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Synthesis of 5-nitro-pyrazole triflones via [3+2] cycloaddition reaction and its application for potential insecticide

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Abstract: *Synthesis of 5-nitro-pyrazole triflones* ***6*** *was achieved via [3+2] cycloaddition reaction of 2-diazo-1-phenyl-2-((trifluoromethyl)sulfonyl)ethan-1-one (****3****) and α-bromonitrostyrene derivatives* ***7*** *under basic conditions in moderate to good yields. An agrochemically attractive 5-amino-N-pyrimidinyl-pyrazole triflone* ***2a*** *was successfully prepared from 5-nitro-pyrazole triflone* ***6c*** *in two steps.*

Key words: *5-nitro-pyrazole triflones, α-bromonitrostyrene, [3+2] cycloaddition*

Introduction: Pyrazoles are often found as an integral part of biologically active molecules [1]. In particular, pyrazoles with aryl or heteroaryl substituents at *N*-1 position and a free NH_2 group at *C*-5 position have gathered much attention because of their promising pharmaceutical [2] and agrochemical [3] properties. More precisely, 1-arylpyrazoles having substituents like alkyl, thioalkyl, acyl or cyano- group at the *C*-3 and *C*-4 positions exhibit potent insecticidal activities [4]. Amongst the pyrazole-type pesticides, Fipronil® (5-amino-1-(2,6-dichloro-4-trifluoromethylphenyl)-4-trifluoromethanesulfinyl-1*H*-pyrazole-3-carbonitrile) is a highly effective broad-spectrum insecticide and veterinary medicine to get rid of fleas and ticks [5] (Figure 1). However, the use of Fipronil® is the matter of discussion due to the recent food safety incident [6]. Thus, the development of safer derivatives of Fipronil® is of great importance. Bayer CropScience AG has filed patents on the sulfur-derivatized pyrimidinyl-pyrazol-5-amines **1** which showed potent activities as insecticides and/or parasiticides [3a,7]. Inspired by their patents, we are interested in triflyl (trifluoromethanesulfonyl, SO_2CF_3) variants (triflones) **2** as potential pesticides.

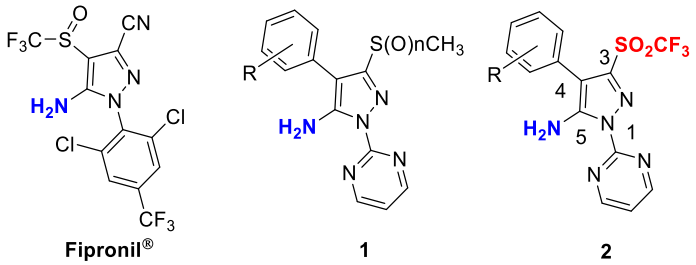
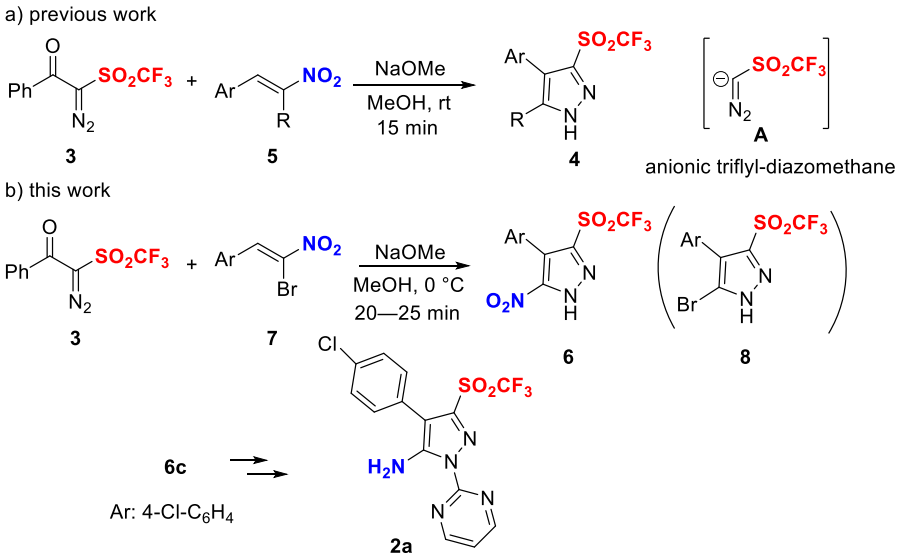


Figure 1. Fipronil® and its biologically attractive derivatives containing aryl or heteroaryl substituent at *N*-1 position and a free NH_2 group at *C*-5 position.

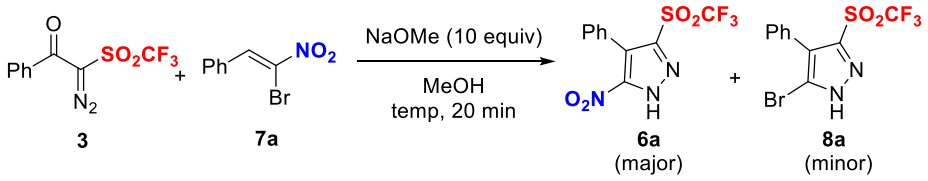
The introduction of fluorine(s) and fluorinated functional groups into organic compounds is one of the effective strategies to improve/alter biological activity and metabolic stability of original molecules [8]. In the case of our target 5-amino-pyrazole triflones **2**, the incorporation of a lipophilic triflyl group (π = 0.55) to *C*-3 position in **2** could potentially perturb the chemical, physical and biological properties of the parent heterocyclic 5-amino-pyrazoles. Besides, the triflone variants **2** are also expected to have a reduced basicity of the amine moiety in **2** due to the strong electron withdrawing effect by the triflyl group (σ_m = 0.79, σ_p = 0.93) [9]. For decades, our group has been focusing on the development of novel shelf-stable reagents for fluoro-functionalization reactions [10,11]. One such kind of unique compounds is 2-diazo-1-phenyl-2-((trifluoromethyl)-sulfonyl)ethan-1-one (**3**) [12]. The compound **3** was originally developed by us as a regent for electrophilic trifluoromethylthiolation reactions. A wide variety of nucleophiles such as enamines, indoles, β-ketoesters, and pyrroles are nicely trifluoromethylthiolated by **3** in the presence of a copper catalyst under mild conditions [12a]. Aromatic coupling reaction is also available by using **3**. On the other hand, **3** also acts as a powerful building block for the preparation of variety of triflones such as β-lactam triflones [12c]. Recently, we have reported the synthesis of pyrazole triflones **4** via [3+2] cycloaddition of **3** with nitrostyrenes **5** (Scheme 1a) [12d]. In the presence of NaOMe, reagent **3** generates a reactive anionic triflyl-diazomethane species **A** *in situ* to react with nitrostyrenes **5**. As an extension of our research work on heterocyclic triflones [12], we herein report the novel strategy for the preparation of 5-amino-*N*-pyrimidinyl-pyrazole triflones **2**. The important precursors to access **2** are the 5-nitro-pyrazole triflones **6**, which can be synthesized by the reaction of **3** with α-bromonitrostyrenes **7** under basic conditions (Scheme 1b). The selective elimination of the bromo group rather than nitro group in **7** during the cyclization step to suppress the formation of 5-bromo-pyrazole triflones **8** is the key for the success [13]. Substrate scope of **7** for the preparation of **6** was examined. Subsequently, the 5-nitro-pyrazole triflone **6c** was successfully transformed to the targeted 5-amino-*N*-pyrimidinyl-pyrazole triflone **2a** via two steps in moderated yield (Scheme 1b).



Scheme 1. a) Synthesis of pyrazole triflons **4** via [3+2] cycloaddition of **3** with nitrostyrenes **5** (previous work); b) Selective synthesis of 5-nitro-pyrazole triflons **6** and transformation of **6c** to 5-amino-*N*-pyrimidinyl-pyrazole triflone **2a** (this work).

Based on our previous work [12d], we initiated to optimize the reaction temperatures for the reactions between **3** and α-bromonitrostyrene **7a** in the presence of 10 equiv of NaOMe in MeOH (Table 1). Desired 5-nitro-pyrazole triflone **6a** was obtained in 62% yield along with 5-bromo-pyrazole triflone **8a** in 17% yield at 0 °C for 20 min (entry 1). While, decreasing the reaction temperature to –10 °C, did not affect the yield and products distribution (entry 2). Increasing the amount of **3** from 1.2 to 1.5 equiv, slightly increased the yields of **6a** to 64% and **8a** to 19% (entry 3) were detected, whereas lowering the temperature with 1.5 equiv of **3** did not affect the formation of nitro product **6a** with slightly increased the yield of bromo **8a** to 21% (entry 4). Thus, the combination of **3** (1.5 equiv) and α-bromonitrostyrenes **7** (1.0 equiv) in the presence of NaOMe (10.0 equiv) in MeOH at 0 °C for 20 min, was selected as the optimized reaction condition (entry 3).

Table 1. Optimization of [3+2] cycloaddition reaction[a]



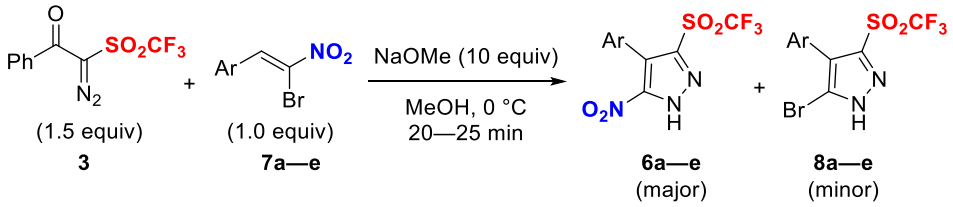
entry	**3** (equiv)	**7a** (equiv)	temp. (°C)	yield (%) **6a**	yield (%) **8a**
1	1.2	1.0	0	62	17
2	1.2	1.0	–10	63	20
3	**1.5**	**1.0**	**0**	**64**	**19**
4	1.5	1.0	–10	64	21

[a]Reaction conditions: Experiments were performed with **3** (1.2 or 1.5 equiv), **7a** (1.0 equiv), NaOMe (10 equiv), MeOH (1.0 mL) at given temperature for 20 min.

With the optimized reaction conditions in hand, the substrate scope of the [3+2] cyclization reaction was explored as shown in Table 2. All the reactions proceeded smoothly to furnish the desired 5-nitro-pyrazole triflones **6b—e** as major products in good yields with similar selectivity as **7a**. Electron donating 4-Me-C_6H_4 substituted substrate **7b** provided the product in similar yield and selectivity (**6b**: 67%, **8b**: 23%). The halogen substituted α-bromonitrostyrenes (**7c**: 4-Cl-C_6H_4; **7d**: 3-Br-C_6H_4; **7e**: 4-F-C_6H_4) provided the corresponding 5-nitro-pyrazole triflones **6** with higher yields (**6c**: 77%; **6d**: 76%; **6e**: 69%) along with corresponding bromo by-products **8** (**8c**: 15%; **8d**: 18%; **8e**: 17%) (Table 2).

Next, we examined the synthesis of 5-amino-*N*-pyrimidinyl-pyrazole triflone **2a**. The reduction of nitro group in **6c** by hydrogenation in the presence of Pd-C in MeOH gave the 5-amino-pyrazole triflone **9**, followed by the nucleophilic addition to 2-chloropyrimidine in the presence of NaH under heating condition to afford the potential biological active 5-amino-*N*-pyrimidinyl-pyrazole triflone **2a** in 35% yield for two steps (Scheme 2).

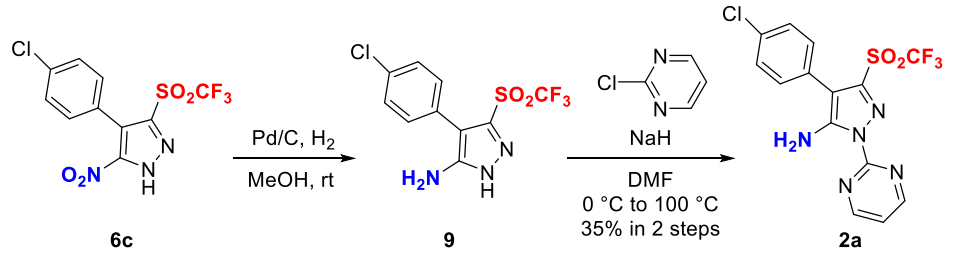
Table 2. Scope of the reaction of diazotriflone **3** with α-bromonitroalkenes **7a-e**[a]



entry	7	Ar	Yield (%)	
			6	8
1	**7a**	Ph	**6a:** 64	**8a:** 19
2	**7b**	4-Me-C_6H_4	**6b:** 67	**8b:** 23
3	**7c**	4-Cl-C_6H_4	**6c:** 77	**8c:** 15
4	**7d**	3-Br-C_6H_4	**6d:** 76	**8d:** 18
5	**7e**	4-F-C_6H_4	**6e:** 69	**8e:** 17

[a]Experiments were performed with **3** (1.5 equiv), **7a-e** (1.0 equiv) and NaOMe (10 equiv) in dry MeOH at 0 °C for 20–25 min.

Scheme 2. Synthesis of 5-amino-*N*-pyrimidinyl-pyrazole triflone **2a**.



In conclusion, we have disclosed the synthesis of 5-nitro-pyrazole triflones **6** via [3+2] cycloaddition reaction of 2-diazo-1-phenyl-2-((trifluoromethyl)sulfonyl)ethan-1-one **3** and α-bromonitrostyrene derivatives **7** under basic conditions in moderate to good yields. The transformation of 5-nitro-pyrazole triflone **6** to an agrochemically attractive 5-amino-*N*-pyrimidinyl-pyrazole triflone **2a** was successfully demonstrated in two steps. The synthesis of a series of 5-amino-*N*-pyrimidinyl-pyrazole triflones and their evaluation of the insecticide property are underway.

Experimental

All reactions were performed in oven-dried glassware under positive pressure of nitrogen or argon unless mentioned otherwise. Solvents were transferred via syringe and were introduced into reaction vessels though a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel (60-F_{254}). The TLC plates were visualized with UV light and $KMnO_4$ in water/heat. Column chromatography was carried out on columns packed with silica gel (60N spherical neutral size 40-50 μm) for flash column chromatography. The ^1H NMR (300 MHz), ^{19}F NMR (282 MHz), and ^{13}C NMR (126 MHz) spectra for solution in $CDCl_3$, CD_3OD were recorded on Varian Mercury 300, and Bruker Avance 500 NMR spectrometers.

Chemical shifts (δ) are expressed in ppm downfield from TMS (δ = 0.00) or C_6F_6 [δ = −162.2 ($CDCl_3$)] as an internal standard. Mass spectra were recorded on a SHIMAZU LCMS-2020 (ESI-MS). High resolution mass spectrometric measurements were recorded on a Waters Synapt G2 HDMS (ESI-MS), a Waters GCT premier (EI-MS). Solvents CH_3CN, CH_2Cl_2, DMF were dried and distilled before use. 2-Diazo-1-phenyl-2-((trifluoromethyl)-sulfonyl)ethan-1-one (**3**) [12c] and (*Z*)- α-bromonitrostyrenes **7a**—**e** [14] were prepared according to the known procedures.

Typical procedure for the synthesis of 5-nitro-4-aryl-pyrazole triflon (6) and 5-bromo-4-aryl-pyrazole triflon (8) from 3 and (*Z*)-1-(2-bromo-2-nitrovinyl) benzene (7) (Procedure A)

To a stirred solution of (*Z*)-α-bromonitrostyrenes **7** (0.1 mmol, 1.0 equiv) and 2-diazo-1-phenyl-2-((trifluoromethyl)-sulfonyl)ethan-1-one (**3**) (0.15 mmol, 1.5 equiv) in dry MeOH (1.0 mL), NaOMe (10.0 equiv) was added at 0 °C and the resulting mixture was stirred for 20-25 minutes under Ar atmosphere (progress of the reaction was monitored by TLC). After completion, the reaction mixture was concentrated under reduced pressure. Water was added and neutralized the solution with 5% HCl and extracted with ethyl acetate. The combined organic phase was washed with brine and dried over Na_2SO_4, and the mixture was evaporated *in vacuo*. The crude product was purified by flash column chromatography (DCM/MeOH = 10:1) to obtain the desired substituted 5-nitro-4-phenyl-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole **6** and 5-bromo-4-phenyl-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole **8**.

5-Nitro-4-phenyl-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (6a) and 5-Bromo-4-phenyl-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (8a):

(*Z*)-(2-Bromo-2-nitrovinyl) benzene **7a** (0.1 mmol, 0.023 g, 1.0 equiv), **3** (0.15 mmol, 0.042 g, 1.5 equiv) and NaOMe (1.0 mmol, 0.054 g, 10.0 equiv) in dry MeOH (1.0 mL) at 0 °C for 20 min provided the pure product **6a** (0.0205 g, 64 %) as a pale yellow solid and **8a** (0.0068 g, 19 %) as a brown solid.

