Supporting Information for

Synthesis of unsymmetrical biaryl ethers through nickel-promoted coupling of polyfluoroarenes with arylboronic acids and oxygen

Jian Zhang, Jingjing Wu, Yang Xiong, and Song Cao*

Shanghai Key Laboratory of Chemical Biology, School of Pharmacy, East China University of Science and Technology, Shanghai, 200237, China

All reagents were of analytical grade, and obtained from commercial suppliers and used without further purification. THF and dioxane were dried by standard method prior to use and degassed. The purity of purchased argon is 99.6%. Melting points were measured in an open capillary using Büchi melting point B-540 apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer (400 MHz and 100 MHz, respectively) using TMS as internal standard, The ^{19}F NMR spectra were obtained using a Bruker AM-400 spectrometer (376 MHz). $CDCl_3$ was used as the NMR solvent in all cases. Gas chromatography-mass spectra (GC-MS) were recorded on HP 5973 MSD with 6890 GC. High resolution mass spectra (HRMS) were recorded under electron impact conditions using a MicroMass GCT CA 055 instrument and recorded on a MicroMass LCTTM spectrometer.

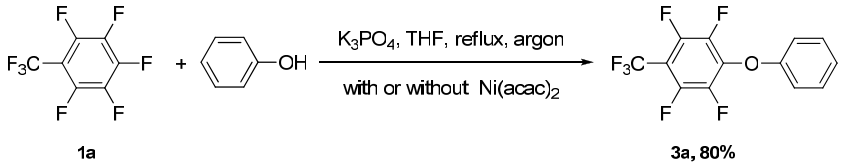
We have evaluated the influences of solvents and bases on the model reaction using the $Ni(acac)_2$ as the catalyst (**Table A**). The results revealed that K_3PO_4 and THF can be used as the most suitable base and solvent, respectively (entry 8). In the absence of a base, the reactivity was attenuated significantly and the starting materials were almost quantitatively recovered (entry 1).

Table A Effects of the solvents and bases on the reaction in an argon atmosphere using the $Ni(acac)_2$ as the catalyst

Entry	Base	Solvent	Yield of **3a** (%) [a]
1	None	THF	None [b]
2	Et_3N	THF	None [b]
3	K_2CO_3	Dioxane	47
4	K_2CO_3	THF	54
5	$CsCO_3$	Dioxane	25
6	$CsCO_3$	THF	40
7	CsF	THF	68
8	K_3PO_4	Toluene	50
9	K_3PO_4	Dioxane	92
10	K_3PO_4	THF	92

[a] Yield determined by GC analysis. [b] The starting materials were recovered.

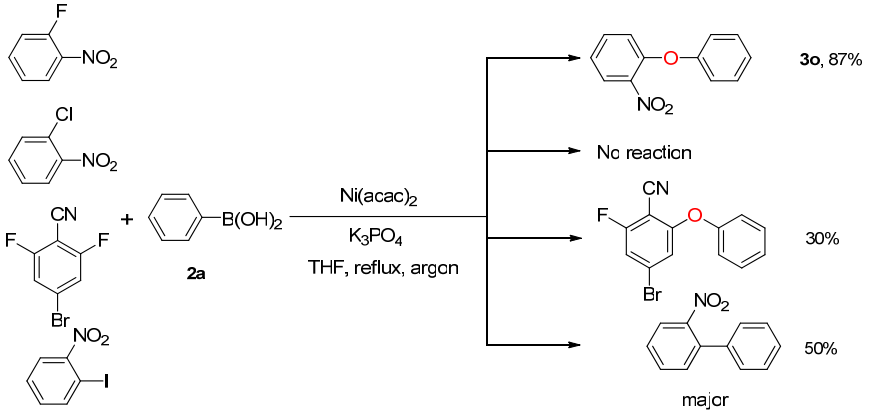
In order to elucidate details of this cross-coupling reaction, octafluorotoluene **1a** was allowed to react with 1 equiv phenol in THF under argon for 12 h at reflux temperature with or without $Ni(acac)_2$. It was found that this S_NAr reaction proceeded smoothly and afforded the biaryl ether **3a** in good yields (**Scheme A**). The results revealed that in the second step of cross-coupling reaction, the $Ni(acac)_2$ exhibited no apparent catalytic activity for S_NAr reaction.



1a 3a, 80%

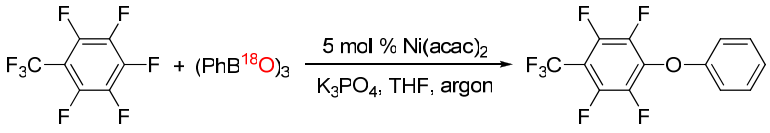
Scheme A S_NAr reactions of 1a with 1 equiv of phenol

For the purpose of comparison, the same reactions were also carried out by treating phenylboronic acid **2a** with 1-fluoro-2-nitrobenzene, 1-chloro-2-nitrobenzene, 4-bromo-2,6-difluorobenzonitrile and 1-iodo-2-nitrobenzene, respectively (**Scheme B**). It was found that the reactivity of fluorine is much higher than those of chlorine, bromine and iodide, where only fluoro-containing benzenes gave the oxygen insertion products. These results demonstrated that the highly electron-deficient fluorinated aromatic compounds could be used as efficient trapping agents of phenoxide intermediate.



Scheme B Reaction of aryl halides with phenylboronic acid in the presence of Ni(acac)$_2$.

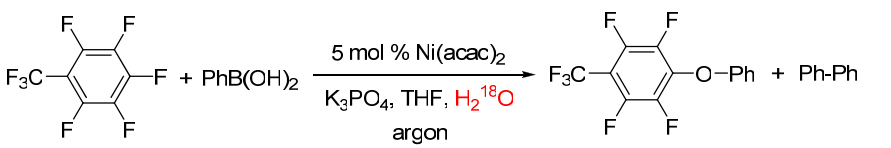
We also made our efforts to elucidate the source of oxygen in the biaryl ether and phenol. Firstly, ^{18}O-labeled phenylboronic acid was synthesized by the reaction of potassium benzyltrifluoroborate with $H_2{}^{18}O$ for the first time.[14] But no isotope was incorporated into the biaryl ether when ^{18}O-labeled phenyl boroxine was treated with octafluorotoluene **1a** and the normal biaryl ether was obtained in good yield (90%) (**Scheme C**). It is proved that the oxygen atom of **3a** did not derive from phenylboronic acid.



1a 3a

Scheme C Reaction of 1a with ^{18}O-labeled phenyl boroxine

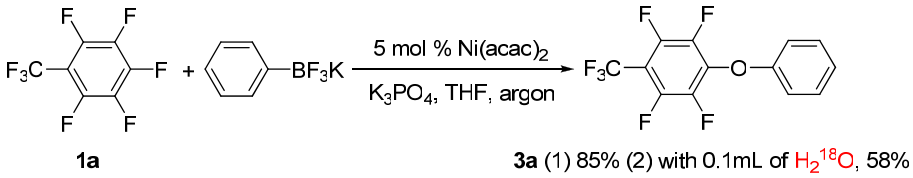
We carried out the Ni-catalyzed reaction of **1a** with phenylboronic acid **2a** in the presence of 0.1mL of ^{18}O water, but unfortunately no isotope incorporation was observed and the yield of homocoupling product **4a** increased. It is suggested that the oxygen atom of **3a** did not derive from water (**Scheme D**).



1a 2a 3a, 43% 4a, 56%

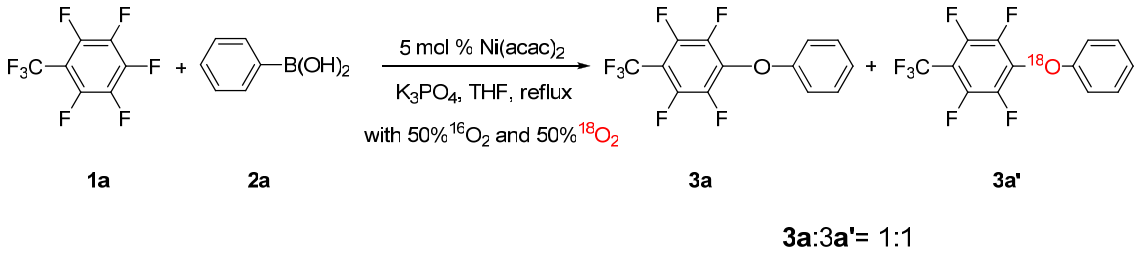
Scheme D Reaction of 1a with 2a in the presence of $H_2{}^{18}O$

In order to further clarify the origin of oxygen in ether and intermediate phenol, two additional experiments were performed. First, we replaced phenylboronic acid **2a** with potassium benzyltrifluoroborate to undergo this reaction under the same reaction conditions. As expected, the same biaryl ether was obtained in good yield (**3a**, 85%) (**Scheme E**). When the reaction was carried out by the addition of 0.1mL of $H_2{}^{18}O$, the reaction did not proceed smoothly and afforded the biaryl ether in lower yield (**3a**, 58%). These results further proved that the oxygen atom of biaryl ether and phenol originated neither from water nor from phenylboronic acid.



Scheme E Reaction of octafluorotoluene 1a with potassium benzyltrifluoroborate

According to the suggestion of reviewer, we performed an additional experiment. We carried out the reaction in the presence of the mixture of 50% $^{16}O_2$ and 50% $^{18}O_2$. The result indicated that both ^{16}O atom and ^{18}O atom are incorporated into the biaryl ethers and the ratio of ^{16}O and ^{18}O biaryl ether products is nearly 1: 1, which is the same as the expected ratio.



Scheme F The reaction of 1a with 2a with the mixture of 50% $^{16}O_2$ and 50% $^{18}O_2$

Reference (Full version)

1 (a) F. González-Bobes, G. C. Fu, *J. Am. Chem. Soc.* 2006, **128**, 5360; (b) F. Alonso, I. P. Beletskaya, M. Yus, *Tetrahedron* 2008, **64**, 3047; (c) I. B. Seiple, S. Su, R. A. Rodriguez, R. Gianatassio, Y. Fujiwara, A. L. Sobel, P. S. Baran, *J. Am. Chem. Soc.* 2010, **132**, 13194.

2 (a) L. Xu, B. J. Li, Z.-H. Wu, X.-Y. Lu, B.-T. Guan, B. Wang, K.-Q. Zhao, Z.-J. Shi, *Org. Lett.* 2010, **12**, 884; (b) Z.-Y. Tang, Q.-S. Hu, *J. Am. Chem. Soc.* 2004, **126**, 3058.

3 M. Moreno-Mañas, M. Pérez, R. Pleixats, *J. Org. Chem.* 1996, **61**, 2346.

4 (a) Y. Yamamoto, R. Suzuki, K. Hattori, H. Nishiyama, *Synlett* 2006, 1027; (b) A. Prastaro, P. Ceci, E. Chiancone, A. Boffi, G. Fabrizi, S. Cacchi, *Tetrahedron Letters* 2010, **51**, 2550; (c) J. Simon, S. Salzbrunn, G. K. S. Prakash, N. A. Petasis, G. A. Olah, *J. Org. Chem.* 2001, **66,** 633; (d) A. D. Chowdhury, S. M. Mobin, S. Mukherjee, S. Bhaduri, G. K. Lahiri, *Eur. J. Inorg. Chem.* 2011, 3232; (e) J. Xu, X. Wang, C. Shao, D. Su, G. Cheng, Y. Hu, *Org. Lett.*, 2010, **12**, 1964.

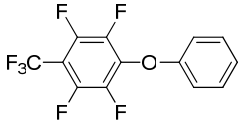
5 (a) A. D. Sagar, R. H. Tale, R. N. Adude, *Tetrahedron Letters* 2003, **44**, 7061; (b) F. Theil, *Angew. Chem. Int. Ed.* 1999, **38**, 2345; (c) D. M. T. Chan, K. L. Monaco, R.-P. Wang, M. P. Winters, *Tetrahedron Letters* 1998, **39**, 2933; (d) D. A. Evans, J. L. Katz, T. R. West, *Tetrahedron Letters* 1998, **39**, 2937; (e) S. Wacharasindhu, S. Bardhan, Z.-K. Wan, K. Tabei, T. S. Mansour, *J. Am. Chem. Soc.* 2009, **131**, 4174; (f) X. Zheng, J. Ding, J. Chen, W. Gao, M. Liu, H. Wu, *Org. Lett.*, 2011, **13**, 1726; (g) W. Wu, J. Xu, S. Huang, W. Su, *Chem. Commun.*, 2011, **47**, 9660; (h) G. Mann, C. Incarvito, A. L. Rheingold, J. F. Hartwig, *J. Am. Chem. Soc.* 1999, **121**, 3224; (g) X. Liu, S. Zhang,

Synlett 2011, 268.
6 (a) J. Liu and M. J. Robins, *Org. Lett.* 2004, **6**, 3421; (b) J. Liu and M. J. Robins, *Org. Lett.* 2005, **7**, 1149.
7 (a) L. H. Jones, A. Randall, O. Barba, M. D. Selby, *Org. Biomol. Chem.* 2007, **5**, 3431, (b) H. Behniafar, M. Sedaghatdoost, *J. Fluorine Chem.* 2011, **132**, 276.
8 H. Amii, K. Uneyama, Chem. Rev. 2009, **109**, 2119.
9 (a) E. Clot, O. Eisenstein, N. Jasim, S. A. Macgregor, J. E. Mcgrady, R. N. Perutz, *Acc. Chem. Res.* 2011, **44**, 333; (b) A. Steffen, M. I. Sladek, T. Braun, B. Neumann, H.-G. Stammler, *Organometallics* 2005**, 24,** 4057; (c) R. P. Hughes, *Eur. J. Inorg. Chem.* 2009, 4591.
10 (a) N. Yoshikai, H. Matsuda, E. Nakamura, *J. Am. Chem. Soc.* 2009, **131**, 9590; (b) D. A. Widdowson, R. Wilhelm, *Chem. Commun.* 2003, 578; (c) N. Yoshikai, H. Mashima, E. Nakamura, *J. Am. Chem. Soc.* 2005, **127**, 17978; (d) C. Wechsler, A. R. Kapdi, A. Althammer, *Synlett*, 2010, 0294–0298; (e) M. Tobisu, T. Xu, T. Shimasaki, N. Chatani, *J. Am. Chem. Soc.* 2011, **133**, 19505; (f) A. D. Sun, J. A. Love, Dalton Trans., 2010, **39**, 10362.
11 T. Schaub, M. Backes, U. Radius, *J. Am. Chem. Soc.* 2006, **128**, 15964.
12 (a) C. Adamo, C. Amatore, I. Ciofini, A. Jutand, H. Lakmini, *J. Am. Chem. Soc.* 2006, **128**, 6829; (b) K. S. Yoo, C. H. Yoon, K. W. Jung, *J. Am. Chem. Soc.* 2006, **128**, 16384; (c) A. C. Negrete-Raymond, B. Weder, L. P. Wackett, *Appl. Environ. Microbiol.*, 2003, 4263; (d) K. Hosoi, Y. Kuriyama, S. Inagi, T. Fuchigami, *Chem. Commun.*, 2010, **46**, 1284; (e) P. Y. S. Lam, D. Bonne, G. Vincent, C. G. Clark, A. P. Combs, *Tetrahedron Letters* 2003, **44**, 1691; (f) Y. Q. Zou, J. R. Chen, X. P. Liu, L. Q. Lu, R. L. Davis, K. A. Jørgensen, W. J. Xiao, *Angew. Chem. Int. Ed.* 2012, **51**, 784; (g) E. Kianmehr, M. Yahyaee, K. Tabatabai, *Tetrahedron Letters* 2007, **48**, 2713.
13 (a) M. Suzuki, *Acc. Chem. Res.* 2007, **40**, 609; (b) M. T. Kieber-Emmons, C. G. Riordan, *Acc. Chem. Res.* 2007, **40**, 618; (c) S. Otsuka, A. Nakamura, Y. Tatsuno, *J. Am. Chem. Soc.*1969, 6994; (e) S. Yao, E. Bill, C. Milsmann, K. Wieghardt, M. Driess, *Angew. Chem. Int. Ed.* 2008, **47**, 7110; (f) J. Zapata-Rivera, R. Caballol, C. J. Calzado, *J. Comput. Chem.* 2012, **33**, 1407.

General procedure for the preparation of 3a – p

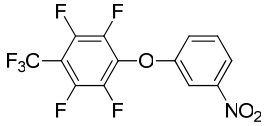
To a dried round-bottom flask was added **1** (1 mmol), **2** (1 mmol), $Ni(acac)_2$ (0.05mmol), K_3PO_4(2 mmol) and THF (10 mL), the reaction mixture was reflux for 8 hours under argon atmosphere(TLC), The resulting suspension was filtered and the filtrate was diluted with CH_2Cl_2, washed successively with H_2O and brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure to leave the crude product. The resultant crude residue was purified by chromatography to give the product **3** (eluent:hexane).

1,2,4,5-tetrafluoro-3-phenoxy-6-(trifluoromethyl)benzene (3a)



Colorless oil, ^{1}H NMR: δ 7.42 – 7.38 (m, 2H), 7.21 (t, J = 7.4 Hz, 1H), 7.05 – 7.03 (m, 2H); ^{13}C NMR: δ 156.6, 130.6, 124.5, 116.0; ^{19}F NMR: δ -55.8 (t, J = 21.8 Hz, 3F), -140.2 - -140.5 (m, 2F), -151.9 (dt, J_1 = 7.4 Hz, J_2 = 13.5 Hz, 2F); HRMS(EI): calc. for $C_{13}H_5F_7O$: 310.0229, found: 310.0233.

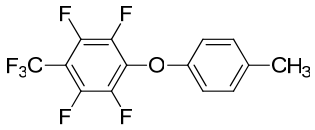
1,2,4,5-tetrafluoro-3-(3-nitrophenoxy)-6-(trifluoromethyl)benzene (3b)



White solid, mp: 80.9 – 81.1°C; ^{1}H NMR: δ 8.10 (d, J = 8.23 Hz, 1H), 7.85 (s, 1H), 7.61 (t, J = 8.26 Hz, 1H), 7.41(d, J = 8.24 Hz, 1H); ^{13}C NMR: δ 156.6, 149.3, 130.9, 122.1, 119.6, 111.2; ^{19}F NMR: δ -55.9 (t, J = 21.9 Hz, 3F), -138.8- -139.0 (m, 2F), -151.3 (dt, J_1 = 7.0 Hz, J_2 = 13.5 Hz, 2F); HRMS(EI): calc. for $C_{13}H_4F_7NO_3$:

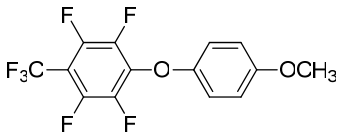
355.0079, found: 355.0072.

1,2,4,5-tetrafluoro-3-(*p*-tolyloxy)-6-(trifluoromethyl)benzene (3c)



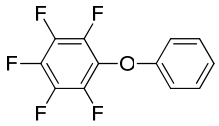
White solid, mp: 33.0 – 33.4°C; ^{1}H NMR: δ 7.18 – 6.92 (m, 4H), 2.37 (s, 3H); ^{13}C NMR: δ 154.6, 134.2, 130.4, 115.9, 20.6; ^{19}F NMR: δ -55.9 (t, J = 21.8 Hz,3F), -140.4 - -140.7 (m, 2F), -152.1 - - 152.2 (m, 2F); HRMS(EI): calc. for $C_{14}H_7F_7O$: 324.0385, found: 324.0386.

1,2,4,5-tetrafluoro-3-(4-methoxyphenoxy)-6-(trifluoromethyl)benzene (3d)



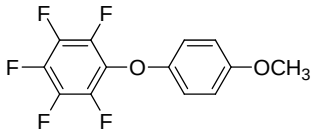
White solid, mp: 42.2 – 42.6°C, ^{1}H NMR: δ 7.01 – 6.88 (m, 4H), 3.82 (s, 3H); ^{13}C NMR: δ 156.5, 150.6, 117.5, 114.9, 55.7; ^{19}F NMR: δ -55.8 (t, J = 21.8 Hz, 3F), -140.4 - -140.7 (m, 2F), -152.5 (dt, J_1 = 7.3 Hz, J_2 = 13.3 Hz, 2F); HRMS(EI): calc. for $C_{14}H_7F_7O_2$: 340.0334, found :340.0332.

1,2,3,4,5-pentafluoro-6-phenoxybenzene (3e)



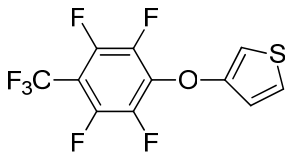
Colorless oil, ^{1}H NMR: δ 7.39 – 7.35 (m, 2H), 7.16 (t, J = 7.4 Hz, 1H), 6.98 (d, J = 8.3 Hz, 2H); ^{13}C NMR: δ 157.1, 129.9, 123.9, 115.4; ^{19}F NMR: δ -153.9 - -154.0 (m, 2F), -160.0 (t, J = 21.8 Hz, 1F), -160.0 - -162.2 (m, 2F); HRMS(EI): calc. for $C_{12}H_5F_5O$: 260.0261, found: 260.0257.

1,2,3,4,5-pentafluoro-6-(4-methoxyphenoxy)benzene (3f)



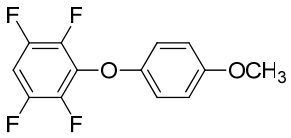
White solid, mp: 45.6 – 46.0 °C, ^{1}H NMR: δ 6.96 – 6.86 (m, 4H), 3.81 (s, 3H); ^{13}C NMR: δ 156.1, 151.3, 116.8, 114.8, 55.7; ^{19}F NMR: δ -154.3 - -154.4 (m, 2F), -160.6 (t, J = 21.8 Hz, 1F), -162.3 - -162.4 (m. 2F); HRMS(EI): calc. for $C_{13}H_7F_5O_2$:290.0366, found: 290.0363.

3-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenoxy)thiophene (3g)



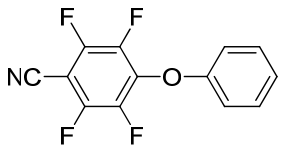
Colorless oil, ^{1}H NMR: δ 7.31 – 7.30 (m, 1H), 6.94 – 6.92 (m, 1H), 6.61 – 6.60 (m, 1H); ^{13}C NMR: δ 153.5, 126.0, 118.7, 105.2; ^{19}F NMR: δ -55.9 (t, J = 21.8, 3F), -140.0 - -140.2 (m, 2F), -152.2 (dt, J_1 = 7.5, J_2 = 13.5, 2F); HRMS(EI): calc. for $C_{11}H_3F_7OS$: 315.9793, found: 315.9791.

