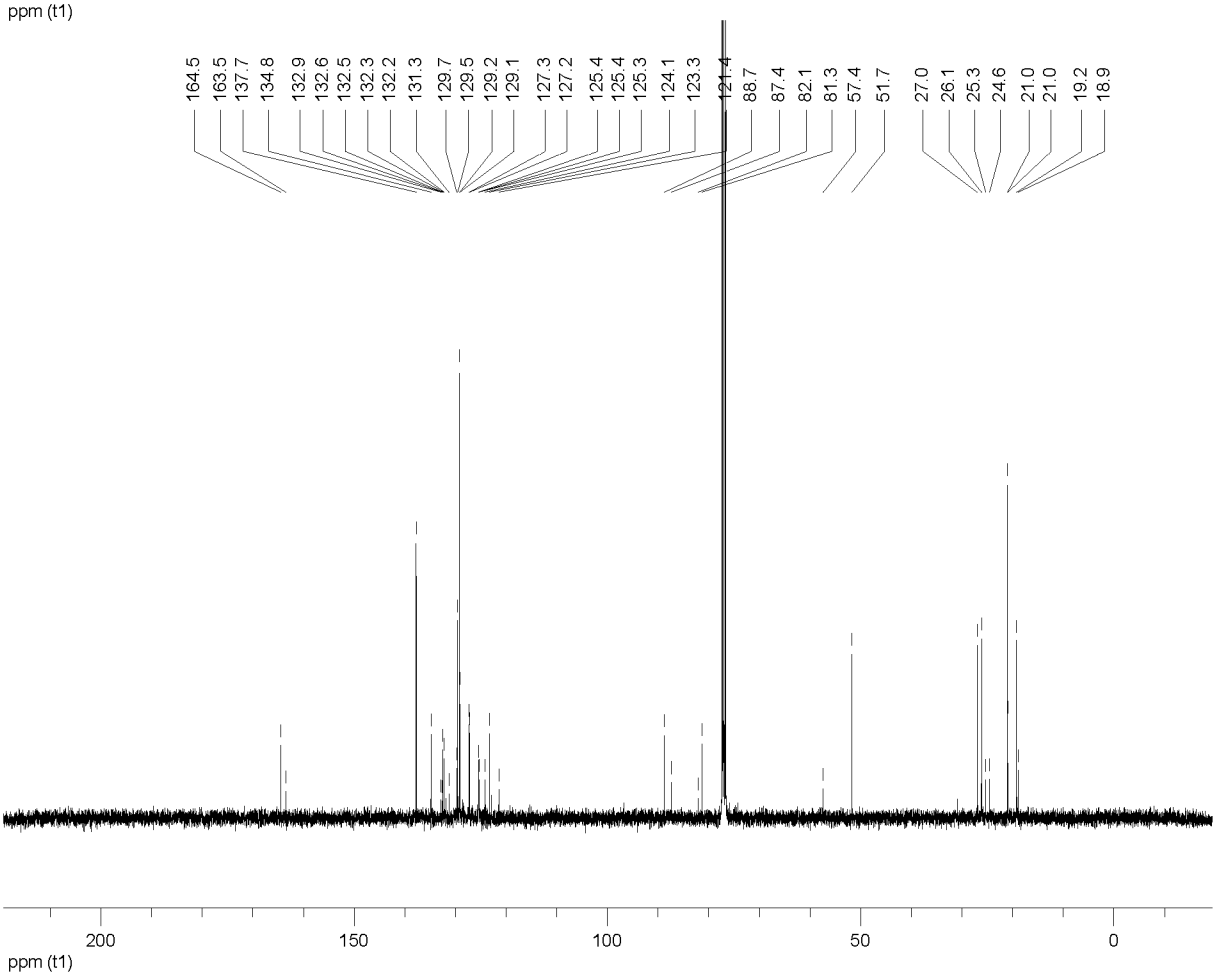




PDF compression, OCR, web optimization using a watermarked evaluation copy of CVISION PDFCompressor





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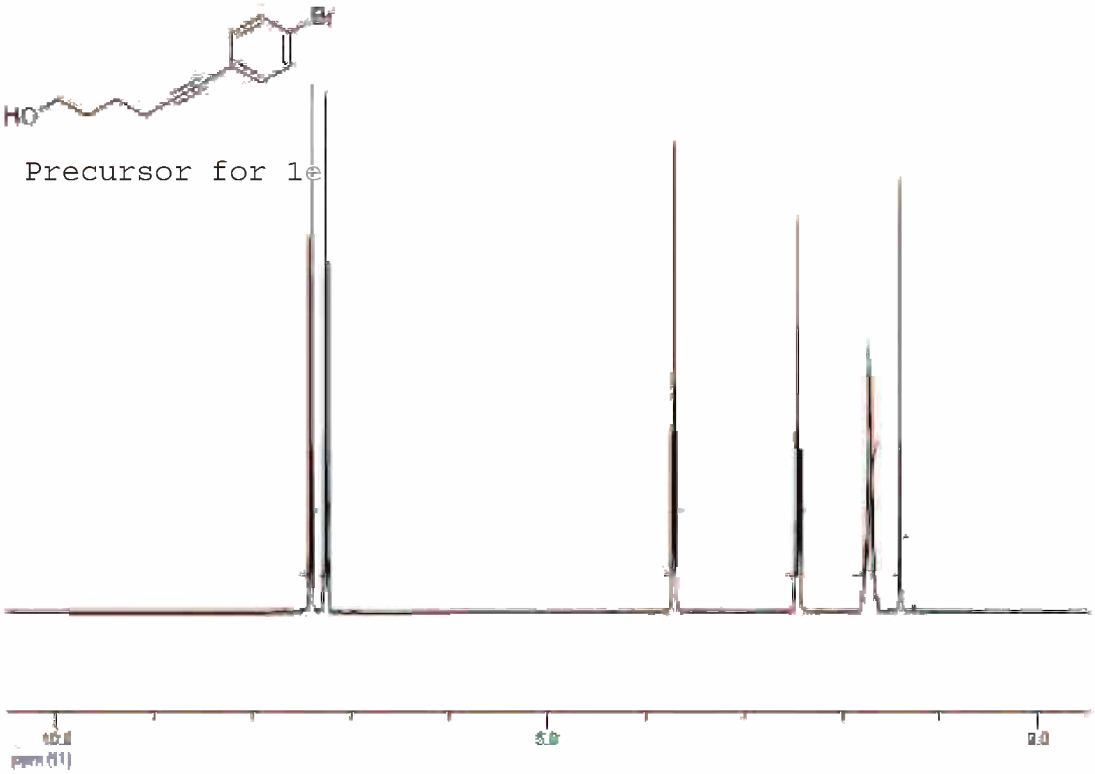

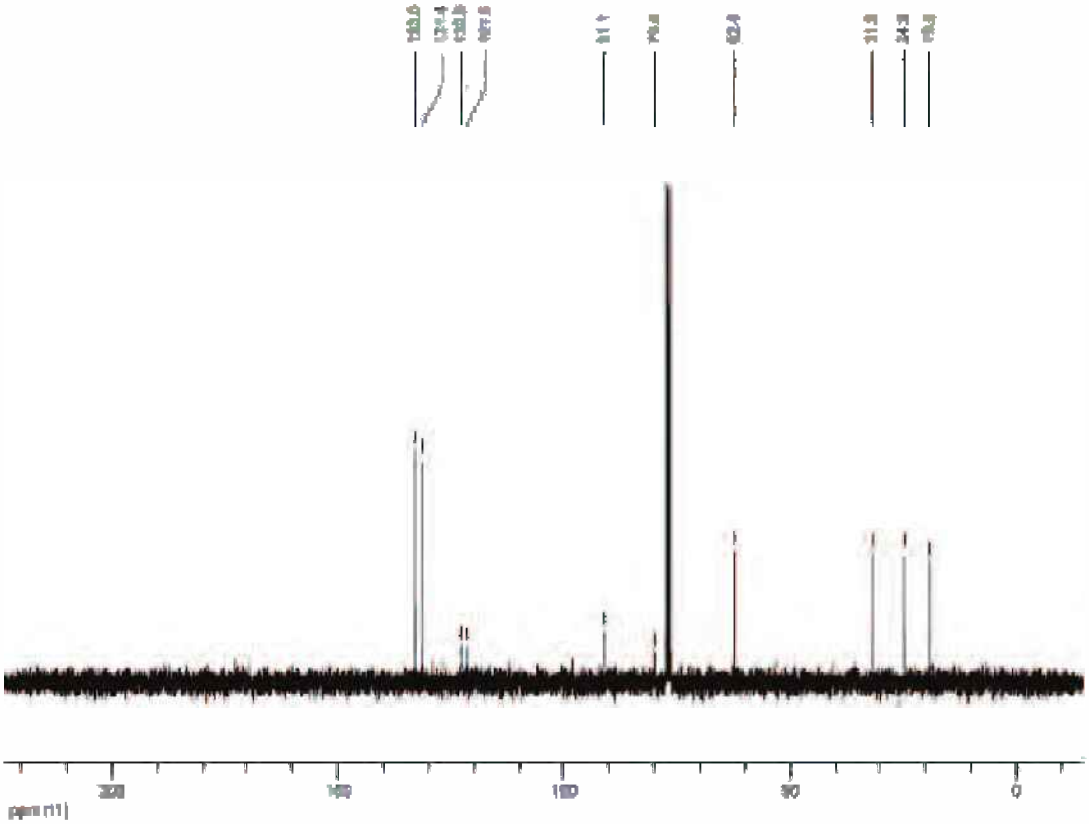

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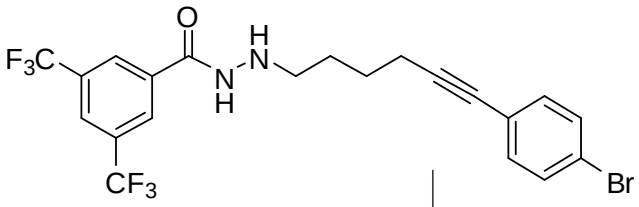

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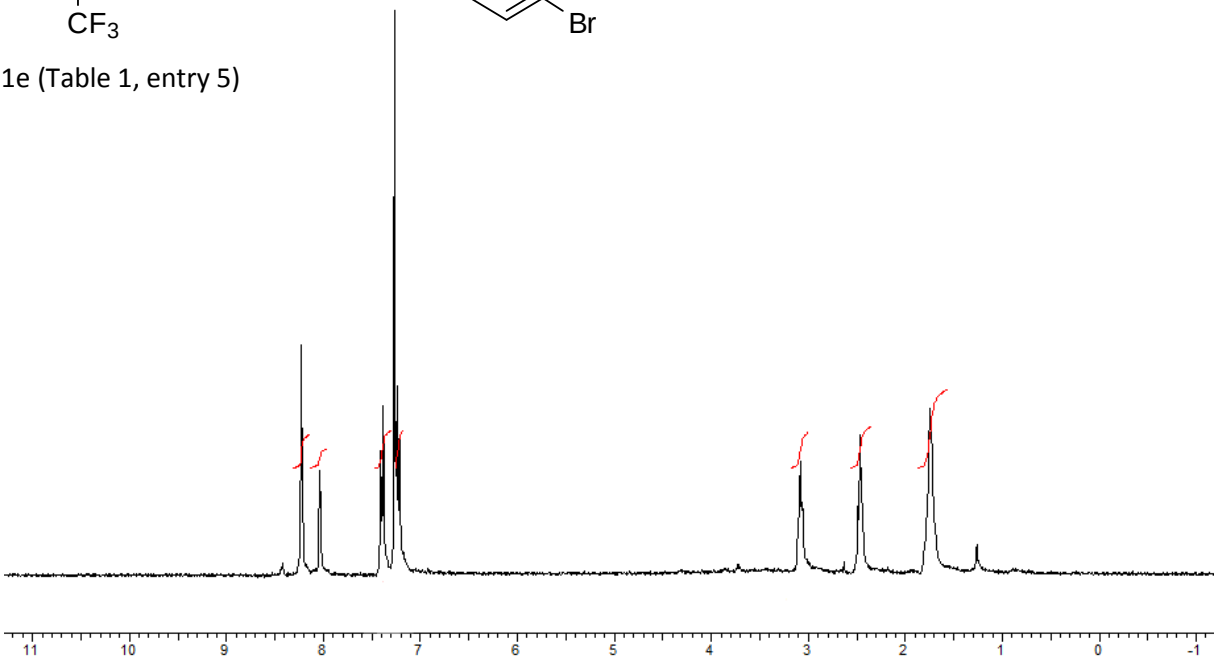

