Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers

Supporting Information for

Copper catalyzed cross-coupling of bromozinc-difluorophosphonate with iodo/bromo-aryl triazenes

Zhang Feng, Yu-Lan Xiao, and Xingang Zhang*

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China

xgzhang@mail.sioc.ac.cn

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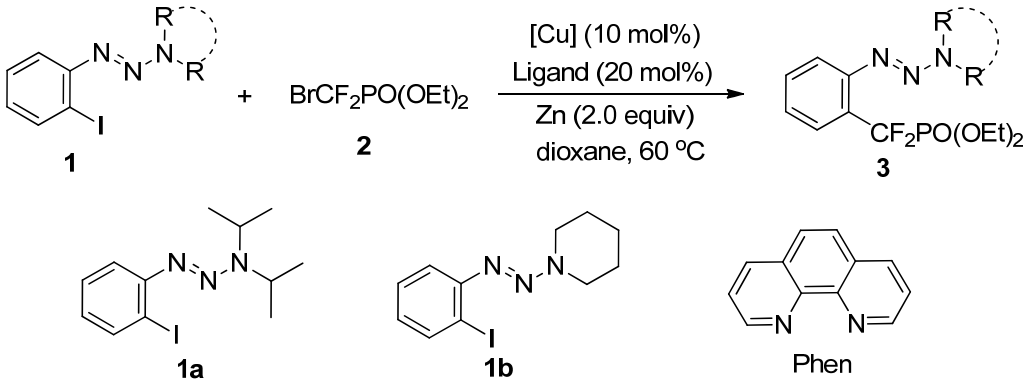
General information: ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM300 and AM400 spectrometer. ^{19}F NMR was recorded on a Bruker AM300 spectrometer ($CFCl_3$ as outside standard and low field is positive). Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. NMR yield was determined by ^{19}F NMR using fluorobenzene as an internal standard before working up the reaction.

Materials: All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature. All reagents were weighed and handled in air, and refilled with an inert atmosphere of N_2 at room temperature. DMF, DMSO, and DMPU were distilled under reduced pressure from CaH_2. THF, 1,4-dioxane, and toluene were distilled from sodium and benzophenone immediately before use.

Screens for Copper-Catalyzed Cross-Coupling of Phenyl Triazene 1 with Bromozinc-difluorophosphonate 4 (Table S1). To a stirred suspension of Zn dust (0.6 mmol, 2.0 equiv) in dioxane (2 mL) was added bromodifluoromethanephosphonate (0.6 mmol, 2.0 equiv) under N_2. After stirring for 3 h at 60 ^{o}C, the resulting mixture was cooled to room temperature. [Cu] (0.1 equiv) and diamine ligand (0.1-0.2 equiv) were added. The reaction mixture was stirred at same temperature for 30 min, phenyl triazene **1** (0.3 mmol) was then added. The reaction was warmed to 60 ^{o}C and stirred for 21 h. The reaction mixture was then cooled to room temperature. The yield was determined by ^{19}F NMR before working up. If necessary, the reaction mixture was diluted with EtOAc, washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/ethyl acetate = 100:1) to provide pure product.

Table S1. Copper-Catalyzed Cross-Coupling of Phenyl Triazene 1 with Bromozinc-Difluorophosphonate 4.[a]



Entry	**1,** R	[Cu]	Solvent	Ligand	**3**, Yield [%][b]
1	**1a**, *i*Pr	CuI	dioxane	Phen	**3aa**, 10
2	**1a**, *i*Pr	CuBr	dioxane	Phen	**3aa**, 14
3	**1a**, *i*Pr	$CuBr_2$	dioxane	Phen	**3aa**, 26
4	**1a**, *i*Pr	CuCN	dioxane	Phen	**3aa**, 28
5	**1a**, *i*Pr	CuSCN	dioxane	Phen	**3aa**, Trace
6	**1a**, *i*Pr	$Cu(MeCN)_2PF_6$	dioxane	Phen	**3aa**, Trace
7	**1a**, *i*Pr	$Cu(OTf)_2$	dioxane	Phen	**3aa**, 12
8	**1a**, *i*Pr	$Cu(acac)_2$	dioxane	Phen	**3aa**, 12
9	**1a**, *i*Pr	$Cu(OAc)_2$	dioxane	Phen	**3aa**, 12
10	**1a**, *i*Pr	$CuCl_2$	dioxane	Phen	**3aa**, Trace
11	**1b**, $(CH_2)_5$	CuCN	dioxane	Phen	**3ba**, 73
12	**1b**, $(CH_2)_5$	CuCN	THF	Phen	**3ba**, 22
13	**1b**, $(CH_2)_5$	CuCN	toluene	Phen	**3ba**, 58
14	**1b**, $(CH_2)_5$	CuCN	DMPU	Phen	**3ba**, NR
15	**1b**, $(CH_2)_5$	CuCN	DMSO	Phen	**3ba**, NR
16	**1b**, $(CH_2)_5$	CuCN	DMF	Phen	**3ba**, NR
17	**1b**, $(CH_2)_5$	CuCN	Diglyme	Phen	**3ba**, 7
18	**1b**, $(CH_2)_5$	CuO	Dioxane	Phen	**3ba**, NR
19	**1b**, $(CH_2)_5$	Cu_2O	Dioxane	Phen	**3ba**, 44
20	**1b**, $(CH_2)_5$	CuTc	Dioxane	Phen	**3ba**, 37
20	**1b**, $(CH_2)_5$	CuCN	Dioxane	Phen (0.1 equiv)	**3ba**, 14

[a] Reaction conditions (unless otherwise specified): **1** (0.3 mmol, 1.0 equiv), **2** (2.0 equiv), Zn (2.0 equiv), [Cu] (10 mol%), Ligand (20 mol%), dioxane (2.0 mL), 21 h, 60 °C. [b] NMR yield determined by ^{19}F NMR using fluorobenzene as internal standard.

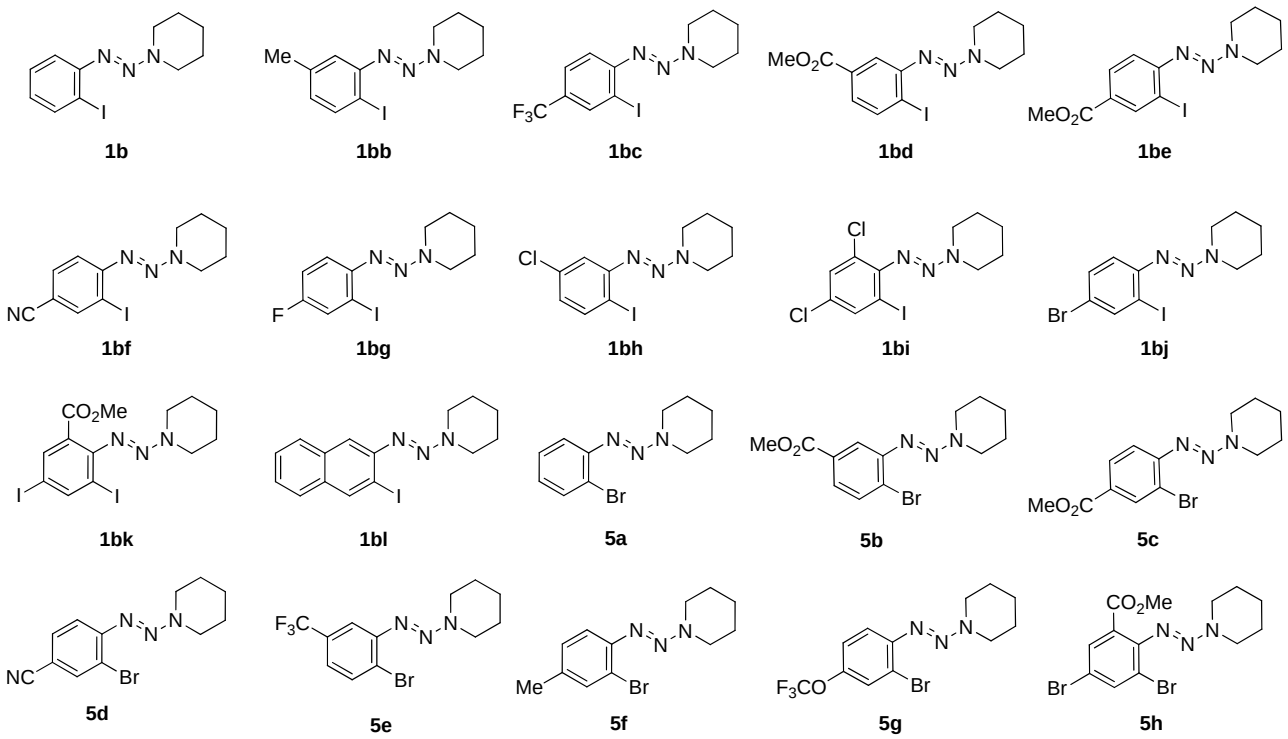
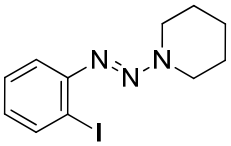
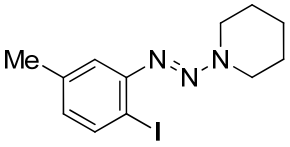


Figure S1. Structures of Iodo/Bromo-Aryl Triazenes

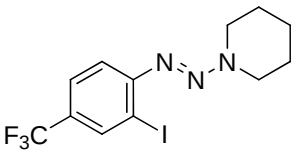
General Procedure for the Preparation of Iodo/Bromo-Aryl Triazenes 1 and 5. The triazenes **1** and **5** were prepared according to reported procedure.[1] 2-iodo/bromoaniline (23 mmol, 1.0 equiv) was dissolved in a mixture of acetonitrile and water (30 mL, 2:1). The resulting mixture was cooled to 0 °C. Concentrated aqeuos HCl (7.6 mL, 91 mmol, 4.0 equiv) was added dropwise. The reaction mixture was then cooled to -5 °C and a solution of $NaNO_2$ (2.4 g, 34 mmol, 1.5 equiv) in water (30 mL) was added slowly, maintaining the reaction temperature below 0 °C. After the addition was complete, the reaction mixture was stirred at -5 °C to 0 °C for 30 min. The resulting mixture was then added slowly to a stirred solution of piperidine (5.6 mL, 57 mmol, 2.5 equiv) and potassium carbonate (16 g, 119 mmol, 5.2 equiv) in a mixture of acetonitrile and water (120 mL, 2:1) at 0°C. The reaction mixture was allowed to warm to room temperature. After stirring for 1 hour at room temperature, the reaction mixture was extracted with ethyl acetate. The combined organic layer was washed with brine, dried over Na_2SO_4, concentrated, and purified with silica gel chromatography to give the corresponding iodo/bromo-aryl triazenes **1** and **5**.



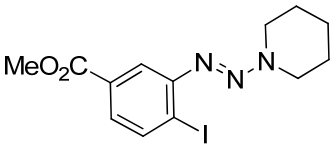
1-((2-Iodophenyl)diazenyl)piperidine (1b). The product (94% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 60:1). This compound is known.[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 8.1 Hz, *J* = 1.2 Hz, 1 H), 7.37 (dd, *J* = 8.1 Hz, *J* = 1.5 Hz, 1 H), 7.27 (td, *J* = 7.2 Hz, *J* = 1.2 Hz,1 H)，6.85 (td, *J* = 7.2 Hz, *J* = 1.5 Hz, 1 H), 3.84 (br, 4 H), 1.72 (s, 6 H).



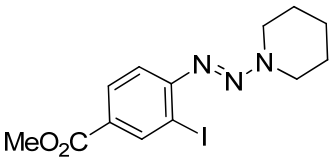
1-((2-iodo-5-methylphenyl)diazenyl)piperidine (1bb). The product (94% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 70:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1 H), 7.30 (d, *J* = 8.2 Hz, 1 H), 7.10 (d, *J* = 8.2 Hz, 1 H), 3.85 (br, 4 H), 2.31 (s, 3 H), 1.73 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 139.3, 136.9, 129.6, 117.1, 96.7, 52.2, 44.4, 25.1, 24.4, 24.2, 20.4. IR (thin film) ν_{max} 2937, 1593, 1431 cm^{-1}. MS (EI): *m/z* (%) 329 (M^+), 217, 69 (100). HRMS calcd. for $C_{12}H_{16}N_3I$: 329.0389; Found: 329.0392.



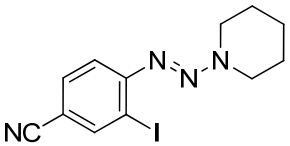
1-((2-iodo-4-(trifluoromethyl)phenyl)diazenyl)piperidine (1bc). The product (78% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 1 H), 7.45 (d, *J* = 8.4 Hz, 1 H), 3.97 (br, 2 H), 3.83 (br, 2 H), 1.74 (s, 6 H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.3 (s, 3 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 136.0 (q, *J* = 3.0 Hz), 128.0 (q, *J* = 32.5 Hz), 125.7 (q, *J* = 3.5 Hz), 123.4 (q, *J* = 270.7 Hz), 117.1, 95.9, 53.2, 44.4, 26.4, 24.3, 24.2. IR (thin film) ν_{max} 2942, 1599, 1421 cm^{-1}. MS (EI): *m/z* (%) 383 (M^+), 299, 271, 69 (100). HRMS calcd. for $C_{12}H_{13}N_3IF_3$: 383.0106; Found: 383.0105.



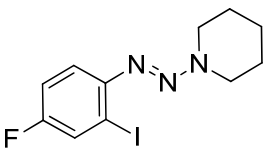
Methyl 4-iodo-3-(piperidin-1-yldiazenyl)benzoate (1bd). The product (96% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 2.0 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1 H), 7.47 (dd, *J* = 8.2 Hz, *J* = 2.0 Hz, 1 H), 3.95-3.85 (br, 4 H), 3.90 (s, 3 H), 1.71 (br, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 150.3, 139.2, 130.8, 127.0, 118.1, 102.7, 53.0, 52.2, 44.3, 26.4, 24.2. IR (thin film) ν_{max} 2942, 1724, 1578 cm^{-1}. MS (EI): *m/z* (%) 373 (M^+), 289, 261 (100). HRMS calcd. for $C_{13}H_{16}N_3IO_2$: 373.0287; Found: 373.0291.



Methyl 3-iodo-4-(piperidin-1-yldiazenyl)benzoate (1be). The product (93% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1). ^{1}H NMR (400 MHz, CDC l_3) δ 8.49 (d, *J* = 2.0 Hz, 1H), 7.91 (dd, *J* = 8.2 Hz, *J* = 2.0 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 3.94 (br, 2 H), 3.87 (s, 3 H), 3.83 (br, 2 H), 1.69 (br, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 153.5, 140.6, 130.1, 127.8, 116.7, 95.8, 53.2, 52.1, 44.4, 26.4, 24.4, 24.2. IR (thin film) ν_{max} 2944, 1719, 1419 cm^{-1}. MS (EI): *m/z* (%) 373 (M^+), 289, 261 (100). HRMS calcd. for $C_{13}H_{16}N_3O_2I$: 373.0287; Found: 373.0282.

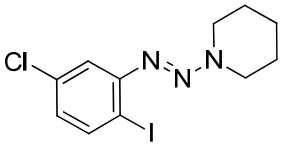


3-Iodo-4-(piperidin-1-yldiazenyl)benzonitrile (1bf). The product (83% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 60:1). ^{1}H NMR (400 MHz, CDC l_3) δ 8.09 (d, *J* = 1.2 Hz, 1H), 7.53 (dd, *J* = 8.4 Hz, *J* = 1.2 Hz, 1 H), 7.44 (d, *J* = 8.4 Hz, 1 H), 4.01 (s, 2 H), 3.87 (s, 2 H), 1.75 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 142.6, 132.3, 118.0, 117.1, 109.1, 95.9, 53.5, 44.6, 26.5, 24.4, 24.1. IR (thin film) ν_{max} 2948, 2220, 1585 cm^{-1}. MS (EI): *m/z* (%) 340 (M^+), 256, 228 (100), 101. HRMS calcd. for $C_{12}H_{13}N_4I$: 340.0185; Found: 340.0184.

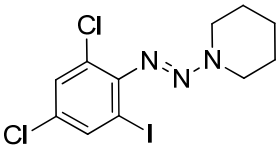


1-((4-Fluoro-2-iodophenyl)diazenyl)piperidine (1bg). The product (73% yield) was purified with

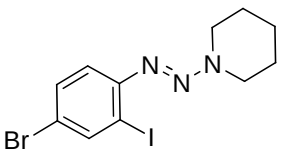
silica gel chromatography (Petroleum ether/EtOAc = 30:1). ^{1}H NMR (400 MHz, CDC l_3) δ 7.58 (dd, *J* = 8.0 Hz, *J* = 2.8 Hz, 1H), 7.36 (dd, *J* = 8.8 Hz, *J* = 5.6 Hz, 1H), 7.03 (td, *J* = 8.8 Hz, *J* = 2.8 Hz, 1H)，3.84 (br, 4 H), 1.71 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1 (d, *J* = 247.5 Hz), 146.6, 125.4 (d, *J* = 24.2 Hz), 117.6 (d, *J* = 8.0 Hz), 115.7 (d, *J* = 22.1 Hz), 95.8 (d, *J* = 8.3 Hz), 52.7, 44.5, 26.0, 24.3. IR (thin film) ν_{max} 2938, 2855, 1586, 1470 cm^{-1}. MS (EI): *m/z* (%) 333 (M^+), 265, 129, 105 (100), 77. HRMS calcd. for $C_{11}H_{13}N_3IF$: 333.0138; Found: 333.0139.



1-((5-Chloro-2-iodophenyl)diazenyl)piperidine (1bh). The product (89% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 2.4 Hz, 1 H), 6.84 (dd, *J* = 8.2 Hz, *J* = 2.4 Hz, 1 H), 3.91 (br, 2 H), 3.82 (br, 2 H)，1.71 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 139.6, 134.9, 126.6, 117.5, 93.8, 53.1, 44.3, 29.7, 26.3, 24.2. IR (thin film) ν_{max} 2939, 1567, 1353 cm^{-1}. MS (EI): *m/z* (%) 349 (M^+), 265, 237 (100). HRMS calcd. for $C_{11}H_{13}N_3ICl$: 348.9843; Found: 348.9839.

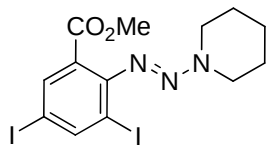


1-((2,4-dichloro-6-iodophenyl)diazenyl)piperidine (1bi). The product (79% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 2.2 Hz, l H), 7.39 (d, *J* = 2.2 Hz, l H), 3.85 (br, 4 H), 1.73 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 136.9, 130.5, 130.2, 126.5, 93.6, 53.0, 43.9, 26.7, 24.3. IR (thin film) ν_{max} 2939, 1535, 1420 cm^{-1}. MS (EI): *m/z* (%) 383 (M^+), 299, 271 (100). HRMS calcd. for $C_{11}H_{12}N_3Cl_2I$: 382.9453; Found: 382.9459.

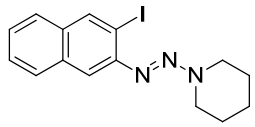


1-((4-Bromo-2-iodophenyl)diazenyl)piperidine (1bj). The product (96% yield) was purified with

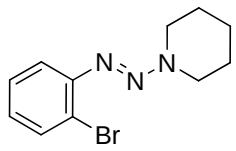
silica gel chromatography (Petroleum ether/EtOAc = 30:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.38 (d, *J* = 8.6 Hz, 1 H), 7.26 (d, *J* = 8.6 Hz, 1 H), 3.85 (br, 4 H)，1.71 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 140.8, 131.7, 118.7, 118.3, 97.1, 53.1, 44.3, 26.4, 24.3. IR (thin film) ν_{max} 2938, 1565, 1454 cm^{-1}. MS (EI): *m/z* (%) 395 (M^+), 393 (M^+), 311, 309, 281, 283, 75 (100). HRMS calcd. for $C_{11}H_{13}N_3BrI$: 392.9338; Found: 392.9336.



Methyl 3,5-diiodo-2-(piperidin-1-yldiazenyl)benzoate (1bk). The product (78% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 100:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 1.6 Hz, l H), 7.76 (d, *J* = 1.6 Hz, l H), 3.96 (br, 2H), 3.76 (s, 3 H), 3.71 (br, 2 H), 1.71 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 148.4, 138.2, 125.8, 97.2, 88.2, 53.2, 52.1, 44.3, 26.5, 24.4, 24.1. IR (thin film) ν_{max} 2941, 1727, 1412 cm^{-1}. MS (EI): *m/z* (%) 499 (M^+), 415, 387, 289, 261 (100). HRMS calcd. for $C_{13}H_{15}N_3I_2O_2$: 498.9254; Found: 498.9258.

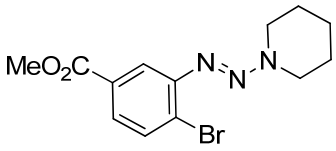


1-((3-Iodonaphthalen-2-yl)diazenyl)piperidine (1bl). The product was purified with silica gel chromatography (Petroleum ether/EtOAc = 80:1). ^{1}H NMR (400 MHz, CDC l_3) δ 8.39 (d, *J* = 8.8 Hz, 1 H), 7.83-7.77 (m, 2 H), 7.69 (d, *J* = 9.2 Hz, 1 H)，7.57 (t, *J* = 8.2 Hz, 1 H), 7.45 (t, *J* = 8.2 Hz, 1 H), 3.93 (br, 4 H), 1.75 (br, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 132.5, 132.0, 128.0, 127.1, 127.0, 125.5, 124.4, 117.8, 53.1, 44.6, 25.4, 24.4. IR (thin film) ν_{max} 2938, 2854, 1593, 1498 cm^{-1}. MS (EI): *m/z* (%) 365 (M^+), 299, 161(100). HRMS calcd. for $C_{15}H_{16}N_3I$: 365.0389; Found: 365.0392.

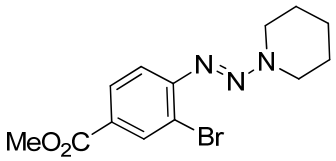


1-((2-Bromophenyl)diazenyl)piperidine (5a). The product (94% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 20:1). This compound is known.[2] ^{1}H NMR (300 MHz,

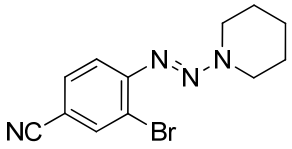
CDC l_3) δ 7.58 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz ,1 H), 7.44 (dd, *J* = 8.0 Hz, *J* = 1.5 Hz, 1 H), 7.26 (td, *J* = 7.2 Hz, *J* = 1.5 Hz ,1 H)，7.00 (td, *J* = 7.2 Hz, *J* = 1.5 Hz, 1 H), 3.85 (s, 4 H), 1.71 (s, 6 H).



Methyl 4-bromo-3-(piperidin-1-yldiazenyl)benzoate (5b). The product (82% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, l H), 7.62 (s, 2 H), 3.95-3.85 (m, 4 H), 3.88 (s, 3 H), 1.71 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 148.3, 133.1, 129.8, 126.7, 125.0, 119.3, 53.0, 52.2, 44.0, 26.4, 24.2. IR (thin film) ν_{max} 2943, 2856, 1724, 1463 cm^{-1}. MS (EI): *m/z* (%) 327 (M^+), 325 (M^+), 243, 241, 213 (100). HRMS calcd. for $C_{13}H_{16}N_3BrO_2$: 325.0426; Found: 325.0421.

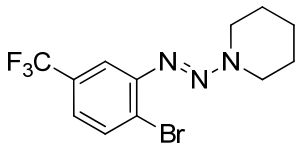


Methyl 3-bromo-4-(piperidin-1-yldiazenyl)benzoate (5c). The product (94% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 80:1). ^{1}H NMR (400 MHz, CDC l_3) δ 8.23 (d, *J* = 2.0 Hz, 1H), 7.87 (dd, *J* = 8.6 Hz, *J* = 2.0 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 3.93 (br, 2 H)，3.87 (s, 3 H), 3.81 (br, 2 H), 1.70 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 151.7, 134.6, 129.1, 127.4, 119.4, 117.7, 53.2, 52.1, 44.1, 26.4, 24.3, 24.2. IR (thin film) ν_{max} 2945, 1720, 1594 cm^{-1}. MS (EI): *m/z* (%) 327 (M^+), 325 (M^+), 243, 241, 215, 213, 84 (100). HRMS calcd. for $C_{13}H_{16}N_3BrO_2$: 325.0426; Found: 325.0429.

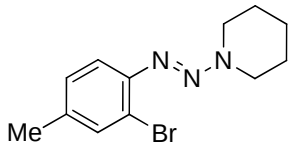


3-Bromo-4-(piperidin-1-yldiazenyl)benzonitrile (5d). The product (90% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 100:1). ^{1}H NMR (400 MHz, CDC l_3) δ 7.84 (d, *J* = 1.6 Hz, 1H), 7.52-7.47 (m, 2 H), 3.98 (s, 2 H)，3.85 (s, 2 H). 1.74 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 136.6, 131.5, 119.6, 118.3, 118.2, 108.6, 53.5, 44.3, 26.4, 24.4, 24.1. IR (thin film)

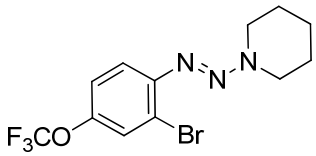
ν_{max} 2941, 2223, 1471 cm^{-1}. MS (EI): *m/z* (%) 294 (M^+), 292 (M^+), 243, 241, 210, 208, 182 (99), 180 (100). HRMS calcd. for $C_{12}H_{13}N_4Br$: 292.0324; Found: 292.0321.



1-((2-Bromo-4-(trifluoromethyl)phenyl)diazenyl)piperidine (5e). The product (74% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 50:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, l H), 7.66 (d, *J* = 8.4 Hz, 1 H), 7.19 (d, *J* = 8.4 Hz, 1 H), 3.92 (br, 2 H), 3.84 (br, 2 H), 1.71 (s, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.6 (s, 3 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.6, 133.6, 130.2 (q, *J* = 32.4 Hz), 124.0 (q, *J* = 271.1 Hz), 123.3, 122.2 (q, *J* = 3.5 Hz), 115.1 (q, *J* = 3.7 Hz), 53.1, 44.0, 26.3, 24.2. IR (thin film) ν_{max} 2942, 1594, 1428 cm^{-1}. MS (EI): *m/z* (%) 337 (M^+), 335 (M^+), 253, 251, 225, 223 (100). HRMS calcd. for $C_{12}H_{13}F_3N_3Br$: 335.0245; Found: 335.0249.

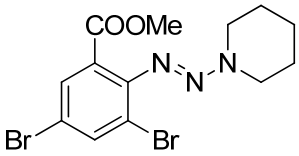


1-((2-Bromo-4-methylphenyl)diazenyl)piperidine (5f). The product (92% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 100:1). ^1H NMR (300 MHz, CDC l_3) δ 7.44 (s, 1 H), 7.37 (d, *J* = 8.0 Hz, 1 H), 7.07 (d, *J* = 8.0 Hz, 1 H), 3.83 (s, 4 H), 2.32 (s, 3 H), 1.70 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.8, 136.5, 133.3, 128.9, 119.8, 118.2, 52.8, 44.6, 25.3, 24.4, 20.7. IR (thin film) ν_{max} 2938, 2855, 1599, 1480 cm^{-1}. MS (EI): *m/z* (%) 283 (M^+), 281 (M^+), 171, 169, 84 (100). HRMS calcd. for $C_{12}H_{16}N_3Br$: 281.0528; Found: 281.0530.



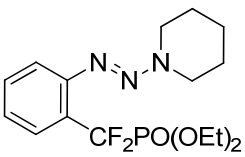
1-((2-Bromo-4-(trifluoromethoxy)phenyl)diazenyl)piperidine (5g). The product (86% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 80:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.47-7.44 (m, 2 H), 7.12 (dd, *J* = 8.8 Hz, *J* = 1.6 Hz, 1 H), 3.85 (br, 4 H). 1.71 (s, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.16 (s, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.1, 146.2, 125.6,

120.6, 120.4 (q, J = 256.1 Hz), 119.6, 118.7, 52.9, 44.0, 26.3, 24.2. IR (thin film) ν_{max} 2942, 2858, 1592 cm^{-1}. MS (EI): *m/z* (%) 353 (M^+), 351 (M^+), 269, 267, 239 (100). HRMS calcd. for $C_{12}H_{13}N_3F_3OBr$: 351.0194; Found: 351.0196.



Methyl 3,5-dibromo-2-(piperidin-1-yldiazenyl)benzoate (5h). The product (95% yield) was purified with silica gel chromatography (Petroleum ether/EtOAc = 30:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 2.0 Hz, l H), 7.57 (d, J = 2.0 Hz, l H), 3.87 (br, 2 H), 3.74 (s, 3 H), 3.69 (br, 2 H), 1.69 (s, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 147.0, 137.2, 131.5, 126.6, 120.4, 117.3, 53.0, 52.1, 44.1, 26.4, 24.1. IR (thin film) ν_{max} 2941, 1731, 1417 cm^{-1}. MS (EI): *m/z* (%) 405 (M^+), 403 (M^+), 321 (100), 293. HRMS calcd. for $C_{13}H_{15}N_3O_2Br_2$: 402.9531; Found: 402.9527.

General Procedure for Copper-Catalyzed Cross-Coupling of Iodo/Bromo-Aryl Triazenes (1 or 5) with Bromozinc-Difluorophosphonate 4: To a stirred suspension of Zn dust (0.9 mmol, 3.0 equiv) in dioxane (2 mL) was added bromodifluoromethanephosphonate (0.9 mmol, 3.0 equiv) under N_2. After stirring for 3 h at 60 °C, the resulting mixture was cooled to room temperature. CuCN (10 mol%) and 3,4,7,8-tetramethyl-1,10-phenanthroline **L1** (20 mol%) were added. The reaction mixture was stirred at same temperature for 30 min, aryl triazene **1** or **5** (0.3 mmol, 1.0 equiv) was then added. The reaction was warmed to 60 °C and stirred for 24-48 h. The reaction mixture was cooled to room temperature, and diluted with EtOAc, washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified with silica gel chromatography to provide pure product.

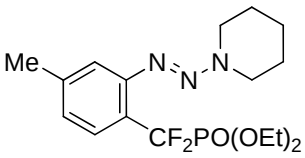


Diethyl (difluoro(2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3ba). The product (103 mg, 91% yield from **1b**; 63 mg, 55% from **5a**) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.0 Hz,

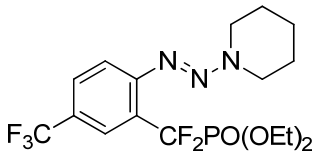
1 H), 7.46 (d, *J* = 8.4 Hz, 1 H), 7.36 (t, *J* = 7.6 Hz, 1 H), 7.16 (t *J* = 7.6 Hz, 1 H), 4.18-4.03 (m, 4 H), 3.81 (br, 4 H), 1.65 (s, 6 H), 1.23 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.3 (d, *J* = 117.0 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 131.3, 127.3 (td, *J* = 9.3 Hz, *J* = 2.6 Hz), 125.8 (td, *J* = 20.1 Hz, *J* = 13.6 Hz), 124.9, 119.2 (td, *J* = 263.6 Hz, *J* = 217.3 Hz), 117.6, 64.28, 64.21, 52.6, 44.2, 27.9, 25.7, 24.3, 16.30, 16.24. IR (thin film) ν_{max} 2940, 1424 cm^{-1}. MS (EI): *m/z* (%) 375 (M^+), 187, 84 (100). HRMS calcd. for $C_{16}H_{24}F_2O_3PN_3$ (M^+): 375.1523; Found: 375.1523.

2-gram-scale synthesis of 3ba.

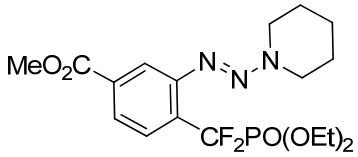
To a stirred suspension of Zn dust (19.4 mmol, 1.26 g) in dioxane (10 mL) was added bromodifluoromethanephosphonate (19.4 mmol, 5.16 g) under N_2. After stirring for 3 h at 60 °C, the resulting mixture was cooled to room temperature and filtered with a syringe filter. To the filtrate were added CuCN (0.1 equiv) and 3,4,7,8-tetramethyl-1,10-phenanthroline (0.2 equiv). The reaction mixture was stirred at same temperature for 30 min, 1-((2-iodophenyl)diazenyl)piperidine (6.3 mmol, 2 g) **1b** was then added. The reaction was warmed to 60 °C and stirred for 48 h. The reaction mixture was cooled to room temperature, and diluted with EtOAc, washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/ethyl acetate = 3:1) to provide pure product (2.07 g, 88% yield).



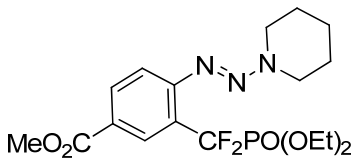
Diethyl (difluoro(4-methyl-2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3bb). The product (100 mg, 86% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (m, 2 H), 7.20 (d, *J* = 8.4 Hz, 1 H), 4.18-4.09 (m, 4 H), 3.81 (br, 4 H), 2.36 (s, 3 H), 1.68 (m, 6 H), 1.28 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.3 (d, *J* = 118.4 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.7, 134.7, 132.0, 127.7 (td, *J* = 9.1 Hz, *J* = 1.9 Hz), 125.6 (td, *J* = 20.4 Hz, *J* = 13.6 Hz), 119.2 (td, *J* = 264.0 Hz, *J* = 217.4 Hz), 117.5, 64.28, 64.22, 51.7, 44.5, 25.3, 24.4, 20.9, 16.32, 16.26. IR (thin film)ν_{max} 2938, 1433 cm^{-1}. MS (EI): *m/z* (%) 389 (M^+), 221, 201 (100), 84. HRMS calcd. for $C_{17}H_{26}F_2O_3PN_3$ (M^+): 389.1680; Found: 389.1682.



Diethyl(difluoro(2-(piperidin-1-yldiazenyl)-5-(trifluoromethyl)phenyl)methyl)phosphonate (3bc). The product (107 mg, 81% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1 H), 7.63 (s, 2 H), 4.12-4.20 (m, 4 H), 4.00 (br, 2 H), 3.84 (br, 2 H), 1.72 (m, 6 H), 1.28 (t, *J* = 6.8 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.1 (s, 3 F), -102.3 (d, *J* = 114.3 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 129.8, 128.0 (q, *J* = 33.2 Hz), 127.8 (td, *J* = 24.1 Hz, *J* = 10.2 Hz), 126.5 (m), 125.8 (q, *J* = 270.2 Hz), 120.4 (td, *J* = 264.6 Hz, *J* = 217.5 Hz), 119.6, 66.16, 66.10, 54.8, 46.0, 28.2, 26.2, 25.9, 17.98, 17.92. IR (thin film) ν_{max} 2942, 1407 cm^{-1}. MS (EI): *m/z* (%) 443 (M^+), 275, 255, 84 (100). HRMS calcd. for $C_{17}H_{23}F_5O_3PN_3$ (M^+): 443.1397; Found: 443.1394.

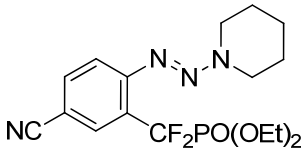


Methyl4-((diethoxyphosphoryl)difluoromethyl)-3-(piperidin-1-yldiazenyl)benzoate (3bd). The product (81 mg, 62% from **1bd**; 90 mg, 69% yield from **5b**) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s,1 H), 7.81 (d, *J* = 8.4 Hz, 1 H), 7.63 (d, *J* = 8.4 Hz, 1 H), 4.06-4.20 (m, 4 H), 3.91 (s, 3 H), 3.87 (br, 4 H), 1.70 (s, 6 H), 1.26 (t, *J* = 6.8 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.3 (d, *J* = 114.3 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 149.4, 132.8, 129.8 (td, *J* = 20.0 Hz, *J* = 13.5 Hz), 127.6 (td, *J* = 9.4 Hz, *J* = 2.6 Hz), 125.3, 118.9 (td, *J* = 263.8 Hz, *J* = 216.2 Hz), 118.8, 64.44, 64.37, 53.0, 52.3, 44.0, 26.4, 24.5, 24.3, 16.32, 16.26. IR (thin film) ν_{max} 2941, 1727, 1436 cm^{-1}. MS (EI): *m/z* (%) 433 (M^+), 265, 245 (100), 84. HRMS calcd. for $C_{18}H_{26}F_2O_5PN_3$ (M^+): 433.1578; Found:433.1581.

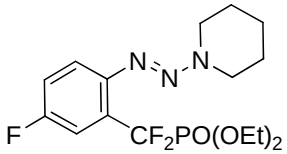


Methyl-3-((diethoxyphosphoryl)difluoromethyl)-4-(piperidin-1-yldiazenyl)benzoate (3be). The product (102 mg, 78% yield from **1be**; 52 mg, 40% yield from **5c** and the reaction was conducted in

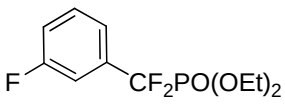
the absence of **L1**) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1 H), 8.05 (d, *J* = 8.6 Hz, 2 H), 7.58 (d, *J* = 8.6 Hz, 2 H), 4.20-4.08 (m, 4 H), 3.99 (br, 2 H), 3.91 (s, 3 H), 3.85 (br, 2 H), 1.72 (m, 6 H), 1.27 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.8 (d, *J* = 115.5 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 154.4, 134.2, 130.9 (td, *J* = 12.0 Hz, *J* = 2.6 Hz), 127.8, 127.6 (td, *J* = 21.0 Hz, *J* = 14.0 Hz), 120.6 (td, *J* = 264.2 Hz, *J* = 217.5 Hz), 119.1, 66.12, 66.05, 54.9, 53.8, 46.0, 28.2, 26.3, 25.9, 18.06, 18.00. IR (thin film) ν_{max} 2943, 1720, 1606 cm^{-1}. MS (EI): *m/z* (%) 433 (M^+), 245, 84 (100). HRMS calcd. for $C_{18}H_{26}F_2N_3O_5P$ (M^+): 433.1578; Found: 433.1575.



Diethyl((5-cyano-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bf). The product (92 mg, 76% yield from **3bf**; 61 mg, 50% yield from **5d**) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1 H), 7.66 (s, 2 H), 4.25-4.11 (m, 4 H), 4.04 (br, 2 H), 3.87 (br, 2 H), 1.75 (m, 6 H), 1.30 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.6 (d, *J* = 99.3 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 134.5, 131.6 (td, *J* = 9.7 Hz, *J* = 1.9 Hz), 126.7 (td, *J* = 20.9 Hz, *J* = 14.1 Hz), 118.7, 118.5 (td, *J* = 264.8 Hz, *J* = 217.5 Hz), 118.1, 107.3, 64.46, 64.39, 53.4, 44.4, 26.5, 24.6, 24.1, 16.28, 16.23. IR (thin film) ν_{max} 2942, 2227, 1603 cm^{-1}. MS (EI): *m/z* (%) 400 (M^+), 212, 84 (100). HRMS calcd. for $C_{17}H_{23}F_2O_3PN_4$ (M^+): 400.1476; Found: 400.1480.



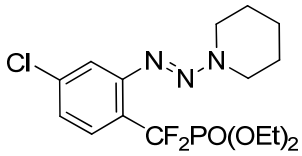
3bg



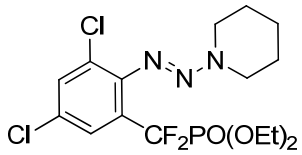
3bg'

Diethyl(difluoro(5-fluoro-2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3bg). The product (87 mg, 74% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1). 4% of **3bg'** was also observed. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 8.4 Hz, *J* = 4.8 Hz, 1 H), 7.28 (dd, *J* = 8.8 Hz, 1.6 Hz, 1 H), 7.11 (td, *J* = 7.6 Hz, *J* = 1.6 Hz, 1 H), 4.23-4.09 (s, 4 H), 3.83 (s, 4 H), 1.70 (s, 6 H), 1.29 (t, *J* = 6.8 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$)

δ -101.8 (d, *J* = 115.5 Hz, 2 F), -117.4 (m, 1 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7 (d, *J* = 243.1 Hz), 147.2, 129.1 (m), 120.9 (d, *J* = 7.6 Hz), 120.8 (m), 120.0 (d, *J* = 22.3 Hz), 115.9 (m), 66.20, 66.13, 54.5, 46.1, 27.8, 26.5, 26.1, 18.08, 18.03. IR (thin film) ν_{max} 2937, 1609, 1486 cm^{-1}. MS (EI): *m/z* (%) 393 (M^+), 202, 85, 58 (100). HRMS calcd. for $C_{16}H_{23}F_3O_3PN_3$ (M^+): 393.1429; Found: 393.1435.

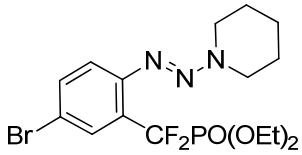


Diethyl ((4-chloro-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bh). The product (80 mg, 65% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1 H), 7.49 (d, *J* = 8.4 Hz, 1 H), 7.15 (d, *J* = 8.4 Hz, 1 H), 4.22-4.08 (m, 4 H), 3.91 (br, 2 H), 3.84 (br, 2 H), 1.71 (s, 6 H), 1.28 (t, *J* = 7.6 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.7 (d, *J* = 115.5 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 139.0, 130.3 (td, *J* = 9.6 Hz, *J* = 2.0 Hz), 126.3, 126.1 (td, *J* = 20.6 Hz, *J* = 13.7 Hz), 120.6 (td, *J* = 264.4 Hz, *J* = 217.8 Hz), 119.2, 66.12, 66.05, 54.7, 45.9, 28.2, 26.3, 26.0, 18.08, 18.03. IR (thin film) ν_{max} 2941, 1590 cm^{-1}. MS (EI): *m/z* (%) 409 (M^+), 221, 84 (100). HRMS calcd. for $C_{16}H_{23}F_2O_3PN_3Cl$ (M^+): 409.1134; Found: 409.1136.

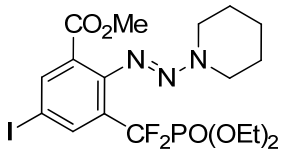


Diethyl((3,5-dichloro-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bi). The product (102 mg, 77% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1 H), 7.49 (s, 1 H), 4.26-4.14 (m, 4 H), 3.83 (s, 4 H), 1.72 (s, 6 H), 1.32 (t, *J* = 6.8 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.0 (d, *J* = 112.8 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.3, 134.1, 131.4, 130.1, 130.0 (td, *J* = 20.9 Hz, *J* = 14.3 Hz), 128.2 (td, *J* = 9.1 Hz, *J* = 1.2 Hz), 119.6 (td, *J* = 265.5 Hz, *J* = 217.1 Hz), 119.5 (td, *J* = 261.0 Hz, *J* = 217.3 Hz), 66.46, 66.40, 54.6, 45.3, 28.4, 26.0, 18.07, 18.01. IR (thin film) ν_{max} 1739, 1436 cm^{-1}. MS (EI): *m/z* (%) 443 (M^+), 255, 84 (100). HRMS calcd. for $C_{16}H_{22}F_2O_3PN_3Cl_2$

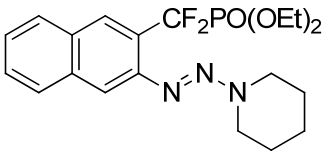
(M^+): 443.0744; Found: 443.0739.



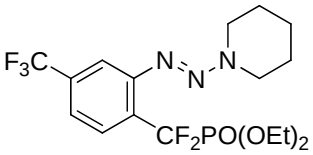
Diethyl ((5-bromo-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bj). The product (118 mg, 87% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1 H), 7.47 (d, *J* = 8.8 Hz, 1 H), 7.39 (d, *J* = 8.8 Hz, 1 H), 4.21-4.07 (m, 4 H), 3.83 (br, 4 H), 1.68 (s, 6 H), 1.27 (t, *J* = 6.8 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.9 (d, *J* = 115.5 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 135.9, 131.8 (td, *J* = 10.0 Hz, *J* = 1.9 Hz), 129.3 (td, *J* = 20.5 Hz, *J* = 13.8 Hz), 120.9, 120.1 (td, *J* = 265.0 Hz, *J* = 217.4 Hz), 119.5, 66.17, 66.11, 54.6, 45.8, 28.2, 26.1, 26.0, 18.07, 18.01. IR (thin film) ν_{max} 2940, 1426 cm^{-1}. MS (EI): *m/z* (%) 453 (M^+), 455 (M^+), 267, 265, 84 (100). HRMS calcd. for $C_{16}H_{23}F_2O_3PN_3Br$ (M^+): 453.0628; Found: 453.0624.



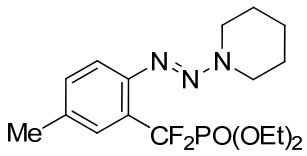
Methyl-3-((diethoxyphosphoryl)difluoromethyl)-5-iodo-2-(piperidin-1-yldiazenyl)benzoate (3bk). A mixture of **3bk** and **3bk'** (96 mg, 57% yield, **3bk**/**3bk'** = 5:1 determined before working up) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 5:1). Further purification by preparative HPLC (Column: Kromasil C18 (150 x 4.5 mm Φ 5 μm); Flow Rate: 1.0 mL/min; Temperature: 25 ^{o}C; Wavelength: UV 210 nm, CH_3CN / H_2O (v/v) = 50:50; Time: 12 min) to give pure **3bk**. **3bk**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1 H), 7.88 (s, 1 H), 4.20-4.12 (m, 4 H), 3.93 (br, 2 H), 3.76 (s, 3 H), 3.72 (br, 2 H), 1.71 (s, 6 H), 1.29 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.8 (d, *J* = 114.3 Hz, 2 F). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 148.4, 140.5, 138.0 (td, *J* = 9.7 Hz, *J* = 2.0 Hz), 128.7 (td, *J* = 17.0 Hz, 11.0 Hz), 126.9, 117.8 (td, *J* = 265.8 Hz, *J* = 218.5 Hz), 64.57, 64.52, 52.9, 52.0, 44.3, 26.5, 24.5, 24.2, 16.31, 16.27. IR (thin film) ν_{max} 2941, 2857, 1730, 1417 cm^{-1}. MS (EI): *m/z* (%) 559 (M^+), 475, 359 (100), 84. HRMS calcd. for $C_{18}H_{25}F_2O_5PN_3I$ (M^+): 559.0545; Found: 559.0539.



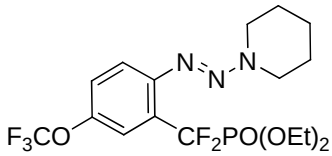
Diethyl (difluoro(3-(piperidin-1-yldiazenyl)naphthalen-2-yl)methyl)phosphonate (3bl). The product (68 mg, 53% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 8.4 Hz, 1 H), 7.83 (d, *J* = 8.8 Hz, 1 H), 7.76 (d, *J* = 8.0 Hz, 1 H), 7.65 (d, *J* = 8.8 Hz, 1 H), 7.50 (t, *J* = 7.6 Hz, 1 H), 7.39 (t, *J* = 7.2 Hz, 1 H), 4.22-4.17 (m, 2 H), 4.13-4.07 (m, 2 H), 3.89 (br, 4 H), 1.72 (s, 6 H), 1.25 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -92.5 (d, *J* = 114.7 Hz, 2 F). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 132.4, 132.3, 131.5, 128.4, 126.8, 126.6 (td, *J* = 9.5 Hz, 1.1 Hz), 124.8, 121.4 (td, *J* = 265.4 Hz, J = 215.3 Hz), 118.0, 64.40, 64.35, 54.0, 44.4, 25.4, 24.2, 16.39, 16.35. IR (thin film) ν_{max} 2938, 1619 cm^{-1}. MS (EI): *m/z* (%) 425 (M^+), 187, 177, 84 (100). HRMS calcd. for $C_{20}H_{26}F_2O_3PN_3$ (M^+): 425.1680; Found: 425.1683.



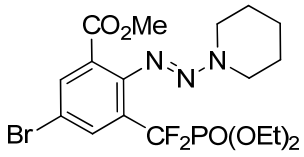
Diethyl(difluoro(2-(piperidin-1-yldiazenyl)-4-(trifluoromethyl)phenyl)methyl)phosphonate (3bm). The product (70 mg, 52% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1 H), 7.68 (d, *J* = 7.8 Hz, 1 H), 7.41 (d, *J* = 7.8 Hz, 1 H), 4.21-4.10 (m, 4 H), 3.96 (br, 2 H), 3.85 (br, 2 H), 1.73 (br, 6 H), 1.29 (t, *J* = 6.8 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.1 (s, 3F), -102.4 (d, *J* = 114.3 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 133.2 (q, *J* = 31.7 Hz), 128.9 (td, *J* = 20.1 Hz, *J* = 12.9 Hz), 128.1 (td, *J* = 11.6 Hz, *J* = 1.9 Hz), 123.7 (q, *J* = 271.6 Hz), 120.9 (q, *J* = 3.1 Hz), 118.7 (td, *J* = 267.1 Hz, *J* = 216.6 Hz), 114.6 (q, *J* = 3.2 Hz), 64.47, 64.41, 53.0, 44.2, 26.5, 24.5, 24.2, 16.32, 16.26. IR (thin film) ν_{max} 2941, 1406 cm^{-1}. MS (EI): *m/z* (%) 443 (M^+), 275, 255, 84 (100). HRMS calcd. for $C_{17}H_{23}F_5O_3PN_3$ (M^+): 443.1397; Found: 443.1394.



Diethyl (difluoro(5-methyl-2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3bn). The product (54 mg, 46% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (m, 2 H), 7.21 (d, *J* = 8.4 Hz, 1 H), 4.23-4.08 (m, 4 H), 3.83 (br, 4 H), 2.39 (s, 3 H), 1.70 (s, 6 H), 1.31 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.3 (d, *J* = 117.3 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 136.5, 133.8, 129.4 (td, *J* = 9.1 Hz, *J* = 1.9 Hz), 127.3 (td, *J* = 19.9 Hz, *J* = 13.5 Hz), 121.0 (td, *J* = 263.7 Hz, *J* = 217.2 Hz), 119.3, 66.08, 66.02, 53.8, 45.9, 27.1, 26.2, 22.7, 18.10, 18.05. IR (thin film) ν_{max} 2936, 1433 cm^{-1}. MS (EI): *m/z* (%) 389 (M^+), 201 (100), 141. HRMS calcd. for $C_{17}H_{26}F_2O_3PN_3$ (M^+): 389.1680; Found: 389.1675.

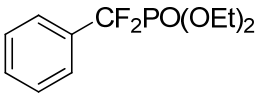


Diethyl(difluoro(2-(piperidin-1-yldiazenyl)-5-(trifluoromethoxy)phenyl)methyl)phosphonate (3bo). The product (76 mg, 55% yield) as a colorless oil was purified with silica gel chromatography (Petroleum ether/EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.6 Hz, 1 H), 7.43 (s, 1 H), 7.26 (d, *J* = 8.6 Hz, 1 H), 4.24-4.10 (m, 4 H), 3.88-3.85 (br, 4 H), 1.71 (s, 6 H), 1.28 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.1 (s, 3 F), -102.3 (*d*, J = 115.5 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 147.6, 128.8 (td, *J* = 21.2 Hz, *J* = 14.2 Hz), 125.8, 122.2 (q, *J* = 255.9 Hz), 122.0 (t, *J* = 9.3 Hz), 120.7, 120.1 (td, *J* = 264.8 Hz, J_{CP} = 218.0 Hz), 66.18, 66.10, 54.6, 45.9, 28.2, 26.2, 26.0, 18.0, 17.9. IR (thin film) ν_{max} 2940, 1438 cm^{-1}. MS (EI): *m/z* (%) 459 (M^+), 211, 109, 184 (100). HRMS calcd. for $C_{17}H_{23}F_5O_4PN_3$ (M^+): 459.1346; Found: 459.1350.

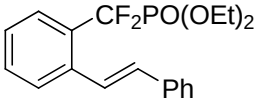


Methyl-5-bromo-3-((diethoxyphosphoryl)difluoromethyl)-2-(piperidin-1-yldiazenyl)benzoate (3bp). The product (65 mg, 42% yield) as a colorless oil was purified with silica gel chromatography

(Petroleum ether/EtOAc = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1 H), 7.71 (s, 1 H), 4.20-4.08 (m, 4 H), 3.93 (br, 2 H), 3.77 (s, 3 H), 3.72 (br, 2 H), 1.71 (m, 6 H), 1.29 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.8 (d, *J* = 112.8 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 147.7, 134.7, 132.3 (td, *J* = 9.5 Hz, *J* = 1.6 Hz), 128.7 (td, *J* = 21.0 Hz, *J* = 6.3 Hz), 126.7, 120.5 (td, *J* = 263.0 Hz, *J* = 219.0 Hz), 116.9, 64.59, 64.52, 52.9, 52.0, 44.3, 26.6, 24.5, 24.2, 16.31, 16.26. IR (thin film) ν_{max} 2943, 1731, 1420 cm^{-1}. MS (EI): *m/z* (%) 513 (M^+), 511 (M^+), 313, 311, 255, 84 (100). HRMS calcd. for $C_{18}H_{25}F_2O_5PN_3Br$ (M^+): 511.0683; Found: 511.0680.

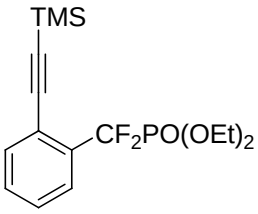


Diethyl (difluoro(phenyl)methyl)phosphonate (6). To a solution of **3ba** (0.2 mmol, 75 mg) in dioxane (2 mL) was added $BF_3.Et_2O$ (75 μL). The resulting mixture was then heated to 60 °C and stirred for 24 h. The reaction mixture was then cooled room temperature and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1) to give compound **6** in 85% yield (45 mg) as an oil. This compound is known.[3] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (m, 2 H), 7.44 (m, 3 H), 4.22-4.10 (m, 4 H), 1.30 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -108.5 (*d*, *J*= 115.8 Hz, 2 F).