1,2,4,5-tetrafluoro-3-(4-methoxyphenoxy)benzene (3h)



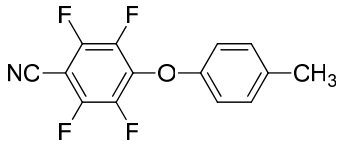
White solid, mp: 47.2 – 47.7 °C, ^{1}H NMR: δ 6.98 – 6.86 (m, 5H), 3.81 (s, 3H), ^{13}C NMR: δ 156.0, 151.3, 117.0, 114.8, 101.5 (t, J = 23.1 Hz), 55.7; ^{19}F NMR: δ -138.9 - -139.0 (m, 2F), -154.5 (td, J_1 = 16.7 Hz, J_2 = 9.3 Hz, 2F); HRMS(EI): calc. for $C_{13}H_8F_4O_2$: 272.0460, found: 272.0462.

2,3,5,6-tetrafluoro-4-phenoxybenzonitrile (3i)



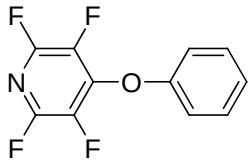
White solid, mp :57.5 – 57.8 °C, ^{1}H NMR: δ 7.42 – 7.38 (m, 2H), 7.23 (t, J = 7.4 Hz, 1H), 7.04 (d, J = 8.3 Hz, 2H); ^{13}C NMR: δ 156.4, 130.1, 124.9, 116.1, 107.2; ^{19}F NMR: δ -132.1 (dt, J_1 = 13.6 Hz, J_2 = 8.1 Hz, 2F), -150.5(dt, J_1 = 13.8 Hz, J_2 = 7.6 Hz, 2F); HRMS(EI): calc. for $C_{13}H_5F_4NO$:267.0307, found; 267.0308.

2,3,5,6-tetrafluoro-4-(*p*-tolyloxy)benzonitrile (3j)



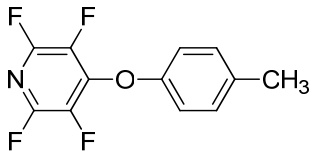
White solid, mp: 94.1 – 94.5 °C, ^{1}H NMR: δ 7.18 (d, J = 8.38 Hz, 2H), 6.92 (d, J = 8.51 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR: δ 154.4, 134.7, 130.5, 116.1, 107.3, 20.7; ^{19}F NMR: δ -132.3 (dt, J_1 = 13.8 Hz, J_2 = 7.7 Hz, 2F), -150.7 (dt, J_1 = 13.6 Hz, J_2 = 7.9 Hz, 2F); HRMS(EI): calc. for $C_{14}H_7F_4NO$: 281.0464, found:281.0465.

2,3,5,6-tetrafluoro-4-(*p*-tolyloxy)pyridine (3k)



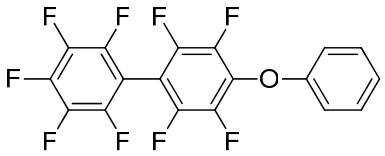
White solid, mp: 28.1 – 28.4 °C, ^{1}H NMR: δ 7.44 – 7.40 (m, 2H), 7.25 (t, J = 7.43 Hz, 1H), 7.09 (d, J = 8.2 Hz, 2H); ^{13}C NMR: δ 155.8, 130.1, 125.2, 116.7; ^{19}F NMR: δ -88.7 (dt, J_1 = 29.5 Hz, J_2 = 15.0 Hz, 2F), -154.3 (dt, J_1 = 29.4 Hz, J_2 = 14.9 Hz, 2F); HRMS(EI): calc. for $C_{11}H_5F_4NO$: 243.0307, found: 243.0305.

2,3,5,6-tetrafluoro-4-(*p*-tolyloxy)pyridine (3l)



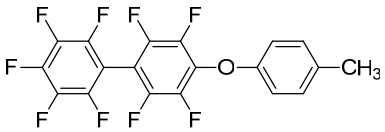
Colorless oil, ^{1}H NMR: δ 7.21 – 6.97 (m, 4H), 2.38 (s, 3H); ^{13}C NMR: δ 153.8, 134.9, 130.4, 116.6, 20.7; ^{19}F NMR: δ -88.9 (dt, J_1 = 29.7 Hz, J_2 = 15.0 Hz, 2F), -154.6 (dt, J_1 = 29,5 Hz, J_2 = 14.9 Hz, 2F); HRMS(EI): calc. for $C_{12}H_7F_4NO$: 257.0464, found: 257.0467.

2,2',3,3',4,5,5',6,6'-nonafluoro-4'-phenoxy-1,1'-biphenyl (3m)



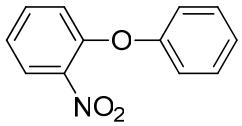
White solid, mp: 113.0 – 113.5°C, ^{1}H NMR: δ 7.42 – 7.07 (m, 5H); ^{13}C NMR: δ 156.9, 129.9, 124.2, 115.9; ^{19}F NMR: δ -137.3 - -137.4 (m, 2F), -138.1 - -138.2 (m, 2F), -150.2 (t, J = 20.8 Hz, 1F), -152.8 (dt, J_1 = 11.7 Hz, J_2 = 4.7 Hz, 2F), -160.4 - -160.6 (m, 2F); HRMS(EI): calc. for $C_{18}H_5F_9O$: 408.0197, found: 408.0199.

2,2',3,3',4,5,5',6,6'-nonafluoro-4'-(*p*-tolyloxy)-1,1'-biphenyl (3n)



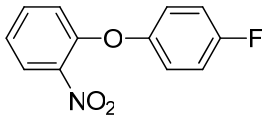
White solid, mp: 102.2 – 102.4°C, ^{1}H NMR: δ 7.20 – 6.96 (m, 4H), 2.37 (s,3H); ^{13}C NMR: δ 154.9, 133.8, 130.3, 115.8, 20.6; ^{19}F NMR: δ -137.3 - -137.4 (m, 2F), -138.3 - -138.4 (m, 2F), -150.3 (t, J = 21.0 Hz, 1F), -153.0 (dt, J_1 = 11.9 Hz, J_2 = 4.9 Hz, 2F), -160.5 - -160.6 (m, 2F); HRMS(EI): calc. for $C_{19}H_7F_9O$: 422.0353, found: 422.0352.

1-nitro-2-phenoxybenzene (3o)



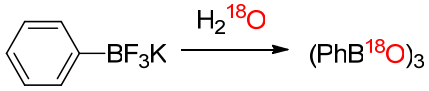
Colorless oil, ^{1}H NMR: δ 7.96 – 7.94 (m, 1H), 7.54 – 7.38 (m, 3H), 7.23 – 7.02 (m, 5H), ^{13}C NMR: δ 155.9, 150.7, 141.4, 134.2, 130.1, 125.7, 124.6, 123.2, 120.5, 119.2; HRMS(EI): calc. for $C_{12}H_9NO_3$: 215.0582, found: 215.0581.

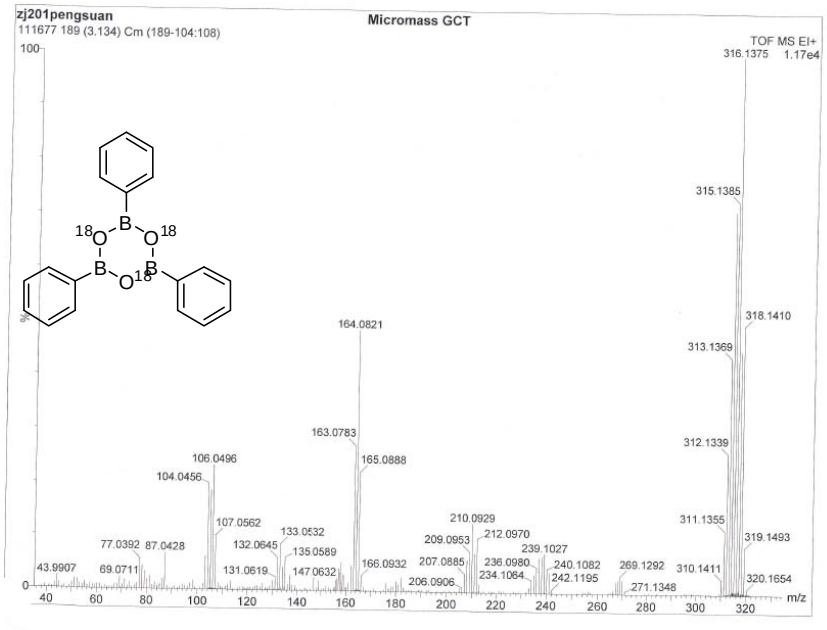
1-(4-fluorophenoxy)-2-nitrobenzene (3p)



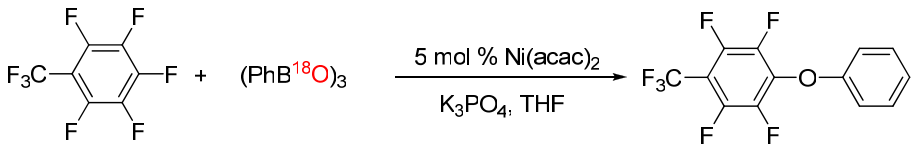
Colorless oil, ^{1}H NMR: δ 7.96 – 7.94 (m,1H), 7.54 – 7.50 (m, 1H), 7.24 – 6.98 (m, 6H); ^{13}C NMR: δ 159.5 (d, J = 243.5 Hz), 151.6 (d, J = 2.4 Hz), 150.9, 141.3, 134.1, 125.7, 123.2, 120.8 (d, J = 8.5 Hz), 119.9, 116.7 (d, J = 23.7 Hz); ^{19}F NMR: δ -118.1 - -118.2 (m, 1F); HRMS(EI): calc. for $C_{12}H_8FNO_3$: 233.0488, found: 233.0490.

HRMS (EI) spectra of **$(PhB^{18}O)_3$**



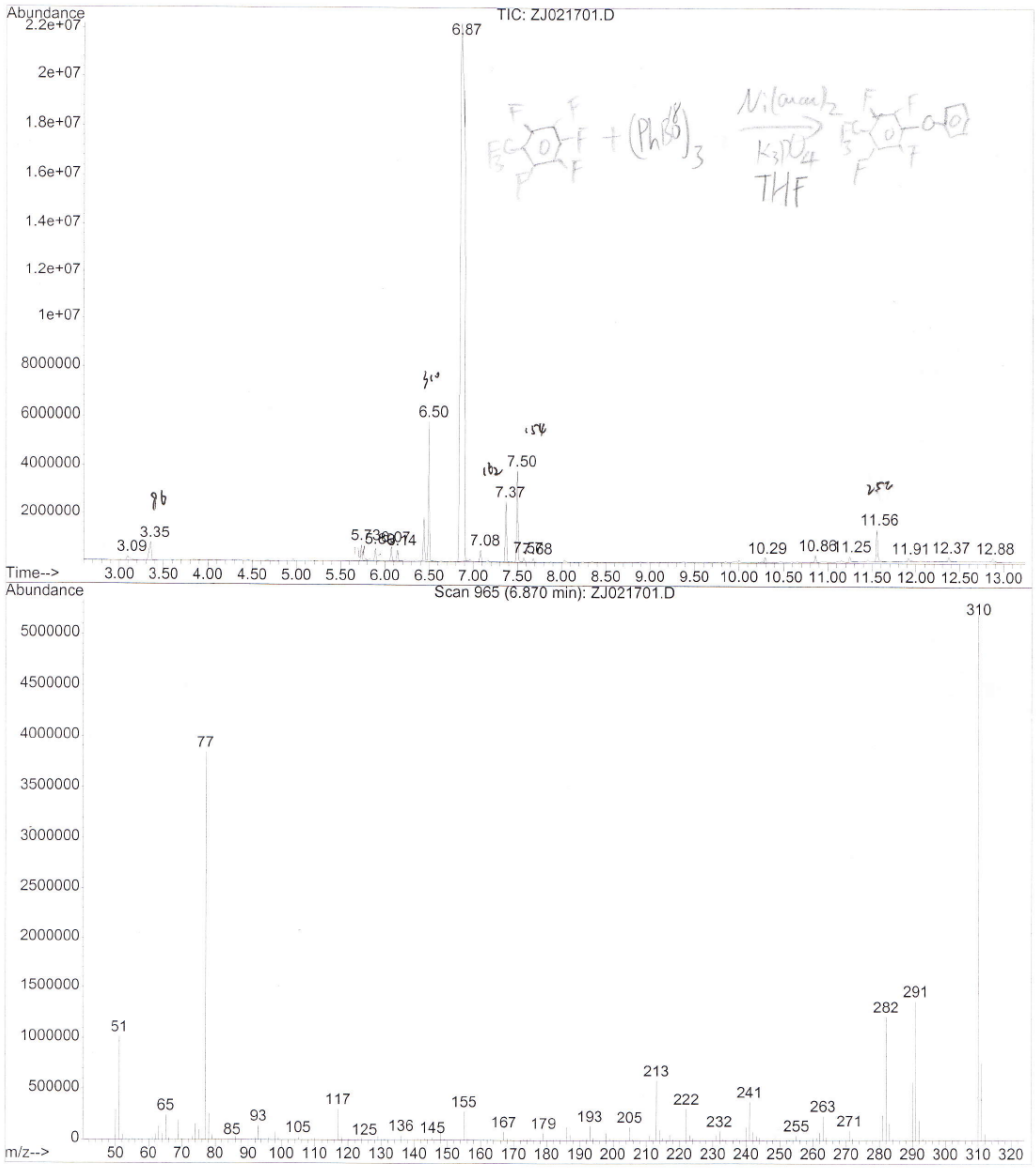


GC-MS of **3a** in reaction of **1a** with ^{18}O-labeled phenylboronic acid **(PhB^{18}O)$_3$**

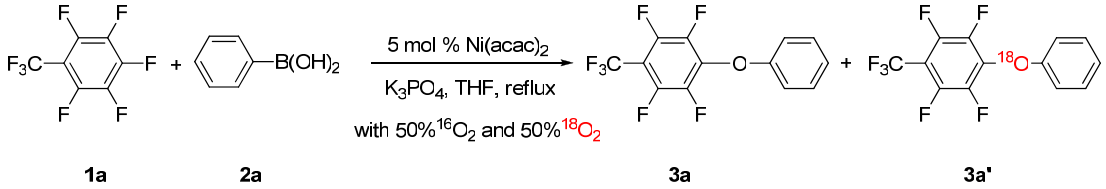


1a **3a**

```
ile        : C:\HPCHEM\1\DATA\ZJ021701.D
perator    : SQF
cquired    : 17 Feb 2012  13:56     using AcqMethod SQF
nstrument :    GC/MS Ins
ample Name:
isc Info   :
ial Number: 1
```

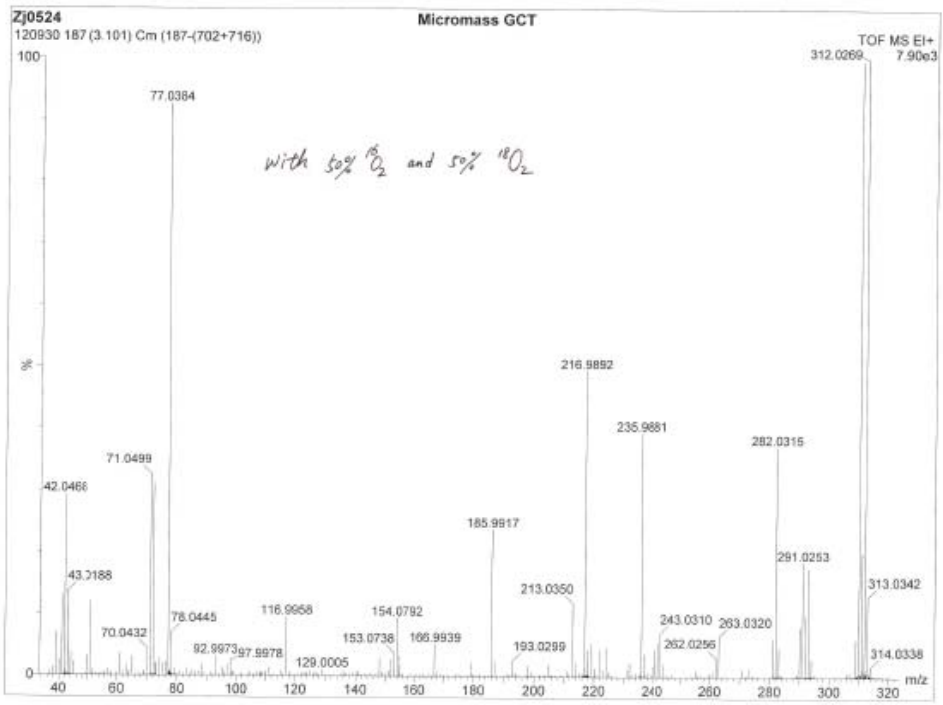


HRMS (EI) spectra of **3a'** in the reaction of **1a** with **2a** in the presence of the mixture of 50% $^{16}O_2$ and 50% $^{18}O_2$.



1a **2a** **3a** **3a'**

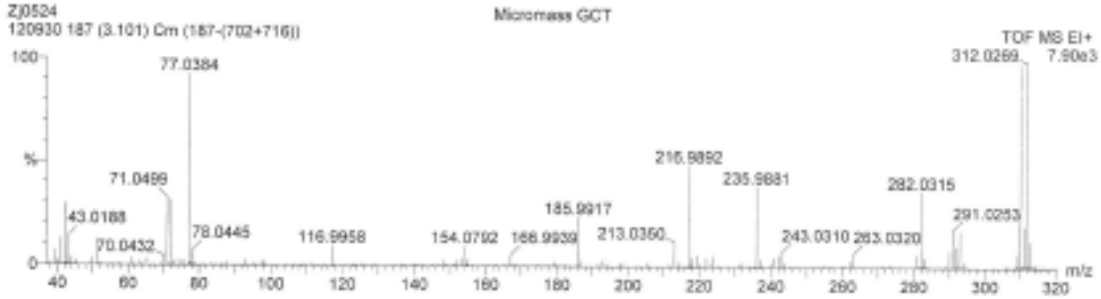
3a:3a'= 1:1



Elemental Composition Report **Page 2**

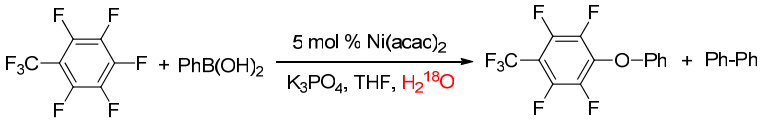
Multiple Mass Analysis: 38 mass(es) processed
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
621 formula(e) evaluated with 40 results within limits (up to 50 closest results for each mass)

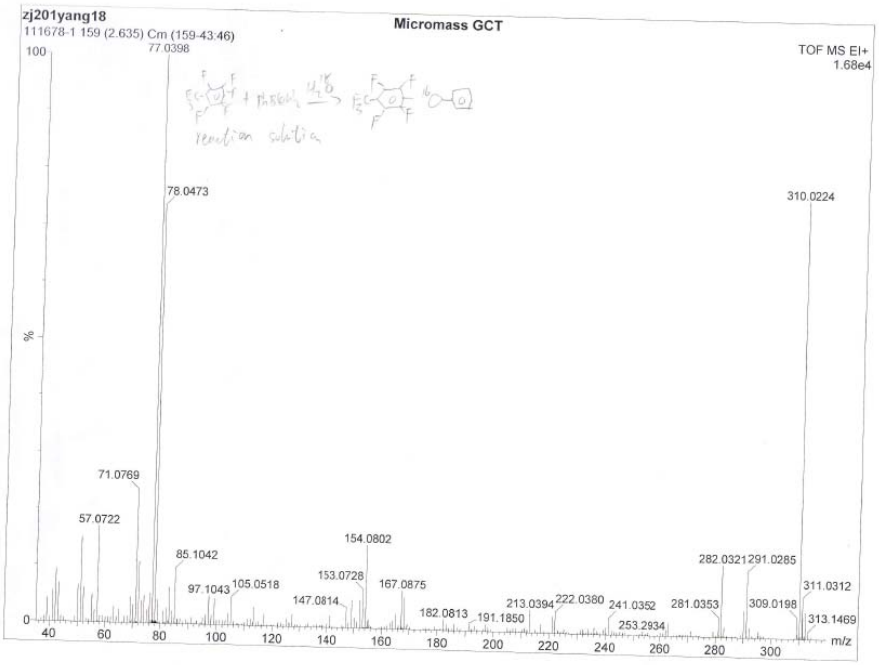


Mass	RA	Calc. Mass	mDa	PPM	DBE	Score	Formula
Minimum:	4.00				-1.5		
Maximum:	100.00		5.0	5.0	50.0		
292.0257	10.07	292.0220	3.7	12.6	5.0	1	C10 H5 16O 18O F7
		292.0209	4.8	16.5	9.0	2	C13 H4 18O F6
293.0311	17.63	293.0287	2.4	8.2	8.5	1	C13 H5 18O F6
309.0156	6.07	309.0150	0.6	1.8	8.5	1	C13 H4 16O F7
310.0230	99.70	310.0229	0.1	0.4	8.0	1	C13 H5 16O F7
311.0265	20.26	---					
312.0269	100.00	312.0271	-0.2	-0.7	8.0	1	C13 H5 18O F7
313.0342	13.05	---					

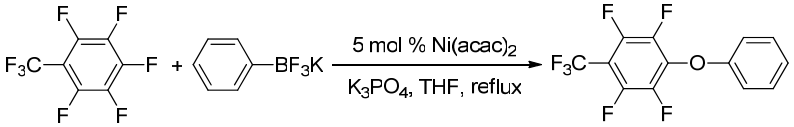
HRMS (EI) spectra of **3a** in the reaction of **1a** with **2a** in the presence of $H_2{}^{18}O$