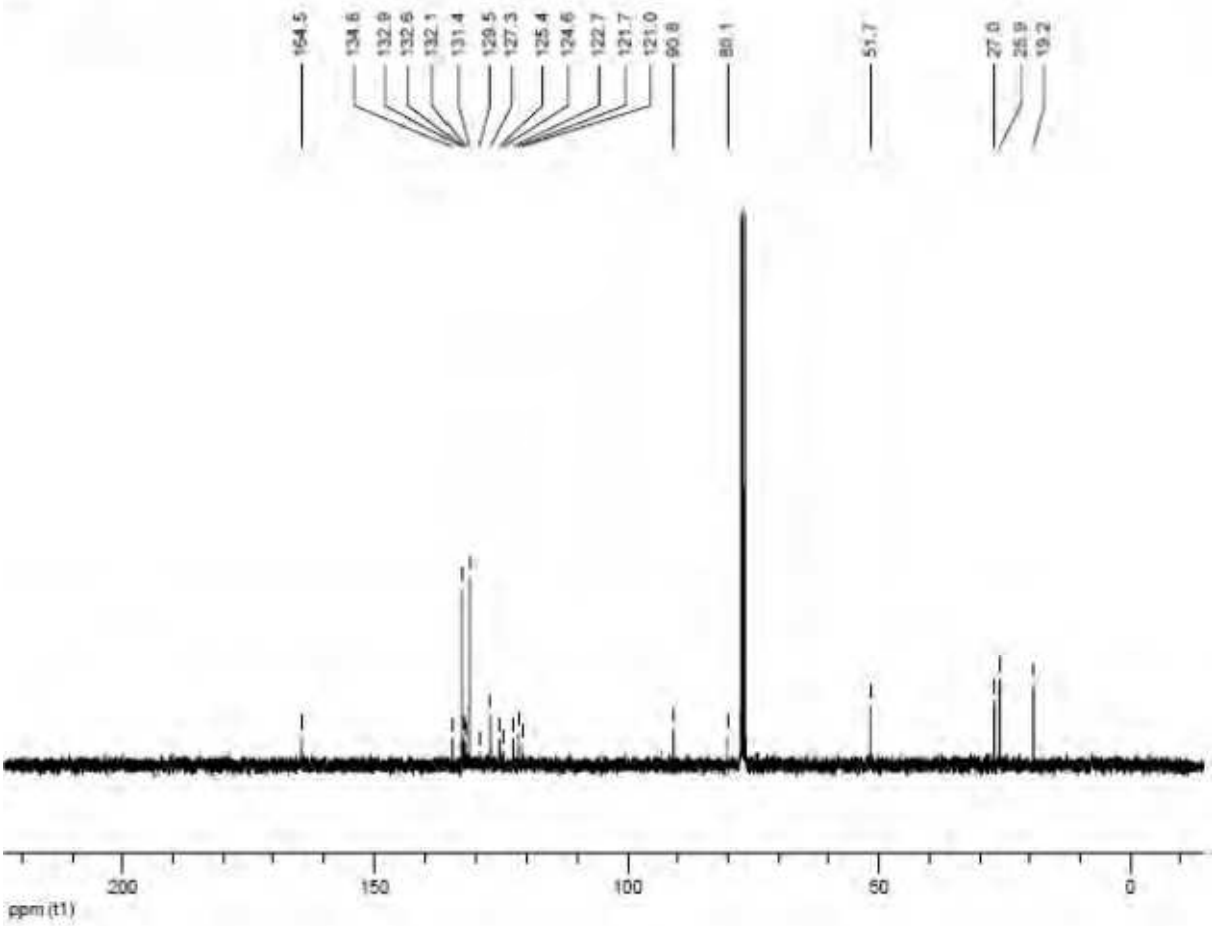

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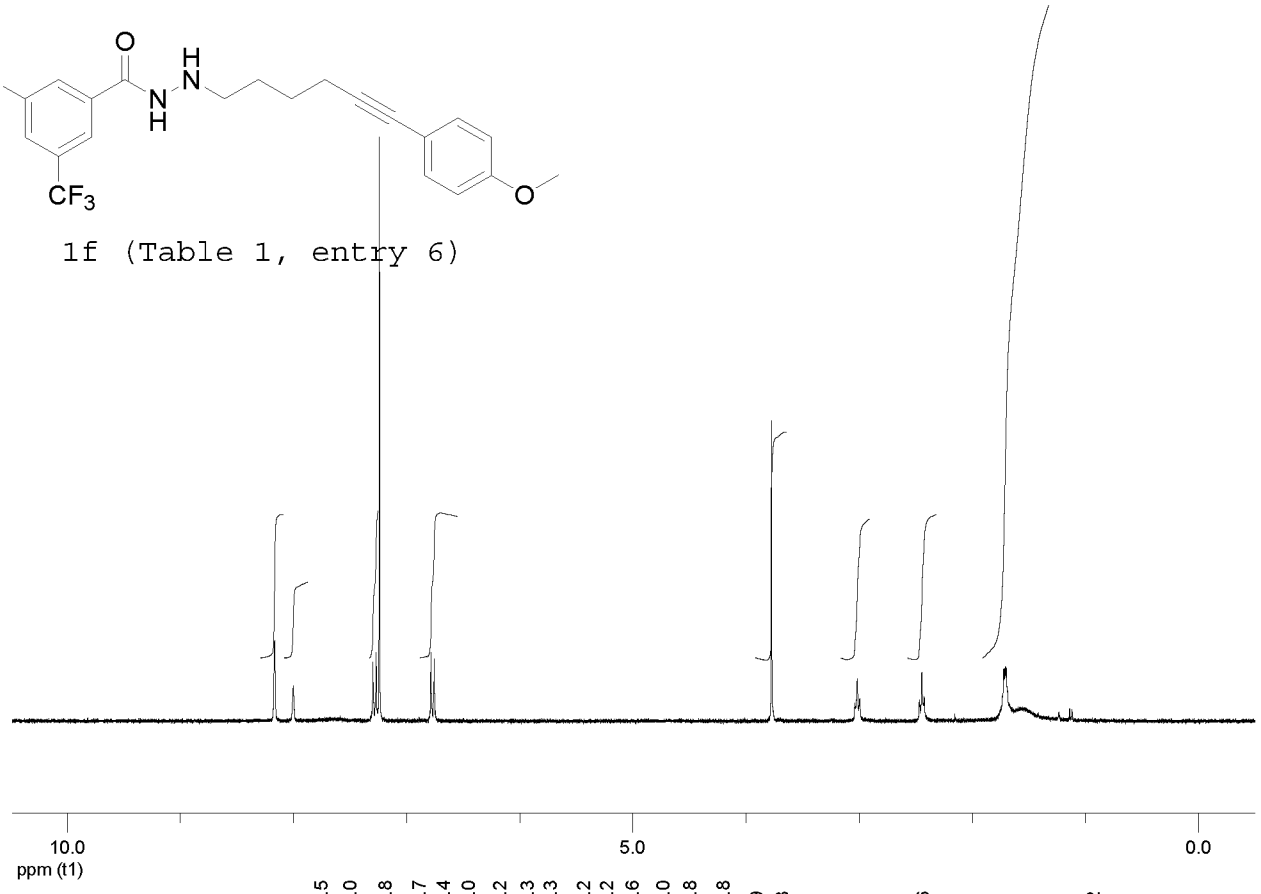

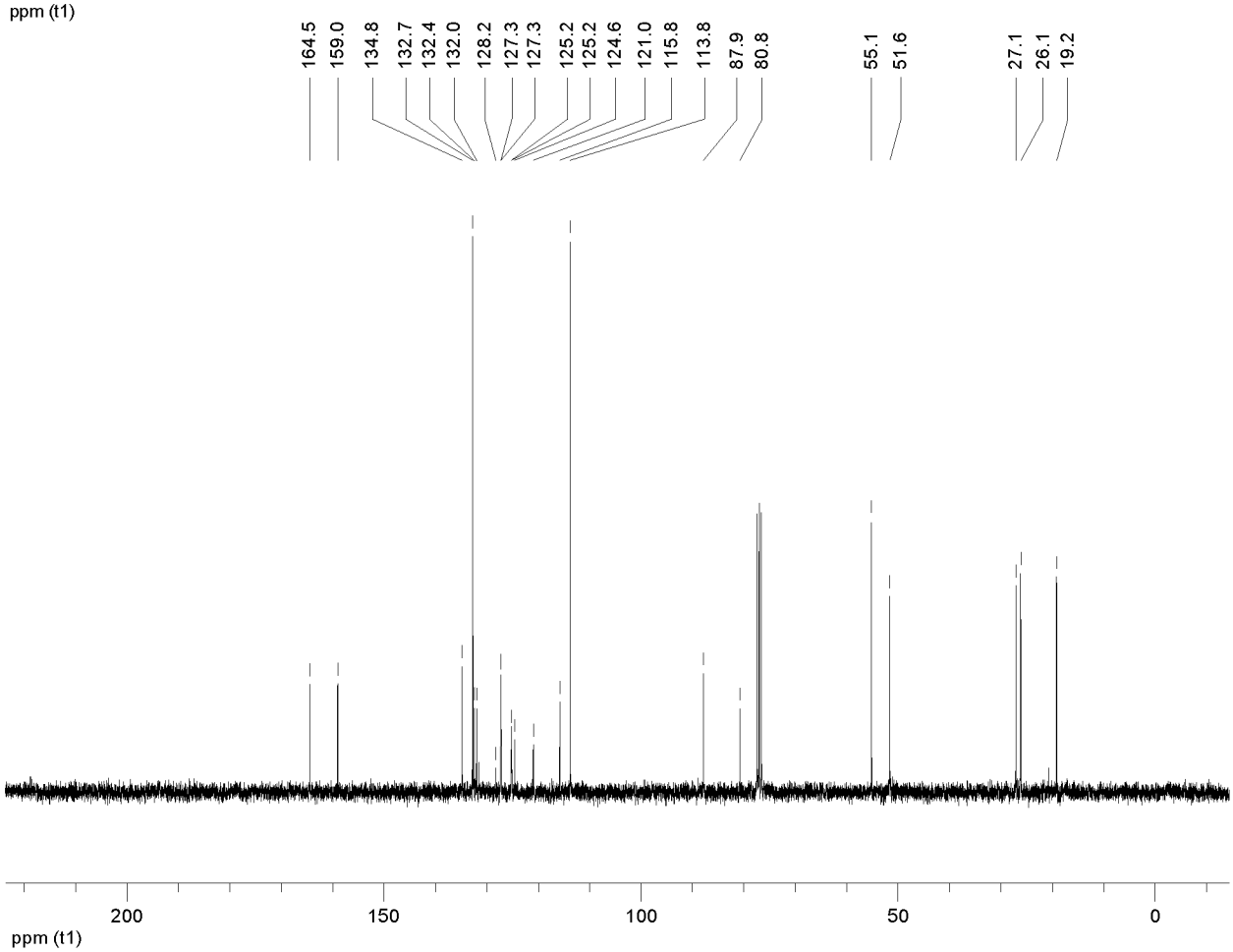

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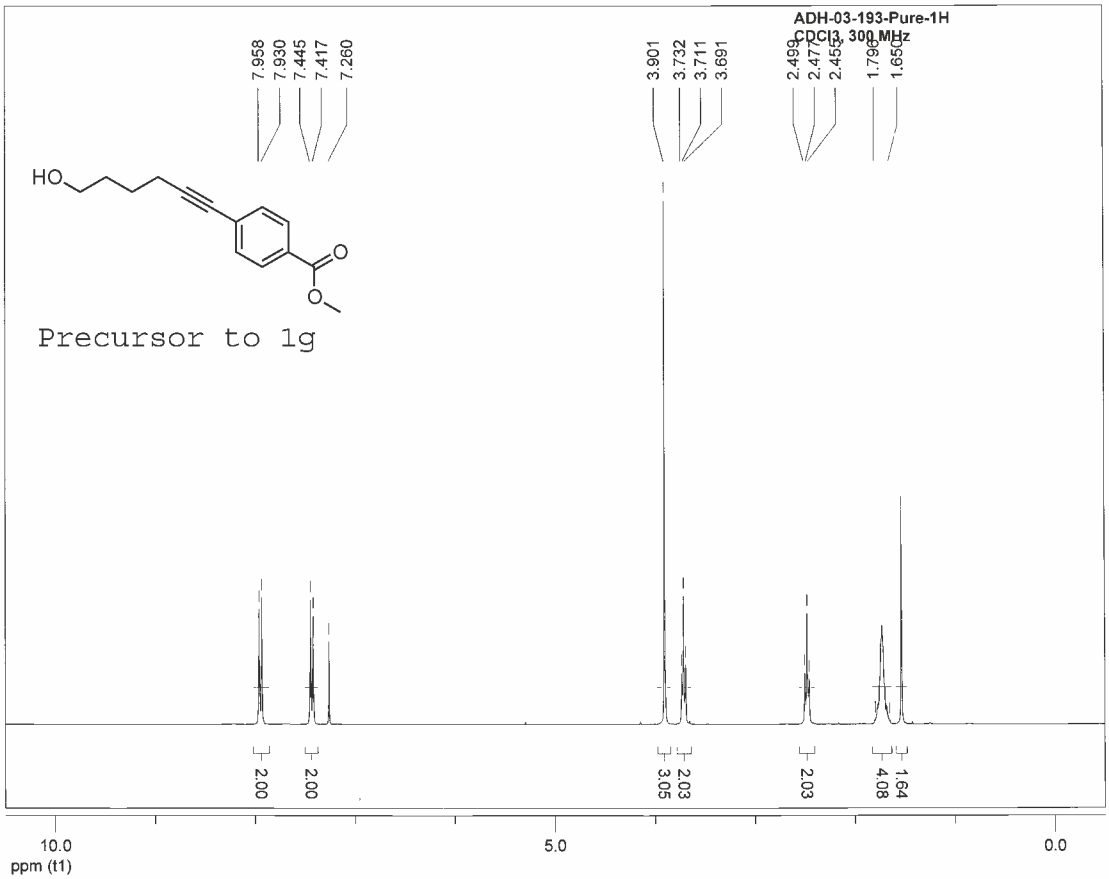

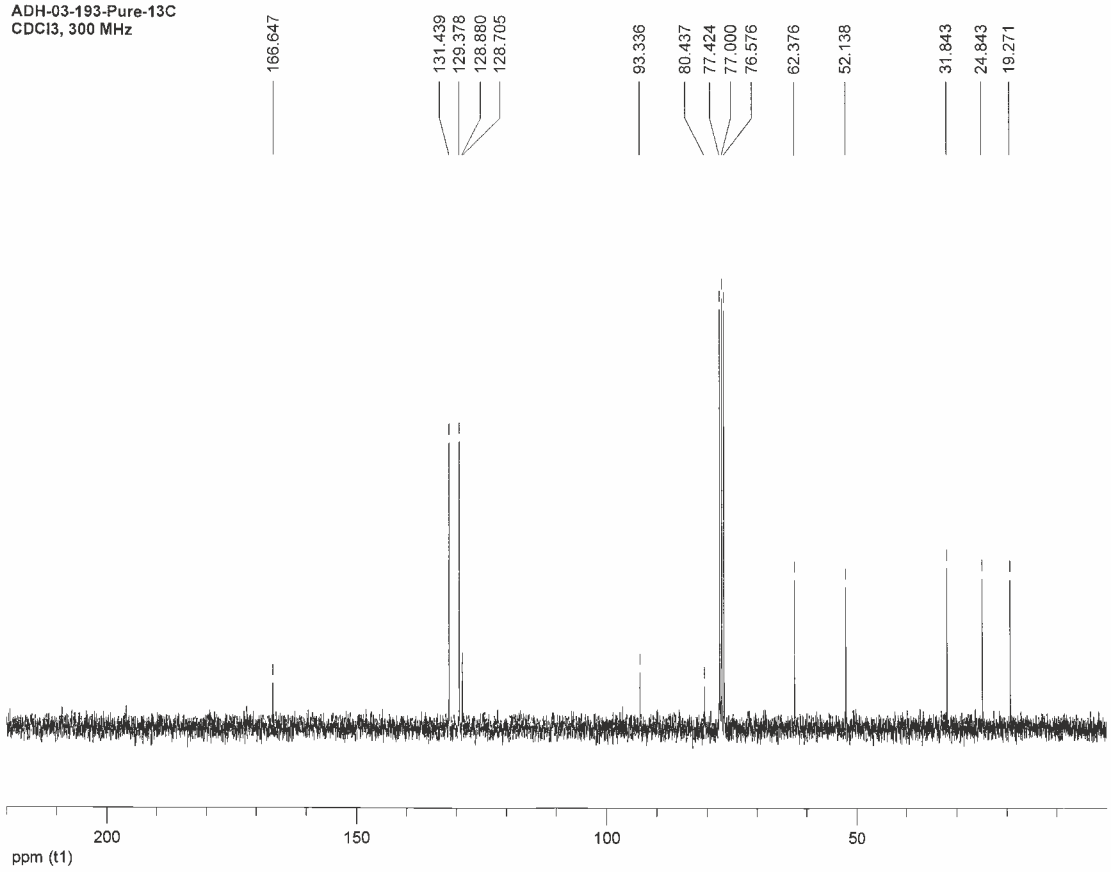

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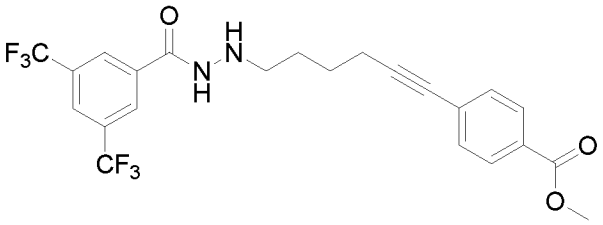