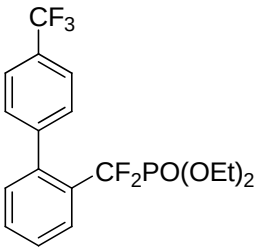


(*E*)-Diethyl (difluoro(2-styrylphenyl)methyl)phosphonate (7.) To a Schlenck tube were added $Pd(OAc)_2$ (0.02 mmol, 6 mg), **3ba** (0.2 mmol, 75 mg), and styrene (0.4 mmol, 46 μL). EtOH (2 mL) and $BF_3{\cdot}Et_2O$ (37 μL) were then added subsequently. The reaction mixture was then heated to 60 °C and stirred for 24 h. The reaction mixture was then cooled room temperature and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1) to give compound **7** in 93% yield (68 mg) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dt, *J* = 16.2 Hz, *J* = 3.2 Hz, 1 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.54 (d, *J* = 7.6 Hz, 2 H), 7.47 (t, *J* = 7.6 Hz, 1 H), 7.36 (m, 3 H), 7.26 (t, *J* = 7.6 Hz, 1 H), 6.97 (d, *J* = 16.2 Hz, 1 H), 4.26-4.12 (m, 4 H), 1.30 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.2 (d, *J* = 115.1 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 138.9 (d, *J* = 2.0 Hz), 133.0, 132.7, 131.4 (td, *J* = 20.0 Hz, *J* = 13.4 Hz), 130.4,

129.5, 129.4 (td, J = 11.4 Hz, J = 1.7 Hz), 129.2, 129.0, 128.9 (t, J = 2.1 Hz), 128.6, 121.1 (td, J = 263.7 Hz, J = 216.0 Hz), 66.57, 66.50, 18.10, 18.05. IR (thin film) ν_{max} 3025, 1599, 1496 cm^{-1}. MS (EI): *m/z* (%) 366 (M^+), 207, 187 (100), 127, 84. HRMS calcd. for $C_{19}H_{21}F_2O_3P$ (M^+): 366.1196; Found: 366.1193.

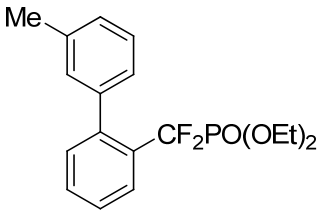


Diethyl (difluoro(2-((trimethylsilyl)ethynyl)phenyl)methyl)phosphonate (8). To a sealed tube was added **3ba** (75 mg, 0.2 mmol), followed by MeI (2 mL). The sealed tube was screwed capped and heated to 100 ^oC. After stirring for 14 h, the reaction mixture was cooled room temperature, and concentrated. To the residue was added $PdCl_2(PPh_3)_2$ (0.02 mmol, 14 mg), CuI (0.02 mmol, 4 mg), ethynyltrimethylsilane (0.4 mmol, 50 mg), and Et_3N (1 mL). After stirring for 24 h at room temperature, the reaction mixture was concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 6:1) to give compound **8** in 82% yield (59 mg, 2 steps) as an oil.^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (m, 2 H), 7.40 (m, 2 H), 4.26-4.19 (m, 4 H), 1.34 (t, J = 7.2 Hz, 3 H), 0.25 (s, 9 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.7 (d, J = 115.5 Hz, 2 F). ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.8, 133.7 (td, J = 20.4 Hz, J = 13.9 Hz), 130.2 (d, J = 1.2 Hz), 128.2 (d, J = 1.2 Hz), 127.9 (td, J = 8.0 Hz, J = 2.0 Hz), 121.4 (q, J = 3.0 Hz), 118.3 (td, J = 264.2 Hz, J = 216.7 Hz), 102.4, 99.2, 64.80, 64.75, 16.42, 16.37, 0.3. IR (thin film) ν_{max} 2961, 2161, 1485 cm^{-1}. MS (EI): *m/z* (%) 360 (M^+), 345 (100), 141, 129. HRMS calcd. for $C_{16}H_{23}F_2O_3PSi$ (M^+): 360.1122; Found: 360.1119.

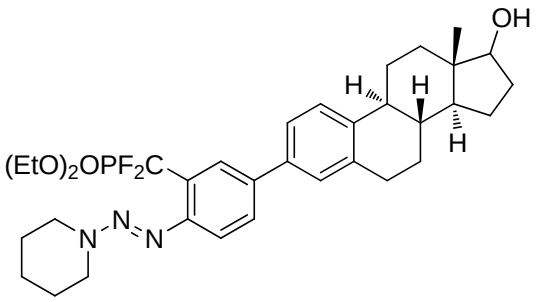


Diethyl(difluoro(4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)methyl)phosphonate (9). To a

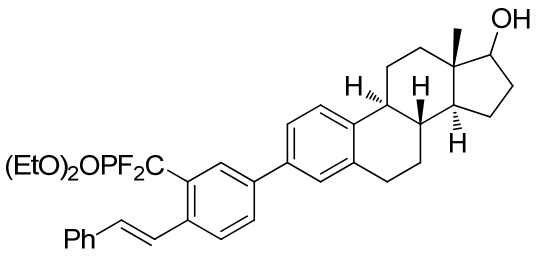
Schlenck tube were added $Pd(OAc)_2$ (0.01 mmol, 3 mg), (4-(trifluoromethyl)phenyl)boronic acid (0.4 mmol, 76 mg), and **3ba** (75 mg, 0.2 mmol). Dioxane (2 mL) and $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol) were subsequently added. After stirring at room temperature for 24 h, the reaction mixture was concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1) to give compound **9** in 85% yield (69 mg) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (m, 1 H), 7.60 (d, *J* = 8.2 Hz, 2 H), 7.52 (d, *J* = 8.2 Hz, 2 H), 7.46 (m, 2 H), 7.19 (m, 1 H), 4.19-4.07 (m, 4 H), 1.28 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.5 (s, 3 F), -95.3 (d, *J* = 114.3 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 140.1, 132.2, 130.3, 130.0 (m), 129.2 (q, *J* = 32.0 Hz), 128.3 (t, *J* = 8.8 Hz), 127.8, 124.3 (q, *J* = 270.4 Hz), 124.1 (q, *J* = 3.6 Hz), 119.3 (td, *J* = 261.0 Hz, *J* = 216.2 Hz), 64.80, 64.73, 16.33, 16.28. IR (thin film) ν_{max} 2917, 1618 cm^{-1}. MS (EI): *m/z* (%) 408 (M^+), 275, 255 (100), 189, 84. HRMS calcd. for $C_{18}H_{18}F_5O_3P$ (M^+): 408.0914; Found: 408.0919.



Diethyl (difluoro(3'-methyl-[1,1'-biphenyl]-2-yl)methyl)phosphonate (10). To a Schlenck tube were added $Pd(OAc)_2$ (0.01 mmol, 3 mg), *m*-tolylboronic acid (0.4 mmol, 61 mg), and **3ba** (75 mg, 0.2 mmol). Dioxane (2 mL) and $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol) were subsequently added. The resulting mixture was stirred at room temperature for 24 h. The reaction mixture was then concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 4:1) to give compound **10** in 97% yield (69 mg) as an oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.2 Hz, 1 H), 7.44 (m, 2 H), 7.25-7.17 (m, 4 H), 7.14 (d, *J* = 7.2 Hz, 1 H), 4.18-4.05 (m, 4 H), 2.37 (s, 3 H), 1.28 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.6 (d, *J* = 115.5 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 141.2, 136.5, 132.5, 130.1, 128.2 (t, *J* = 7.1 Hz), 127.6, 127.1, 127.0, 126.4, 119.3 (td, *J* = 261.2 Hz, *J* = 216.7 Hz), 64.67, 64.60, 21.4, 16.35, 16.29. IR (thin film) ν_{max} 2984, 1478 cm^{-1}. MS (EI): *m/z* (%) 354 (M^+), 217, 197 (100). HRMS calcd. for $C_{18}H_{21}F_2O_3P$ (M^+): 354.1196; Found:354.1200.

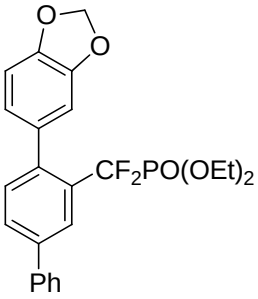


Diethyl(difluoro(5-((8*R*,9*S*,13*S*,14*S*)-17-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)-2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (12). To a solution of **3bj** (0.3 mmol, 136 mg) in dioxane (2 mL) were added $Pd(OAc)_2$ (4 mg, 0.015 mmol), PPh_3 (8 mg, 0.03 mmol), aryl boronic acid **11** (169 mg, 0.45 mmol), K_3PO_4 (223 mg, 1.05 mmol), and H_2O (40 μL). The resulting mixture was heated to 60 ^oC and stirred for 24 h. The reaction was cooled room temperature and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 3:1) to give compound **12** in 83% yield (155 mg) as a solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1 H), 7.63 (d, *J* = 8.4 Hz, 1 H), 7.56 (d, *J* = 8.4 Hz, 1 H), 7.36 (q, *J* = 8.4 Hz, 2 H), 7.32 (s, 1 H), 4.24-4.10 (m, 4 H), 3.87 (br, 4 H), 3.71 (t, *J* = 8.4 Hz, 1 H), 2.93 (m, 2 H), 2.36 (d, *J* = 8.4 Hz, 1 H), 2.23 (m, 1 H), 2.09 (m, 1 H), 2.02 (s, 1 H), 1.98-1.87 (m, 3 H), 1.71 (m, 6H), 1.56-1.45 (m, 3 H), 1.39-1.16 (m, 4 H), 1.26 (t, *J* = 7.2 Hz, 6 H), 0.75 (s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.3 (d, *J* = 117.0 Hz, 2 F). IR (thin film) ν_{max} 3433, 2926, 1481 cm^{-1}. MS (TOF): *m/z* (%) 629 (M^+), 518 (100). HRMS calcd. for $C_{34}H_{46}N_3F_2O_4P$ (M^+): 629.3194; Found: 629.3192.



Diethyl(difluoro(5-((8*R*,9*S*,13*S*,14*S*)-17-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)-2-(styryl)phenyl)methyl)phosphonate (13). To a solution of compound **12** (63 mg, 0.11 mmol) in EtOH (2 mL) were added $Pd(OAc)_2$ (3 mg, 0.011 mmol), styrene (24 μL, 0.21 mmol), and $BF_3{\cdot}Et_2O$ (20 μL, 0.15 mmol). The resulting mixture was then heated to 60 ^oC and stirred for 24 h. The reaction mixture was cooled to room temperature and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc =

3:1) to give compound **13** in 92% yield (62 mg) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (m, 3 H), 7.68 (d, *J* = 8.0 Hz, 1 H), 7.55 (d, *J* = 7.2 Hz, 2 H), 7.41-7.35 (m, 5 H), 7.25 (m, 1 H), 7.01 (d, *J* = 16.4 Hz, 1 H), 4.28-4.11 (m, 4 H), 3.74 (t, *J* = 8.4 Hz, 1 H), 2.95 (dd, *J* = 8.4 Hz, *J* = 3.2 Hz, 2 H), 2.38 (m, 1 H), 2.29 (m, 1 H), 2.12 (m, 1 H), 2.03 (s, 1 H), 1.99-1.92 (m, 2 H), 1.60-1.48 (m, 4 H), 1.39-1.17 (m, 4 H), 1.28 (t, *J* = 7.2 Hz, 6 H), 0.78 (s, 3 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.1 (d, *J* = 115.1 Hz, 2 F). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.2, 140.0, 137.5, 137.4, 136.9, 135.7, 131.0, 130.0 (td, *J* = 19.9 Hz, *J* = 13.6 Hz), 129.2, 128.7, 127.8, 127.4, 126.83, 126.79 (t, *J* = 3.9 Hz), 126.00, 126.99 (td, *J* = 10.1 Hz, *J* = 2.5 Hz), 124.2, 119.4 (td, *J* = 263.5 Hz, *J* = 215.8 Hz), 81.8, 64.86, 64.81, 50.2, 44.4, 43.2, 38.6, 36.7, 30.6, 29.7, 27.2, 26.2, 23.1, 16.39, 16.34, 11.1. IR (thin film) ν_{max} 3451, 2927, 1483 cm^{-1}. MS (TOF): *m/z* (%) 620 (M^+, 100), 463. HRMS calcd. for $C_{37}H_{43}F_2O_4P$ (M^+): 620.2867; Found: 620.2870.



Diethyl((4-(benzo[d][1,3]dioxol-5-yl)-[1,1'-biphenyl]-3-yl)difluoromethyl)phosphonate (16). To a Schlenck tube were added $Pd(OAc)_2$ (2 mg, 0.0065 mmol), **3bj** (0.13 mmol, 60 mg), benzo[d][1,3]dioxol-5-ylboronic acid (0.26 mmol，44 mg). Dioxane (2 mL) and $BF_3{\cdot}Et_2O$ (25 μL, 0.2 mmol) were subsequently added. The reaction mixture was stirred at room temperature for 24 h. The reaction mixture was filtered through a silica gel pad, and the filtrate was concentrated. The residue was used for next step without further purification.To a second Schlenck bube were added $Pd_2(dba)_3$ (0.01 mmol, 10 mg), SPhos (0.017 mmol, 8 mg), K_3PO_4 (0.258 mmol, 64 mg), crude compound **15** obtained as above, and phenylboronic acid (21 mg, 0.172 mmol). Dioxane (2 mL) was then added. The resulting mixture was heated to 100 ^{o}C and stirred for 14 h. The reaction mixture was cooled room temperature and concentrated. The residue was purified with silica gel chromatography (Petroleum ether/EtOAc = 2:1) to give compound **16** in 68% yield (41 mg, 2 steps) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1 H), 7.66 (d, *J* = 8.8 Hz, 1 H), 7.62 (d, *J* = 7.6 Hz,

2 H), 7.45 (t, *J* = 7.6 Hz, 2 H), 7.36 (t, *J* = 7.6 Hz, 1 H), 7.28 (d, *J* = 8.4 Hz, 1 H), 6.93 (s, 1 H), 6.86 (dd, *J* = 8.4 Hz, *J* = 1.6 Hz ,1 H), 6.80 (d, *J* = 8.4 Hz, 1 H), 5.98 (s, 2 H), 4.22-4.12 (m, 4 H), 1.28 (t, *J* = 7.2 Hz, 6 H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.9 (d, *J* = 115.5 Hz, 2 F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.62, 146.54, 140.0, 139.6, 134.7, 133.3, 130.5 (td, *J* = 20.0 Hz, *J* = 14.5 Hz), 128.9, 128.6, 127.8, 127.1 127.0 (td, *J* = 6.4 Hz, *J* = 1.2 Hz), 122.8, 119.3 (td, *J* = 264.2 Hz, *J* = 216.5 Hz), 110.3, 107.8, 100.9, 67.05, 64.74, 64.67, 16.35, 16.30. IR (thin film) ν_{max} 2917, 1504, 1478 cm^{-1}. MS (EI): *m/z* (%) 460 (M^+), 203, 86, 84 (100). HRMS calcd. for $C_{24}H_{23}F_2O_5P$ (M^+): 460.1251; Found: 460.1253.

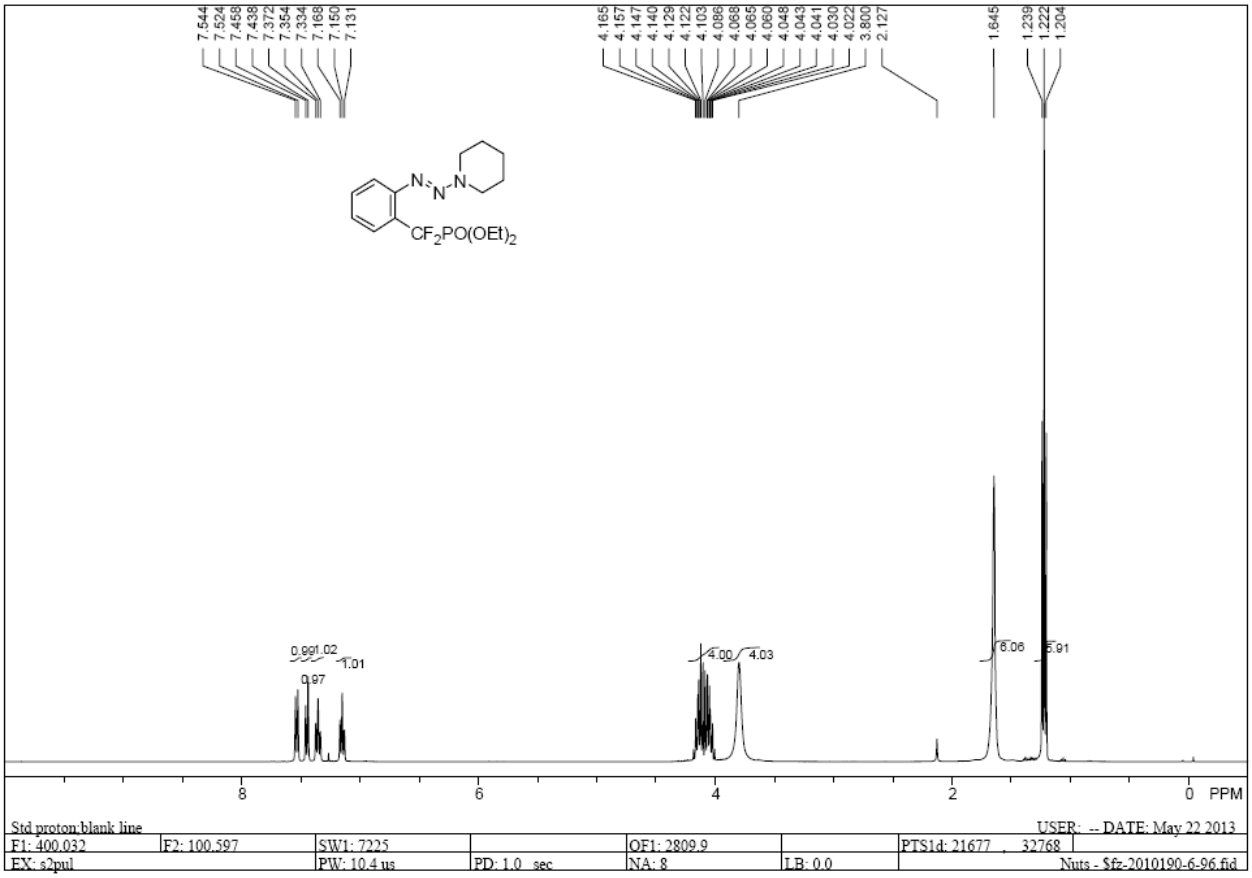
References:

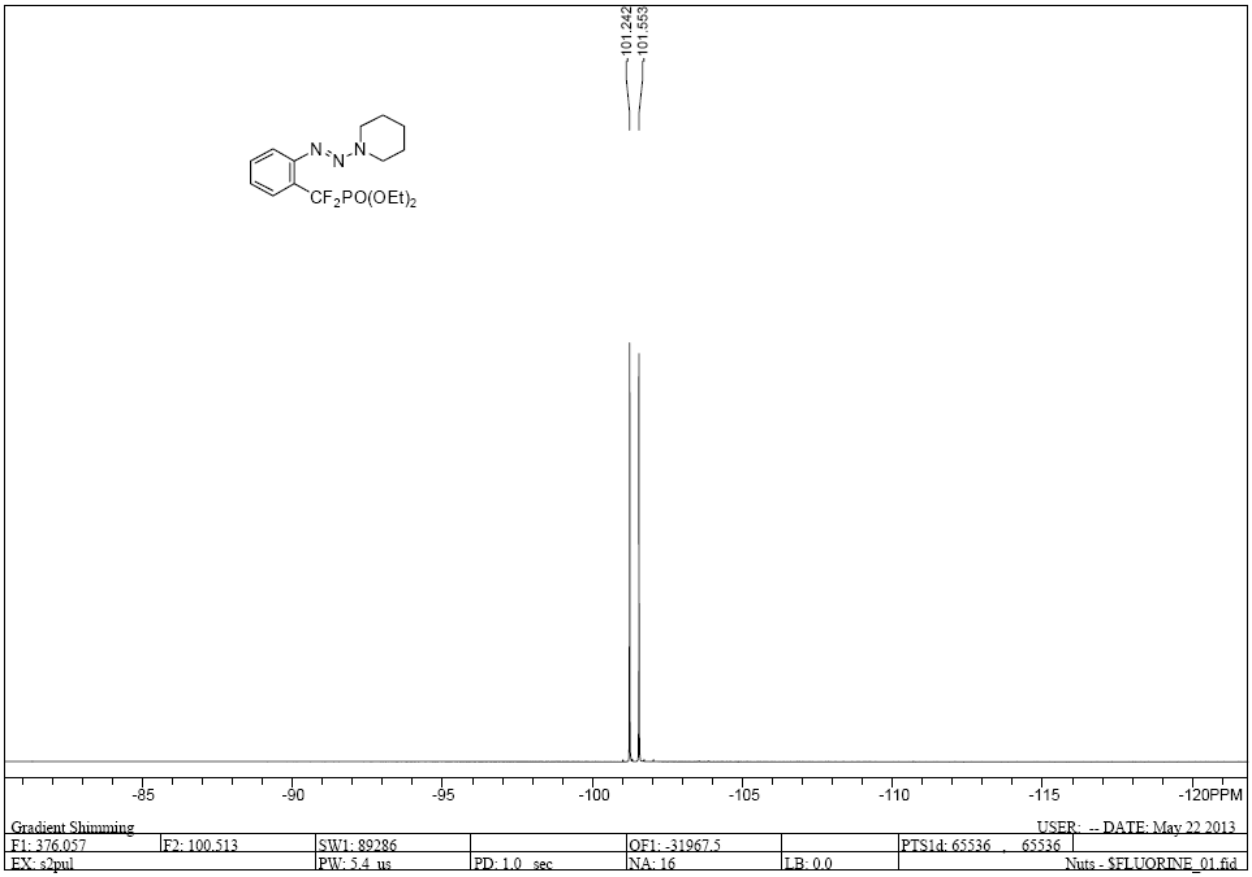
(1) Goeminne,A.; Scammells,P.J.; Devine,S.M.; Flynn, B.L. *Tetrahedron .Lett.* **2010**, *51*, 6882.

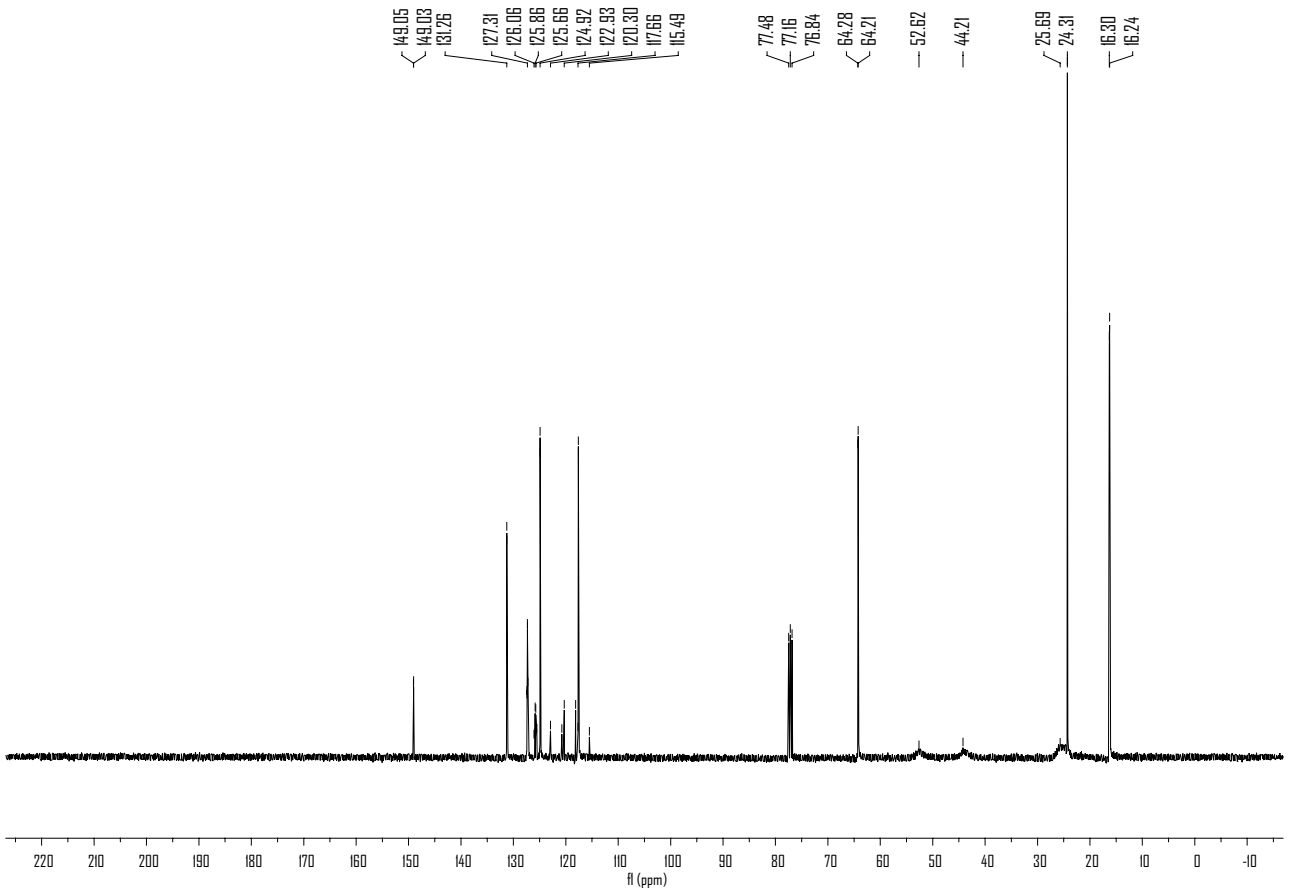
(2) Tonelli, M.; Vazzana, I.; Tasso, B.; Boido, V.; Sparatore, F.; Fermeglia, M.; Paneni, M.S.; Posocco, P.; Pricl, S.; La Colla, P.; Ibba, C.; Secci, B.; Collu, G.; Loddo, R. *Bioorg. Med.Chem.*, **2009**, 17, 4425.

(3) Yokomatsu, T.; Murano, T.; Suemune, K.; Shibuya, S. *Tetrahedron* **1997**, *53*, 815.

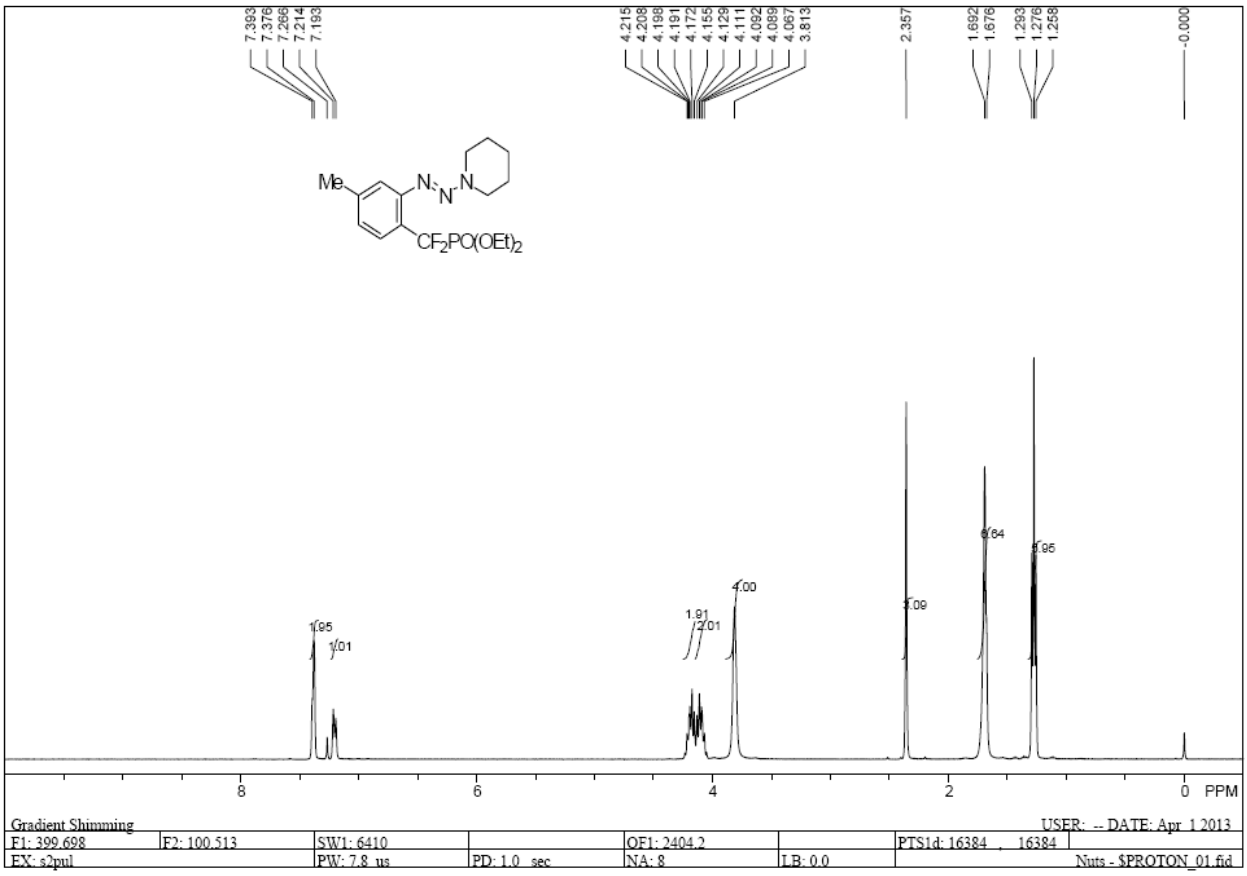
Diethyl (difluoro(2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3ba).

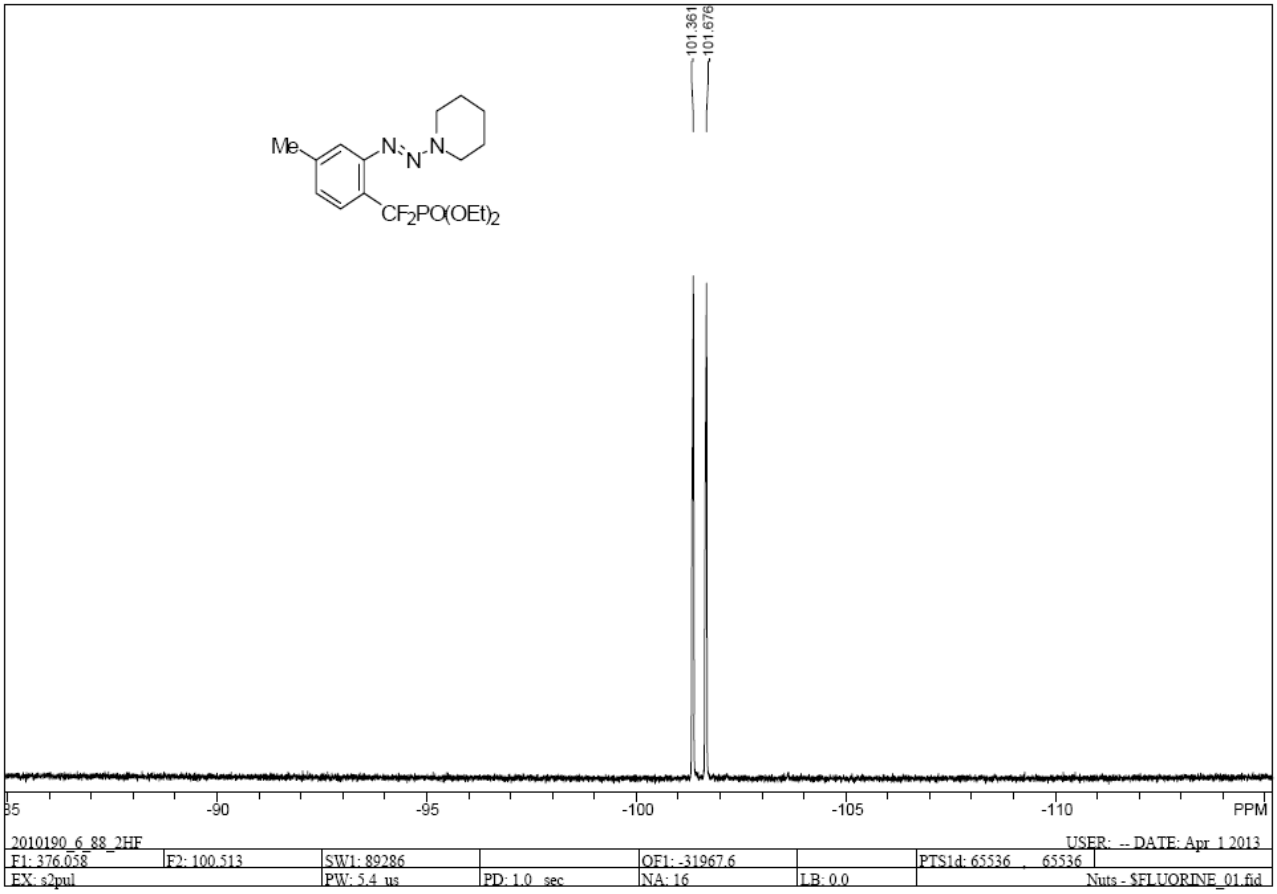






Diethyl (difluoro(4-methyl-2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3bb).

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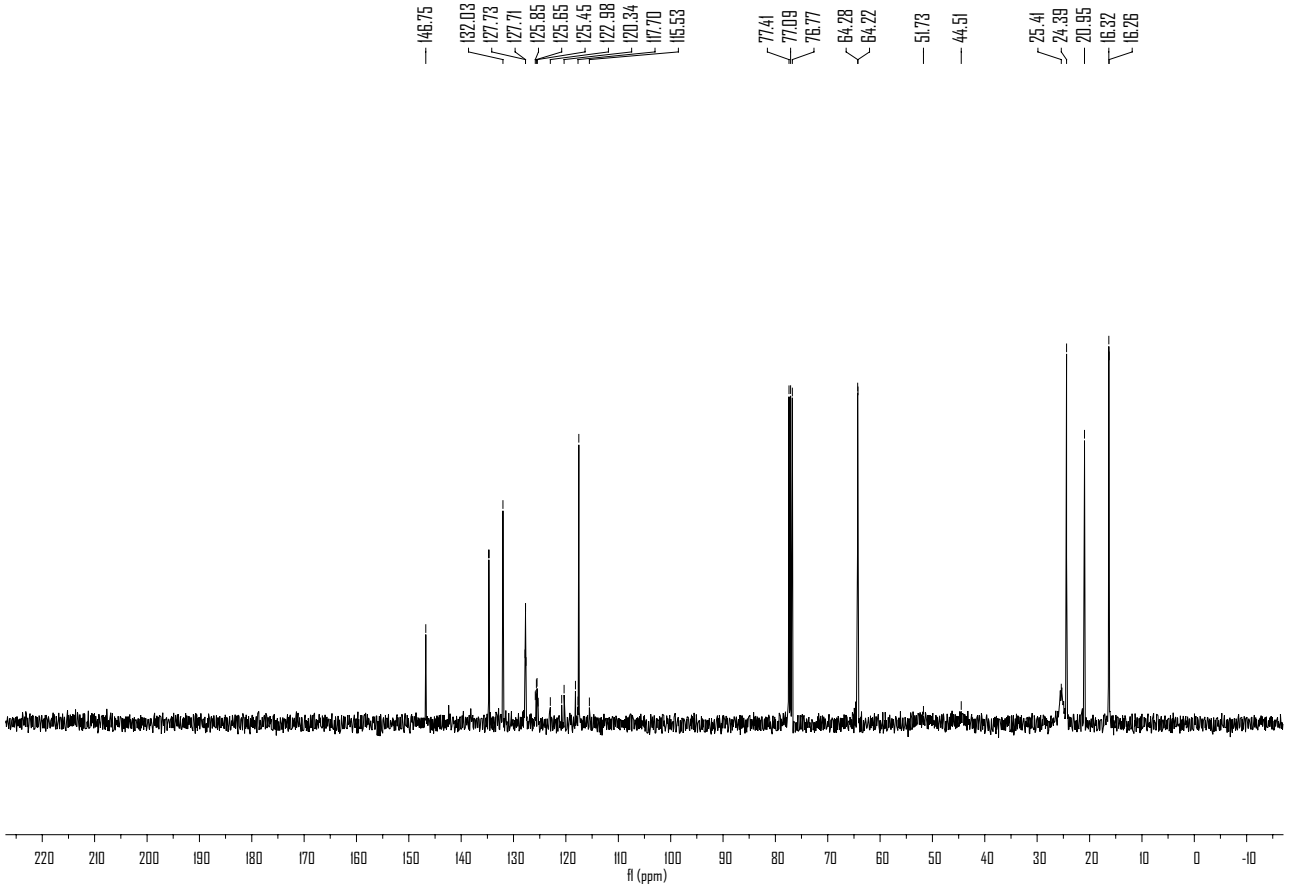
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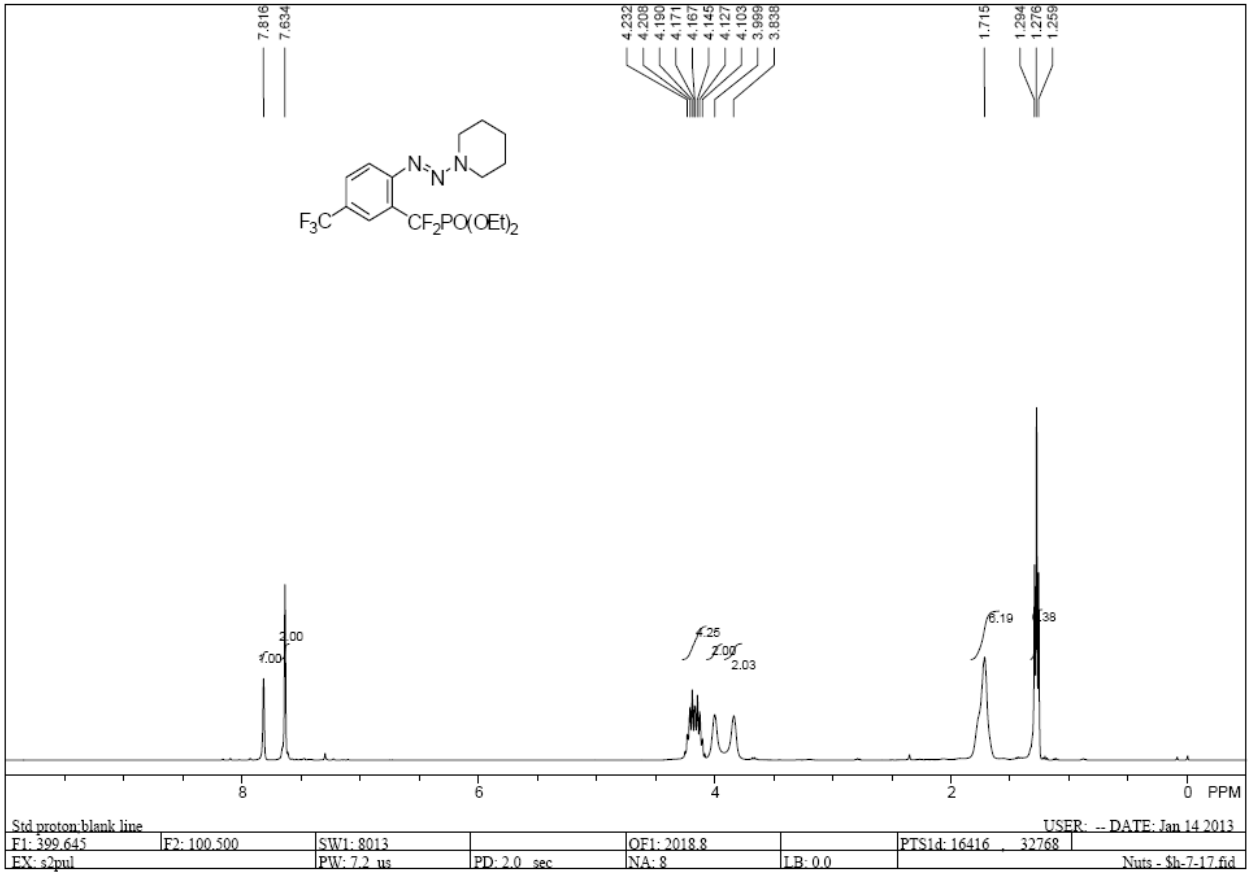
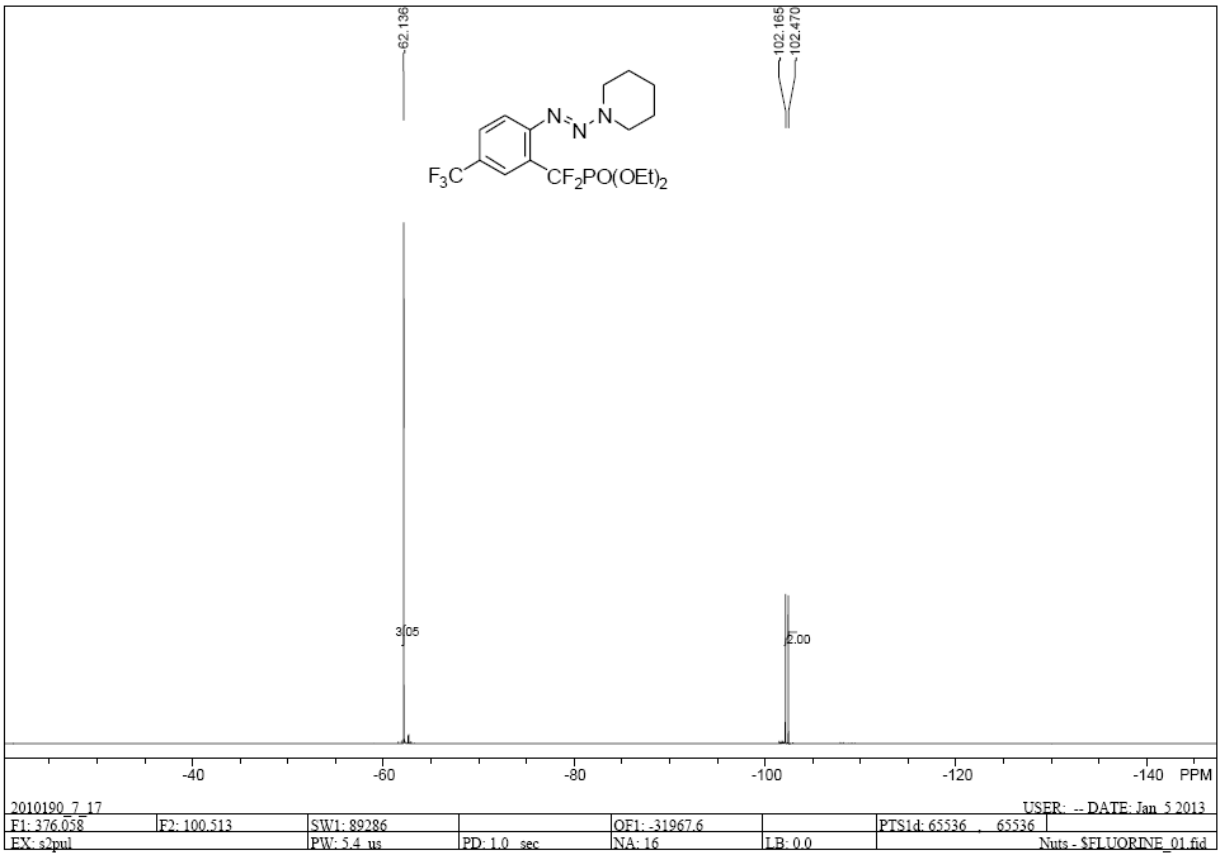
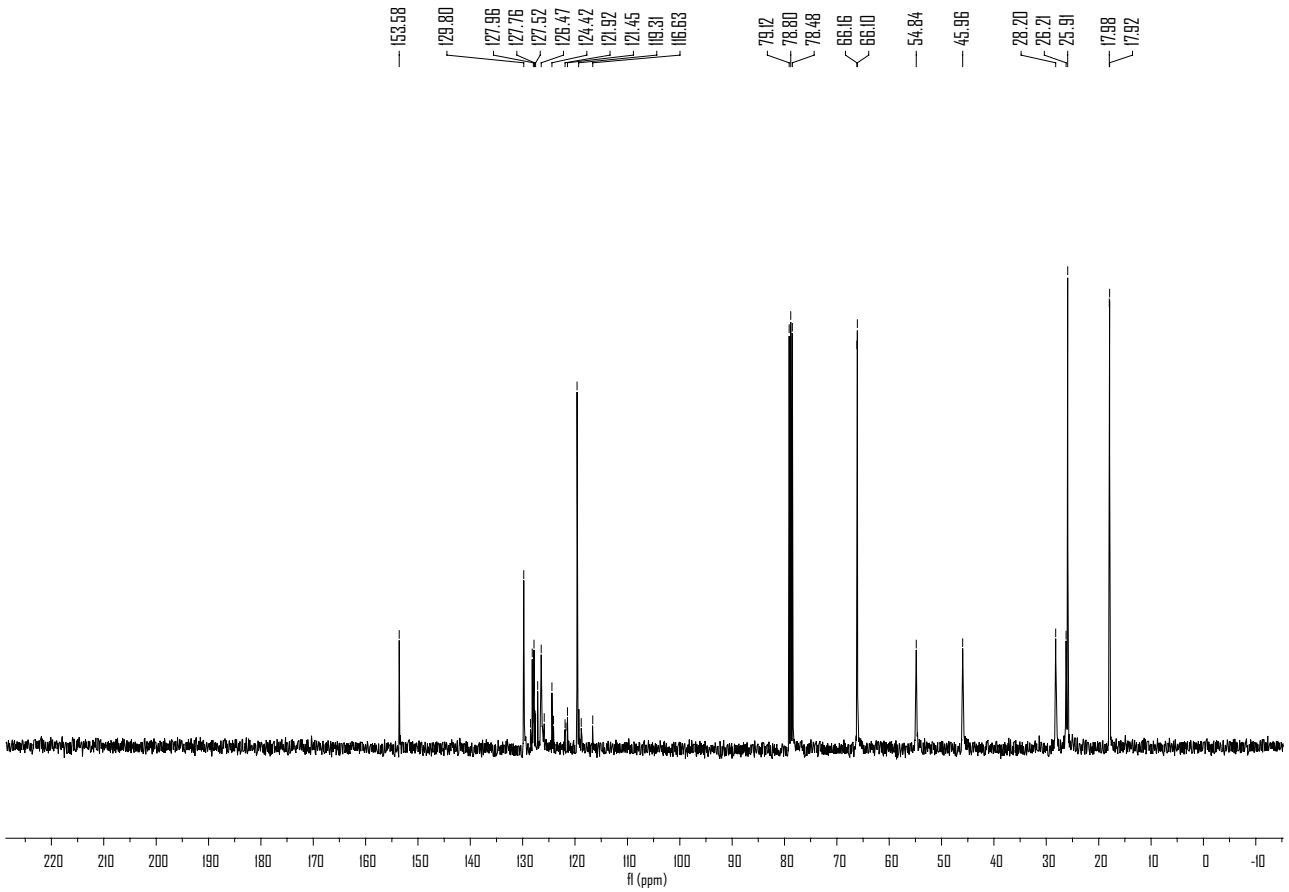
Diethyl(difluoro(2-(piperidin-1-yldiazenyl)-5-(trifluoromethyl)phenyl)methyl)phosphonate (3bc).