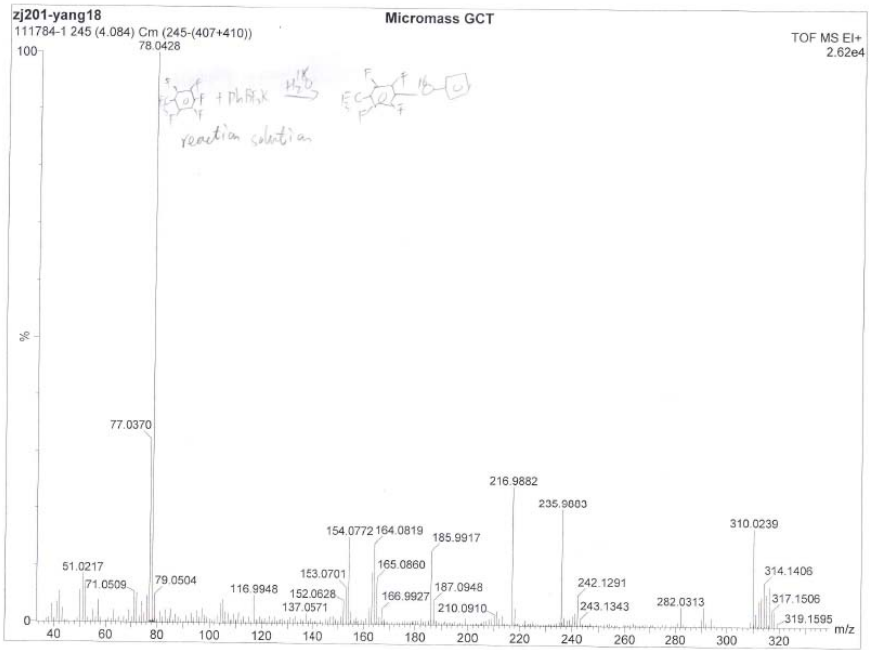
1a **2a** **3a**, 43% **4a**, 56%



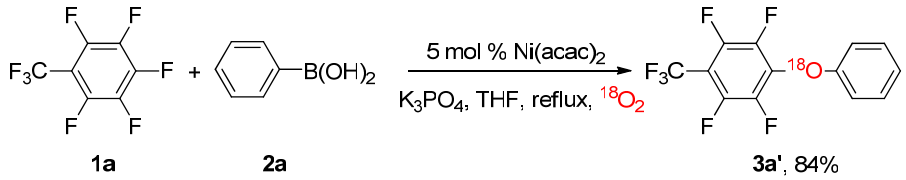
HRMS (EI) spectra of **3a** in the reaction of **1a** with **9** in the presence of $H_2{}^{18}O$



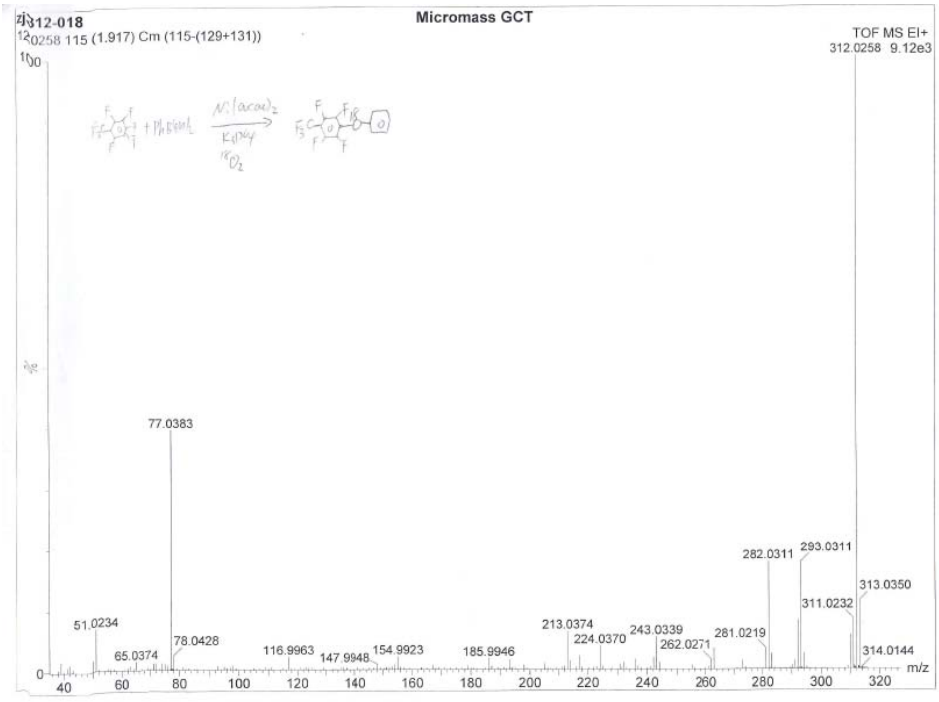
1a **9** **3a** (1) 85% (2) with 0.1mL of $H_2{}^{18}O$, 58%



HRMS (EI) spectra of **3a'** in the reaction of **1a** with **2a** in the presence of $^{18}O_2$



1a **2a** **3a'**, 84%

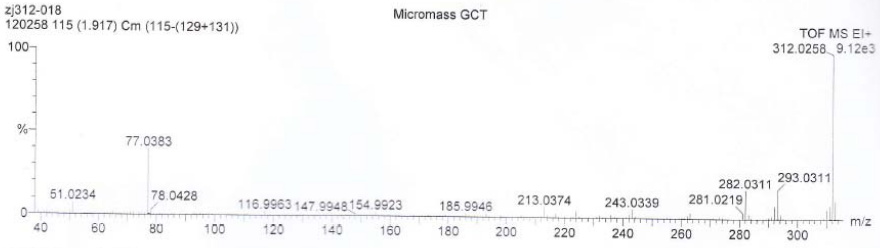


Elemental Composition Report

Page 1

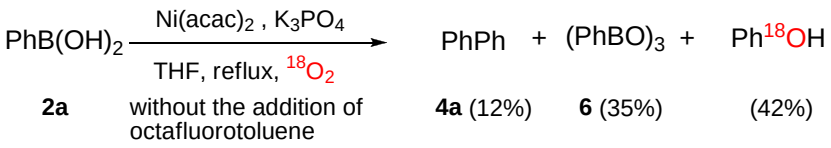
Multiple Mass Analysis: 14 mass(es) processed
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
279 formula(e) evaluated with 15 results within limits (up to 50 closest results for each mass)

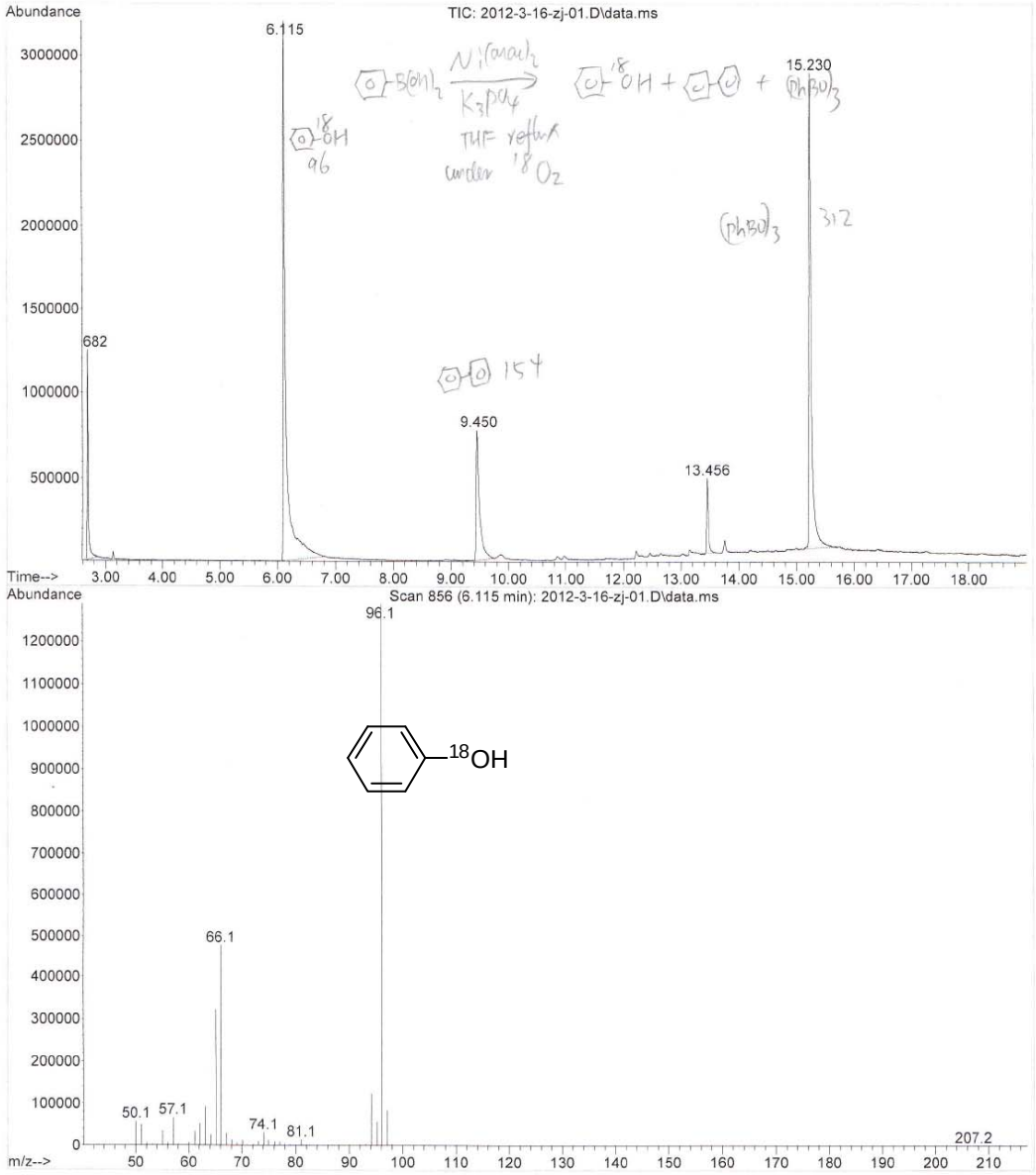


Minimum:	3.00				-1.5		
Maximum:	100.00		5.0	5.0	50.0		
Mass	RA	Calc. Mass	mDa	PPM	DBE	Score	Formula
51.0234	6.88	51.0235	-0.1	-1.5	3.5	1	C4 H3
		51.0246	-1.2	-23.9	-0.5	2	C H4 16O F
77.0383	39.22	77.0391	-0.8	-10.7	4.5	1	C6 H5
213.0374	6.17	213.0327	4.7	21.9	7.5	1	C11 H5 F4
224.0370	3.77	224.0335	3.5	15.6	9.0	1	C12 H5 18O F3
243.0339	5.25	243.0319	2.0	8.2	8.5	1	C12 H5 18O F4
263.0303	3.31	263.0295	0.8	2.9	7.5	1	C12 H5 F6
281.0219	3.36	281.0201	1.8	6.3	7.5	1	C12 H4 F7
282.0311	17.49	282.0279	3.2	11.2	7.0	1	C12 H5 F7
292.0244	7.94	292.0220	2.4	8.1	5.0	2	C10 H5 16O 18O F7
		292.0209	3.5	12.1	9.0	1	C13 H4 18O F6
293.0311	17.47	293.0287	2.4	8.2	8.5	1	C13 H5 18O F6
310.0246	5.55	310.0229	1.7	5.6	8.0	1	C13 H5 16O F7
311.0232	8.12	311.0193	3.9	12.6	8.5	1	C13 H4 18O F7
312.0258	100.00	312.0271	-1.3	-4.2	8.0	1	C13 H5 18O F7
313.0350	11.11	---					

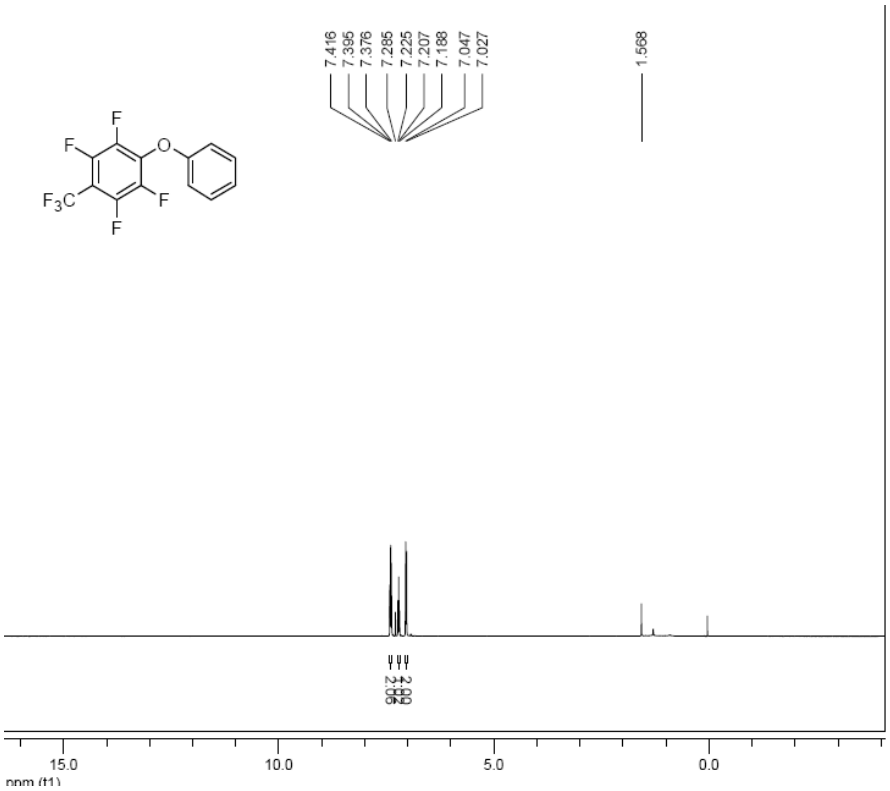
GC-MS spectra of intermediate $Ph^{18}OH$




```
.le       :D:\data\2012-3-16\2012-3-16-zj-01.D
erator    : sqf
quired    : 16 Mar 2012    8:53     using AcqMethod METHOD-04.M
strument :    GC-MSD
mple Name: 2012-3-16-1
sc Info   :
al Number: 1
```



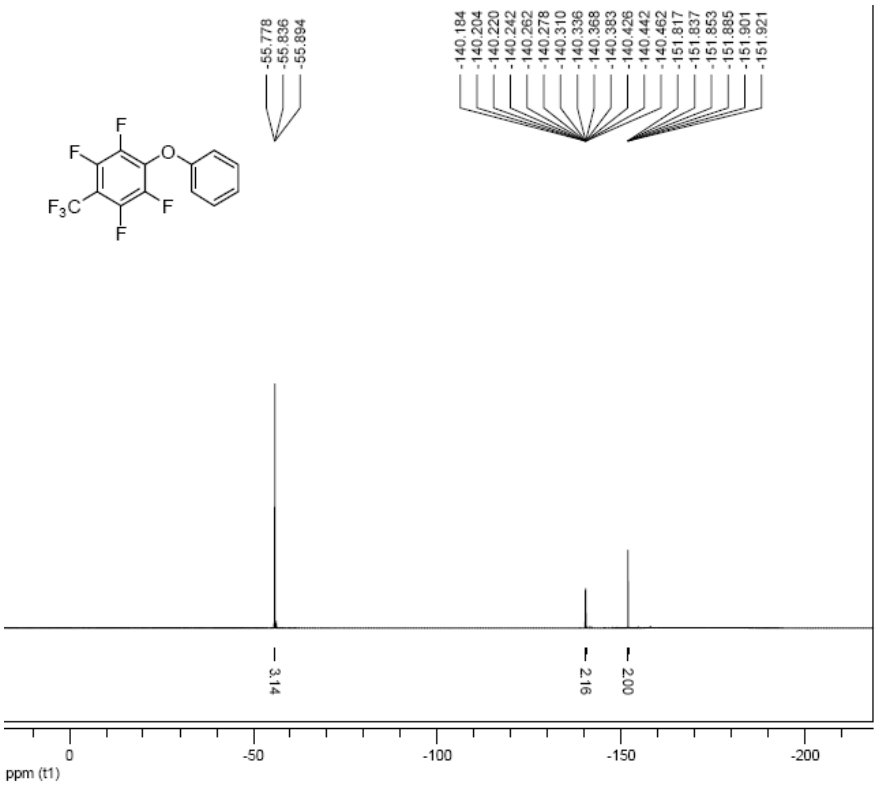
^{1}H NMR spectra of **3a**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

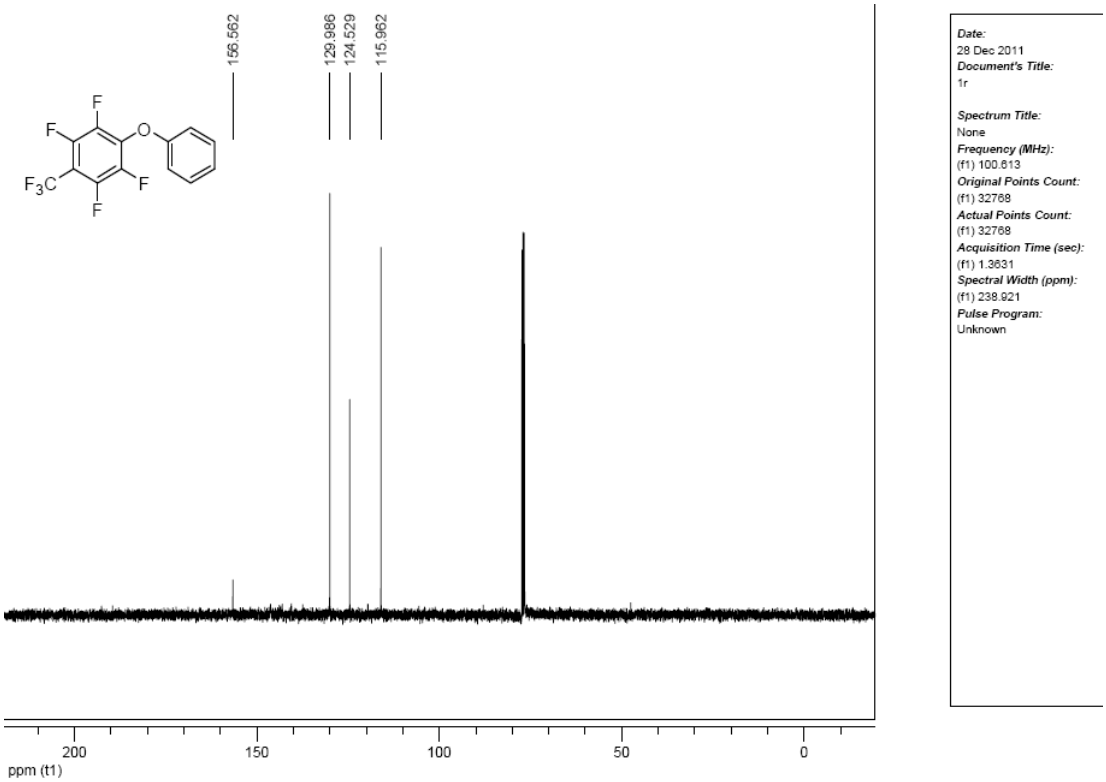
^{19}F NMR spectra of **3a**



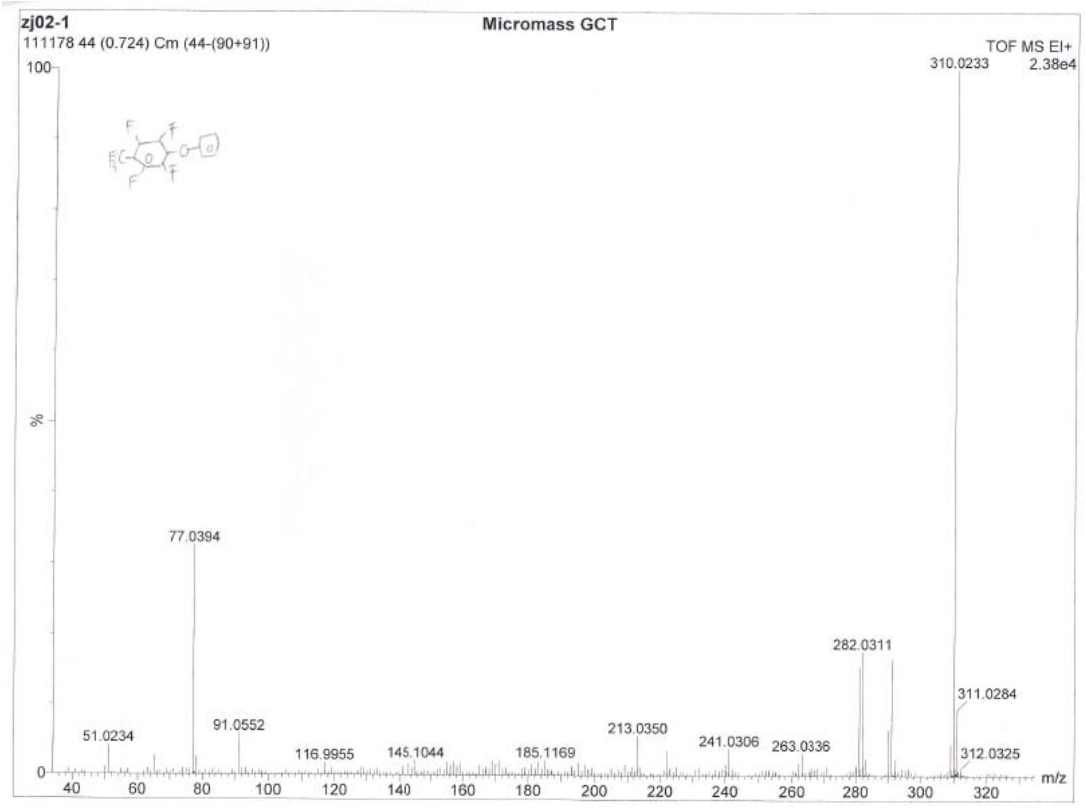
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