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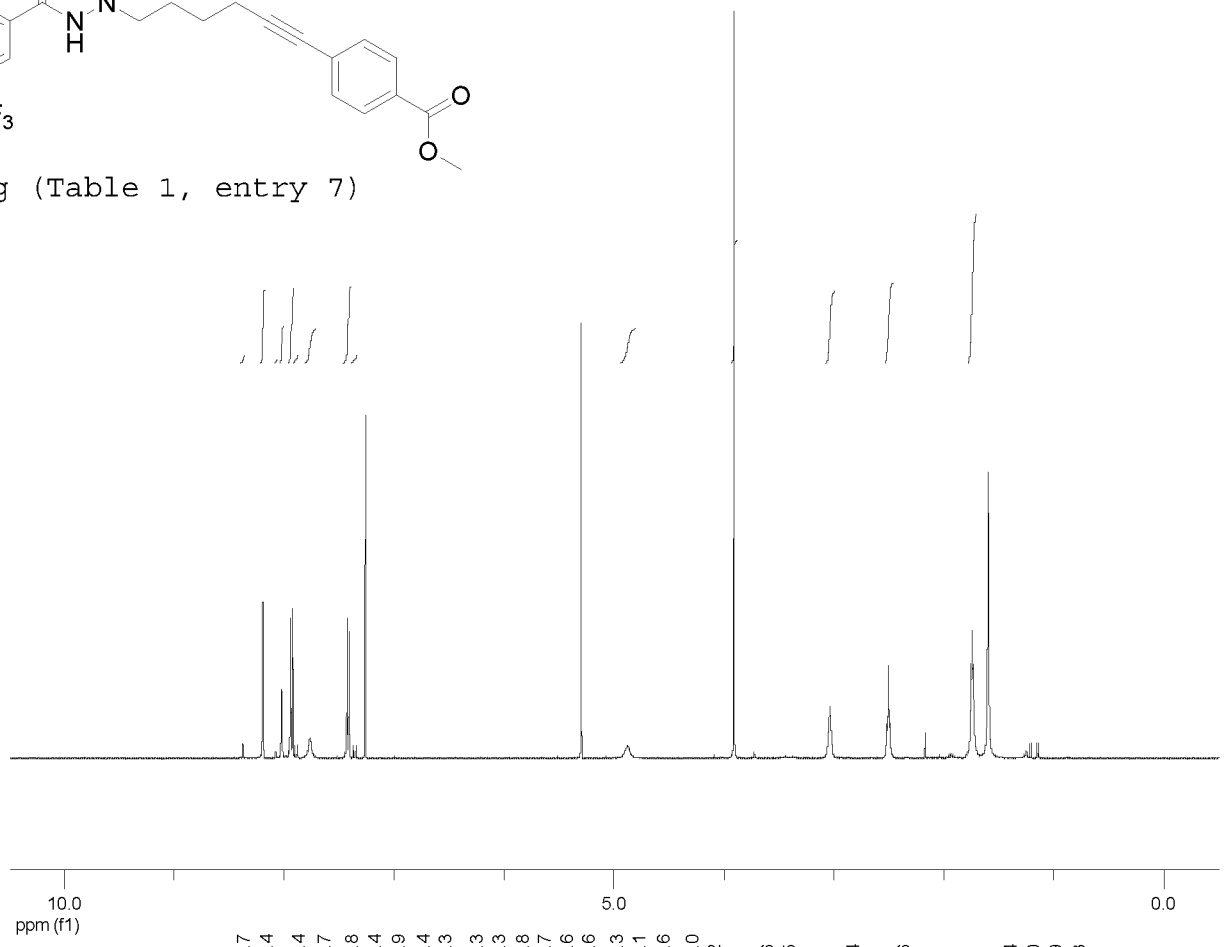

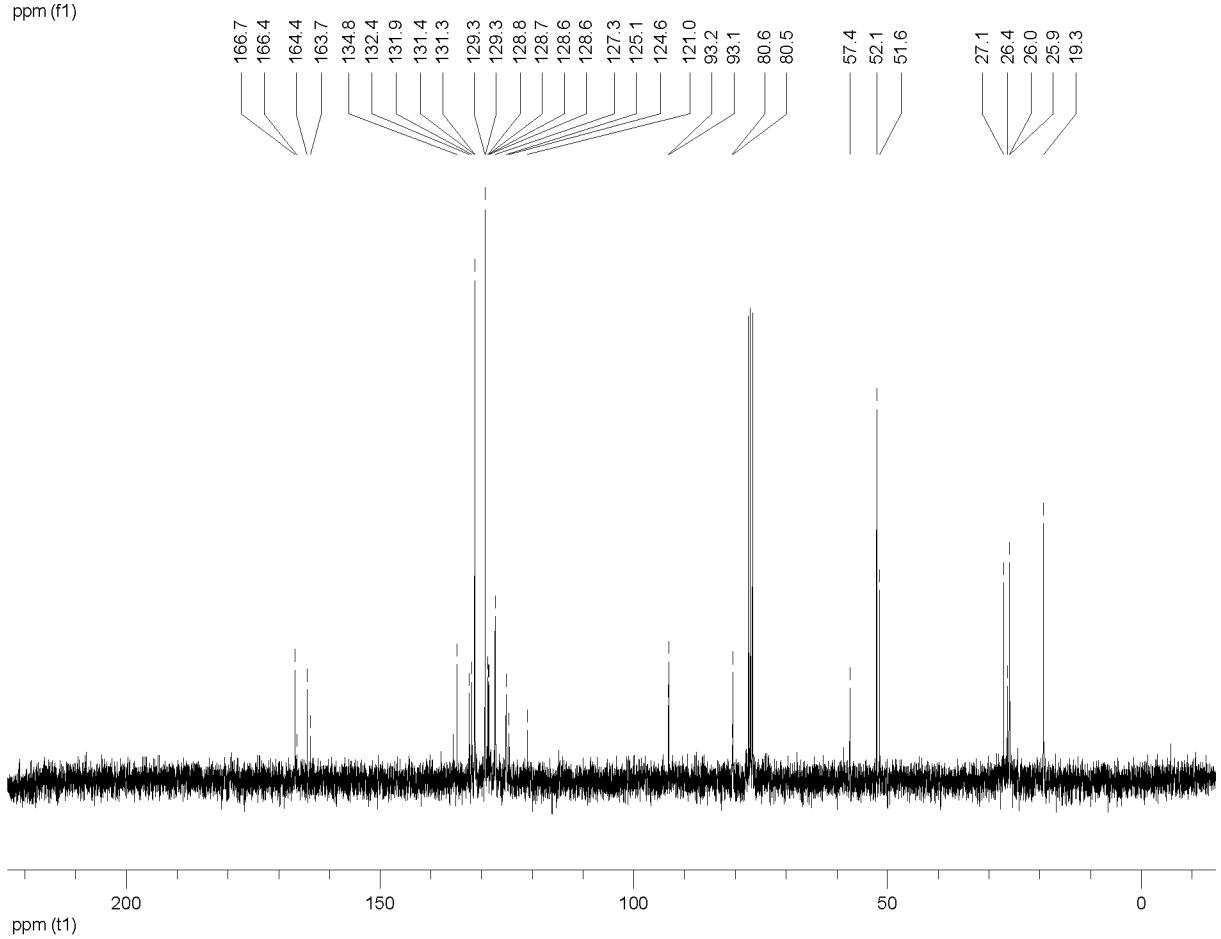

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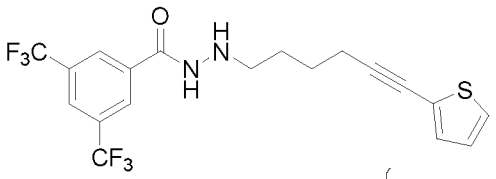

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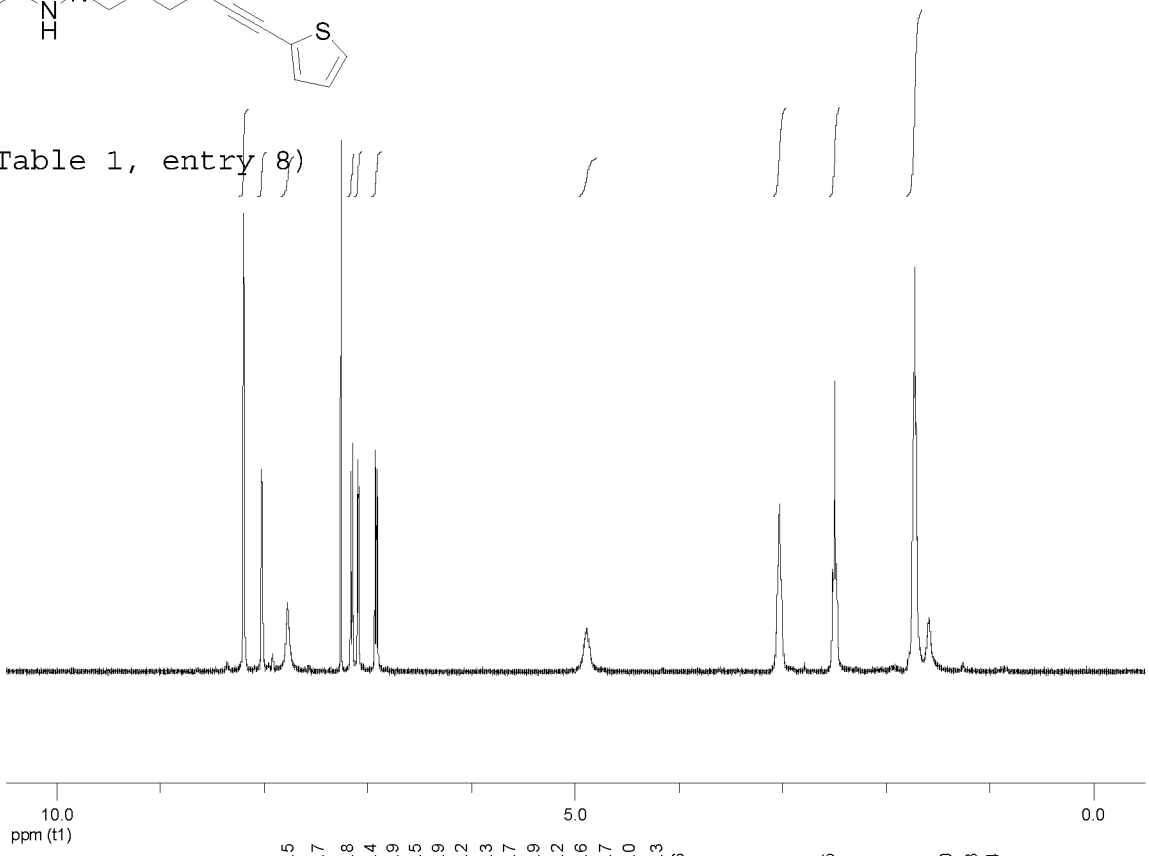

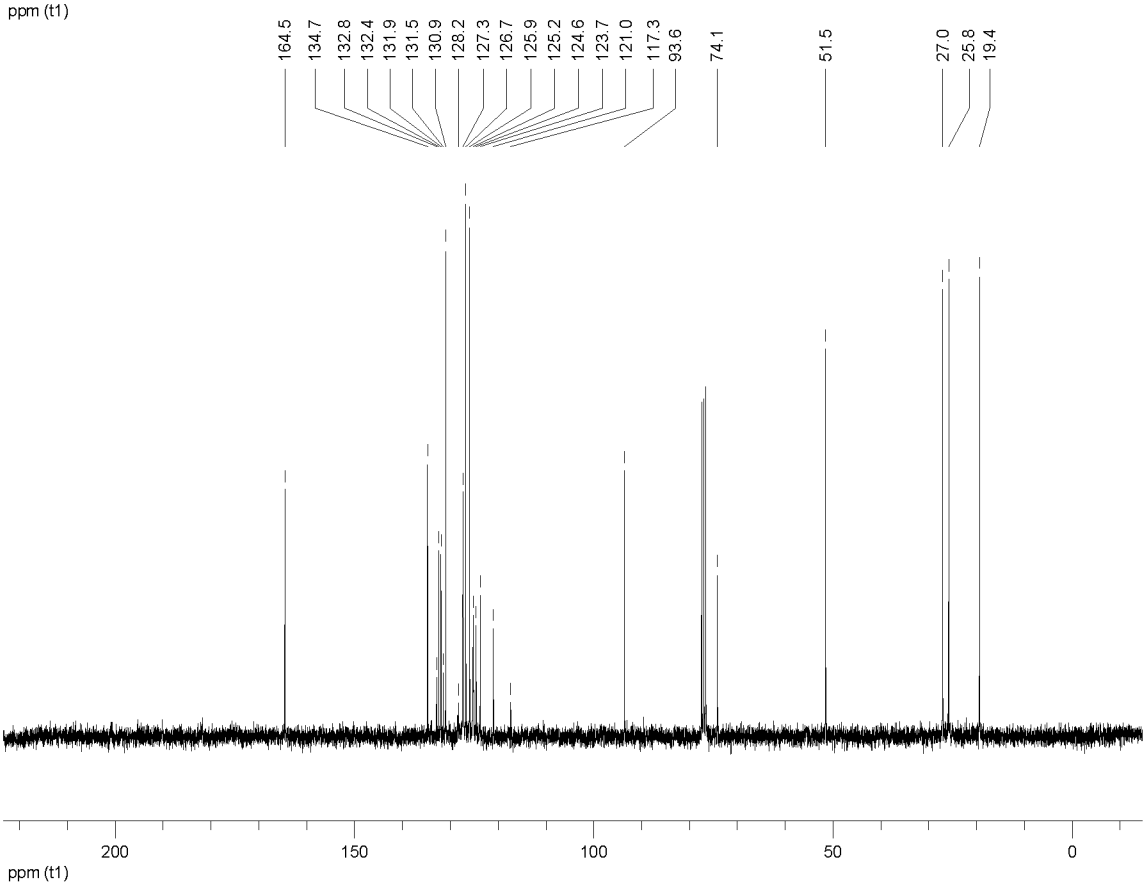

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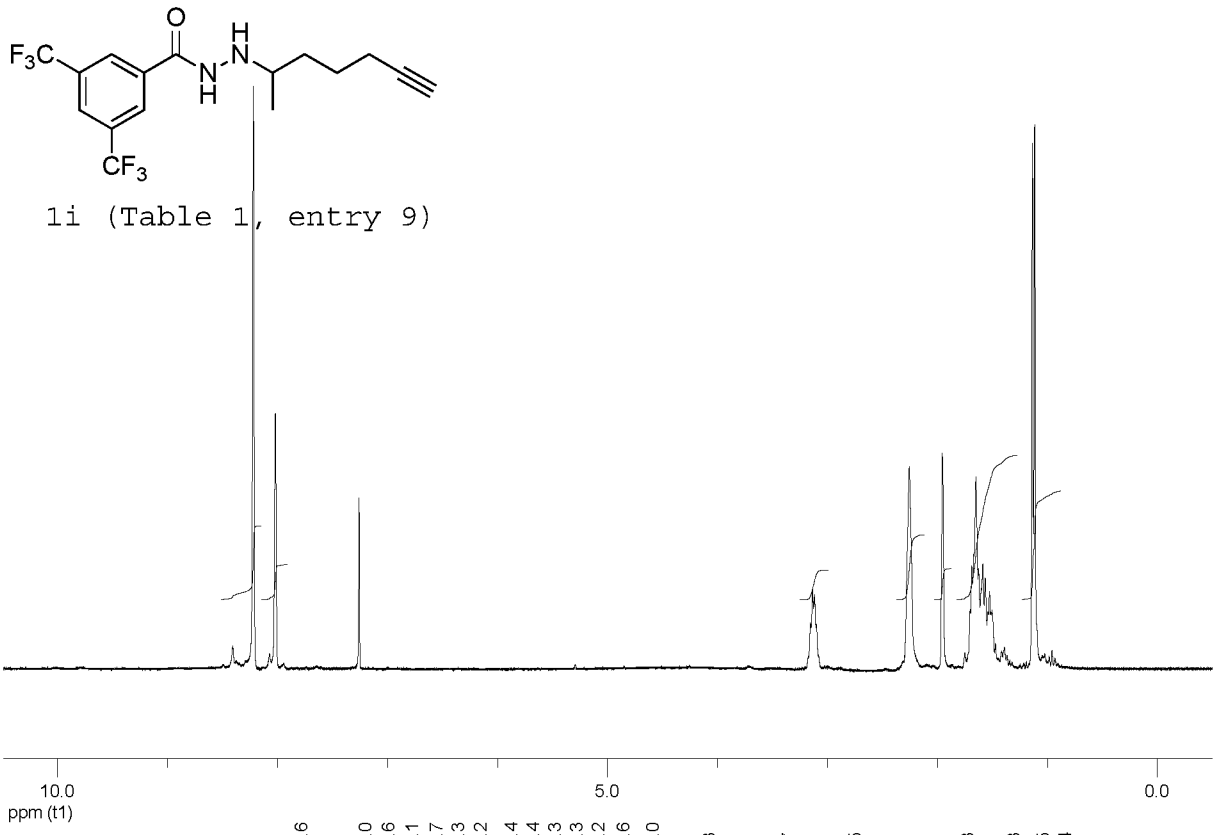