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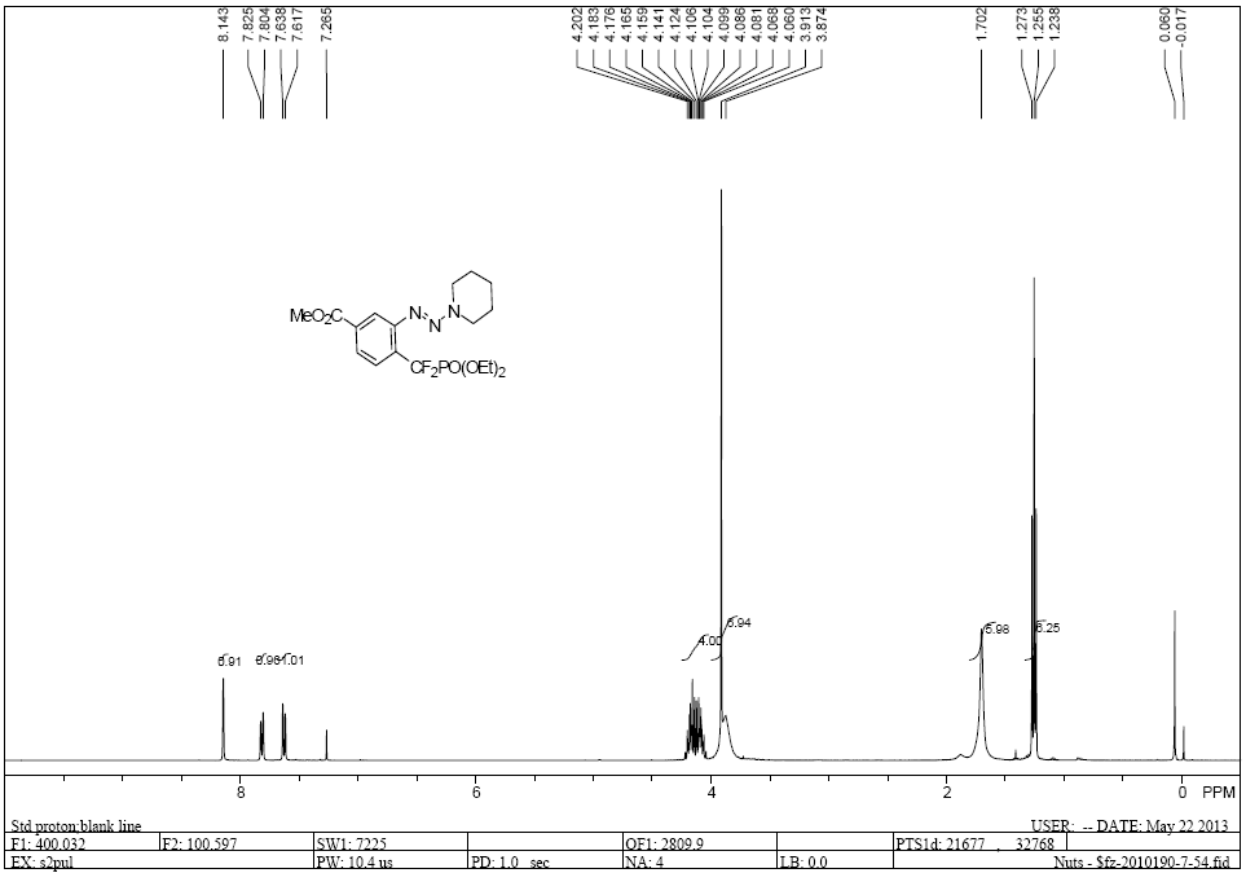

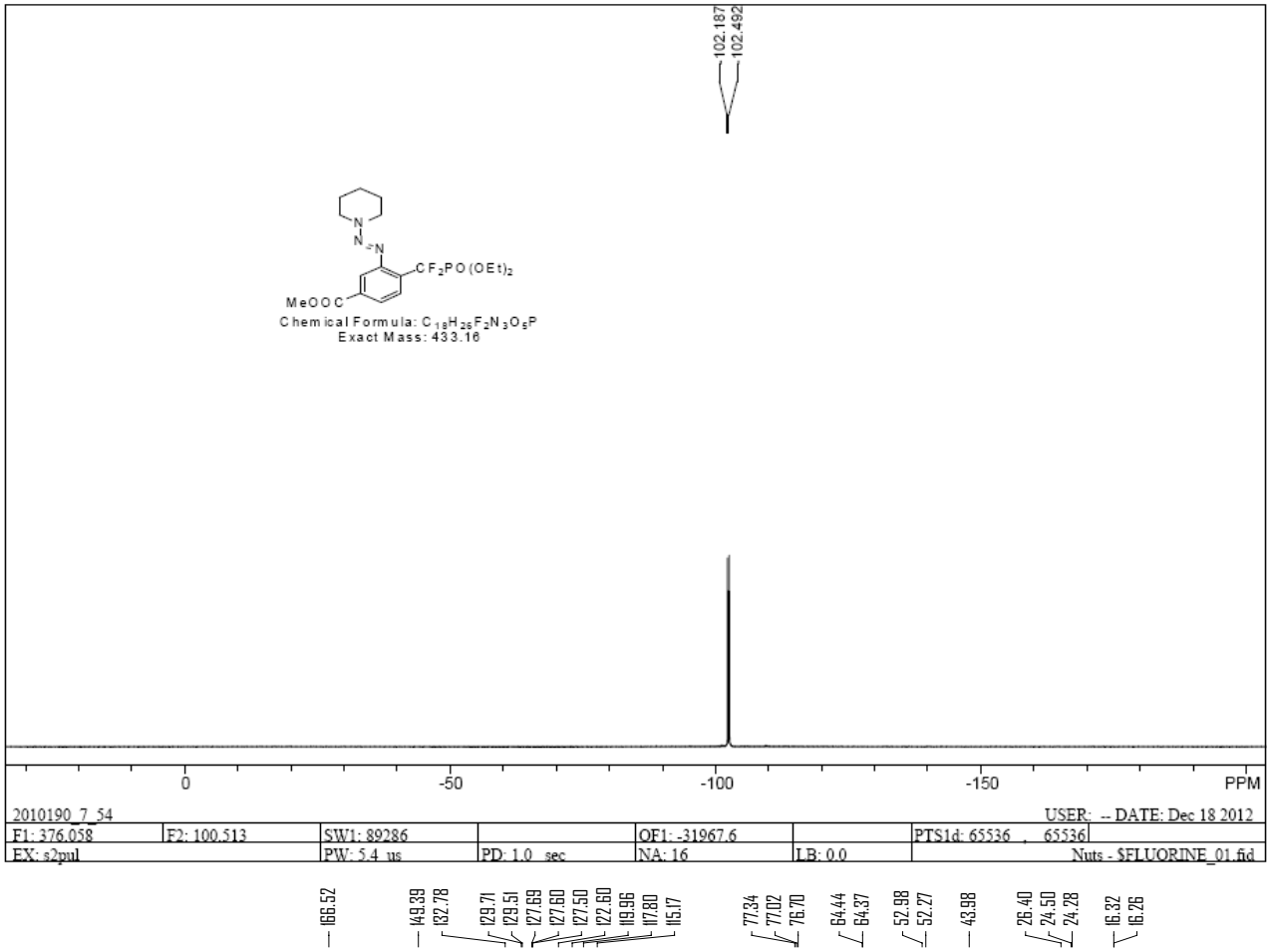
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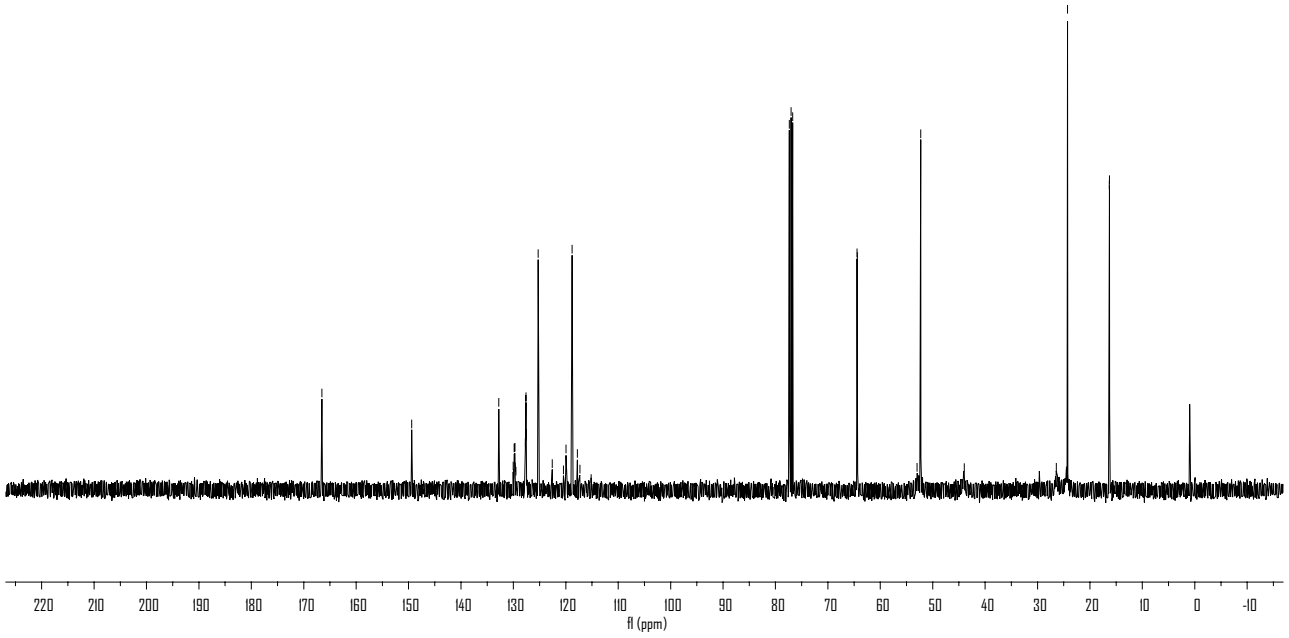
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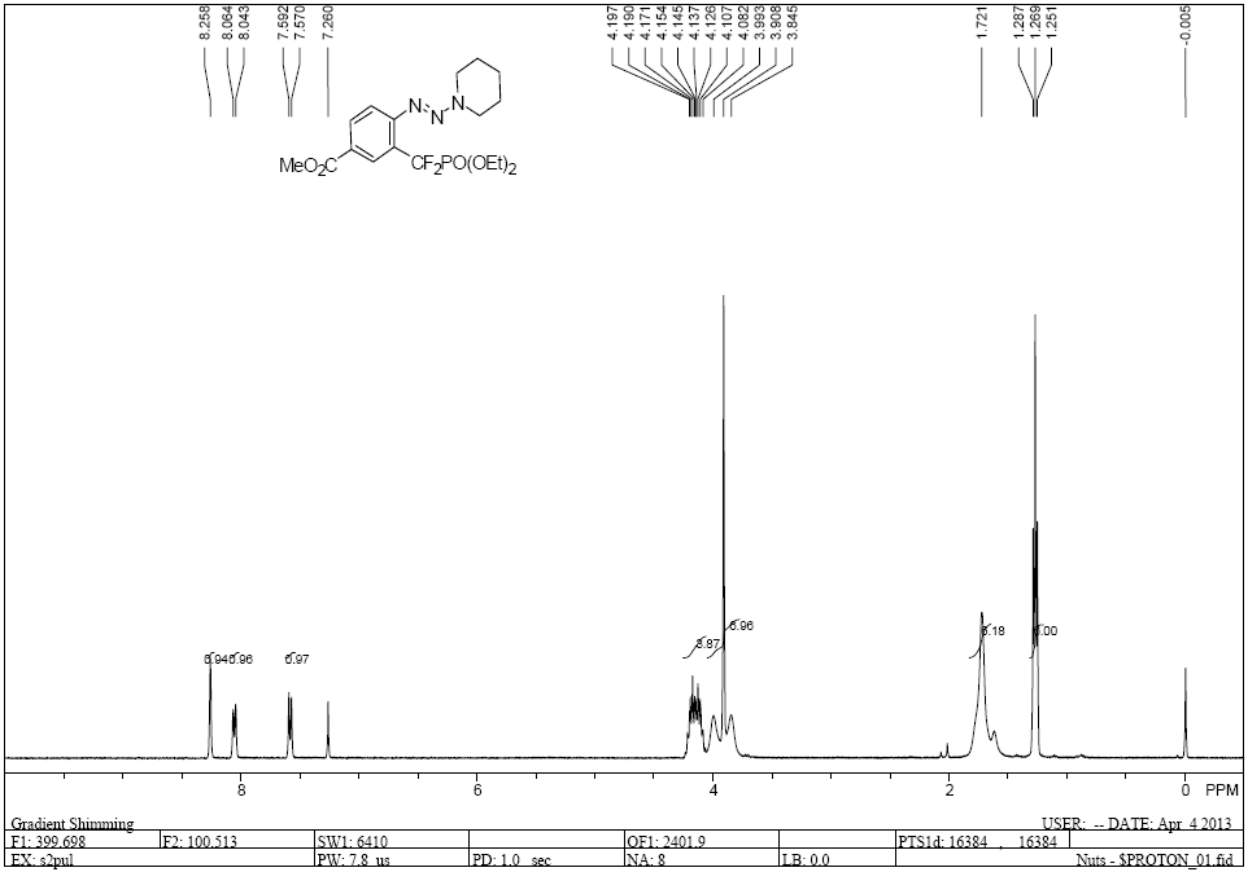
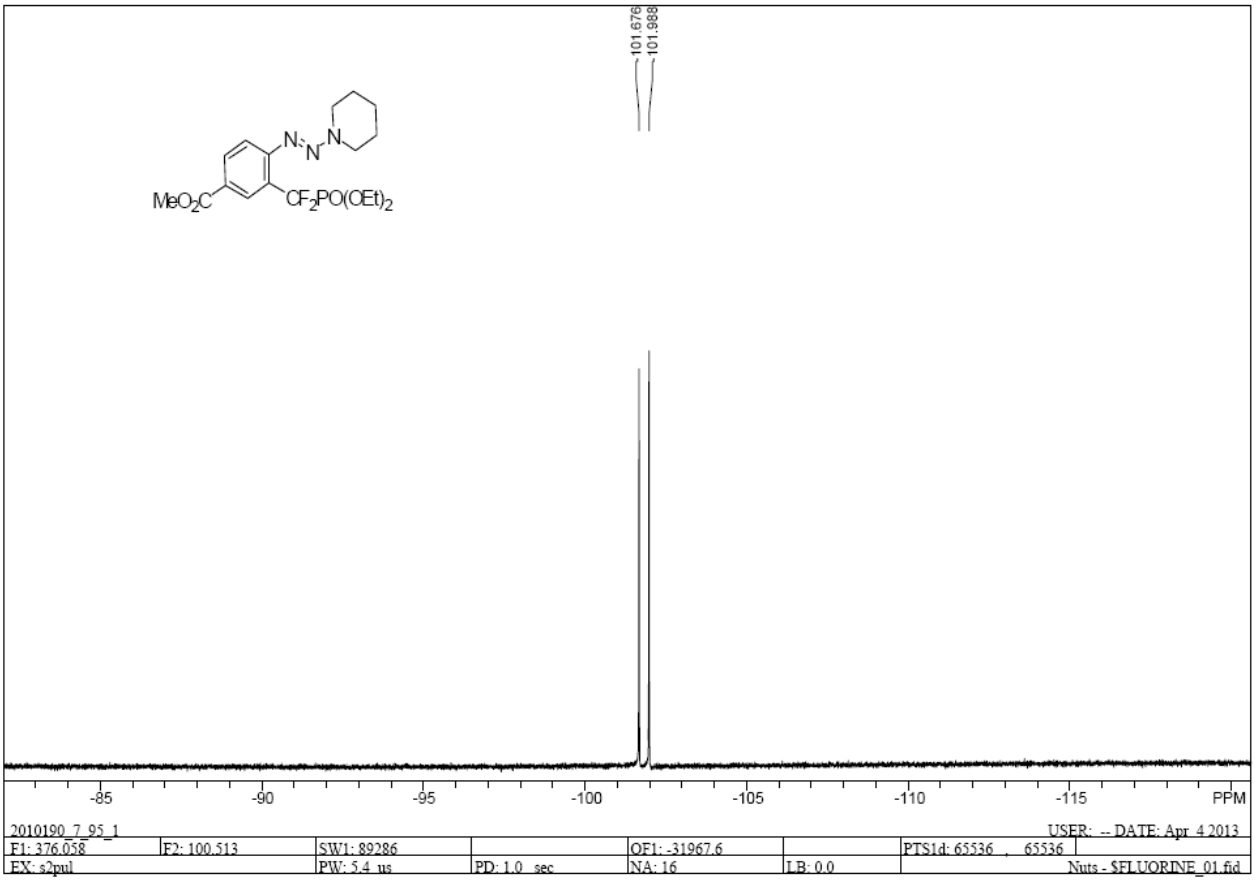
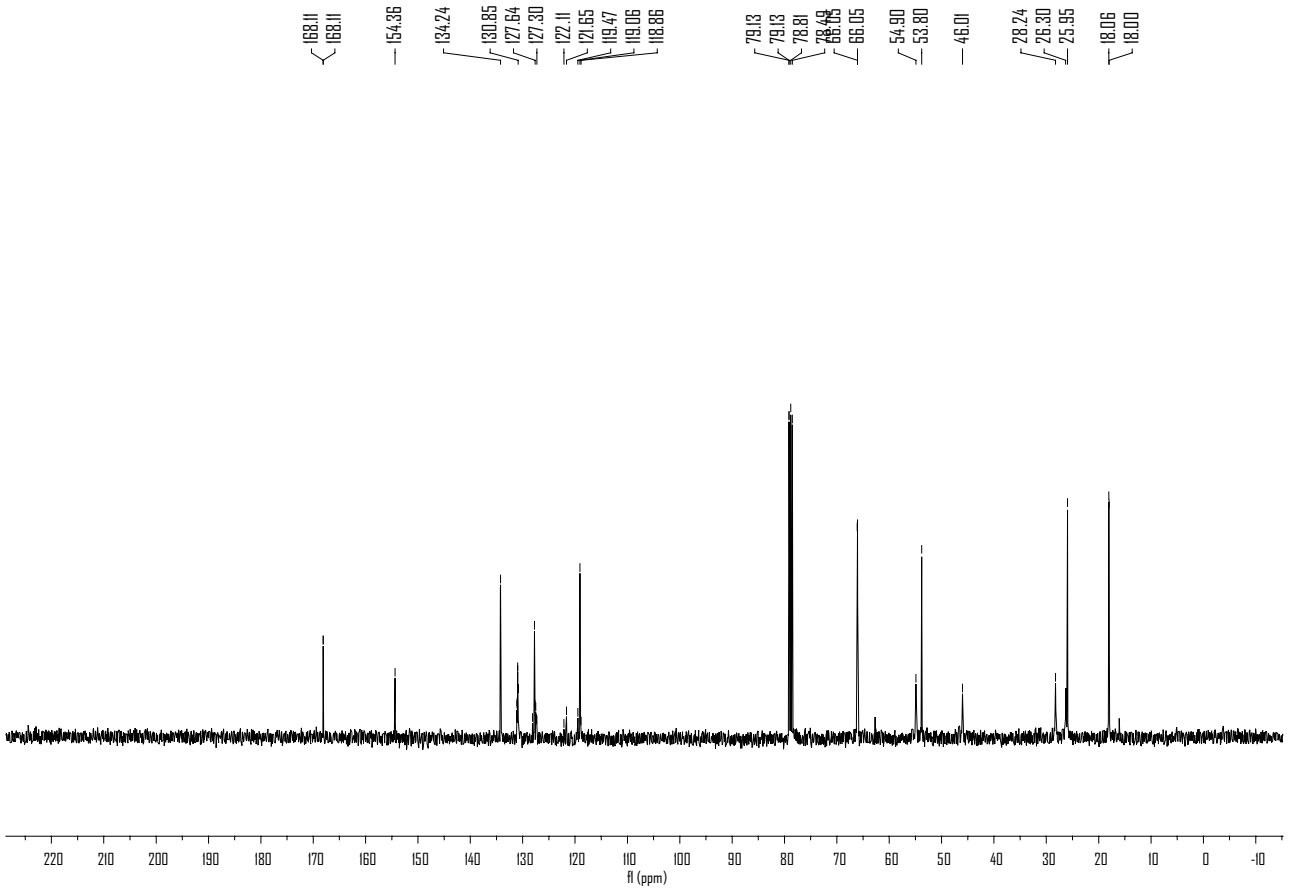
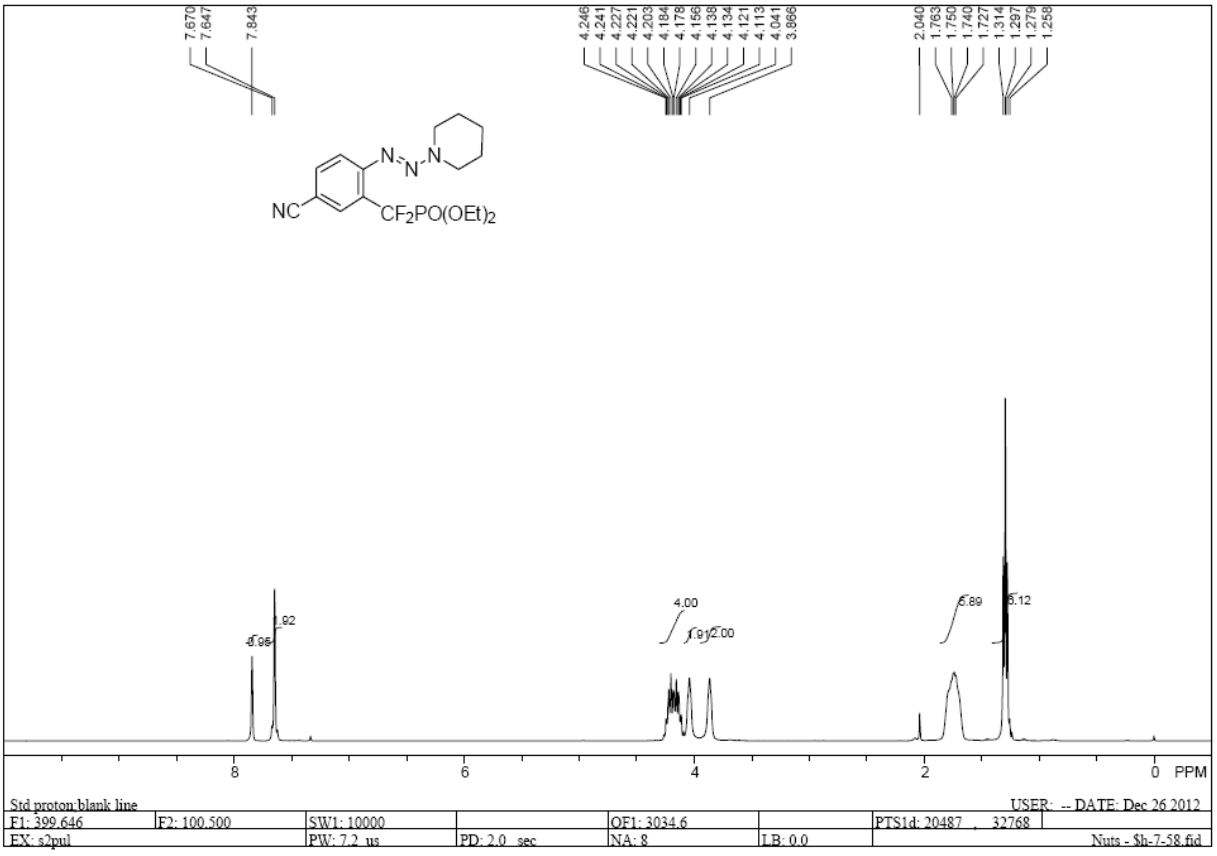
Methyl-3-((diethoxyphosphoryl)difluoromethyl)-4-(piperidin-1-yldiazenyl)benzoate (3be).

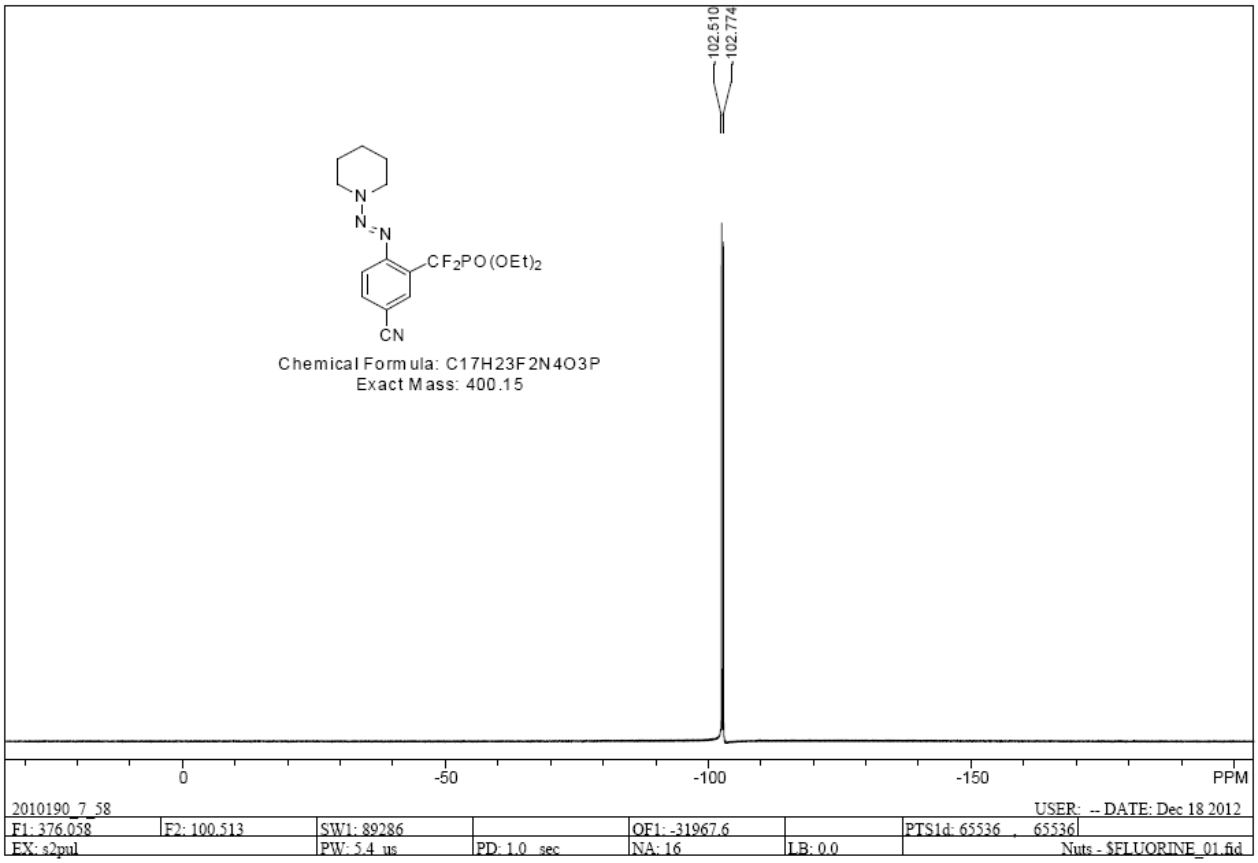


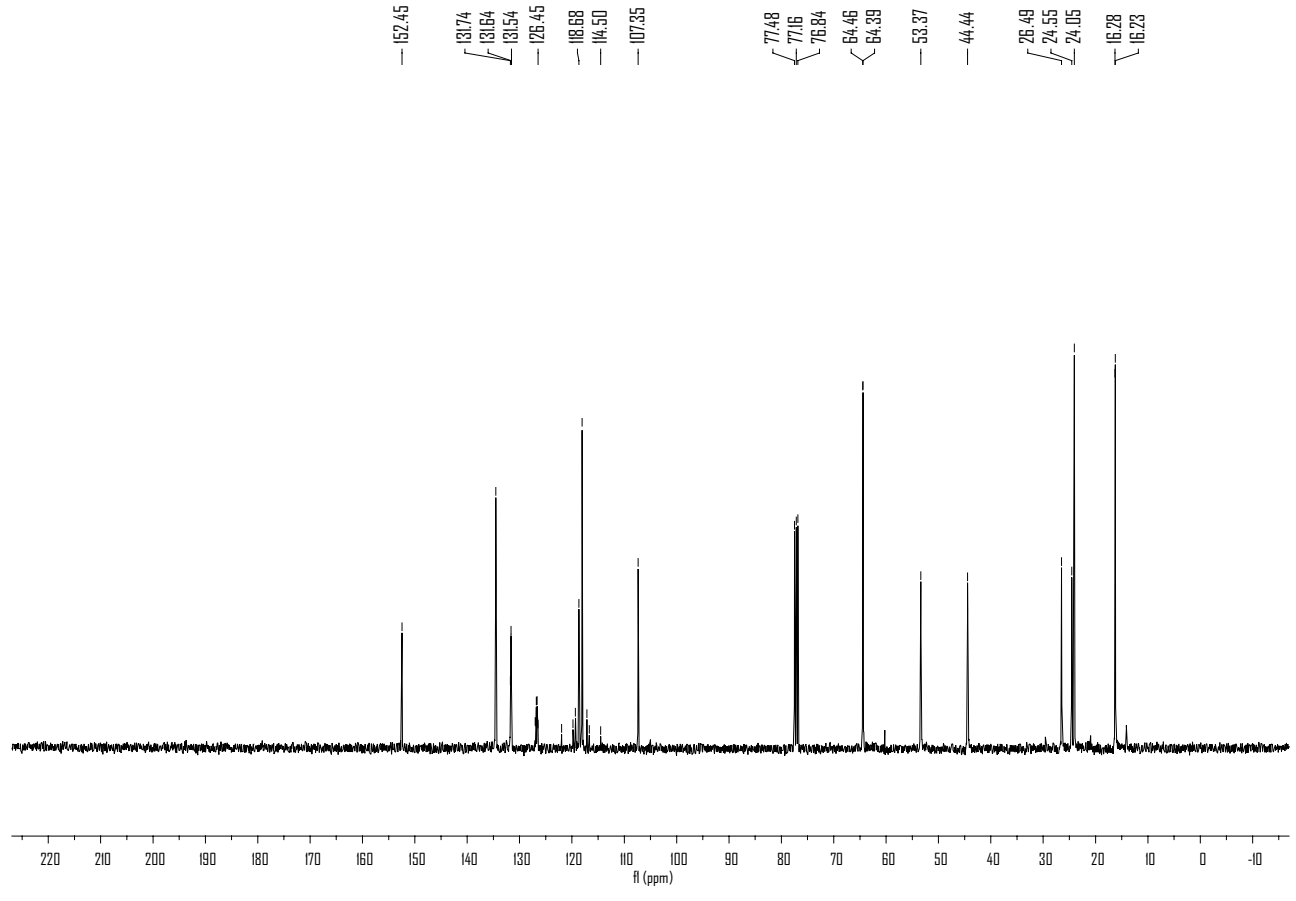




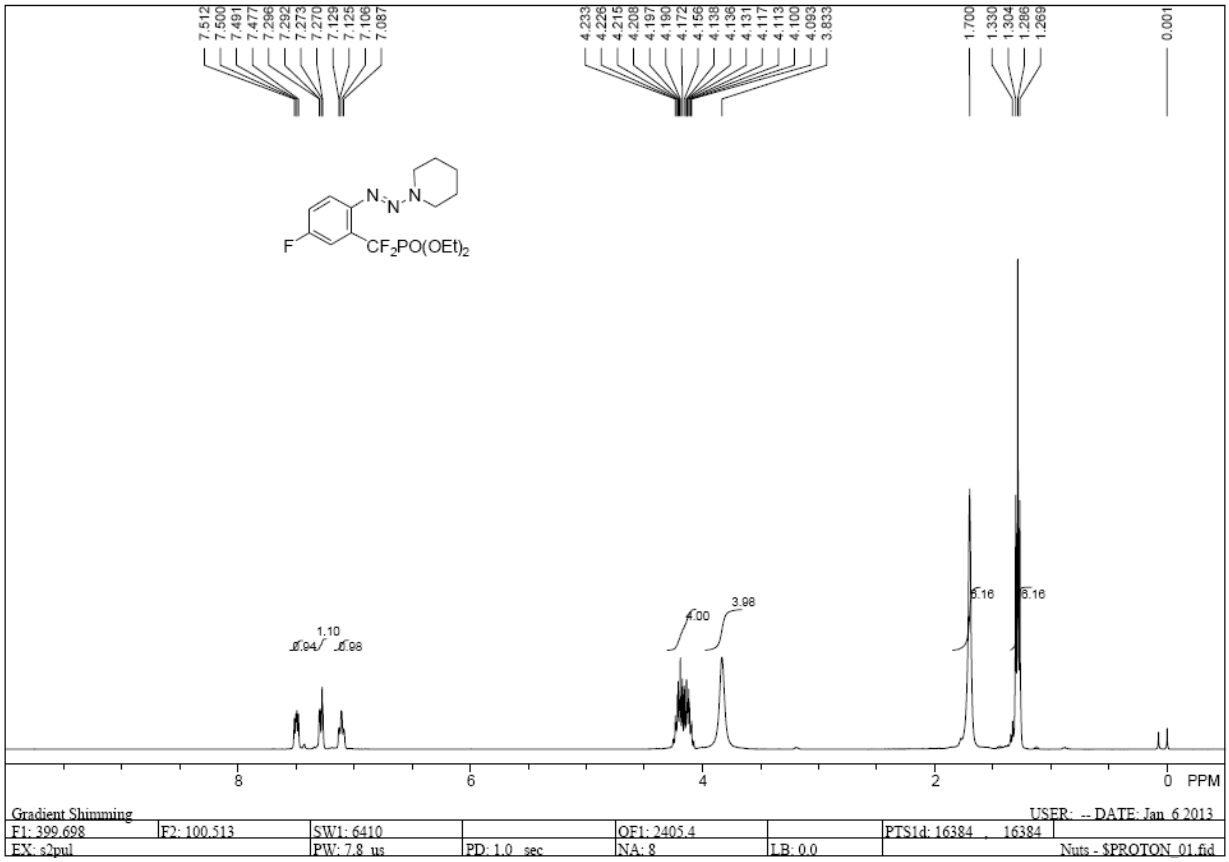
Diethyl((5-cyano-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bf).

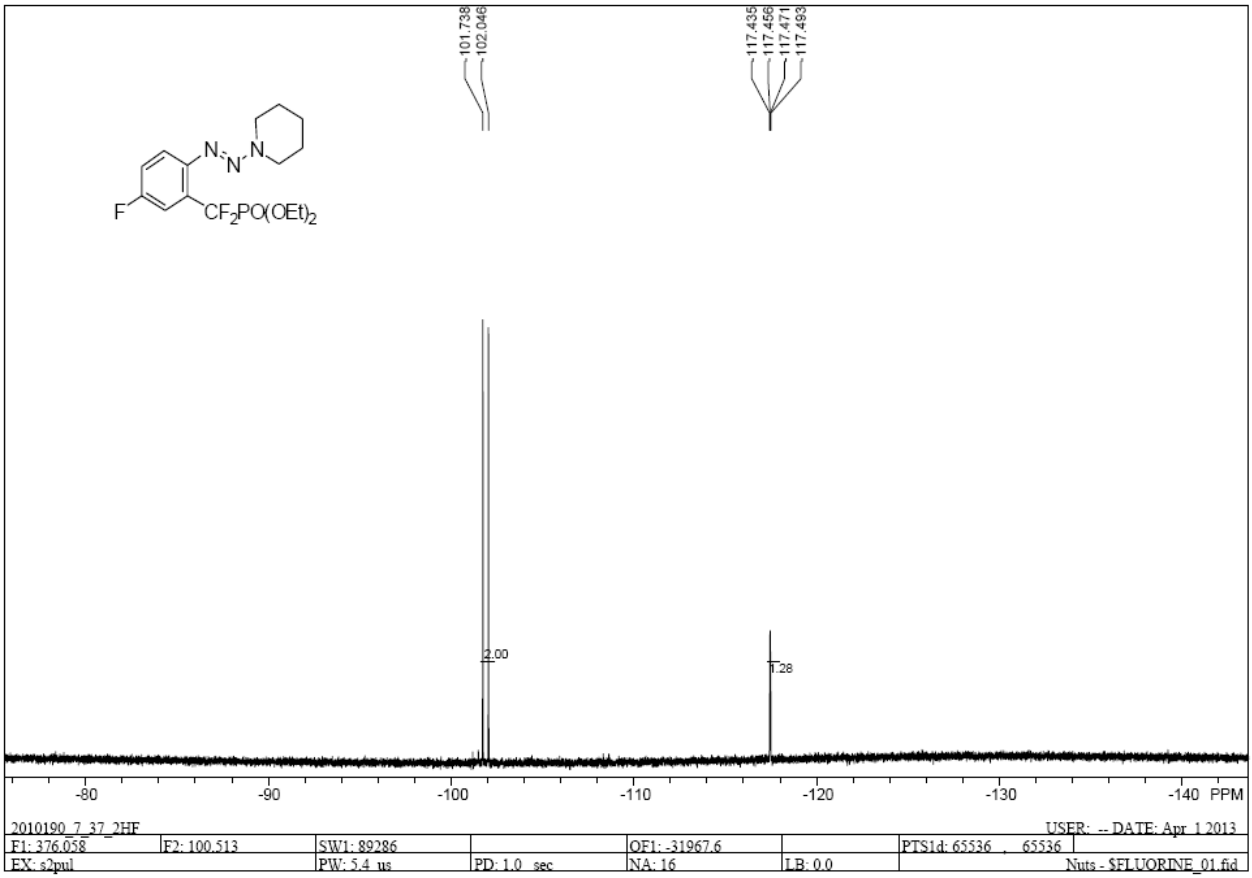


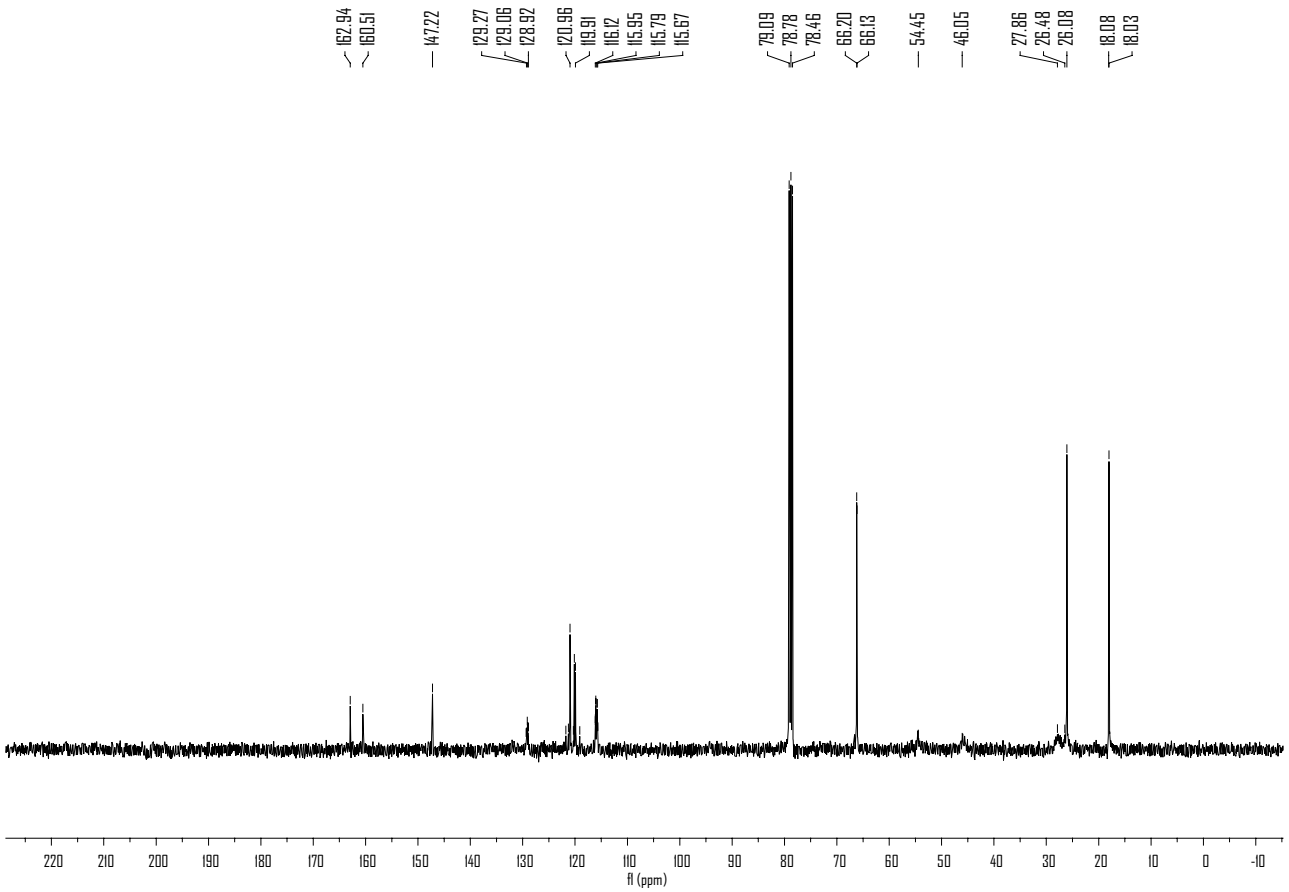




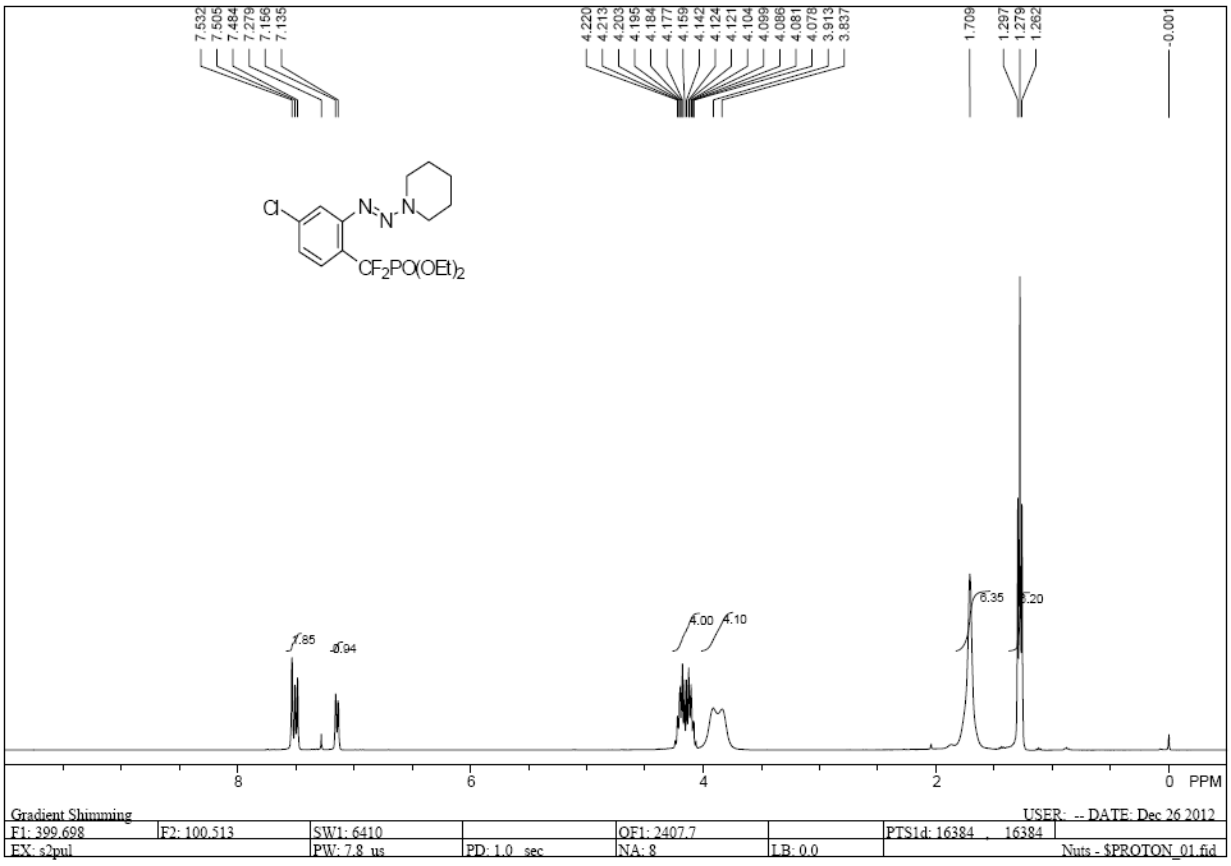
Diethyl(difluoro(5-fluoro-2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3bg).

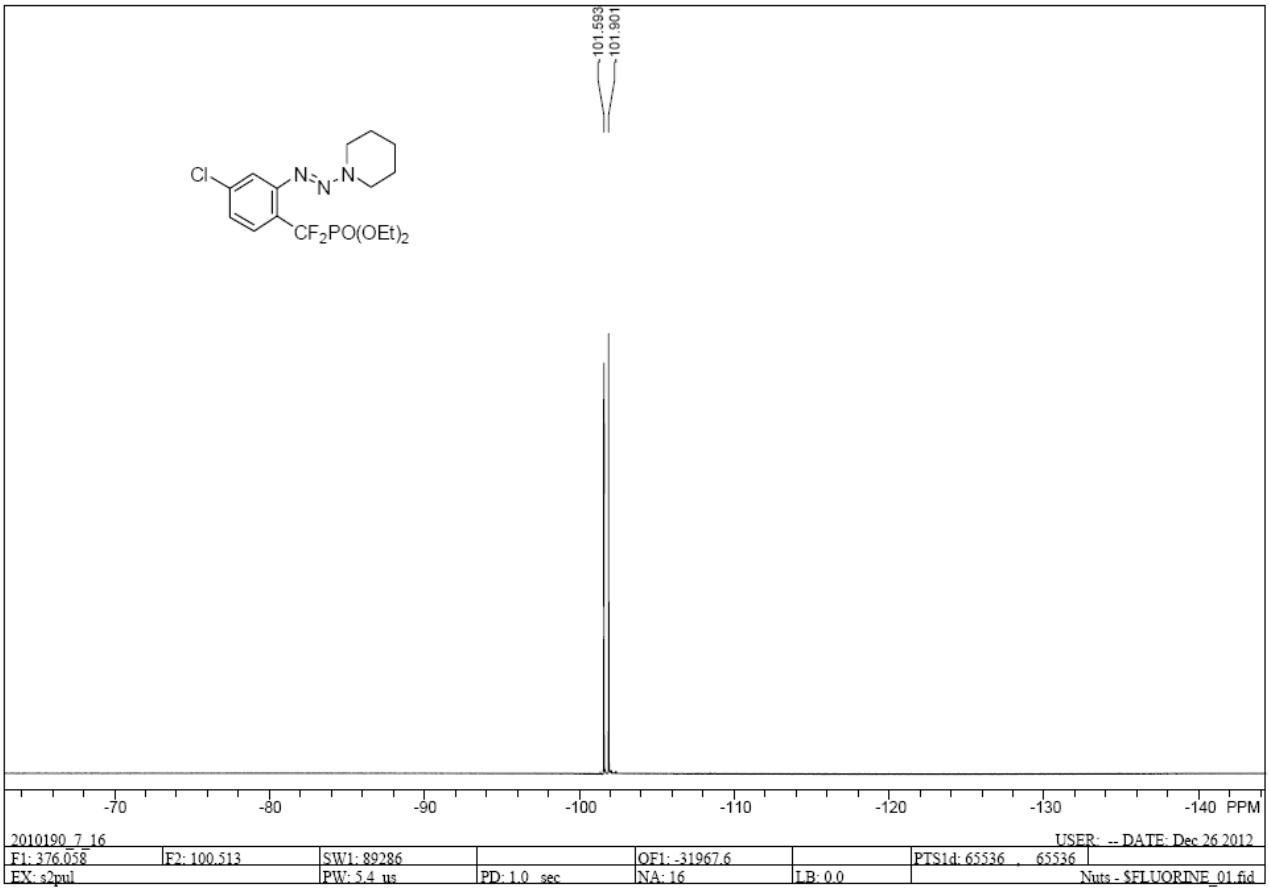


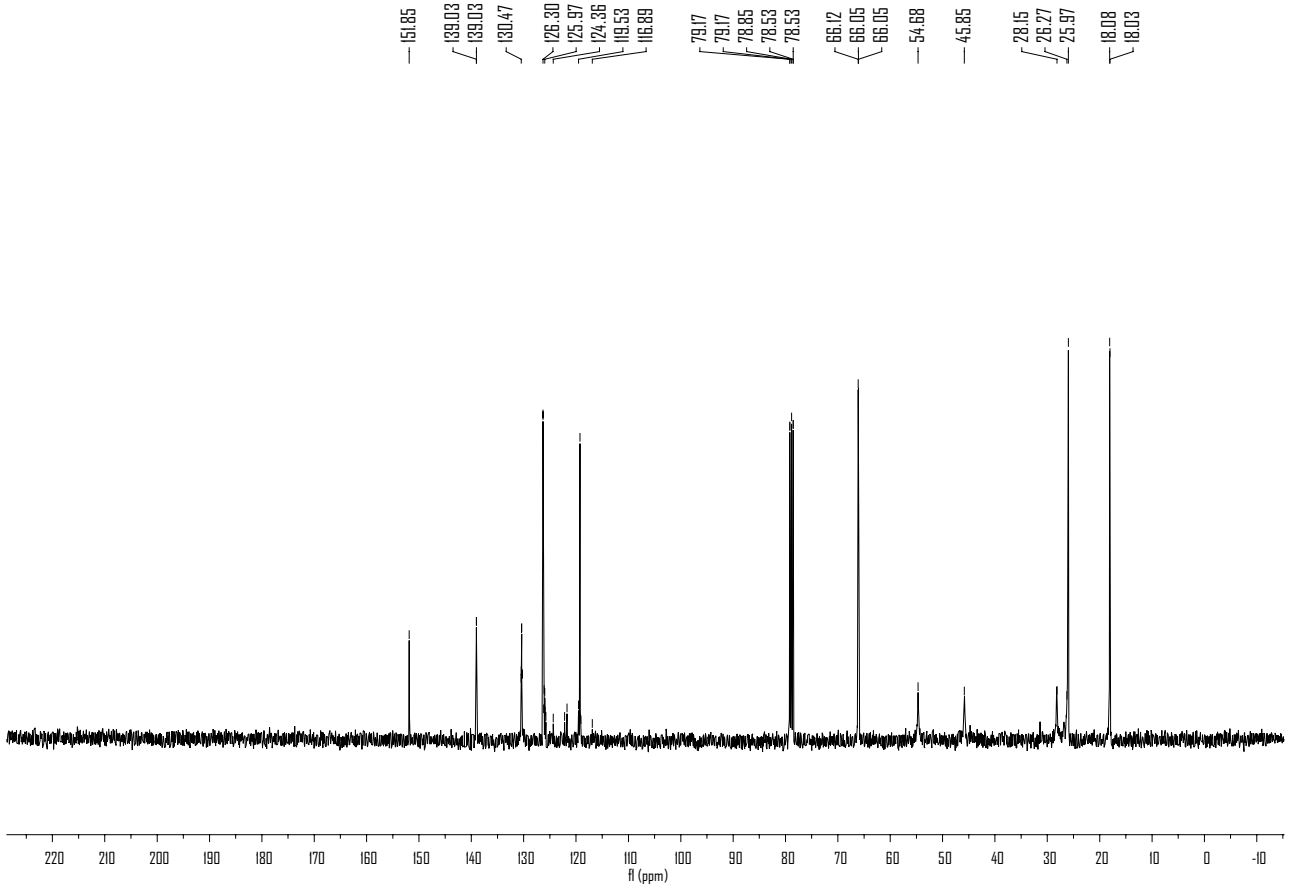




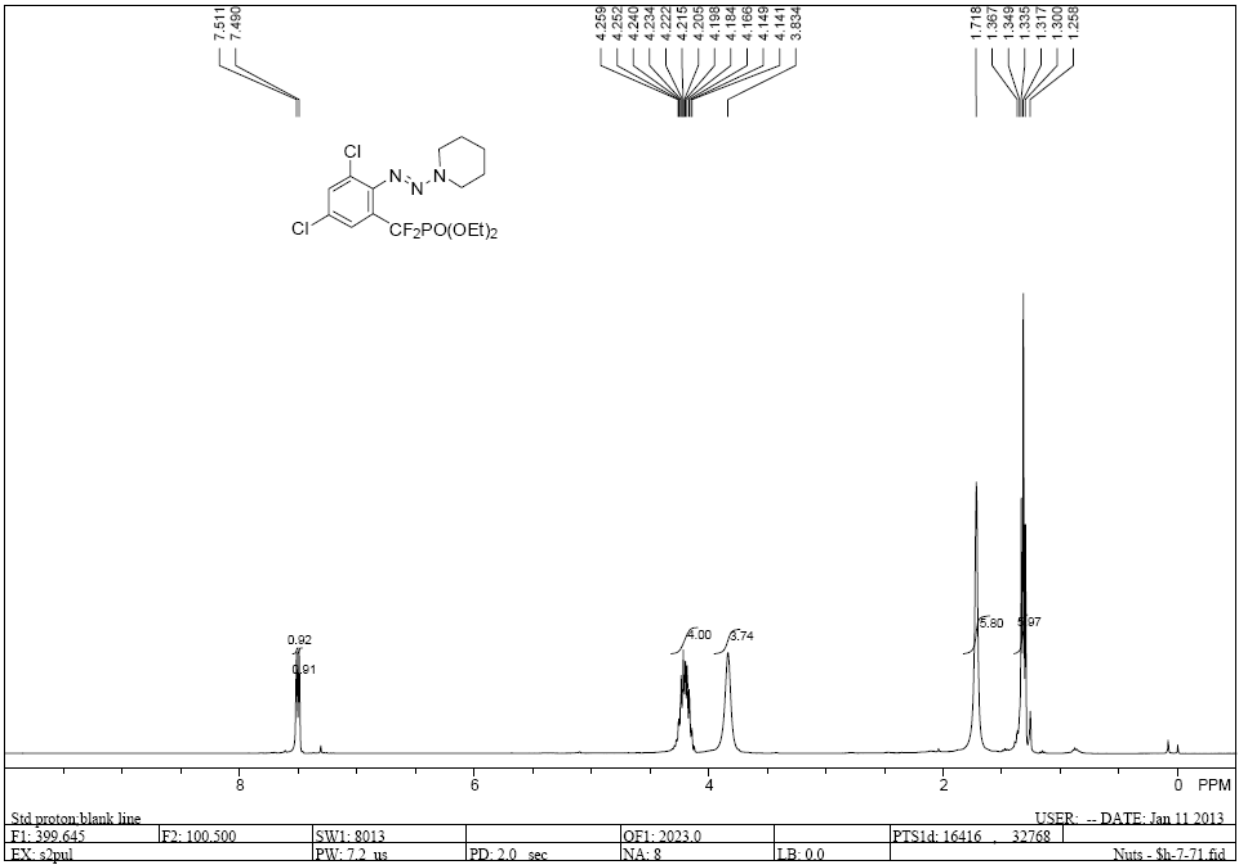
Diethyl ((4-chloro-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bh).

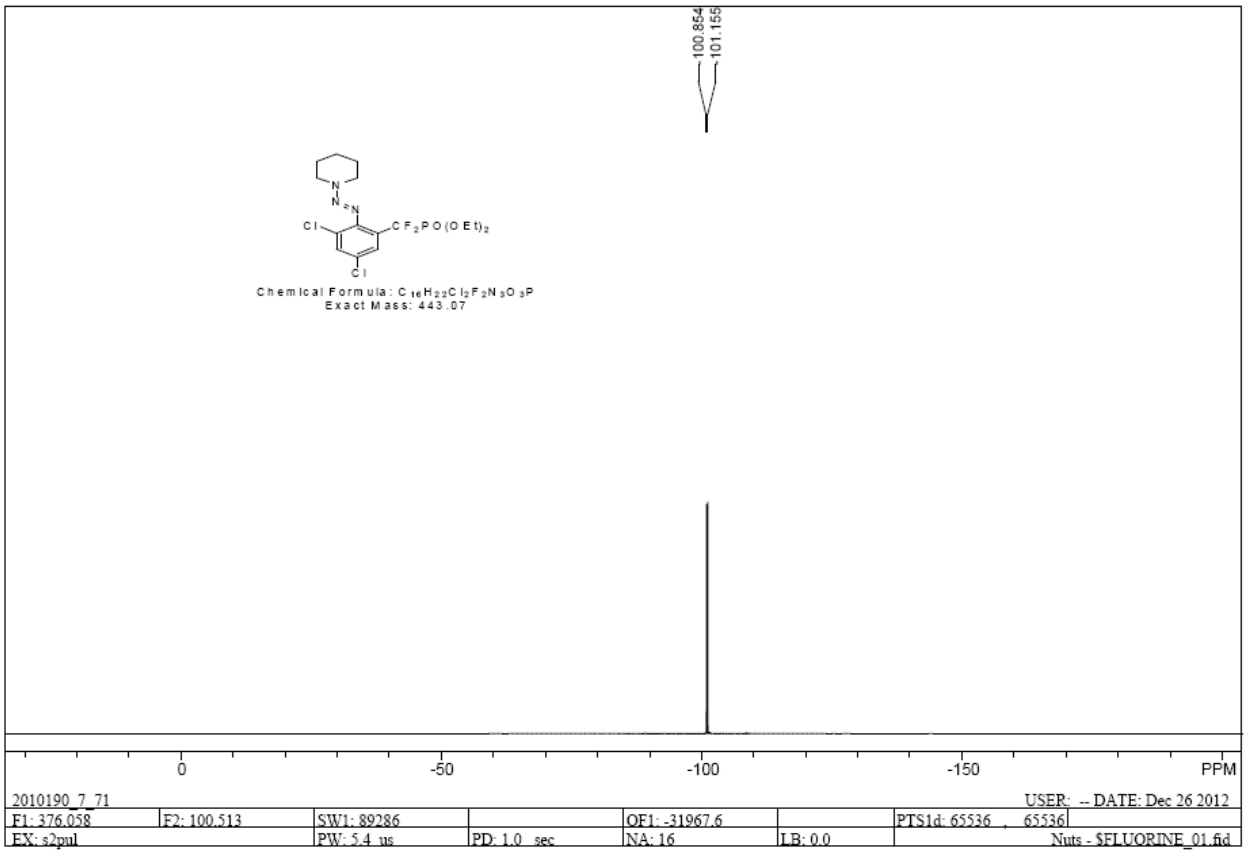


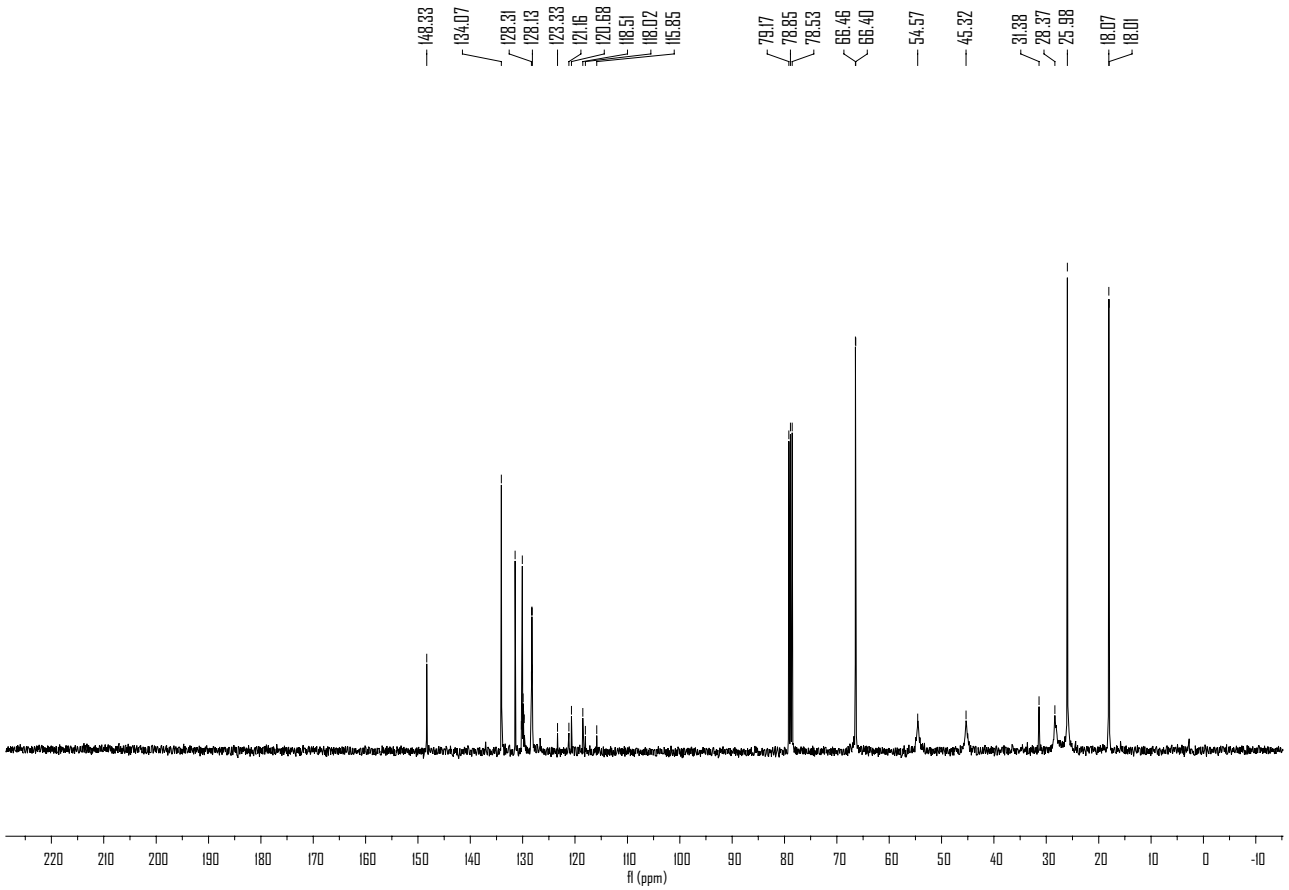




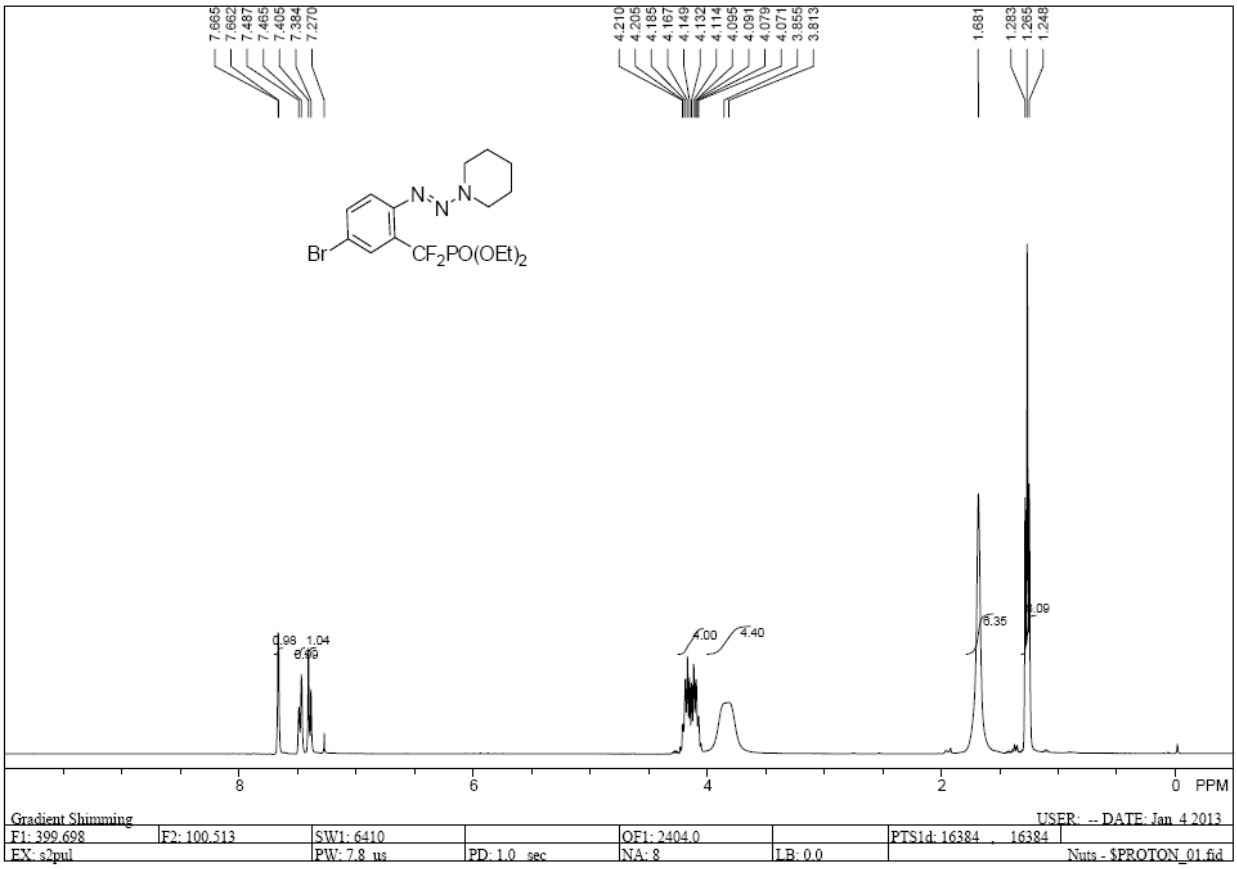
Diethyl((3,5-dichloro-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bi).