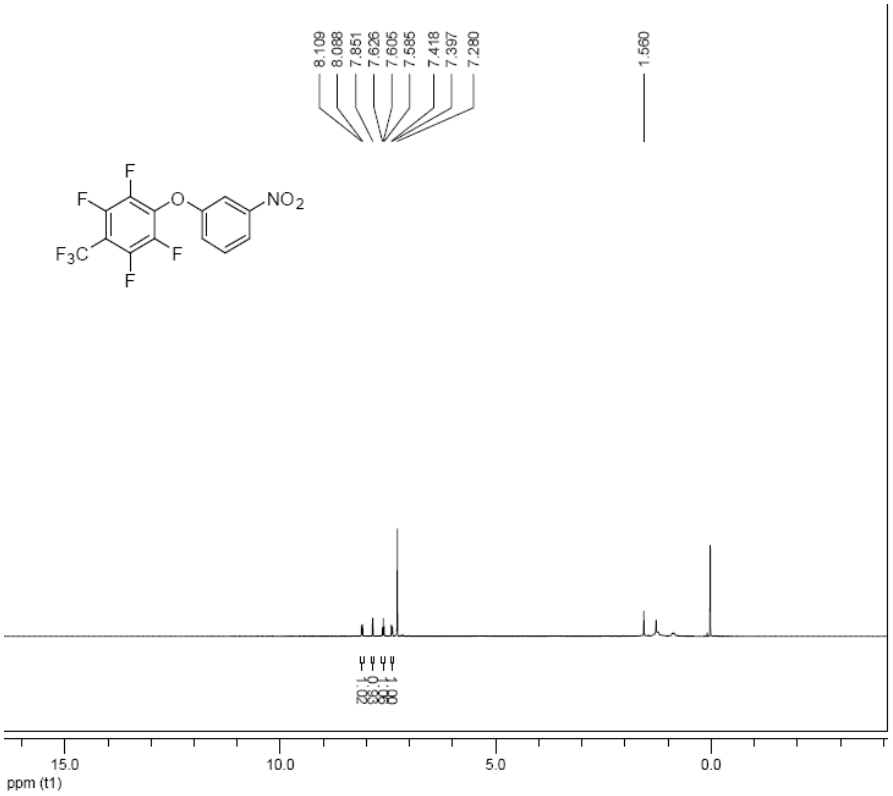
^{13}C NMR spectra of **3a**



HRMS (EI) spectra of **3a**



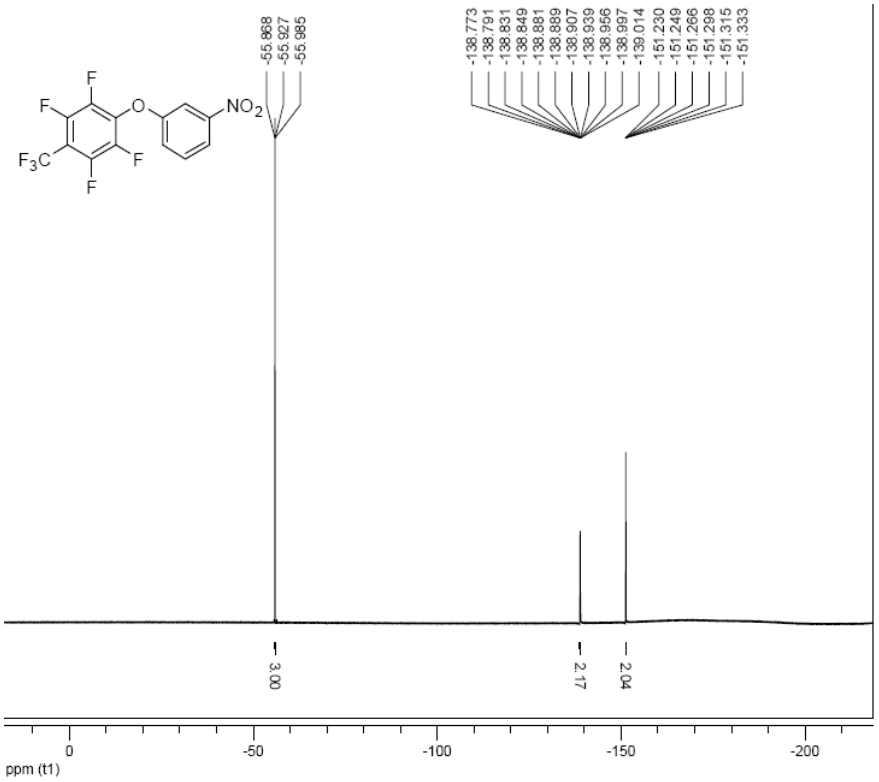
^{1}H NMR spectra of **3b**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

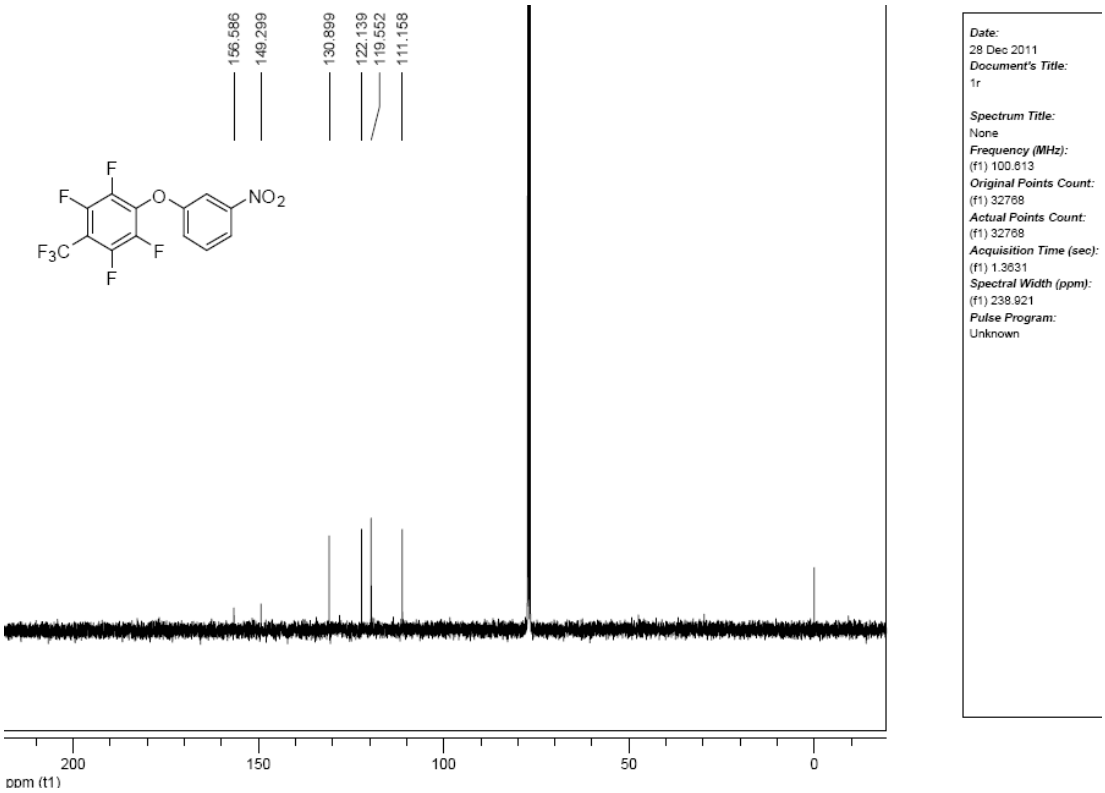
^{19}F NMR spectra of **3b**



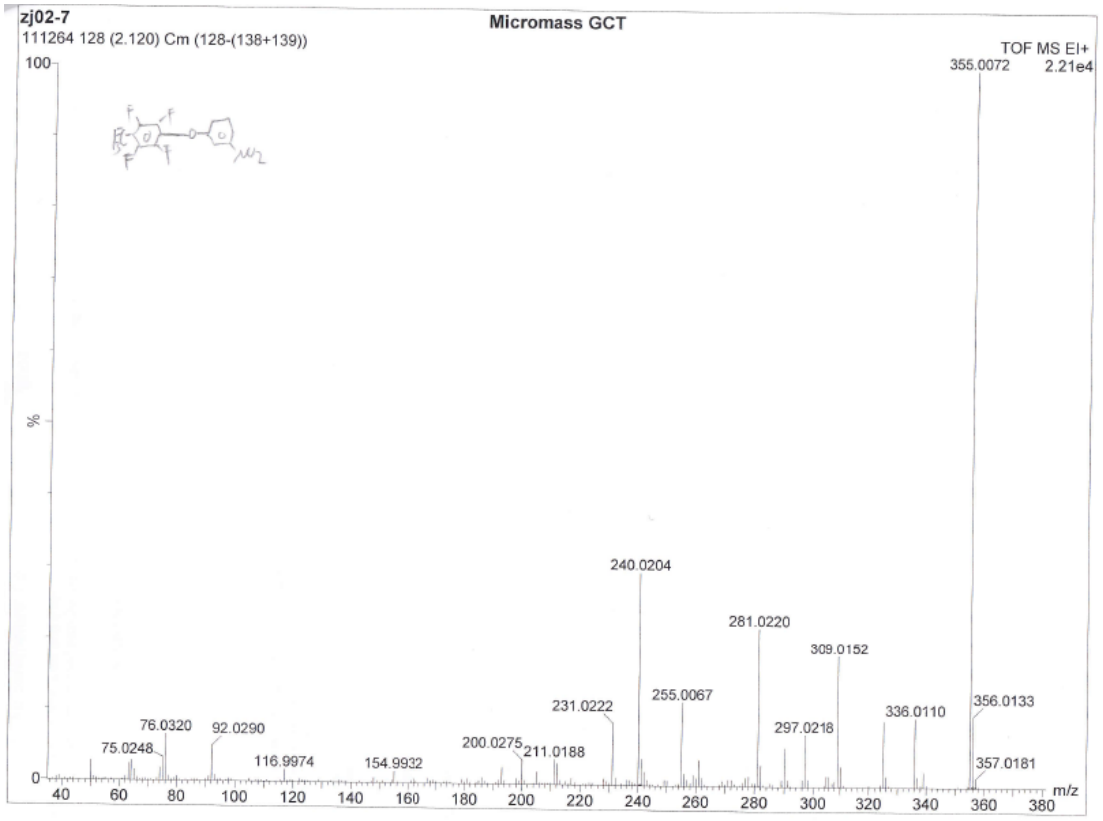
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

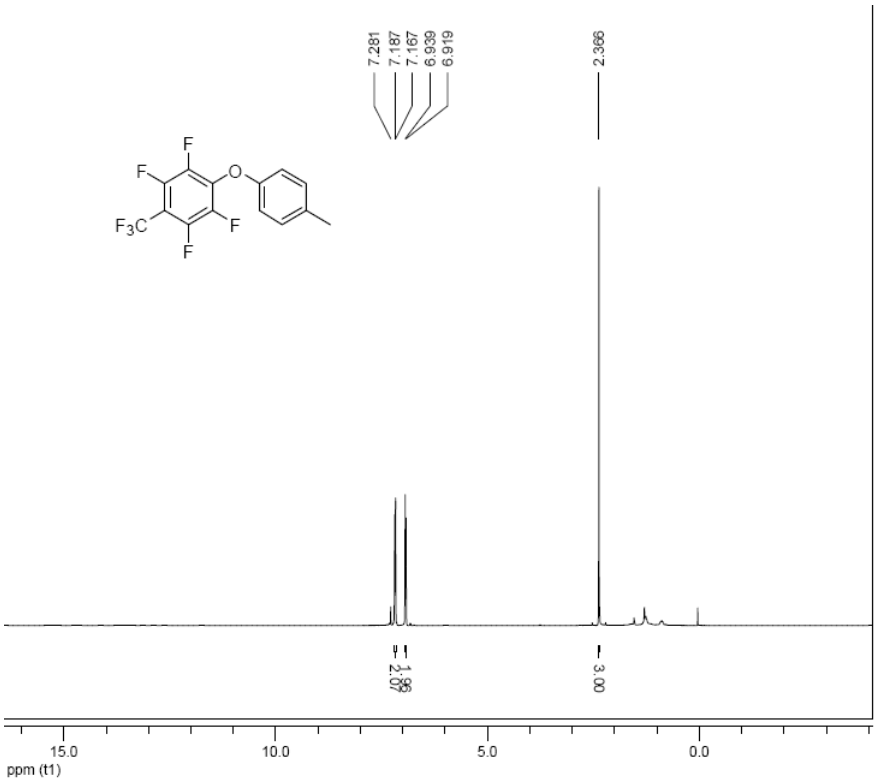
^{13}C NMR spectra of **3b**



HRMS (EI) spectra of **3b**



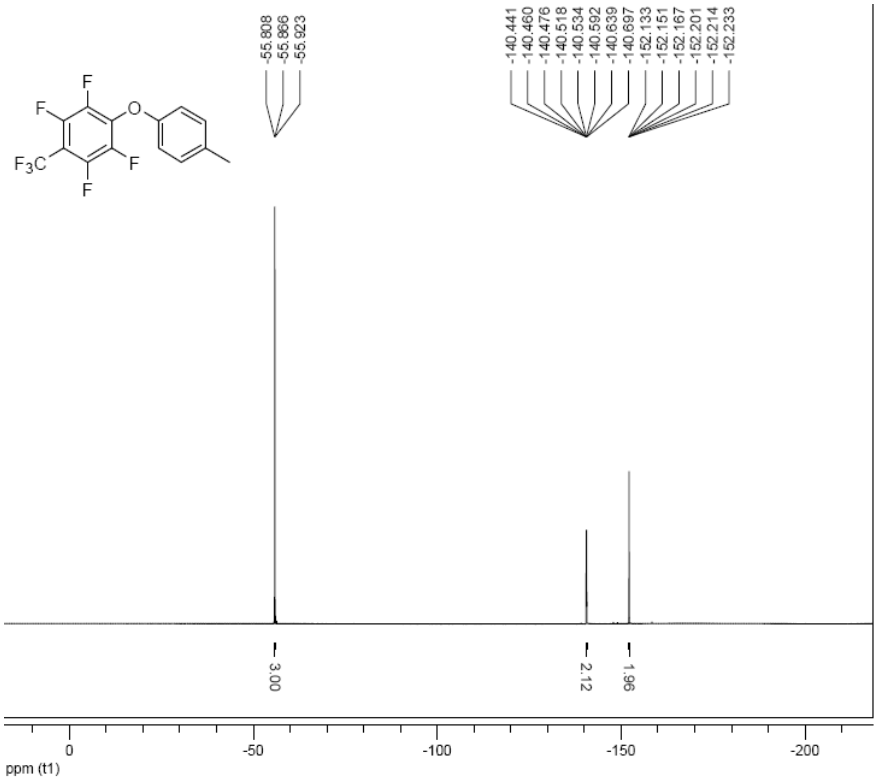
^{1}H NMR spectra of **3c**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

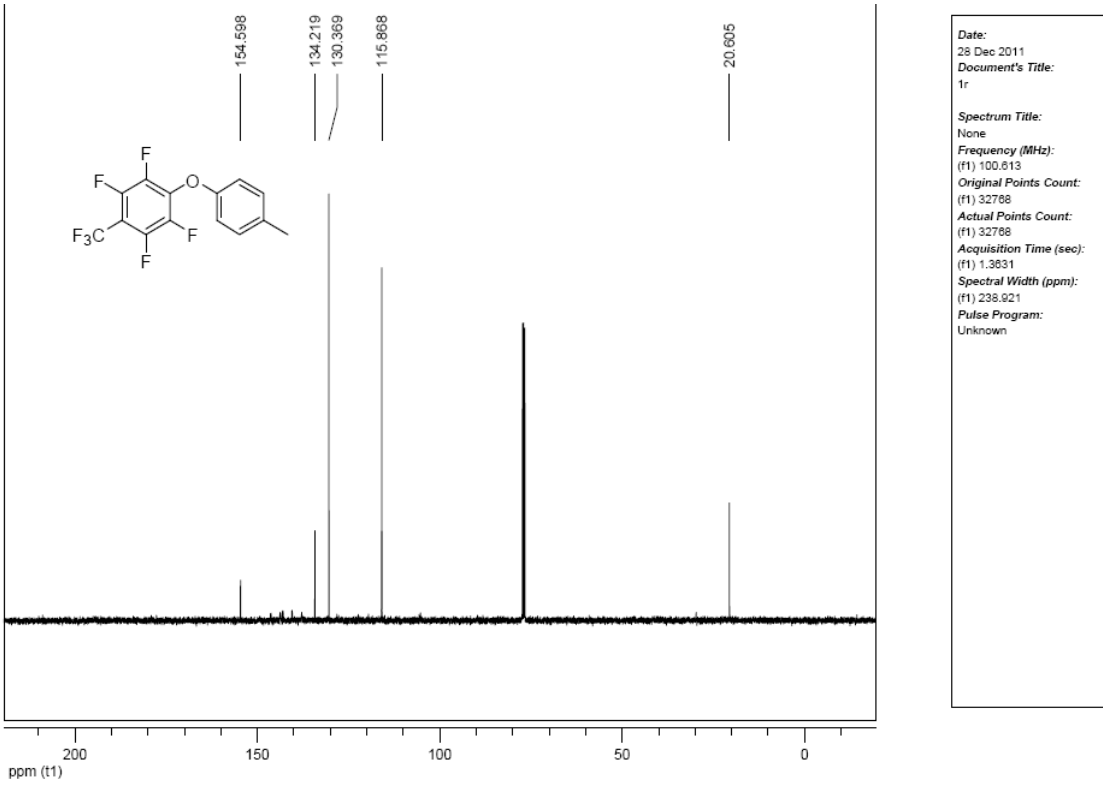
^{19}F NMR spectra of **3c**



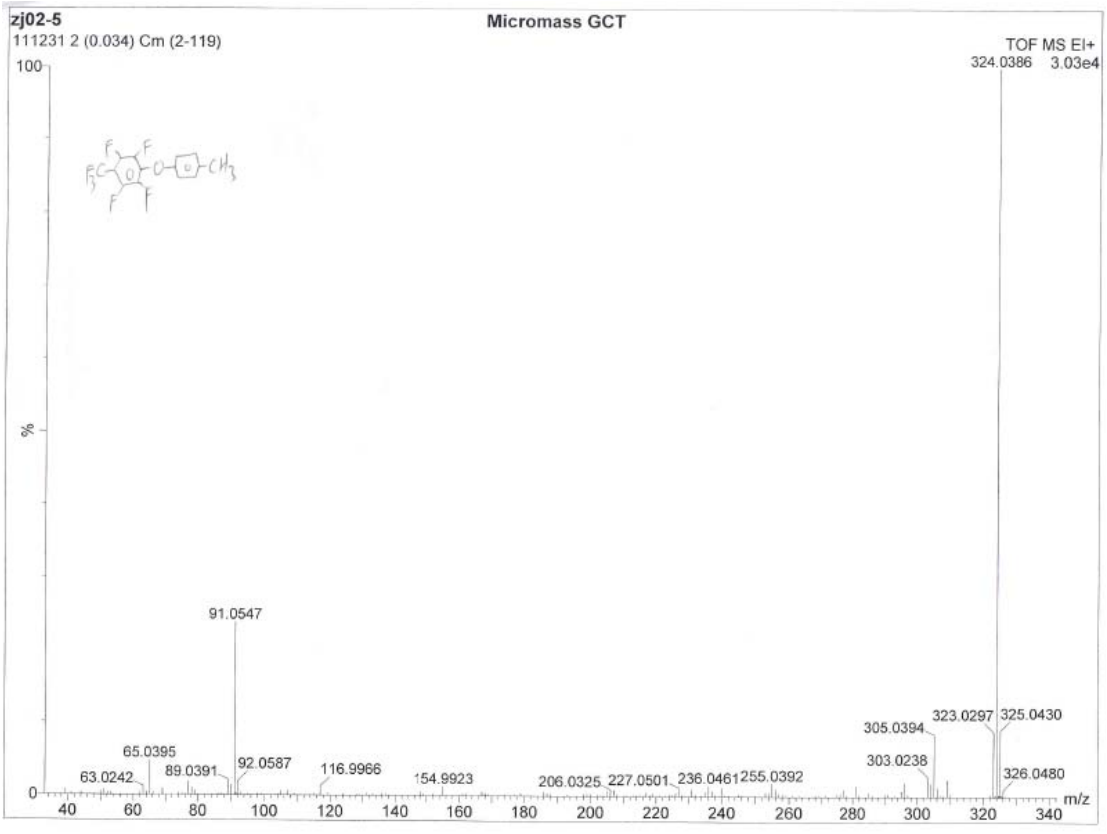
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