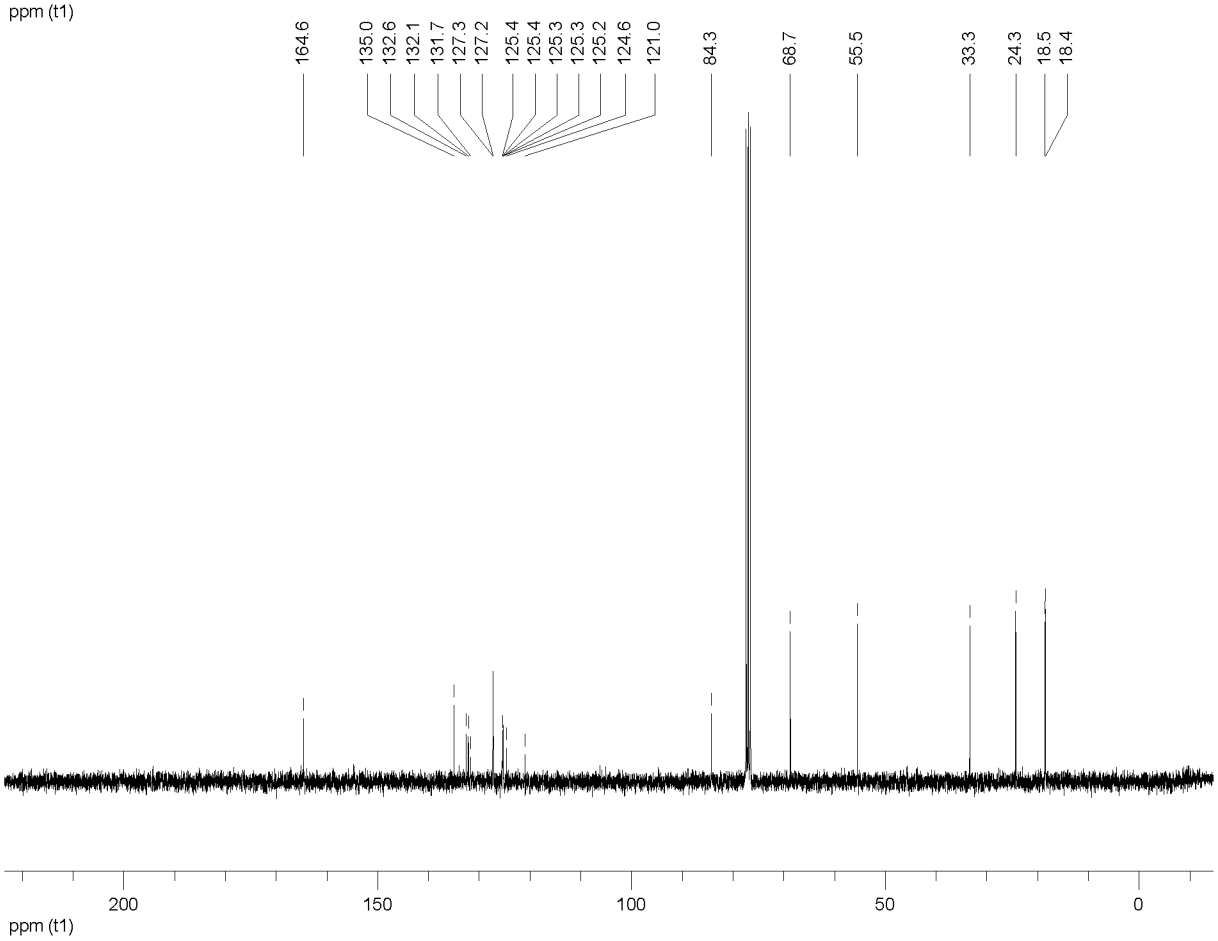

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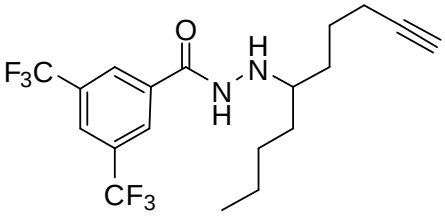

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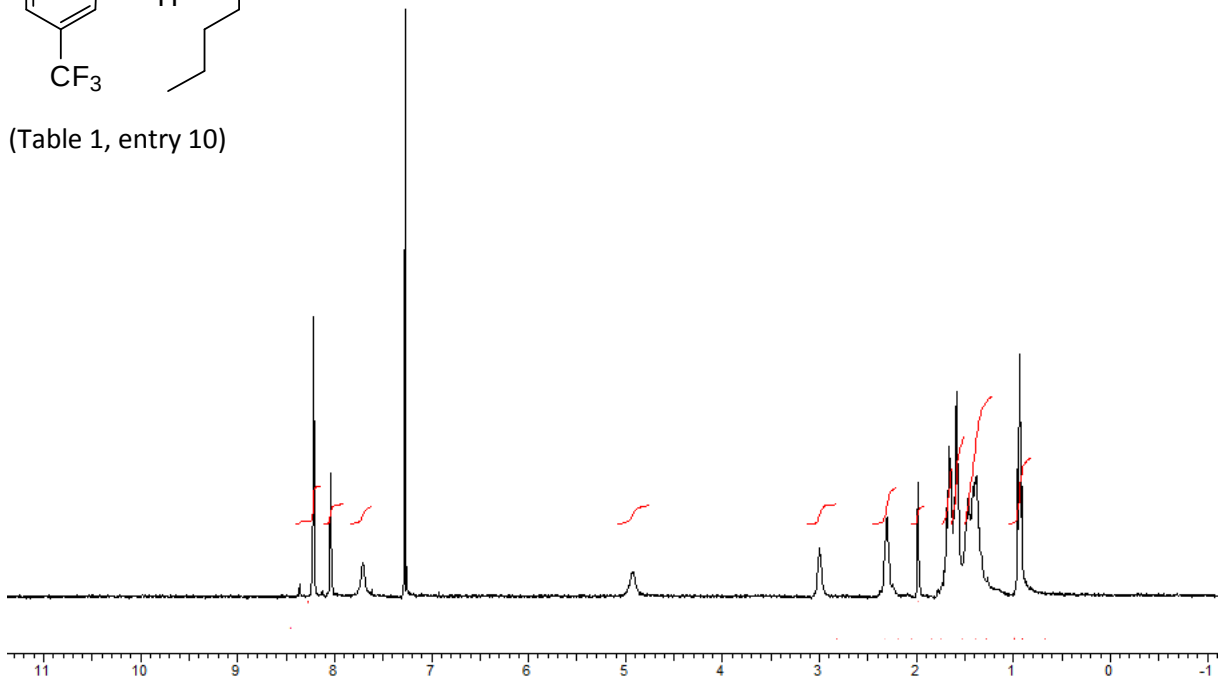

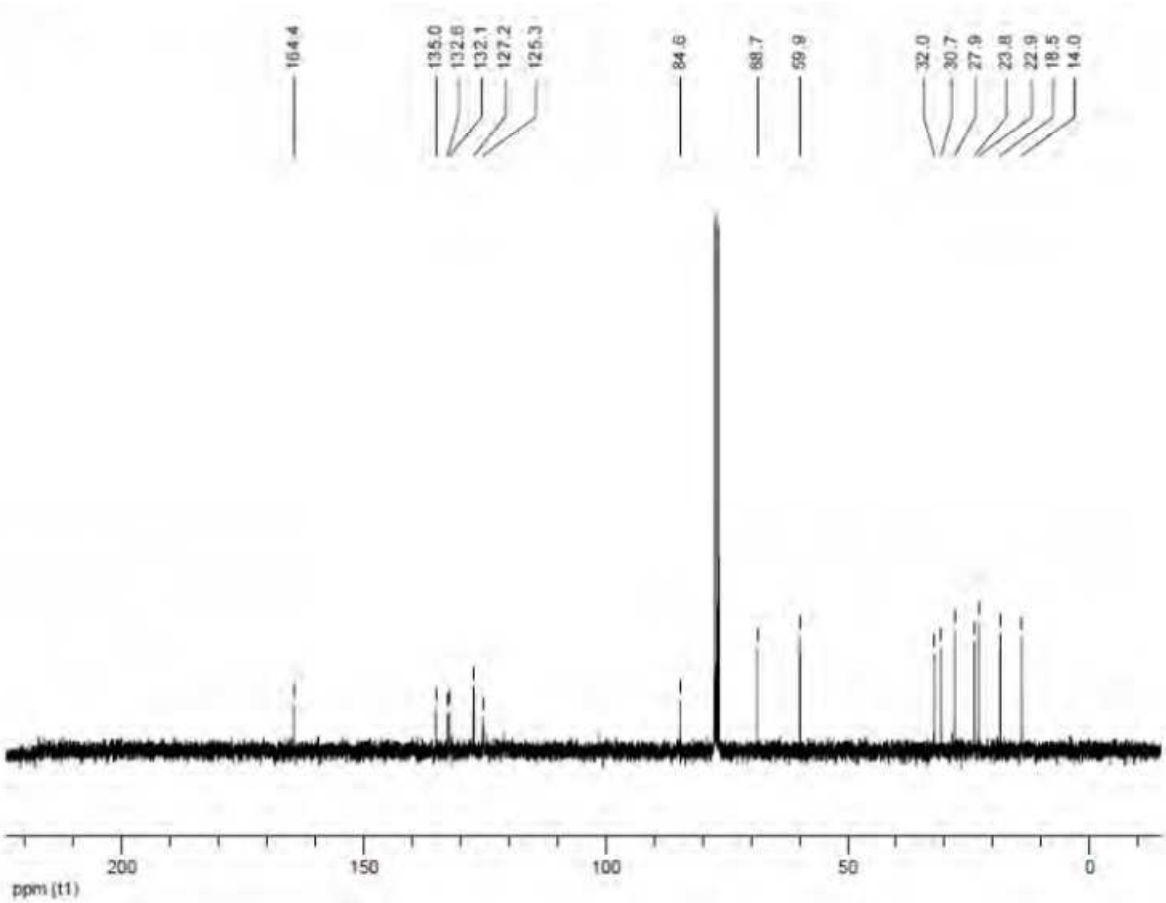

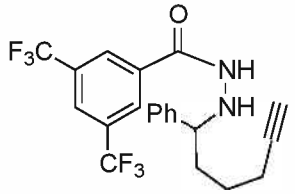

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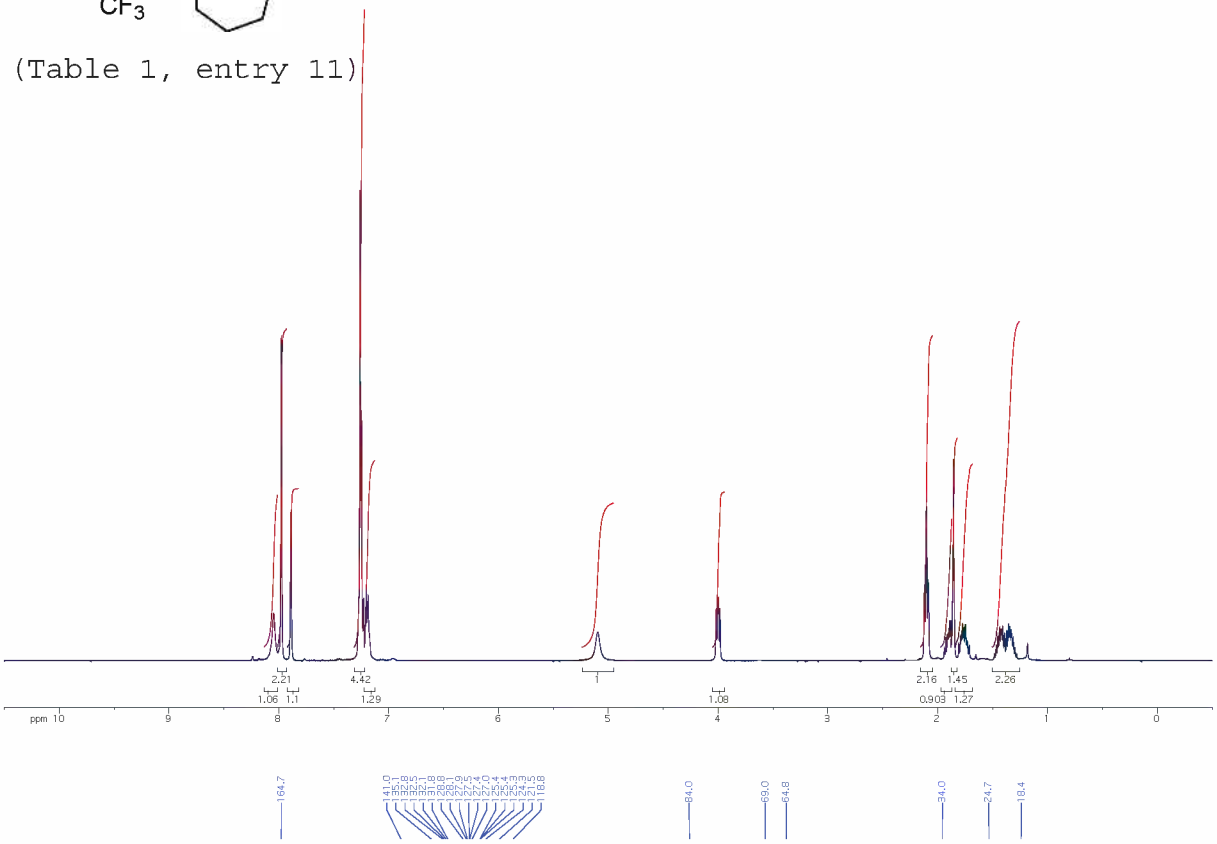