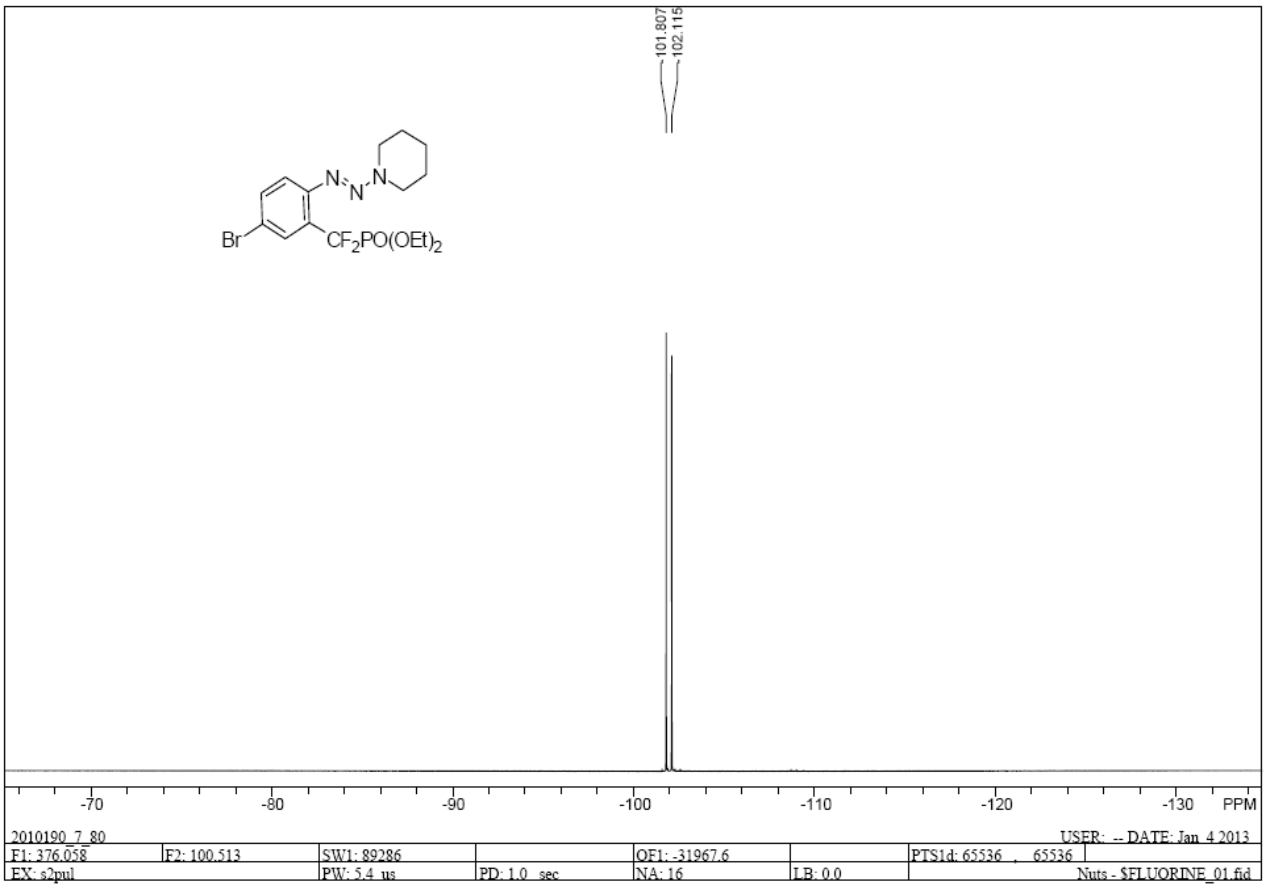


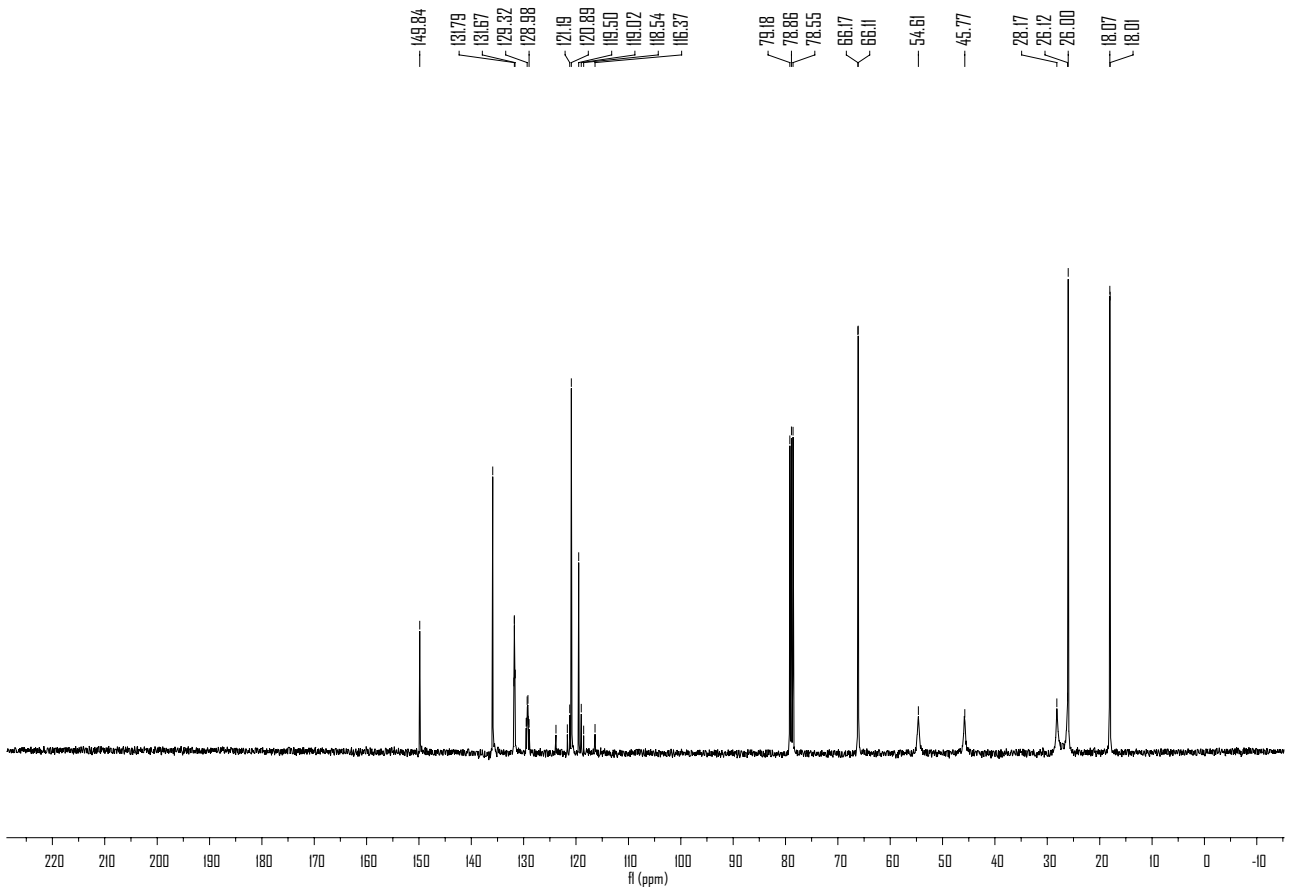




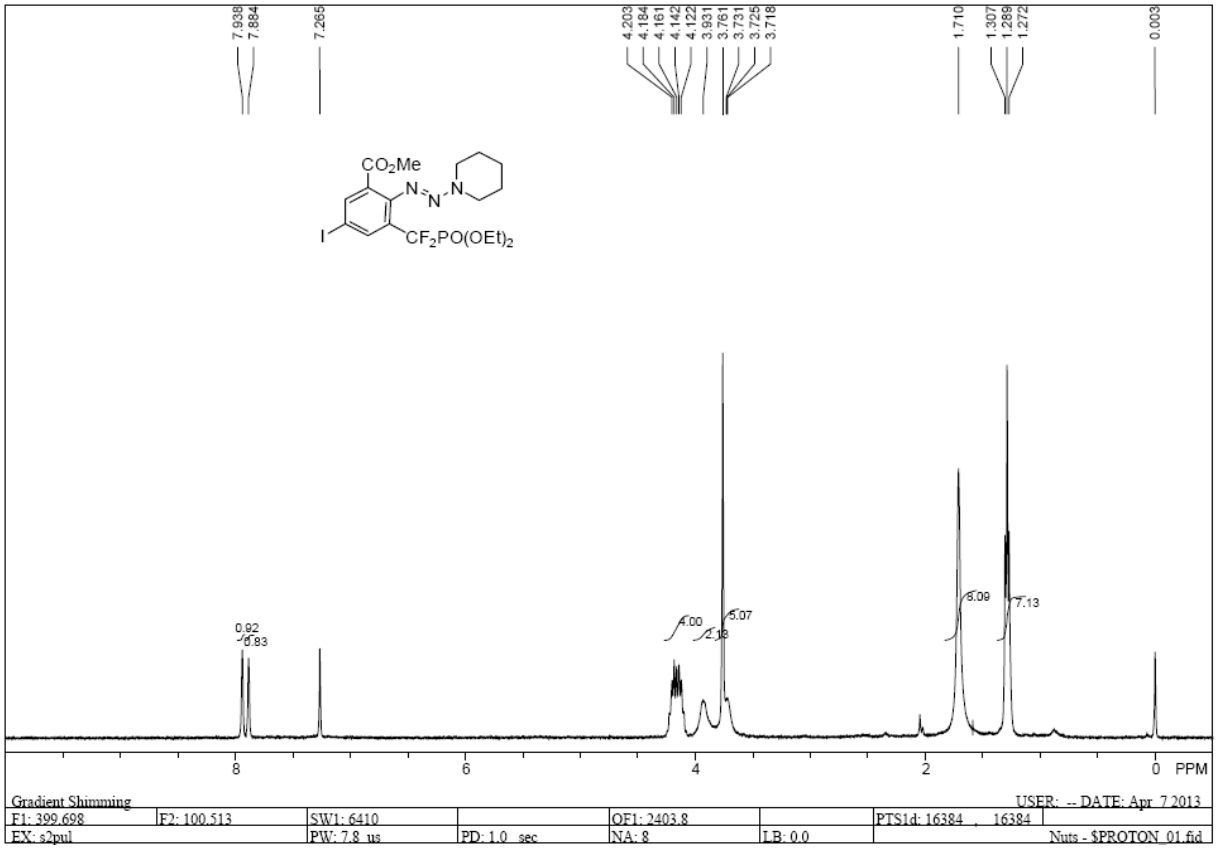
Diethyl ((5-bromo-2-(piperidin-1-yldiazenyl)phenyl)difluoromethyl)phosphonate (3bj).

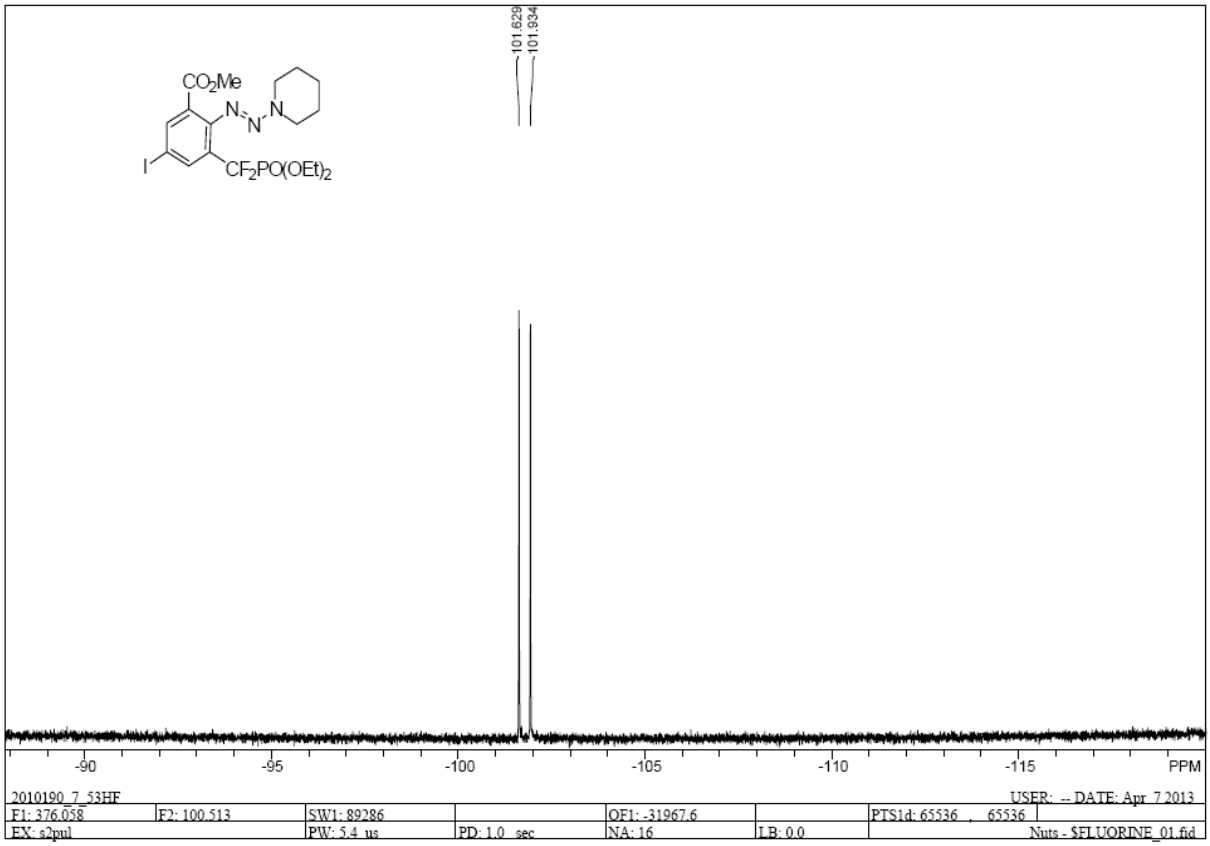


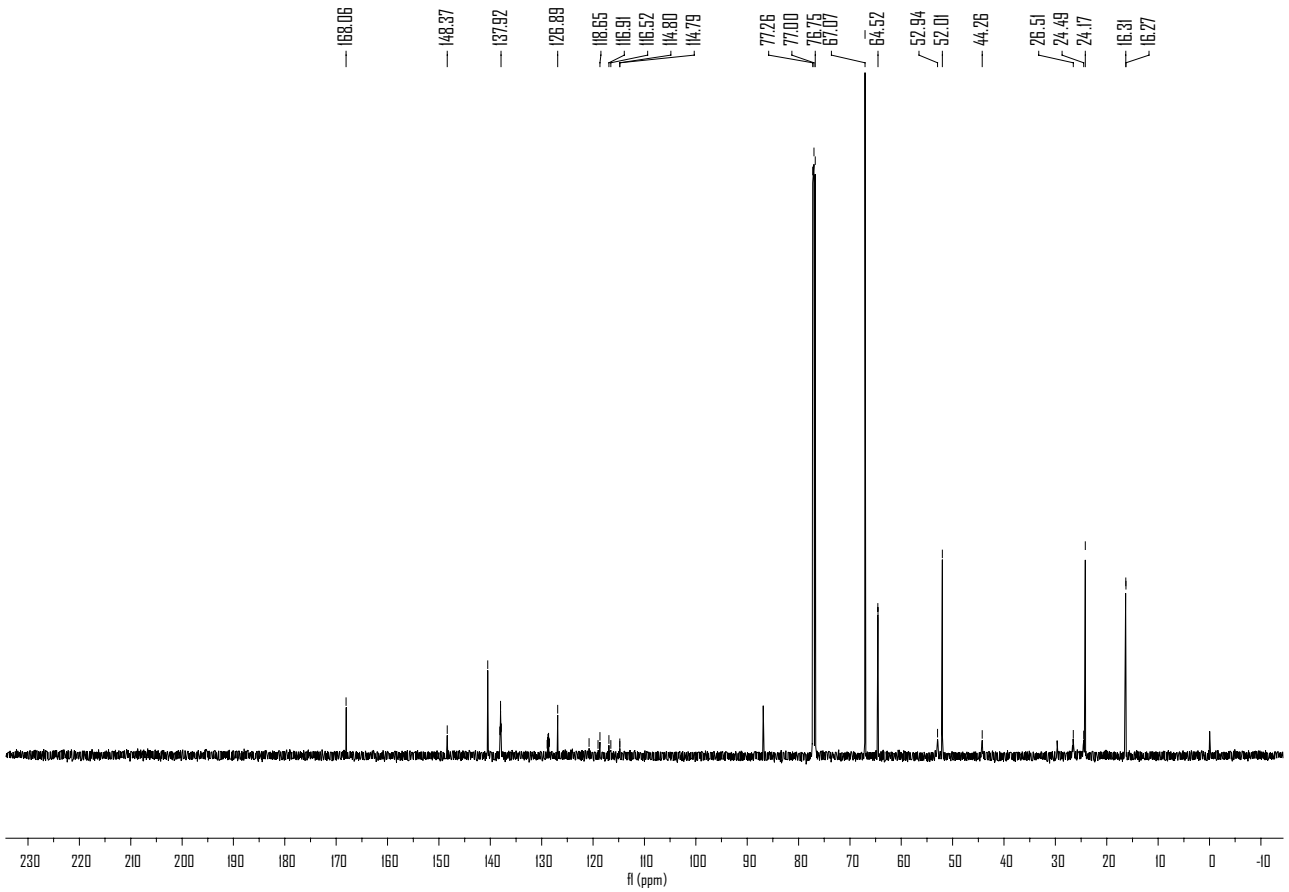

101.807
102.115
Br
CF2PO(OEt)2
-70
-80
-90
-100
-110
-120
-130
PPM
2010190_7_80
USER: -- DATE: Jan 4 2013
F1: 376.058
F2: 100.513
SW1: 89286
OF1: -31967.6
PTS1d: 65536 , 65536
EX: s2pul
PW: 5.4 us
PD: 1.0 sec
NA: 16
LB: 0.0
Nuts - $FLUORINE_01.fid


149.84
131.79
131.67
129.32
128.98
121.19
120.89
119.50
119.02
118.54
116.37
79.18
78.86
78.55
66.17
66.11
54.61
45.77
28.17
26.12
26.00
18.07
18.01
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

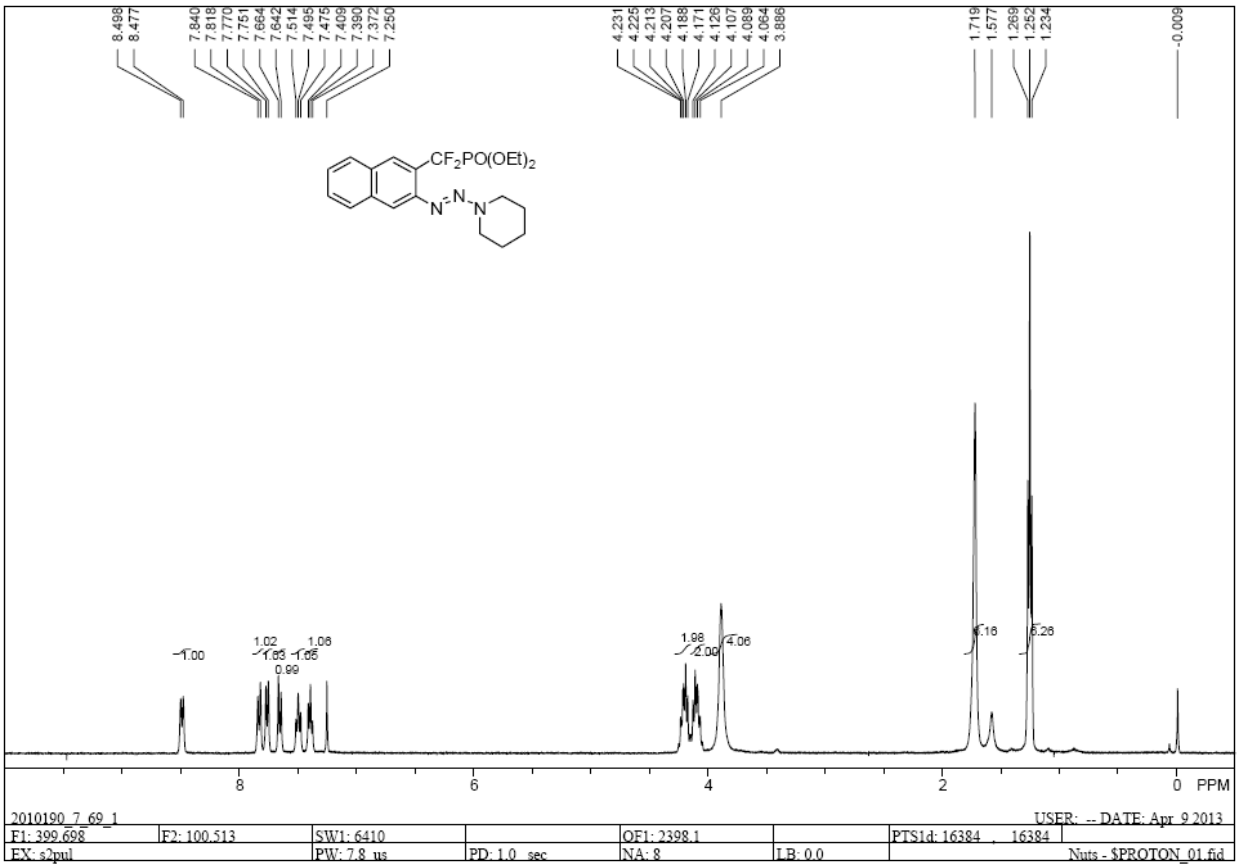
Methyl-3-((diethoxyphosphoryl)difluoromethyl)-5-iodo-2-(piperidin-1-yldiazenyl)benzoate (3bk).

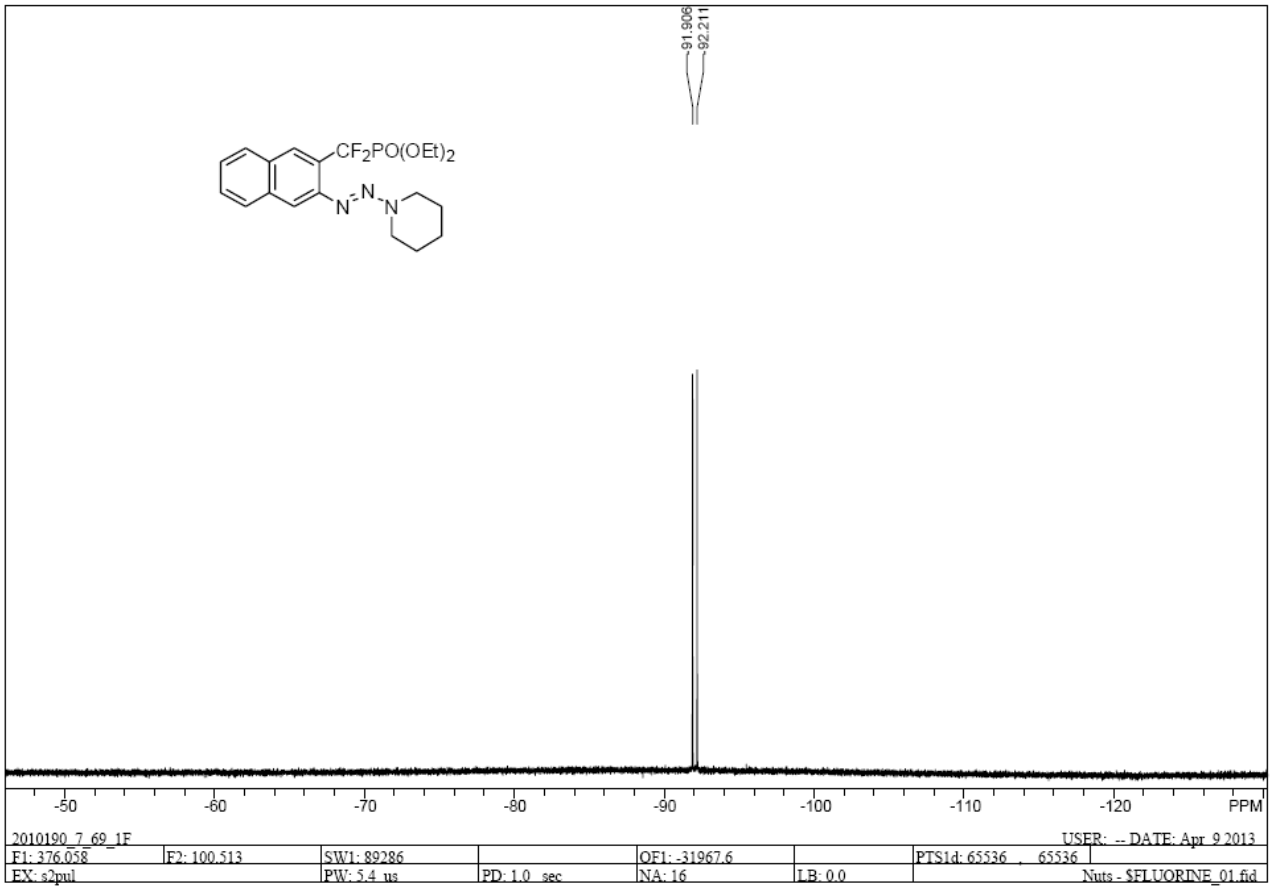


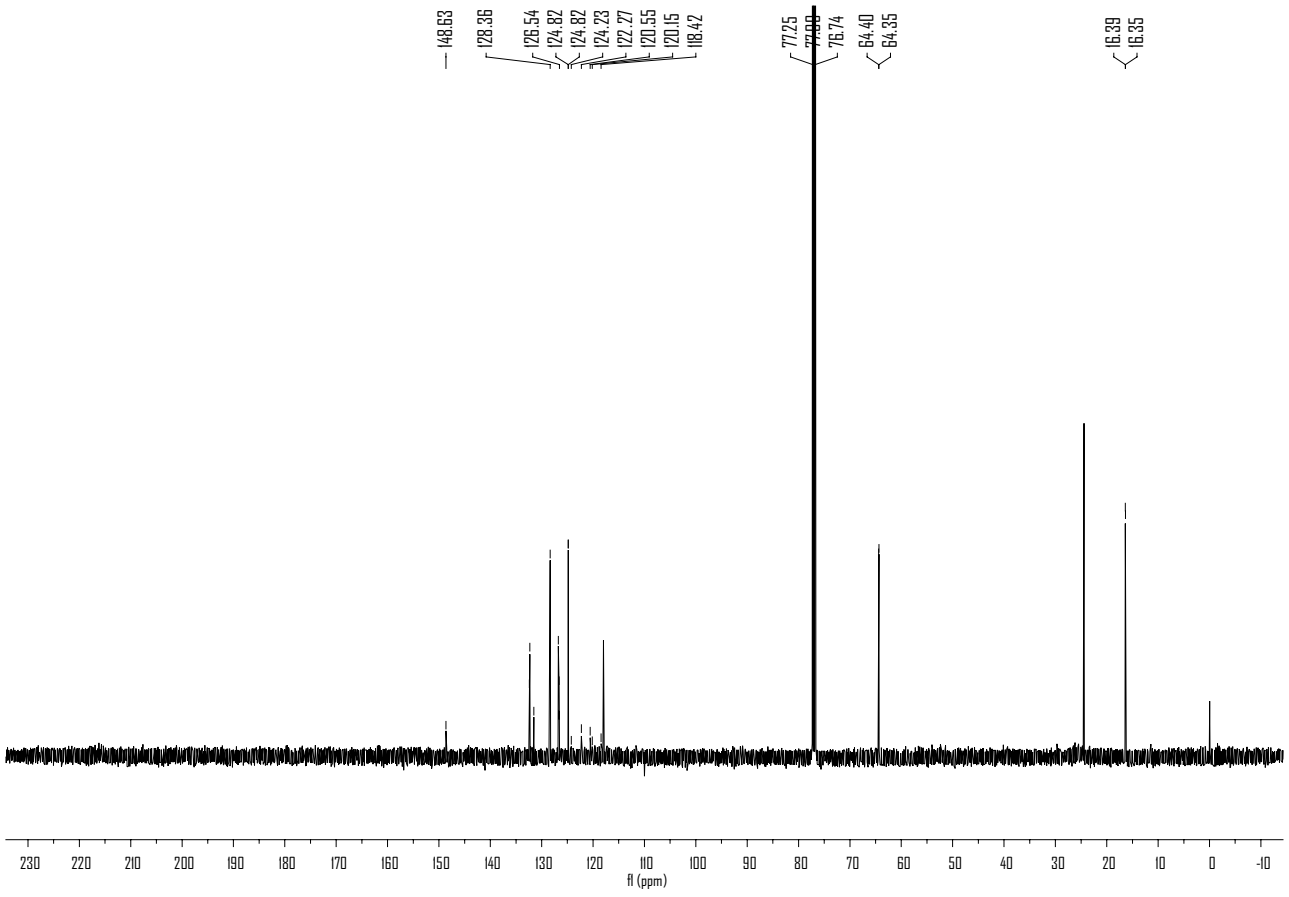




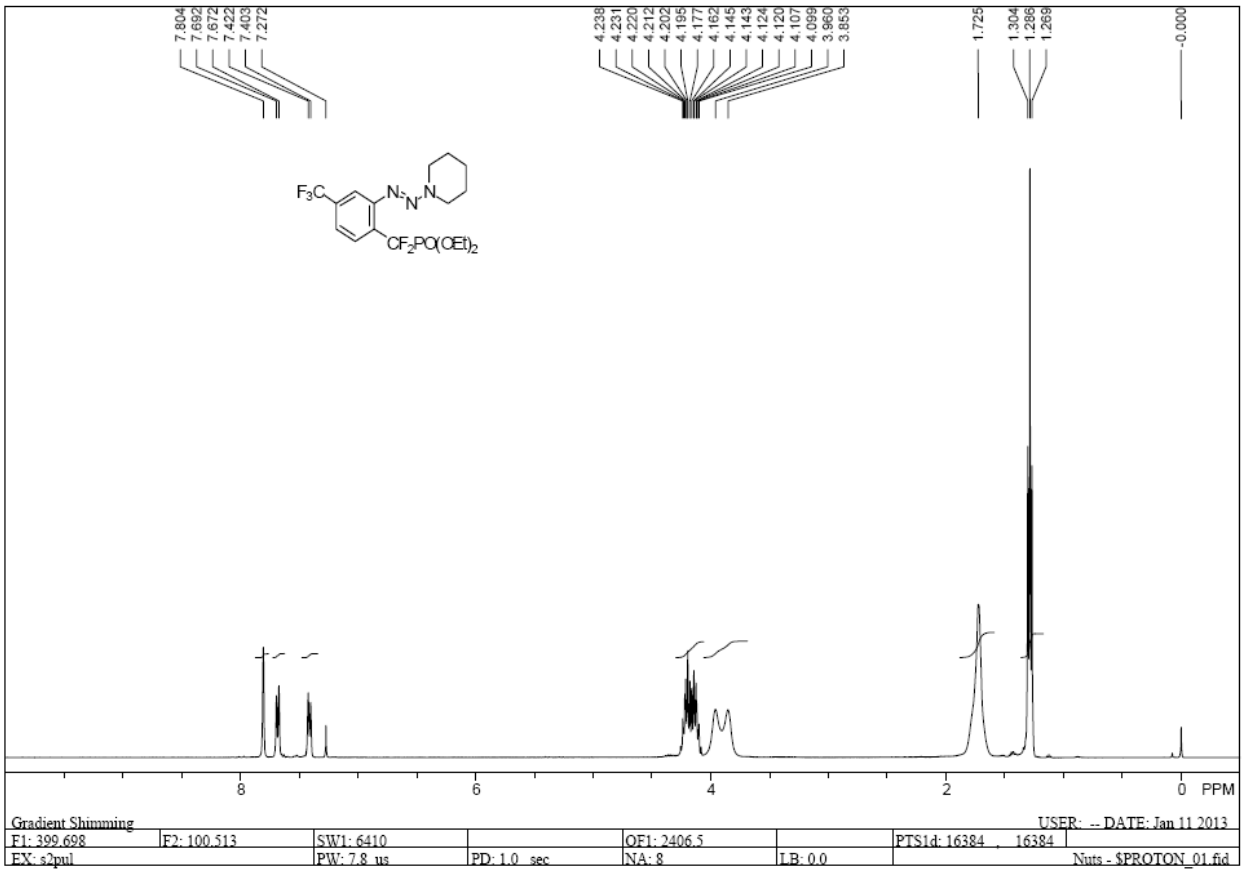
Diethyl (difluoro(3-(piperidin-1-yldiazenyl)naphthalen-2-yl)methyl)phosphonate (3bl).

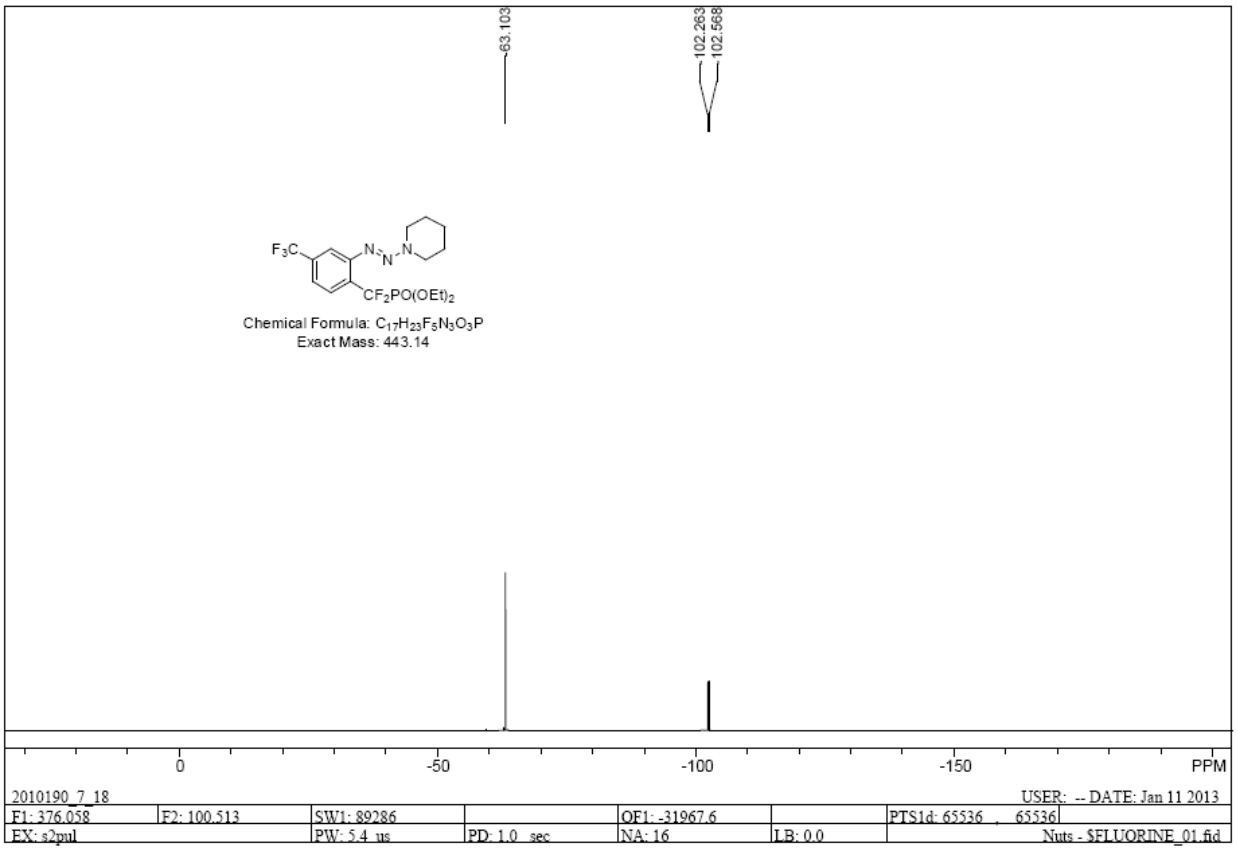


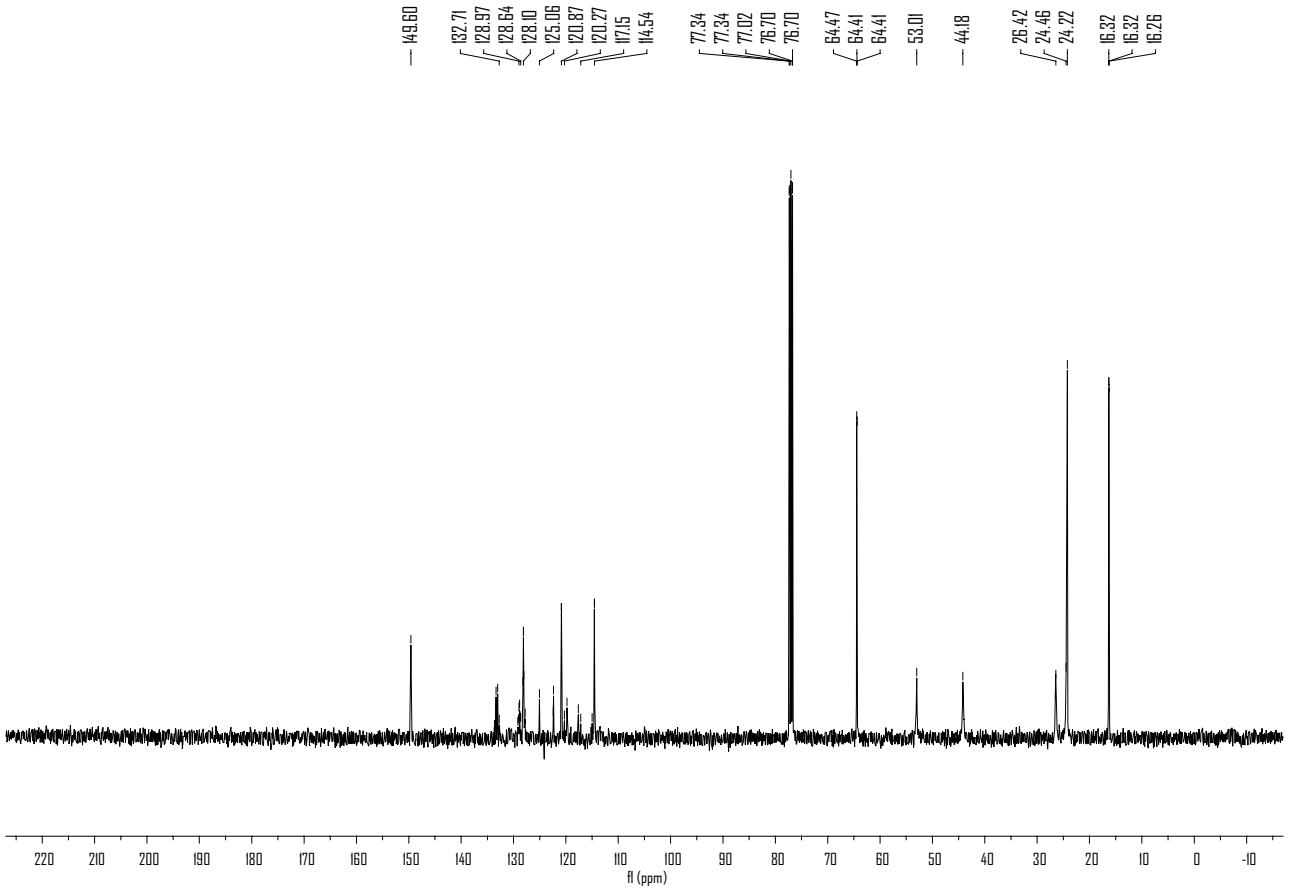




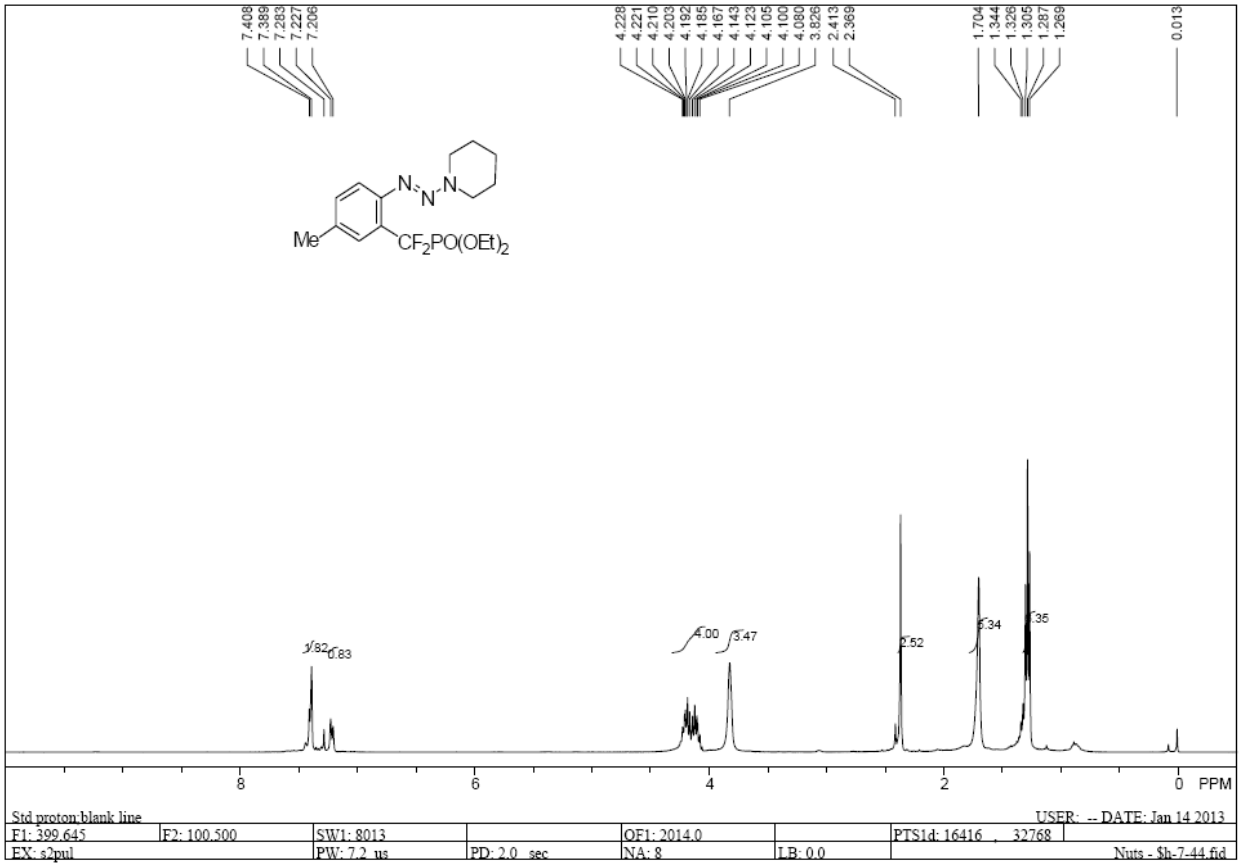
Diethyl(difluoro(2-(piperidin-1-yldiazenyl)-4-(trifluoromethyl)phenyl)methyl)phosphonate (3bm).

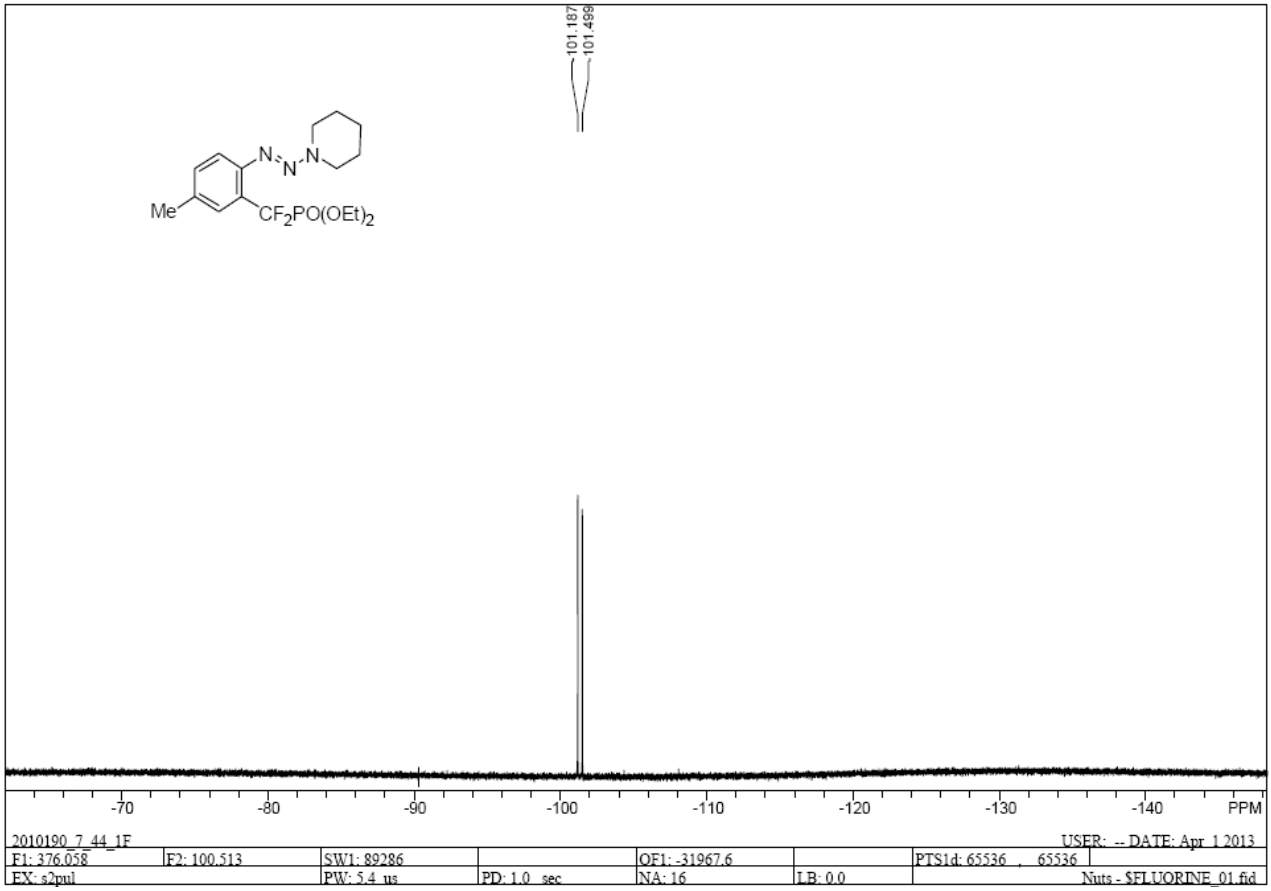


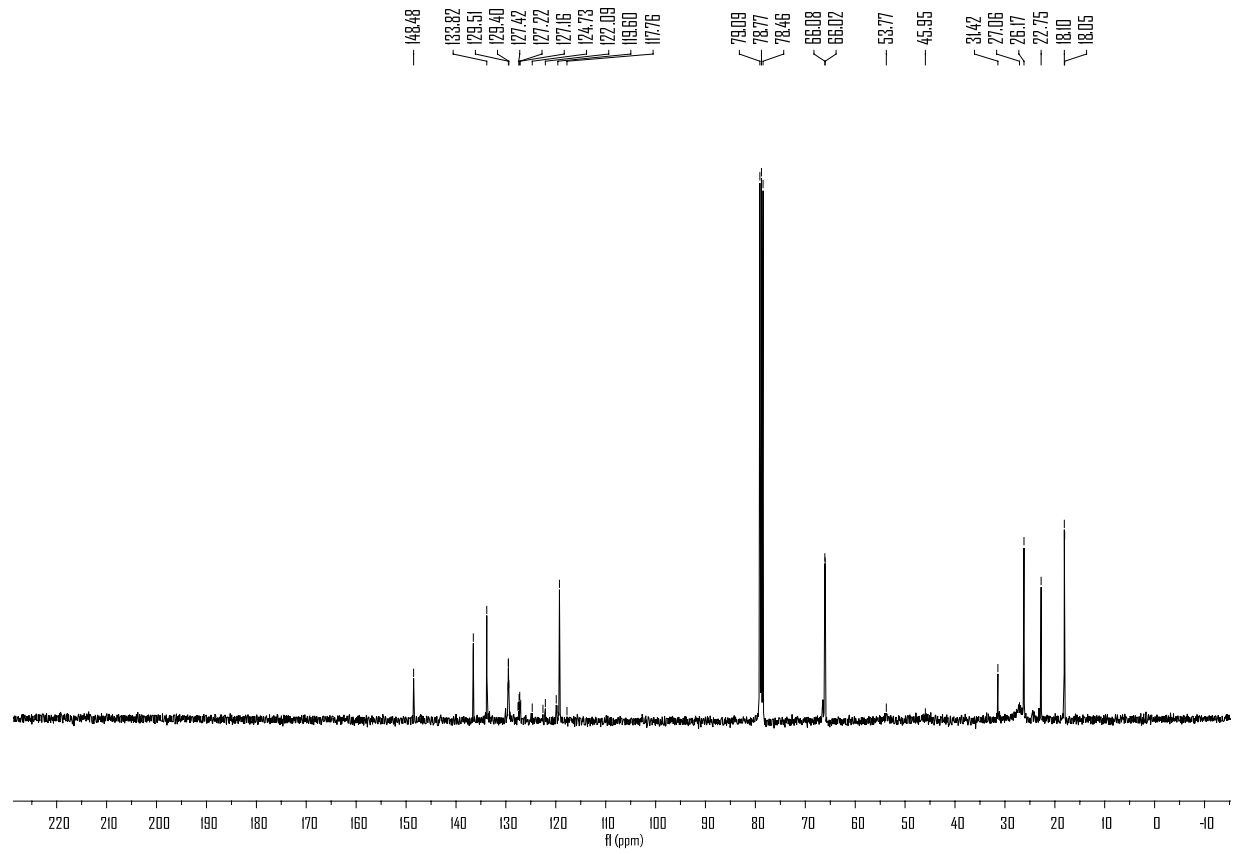




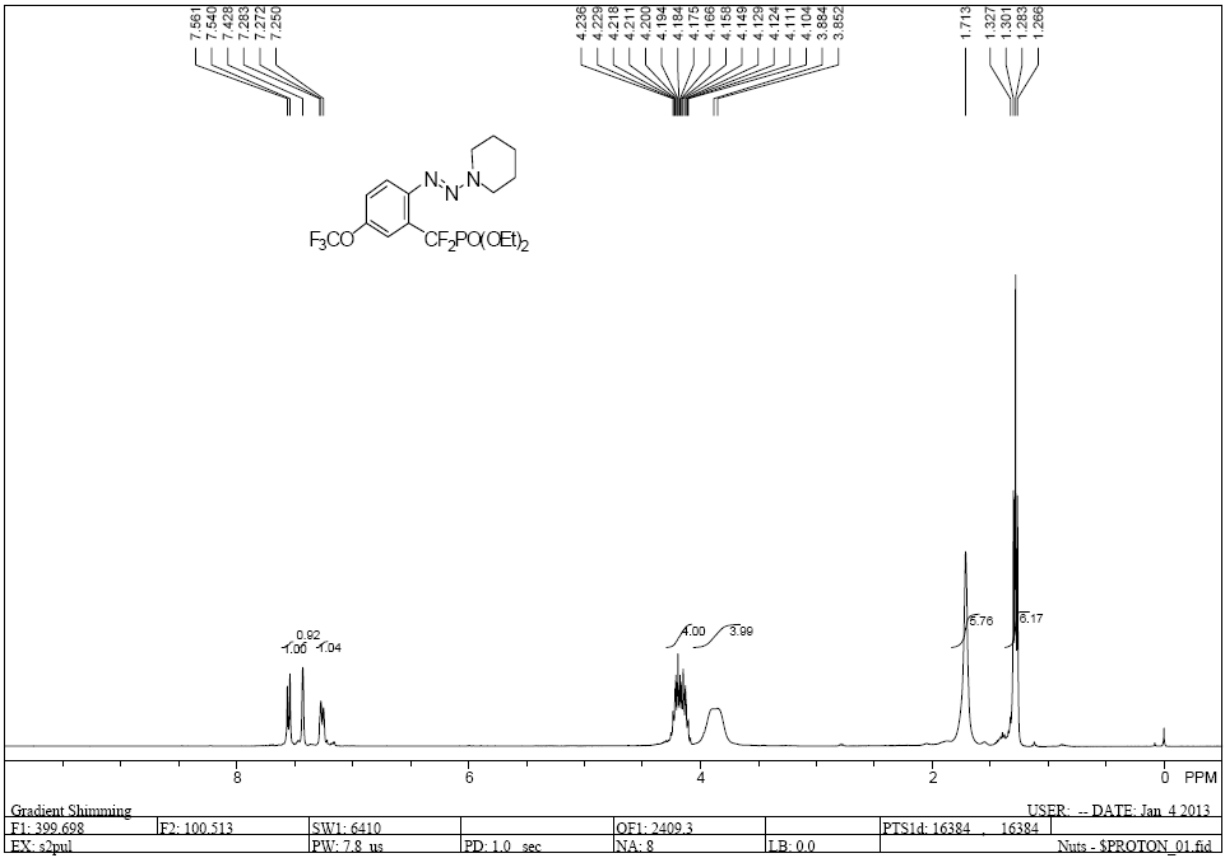
Diethyl (difluoro(5-methyl-2-(piperidin-1-yldiazenyl)phenyl)methyl)phosphonate (3bn).