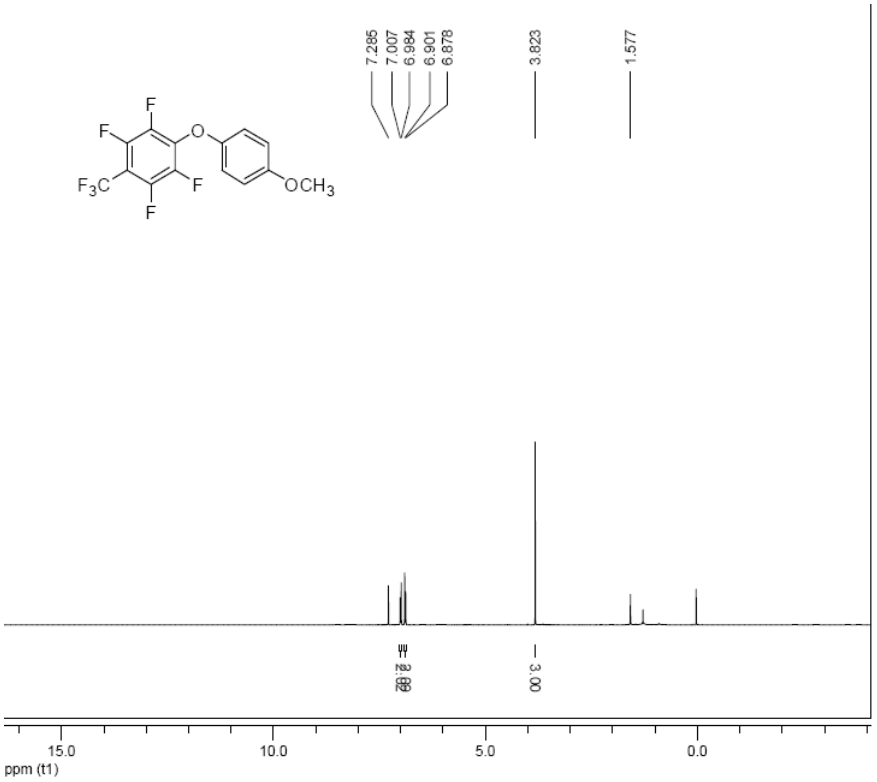
^{13}C NMR spectra of **3c**



HRMS (EI) spectra of **3c**



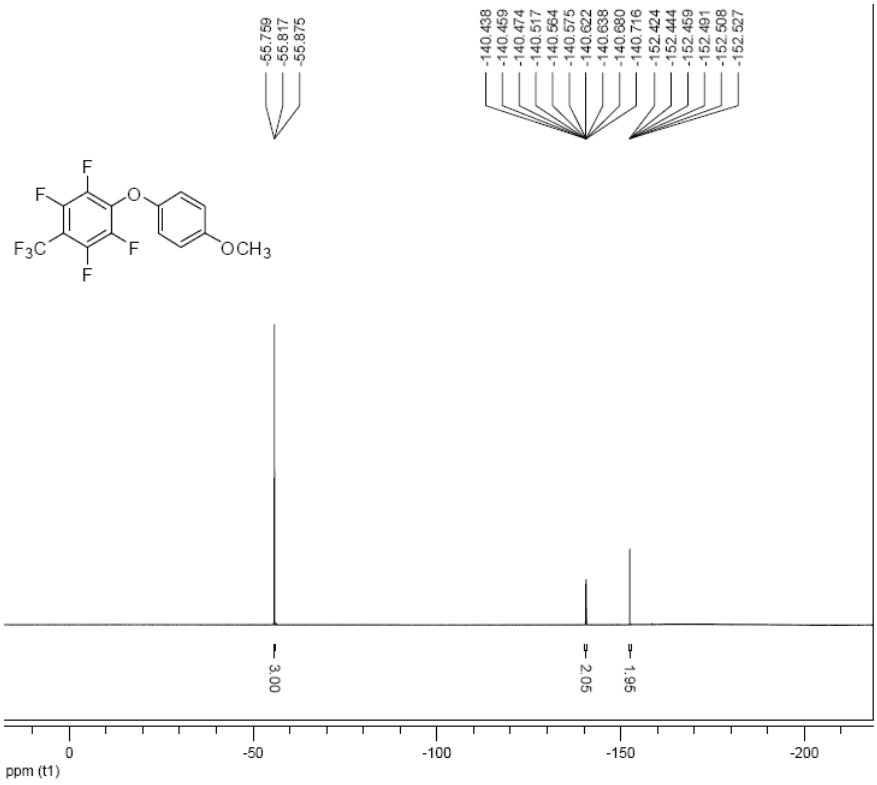
^{1}H NMR spectra of **3d**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.563
Pulse Program:
Unknown

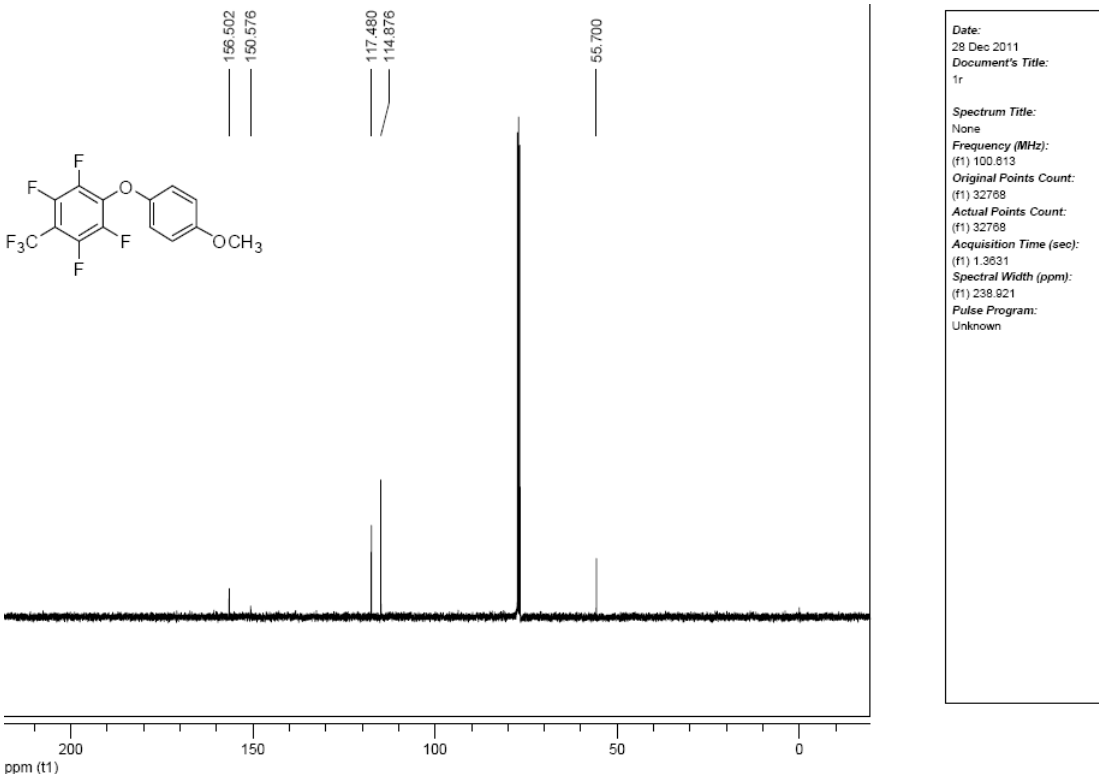
^{19}F NMR spectra of **3d**



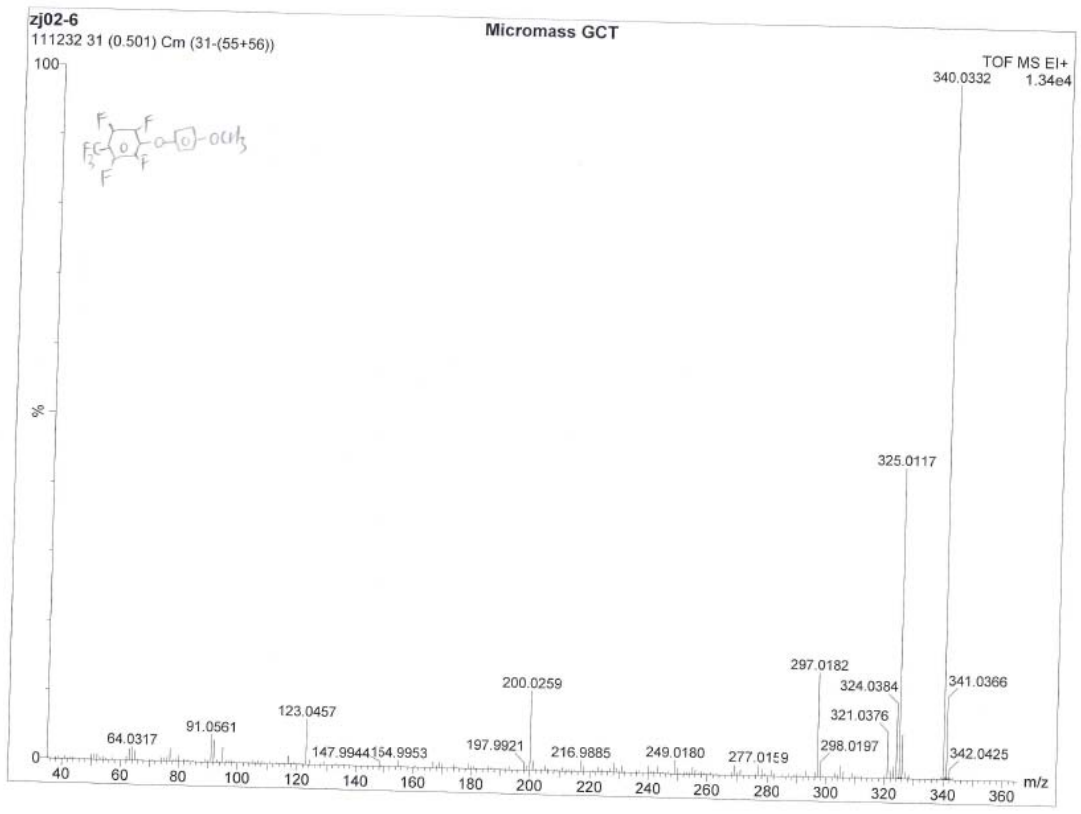
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

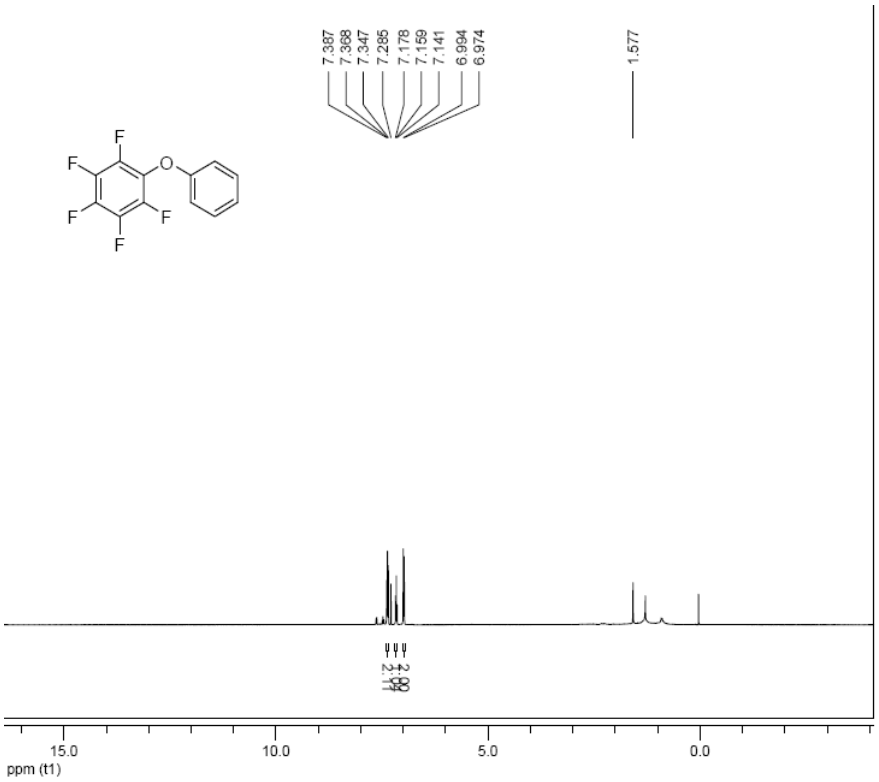
^{13}C NMR spectra of **3d**



HRMS (EI) spectra of **3d**



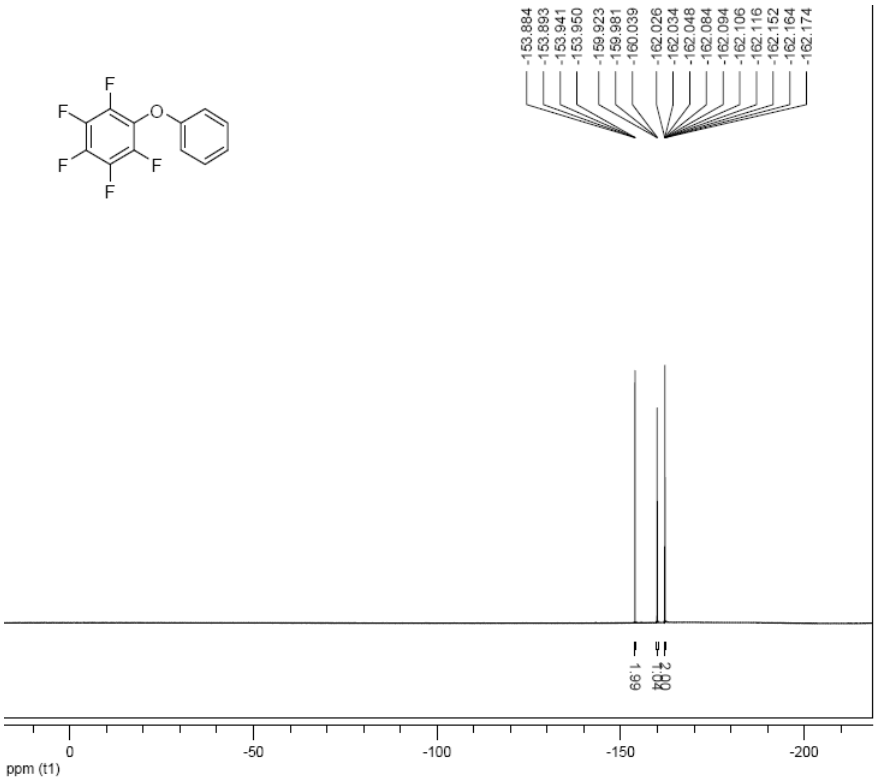
^{1}H NMR spectra of **3e**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

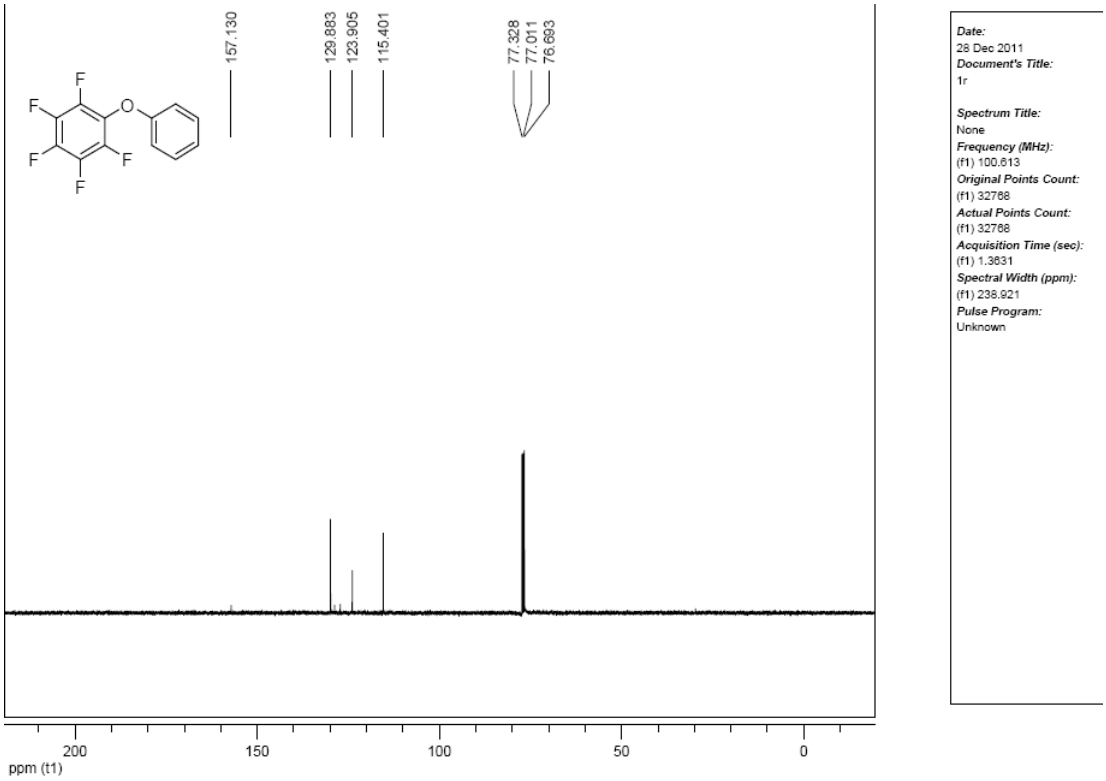
^{19}F NMR spectra of **3e**



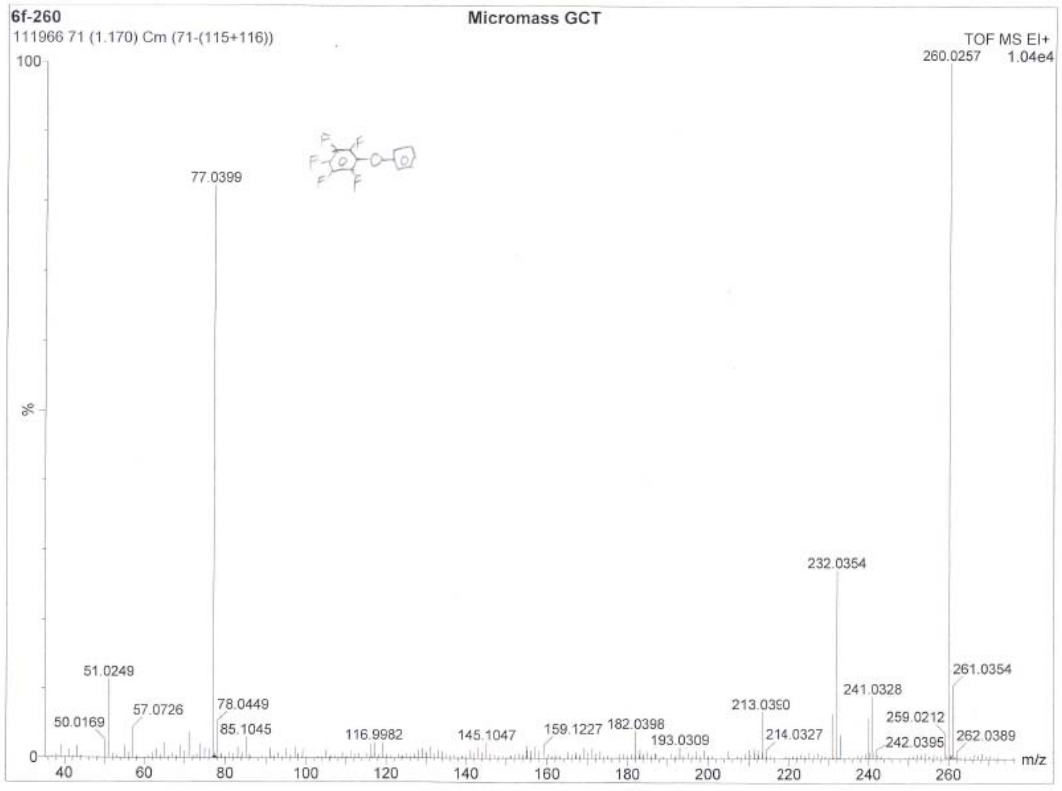
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

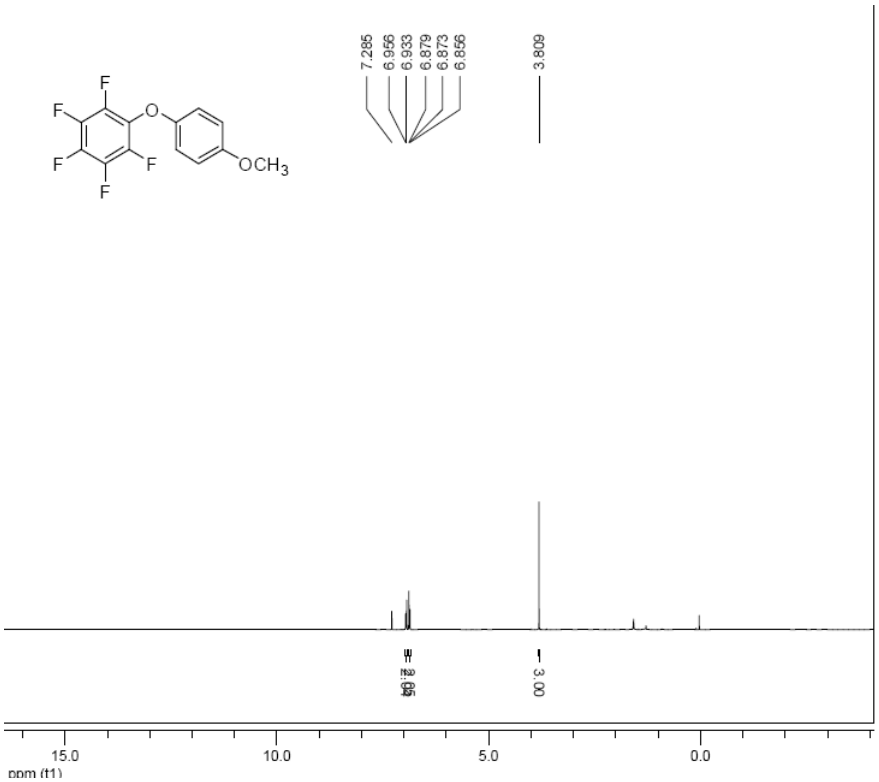
^{13}C NMR spectra of **3e**



HRMS (EI) spectra of **3e**



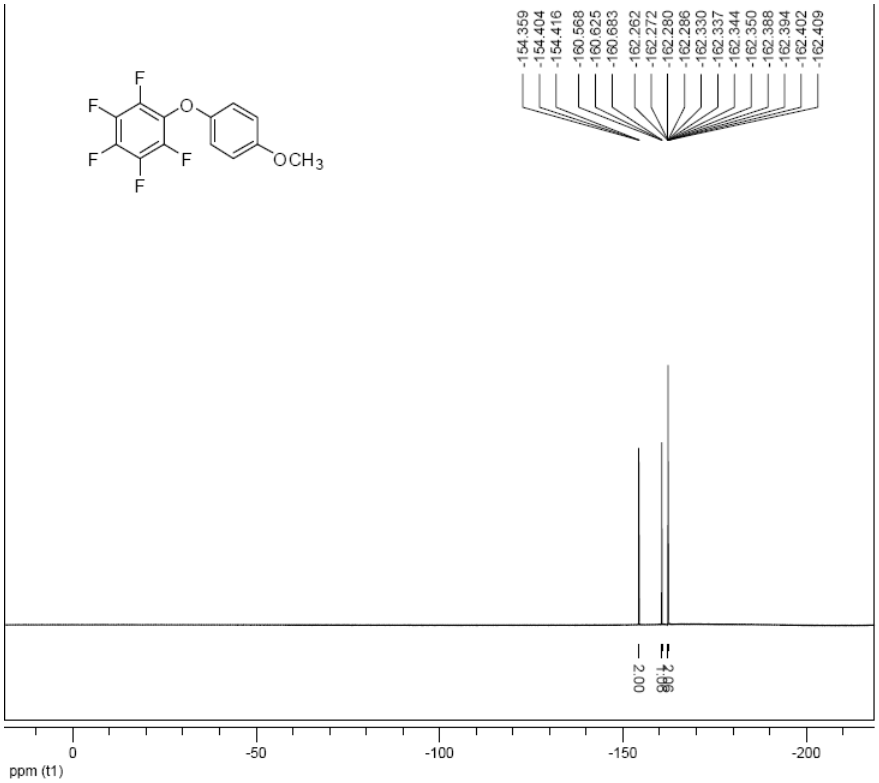
^{1}H NMR spectra of **3f**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