6a: Mp: 313–315 °C (methanol); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.56–7.44 (m, 3H), 7.40–7.31 (m, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –77.96 (s, 3F); ^{13}C NMR (CD_3OD, 126 MHz) δ: 151.51, 138.17, 131.37, 130.22, 128.86, 127.58, 125.48, 120.81 (q, *J* = 324.8 Hz); IR (KBr): 3581, 3334, 3066, 1963, 1673, 1560, 1506, 1378, 1232, 1110, 921 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{10}H_5F_3N_3O_4S$ $[M–H]^–$ 319.9953; found 319.9981.

8a: Mp: 152–155 °C (DCM); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.49–7.43 (m, 3H), 7.41–7.36 (m, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.30 (s, 3F); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 130.49, 129.92, 129.55, 129.28, 128.49, 127.82, 126.77, 119.51 (q, *J* = 326.0 Hz); IR (KBr): 3642, 3210, 3116, 2672, 1959, 1654, 1533, 1386, 1114, 987, 717 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{10}H_6F_3N_2O_2SBrNa$ $[M+Na]^+$ 376.9183; found 376.9177.

5-Nitro-4-(*p*-tolyl)-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (6b) and 5-Bromo-4-(*p*-tolyl)-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (8b):

(*Z*)-1-(2-Bromo-2-nitrovinyl)-4-methylbenzene **7b** (0.3 mmol, 0.0726 g, 1.0 equiv), **3** (0.45 mmol, 0.125 g, 1.5 equiv) and NaOMe (3.0 mmol, 0.162 g, 10.0 equiv) in dry MeOH (3.0 mL) at 0 °C for 25 min provided the pure product **6b** (0.0677 g, 67%) as a pale yellow solid and **8b** (0.0251 g, 23%) as a brown solid.

6b: Mp: 305–308 °C (methanol); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.34–7.15 (m, 4H), 2.43 (s, 3H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.12 (s, 3F); ^{13}C NMR (CD_3OD, 126 MHz) δ: 155.17, 139.39, 139.21, 131.23, 129.18, 126.95, 125.27, 121.20 (q, *J* = 325.0 Hz), 21.37; IR (KBr): 3596, 3210, 3035, 1720, 1670, 1529, 1371, 1224, 1110, 995 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{11}H_7F_3N_3O_4S$ $[M–H]^-$ 334.0109, found 334.0108.

8b: Mp: 133–134 °C (DCM); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.29–7.25 (m, 4H), 2.41 (s, 3H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.33 (s, 3F); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 139.55, 130.33, 129.72, 129.23, 127.77, 125.33, 123.79, 119.53 (q, *J* = 325.7 Hz), 21.56; IR (KBr): 3612, 3237, 3097, 2350, 1901, 1662, 1498, 1382, 1106, 975, 717 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{11}H_8F_3N_2O_2SBrNa$ $[M+Na]^+$ 390.9340, found 390.9333.

4-(4-Chlorophenyl)-5-nitro-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (6c) and 5-Bromo-4-(4-chlorophenyl)-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (8c):

(*Z*)-1-(2-Bromo-2-nitrovinyl)-4-chlorobenzene **7c** (0.3 mmol, 0.0787 g, 1.0 equiv), **3** (0.45 mmol, 0.125 g, 1.5 equiv) and NaOMe (3.0 mmol, 0.162 g, 10.0 equiv) in dry MeOH (3.0 mL) at 0 °C for 20 min provided the pure product **6c** (0.0825 g, 77 %) as a brownish yellow solid and **8c** (0.0177 g, 15 %) as a brown solid.

6c: Mp: 271–273 °C (methanol); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.38 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.2 Hz, 2H), 3.04 (br s, 1H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.47 (s, 3F); ^{13}C NMR (CD_3OD, 126 MHz) δ: 156.09, 139.82, 135.04, 132.99, 129.66, 128.60, 123.65, 121.26 (q, *J* = 325.2 Hz); IR (KBr): 3507, 3241, 3073, 2609, 1897, 1635, 1529, 1367, 1220, 1106, 848 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{10}H_4F_3N_3O_4SCl$ $[M–H]^-$ 353.9563; found 353.9581.

8c: Mp: 136–138 °C (DCM); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.45 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.32 (s, 3F); ^{13}C NMR ($CDCl_3$, 126 MHz) δ: 135.73, 133.76, 131.71, 130.22, 128.75, 126.43, 125.12, 119.34 (q, *J* = 325.9 Hz); IR (KBr): 3619, 3131, 2923, 2327, 1540, 1459, 1390, 1110, 987, 829, 717 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{10}H_4F_3N_2O_2SClBr$ $[M–H]^-$ 386.8817; found 386.8824.

4-(3-Bromophenyl)-5-nitro-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (6d) and 5-Bromo-4-(3-bromophenyl)-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (8d):

(*Z*)-1-Bromo-3-(2-bromo-2-nitrovinyl)benzene **7d** (0.3 mmol, 0.092 g, 1.0 equiv), **3** (0.45 mmol, 0.125 g, 1.5 equiv) and NaOMe (3.0 mmol, 0.162 g, 10.0 equiv) in dry MeOH (3.0 mL) at 0 °C for 20 min provided the pure product **6d** (0.0917 g, 76 %) as a brownish yellow solid and **8d** (0.024 g, 18%) as a brown solid.

6d: Mp: 266–268 °C (methanol); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.59 (d, *J* = 7.5 Hz, 1H), 7.43 (s, 1H), 7.36–7.26 (m, 1H), 7.20 (d, *J* = 7.4 Hz, 1H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.54 (s, 3F); ^{13}C NMR (CD_3OD, 126 MHz) δ: 156.12, 139.87, 134.13, 133.27, 131.95, 130.31, 130.17, 123.17, 122.15, 121.26 (q, *J* = 325.3 Hz); IR (KBr): 3569, 3226, 3085, 2613, 1743, 1552, 1521, 1378, 1205, 1106, 840, 624 cm^{-1}. HRMS (ESI–TOF): calcd for $C_{10}H_4F_3N_3O_4SBr$ $[M–H]^-$ 397.9058; found 397.9055.

8d: Mp: 115–116 °C (DCM); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.61 (d, *J* = 5.9 Hz, 1H), 7.54 (s, 1H), 7.40–7.31 (m, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.27 (s, 3F); ^{13}C NMR (CD_3OD, 126 MHz) δ: 134.51, 134.04, 133.04, 131.41, 130.96, 130.67, 129.47, 126.43, 122.86, 120.90 (q, *J* = 325.3 Hz); IR (KBr): 3667, 3139, 2938, 2373, 1556, 1459, 1375, 1106, 987, 871, 790, 655 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{10}H_4F_3N_2O_2SBr_2$ $[M–H]^-$ 430.8312; found 430.8305.

4-(4-Fluorophenyl)-5-nitro-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (6e) and 5-Bromo-4-(4-fluorophenyl)-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole (8e):

(*Z*)-1-(2-Bromo-2-nitrovinyl)-4-fluorobenzene **7e** (0.3 mmol, 0.0738 g, 1.0 equiv), **3** (0.45 mmol, 0.125 g, 1.5 equiv) and NaOMe (3.0 mmol, 0.162 g, 10.0 equiv) in dry MeOH (3.0 mL) at 0 °C for 20 min provided the pure product **6e** (0.0706 g, 69 %) as a brownish yellow solid and **8e** (0.0188 g, 17 %) as a brown solid.

6e: Mp: 352–354 °C (methanol); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.26–7.23 (m, 2H), 7.18–7.07 (m, 2H), 2.20 (br s, 1H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.65 (s, 3F), –111.50 (s, 1F); ^{13}C NMR (CD_3OD, 126 MHz) δ: 162.65 (d, *J* = 245.3 Hz), 155.03, 138.54, 131.98 (d, *J* = 8.6 Hz), 125.71 (d, *J* = 3.8 Hz), 122.47, 119.91 (q, *J* = 325.2 Hz), 113.82 (d, *J* = 22.0 Hz); IR (KBr): 3519, 3318, 3097, 2562, 1654, 1521, 1375, 1224, 1106, 991 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{10}H_4F_4N_3O_4S$ $[M–H]^-$ 337.9859; found 337.9861.

8e: Mp: 116–118 °C (DCM); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.40–7.33 (m, 2H), 7.19–7.12 (m, 2H); ^{19}F NMR ($CDCl_3$, 282 MHz) δ: –78.35 (s, 3F), –111.67– –111.86 (m, 1F); ^{13}C NMR (CD_3OD, 126 MHz) δ: 164.57 (d, *J* = 247.0 Hz), 133.89 (d, *J* = 8.7 Hz), 130.72, 129.47, 127.02, 125.31 (d, *J* = 3.6 Hz), 120.92 (q, *J* = 325.1 Hz), 116.10 (d, *J* = 22.1 Hz); IR (KBr): 3679, 3127, 2931, 2377, 1548, 1475, 1382, 1228, 1114, 983, 755, 640 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{10}H_4F_4N_2O_2SBr$ $[M–H]^-$ 370.9113; found 370.9113.

Synthesis of 4-(4-chlorophenyl)-1-(pyrimidin-2-yl)-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazol-5-amine (2a)

To a solution of 4-(4-chlorophenyl)-5-nitro-3-((trifluoromethyl)sulfonyl)-1*H*-pyrazole **6c** (0.0355 g, 0.1 mmol) in MeOH was added Pd/C (0.006 g), and the mixture was stirred at rt under H_2 atmosphere (balloon) for 2.5 h. The mixture was filtered through a pad of Celite® to give the amine **9**. The crude product was used for the next reaction without further purification.

The crude amine **9** was dissolved in DMF (1.0 mL). NaH (60% w/w in mineral oil, 0.0024 g, 0.1 mmol) was added to the mixture at 0 °C, and the mixture was stirred at rt for 30 min. 2-Chloropyrimidine (0.0115 g, 0.1 mmol) was added to the mixture and the mixture was stirred at 100 °C for 12 h. H_2O was added to the mixture and the mixture was extracted with EtOAc. The combined organic phase was washed with brine and dried with Na_2SO_4, and the mixture was evaporated *in vacuo*. The crude product was purified with flash column chromatography (eluted with CH_2Cl_2:MeOH = 20:1, the silica gel was neutralized with 1% ammonia solution in DCM prior to using) to give the 5-amino-*N*-pyrimidinyl-pyrazole triflone **2a** (0.014 g, 35% yield) as a white solid.

Mp (DCM): 150–151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.90 (d, *J* = 4.9 Hz, 2H), 7.48–7.41 (m, 3H), 7.40–7.34 (m, 2H), 6.09 (br s, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ: –78.18 (s, 3F).; ^{13}C NMR (126 MHz, $CDCl_3$) δ: 158.96, 157.28,

148.99, 143.03, 130.72, 129.02, 128.75, 128.20, 119.74, 119.68 (q, *J* = 326.3 Hz), 106.98; IR (KBr): 3411, 3255, 3060, 1600, 1567, 1511, 1428, 1376, 1297, 1213, 1120, 979, 838, 794, 701, 657 cm^{-1}; HRMS (ESI–TOF): calcd for $C_{14}H_8F_3N_5O_2SCl$ $[M–H]^-$ 402.0039; found 402.0029.

Acknowledgements

This work was supported by JSPS KAKENHI grants JP 16H01142 (Middle Molecular Strategy) and JP16H01017 (Precisely Designed Catalysts with Customized Scaffolding), and ACT-C from the JST (JPMJCR12Z7). ET thanks the Pesticide Science Society of Japan for support.

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Supporting Information

Synthesis of 5-nitro-pyrazole triflones via [3+2] cycloaddition reaction and its application for potential insecticide