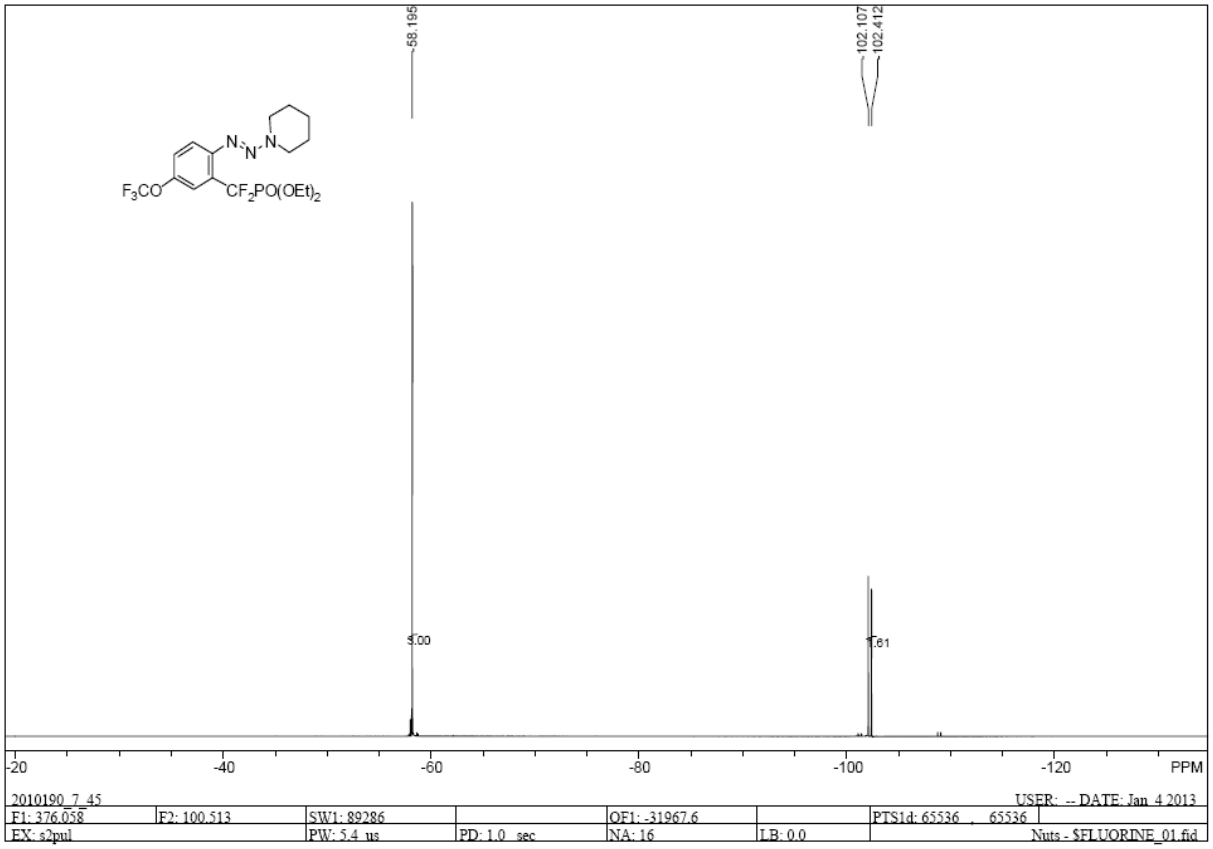


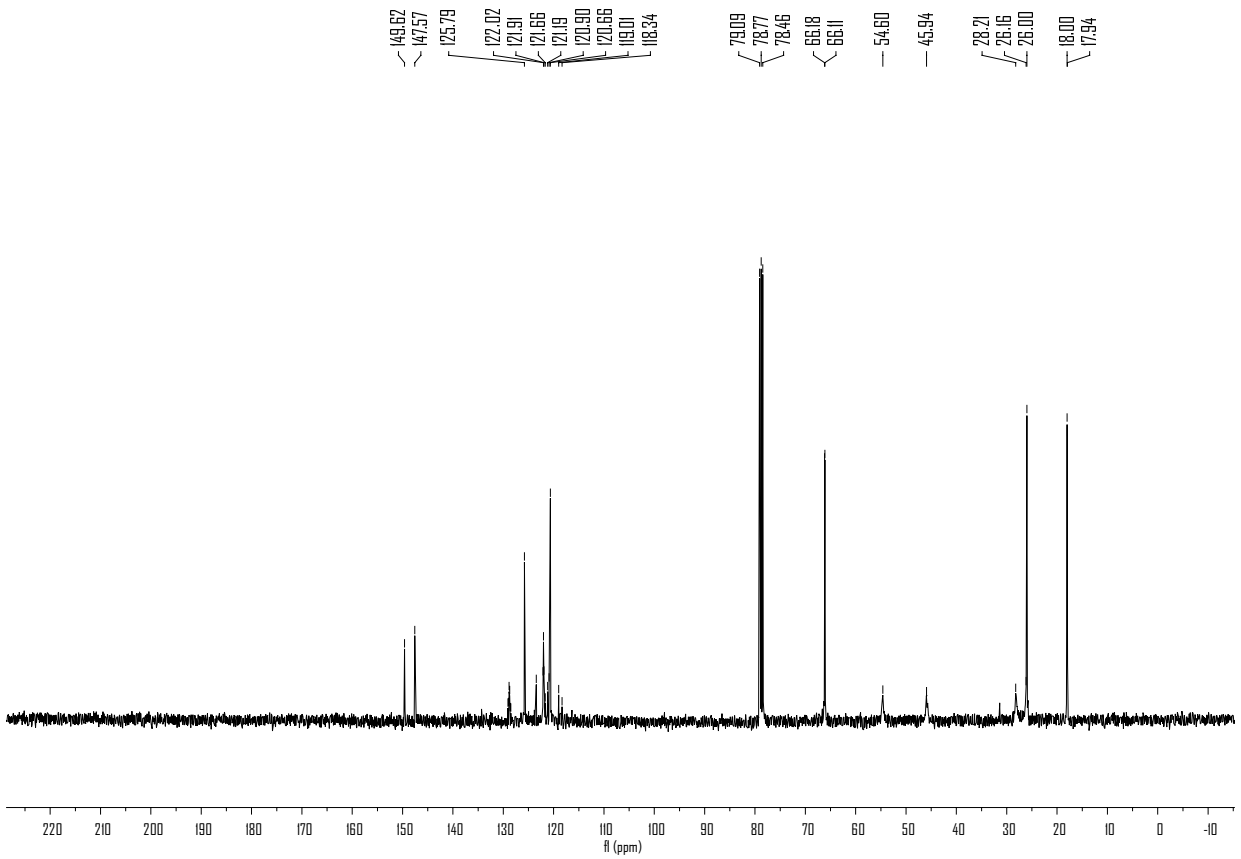

-101.187
-101.499
Me
CF2PO(OEt)2
-70
-80
-90
-100
-110
-120
-130
-140
PPM
2010190_7_44_1F
USER: -- DATE: Apr 1 2013
F1: 376.058
F2: 100.513
SW1: 89286
OF1: -31967.6
PTS1d: 65536 , 65536
EX: s2pul
PW: 5.4 us
PD: 1.0 sec
NA: 16
LB: 0.0
Nuts - $FLUORINE_01.fid


148.48
133.82
129.51
129.40
127.42
127.22
127.16
124.73
122.09
119.60
117.76
79.09
78.77
78.46
66.08
66.02
53.77
45.95
31.42
27.06
26.17
22.75
18.10
18.05
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

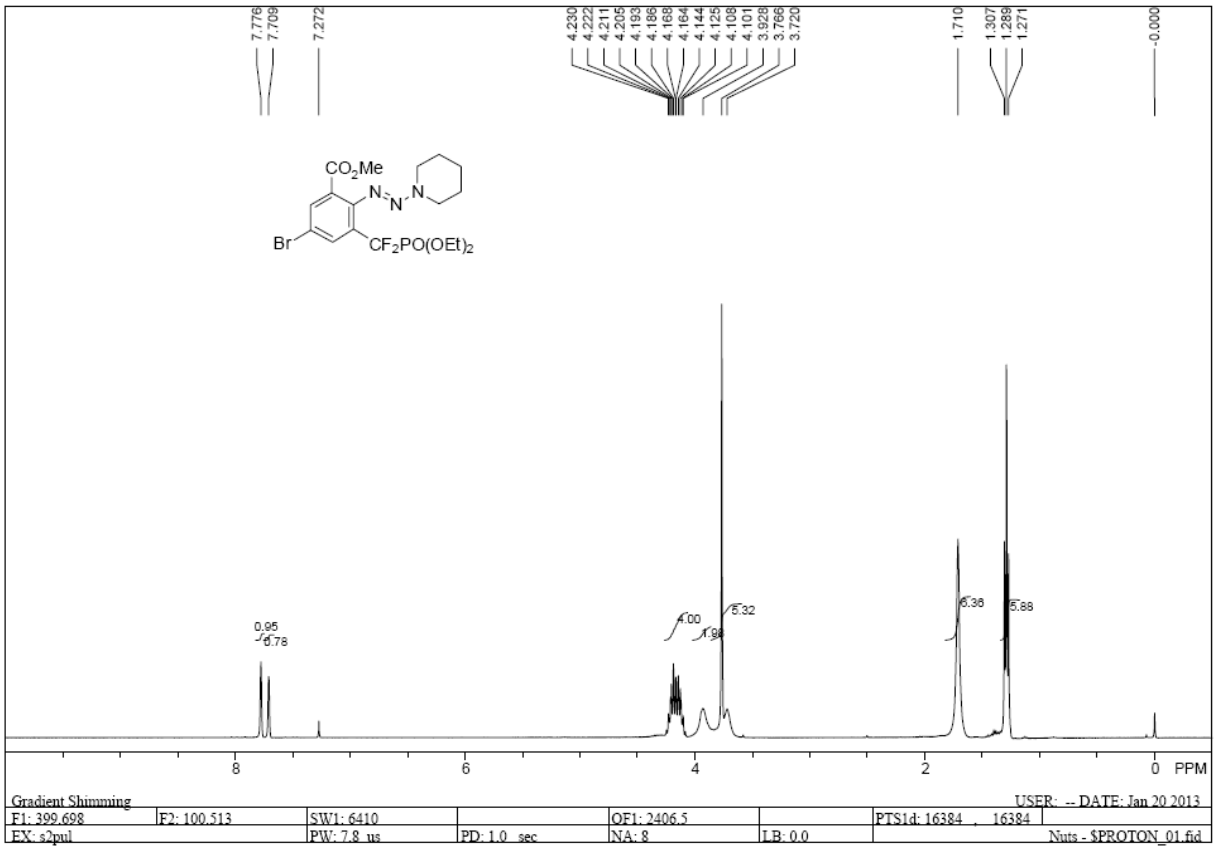
Diethyl(difluoro(2-(piperidin-1-yldiazenyl)-5-(trifluoromethoxy)phenyl)methyl)phosphonate (3bo).

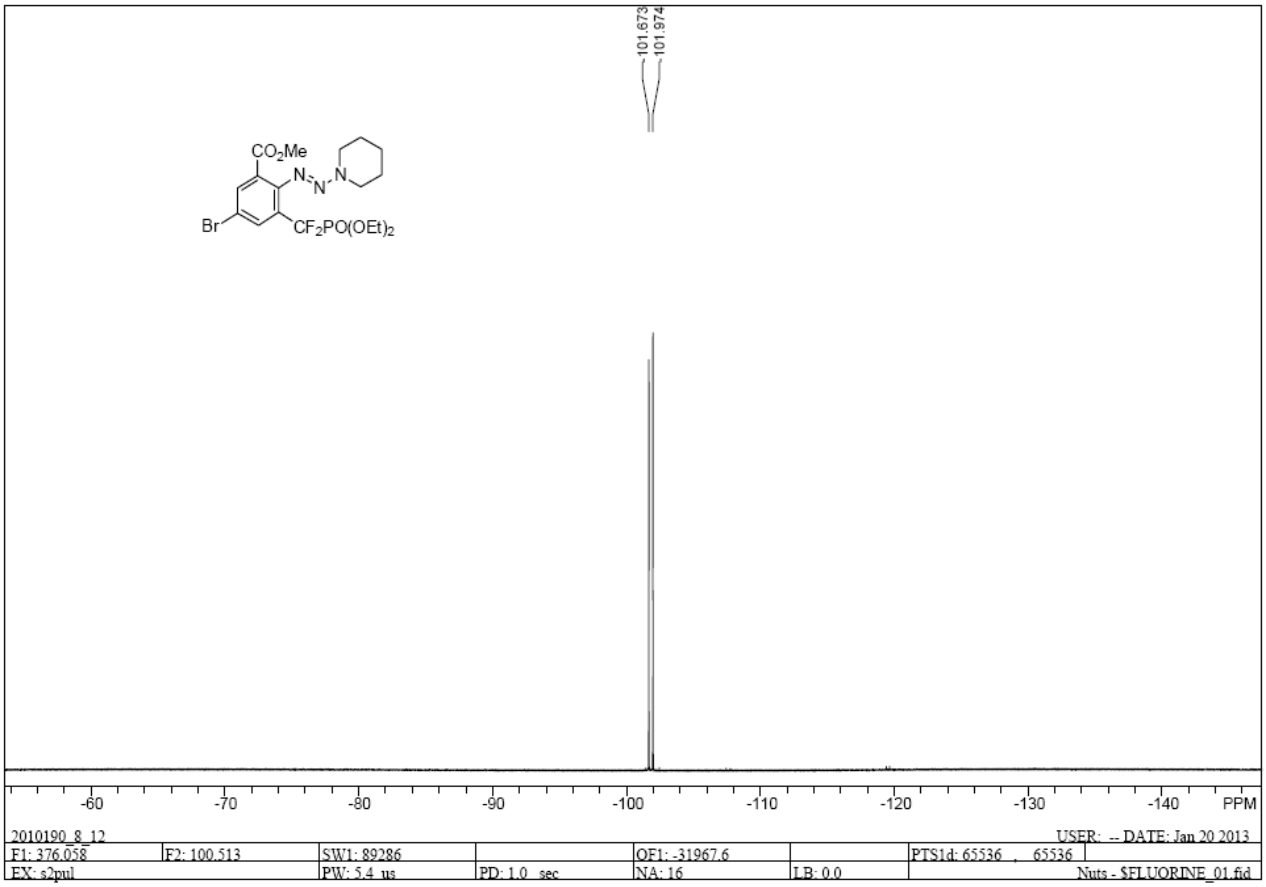


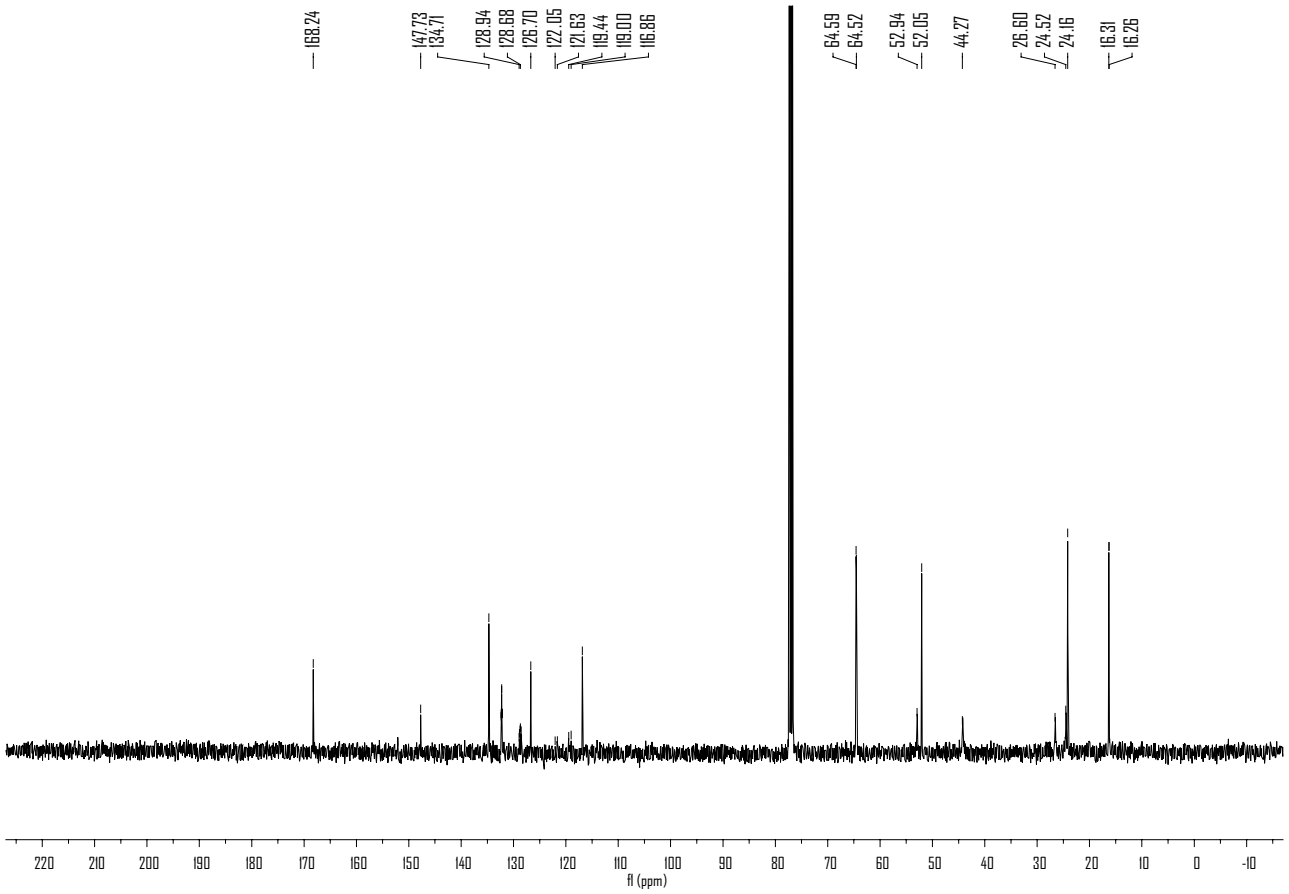




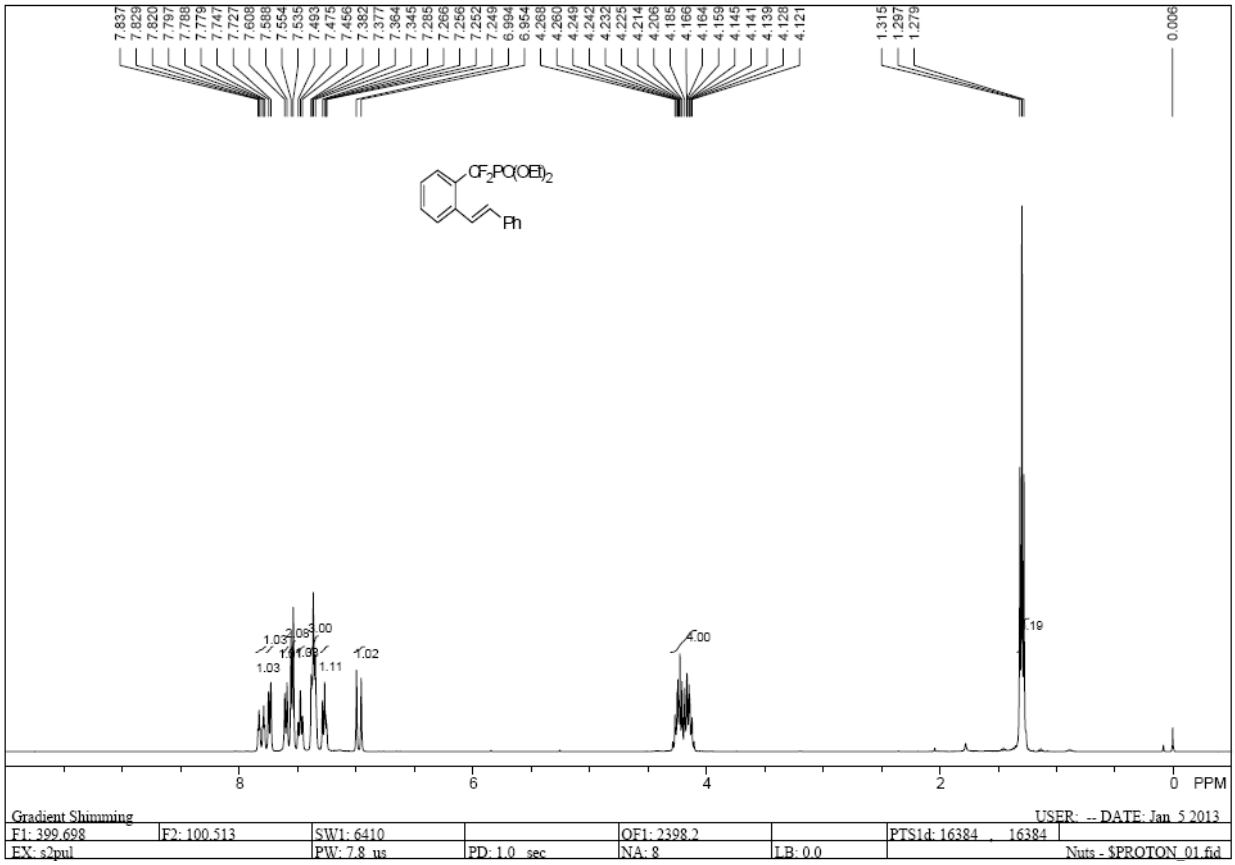
Methyl-5-bromo-3-((diethoxyphosphoryl)difluoromethyl)-2-(piperidin-1-yldiazenyl)benzoate (3bp).

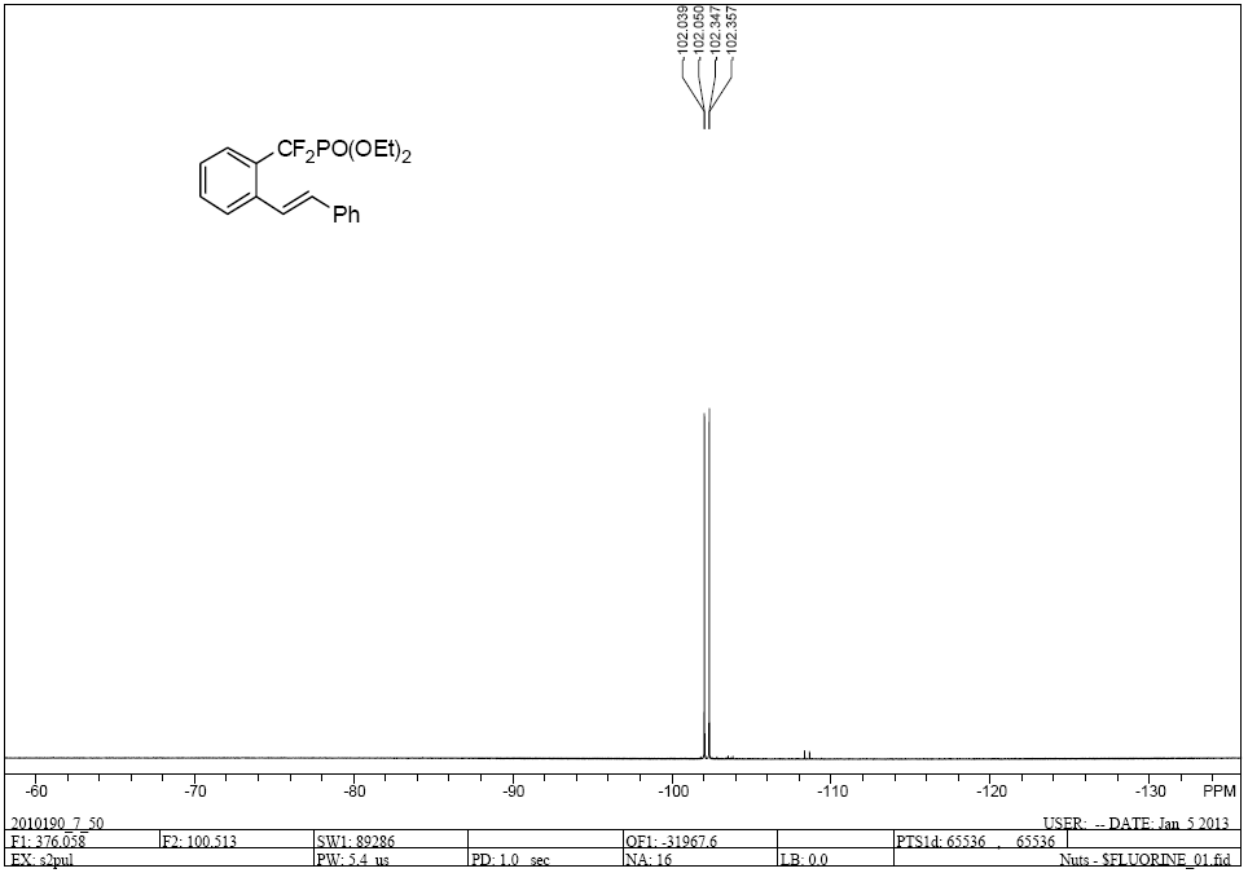


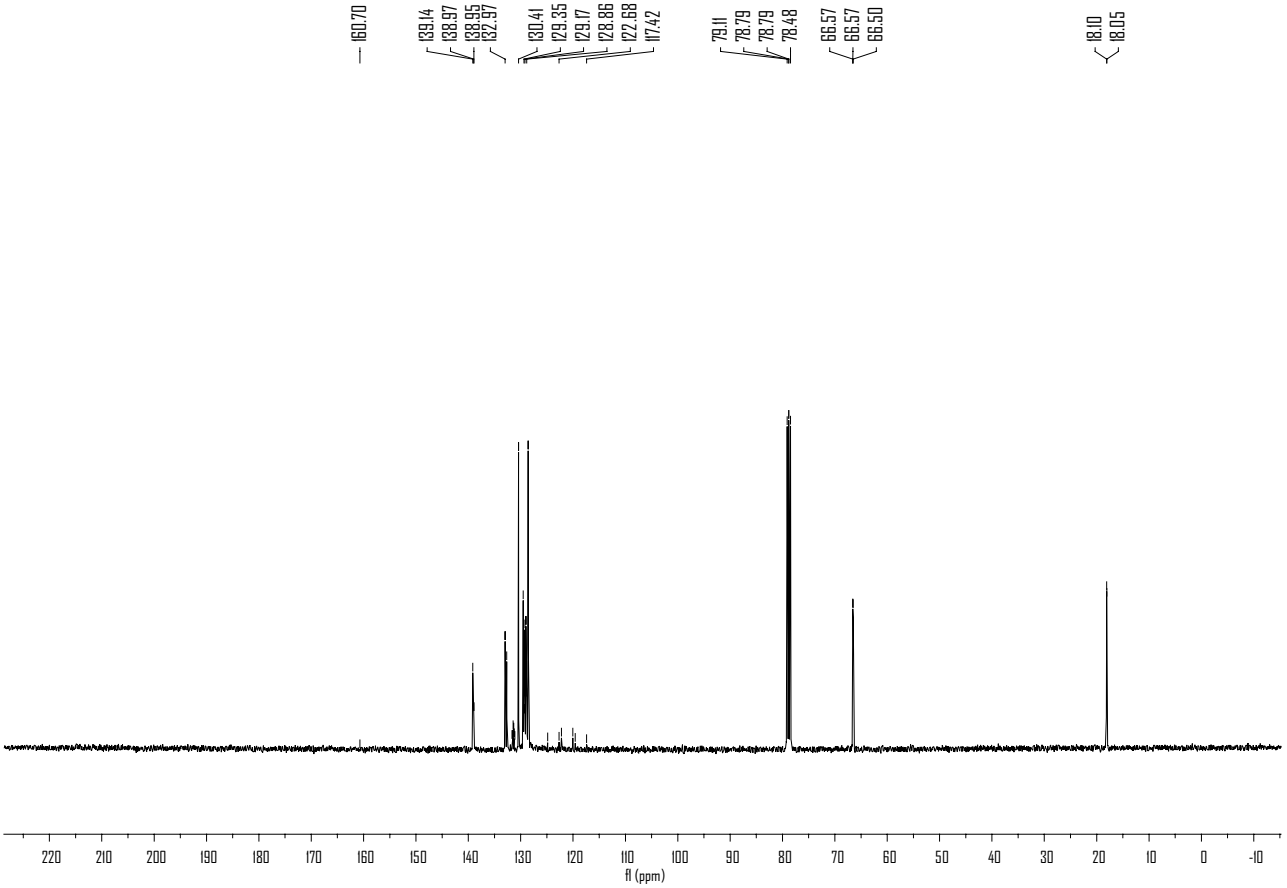

101.673
101.974
CO2Me
N
N
N
Br
CF2PO(OEt)2
-60
-70
-80
-90
-100
-110
-120
-130
-140
PPM
2010190_8_12
USER: -- DATE: Jan 20 2013
F1: 376.058
F2: 100.513
SW1: 89286
OF1: -31967.6
PTS1d: 65536 , 65536
EX: s2pul
PW: 5.4 us
PD: 1.0 sec
NA: 16
LB: 0.0
Nuts - $FLUORINE_01.fid


168.24
147.73
134.71
128.94
128.68
126.70
122.05
121.63
119.44
119.00
116.86
64.59
64.52
52.94
52.05
44.27
26.60
24.52
24.16
16.31
16.26
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

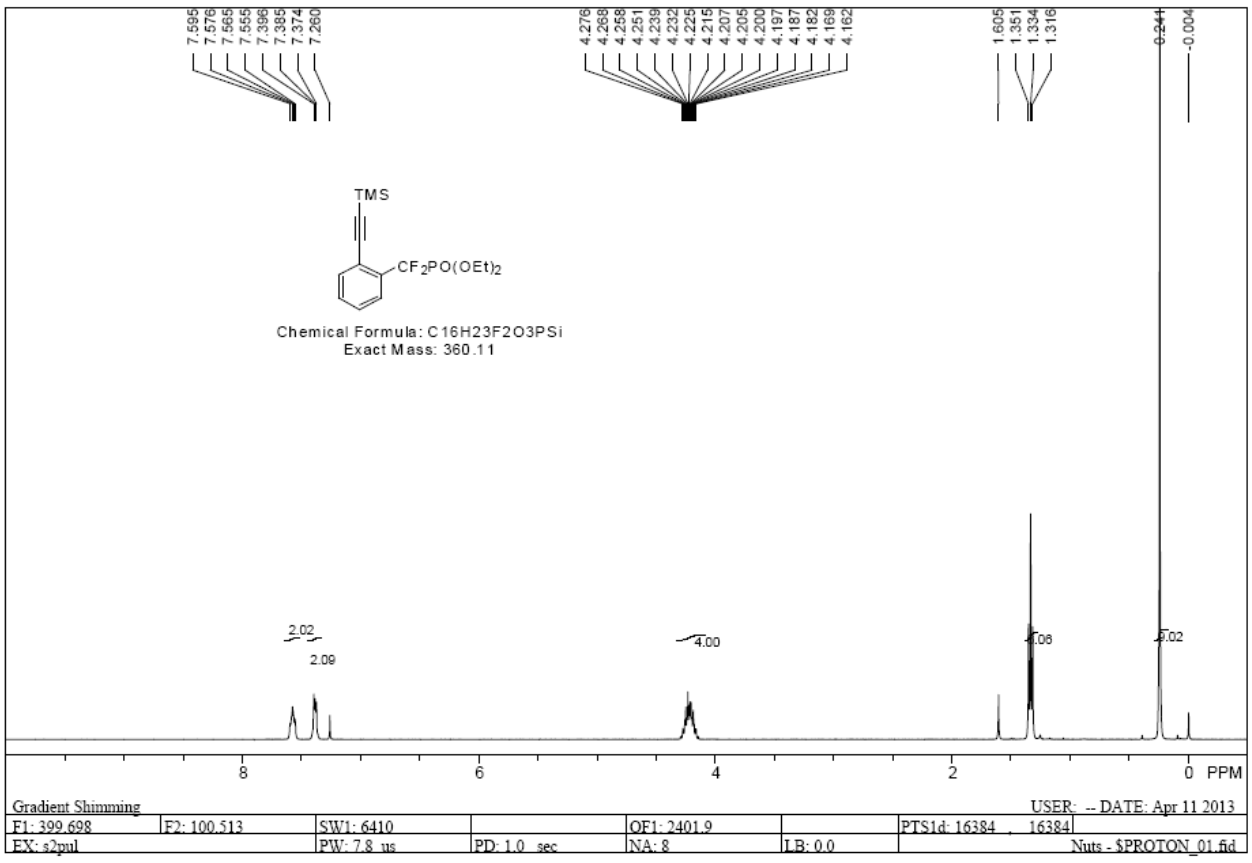
(*E*)-Diethyl (difluoro(2-styrylphenyl)methyl)phosphonate (7)

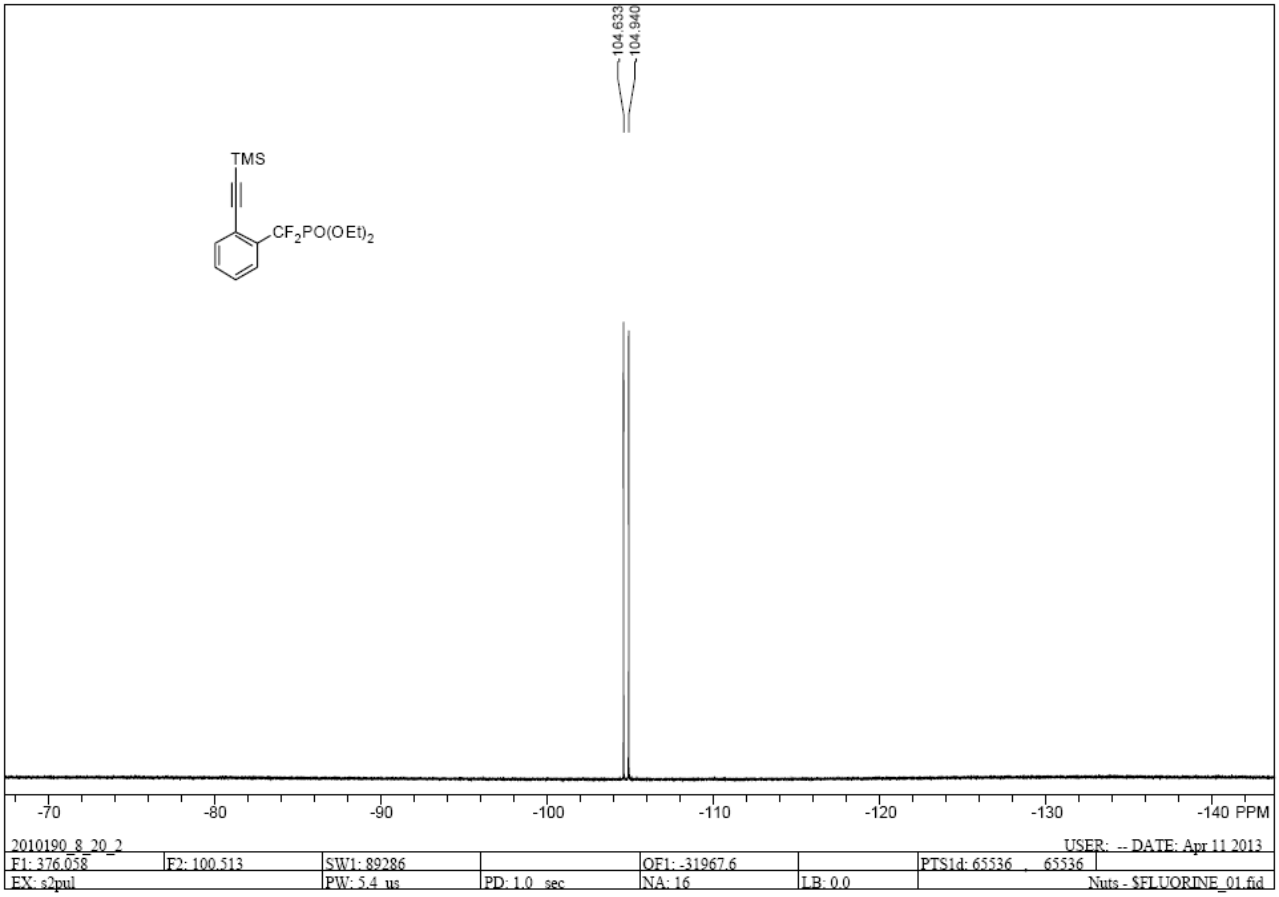


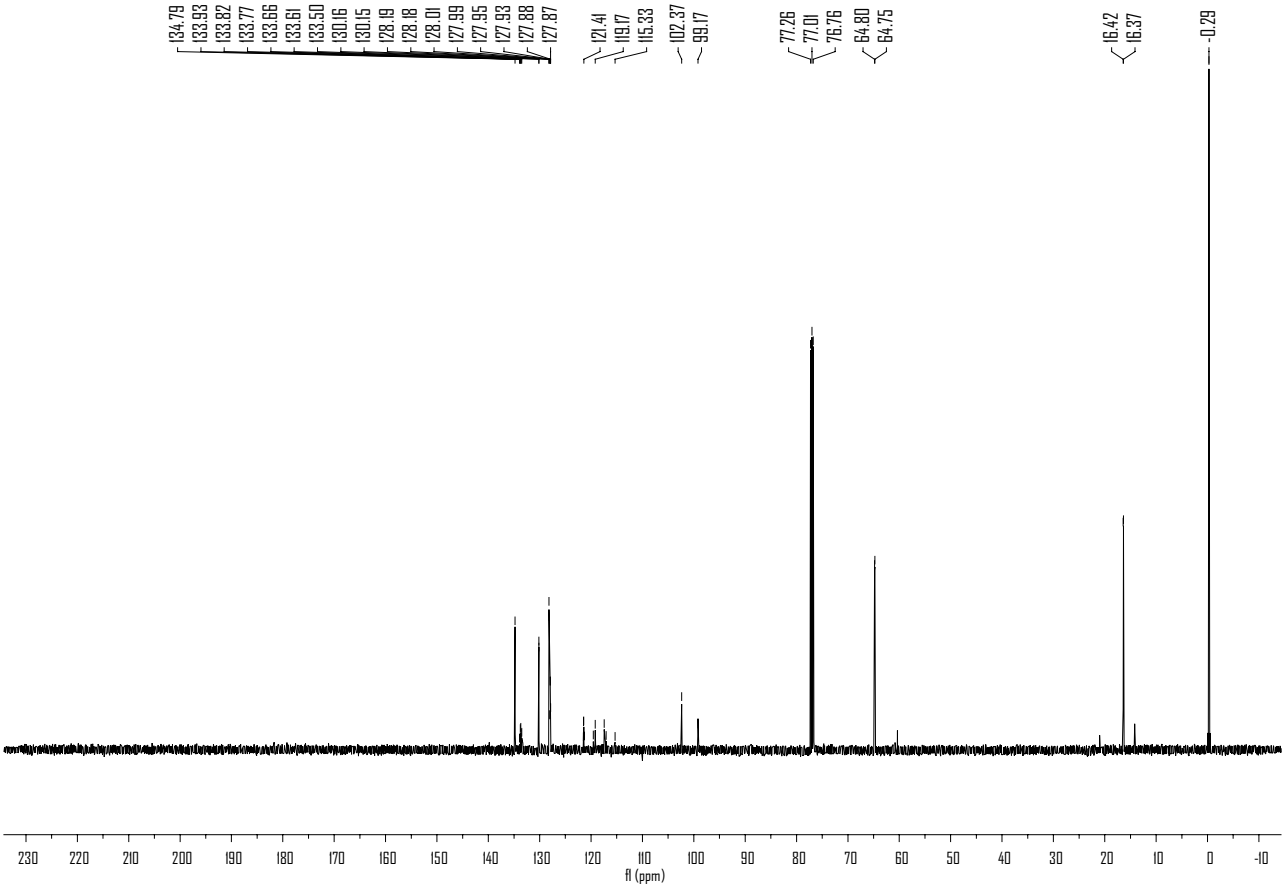




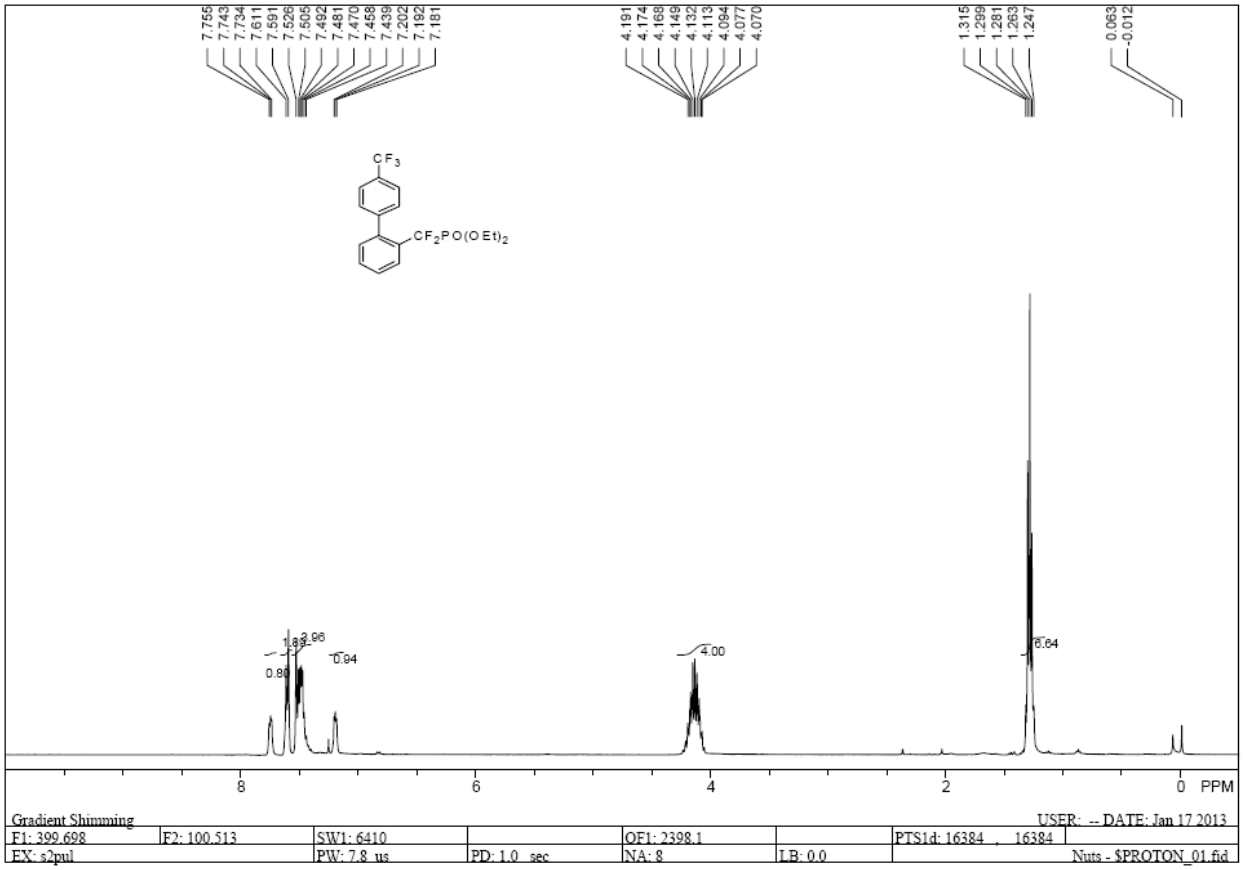
Diethyl (difluoro(2-((trimethylsilyl)ethynyl)phenyl)methyl)phosphonate (8).

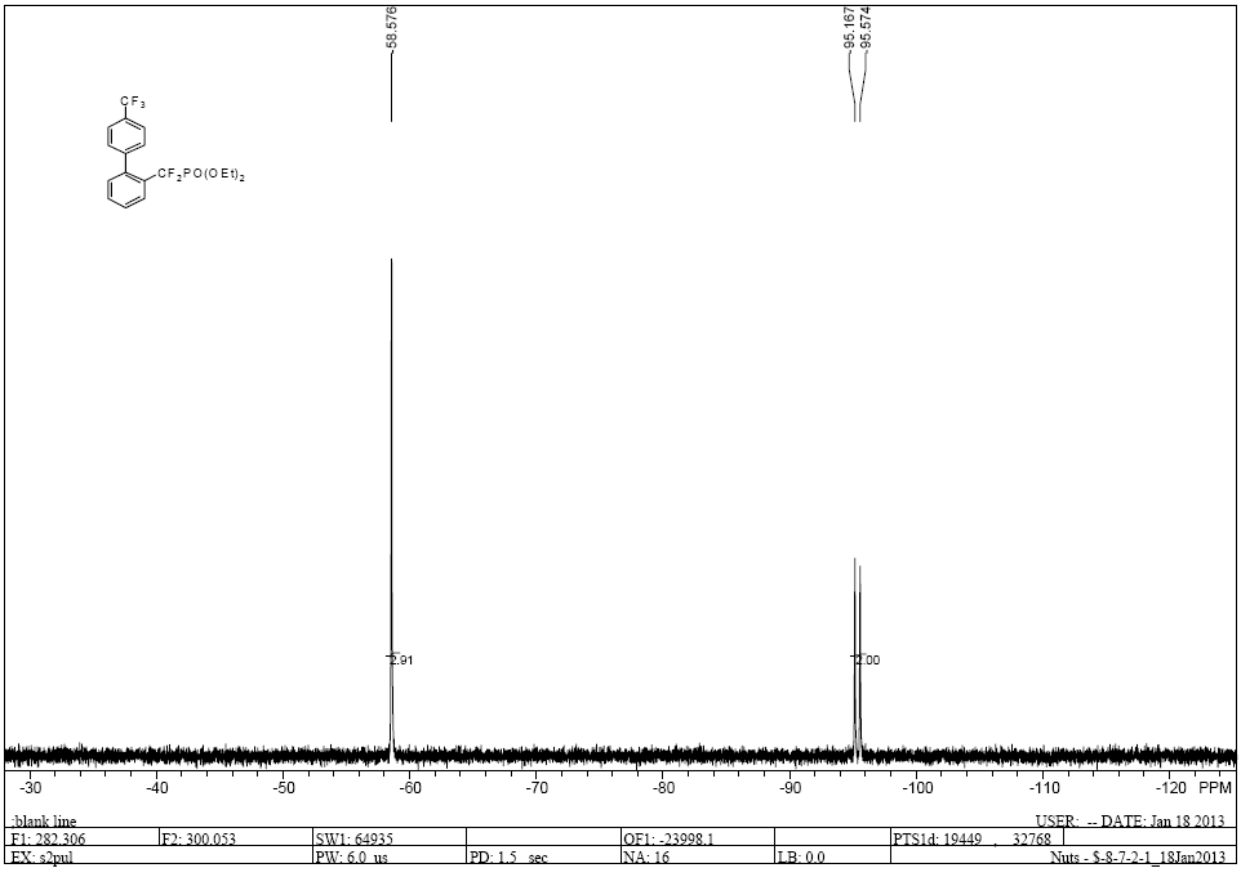


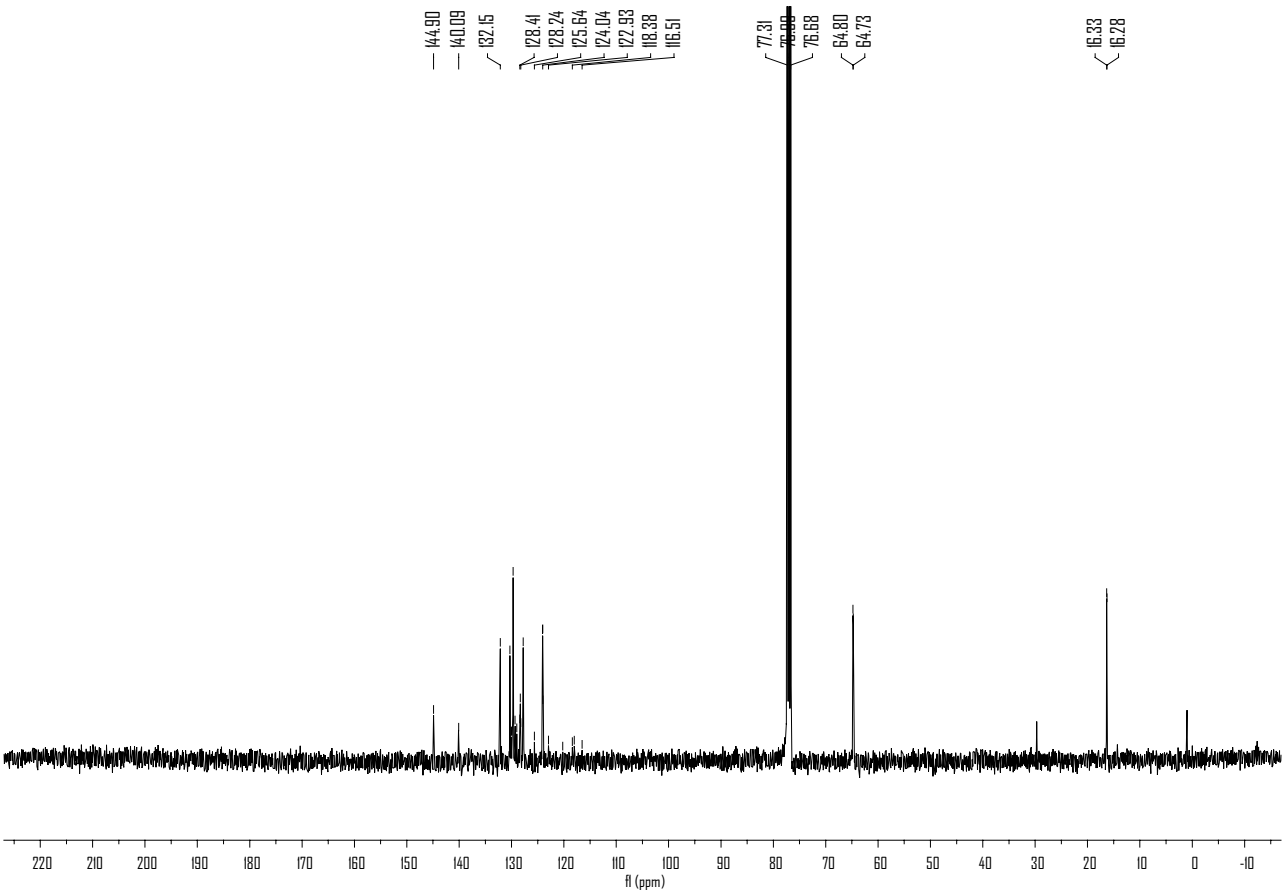

104.633
104.940
TMS
CF2PO(OEt)2
-70
-80
-90
-100
-110
-120
-130
-140 PPM
2010190_8_20_2
USER: -- DATE: Apr 11 2013
F1: 376.058
F2: 100.513
SW1: 89286
OF1: -31967.6
PTS1d: 65536 , 65536
EX: s2pul
PW: 5.4 us
PD: 1.0 sec
NA: 16
LB: 0.0
Nuts - SFLUORINE_01.fid


134.79
133.93
133.82
133.77
133.66
133.61
133.50
130.16
130.15
128.19
128.18
128.01
127.99
127.95
127.93
127.88
127.87
121.41
119.17
115.33
102.37
99.17
77.26
77.01
76.76
64.80
64.75
16.42
16.37
-0.29
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

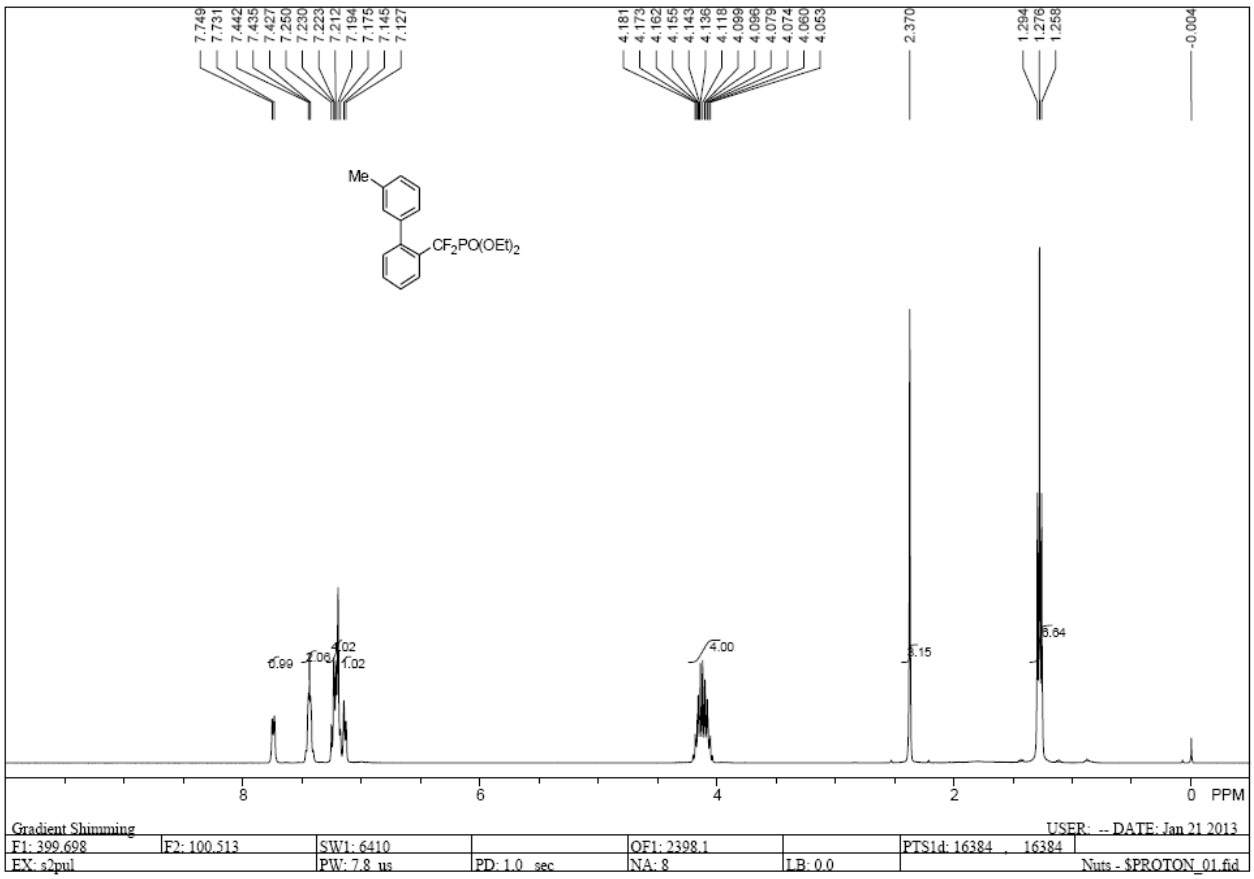
Diethyl(difluoro(4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)methyl)phosphonate (9).