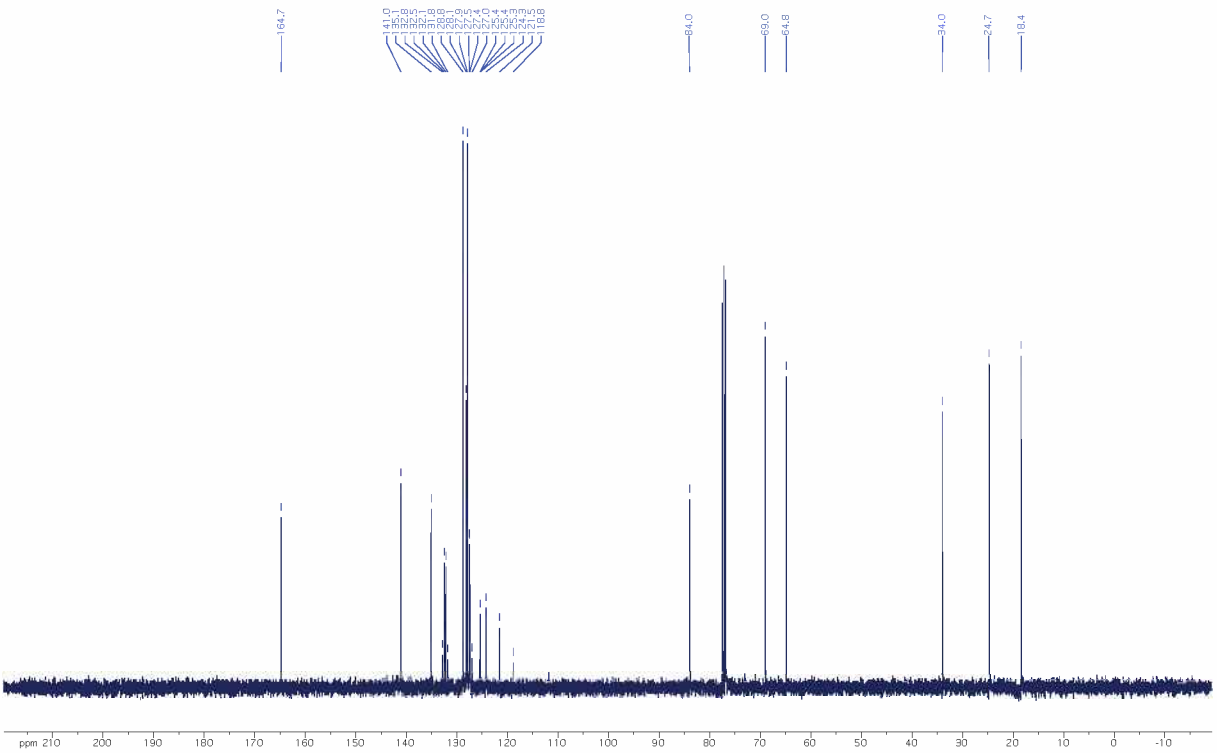

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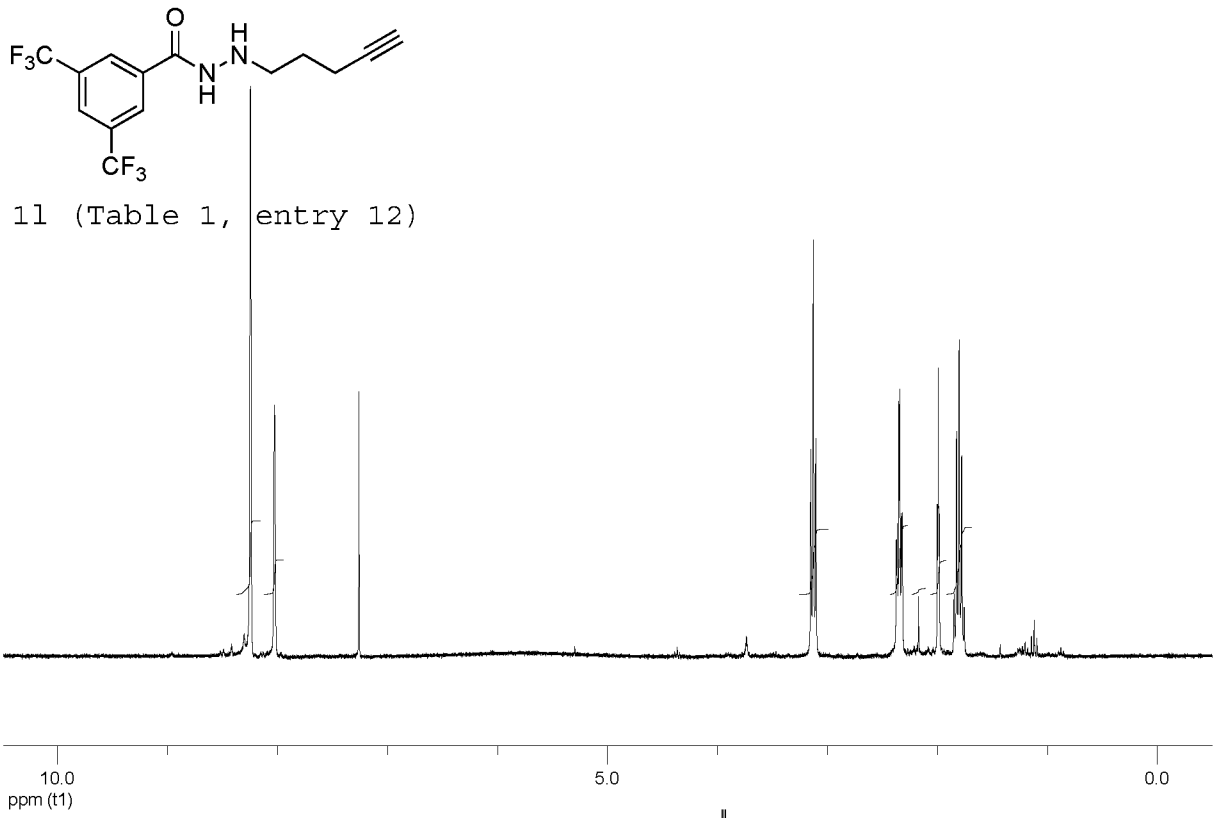

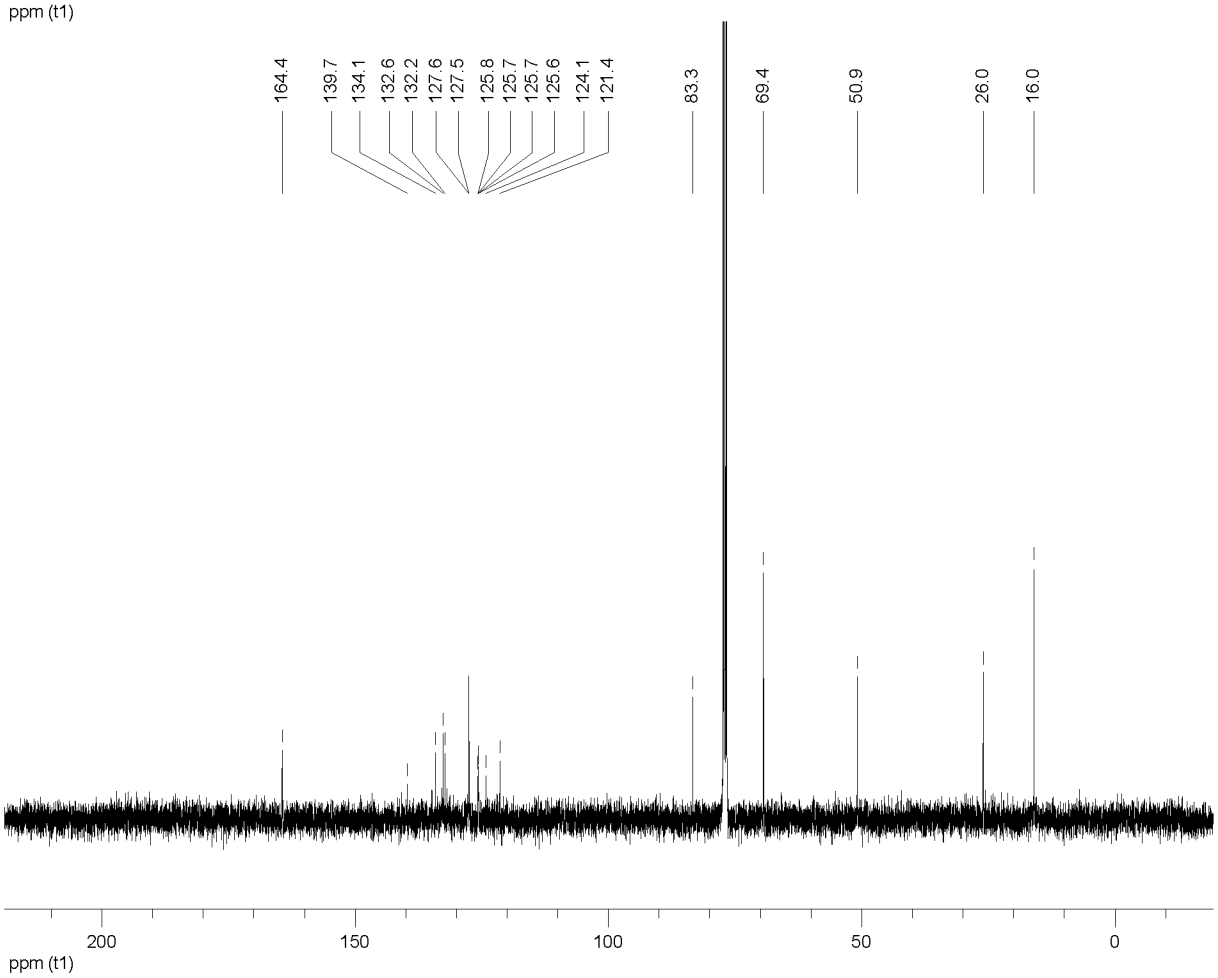

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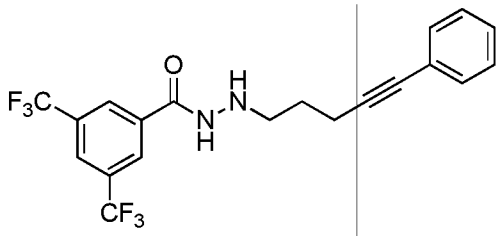

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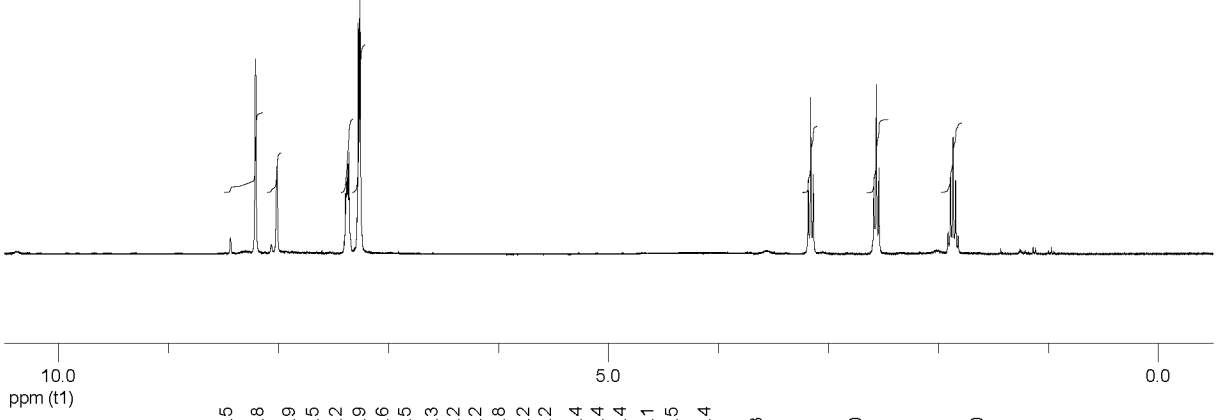

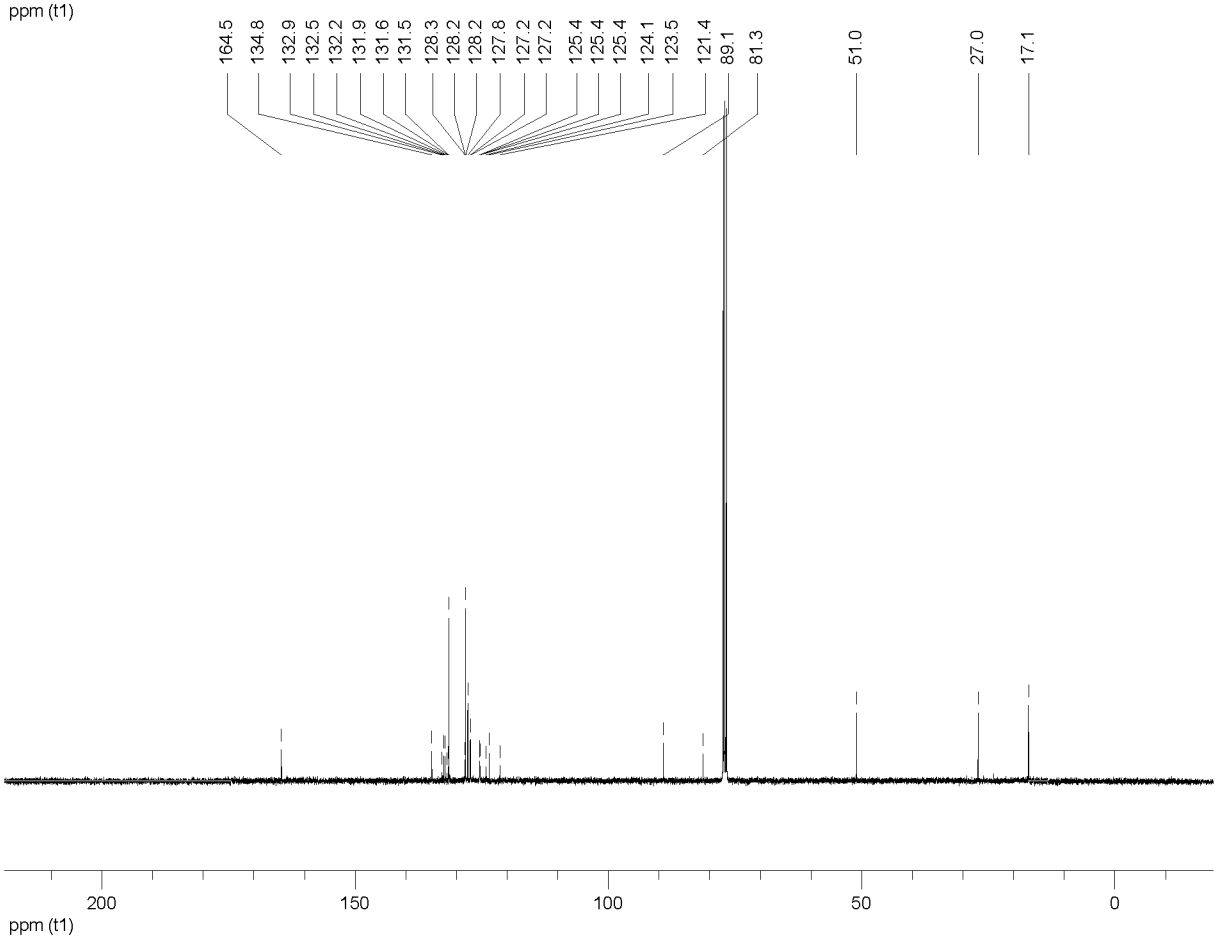

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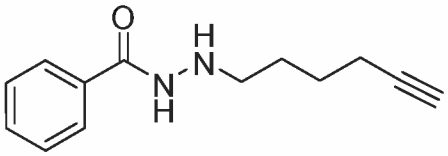