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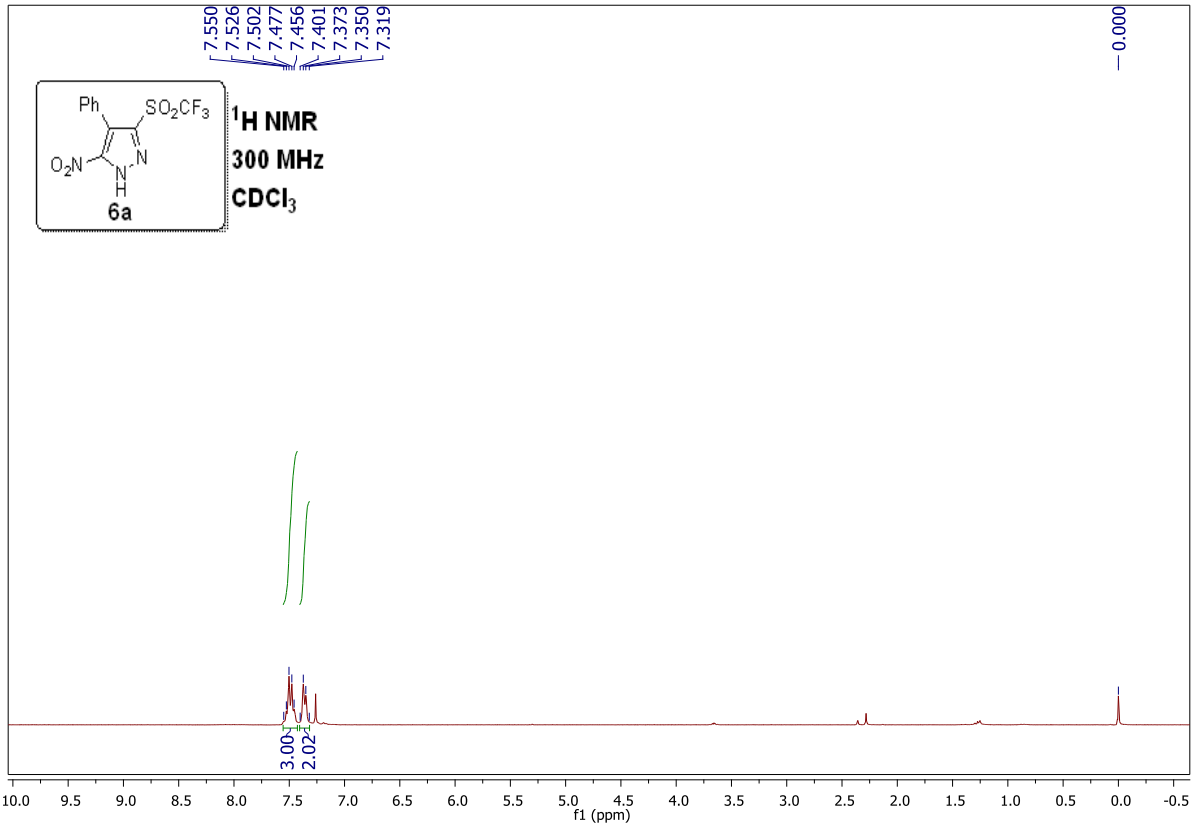
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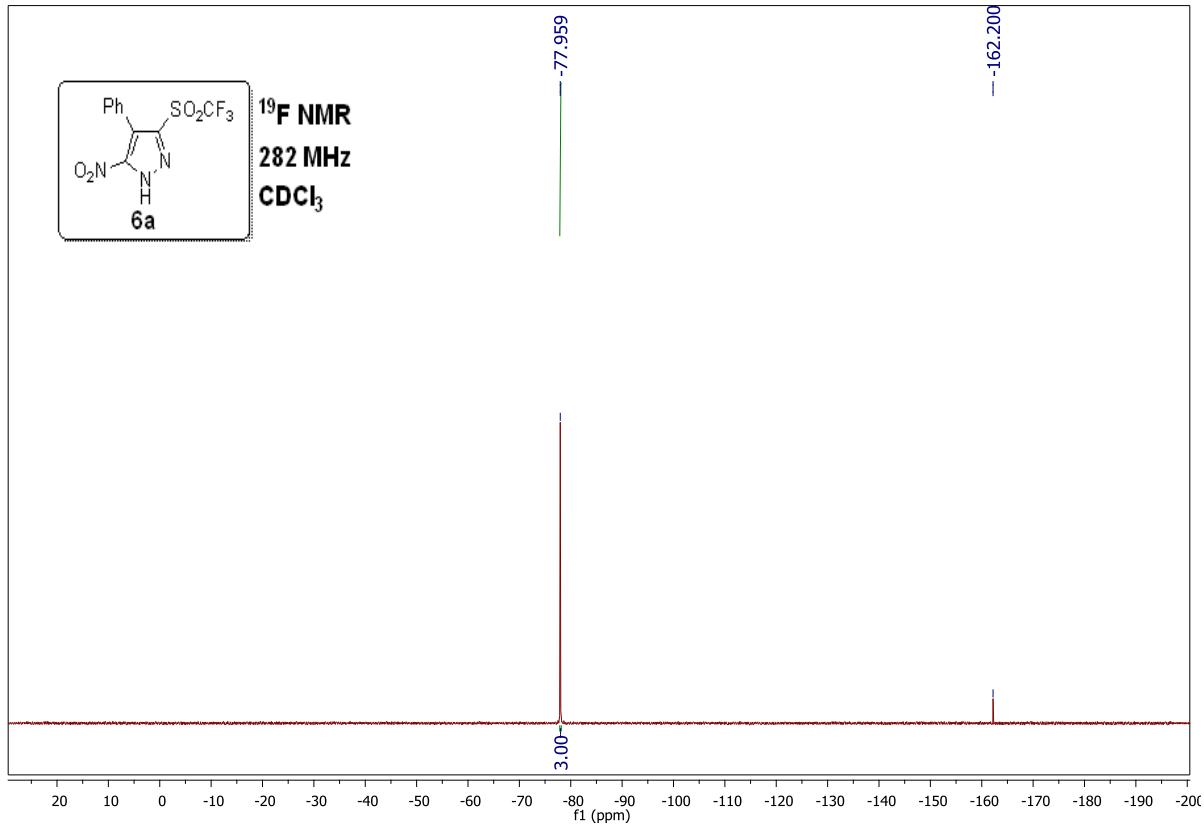
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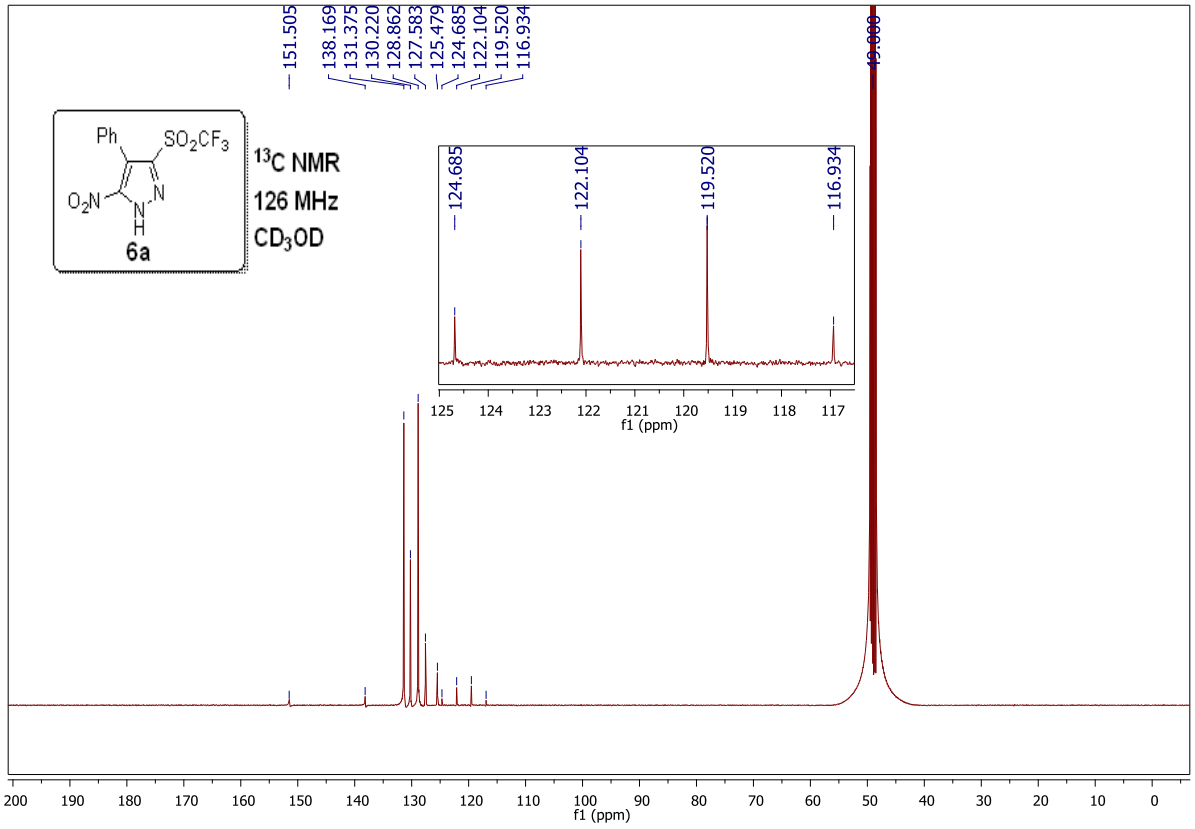
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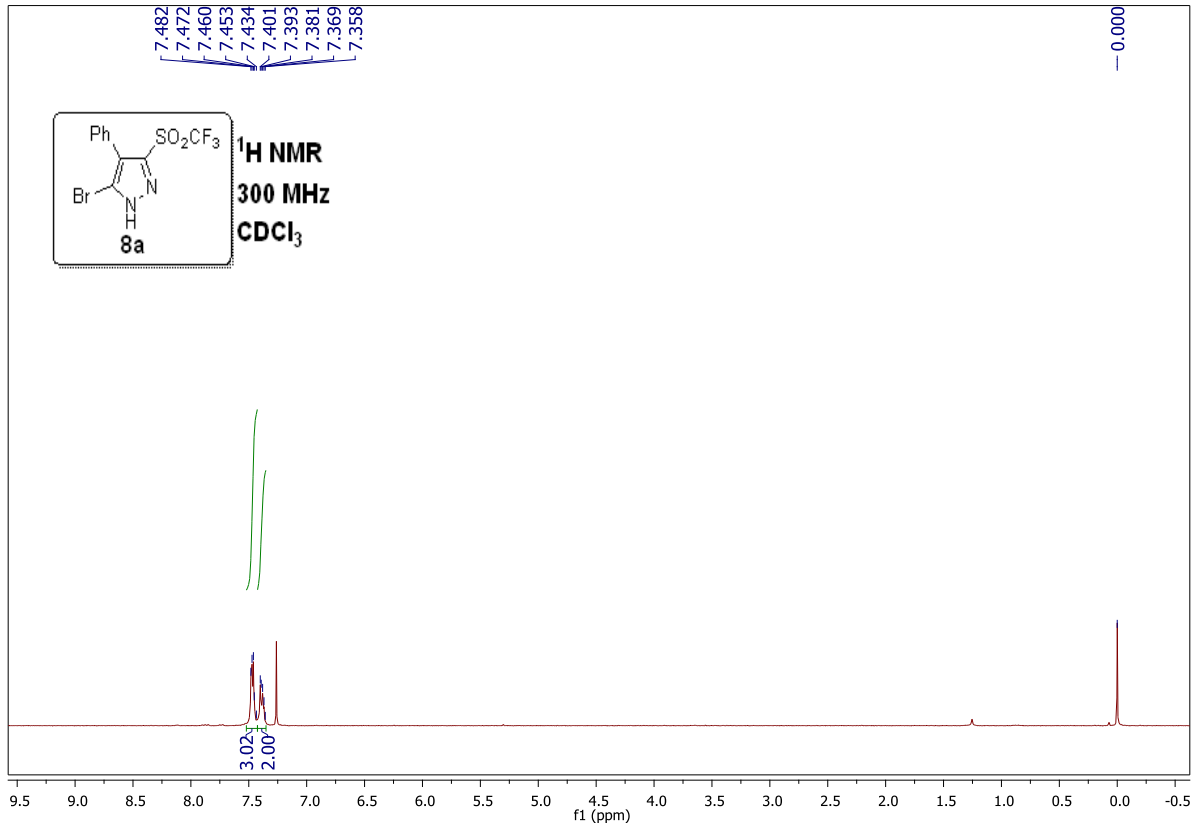
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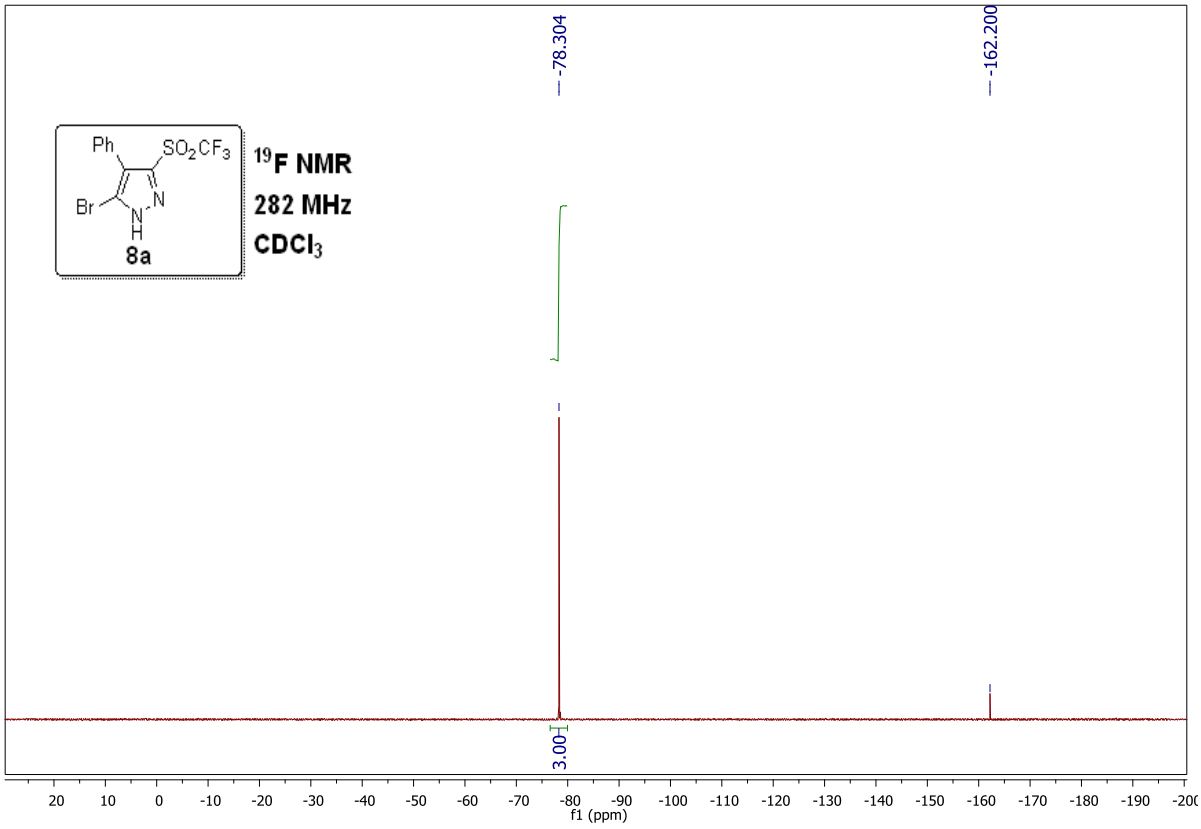
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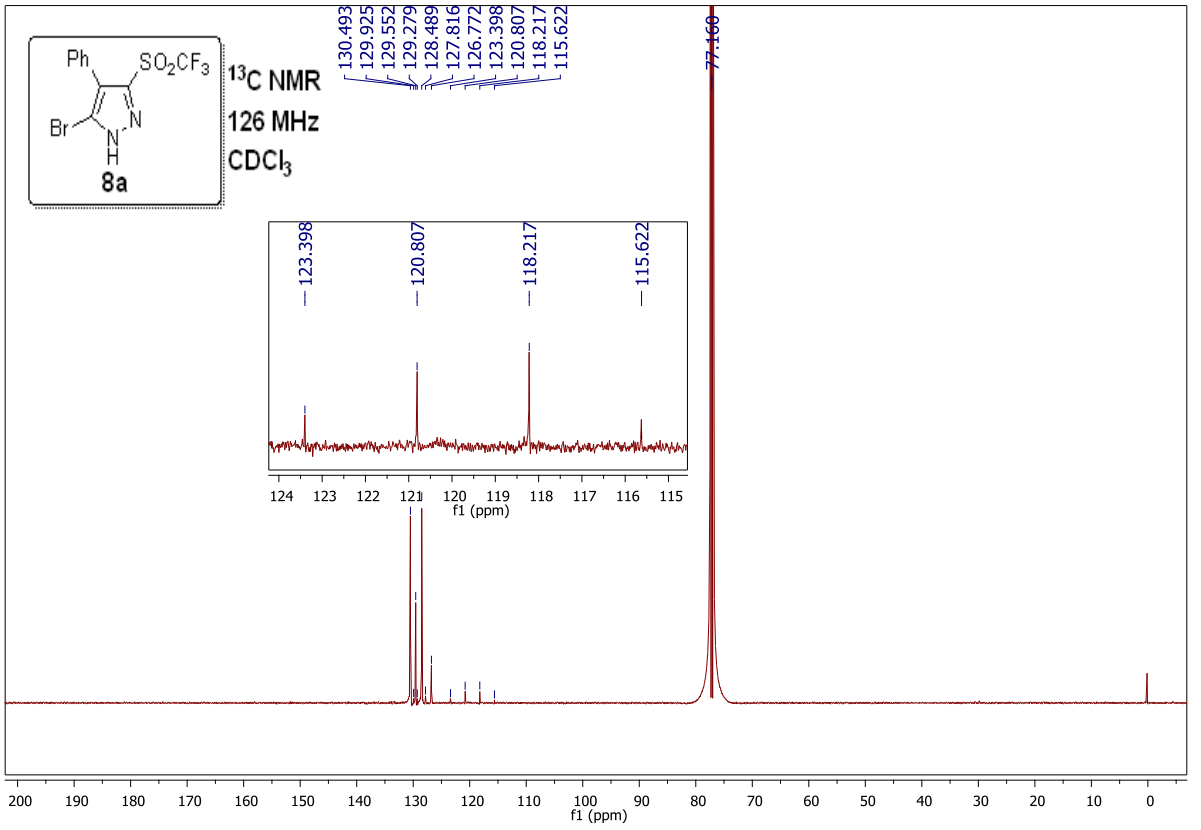