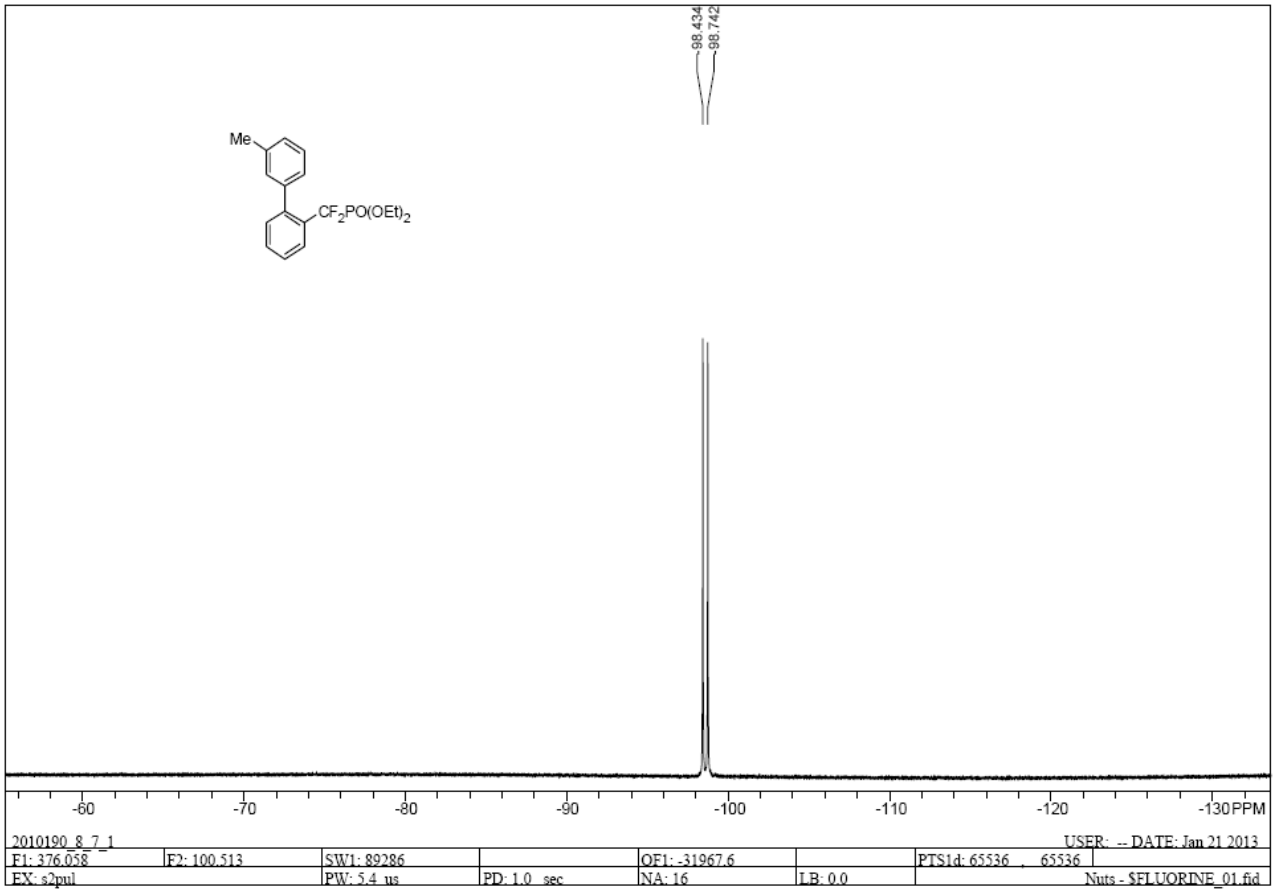


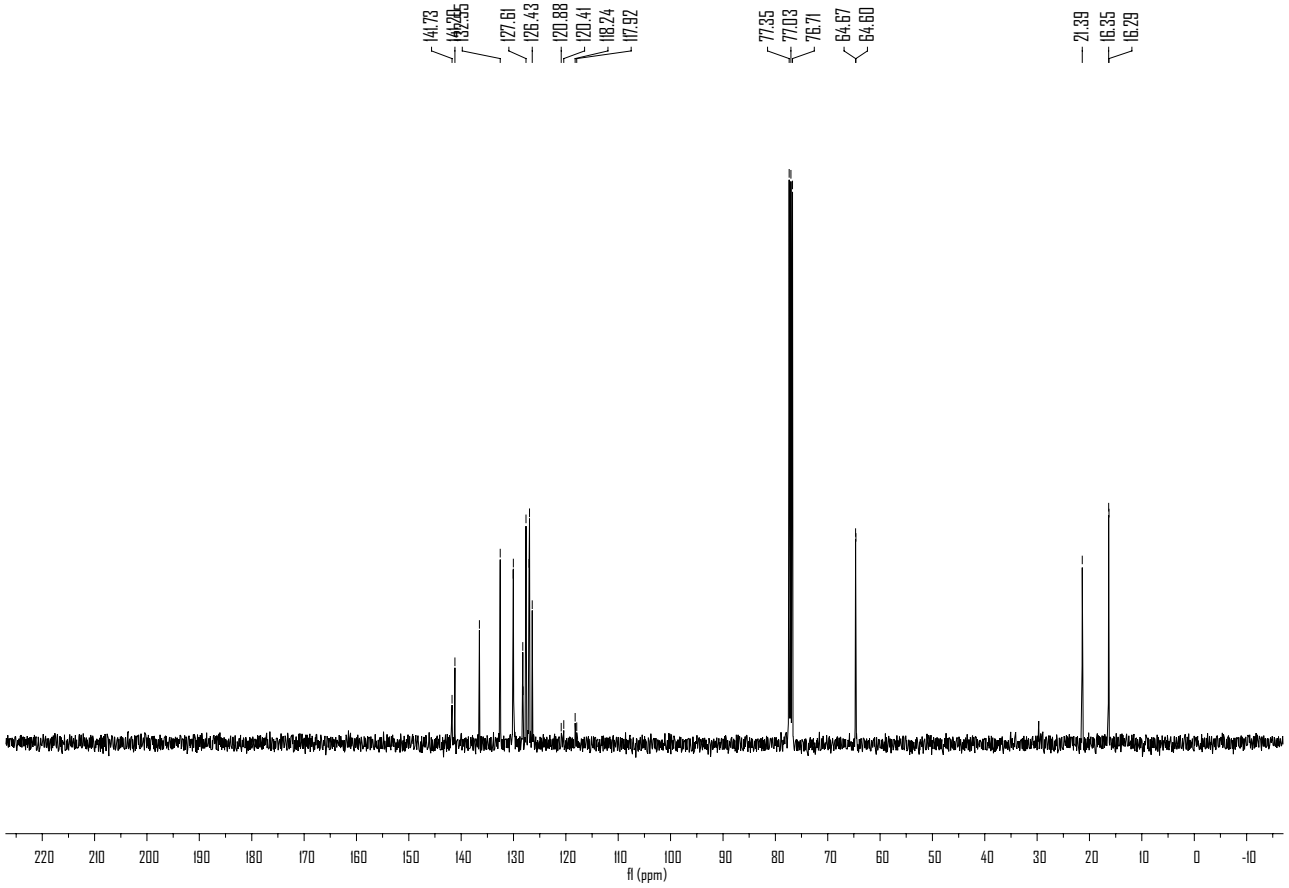




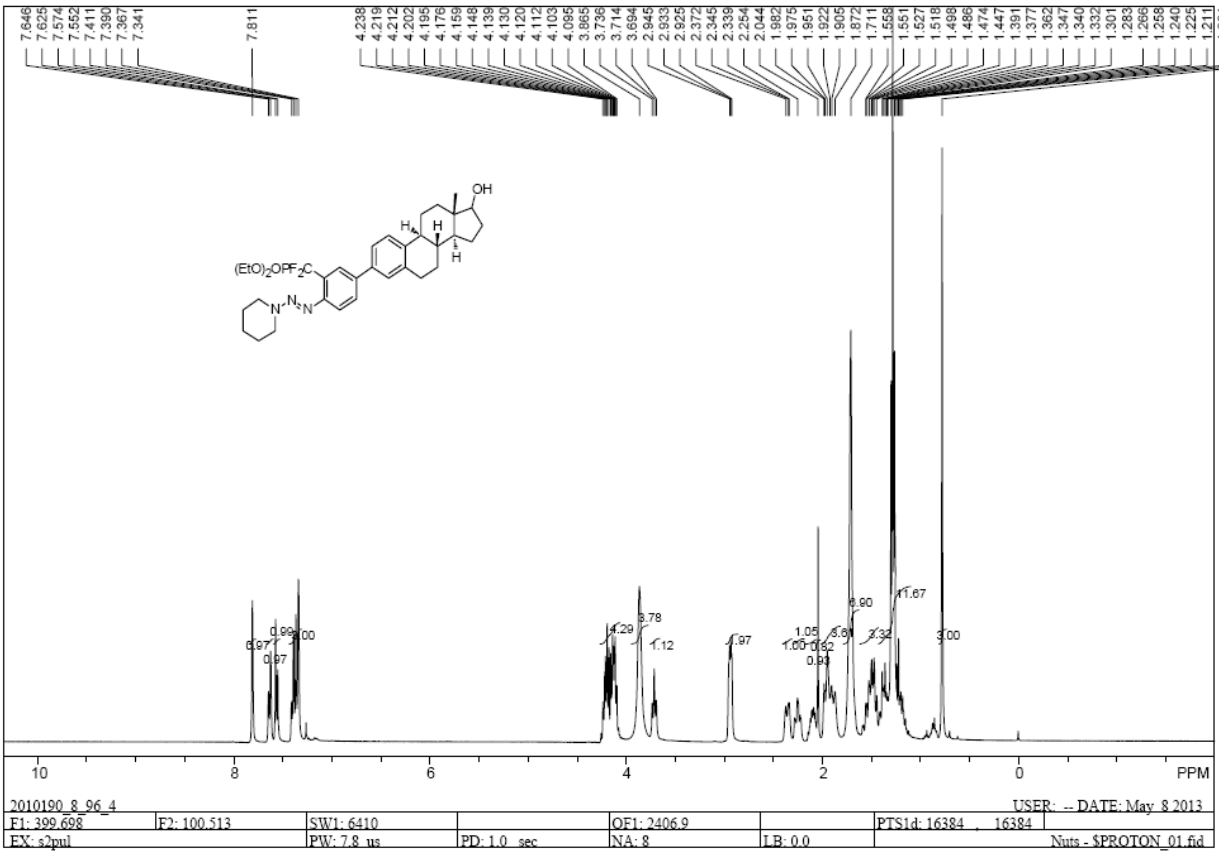
Diethyl (difluoro(3'-methyl-[1,1'-biphenyl]-2-yl)methyl)phosphonate (10).

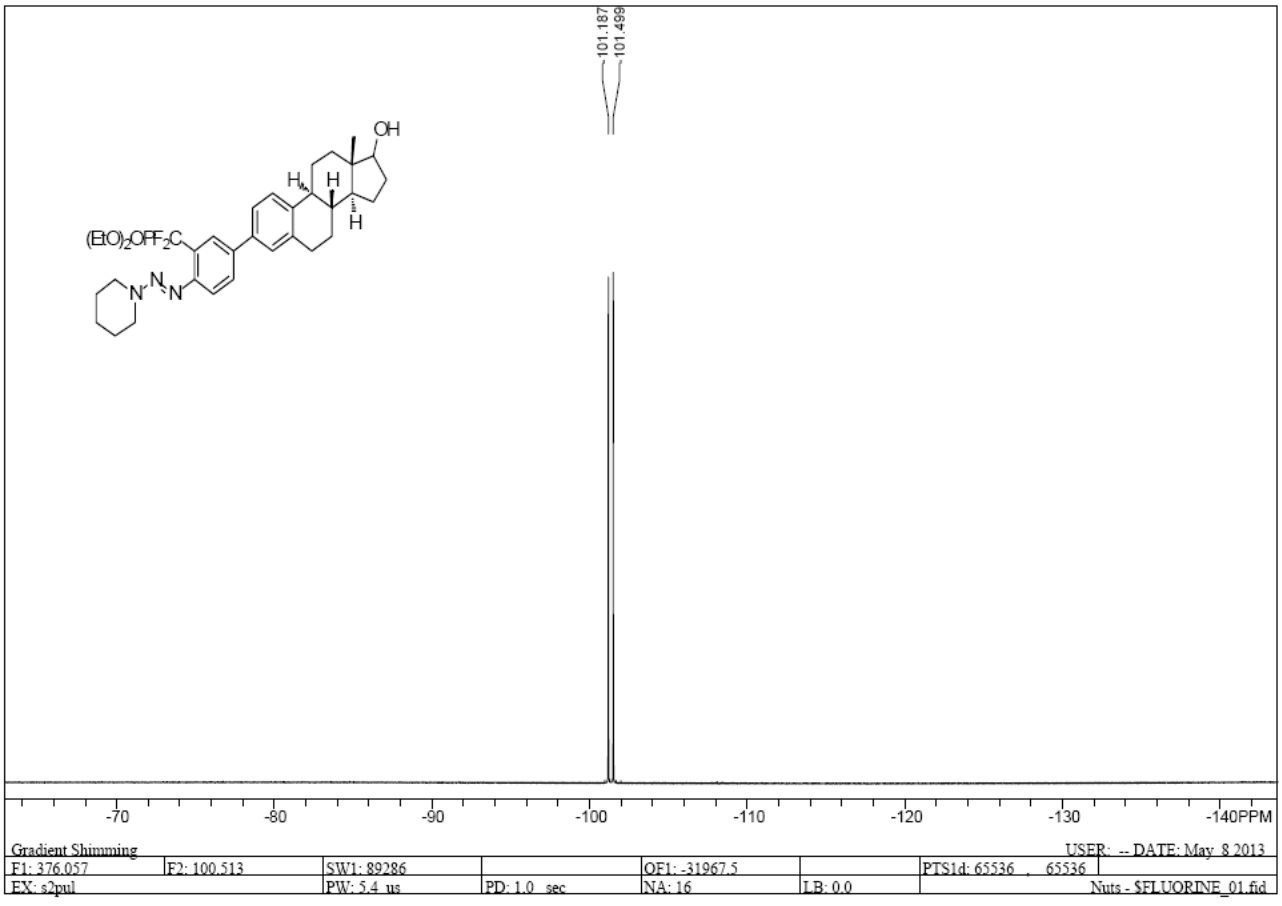




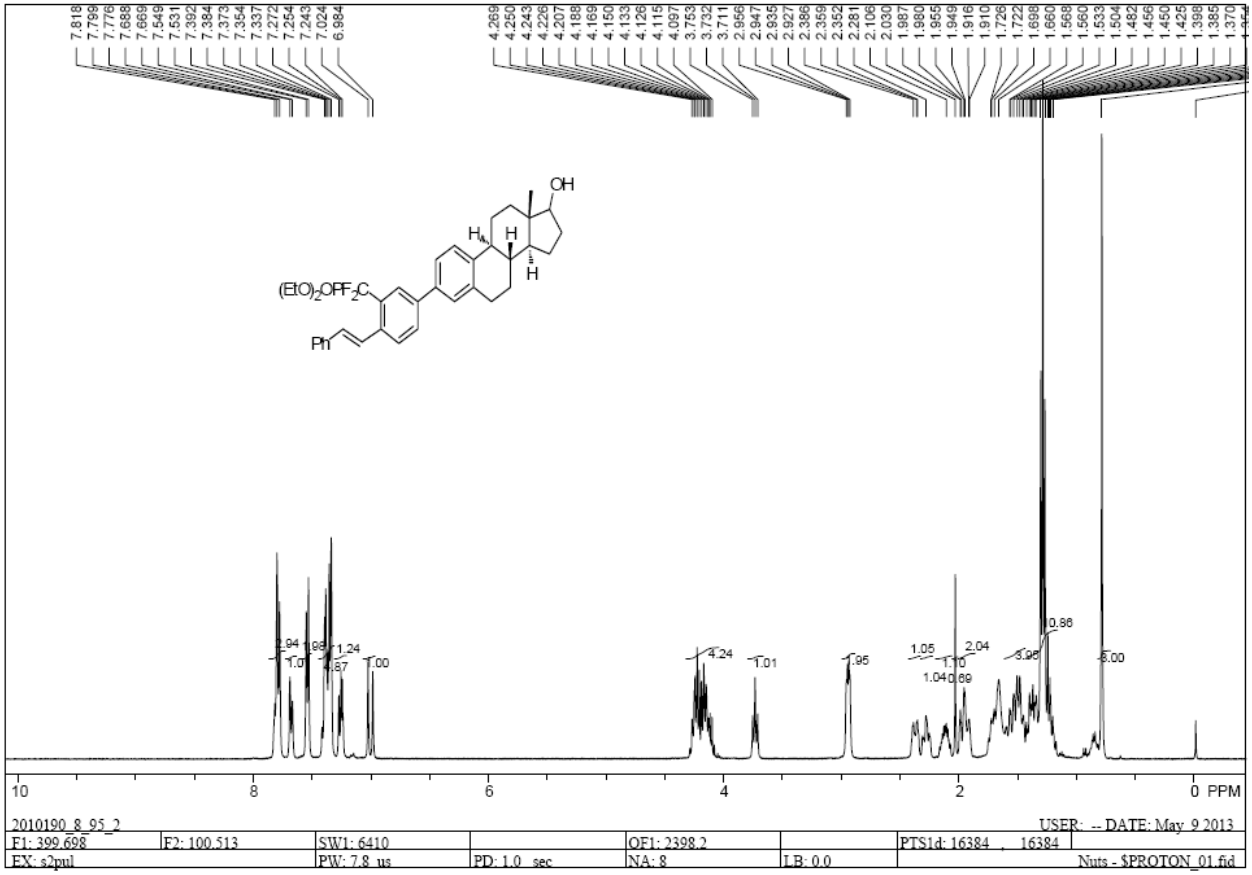


(12)


7.646
7.625
7.574
7.552
7.411
7.390
7.367
7.341
7.811
4.238
4.219
4.212
4.202
4.195
4.176
4.159
4.148
4.139
4.130
4.120
4.112
4.103
4.095
3.885
3.736
3.714
3.694
2.945
2.933
2.925
2.372
2.345
2.339
2.254
2.044
1.982
1.975
1.951
1.922
1.905
1.872
1.711
1.558
1.551
1.527
1.518
1.498
1.486
1.474
1.447
1.391
1.377
1.362
1.347
1.340
1.332
1.301
1.283
1.266
1.258
1.240
1.225
1.211
OH
H
H
H
(EtO)2OPF2C
N
N
N
0.97
0.99
3.00
0.97
4.29
3.78
1.12
0.97
1.05
1.00
0.52
0.91
6.90
11.67
3.34
3.00
10
8
6
4
2
0
PPM
2010190_8_96_4
USER: -- DATE: May 8 2013
F1: 399.698
F2: 100.513
SW1: 6410
OF1: 2406.9
PTS1d: 16384 , 16384
EX: s2pul
PW: 7.8 us
PD: 1.0 sec
NA: 8
LB: 0.0
Nuts - $PROTON_01.fid


101.187
101.499
OH
H
H
H
(EtO)2OPF2C
N
N
N
-70
-80
-90
-100
-110
-120
-130
-140PPM
Gradient Shimming
USER: -- DATE: May 8 2013
F1: 376.057
F2: 100.513
SW1: 89286
OF1: -31967.5
PTS1d: 65536 , 65536
EX: s2pul
PW: 5.4 us
PD: 1.0 sec
NA: 16
LB: 0.0
Nuts - $FLUORINE_01.fid

(13)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7.024
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4.226
4.207
4.188
4.169
4.150
4.133
4.128
4.115
4.097
3.753
3.732
3.711
2.966
2.947
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2.352
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2.106
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1.987
1.980
1.955
1.949
1.916
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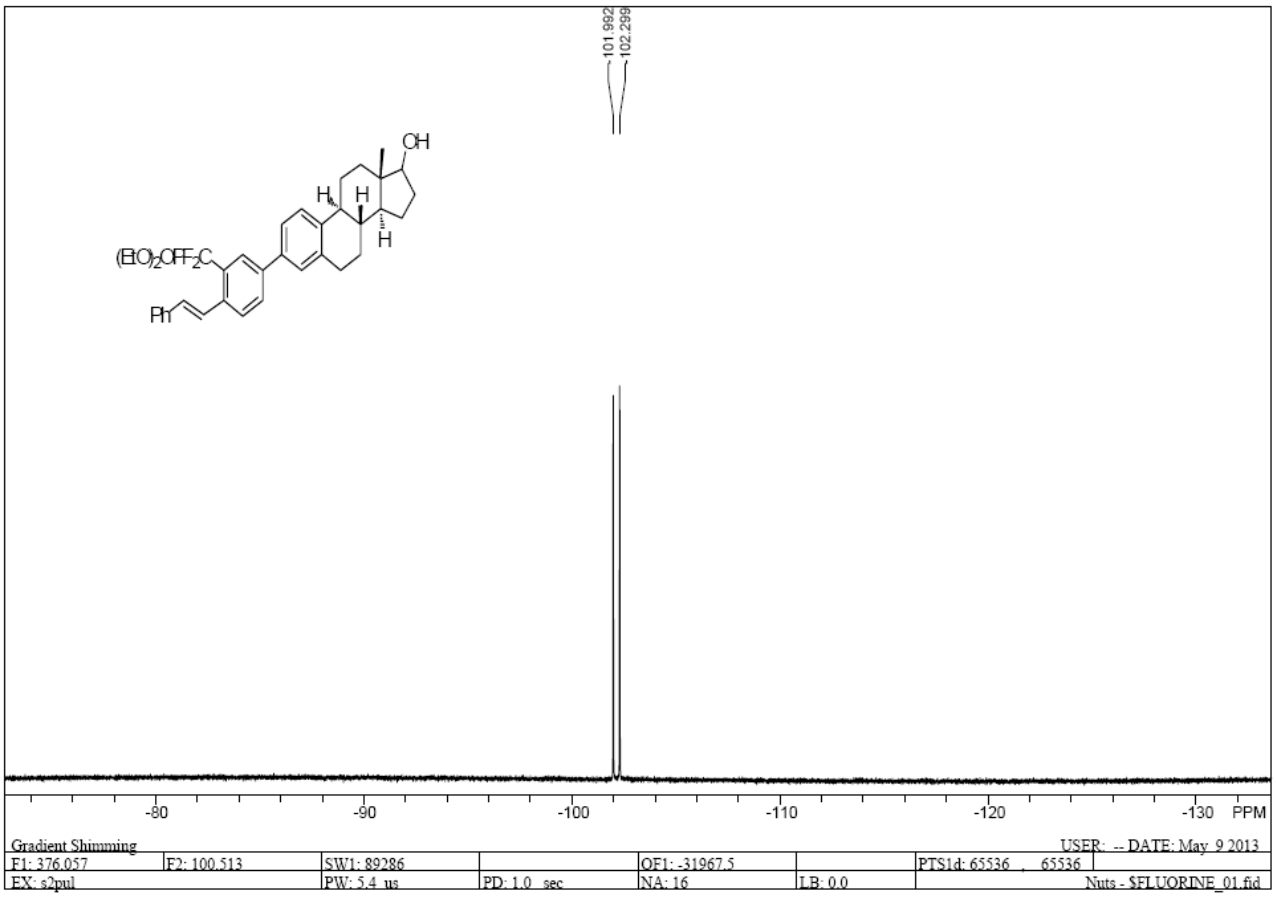
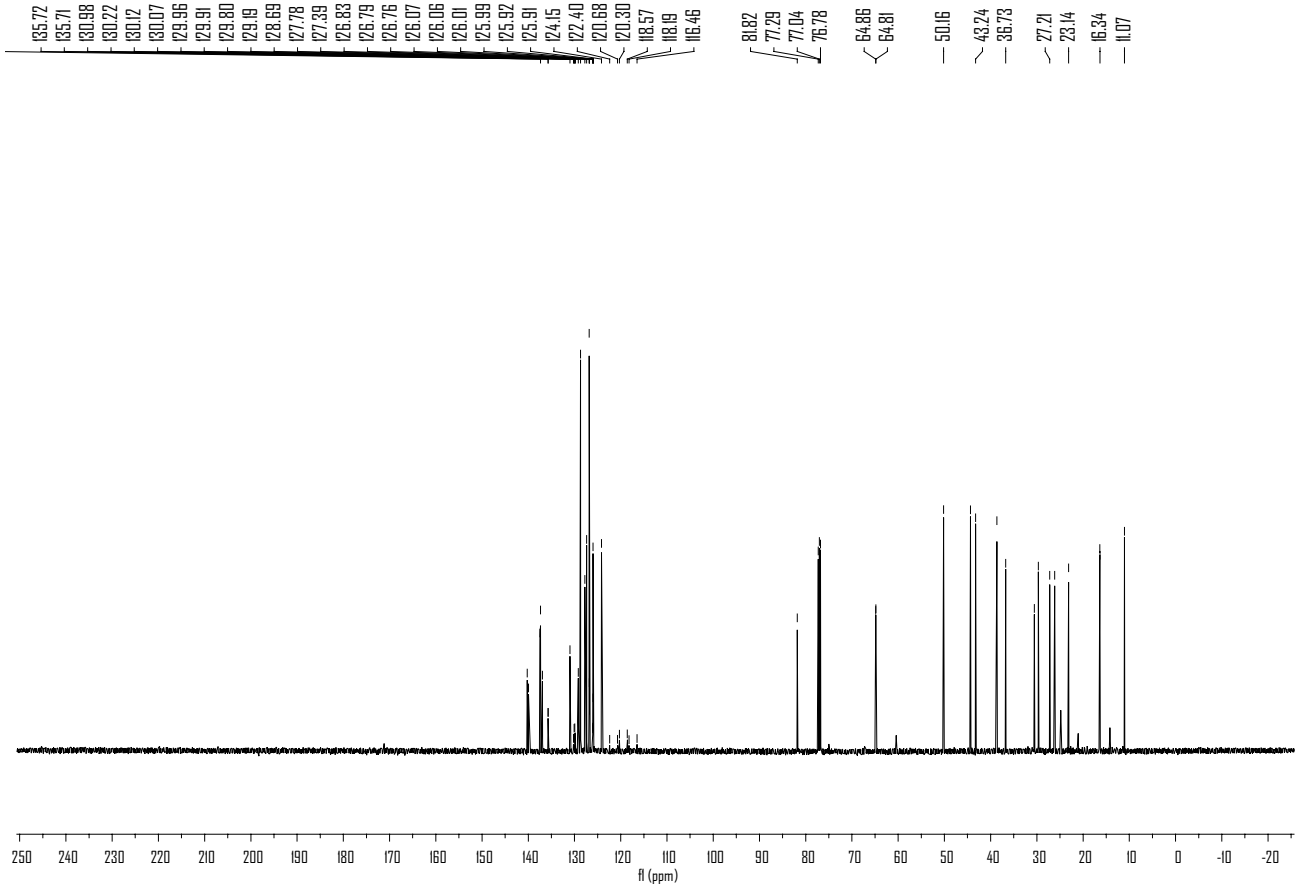
1.722
1.698
1.660
1.568
1.560
1.533
1.504
1.482
1.456
1.450
1.425
1.398
1.385
1.370
OH
H
H
H
(EtO)2OPF2C
Ph
2.94
1.98
1.24
1.00
1.87
4.24
1.01
1.95
1.05
2.04
1.10
1.04
0.89
0.86
3.98
3.00
10
8
6
4
2
0 PPM
2010190_8_95_2
USER: -- DATE: May 9 2013
F1: 399.698
F2: 100.513
SW1: 6410
OF1: 2398.2
PTS1d: 16384 , 16384
EX: s2pul
PW: 7.8 us
PD: 1.0 sec
NA: 8
LB: 0.0
Nuts - $PROTON_01.fid


101.992
102.299
OH
H
H
H
(EtO)2OPF2C
Ph
-80
-90
-100
-110
-120
-130 PPM
Gradient Shimming
USER: -- DATE: May 9 2013
F1: 376.057
F2: 100.513
SW1: 89286
OF1: -31967.5
PTS1d: 65536 , 65536
EX: s2pul
PW: 5.4 us
PD: 1.0 sec
NA: 16
LB: 0.0
Nuts - $FLUORINE_01.fid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130.12
130.07
129.96
129.91
129.80
129.19
128.69
127.78
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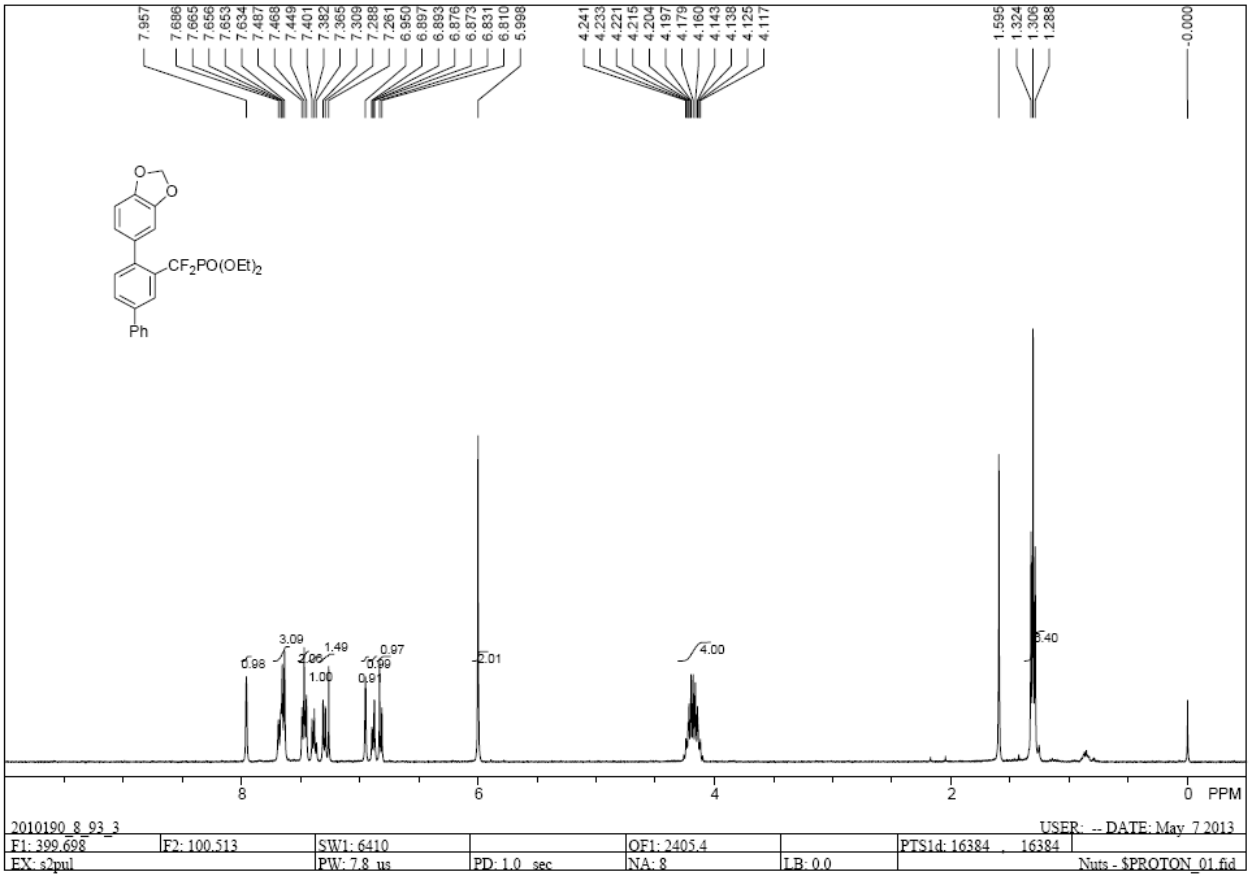
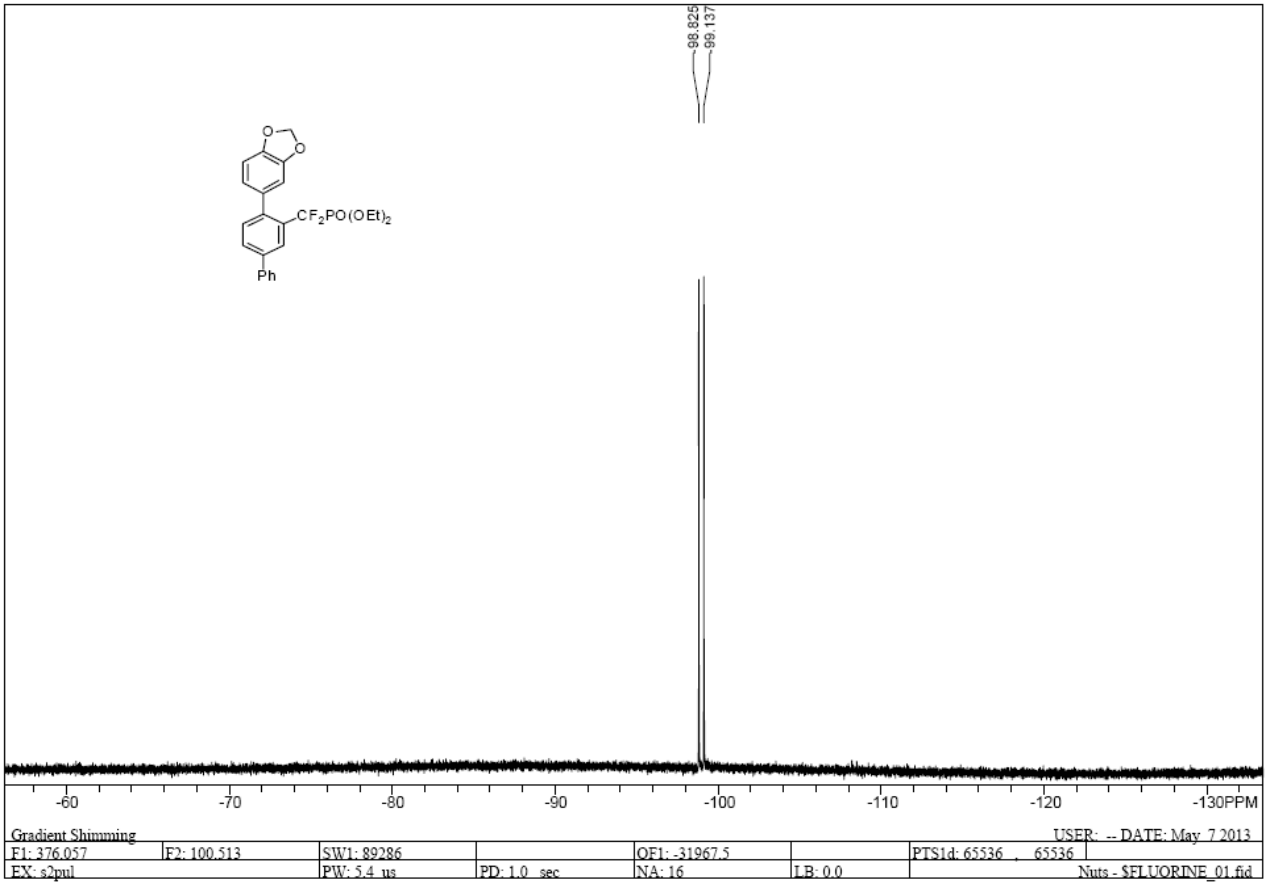
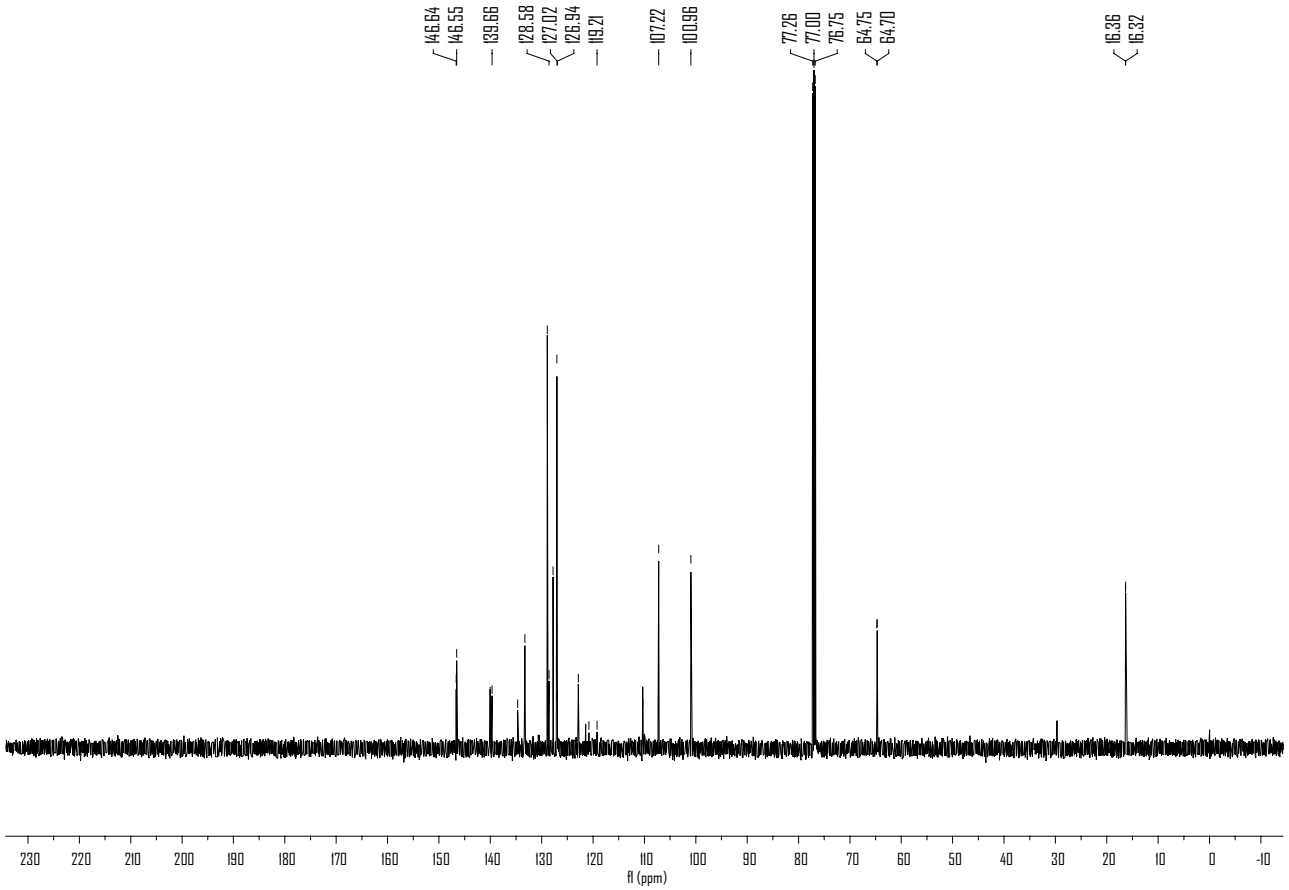
126.83
126.79
126.76
126.07
126.06
126.01
125.99
125.92
125.91
124.15
122.40
120.68
120.30
118.57
118.19
116.46
81.82
77.29
77.04
76.78
64.86
64.81
50.16
43.24
36.73
27.21
23.14
16.34
11.07
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

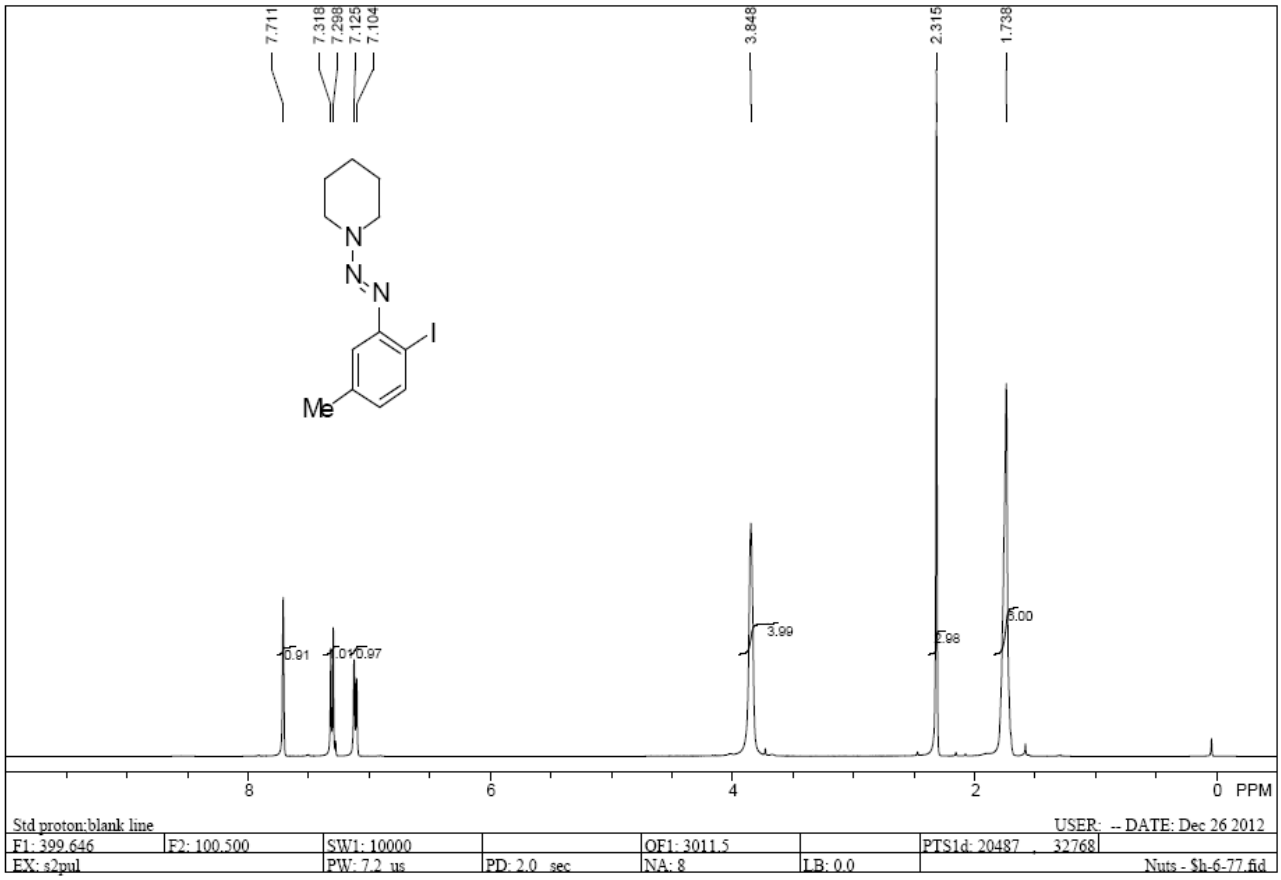
Diethyl((4-(benzo[d][1,3]dioxol-5-yl)-[1,1'-biphenyl]-3-yl)difluoromethyl)phosphonate (16).

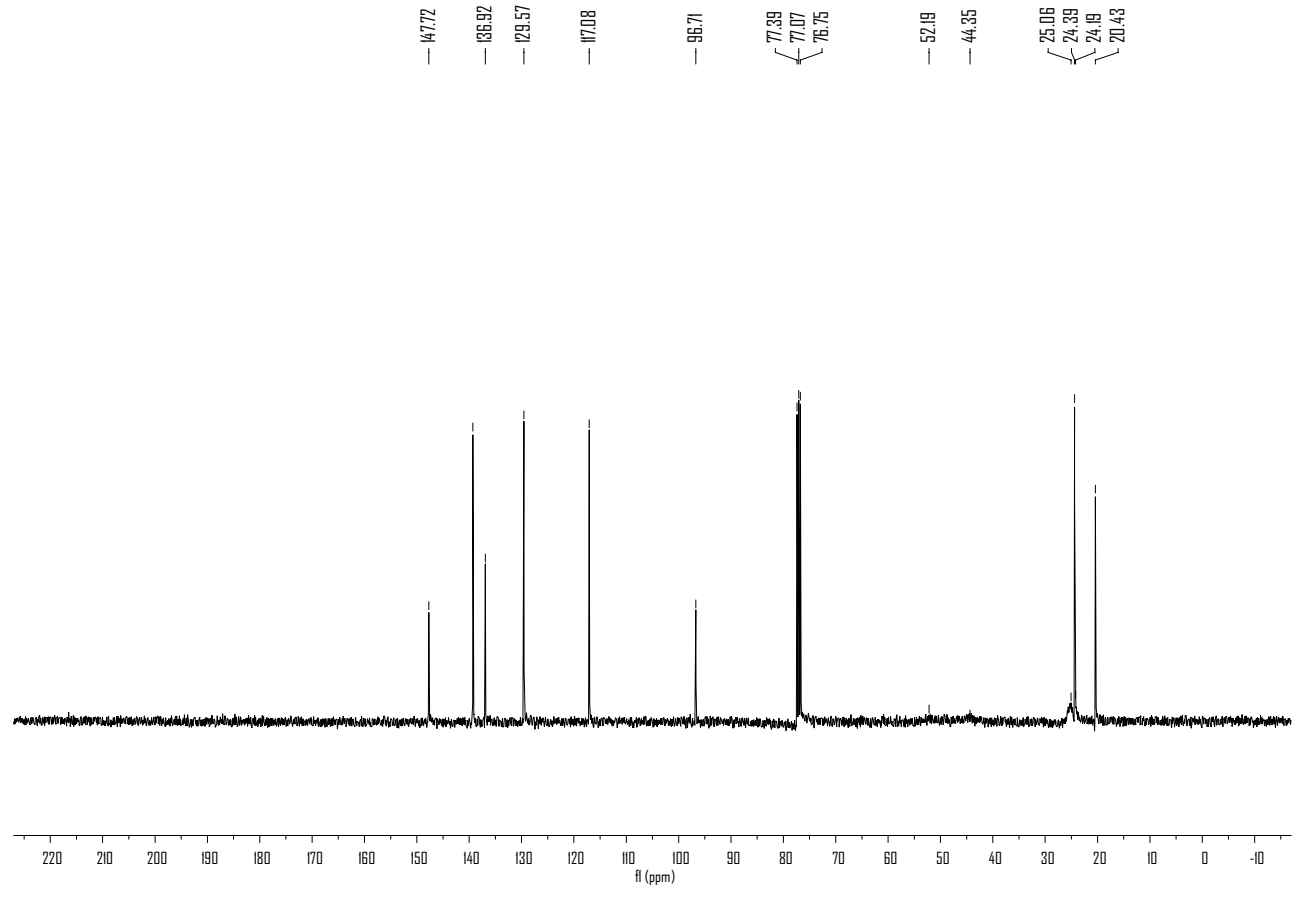




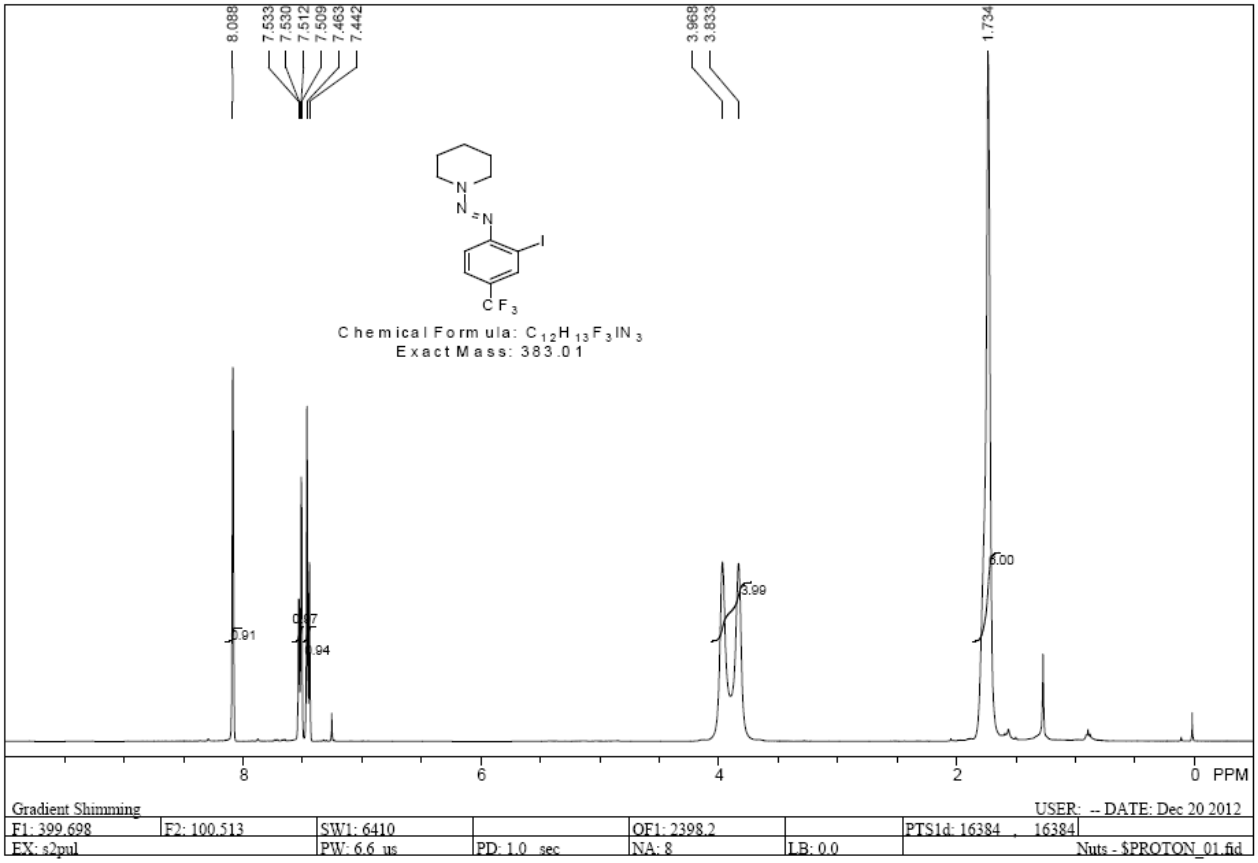


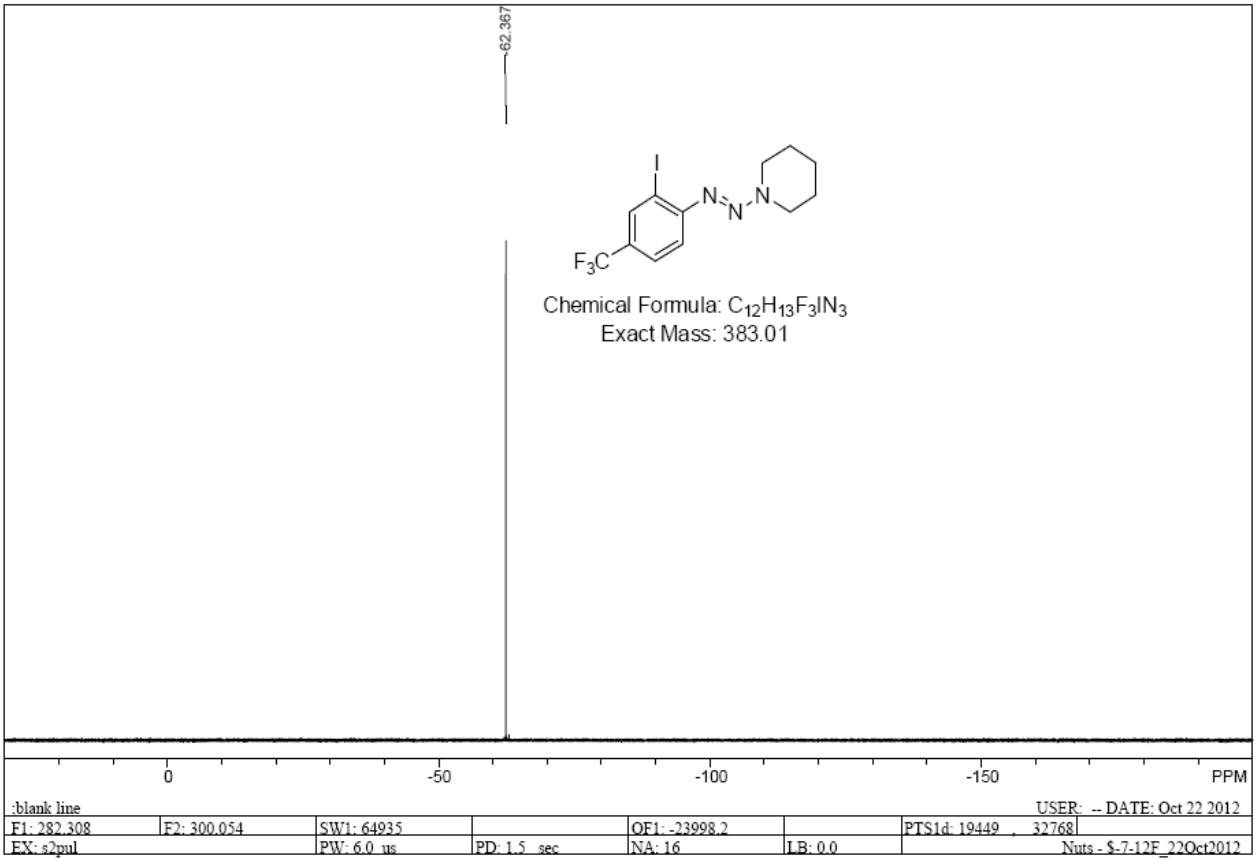
1-((2-iodo-5-methylphenyl)diazenyl)piperidine (1bb).