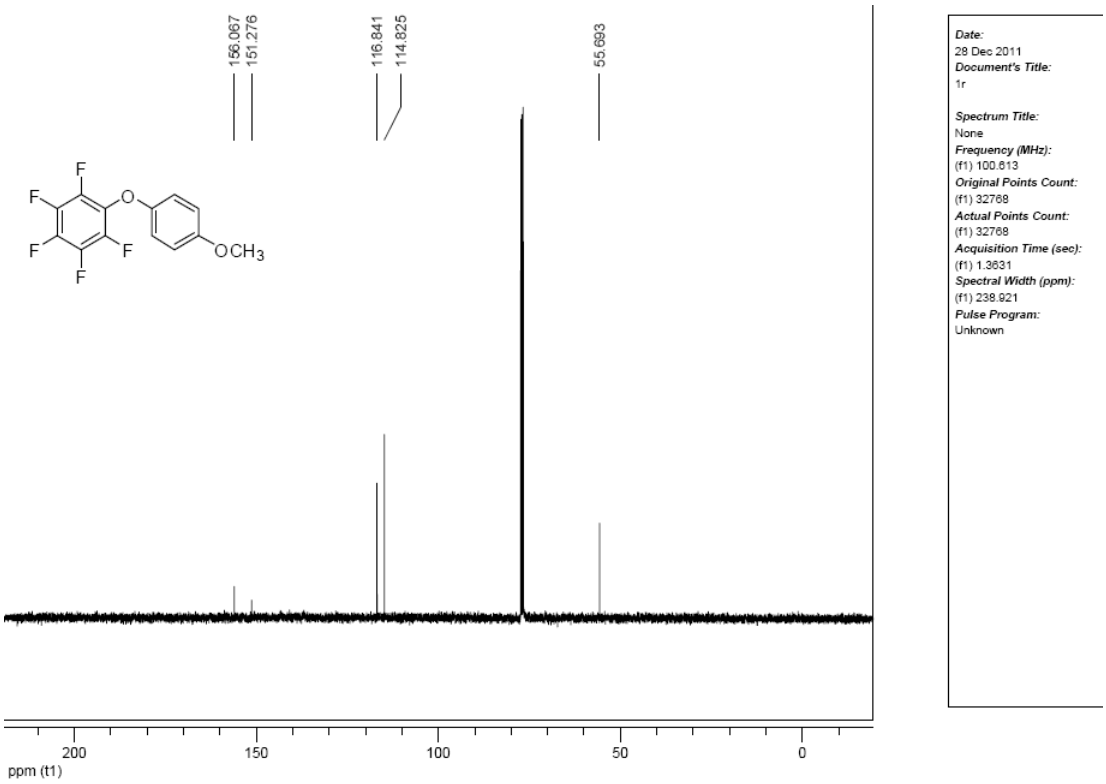
^{19}F NMR spectra of **3f**



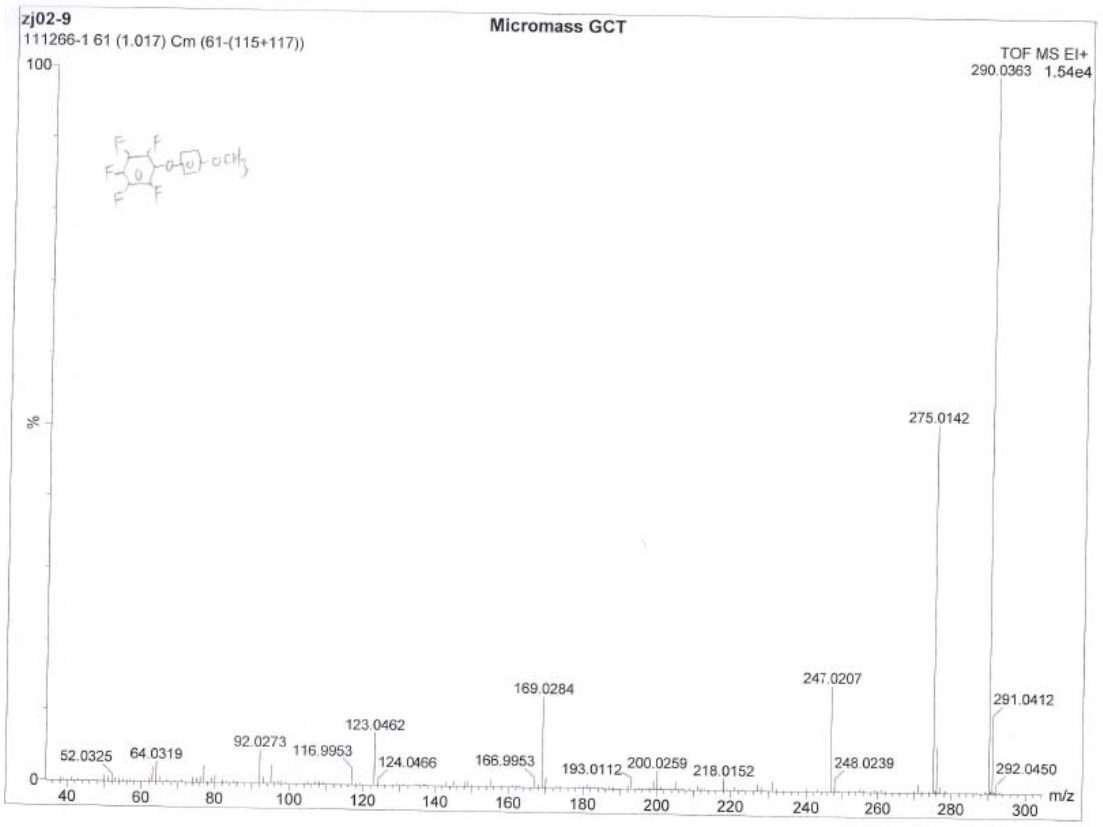
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

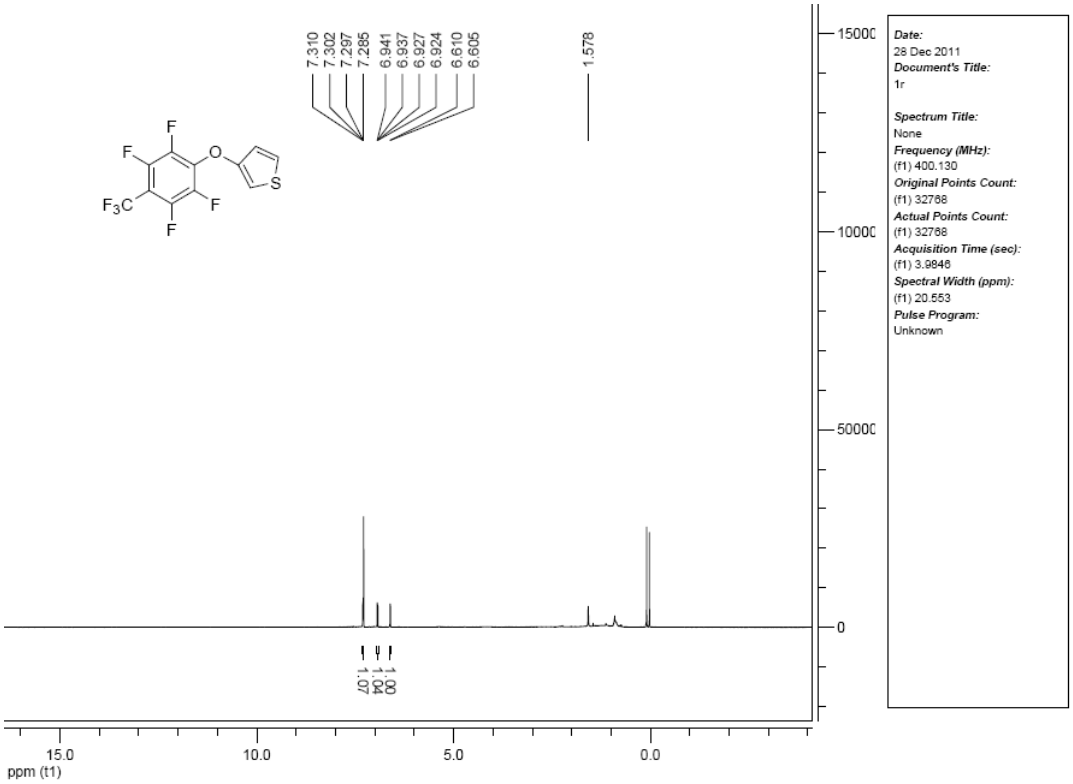
^{13}C NMR spectra of **3f**



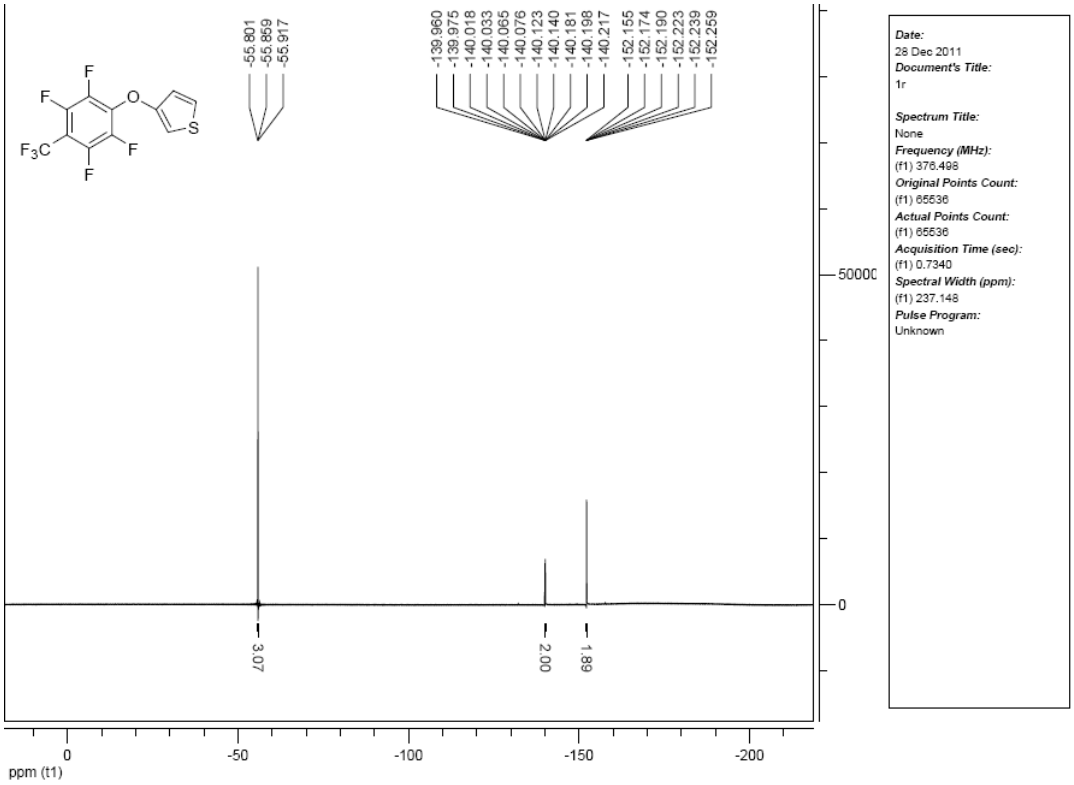
HRMS (EI) spectra of **3f**



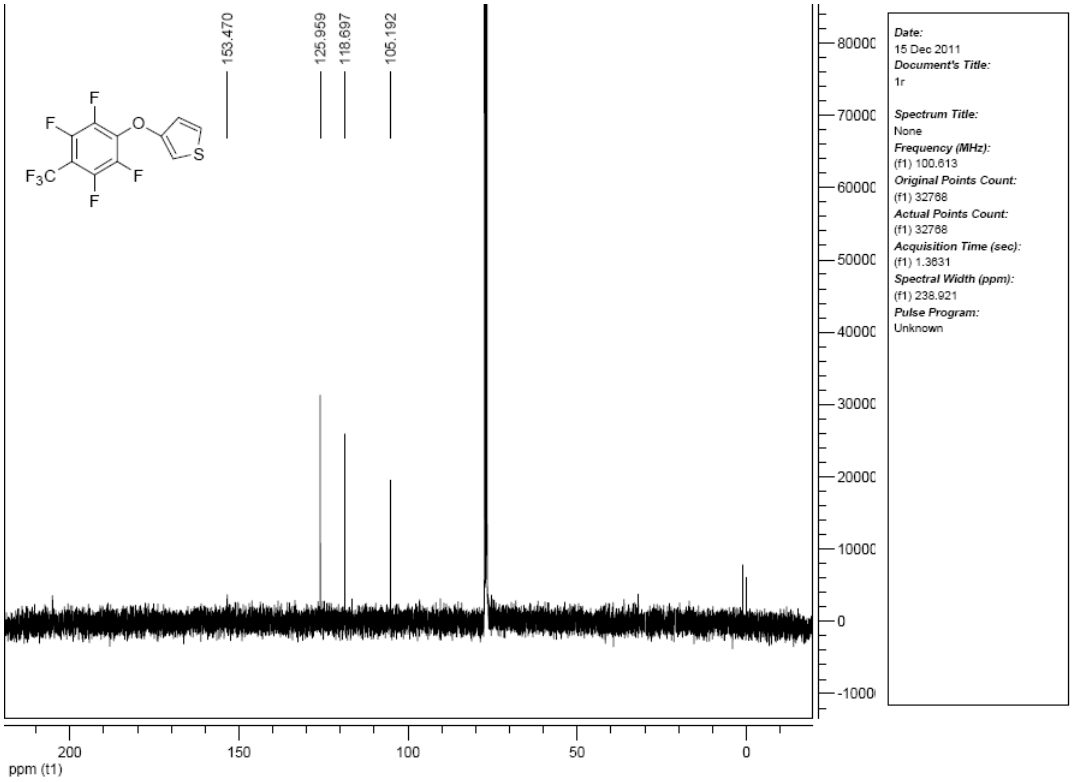
^{1}H NMR spectra of **3g**



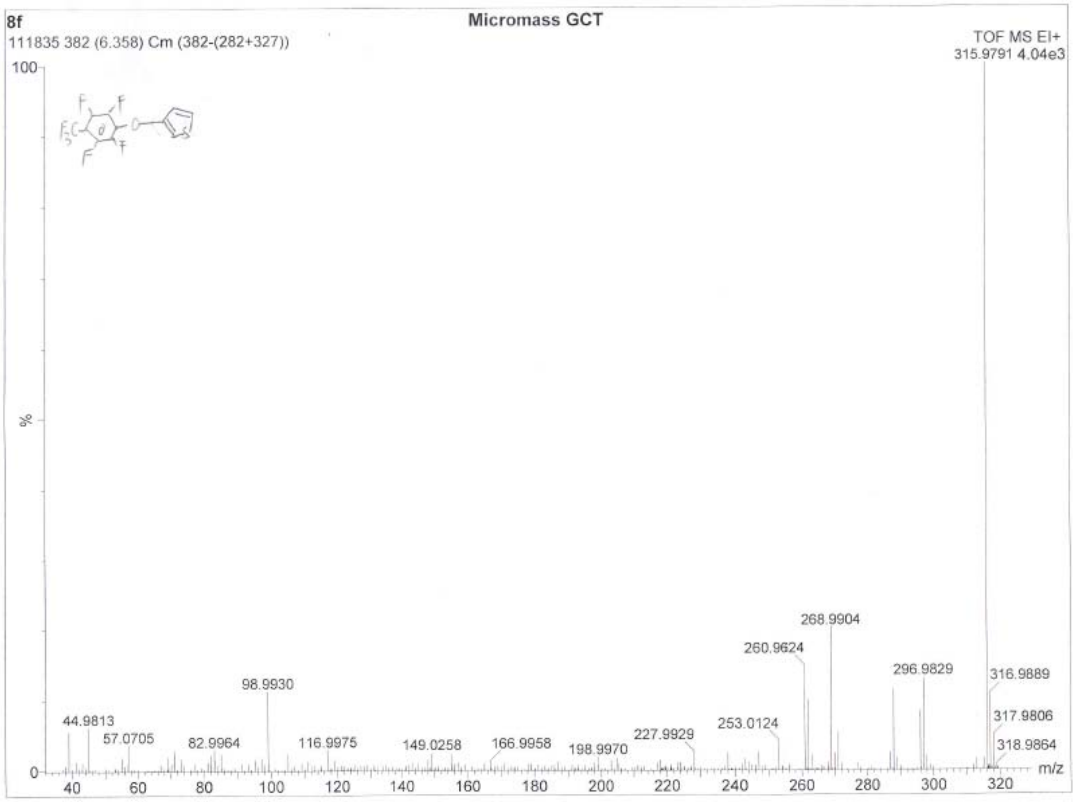
^{19}F NMR spectra of **3g**



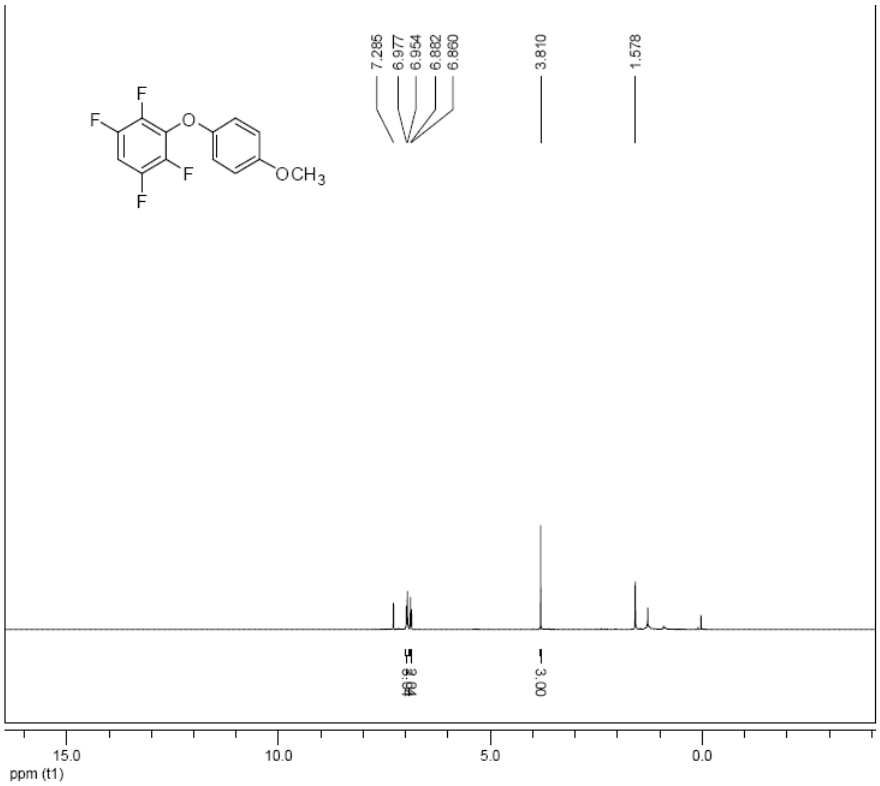
^{13}C NMR spectra of **3g**



HRMS (EI) spectra of **3g**



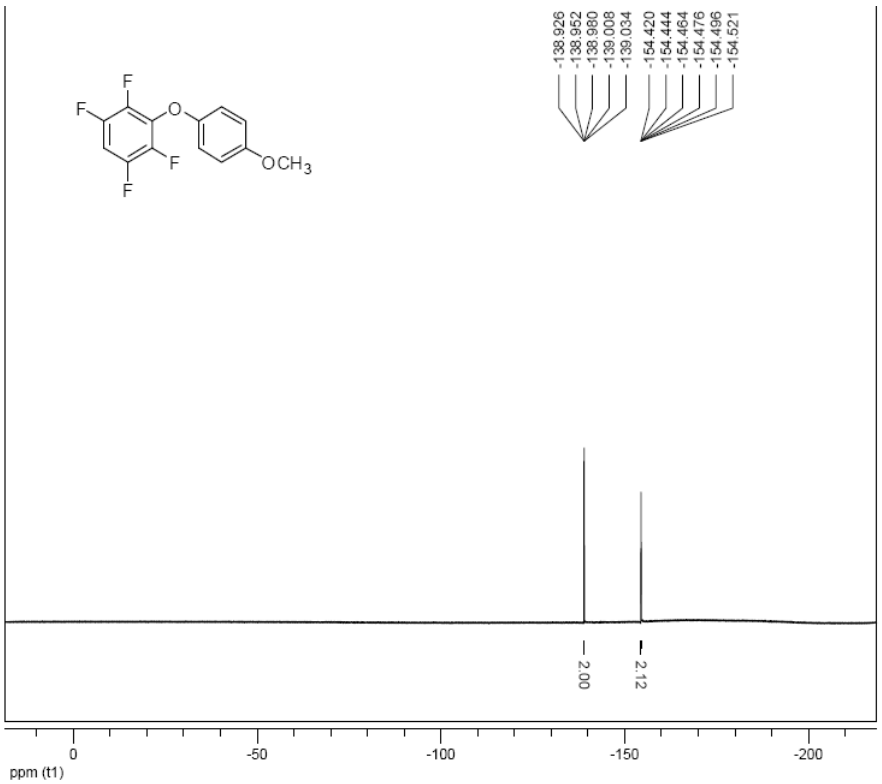
^{1}H NMR spectra of **3h**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