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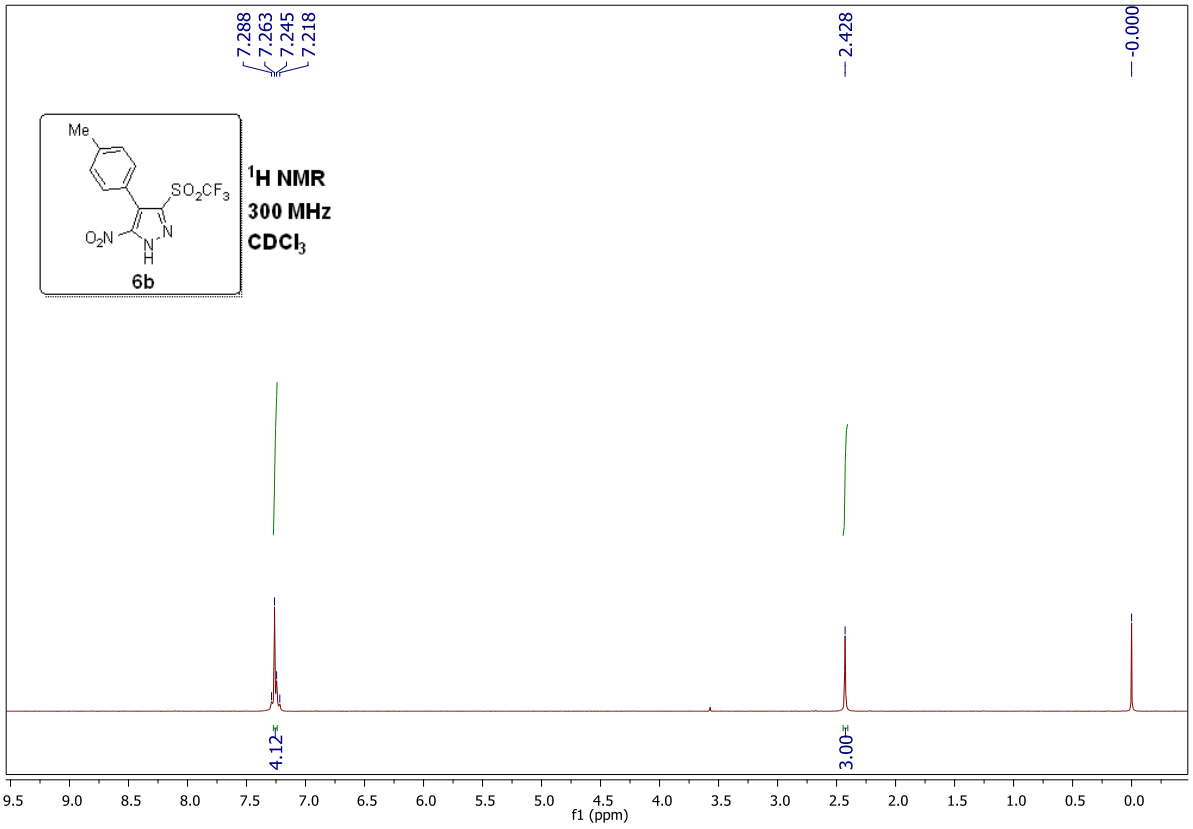
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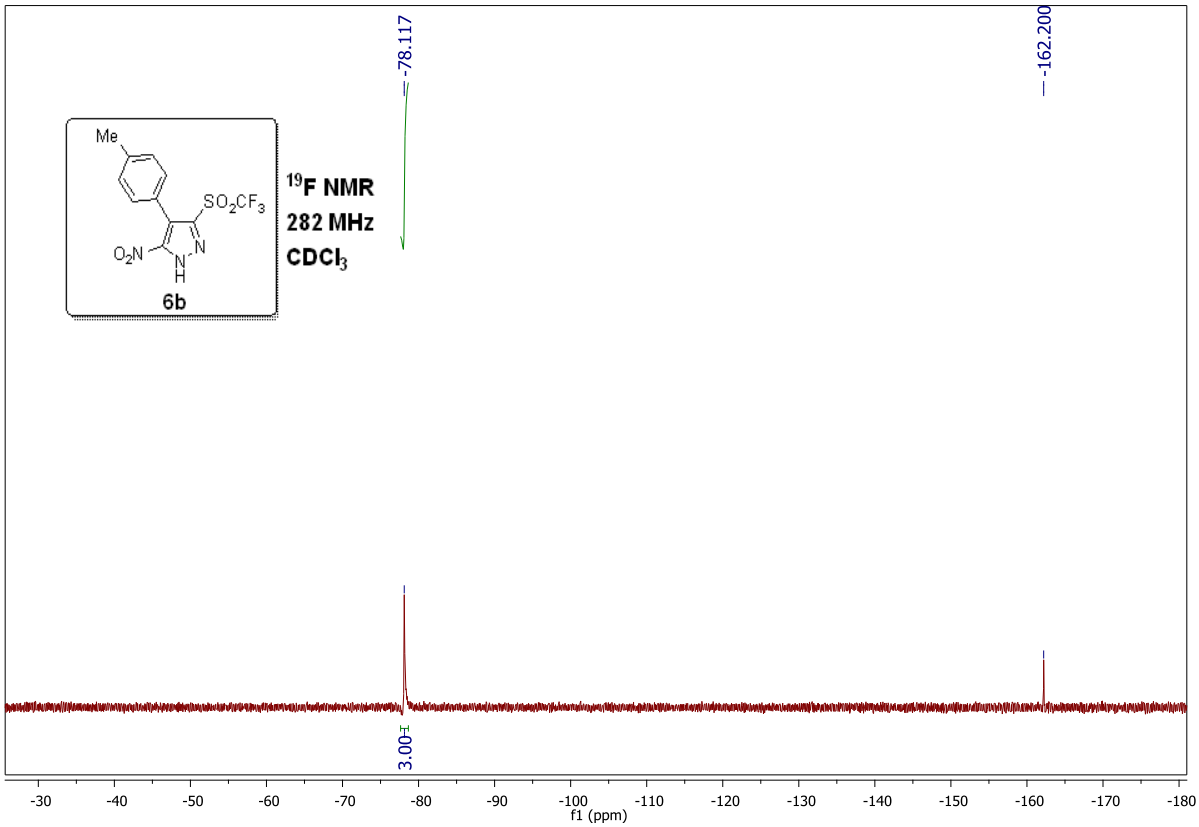
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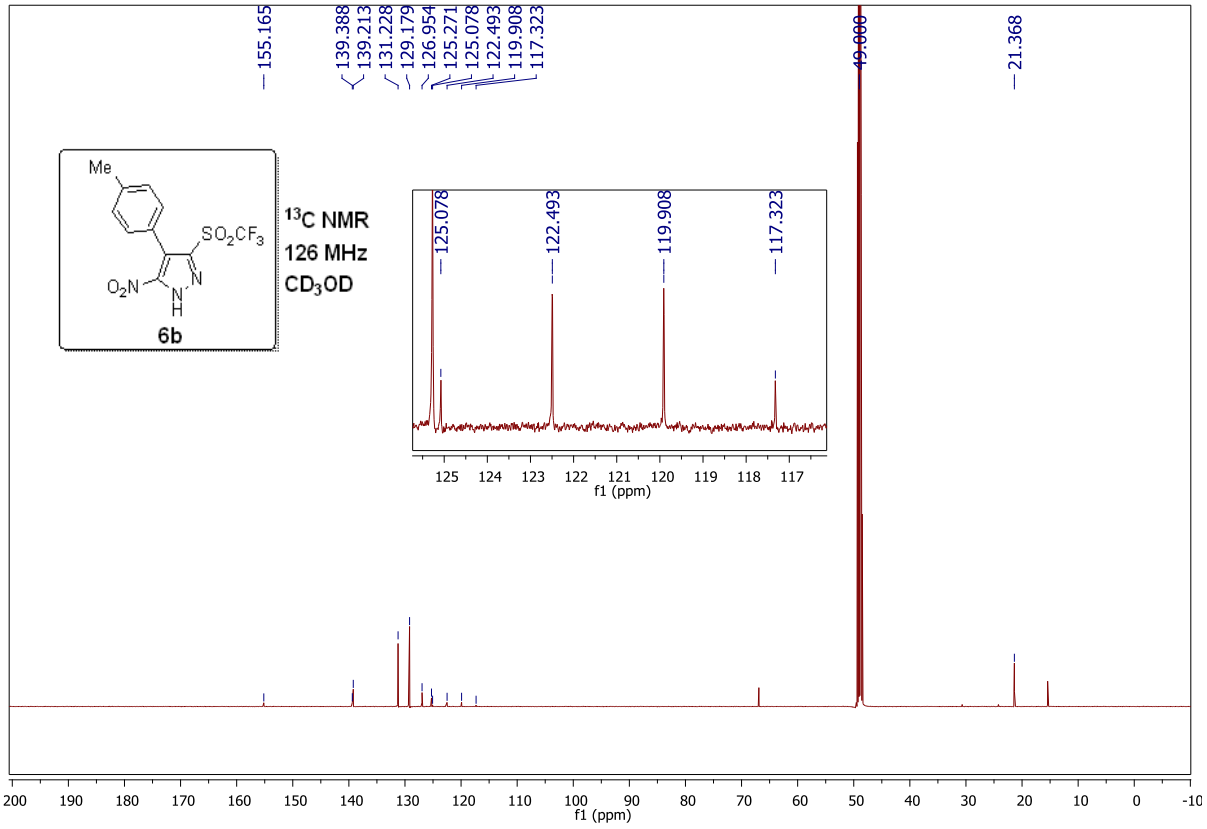
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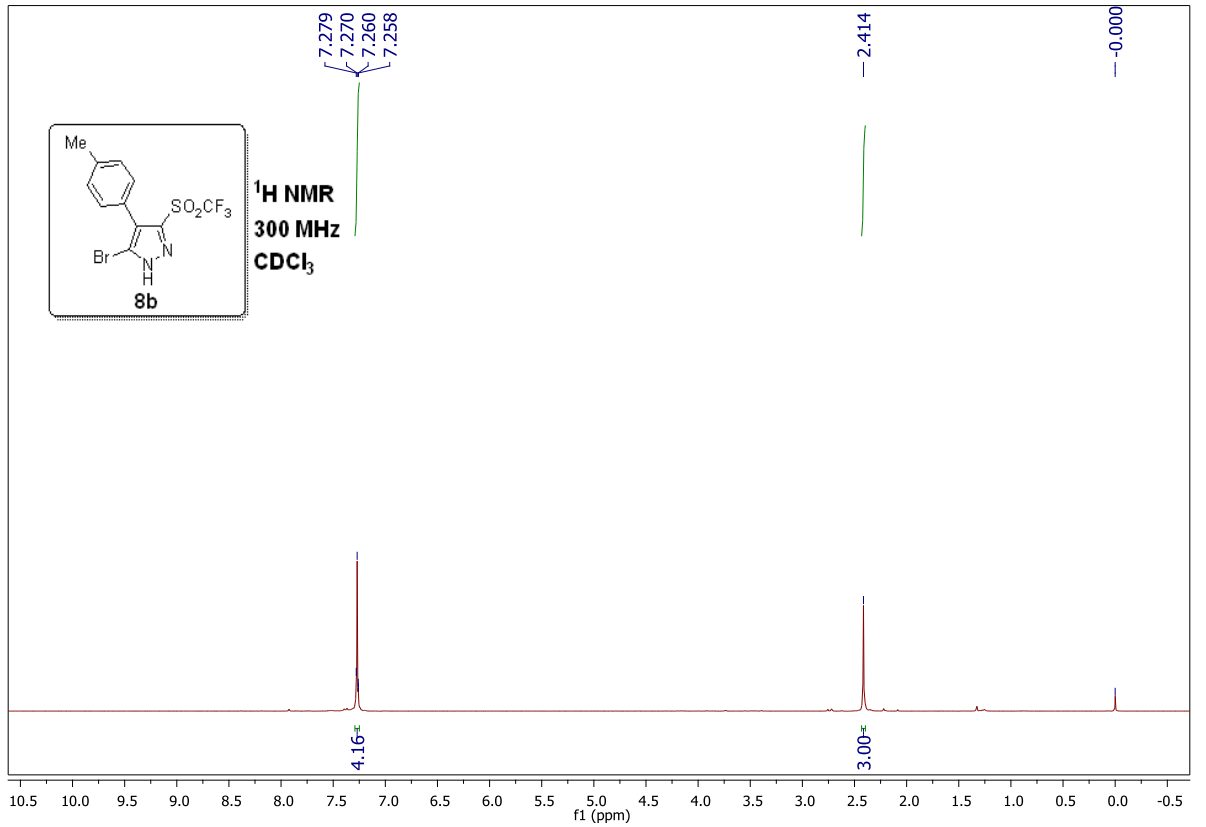
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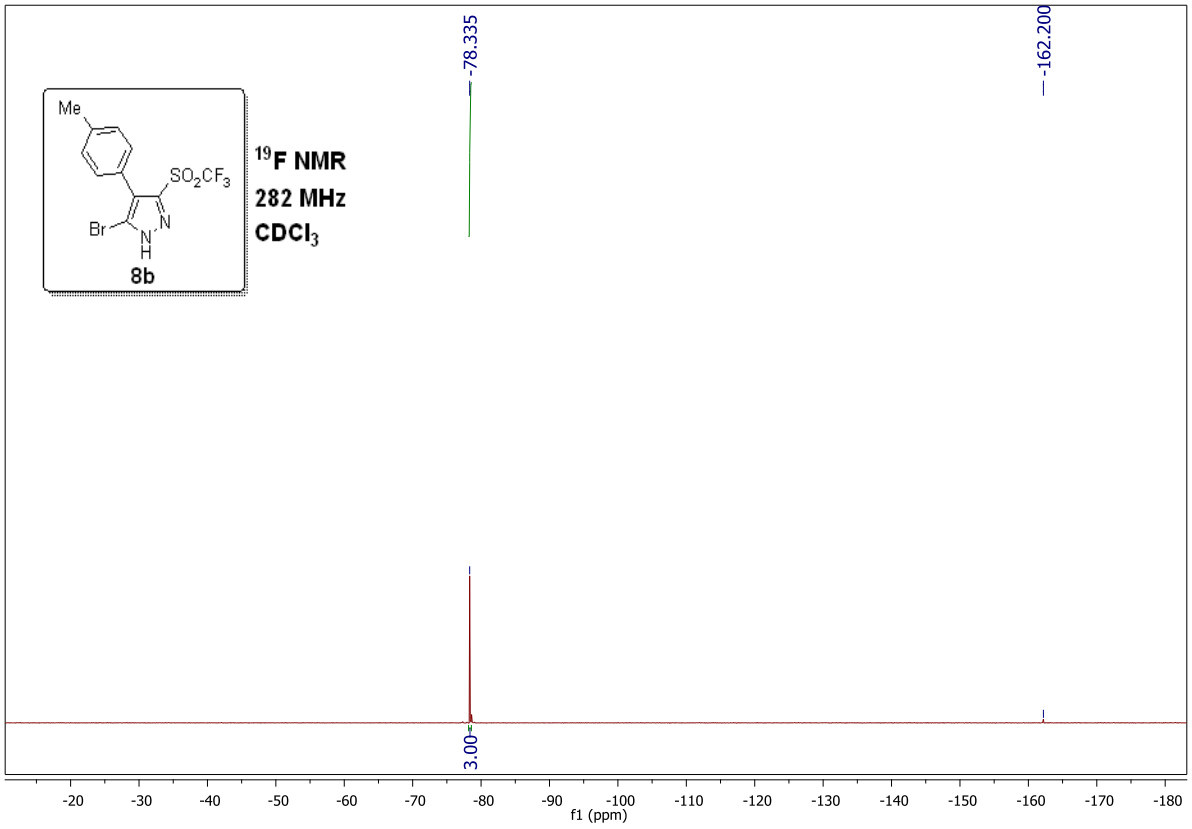