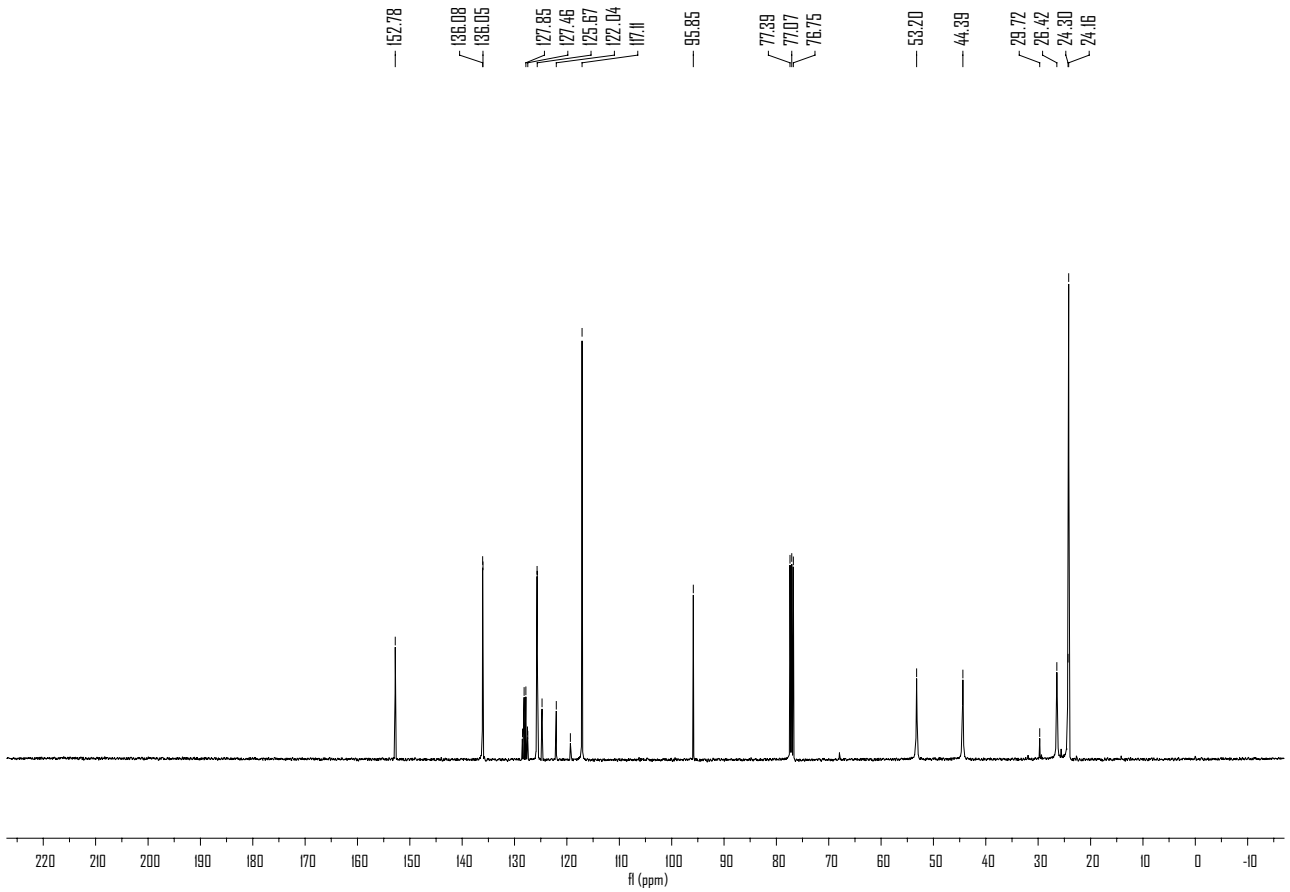




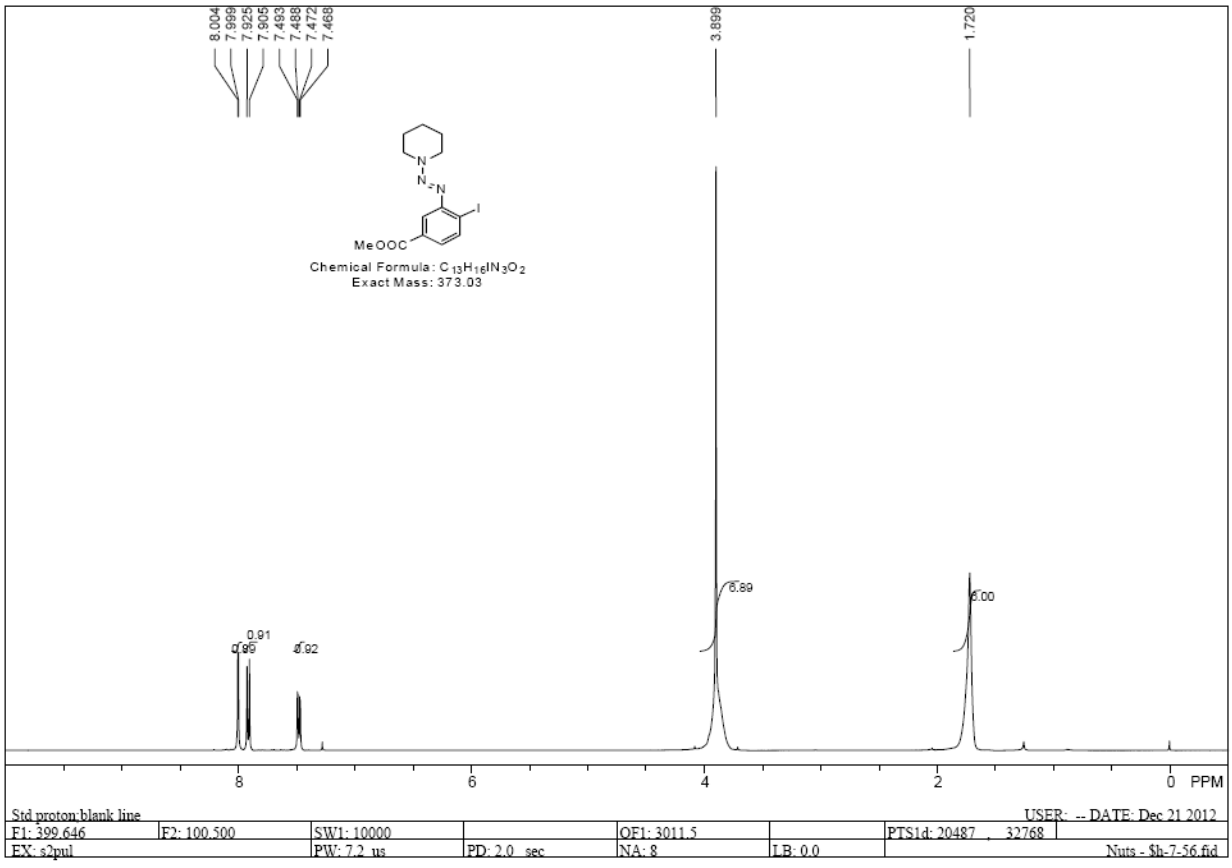
1-((2-Iodo-4-(trifluoromethyl)phenyl)diazenyl)piperidine (1bc).

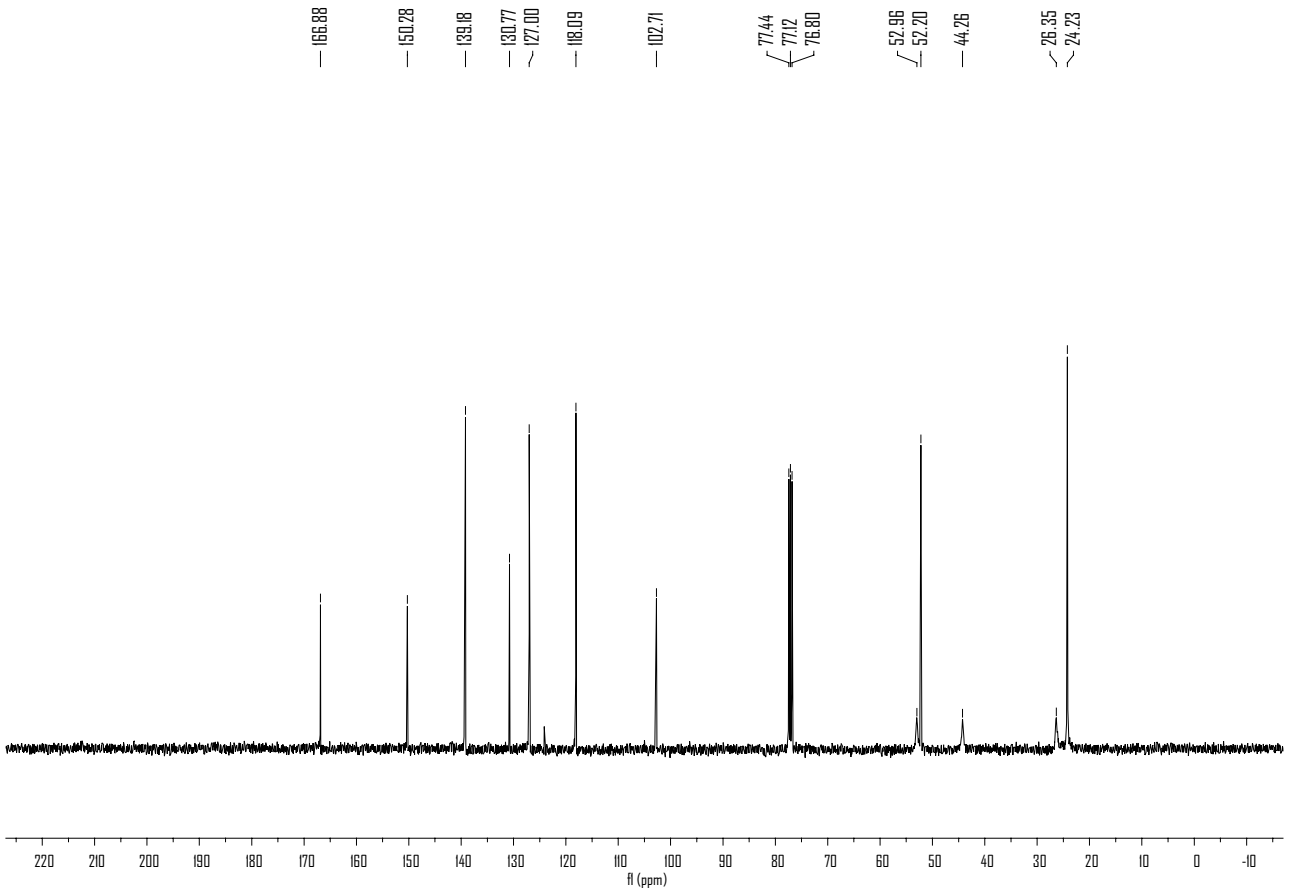




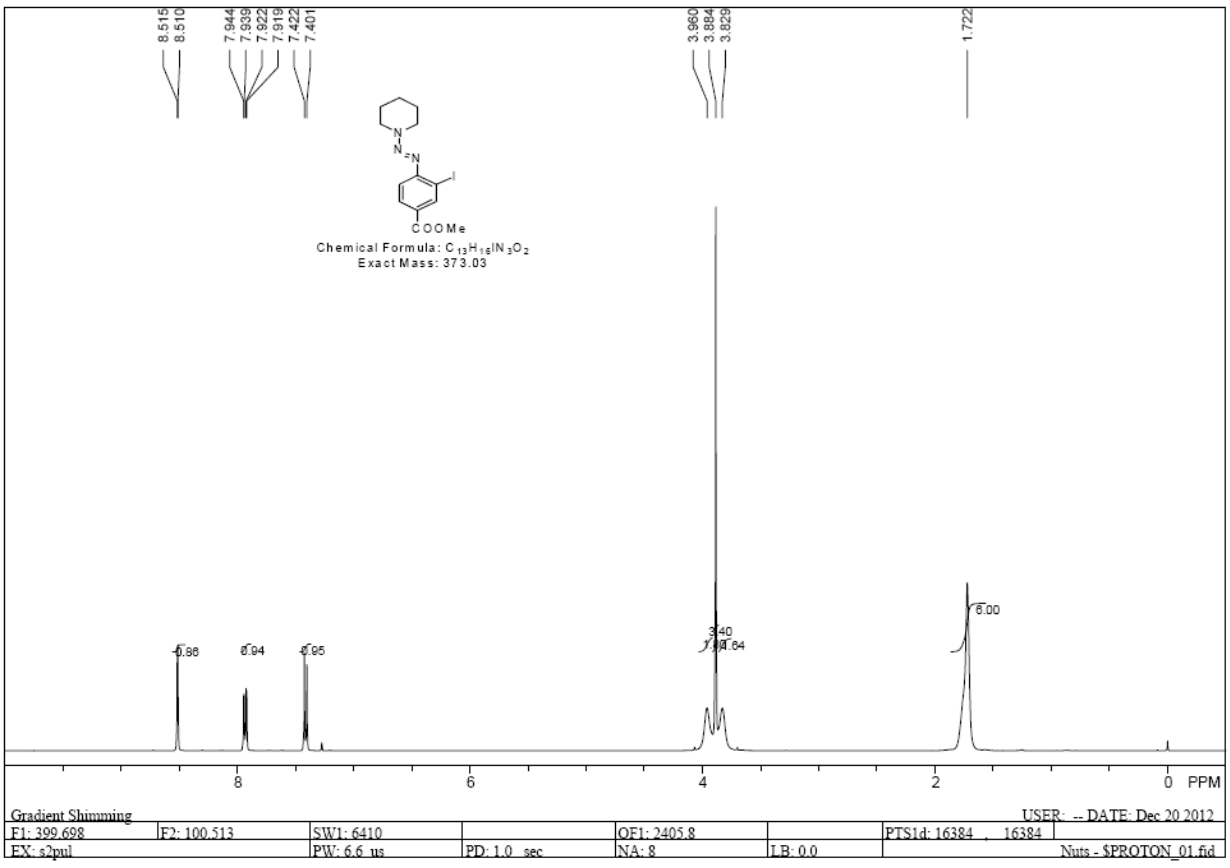


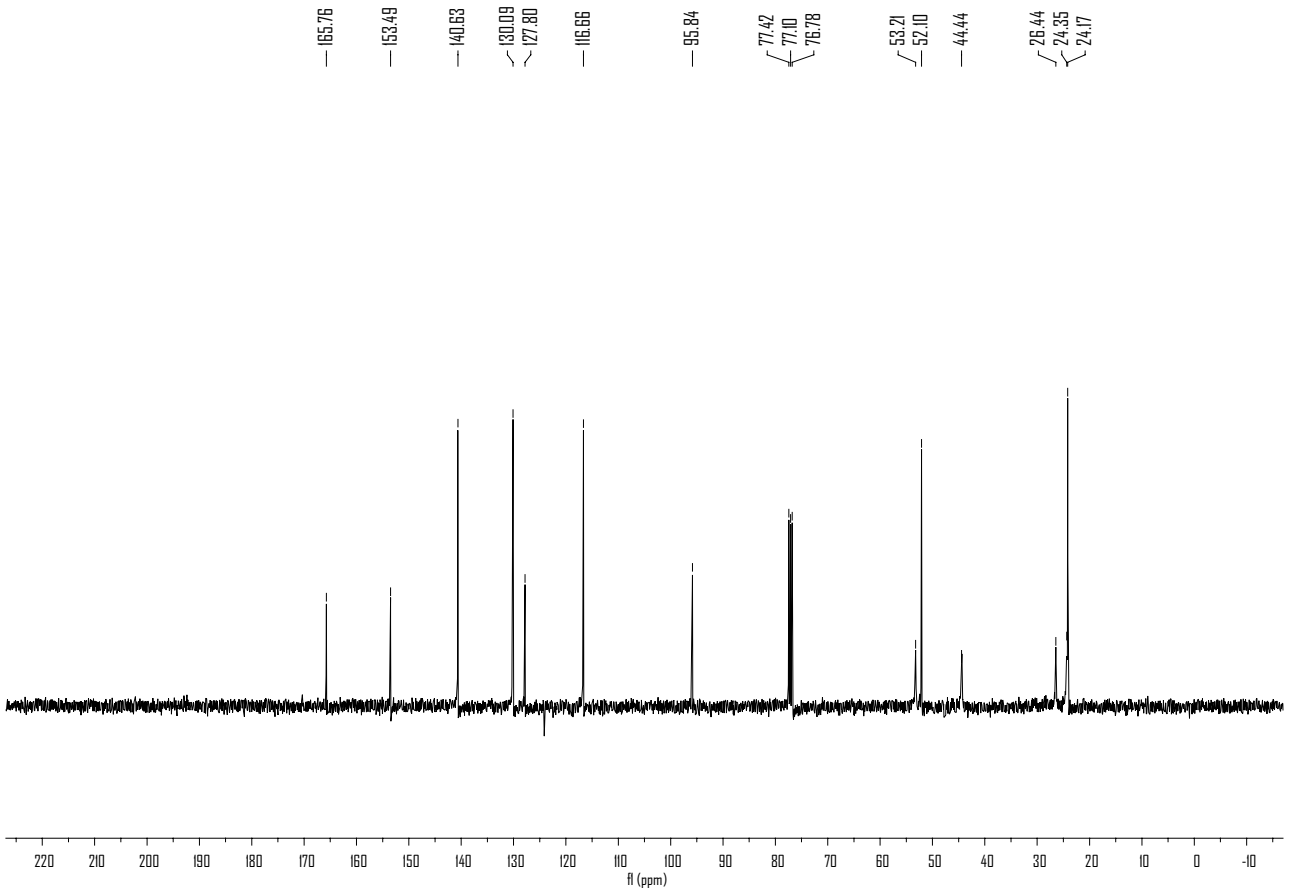
Methyl 4-iodo-3-(piperidin-1-yldiazenyl)benzoate (1bd).



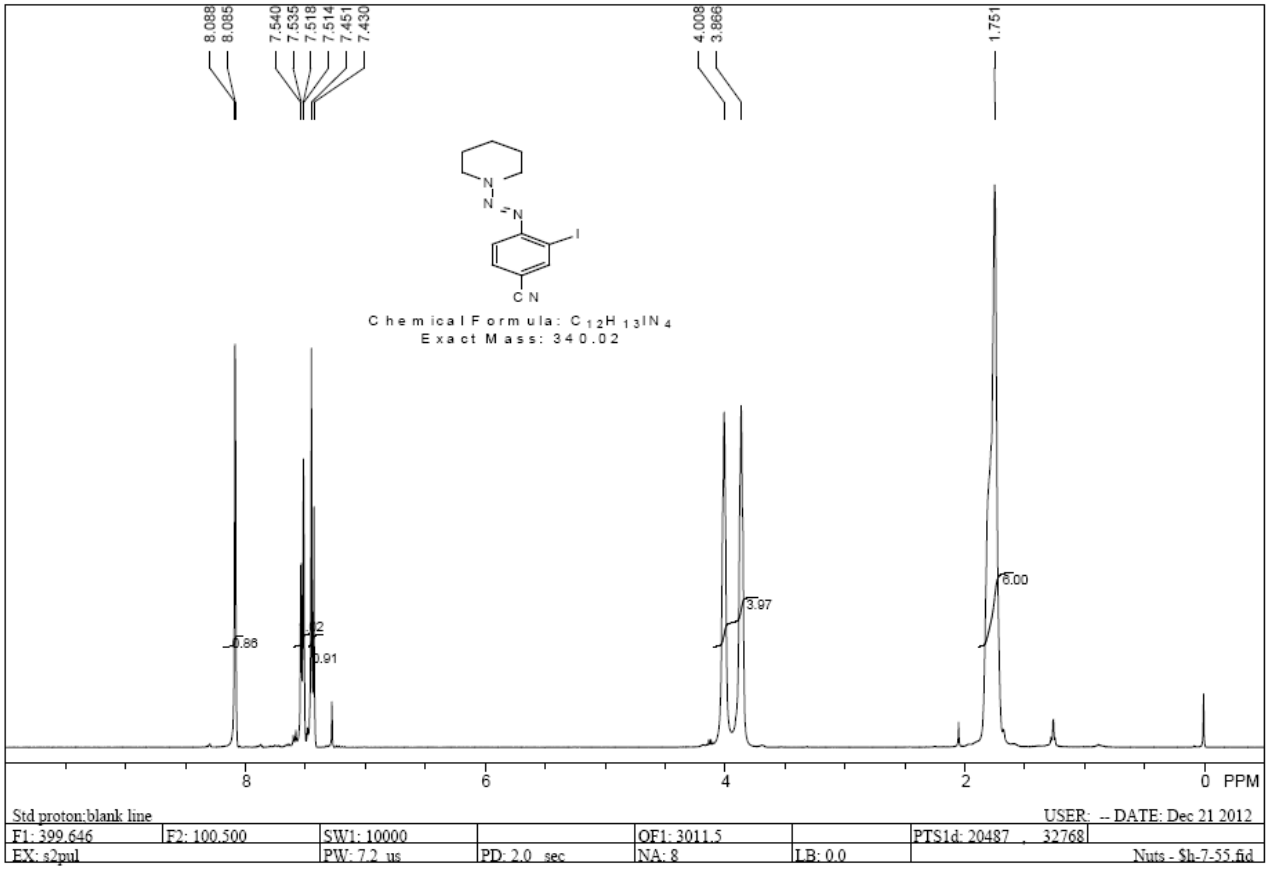


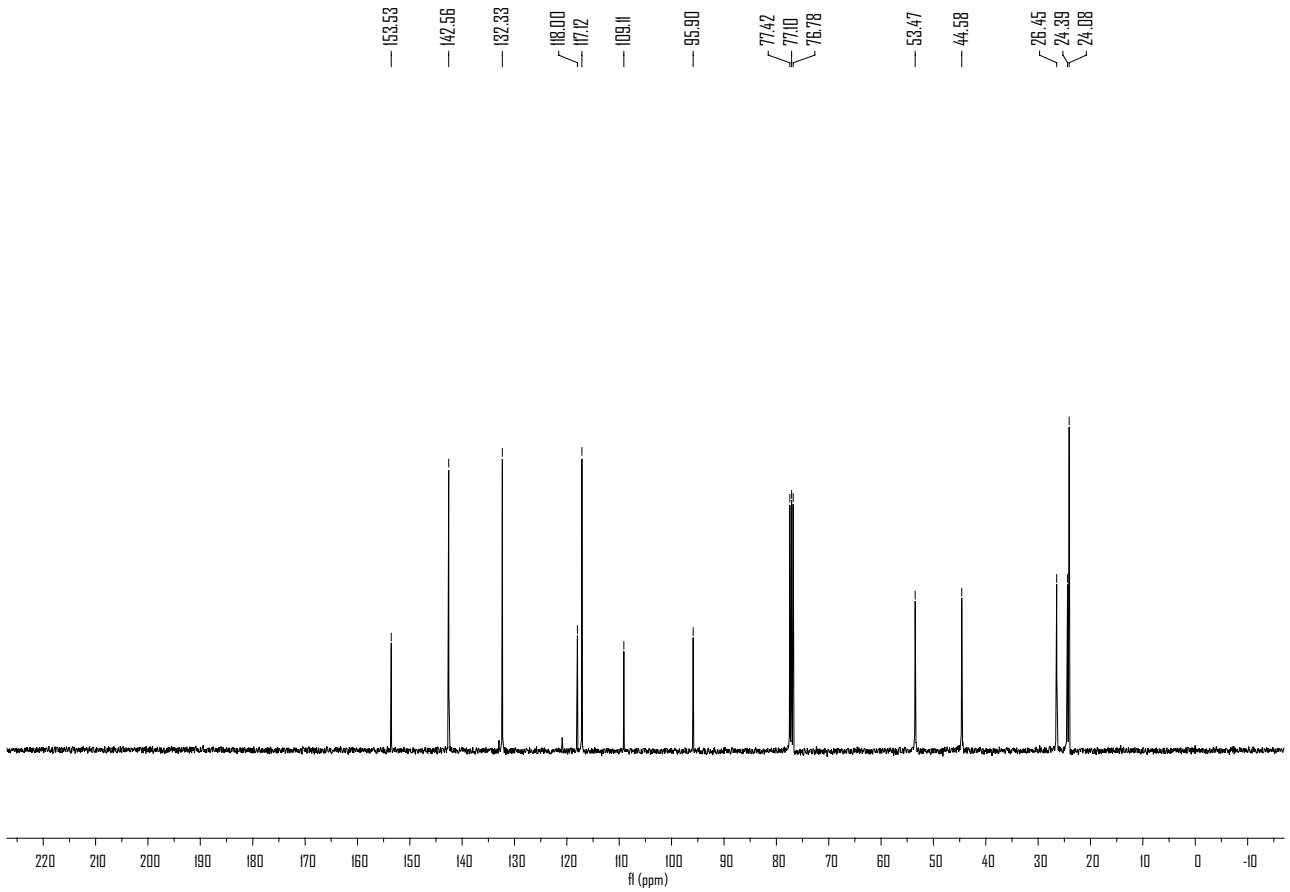
Methyl 3-iodo-4-(piperidin-1-yldiazenyl)benzoate (1be).



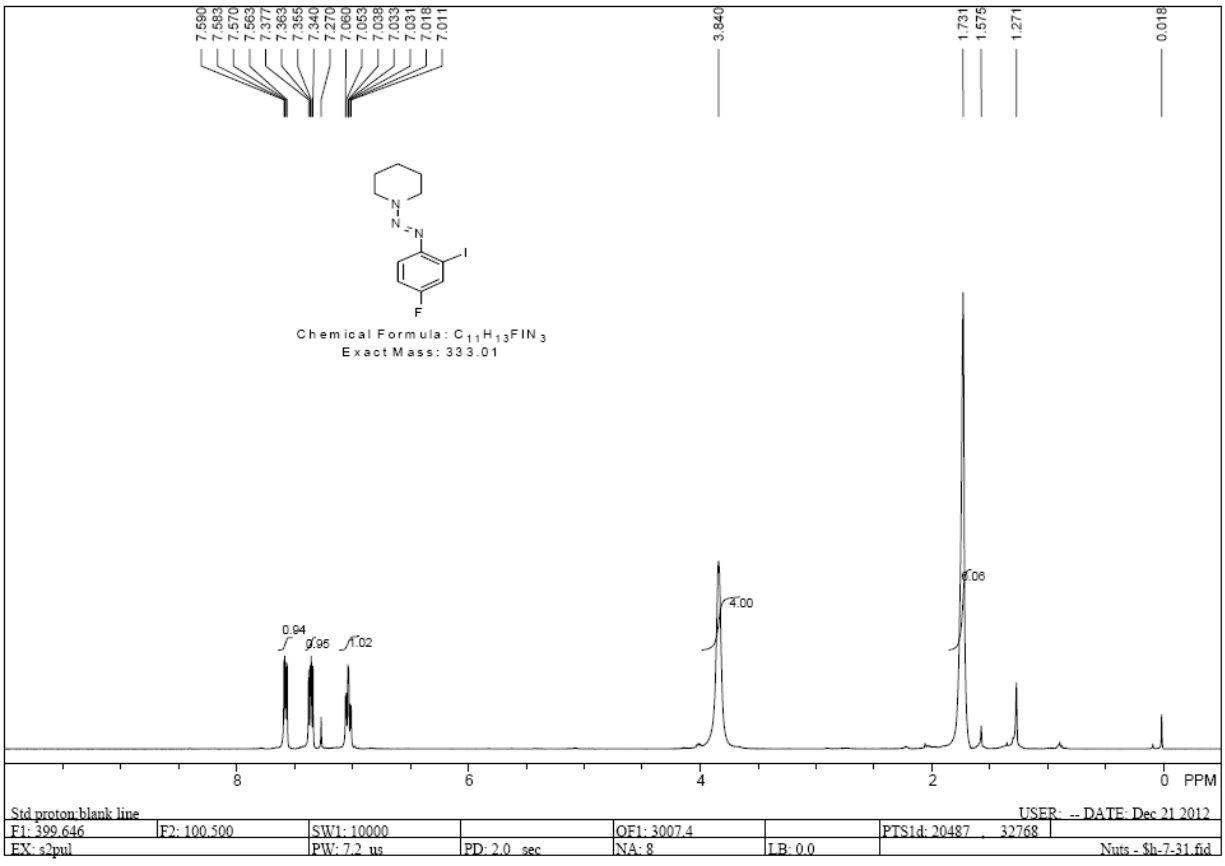


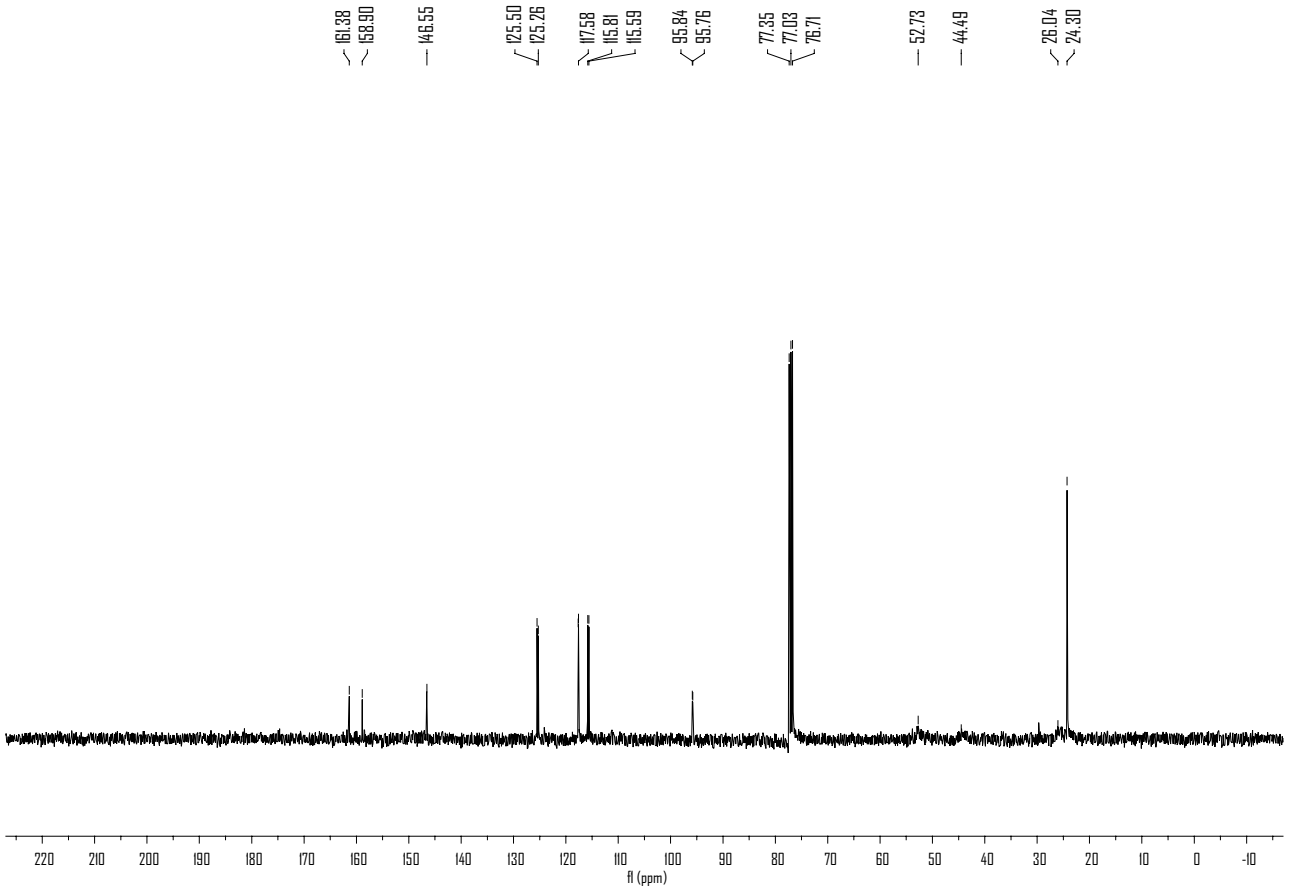
3-Iodo-4-(piperidin-1-yldiazenyl)benzonitrile (1bf).



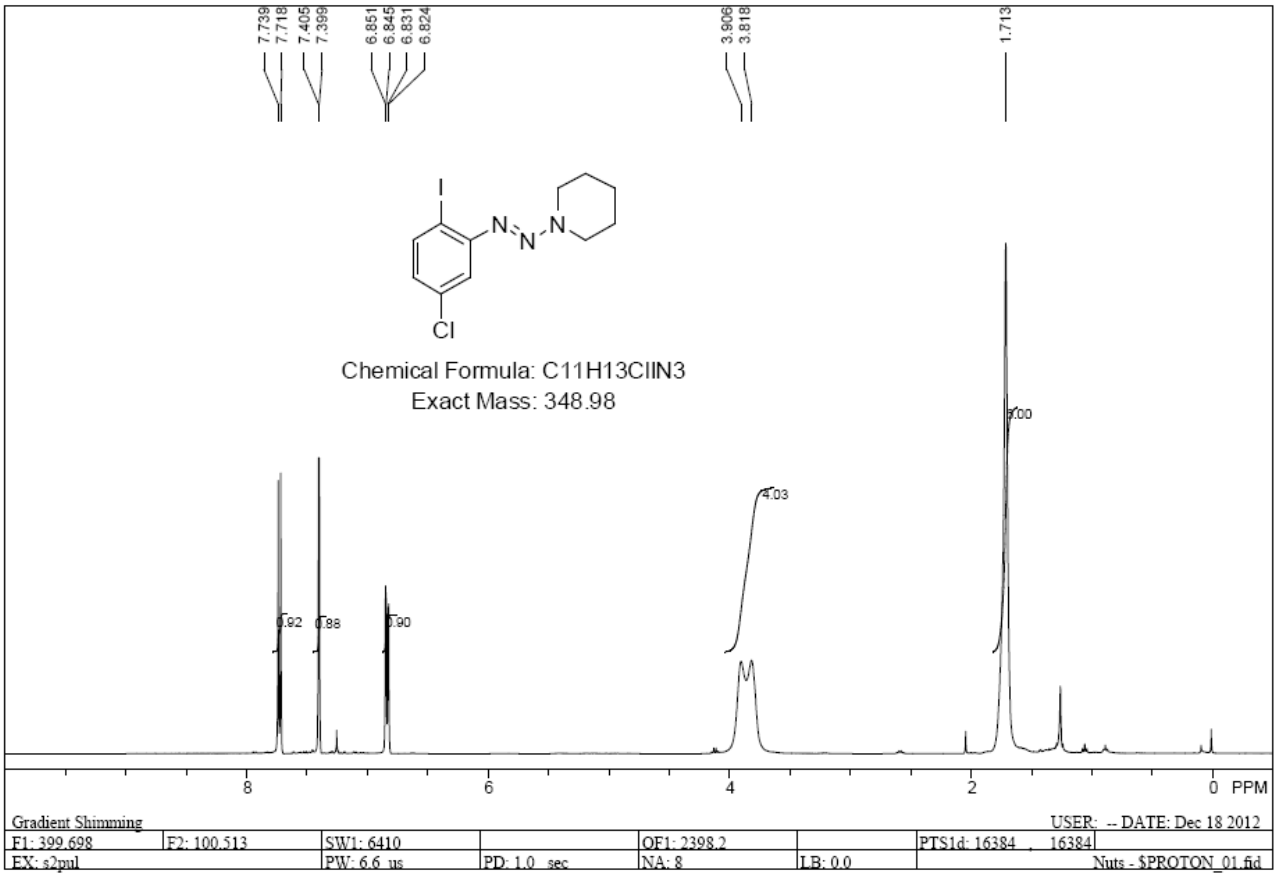


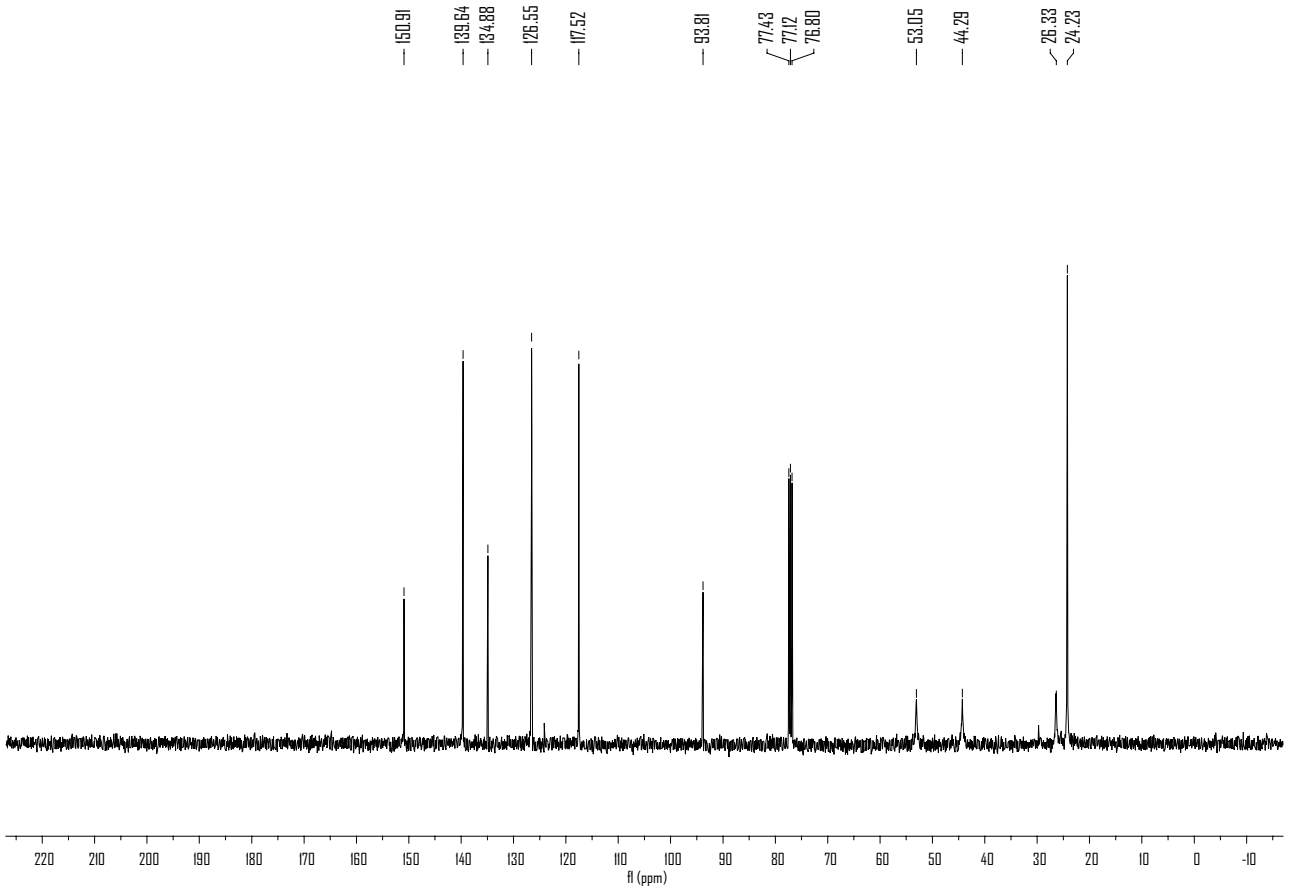
1-((4-Fluoro-2-iodophenyl)diazenyl)piperidine (1bg).



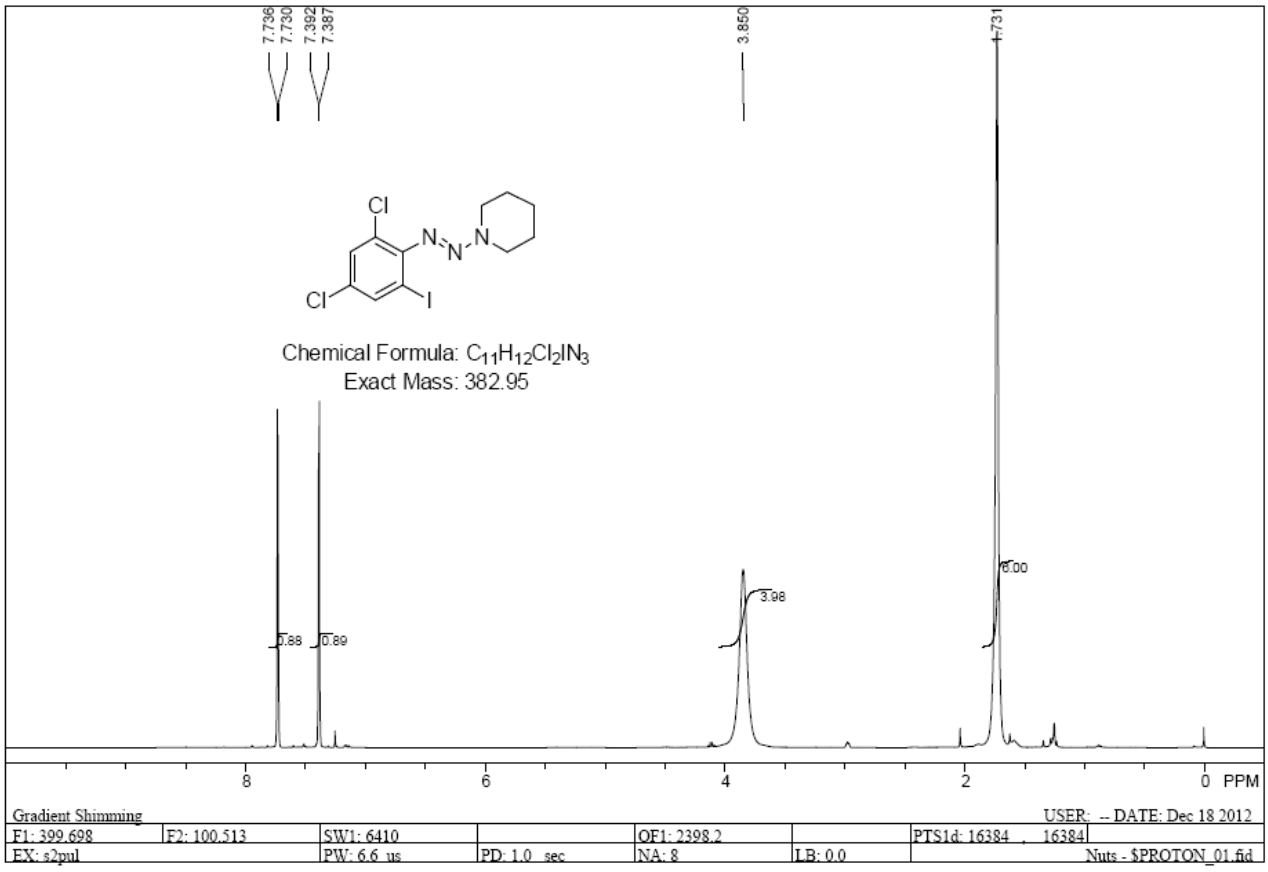


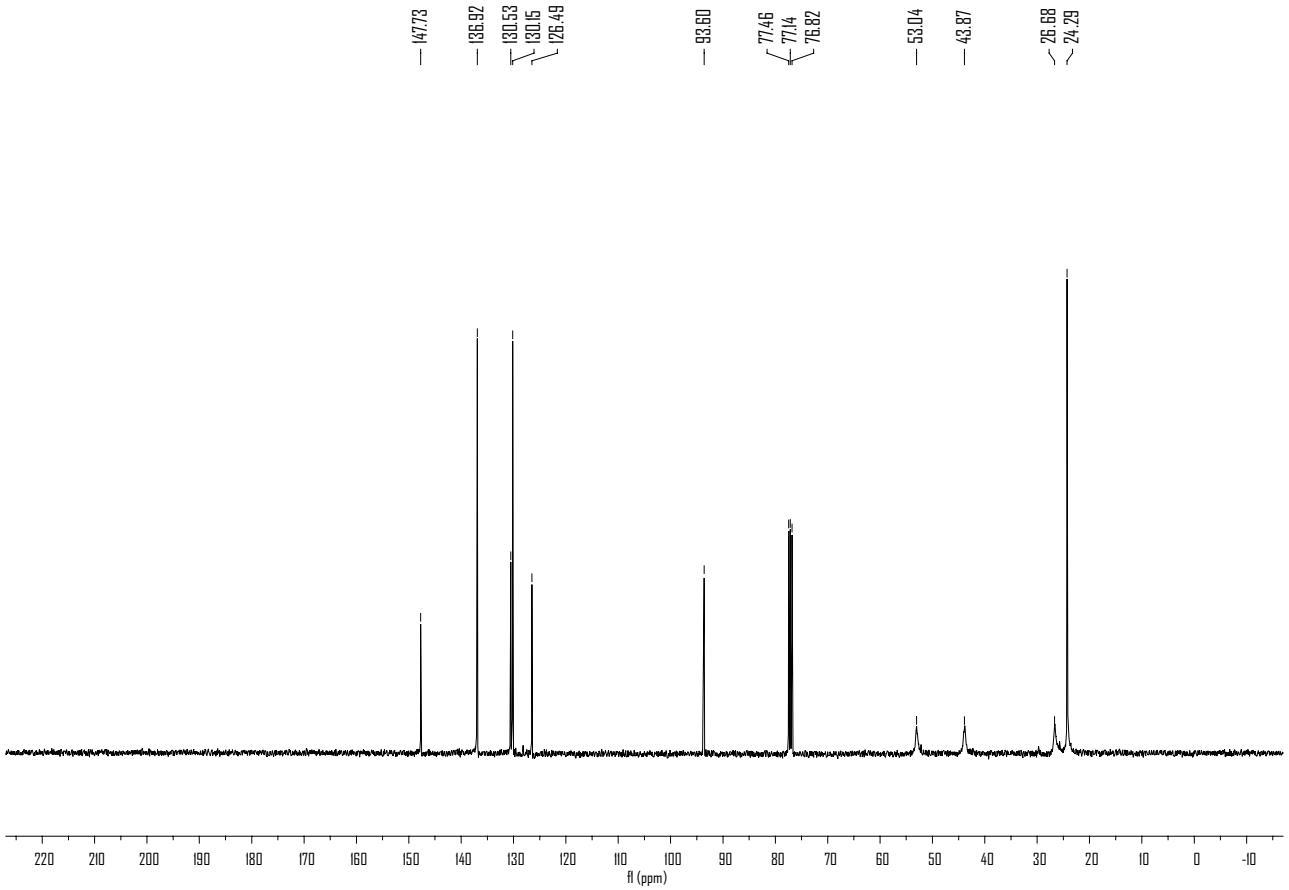
1-((5-Chloro-2-iodophenyl)diazenyl)piperidine (1bh).



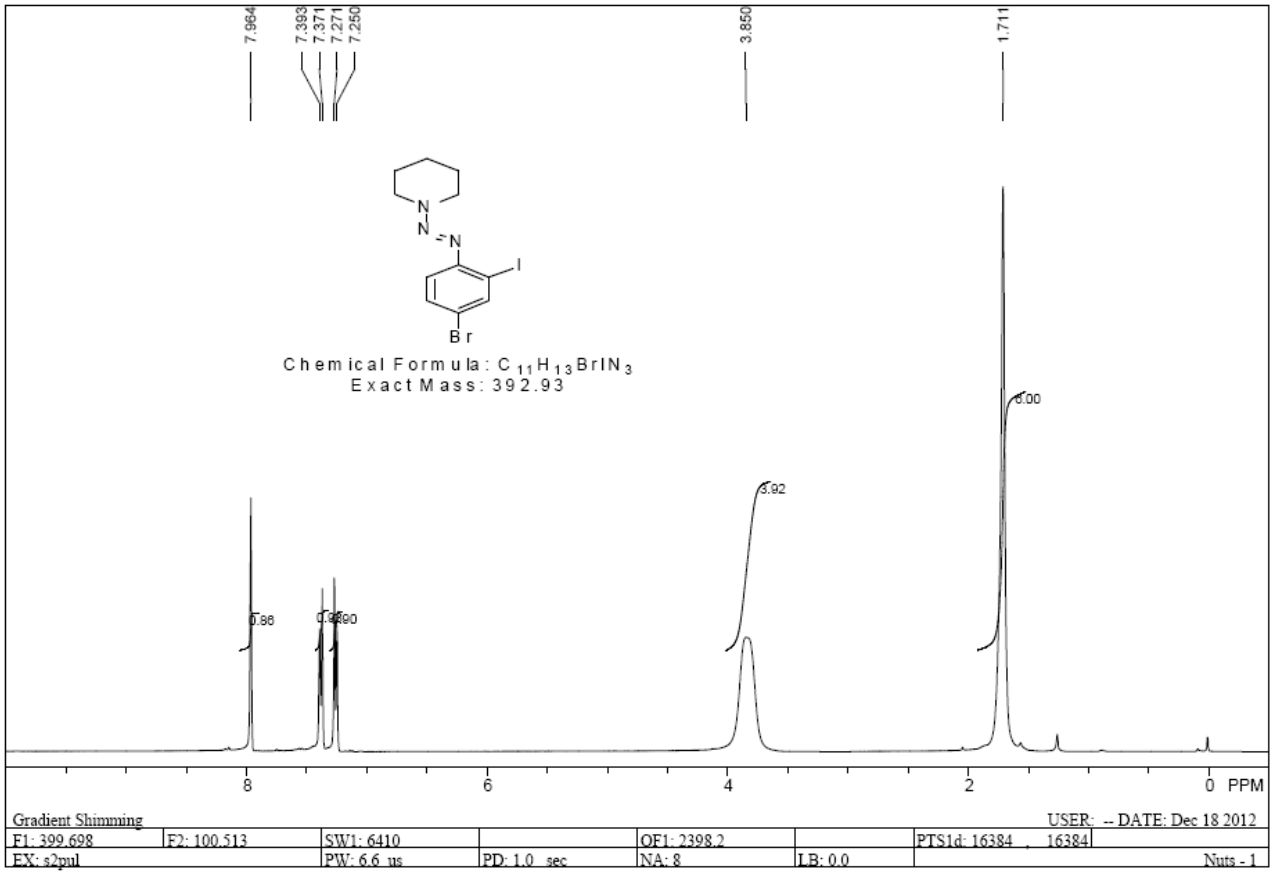


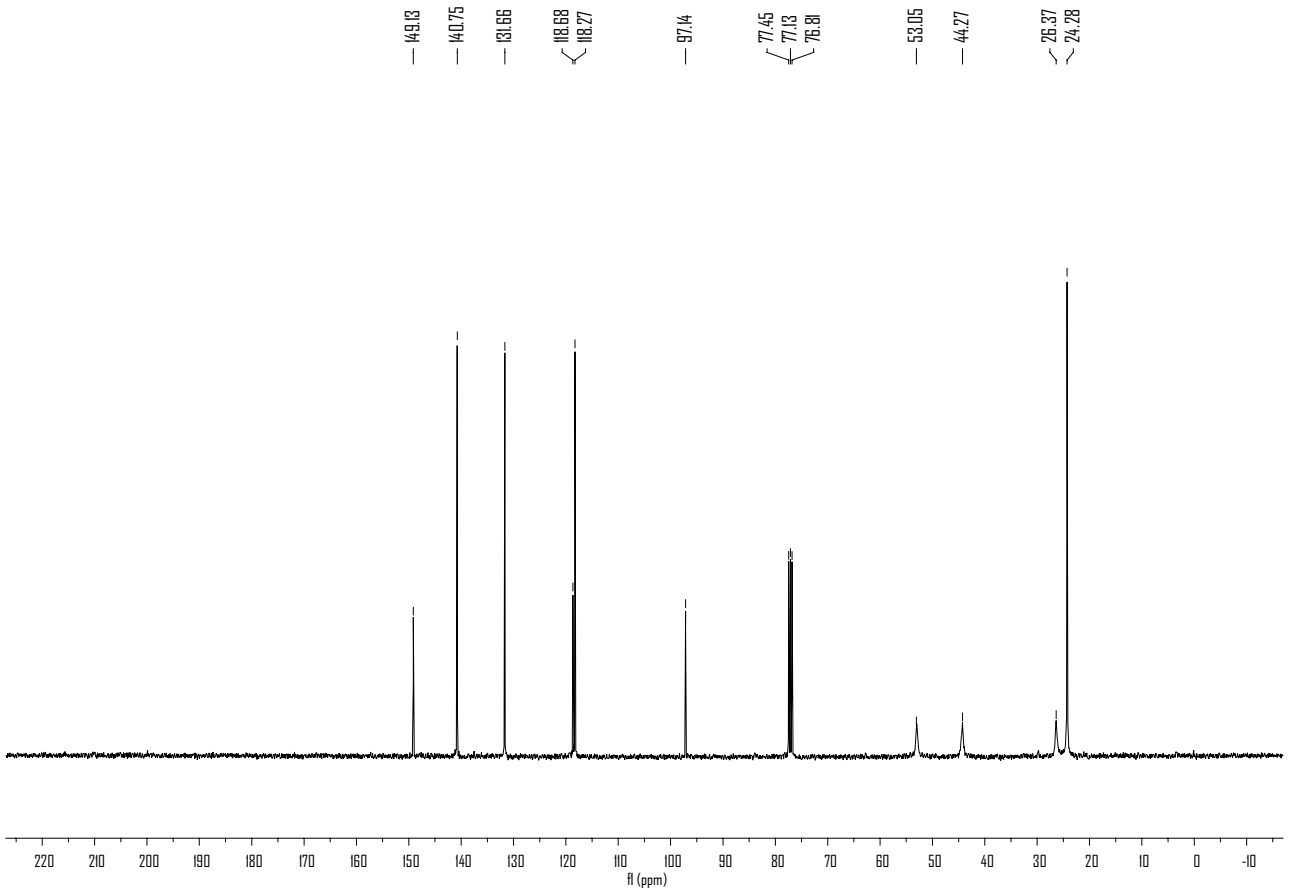
1-((2,4-Dichloro-6-iodophenyl)diazenyl)piperidine (1bi).