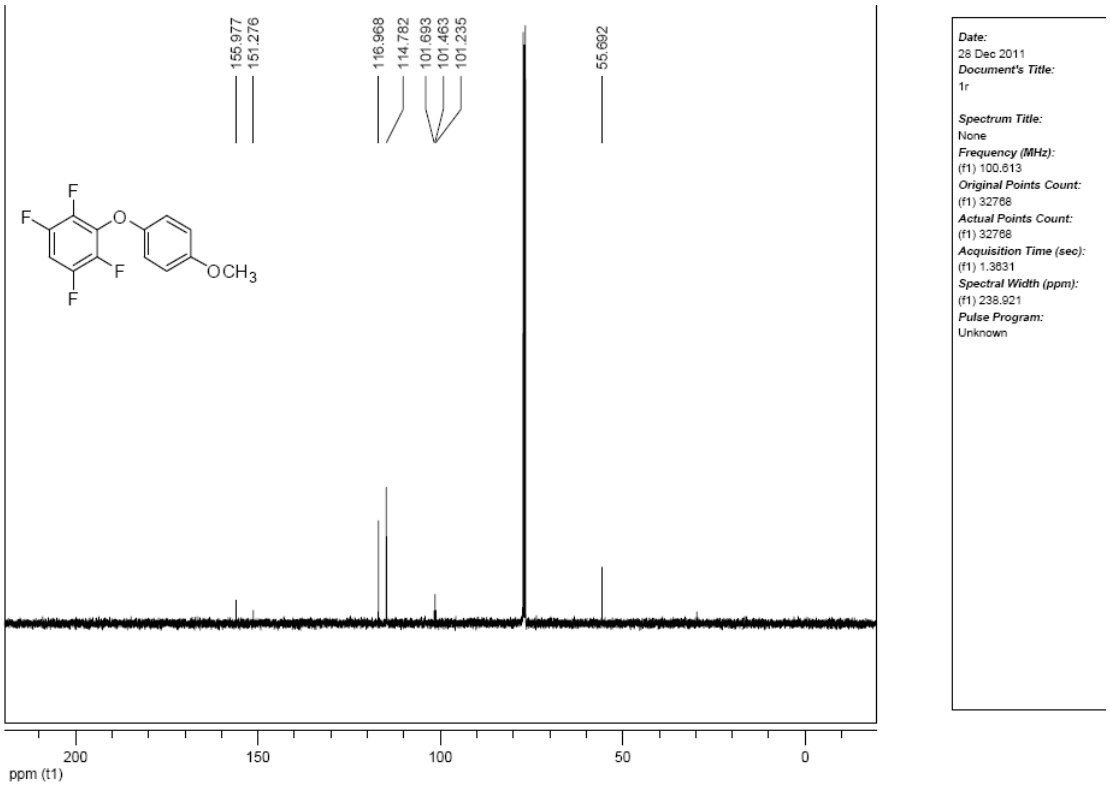
^{19}F NMR spectra of **3h**



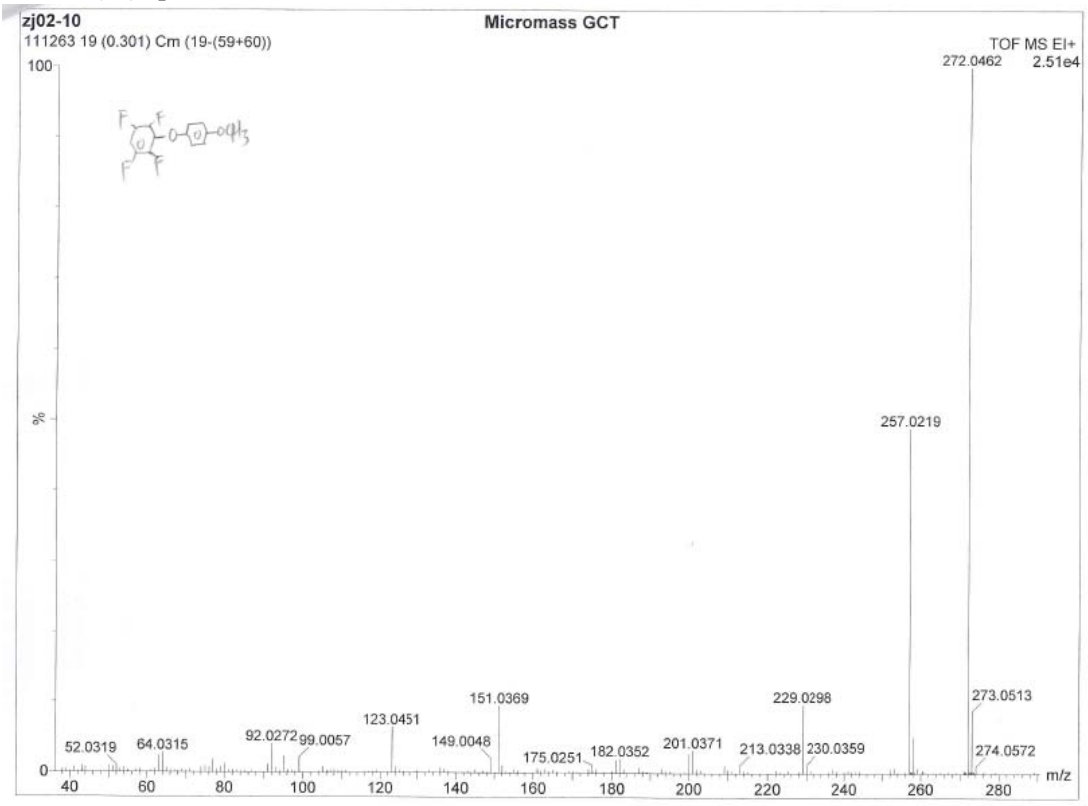
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

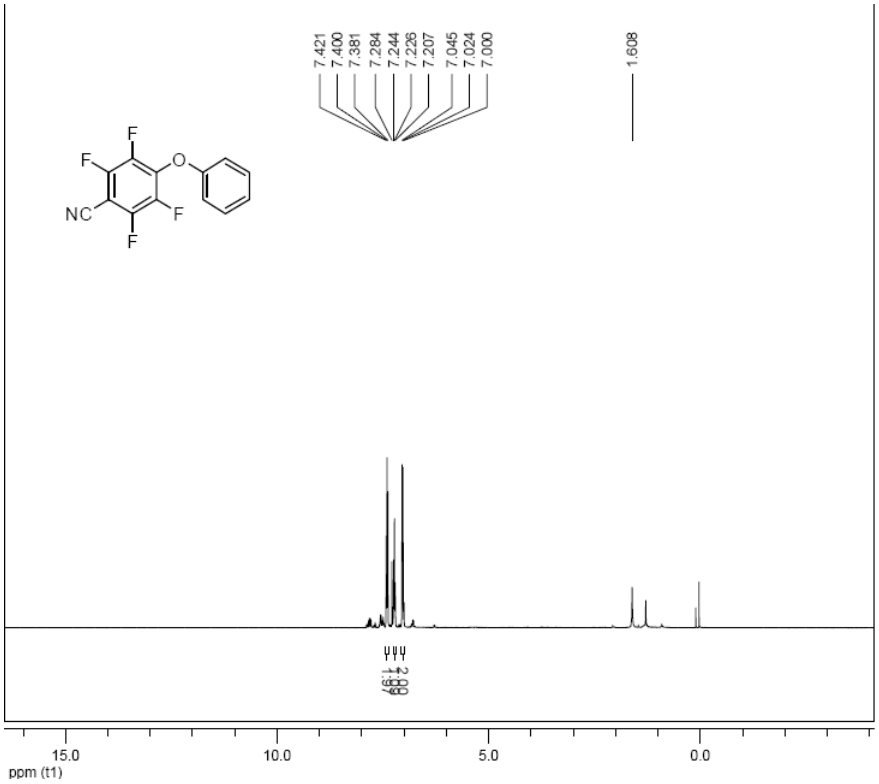
^{13}C NMR spectra of **3h**



HRMS (EI) spectra of **3h**



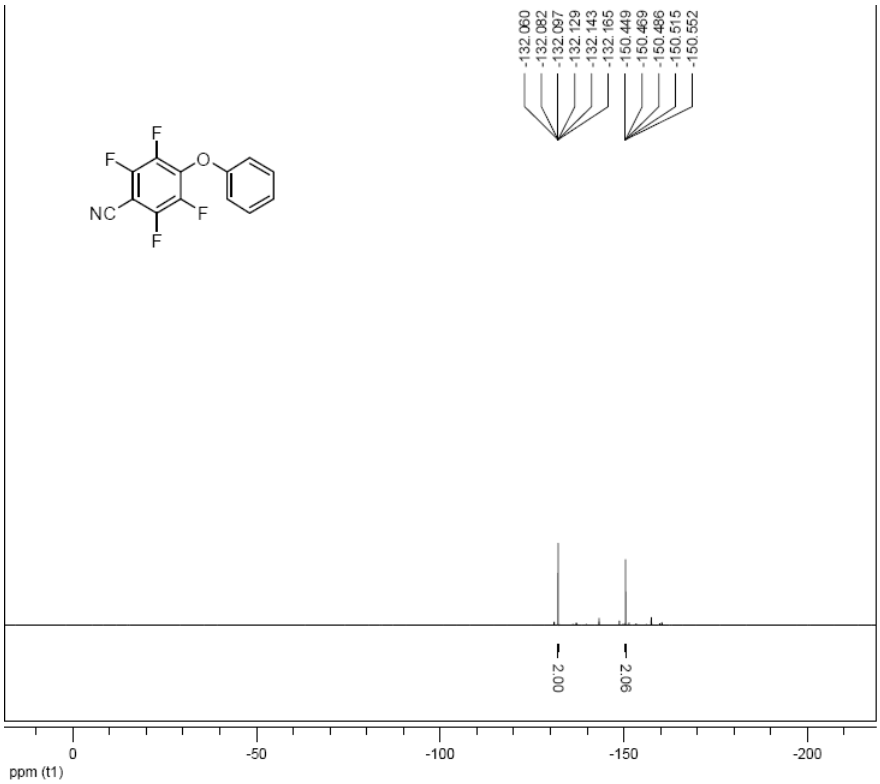
^{1}H NMR spectra of **3i**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

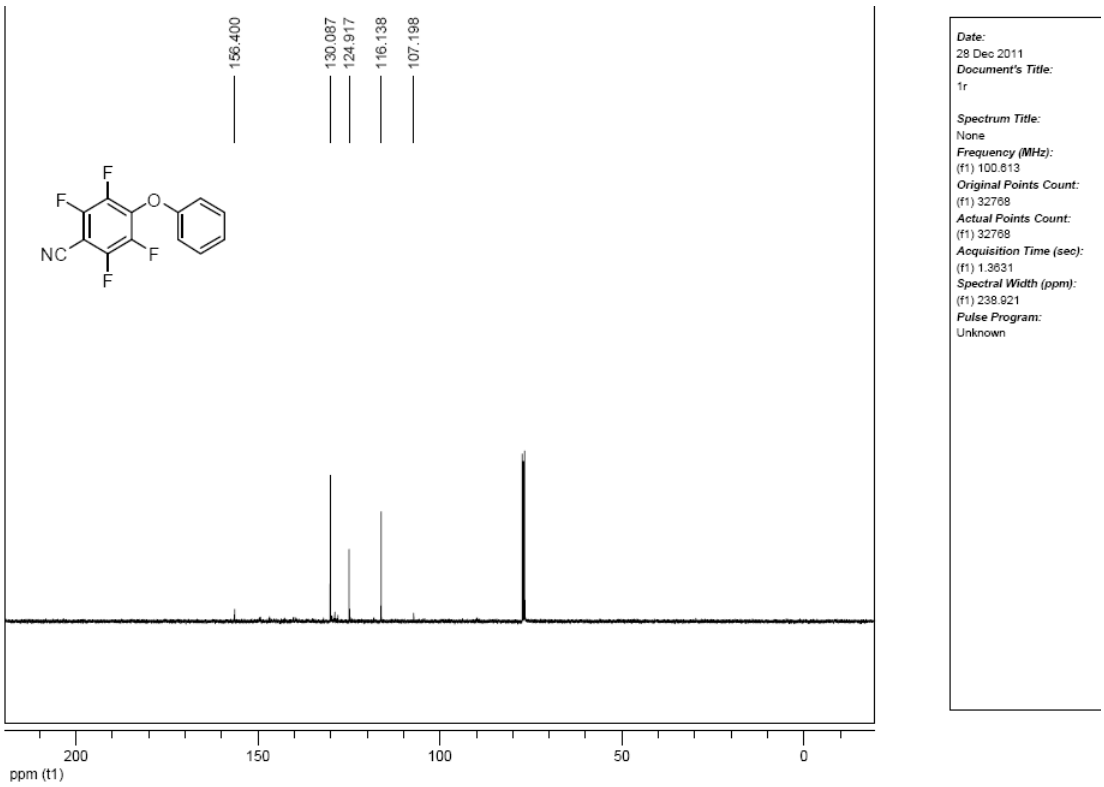
^{19}F NMR spectra of **3i**



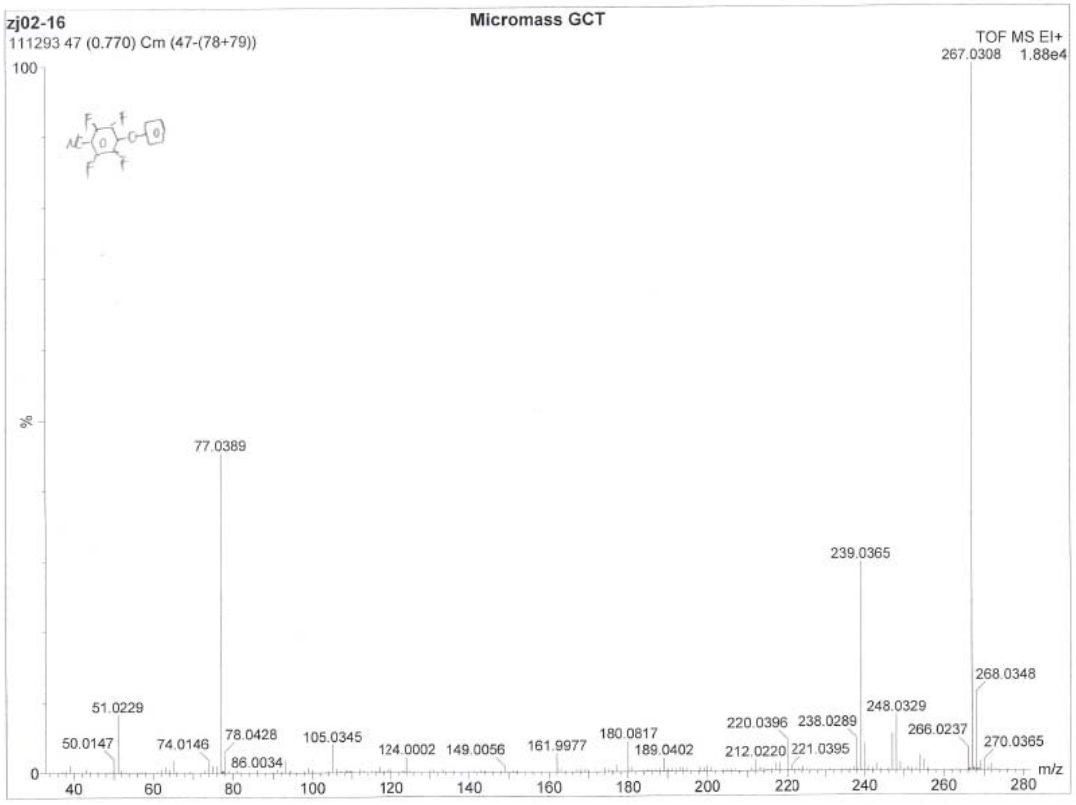
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