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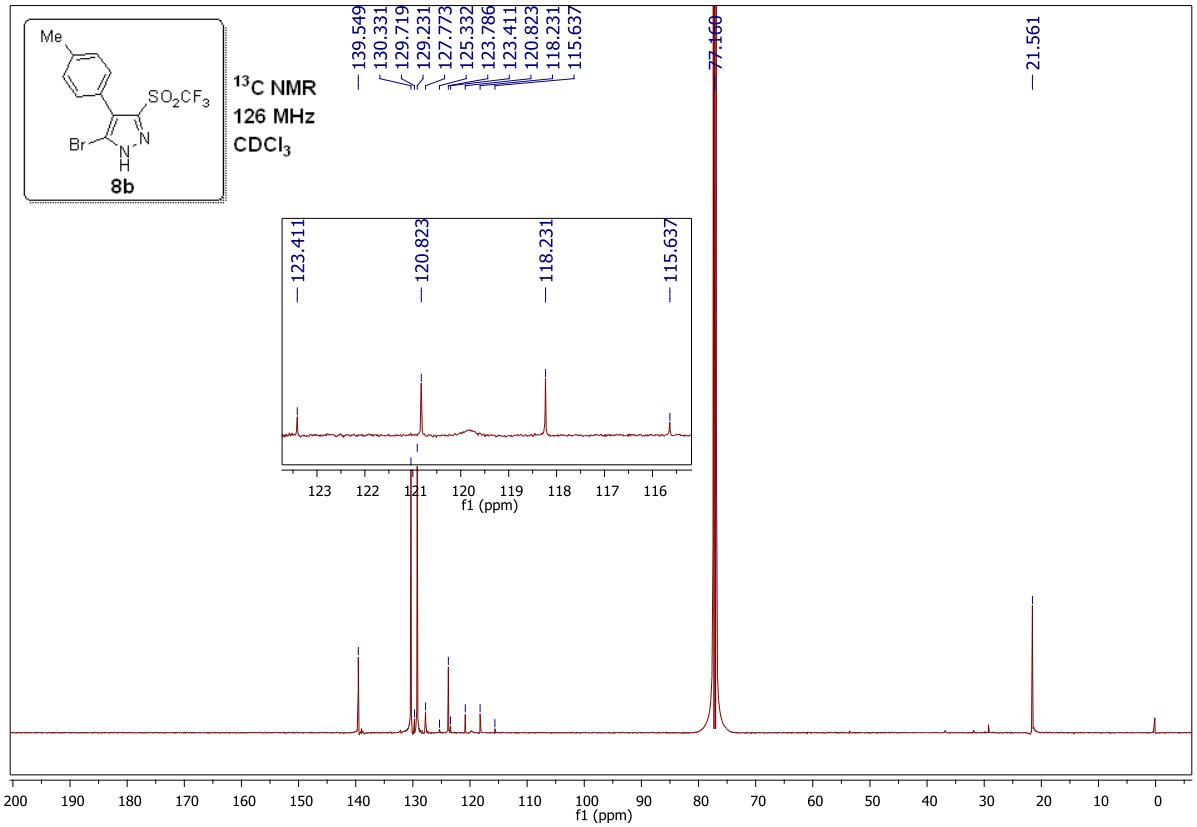
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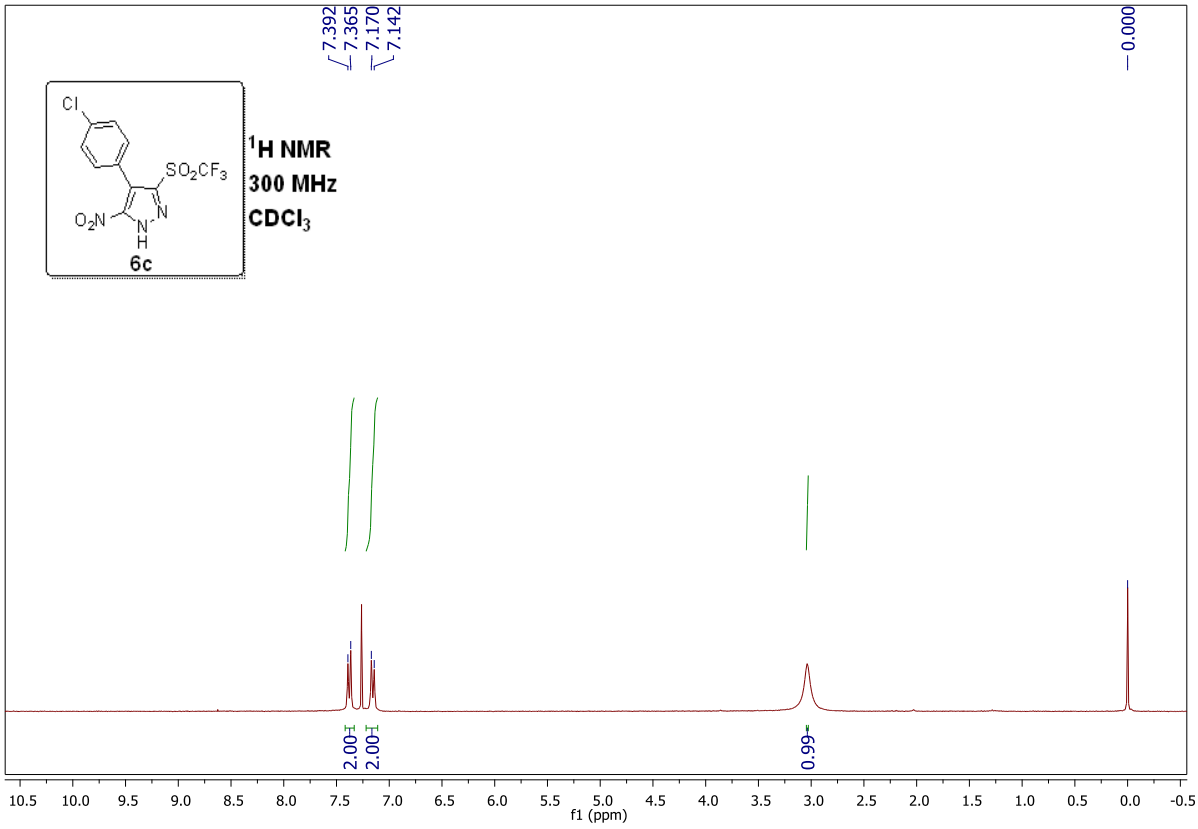
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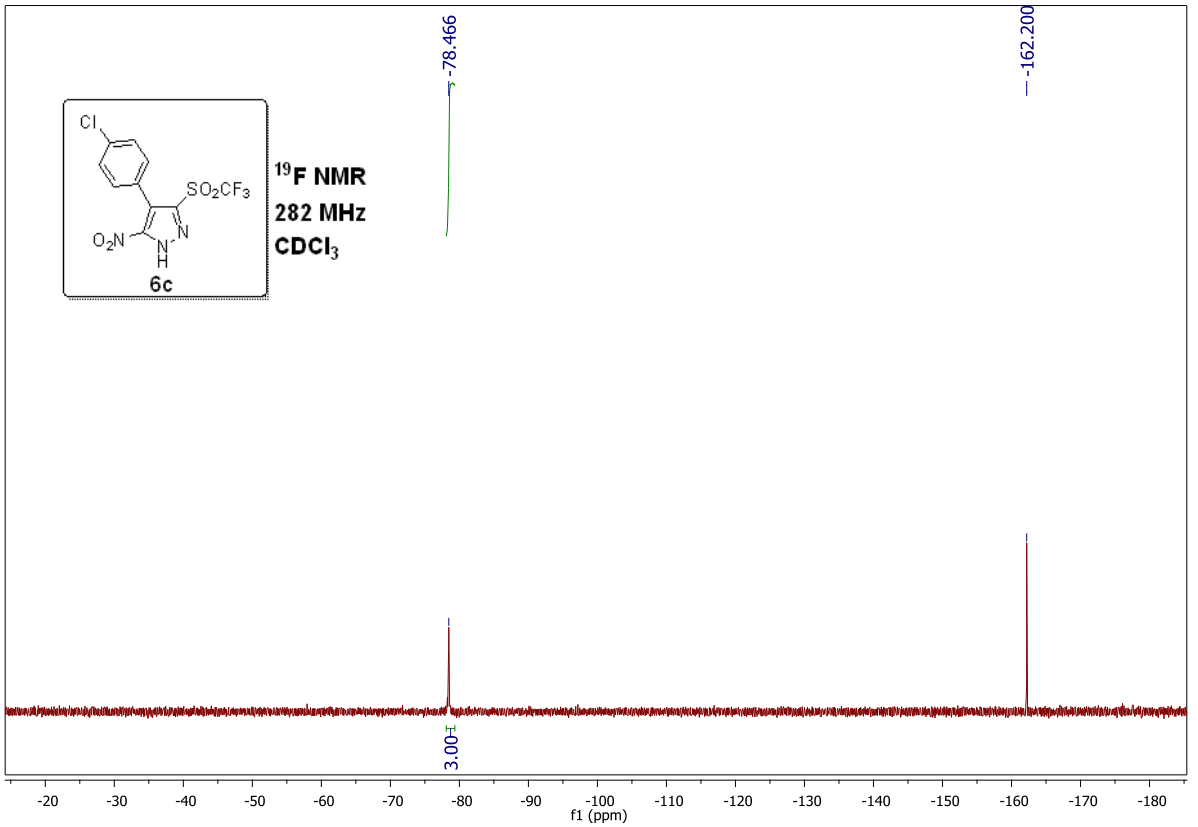
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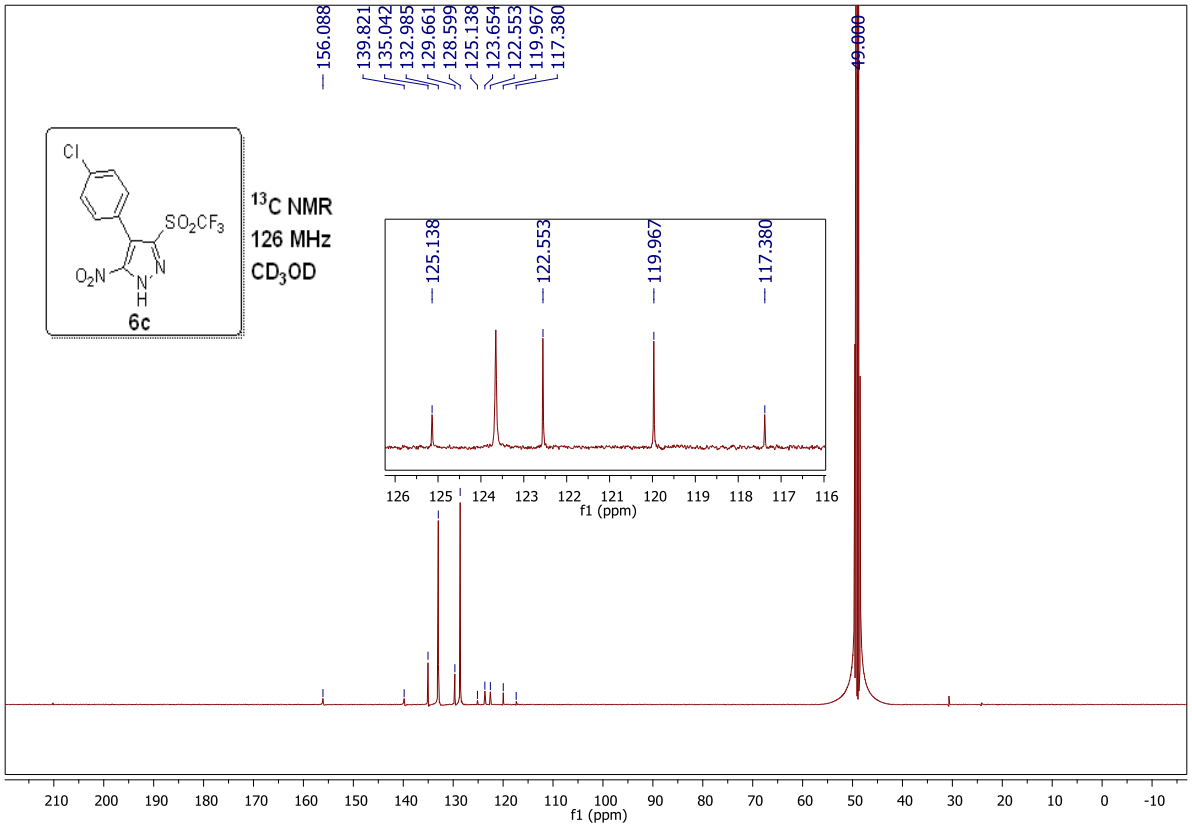
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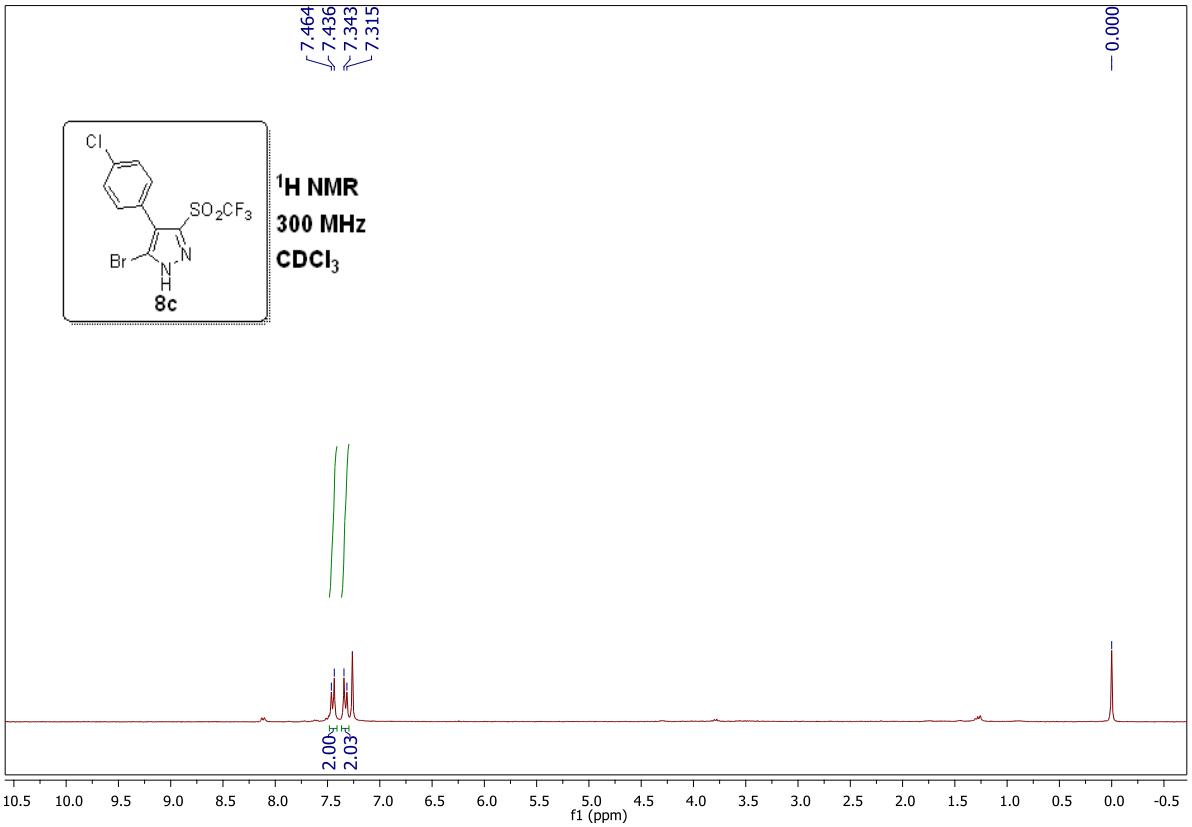
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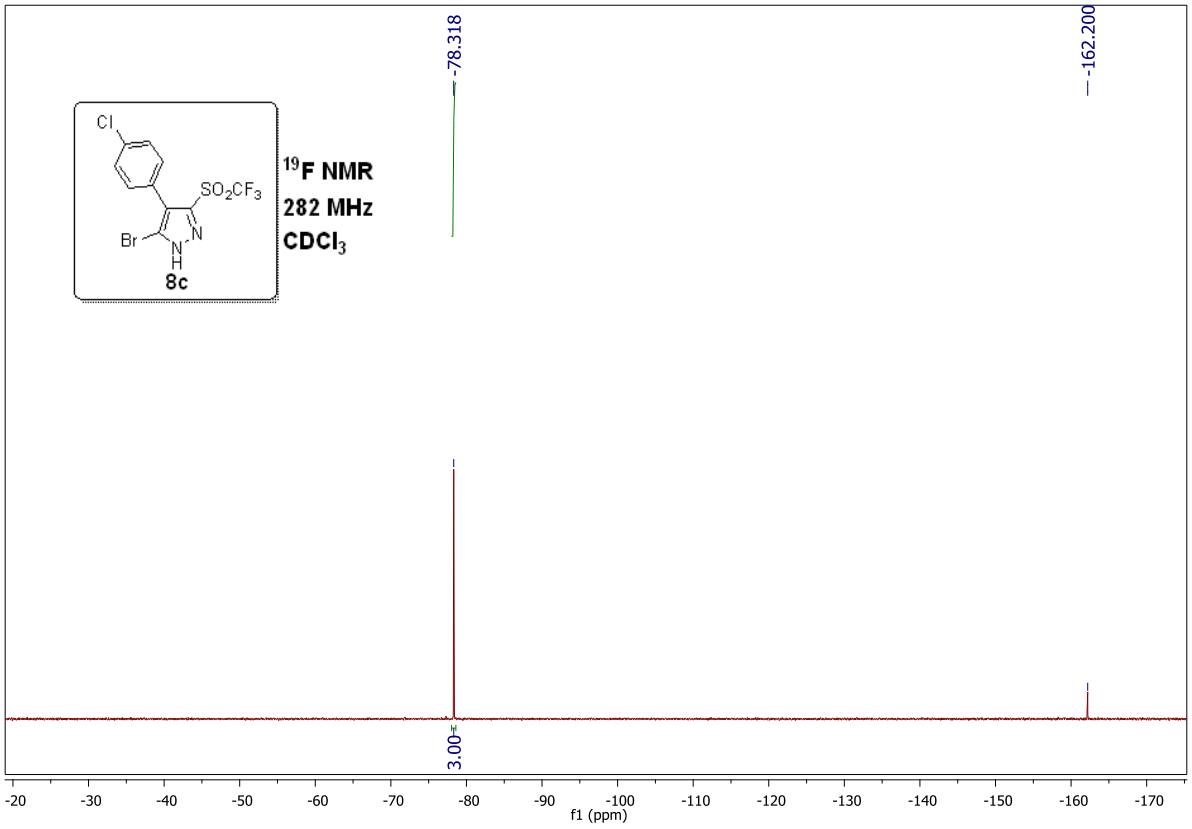