1-((4-Bromo-2-iodophenyl)diazenyl)piperidine (1bj).

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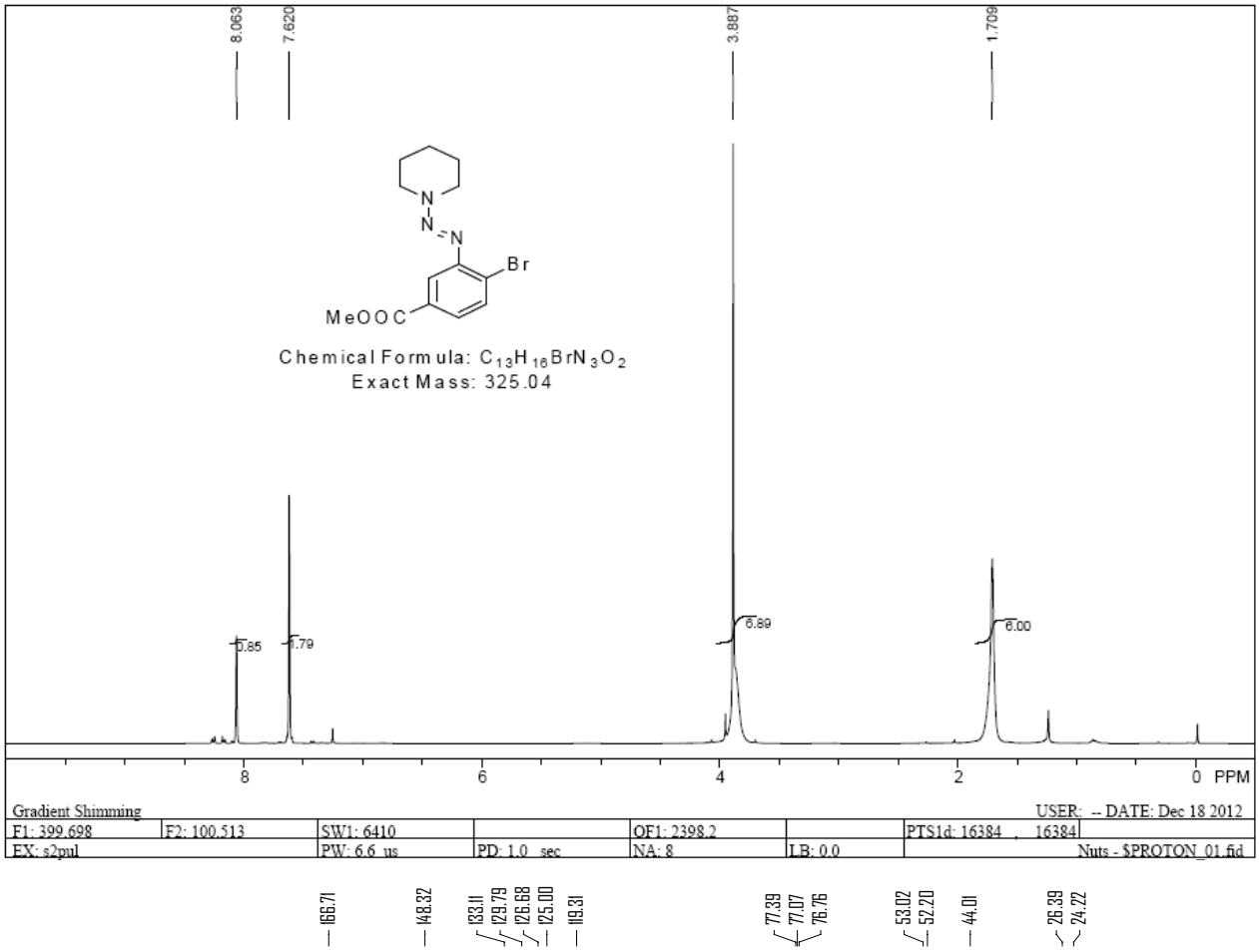
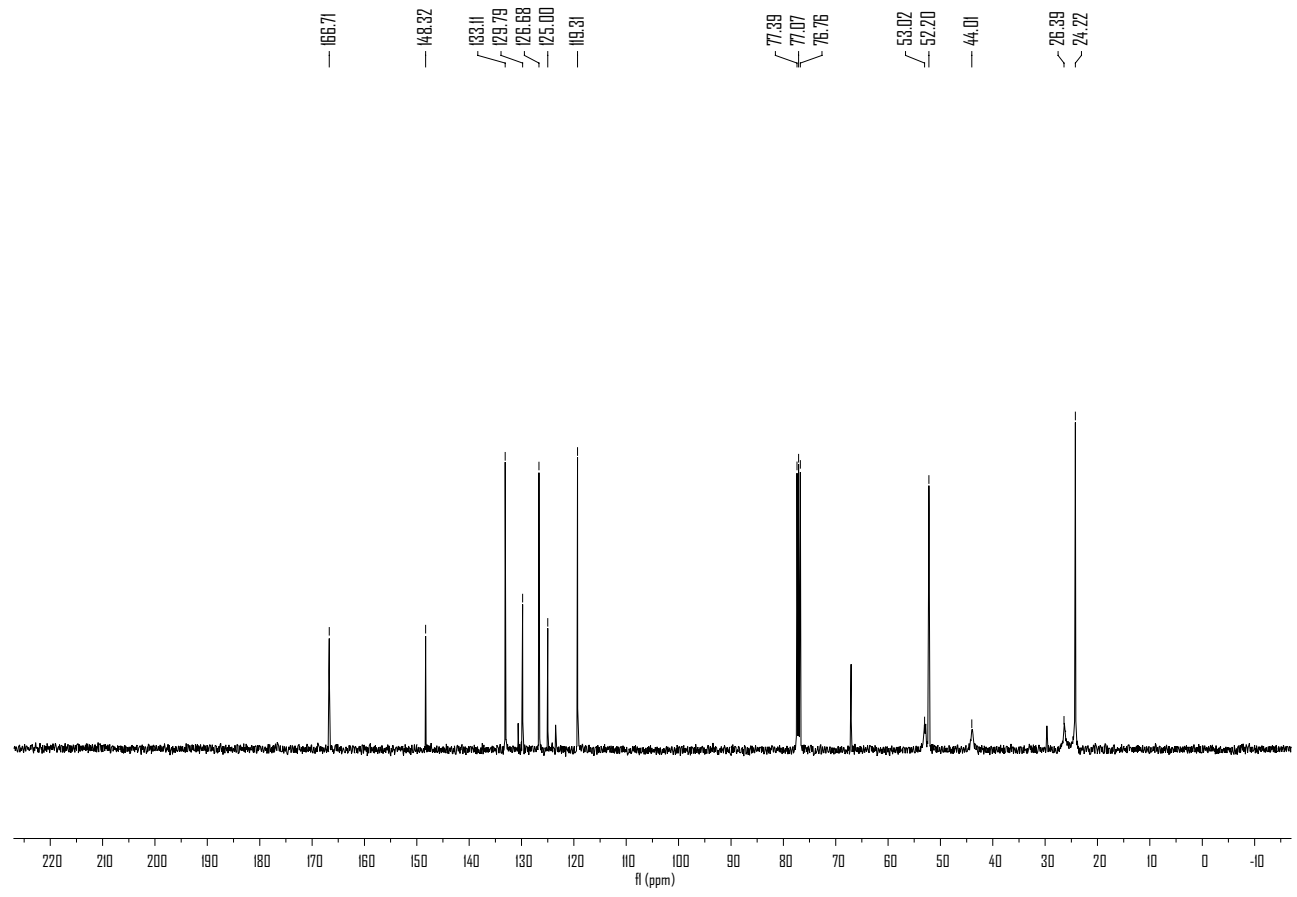
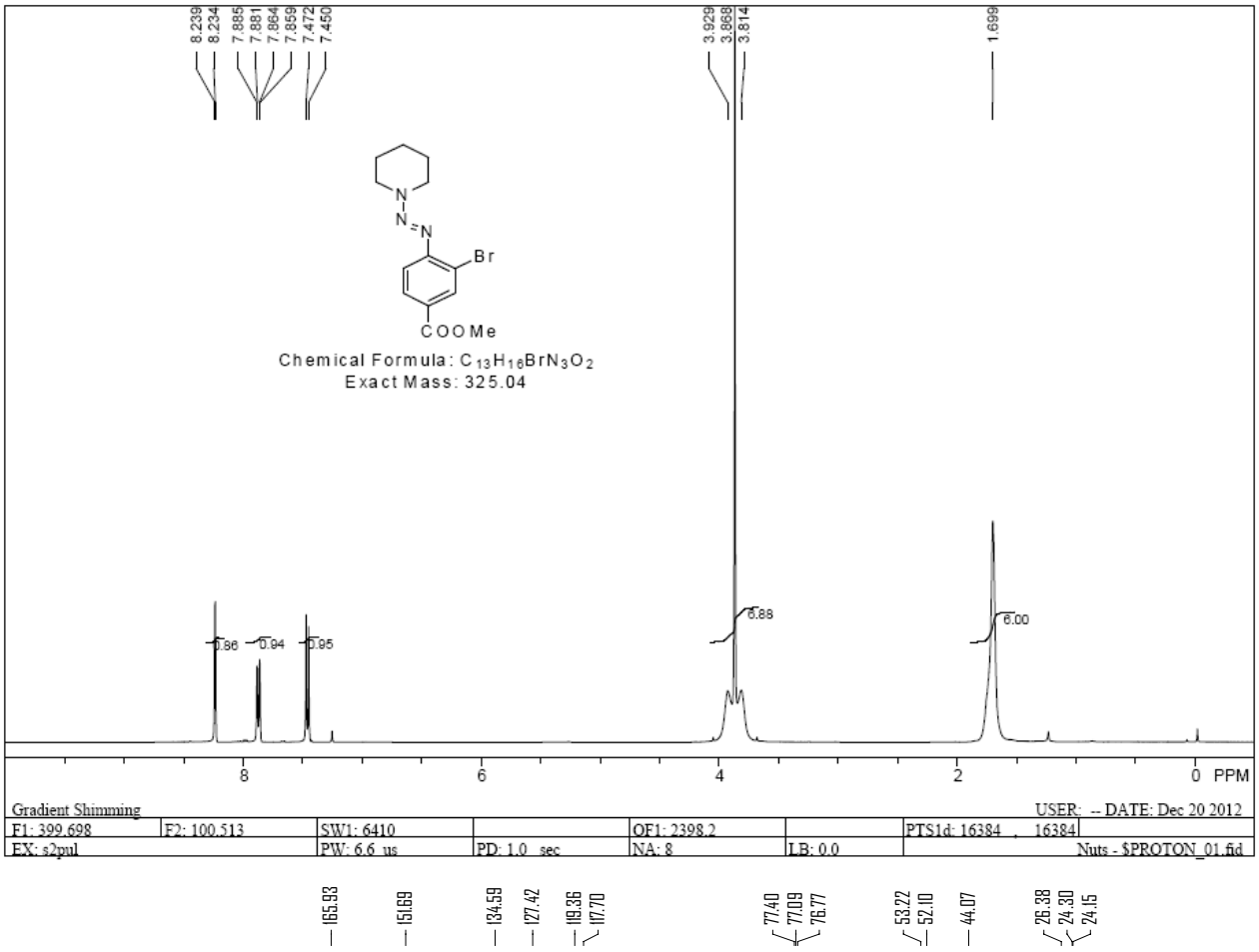
118.68
118.27
97.14
77.45
77.13
76.81
53.05
44.27
26.37
24.28
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

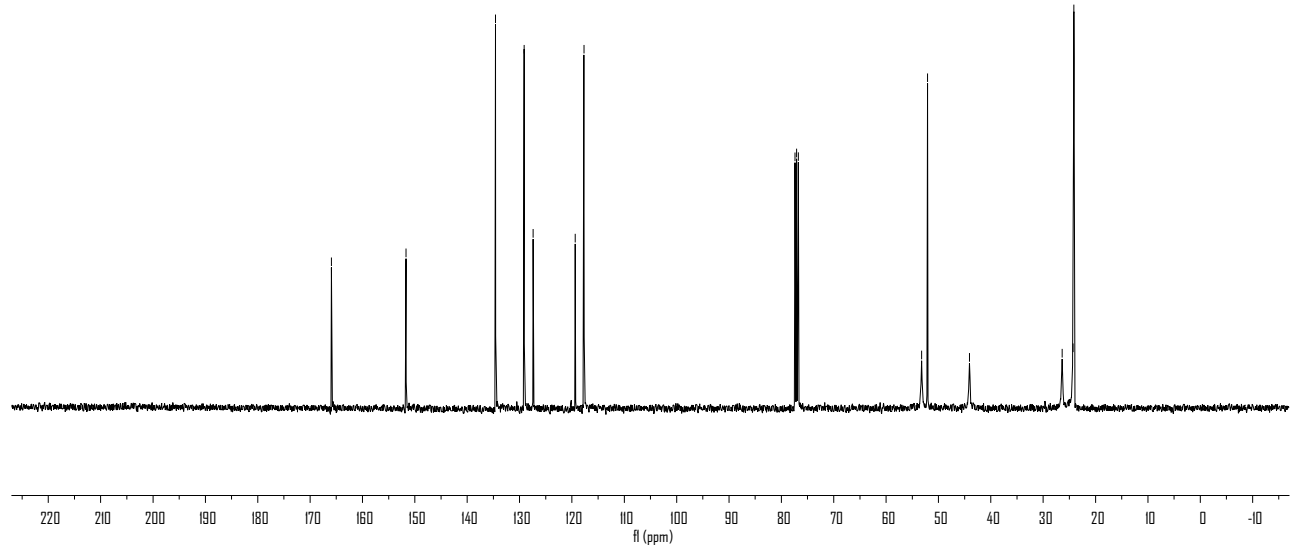
Methyl 4-bromo-3-(piperidin-1-yldiazenyl)benzoate (5b).



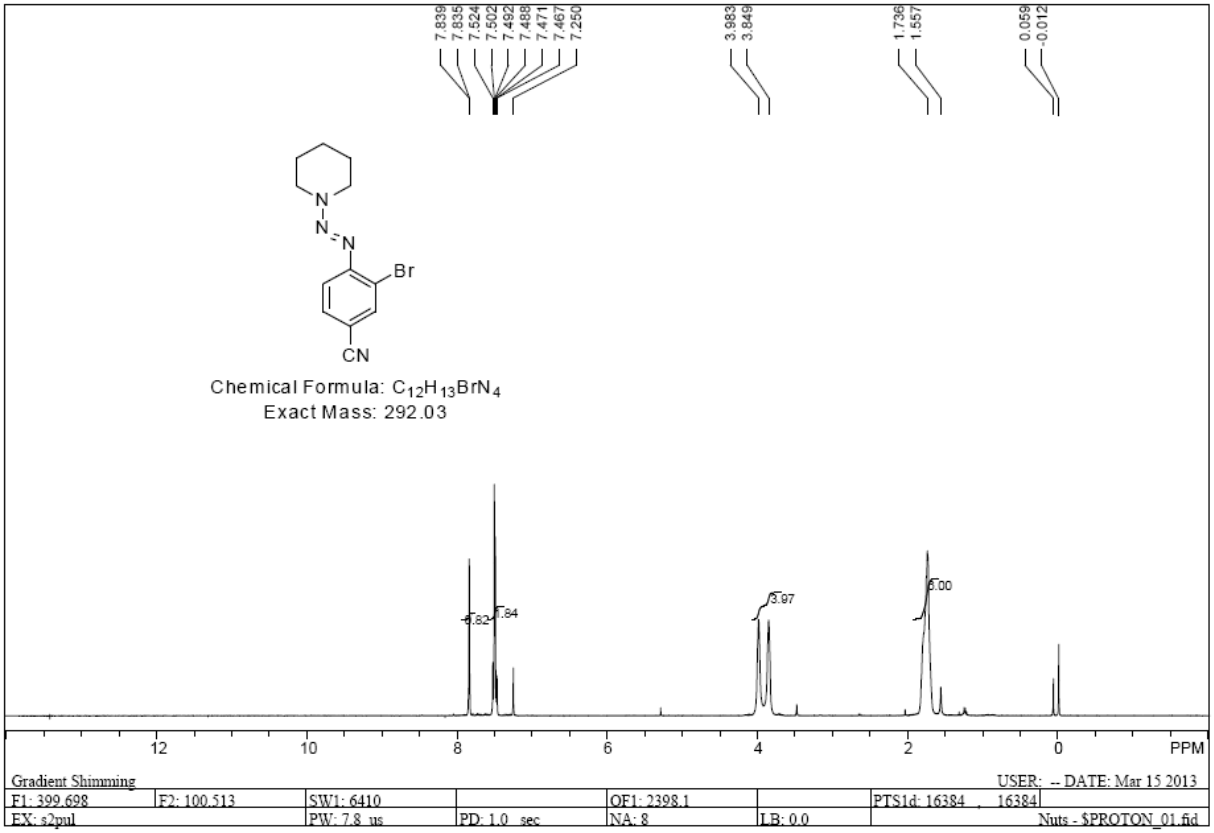


Methyl 3-bromo-4-(piperidin-1-yldiazenyl)benzoate (5c).

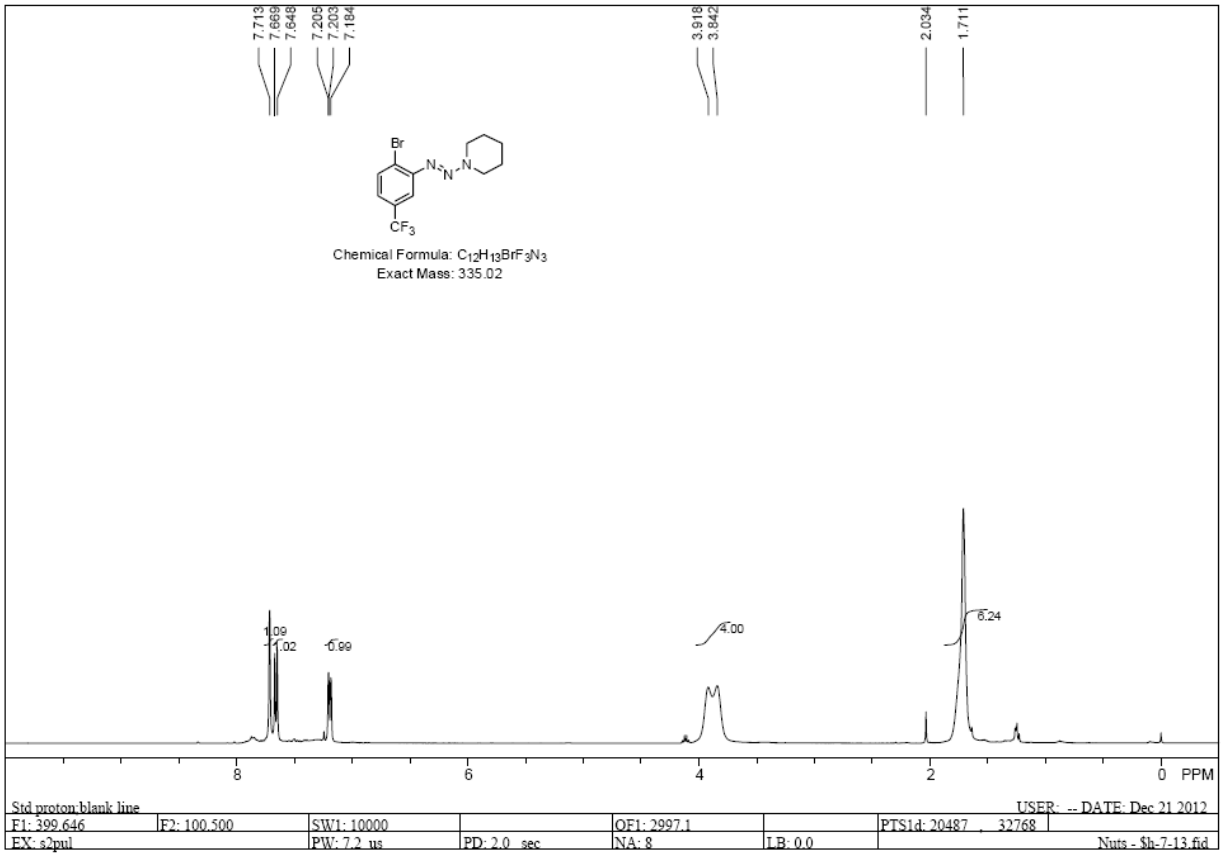


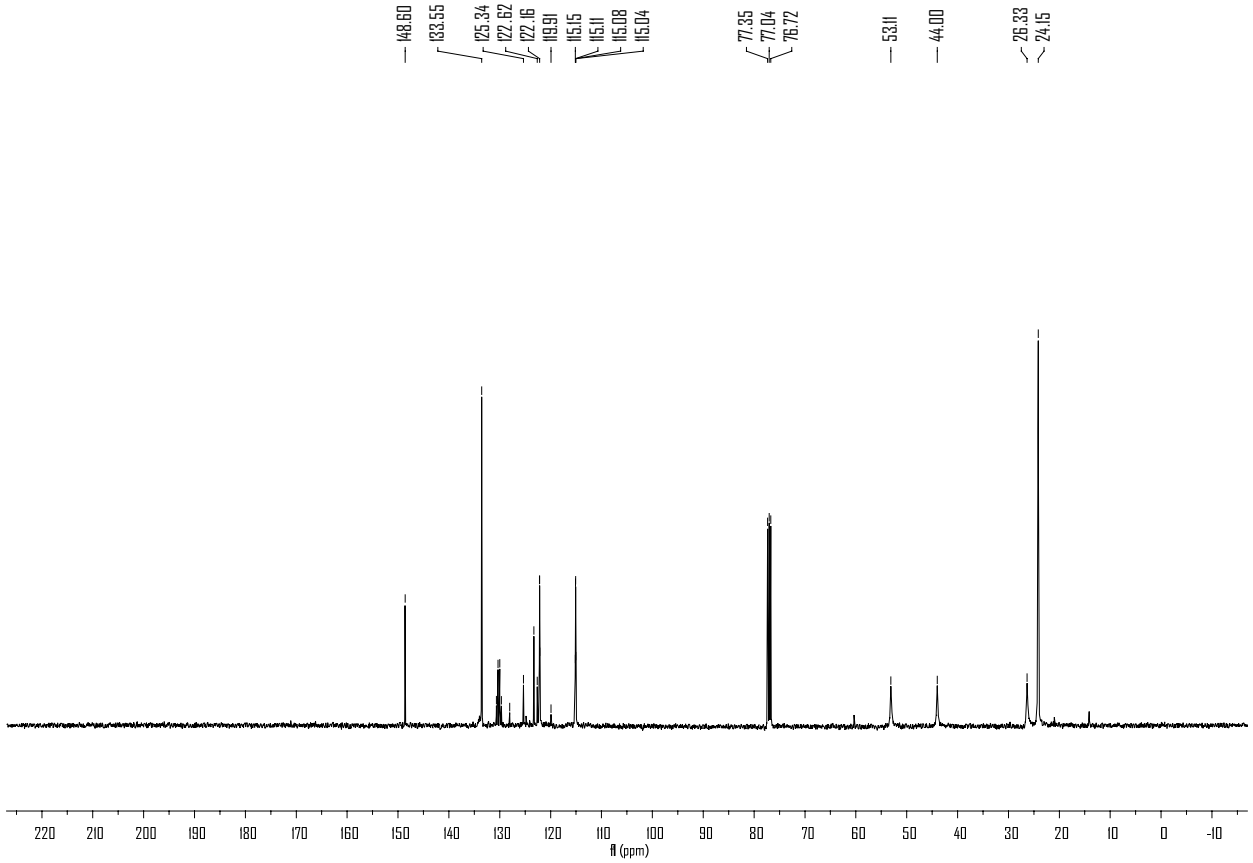


3-Bromo-4-(piperidin-1-yldiazenyl)benzonitrile (5d).



1-((2-Bromo-4-(trifluoromethyl)phenyl)diazenyl)piperidine (5e).

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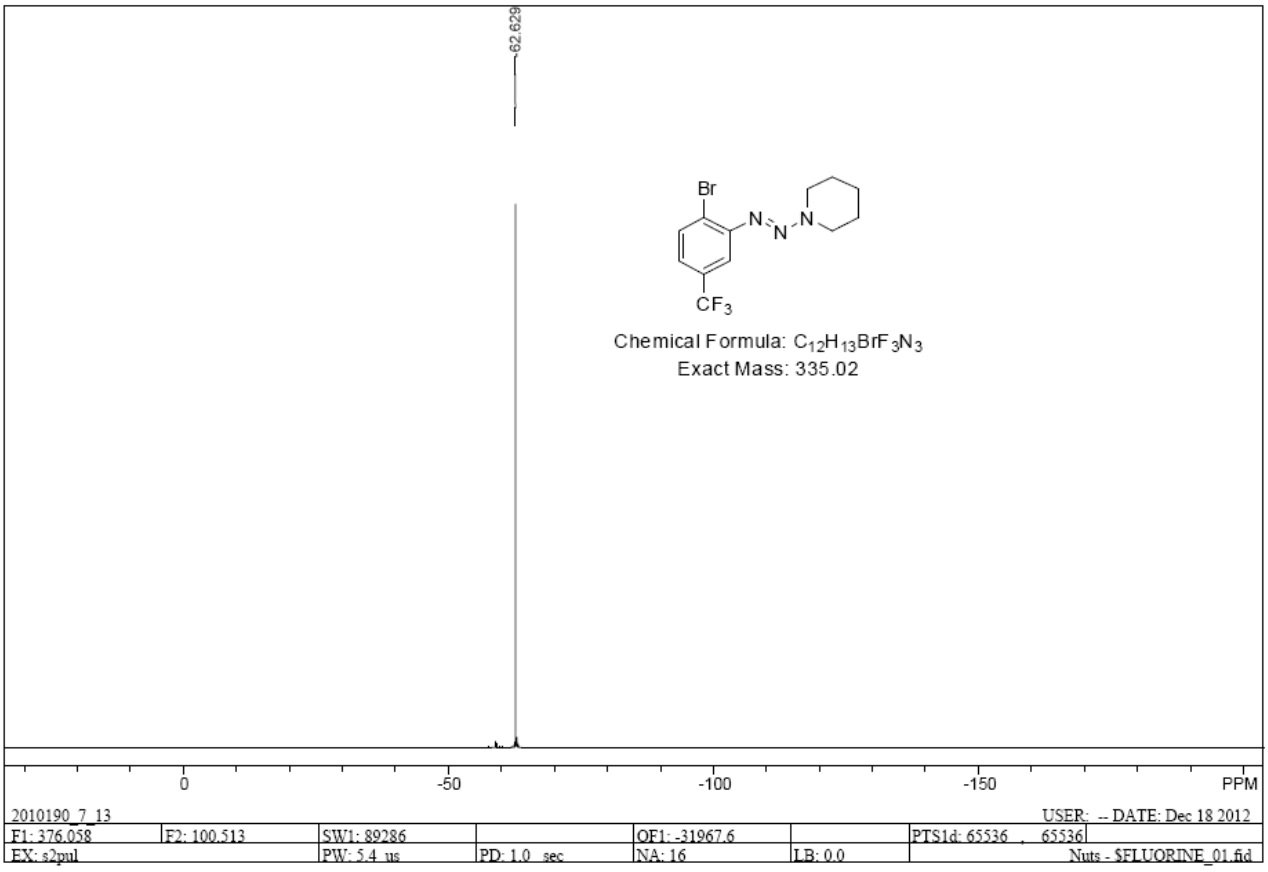
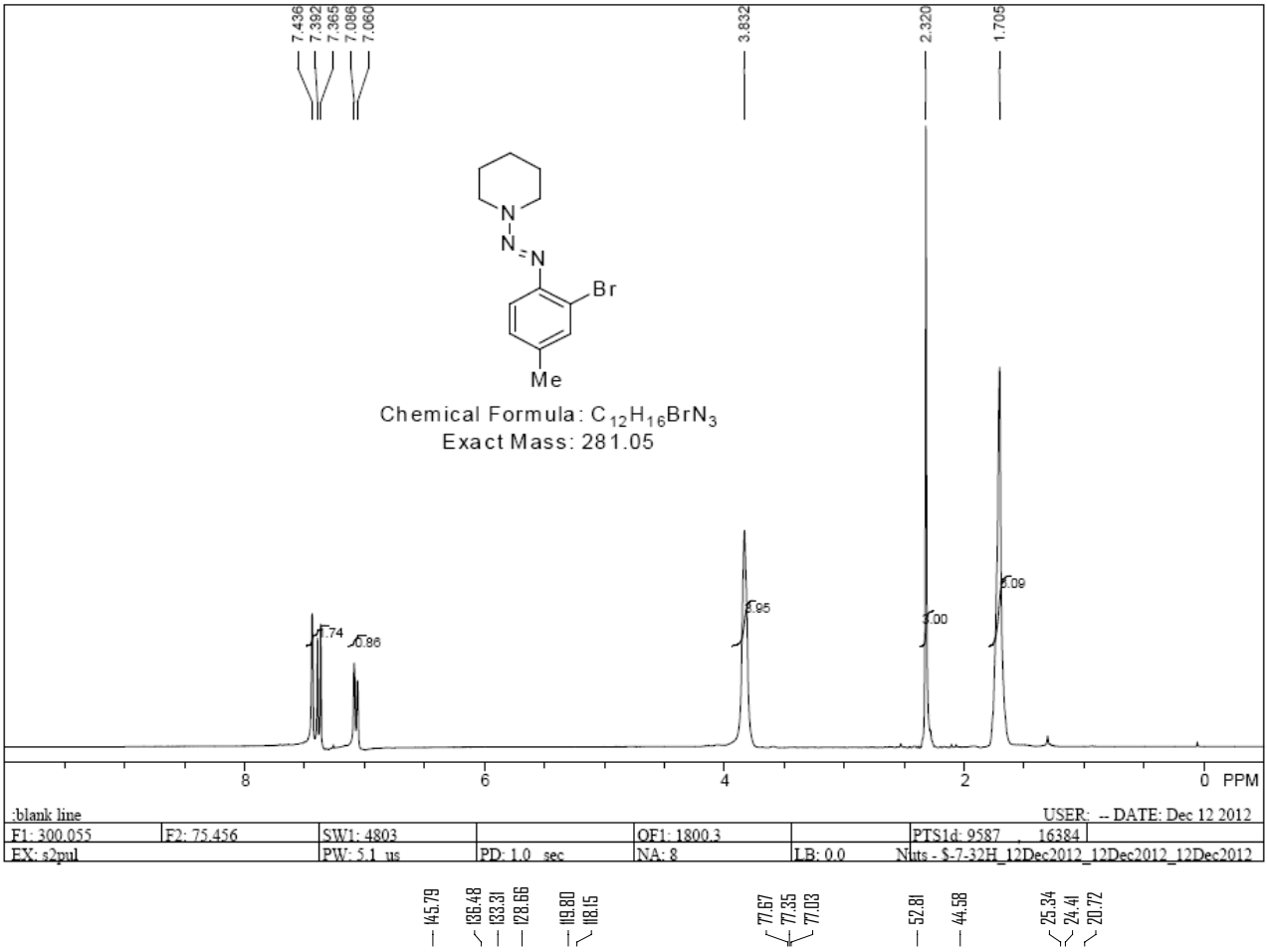
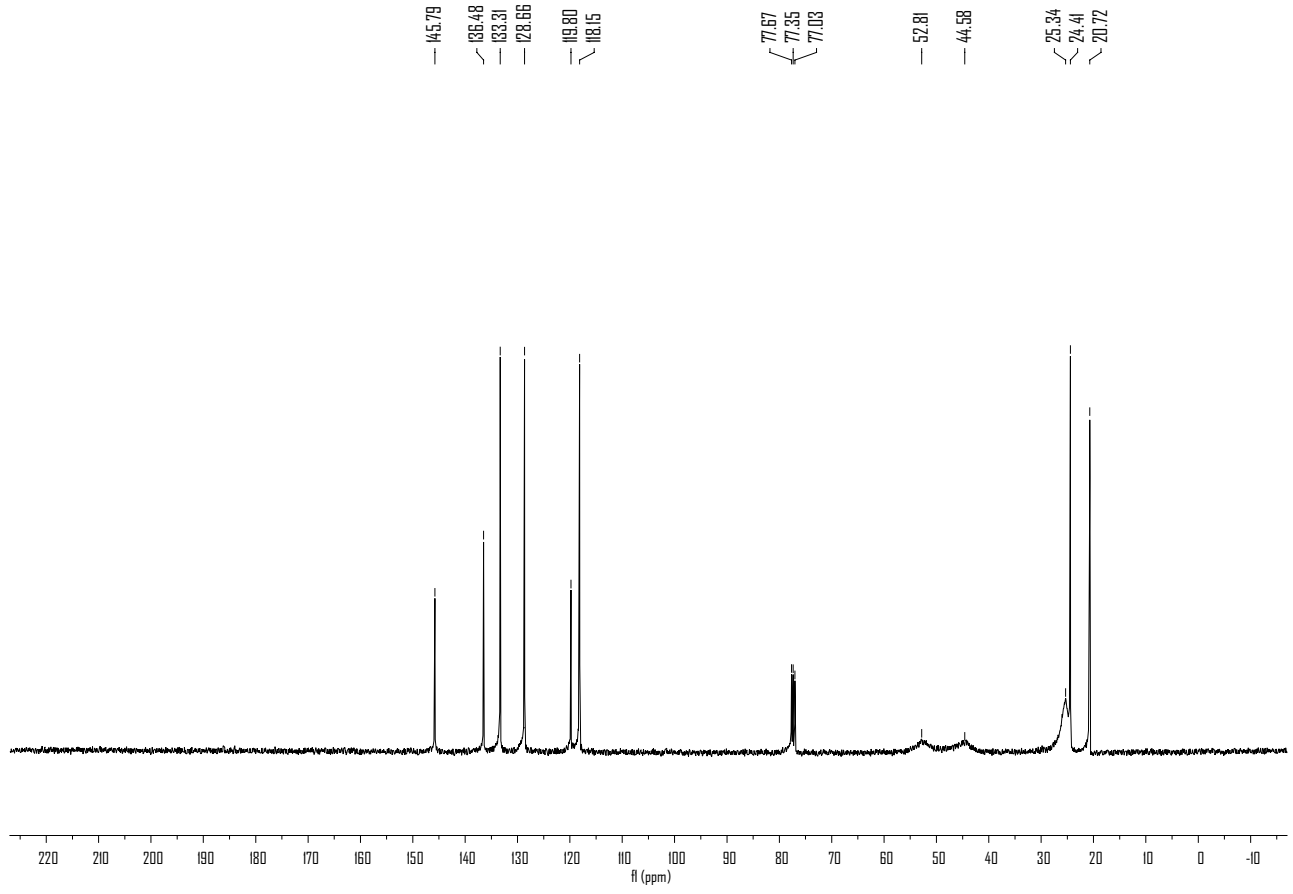
125.34
122.62
122.16
119.91
115.15
115.11
115.08
115.04
77.35
77.04
76.72
53.11
44.00
26.33
24.15
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

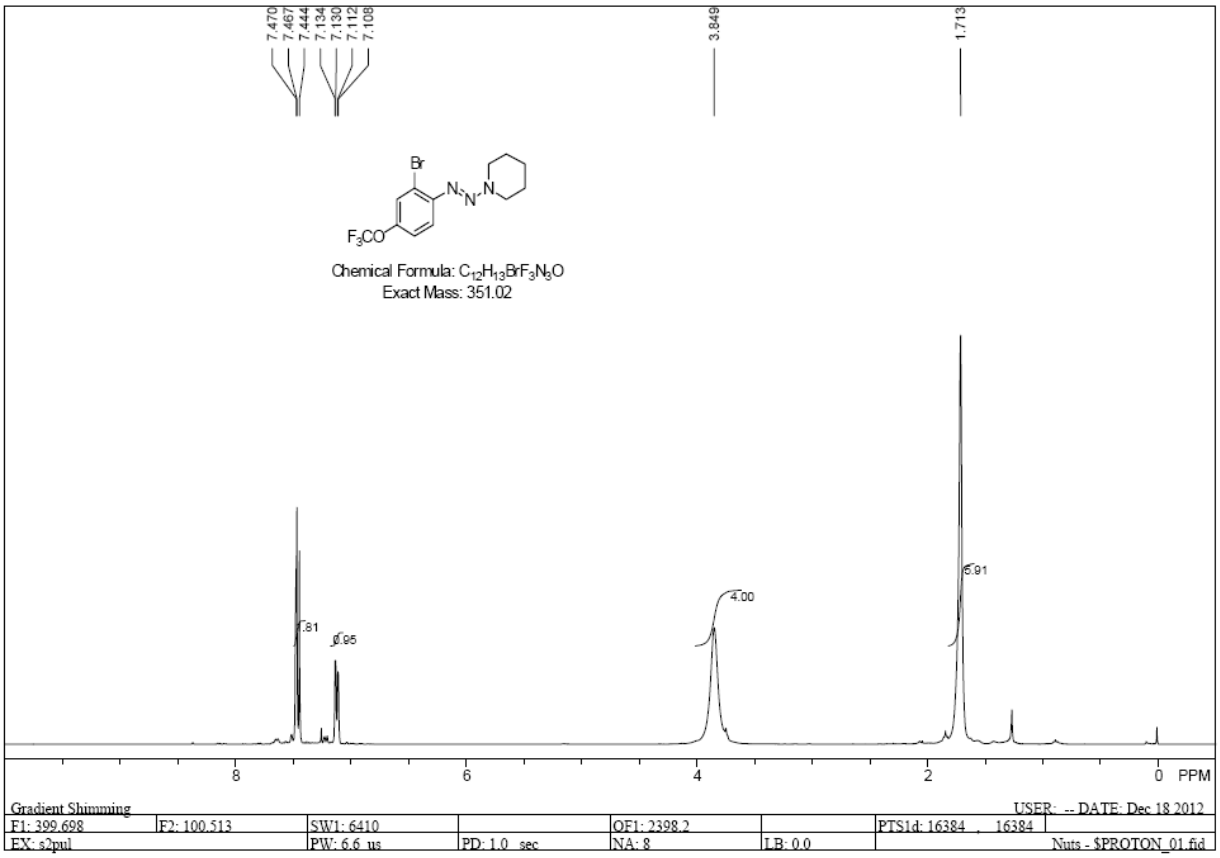

-62.629
Br
N
N
N
CF3
Chemical Formula: C12H13BrF3N3
Exact Mass: 335.02
0 -50 -100 -150 PPM
2010190_7_13
USER: -- DATE: Dec 18 2012
F1: 376.058
F2: 100.513
SW1: 89286
OF1: -31967.6
PTS1d: 65536 , 65536
EX: s2pul
PW: 5.4 us
PD: 1.0 sec
NA: 16
LB: 0.0
Nuts - $FLUORINE_01.fid

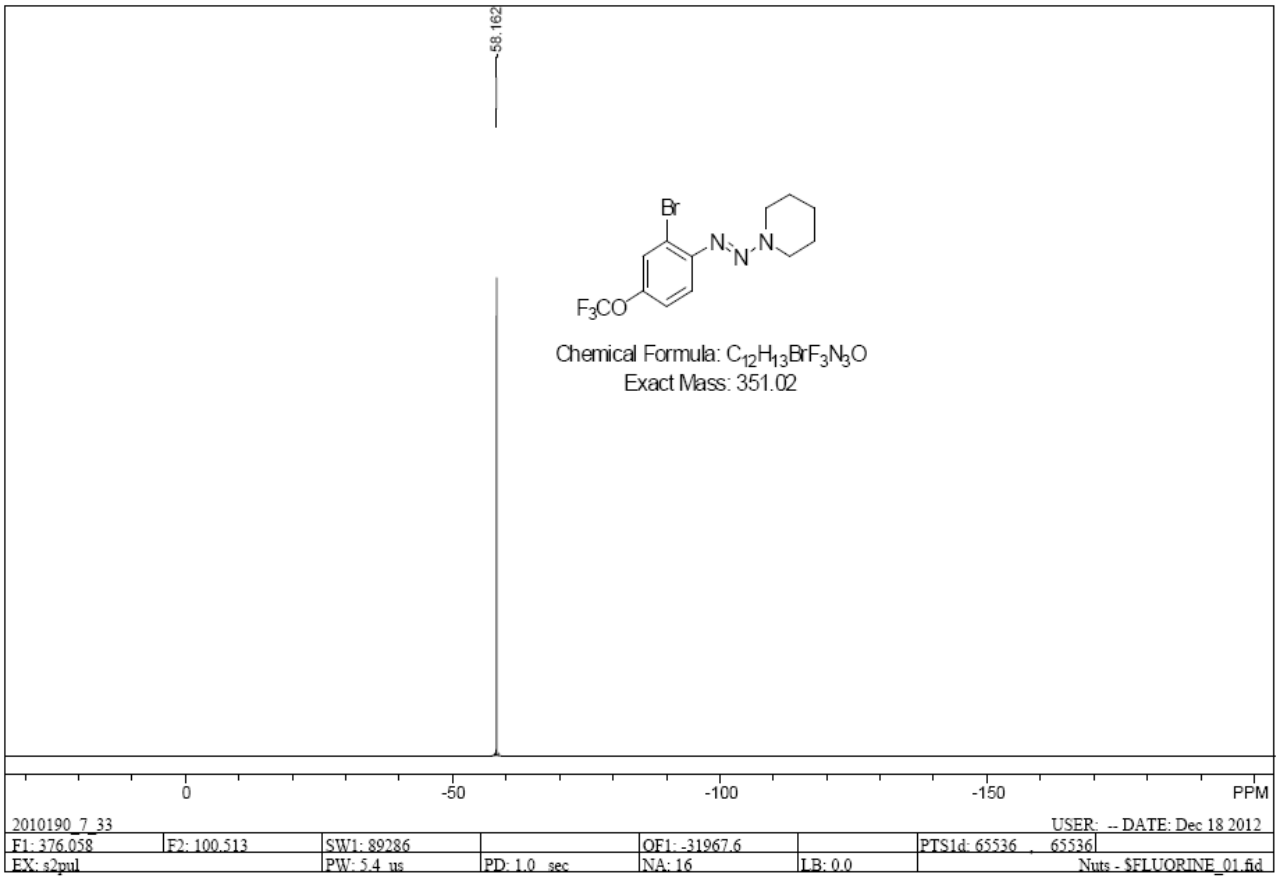
1-((2-Bromo-4-methylphenyl)diazenyl)piperidine (5f).

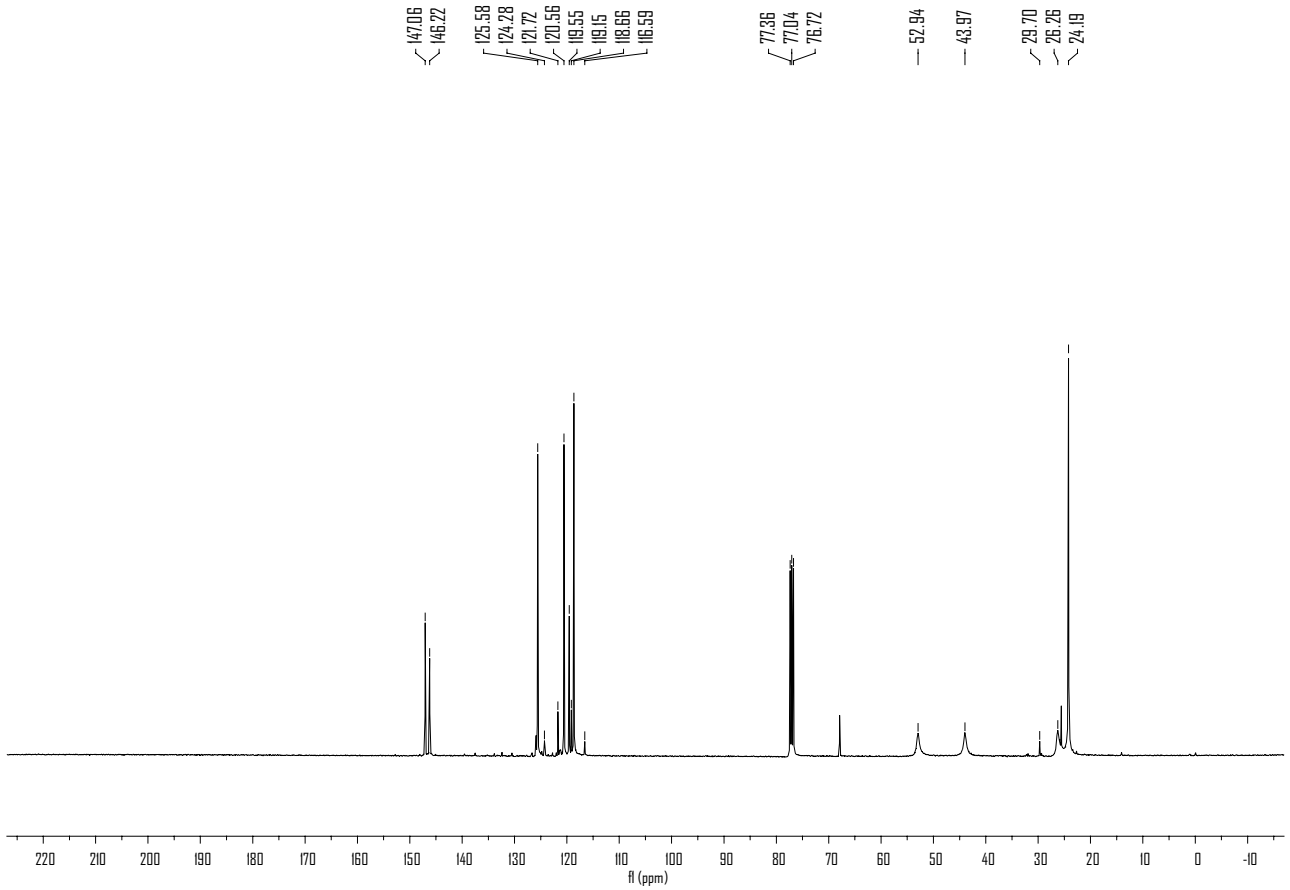




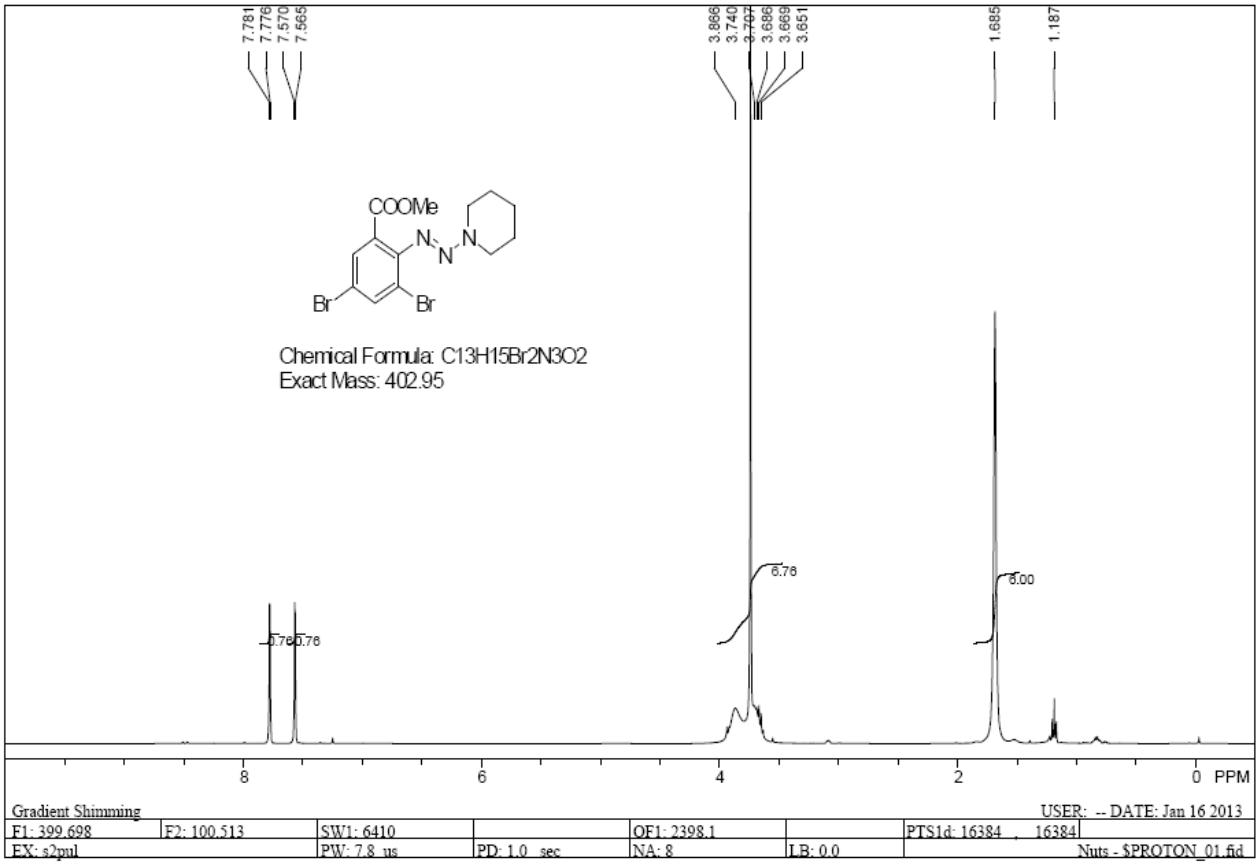
1-((2-Bromo-4-(trifluoromethoxy)phenyl)diazenyl)piperidine (5g).

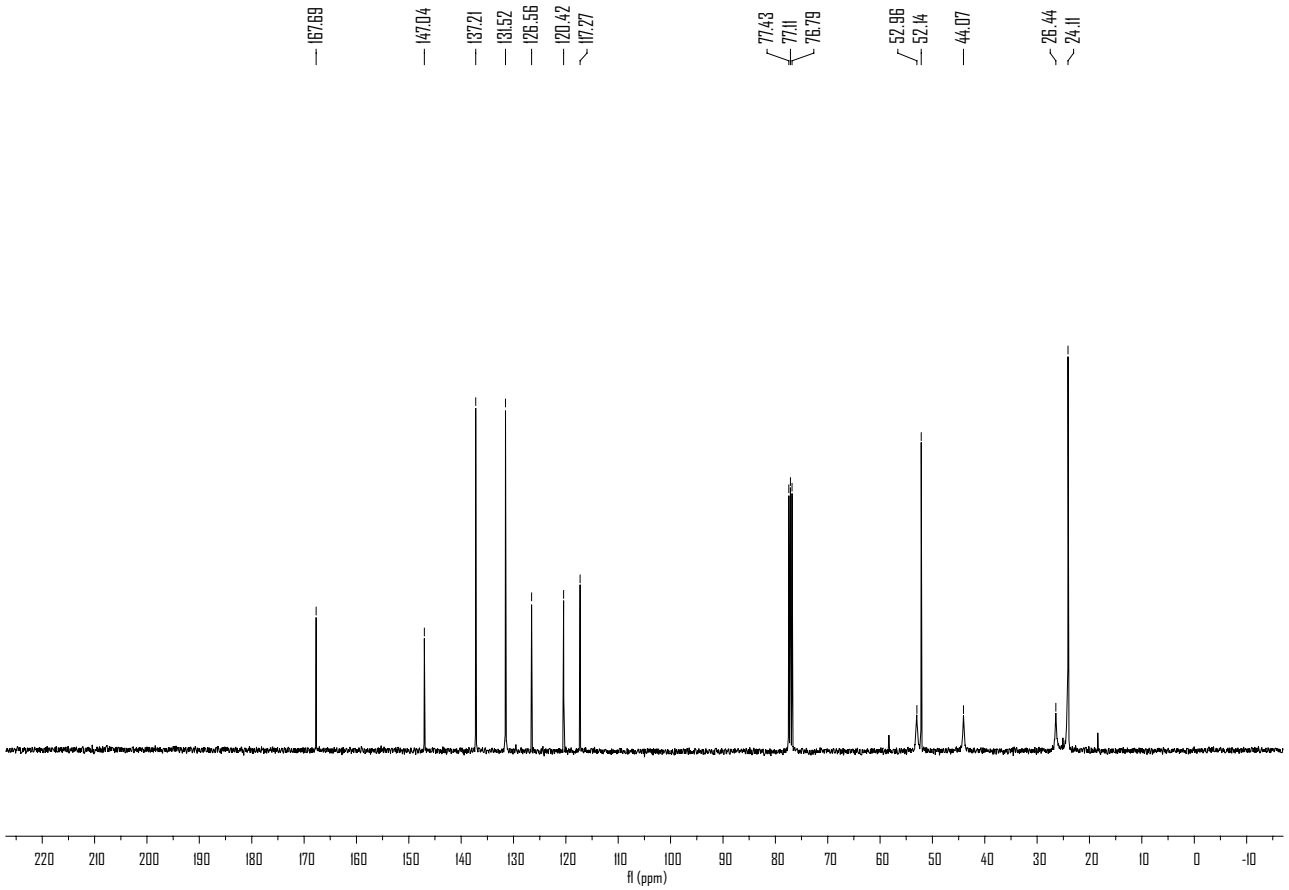






Methyl 3,5-dibromo-2-(piperidin-1-yldiazenyl)benzoate (5h).




167.69
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131.52
126.56
120.42
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77.43
77.11
76.79
52.96
52.14
44.07
26.44
24.11
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)