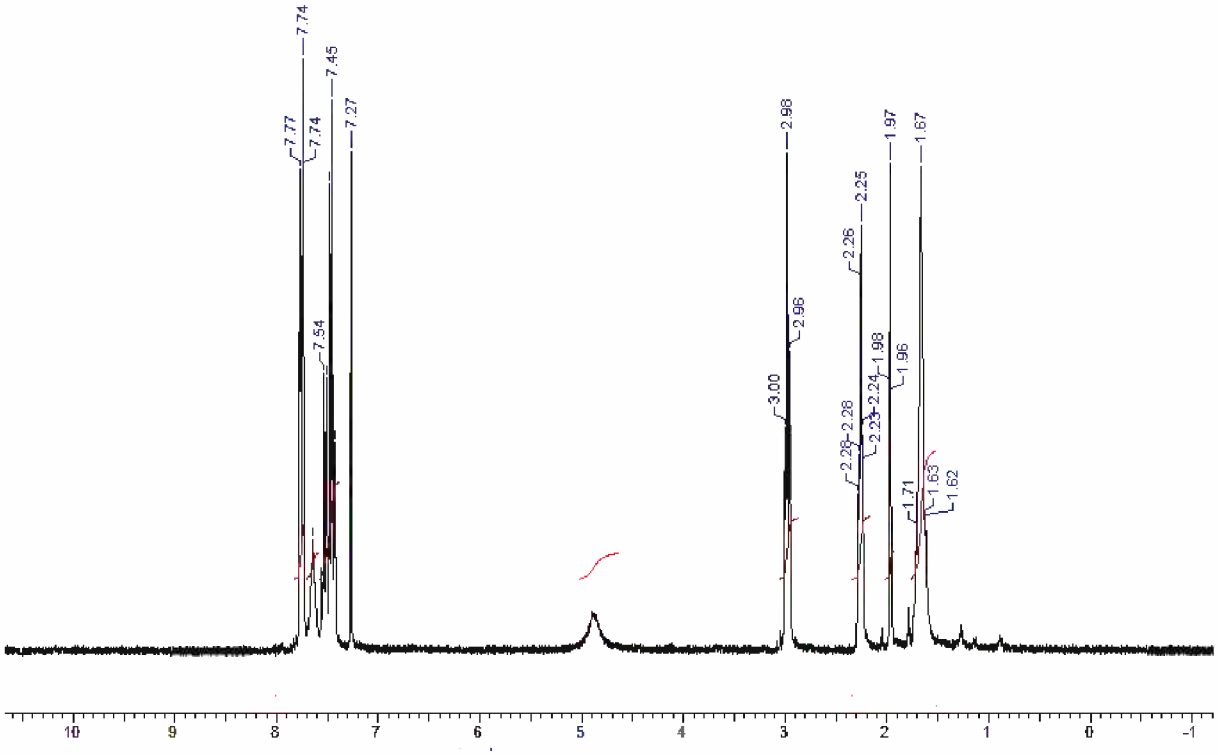

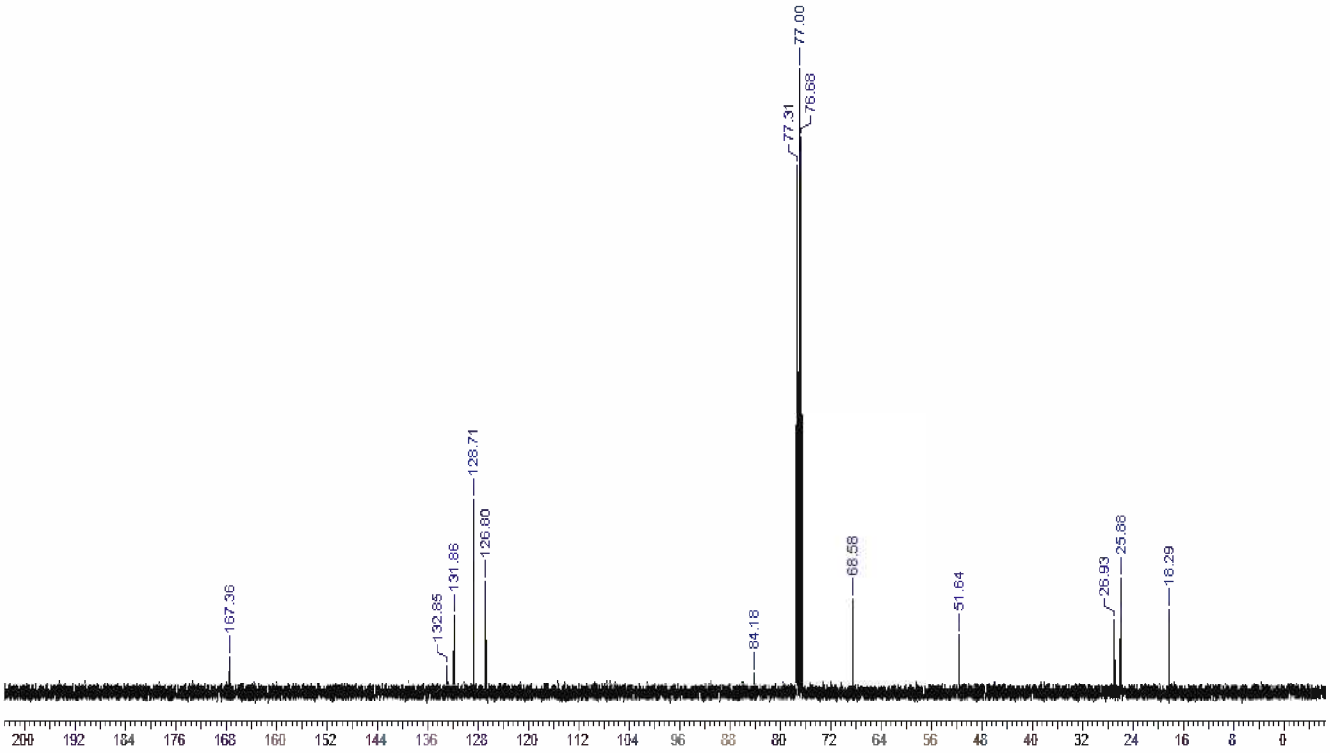

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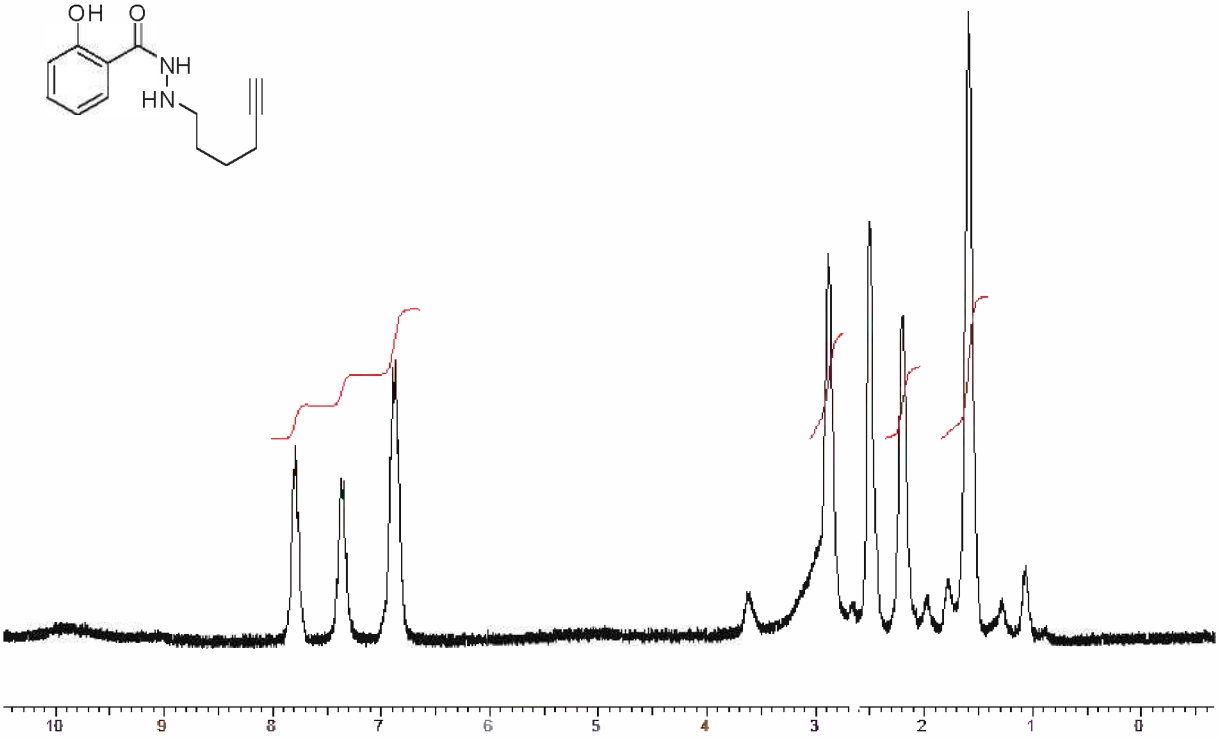

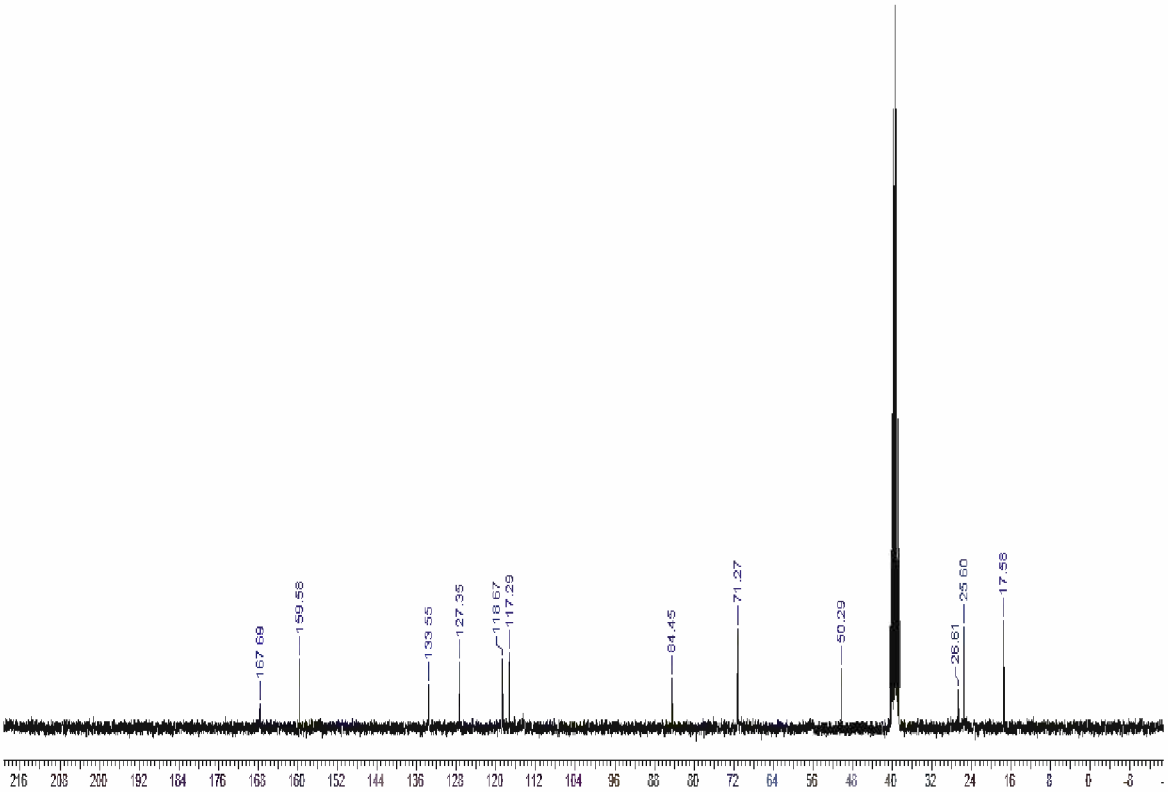

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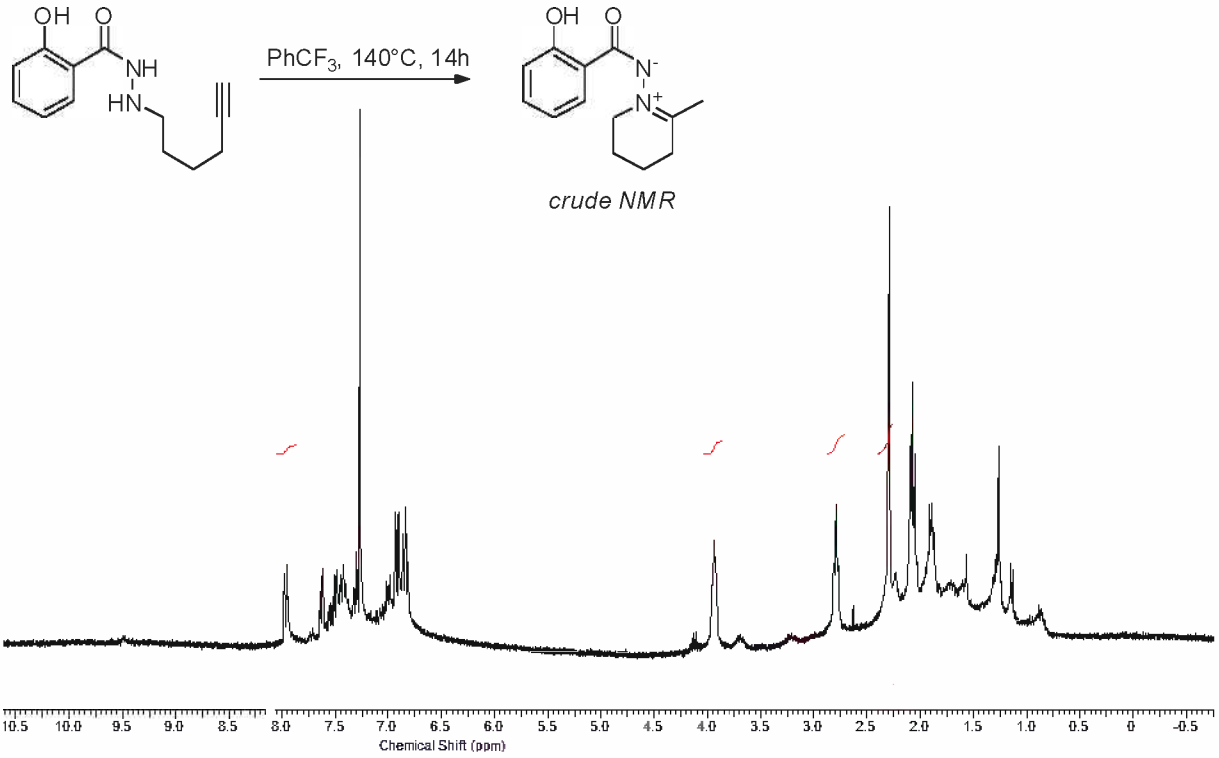