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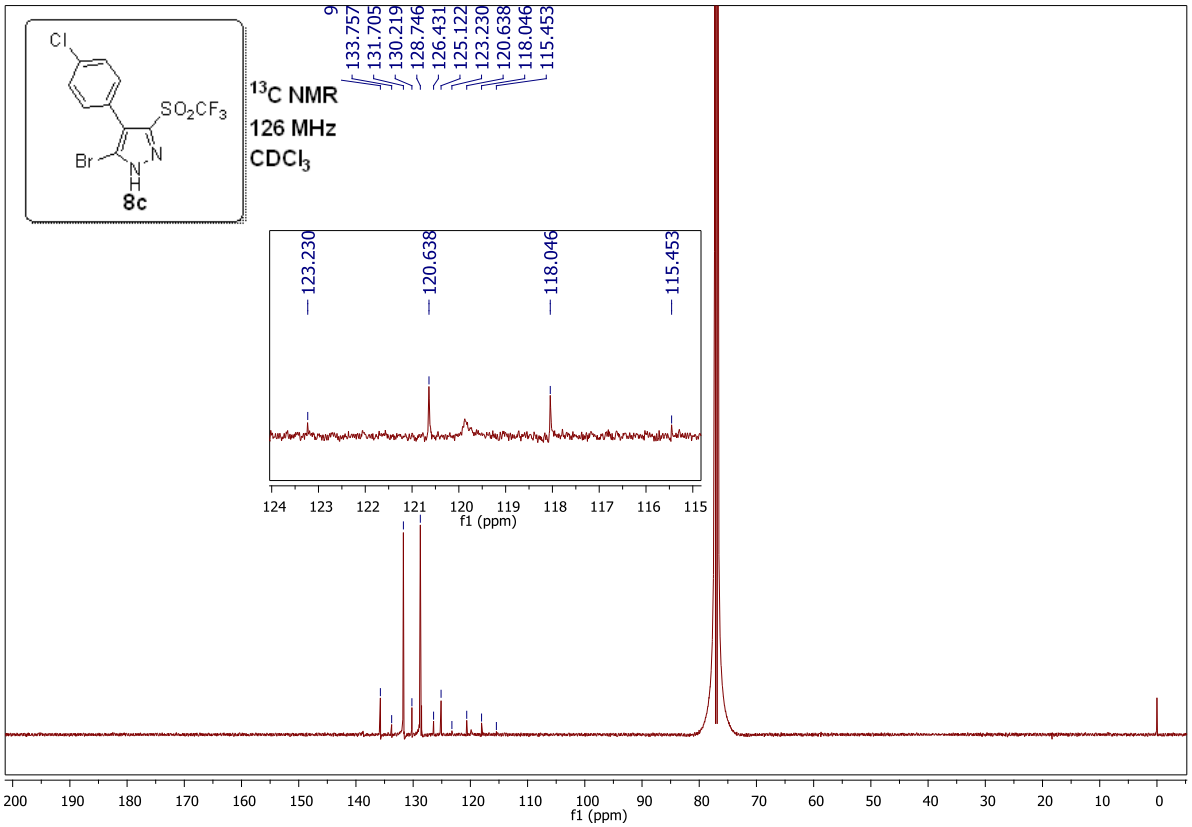
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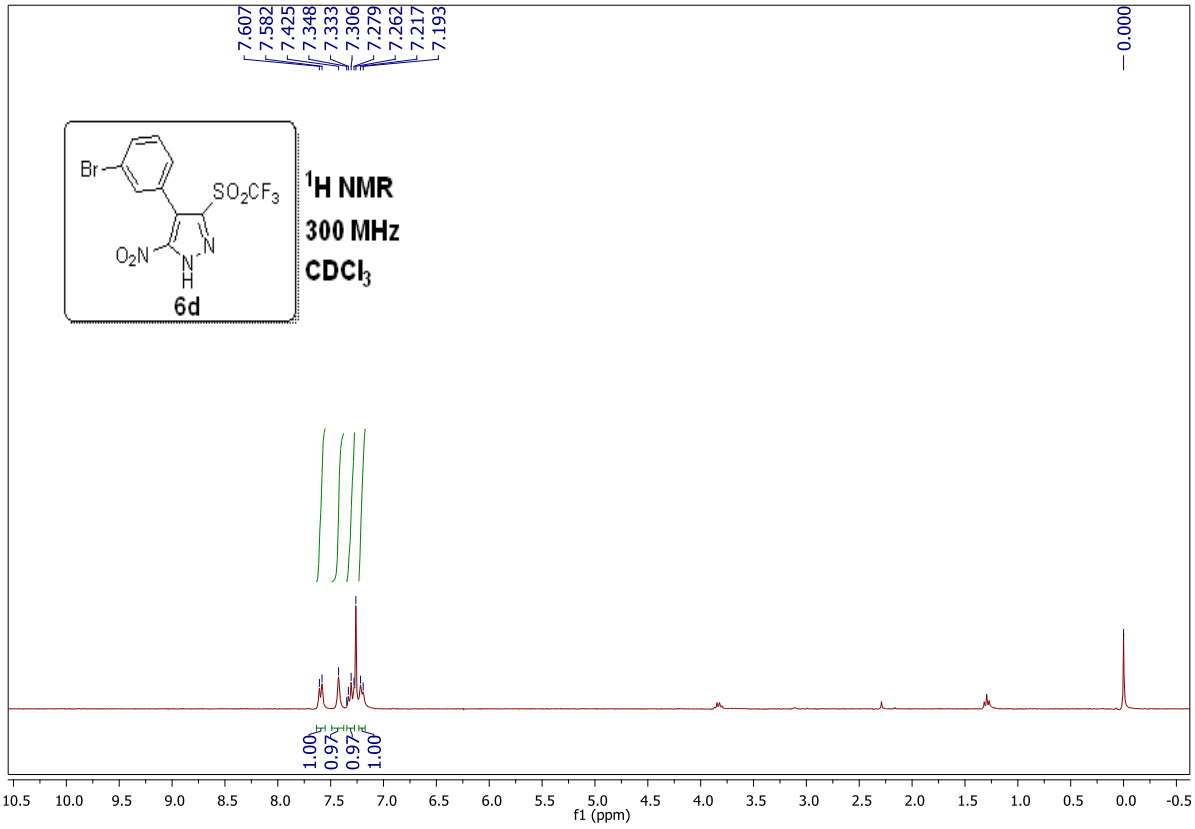
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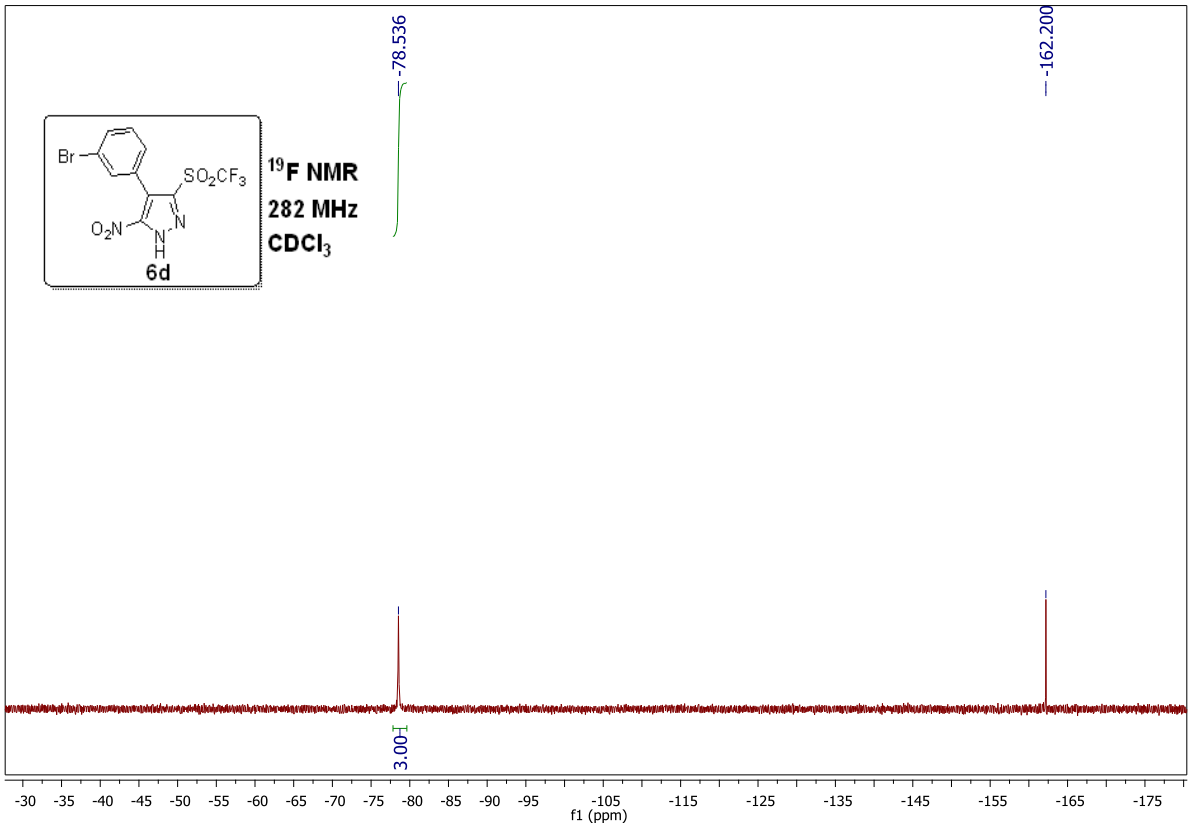
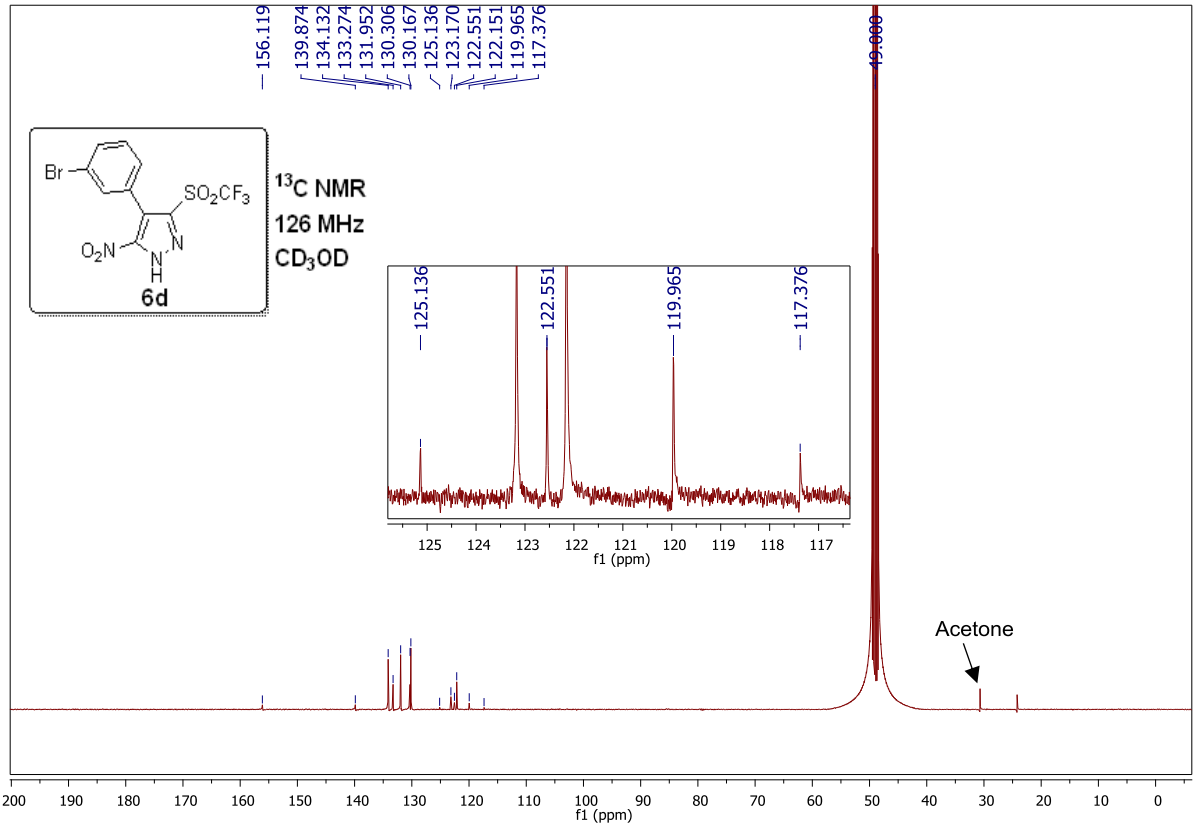
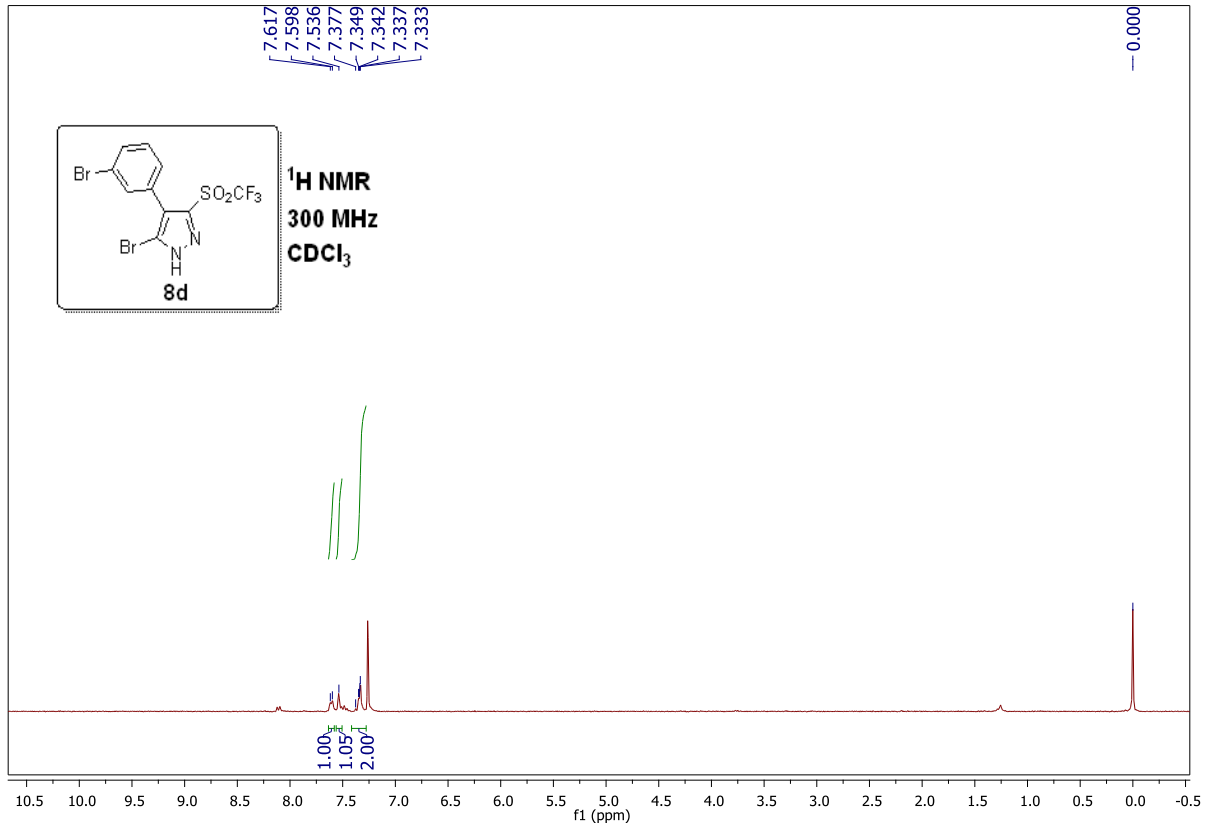
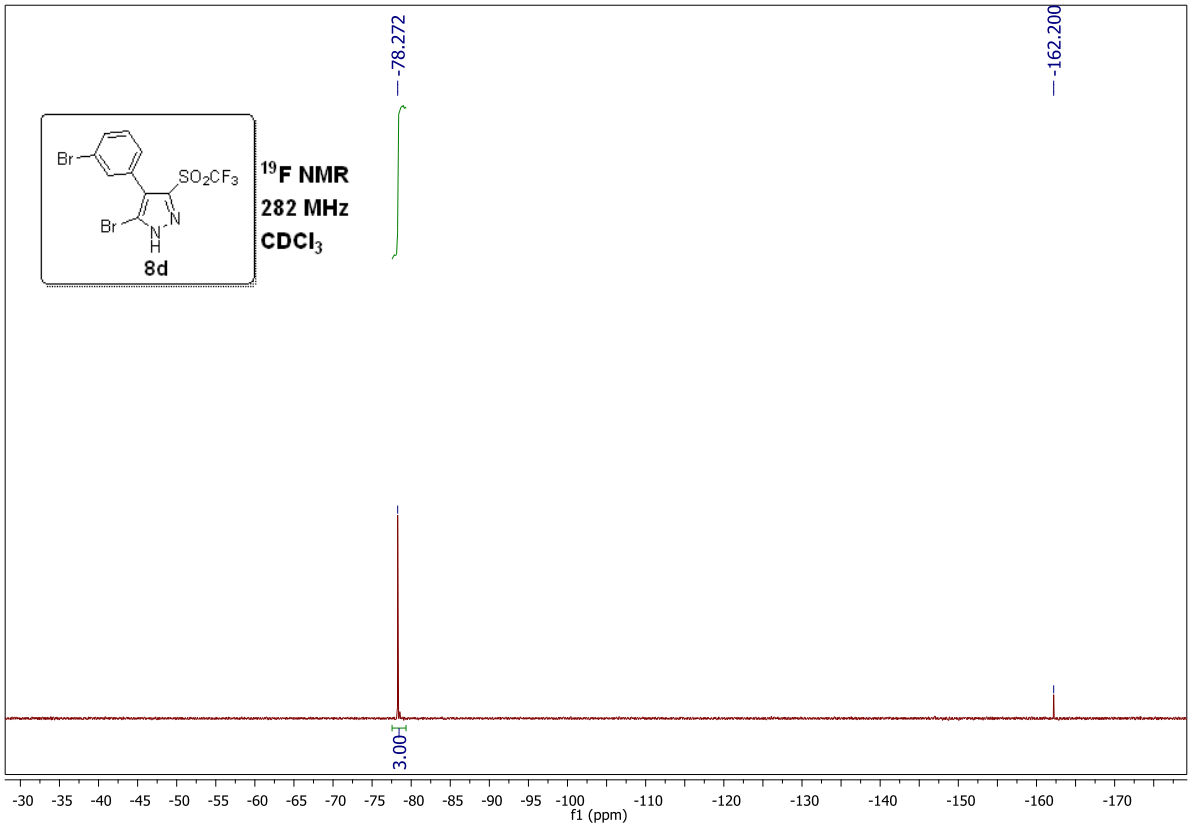
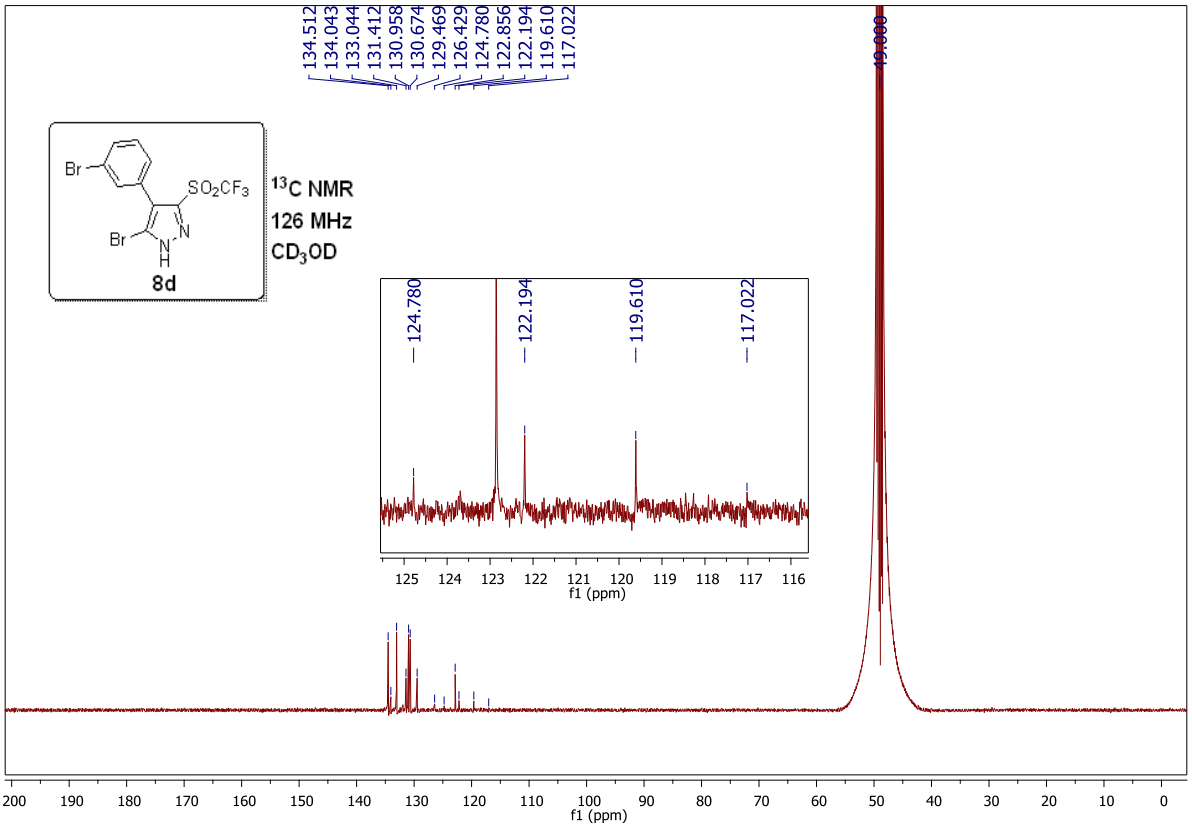
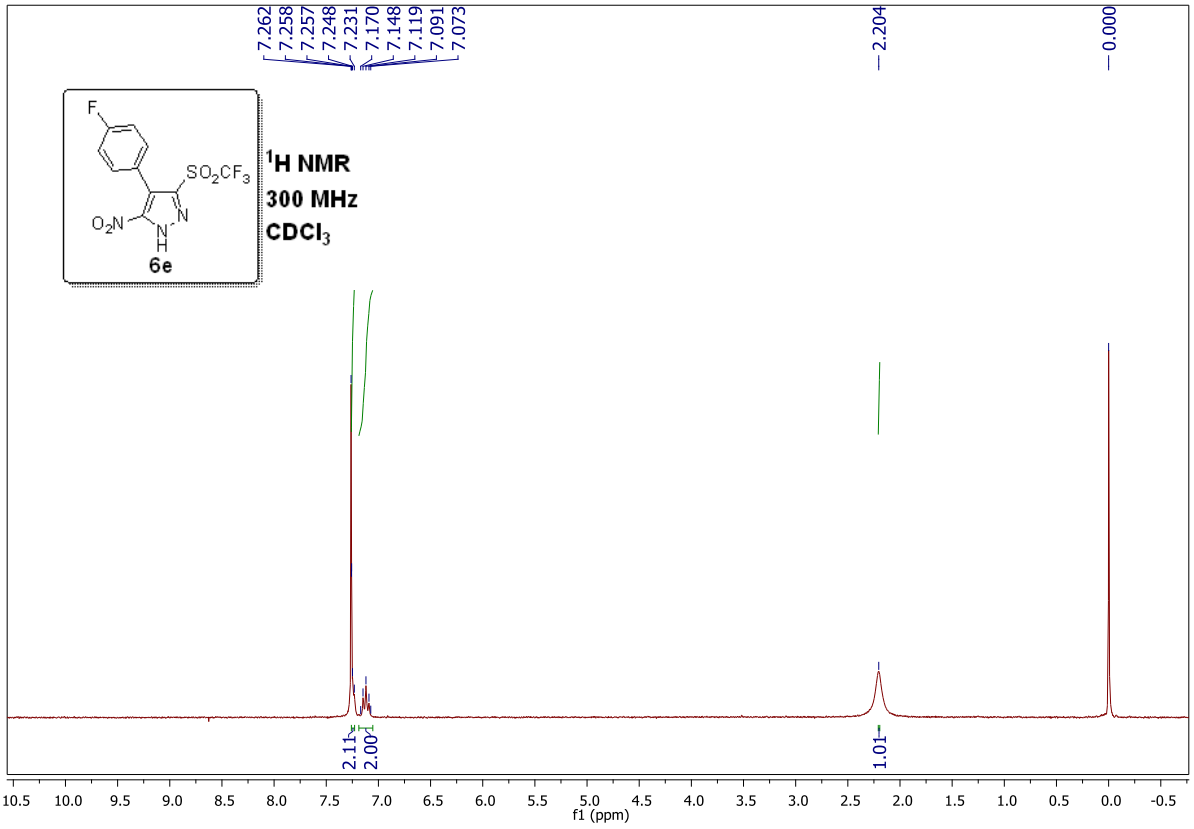

-78.536
-162.200
Br
SO2CF3
O2N
N
H
6d
19F NMR
282 MHz
CDCl3
3.00
f1 (ppm)

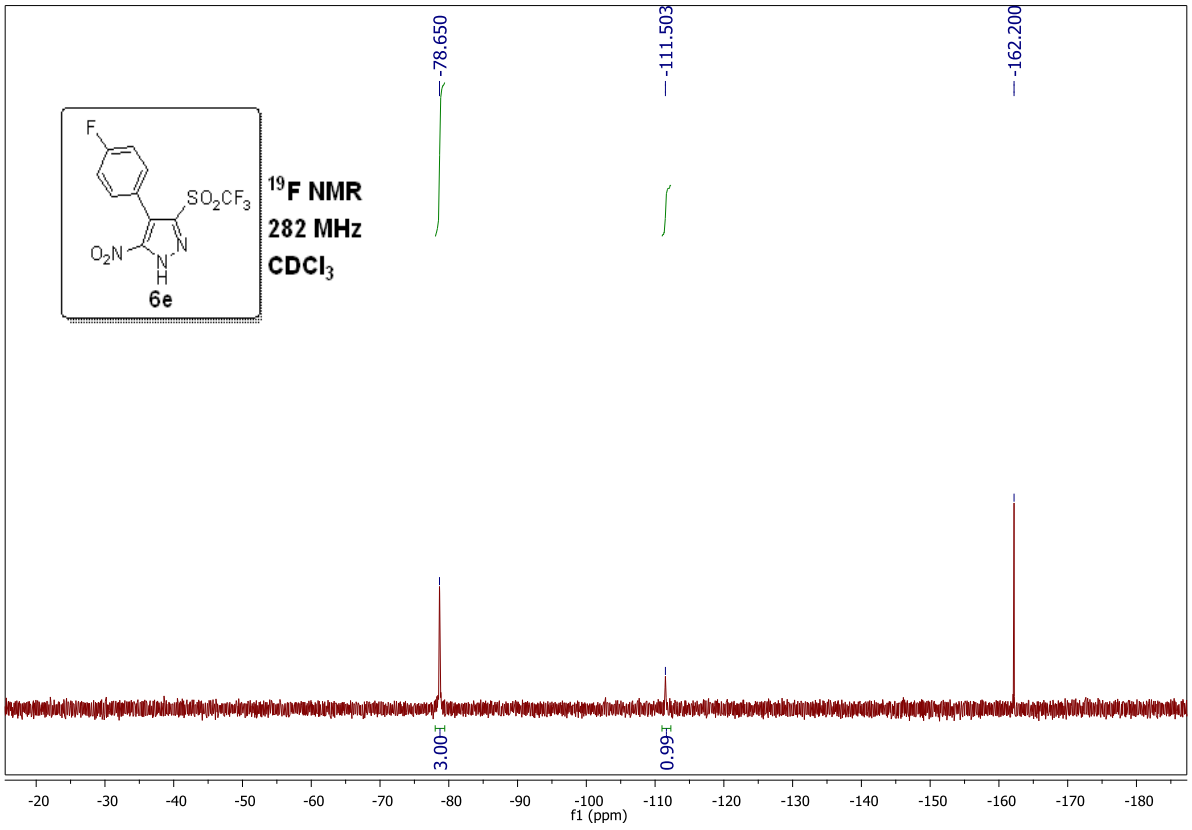

156.119
139.874
134.132
133.274
131.952
130.306
130.167
125.136
123.170
122.551
122.151
119.965
117.376
49.000
Br
SO2CF3
O2N
N
H
6d
13C NMR
126 MHz
CD3OD
125.136
122.551
119.965
117.376
125 124 123 122 121 120 119 118 117
f1 (ppm)
Acetone
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

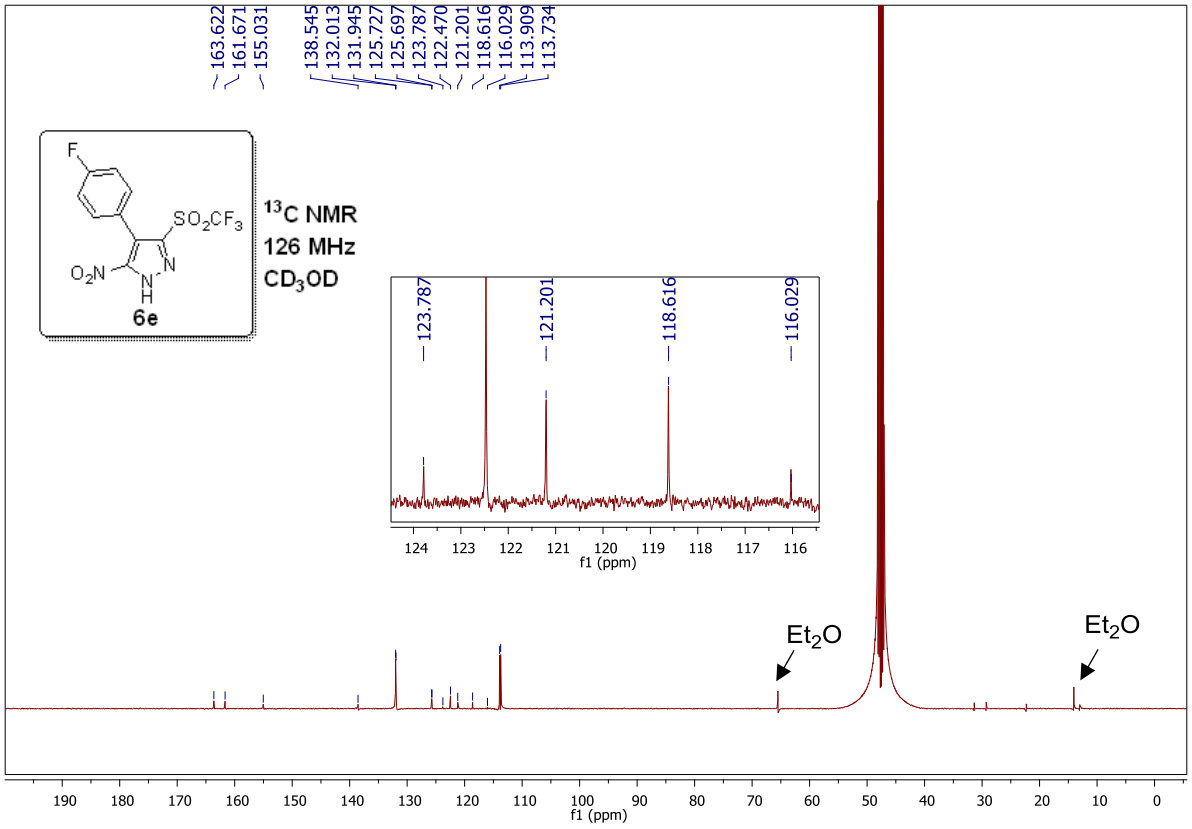

7.617
7.598
7.536
7.377
7.349
7.342
7.337
7.333
0.000
Br
SO2CF3
Br
N
H
8d
1H NMR
300 MHz
CDCl3
1.00
1.05
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

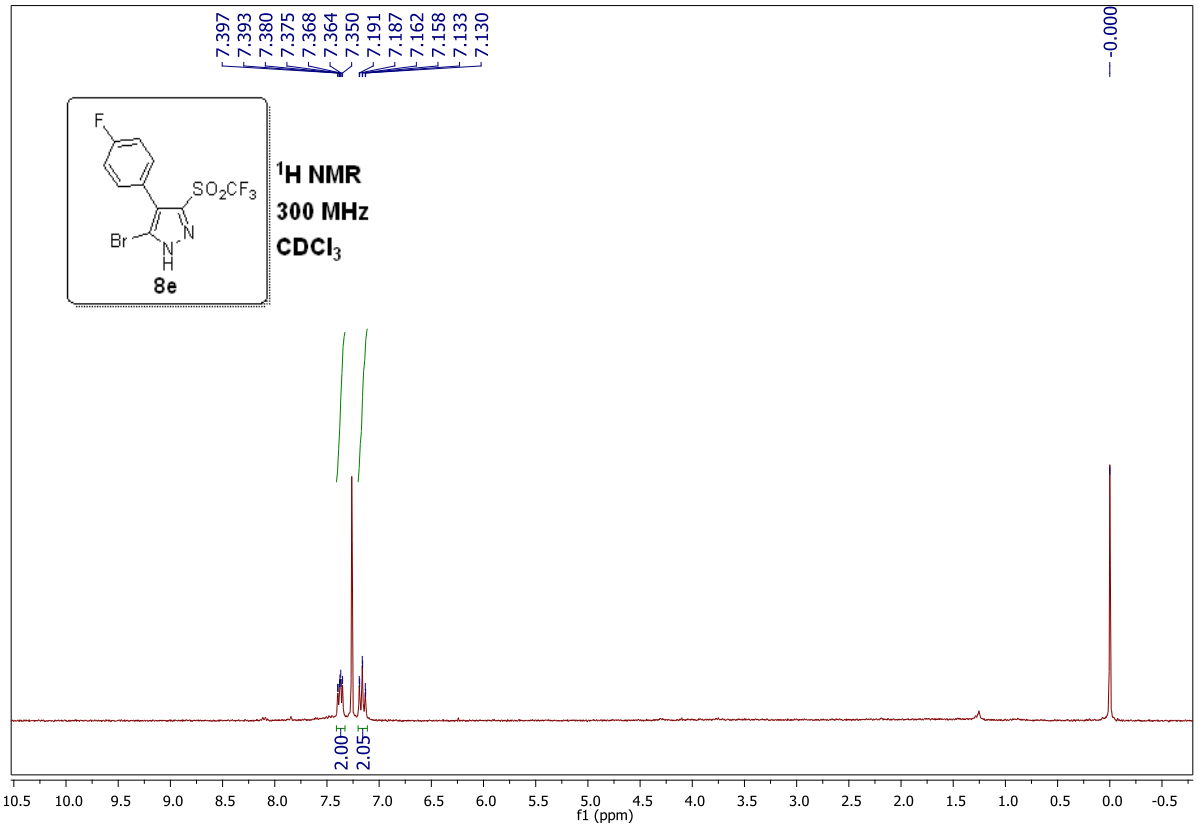

-78.272
-162.200
Br
SO2CF3
Br
N
H
8d
19F NMR
282 MHz
CDCl3
3.00
-30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -110 -120 -130 -140 -150 -160 -170
f1 (ppm)