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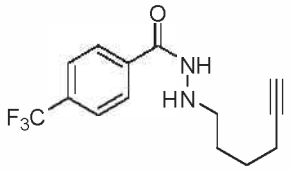

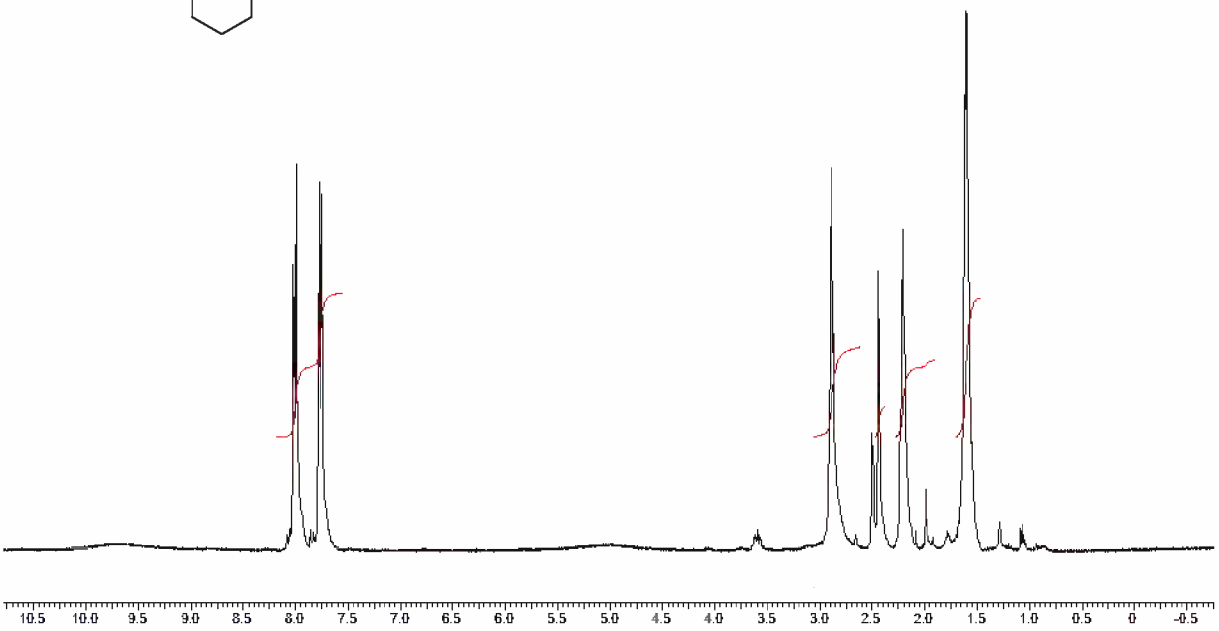

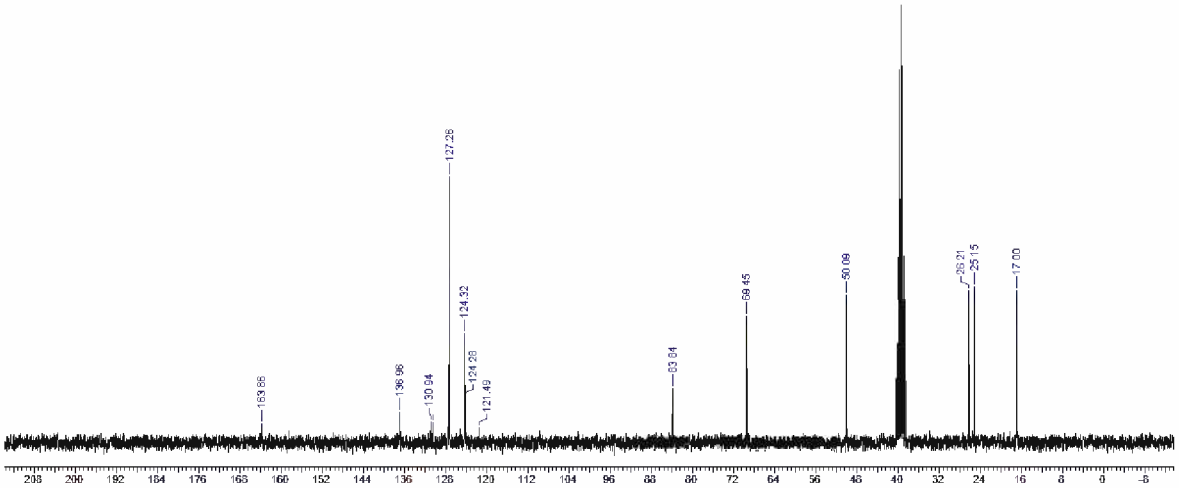

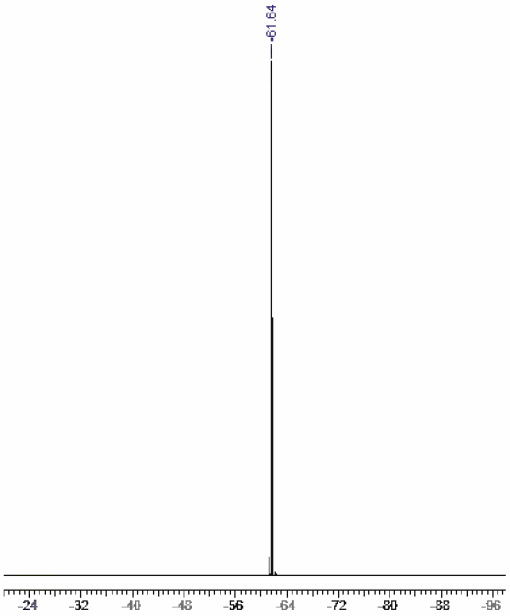

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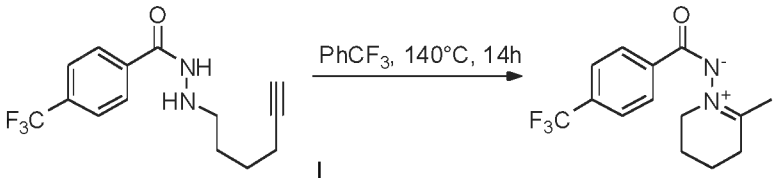
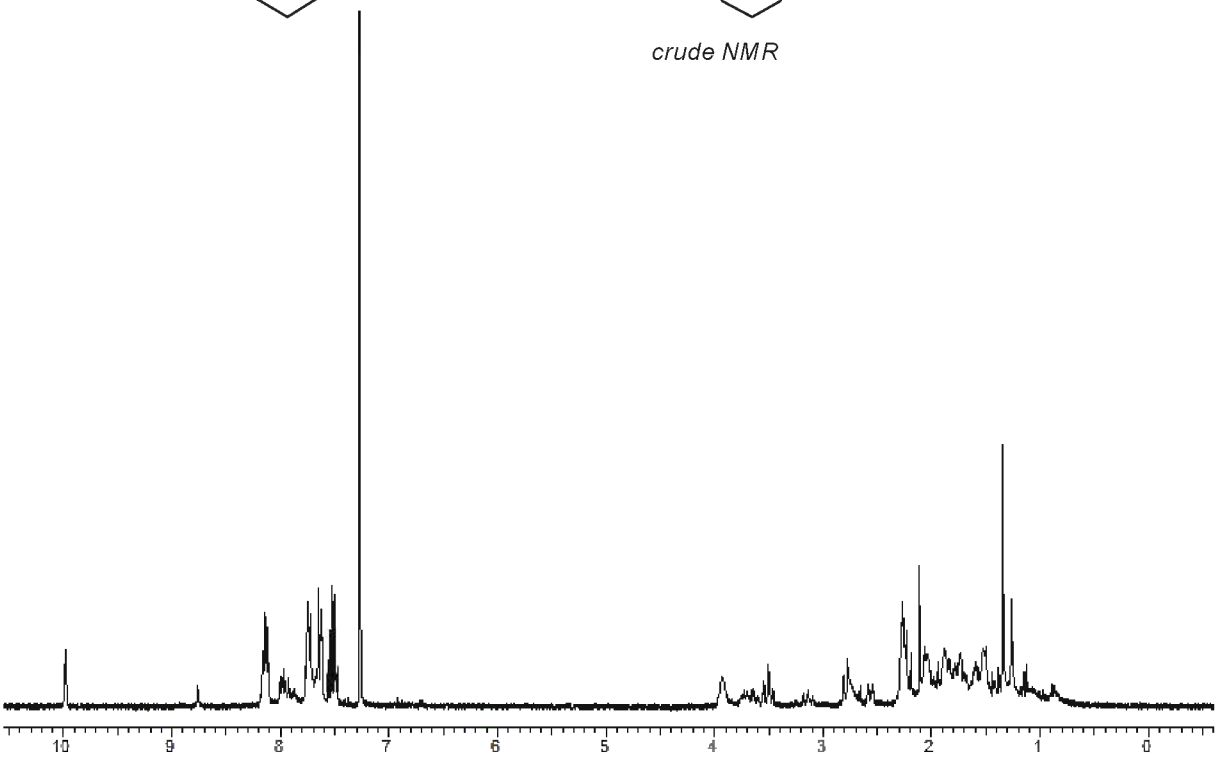
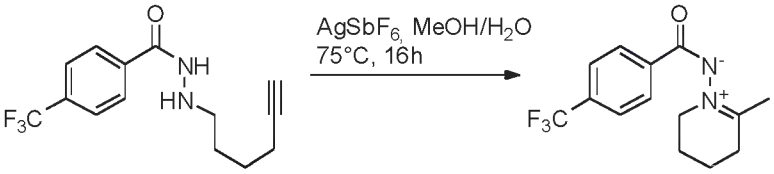


crude NMR





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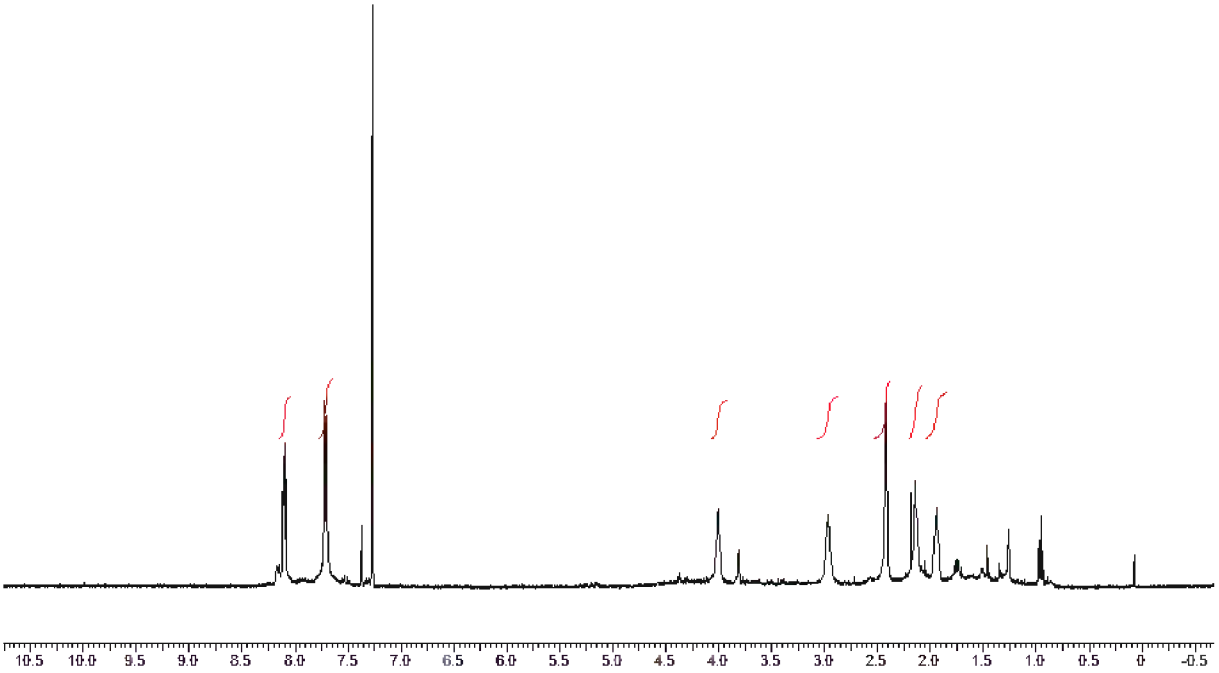

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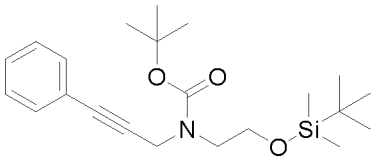