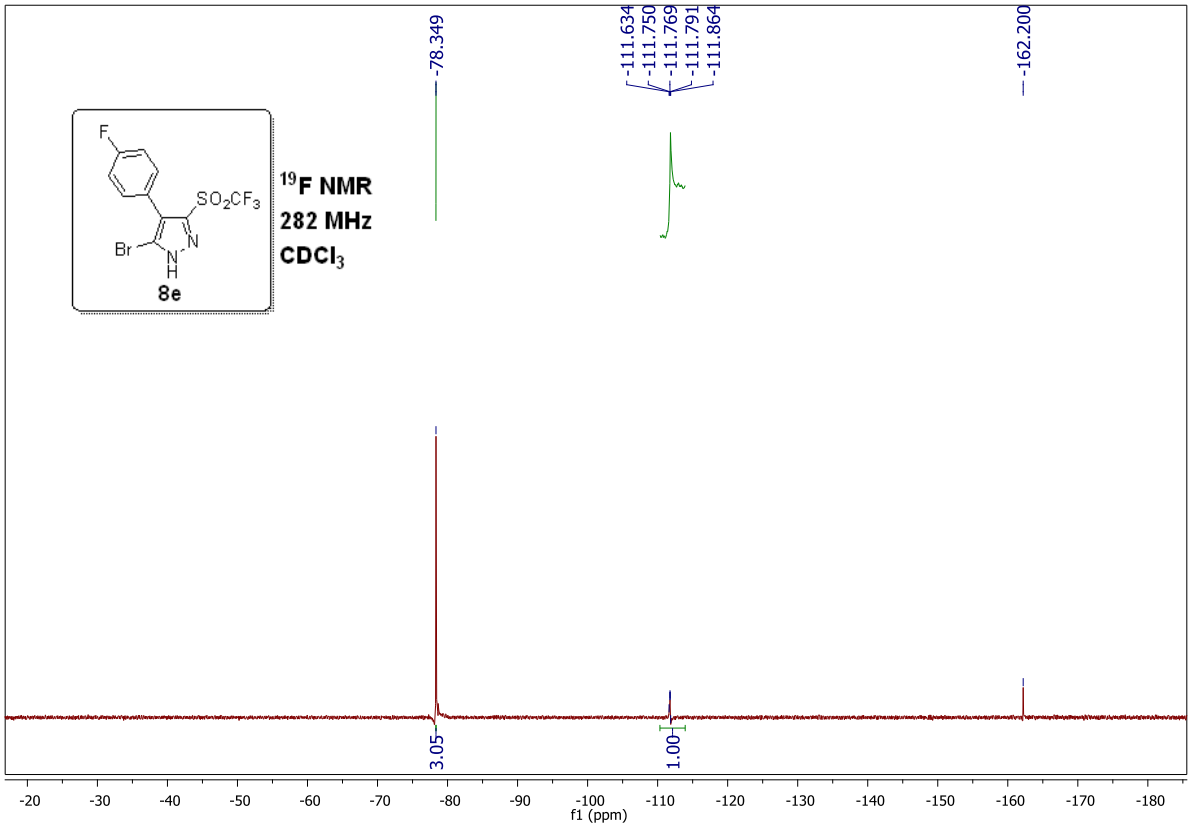

134.512
134.043
133.044
131.412
130.958
130.674
129.469
126.429
124.780
122.856
122.194
119.610
117.022
49.000
Br
SO2CF3
Br
N
H
8d
13C NMR
126 MHz
CD3OD
124.780
122.194
119.610
117.022
125 124 123 122 121 120 119 118 117 116
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

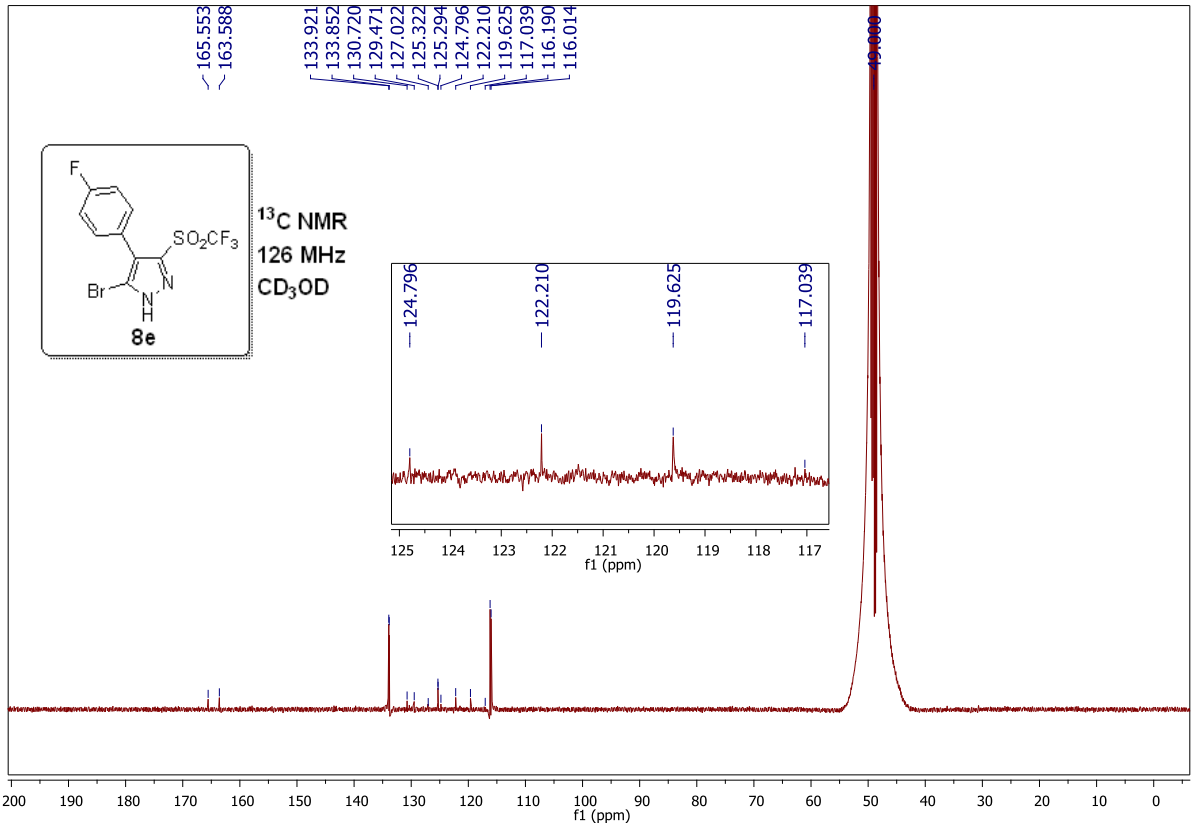

7.262
7.258
7.257
7.248
7.231
7.170
7.148
7.119
7.091
7.073
2.204
0.000
F
SO2CF3
O2N
N
N
H
6e
1H NMR
300 MHz
CDCl3
2.11
2.00
1.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

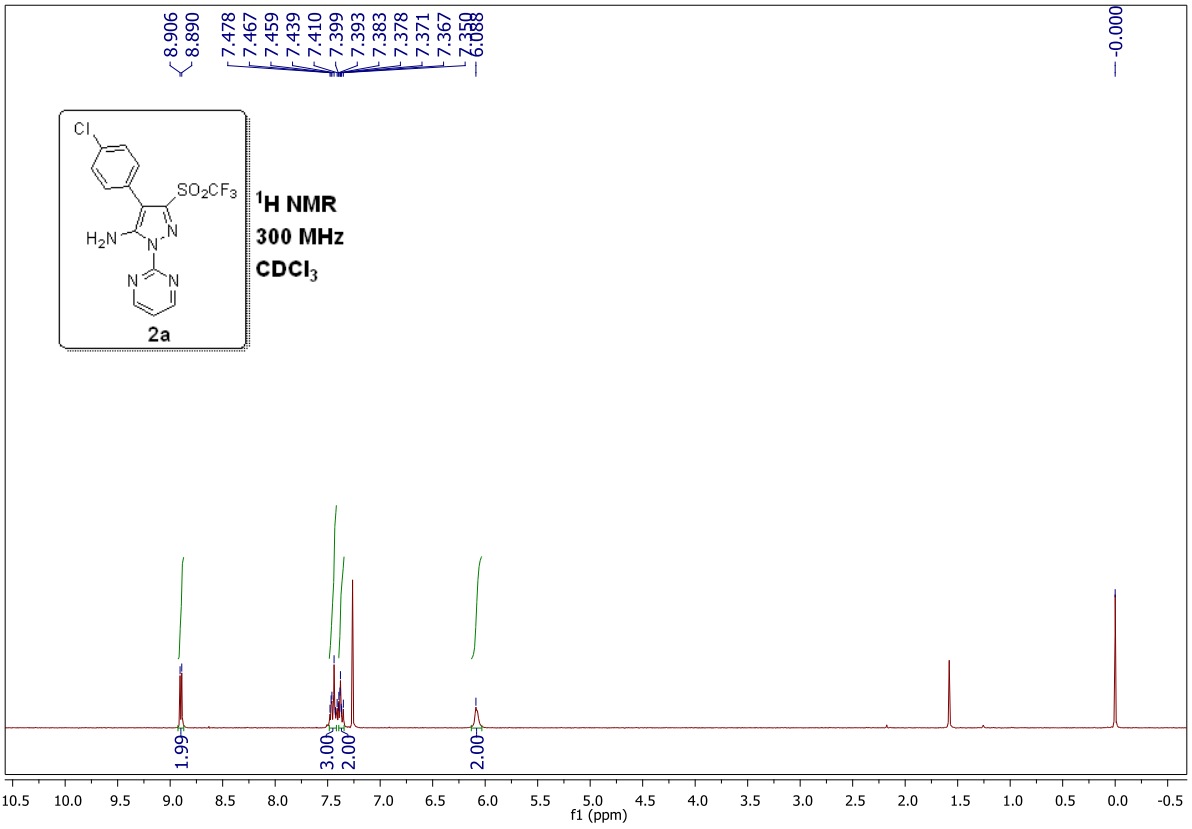

-78.650
-111.503
-162.200
F
SO2CF3
O2N
N
N
H
6e
19F NMR
282 MHz
CDCl3
3.00
0.99
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)

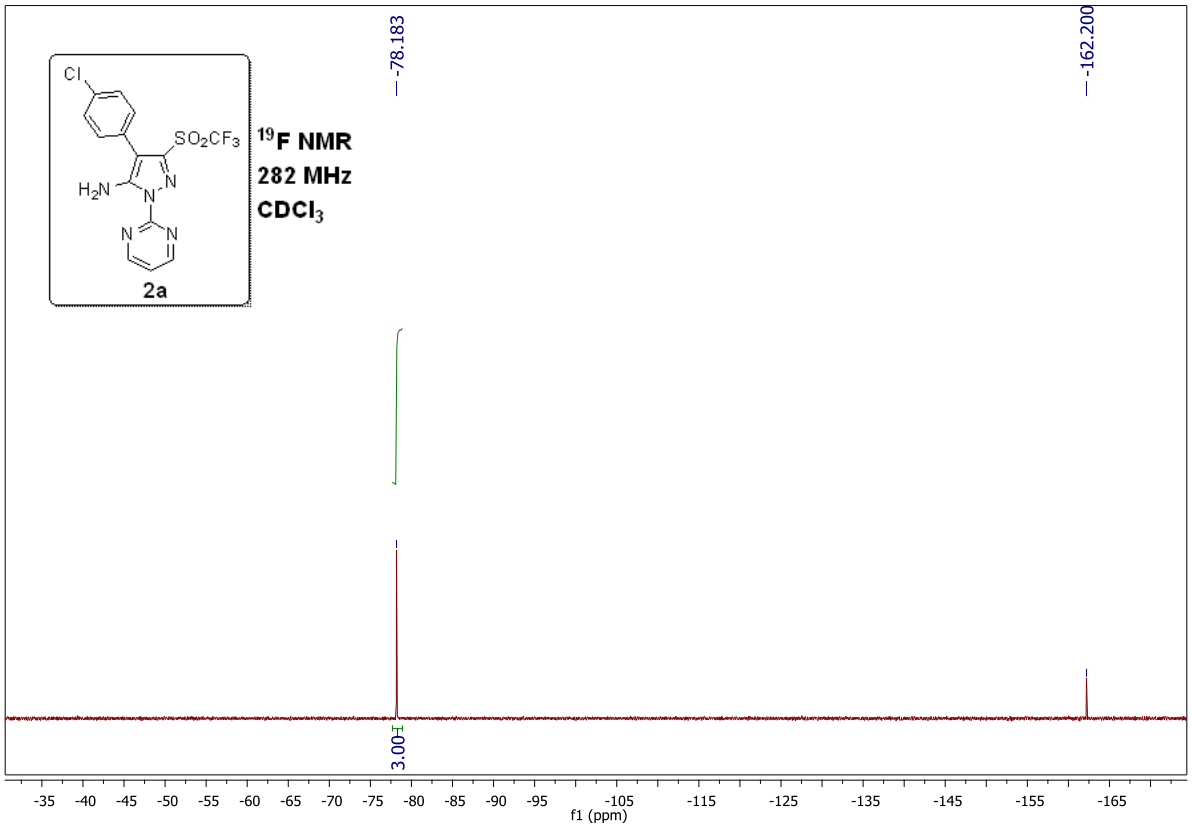

163.622
161.671
155.031
138.545
132.013
131.945
125.727
125.697
123.787
122.470
121.201
118.616
116.029
113.909
113.734
F
SO2CF3
O2N
N
H
6e
13C NMR
126 MHz
CD3OD
123.787
121.201
118.616
116.029
124 123 122 121 120 119 118 117 116
f1 (ppm)
Et2O
Et2O
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

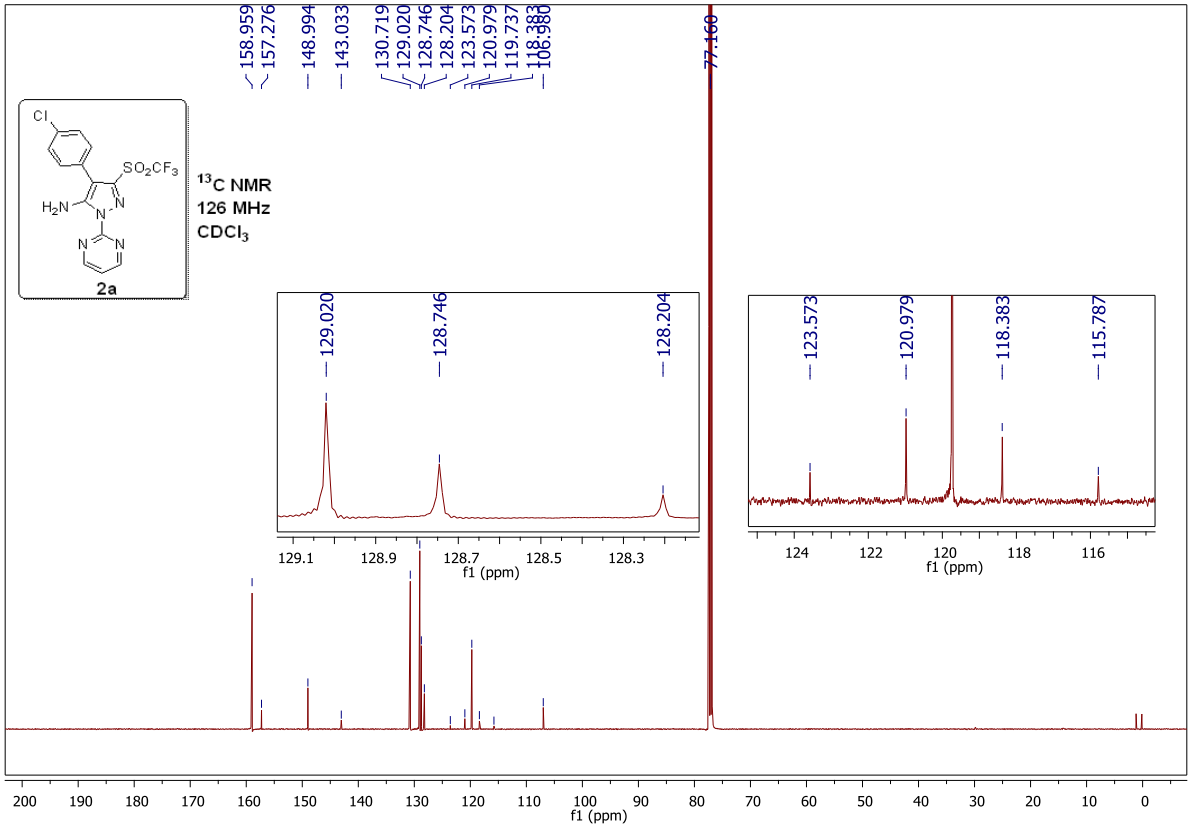

7.397
7.393
7.380
7.375
7.368
7.364
7.350
7.191
7.187
7.162
7.158
7.133
7.130
-0.000
F
SO2CF3
Br
N
H
8e
1H NMR
300 MHz
CDCl3
2.00
2.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


-78.349
-111.634
-111.750
-111.769
-111.791
-111.864
-162.200
F
SO2CF3
Br
N
H
8e
19F NMR
282 MHz
CDCl3
3.05
1.00
-20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180
f1 (ppm)


165.553
163.588
133.921
133.852
130.720
129.471
127.022
125.322
125.294
124.796
122.210
119.625
117.039
116.190
116.014
49.000
F
SO2CF3
Br
N
H
8e
13C NMR
126 MHz
CD3OD
124.796
122.210
119.625
117.039
125 124 123 122 121 120 119 118 117
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.906
8.890
7.478
7.467
7.459
7.439
7.410
7.399
7.393
7.383
7.378
7.371
7.367
6.088
-0.000
Cl
SO2CF3
H2N
N
N
N
2a
1H NMR
300 MHz
CDCl3
1.99
3.00
2.00
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


-78.183
-162.200
Cl
SO2CF3
H2N
N
N
N
2a
19F NMR
282 MHz
CDCl3
3.00
-35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145 -155 -165
f1 (ppm)


158.959
157.276
148.994
143.033
130.719
129.020
128.746
128.204
123.573
120.979
119.737
118.383
115.787
106.980
77.160
Cl
SO2CF3
H2N
N
N
N
N
2a
13C NMR
126 MHz
CDCl3
129.020
128.746
128.204
123.573
120.979
118.383
115.787
129.1
128.9
128.7
128.5
128.3
f1 (ppm)
124
122
120
118
116
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)