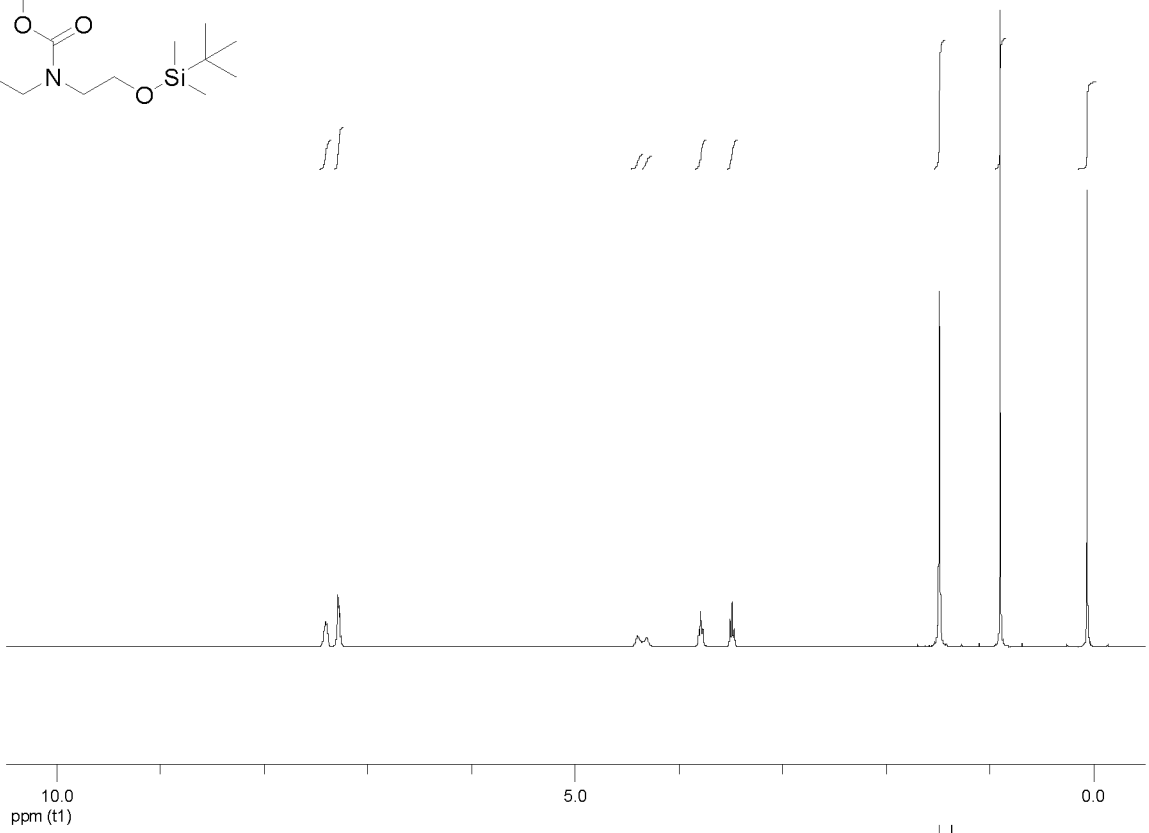

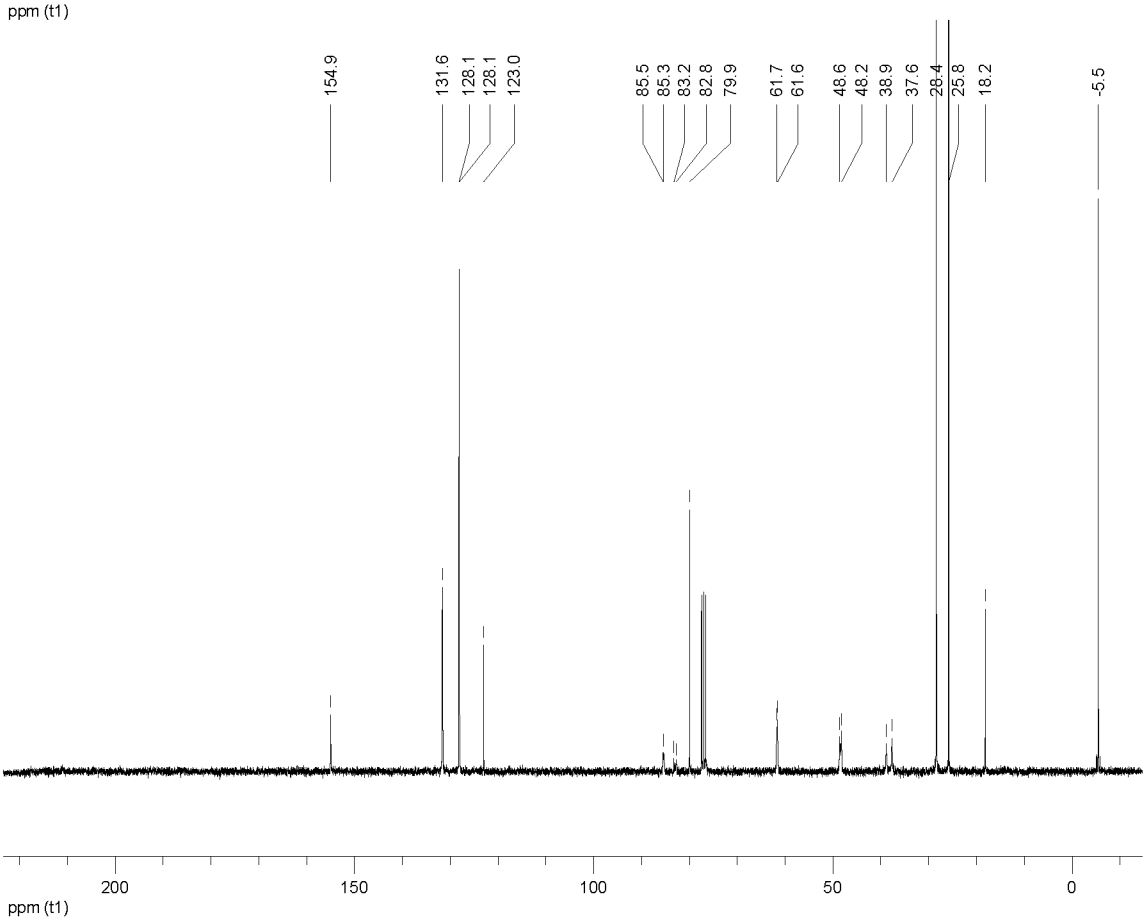

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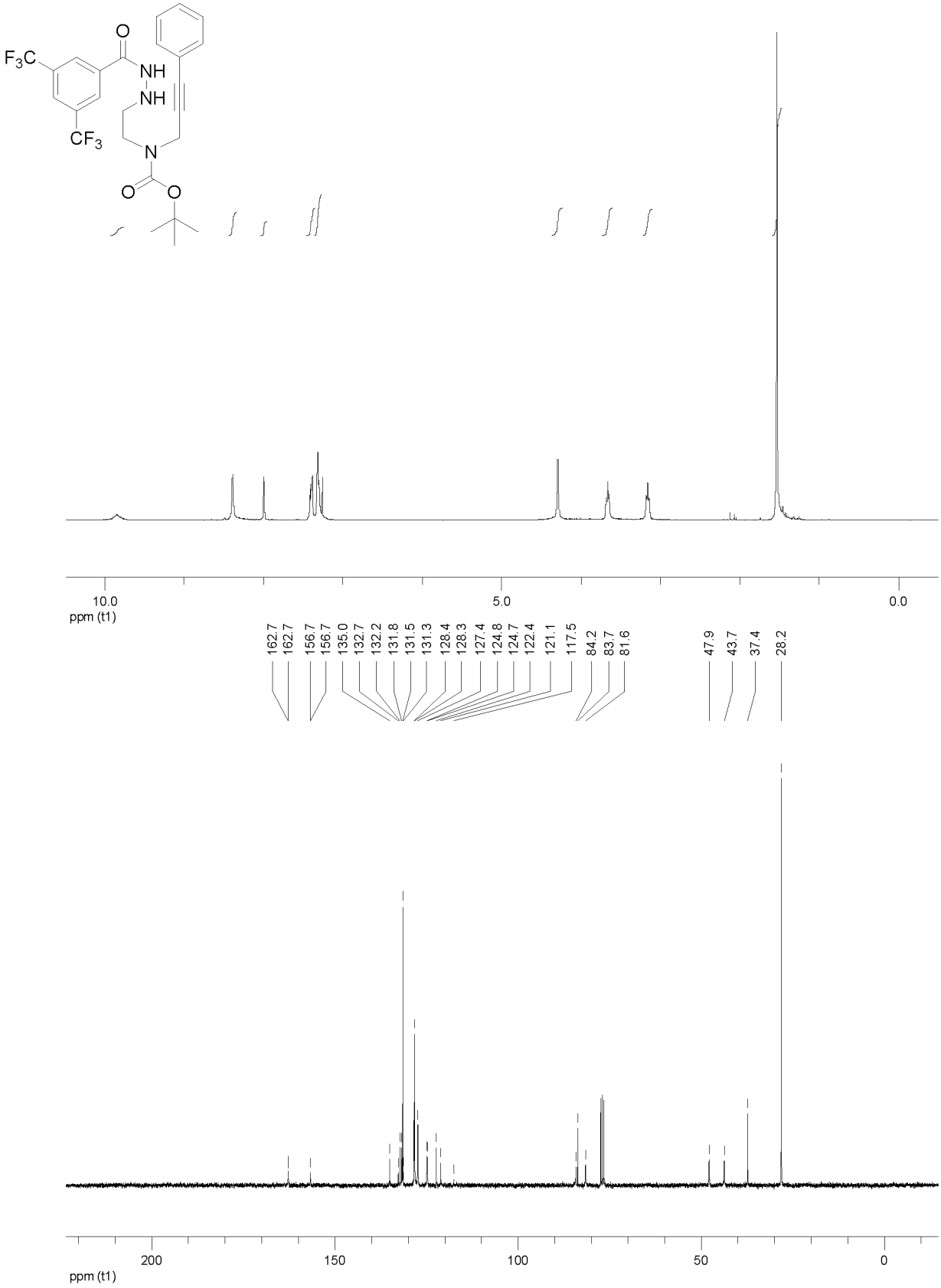

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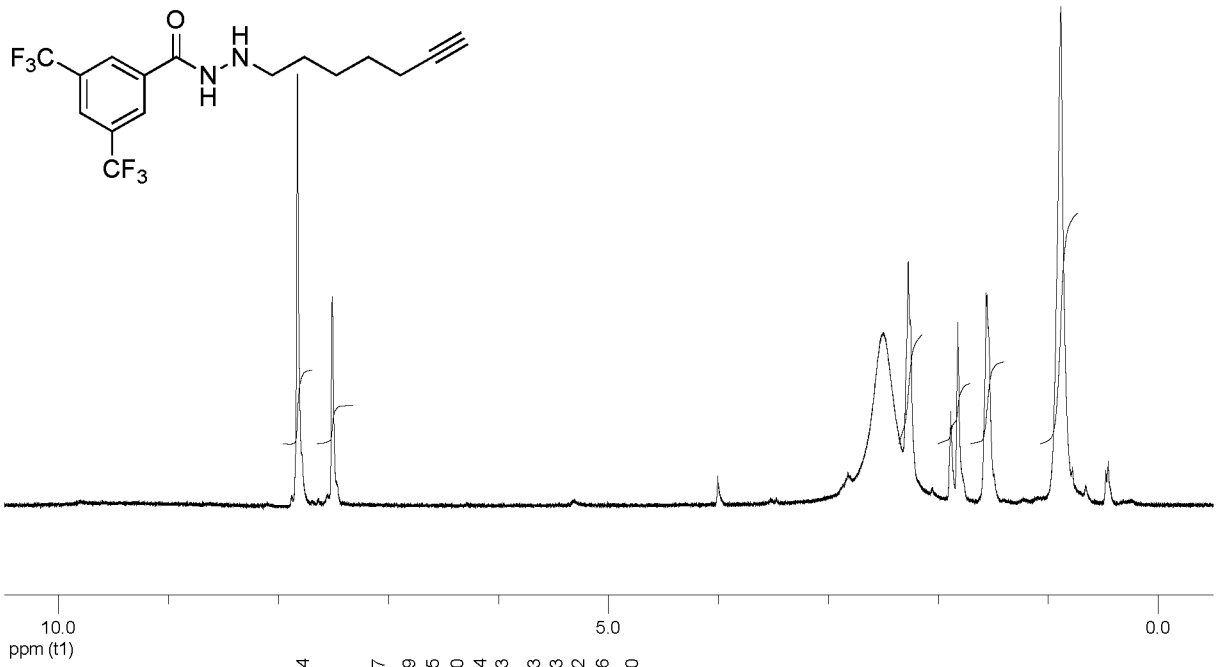

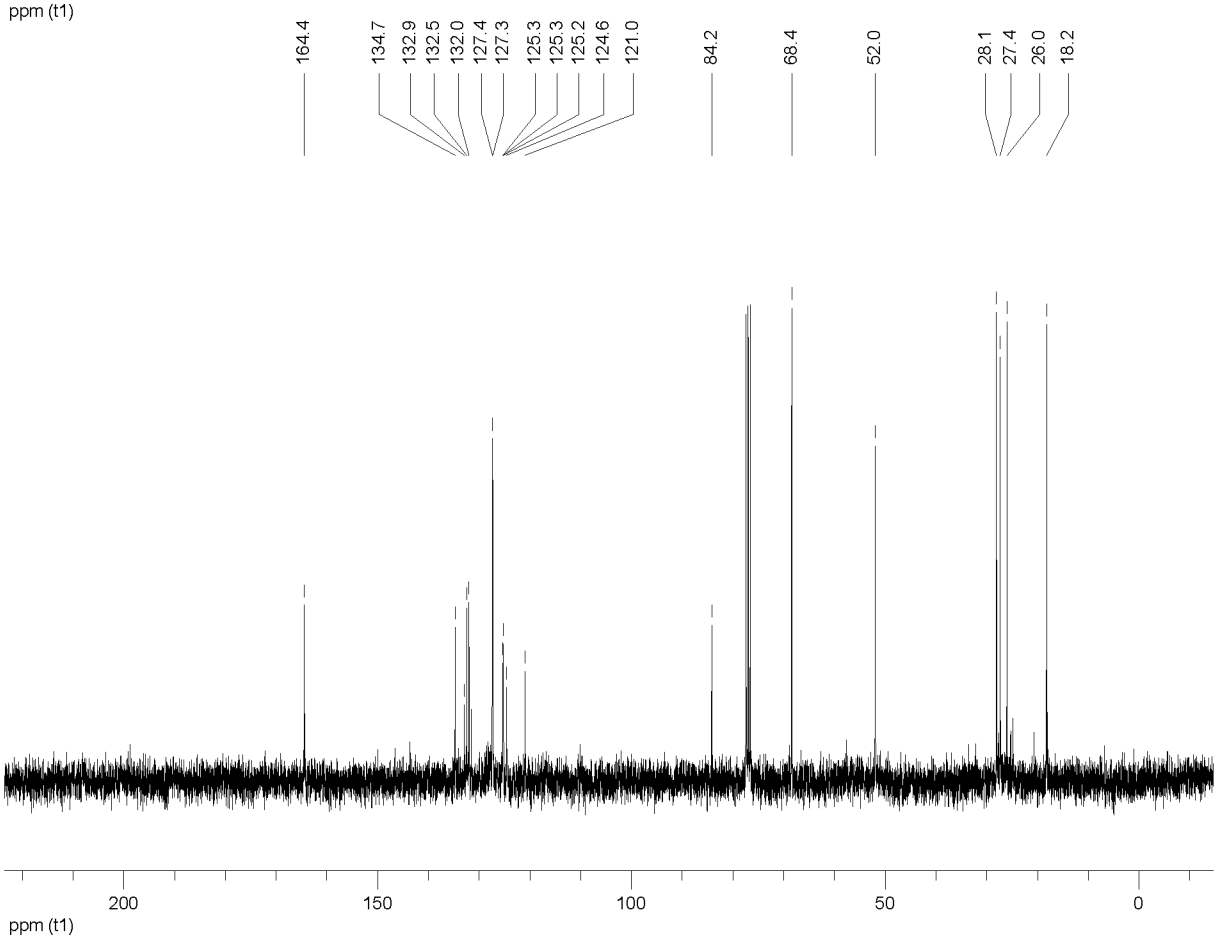

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