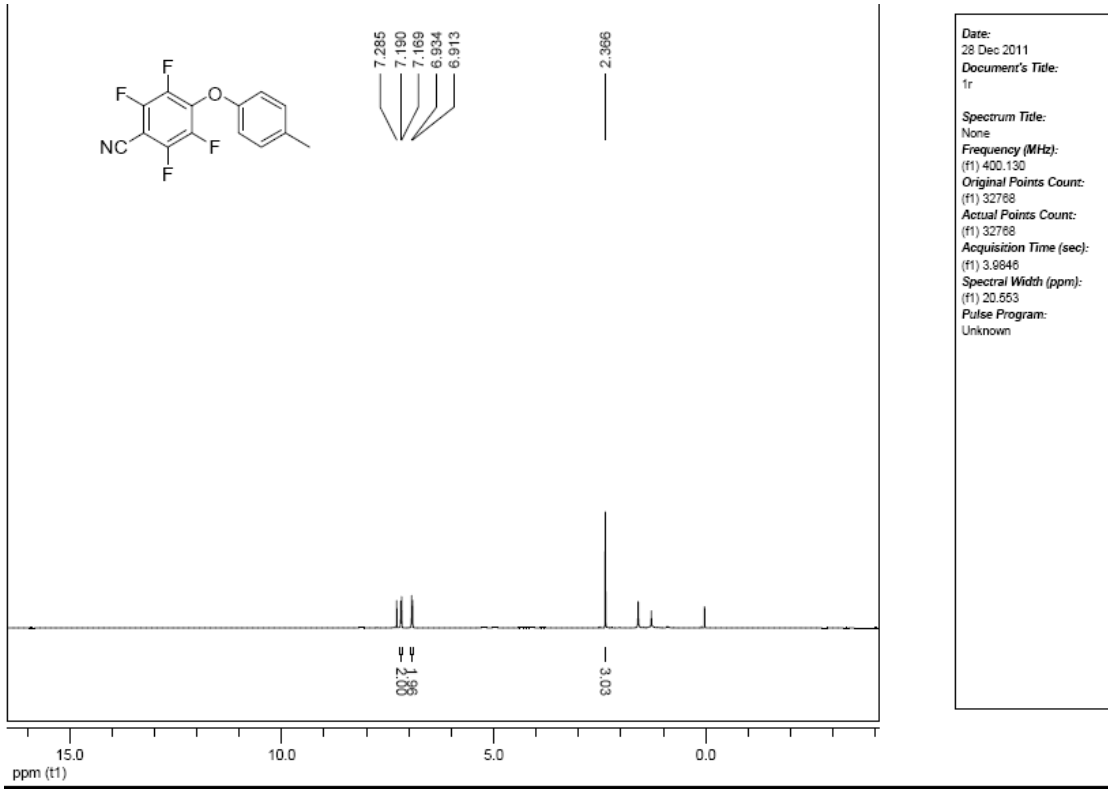
^{13}C NMR spectra of **3i**



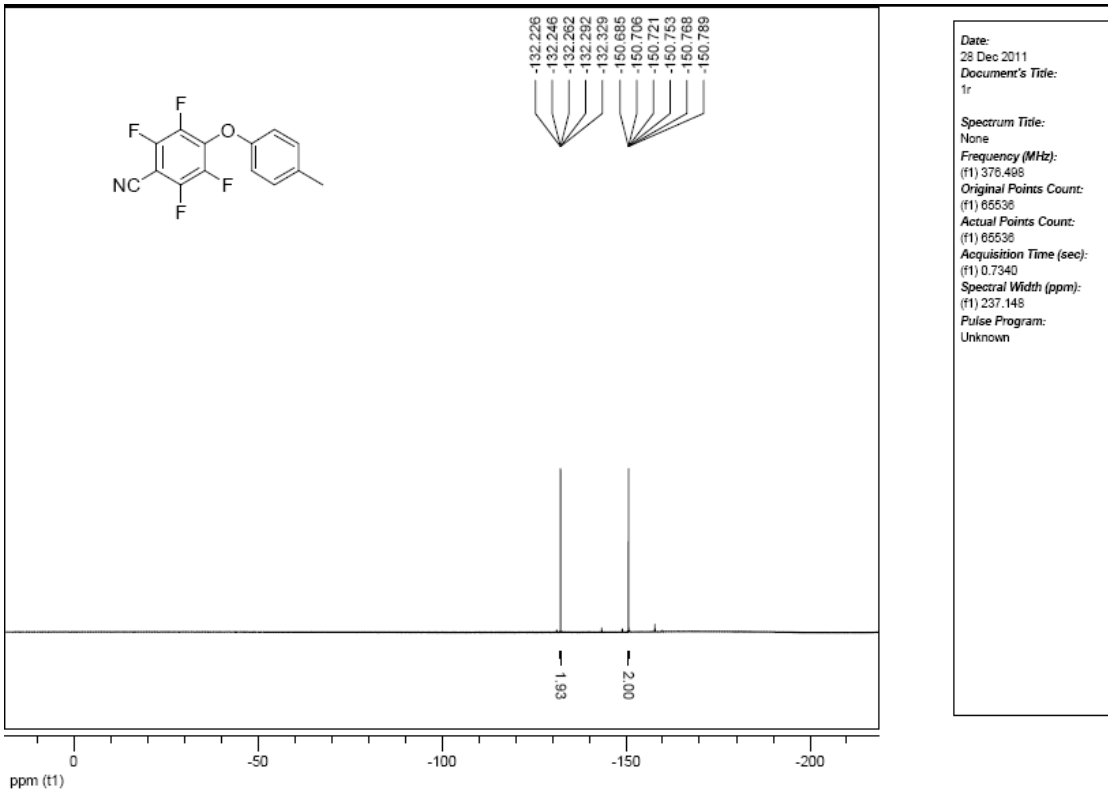
HRMS (EI) spectra of **3i**



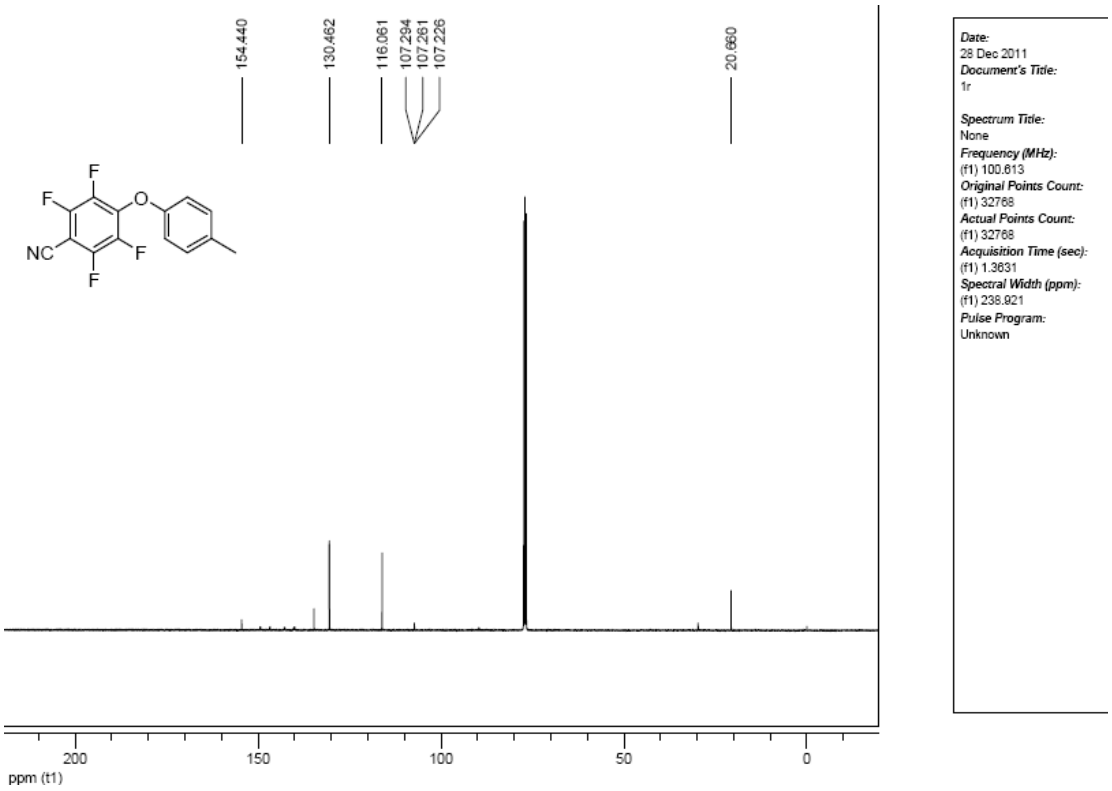
^{1}H NMR spectra of **3j**



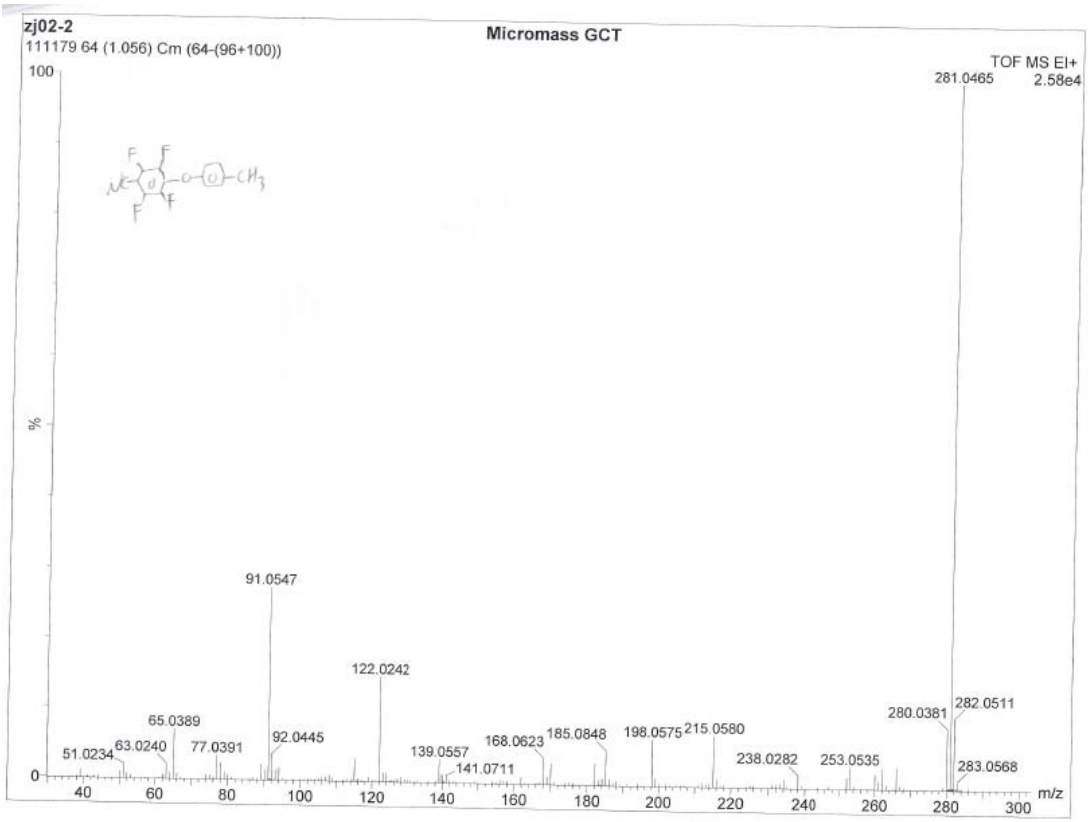
^{19}F NMR spectra of **3j**



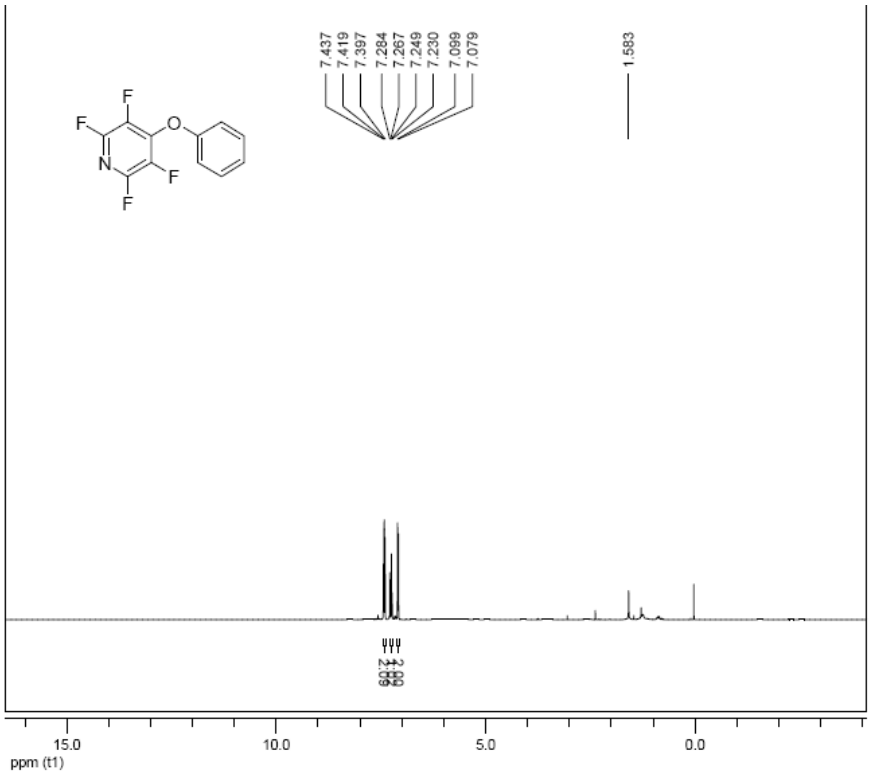
^{13}C NMR spectra of **3j**



HRMS (EI) spectra of **3j**



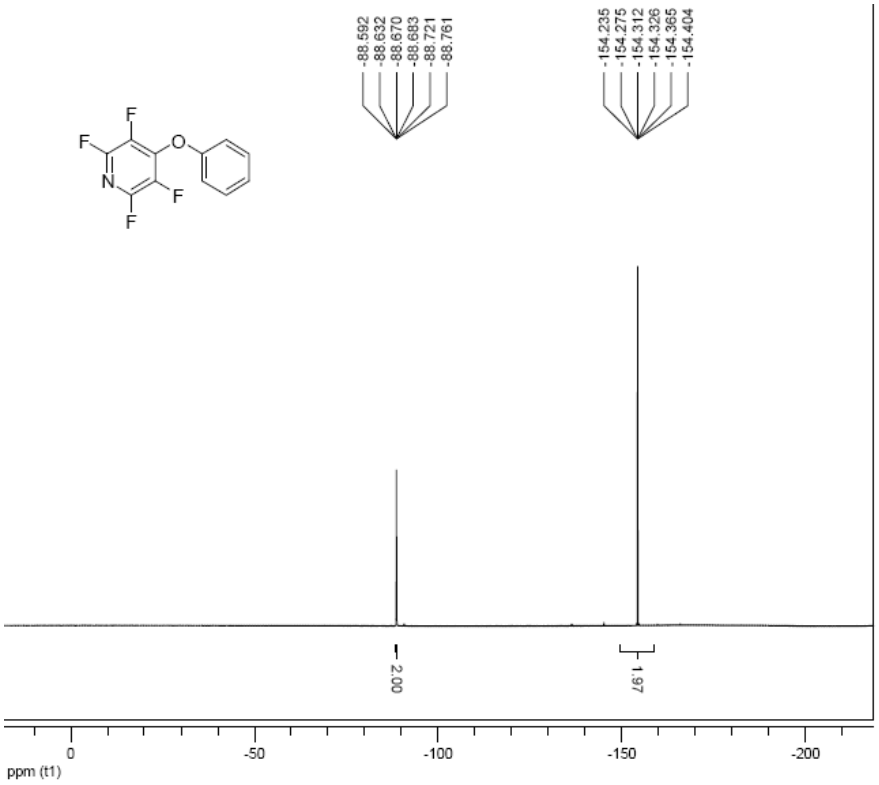
^{1}H NMR spectra of **3k**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

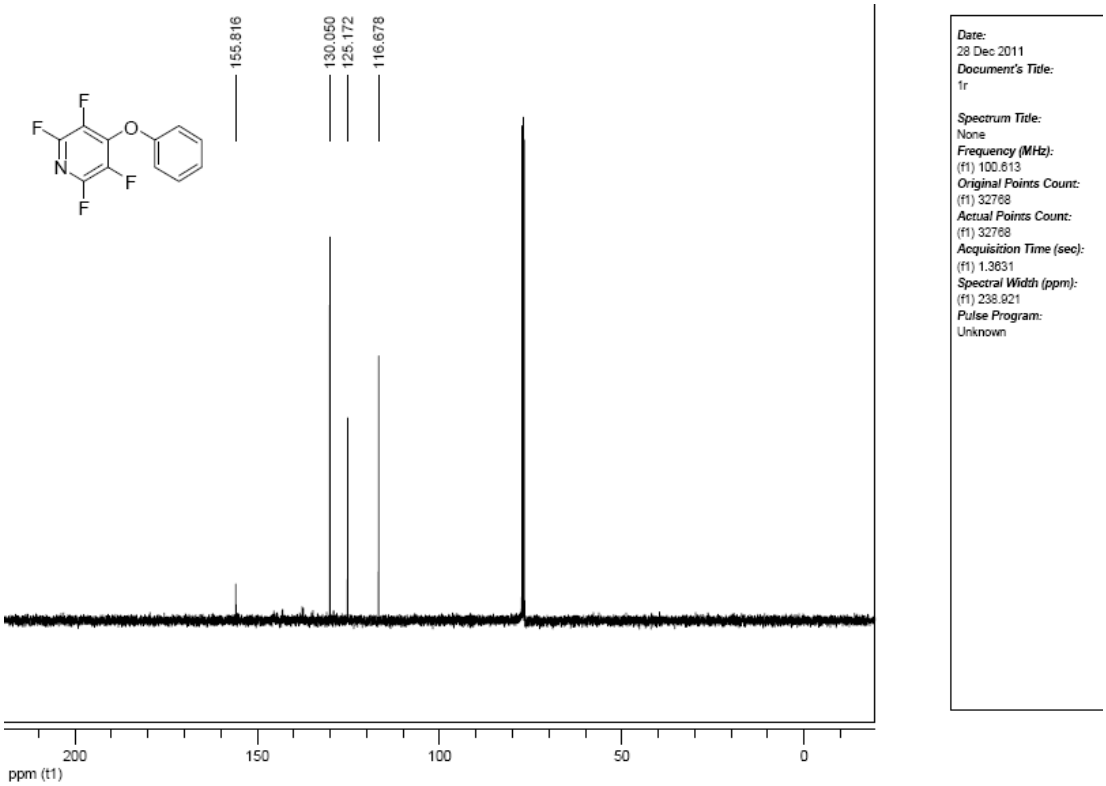
^{19}F NMR spectra of **3k**



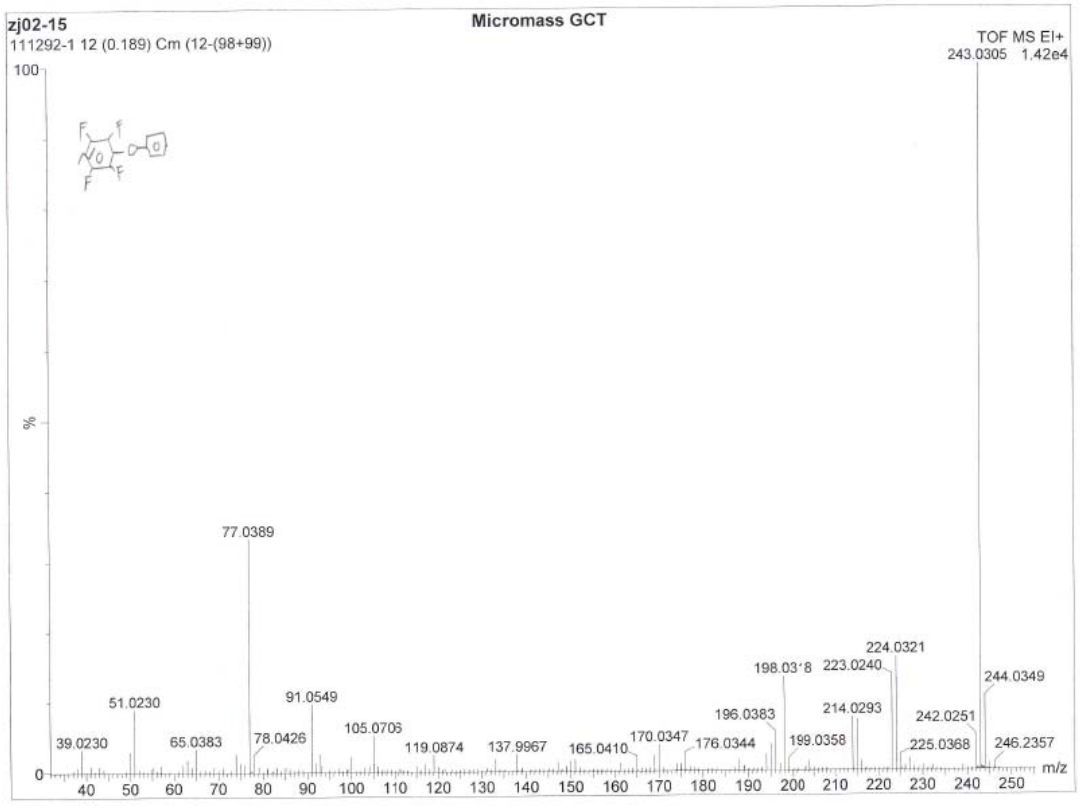
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

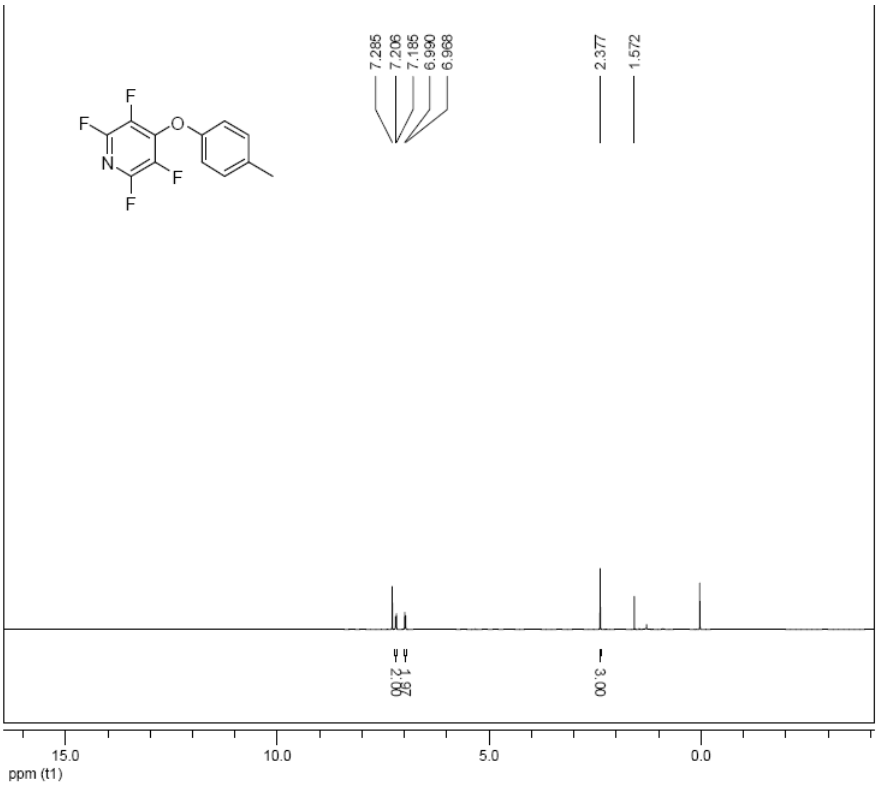
^{13}C NMR spectra of **3k**



HRMS (EI) spectra of **3k**



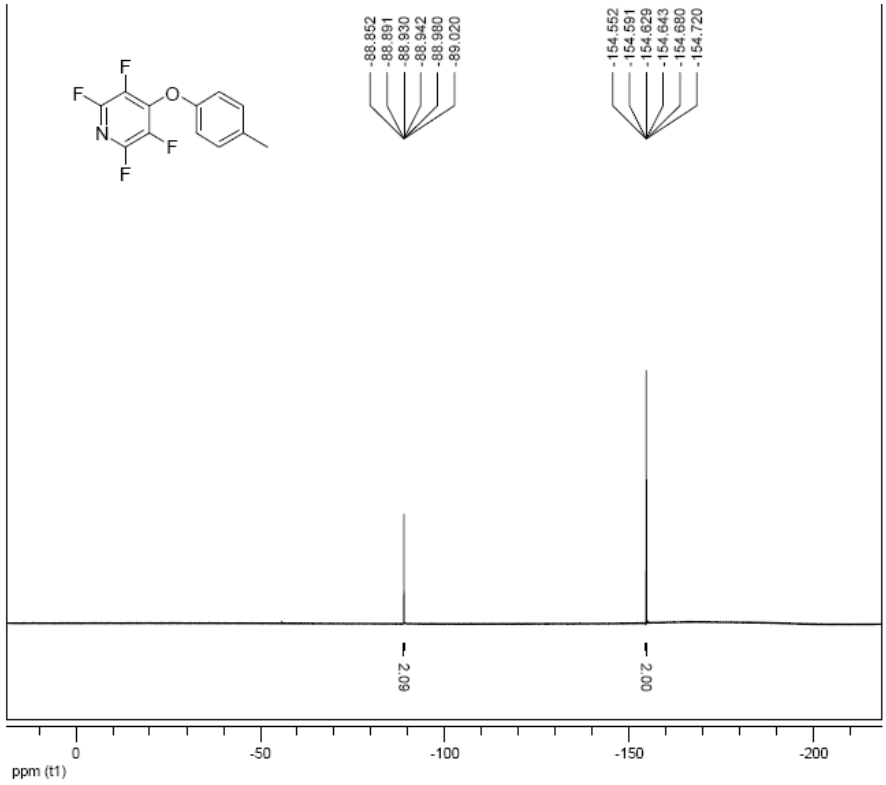
^{1}H NMR spectra of **3l**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

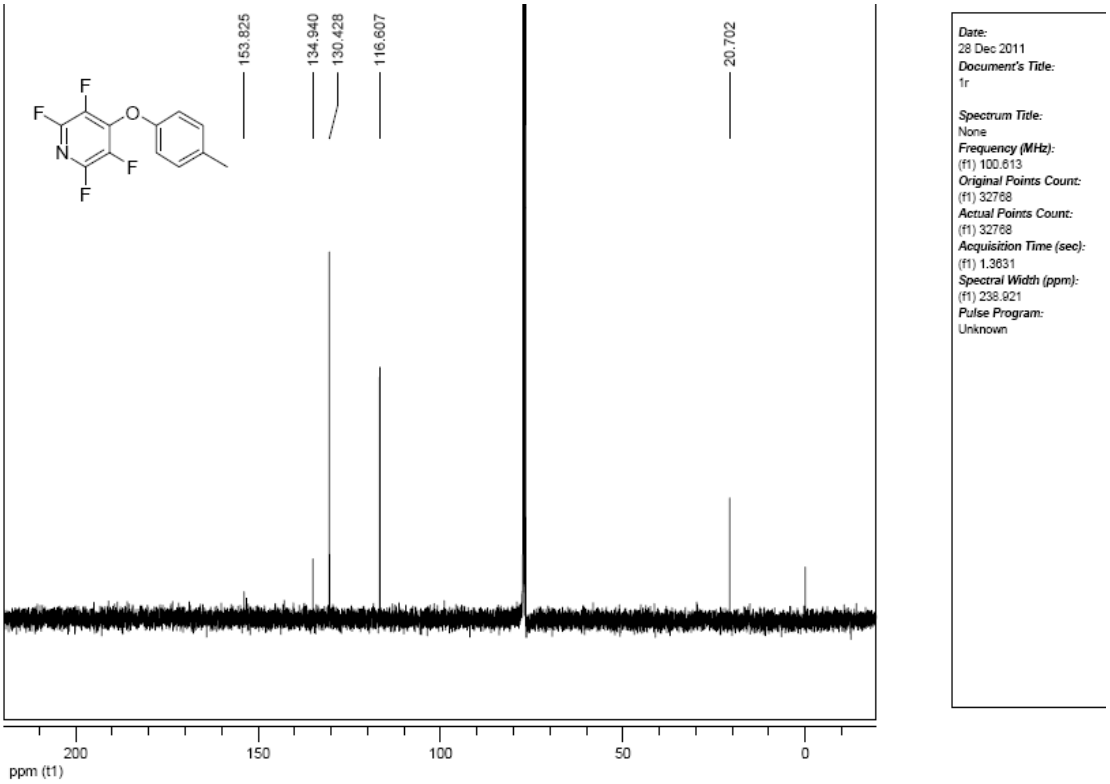
^{19}F NMR spectra of **3l**



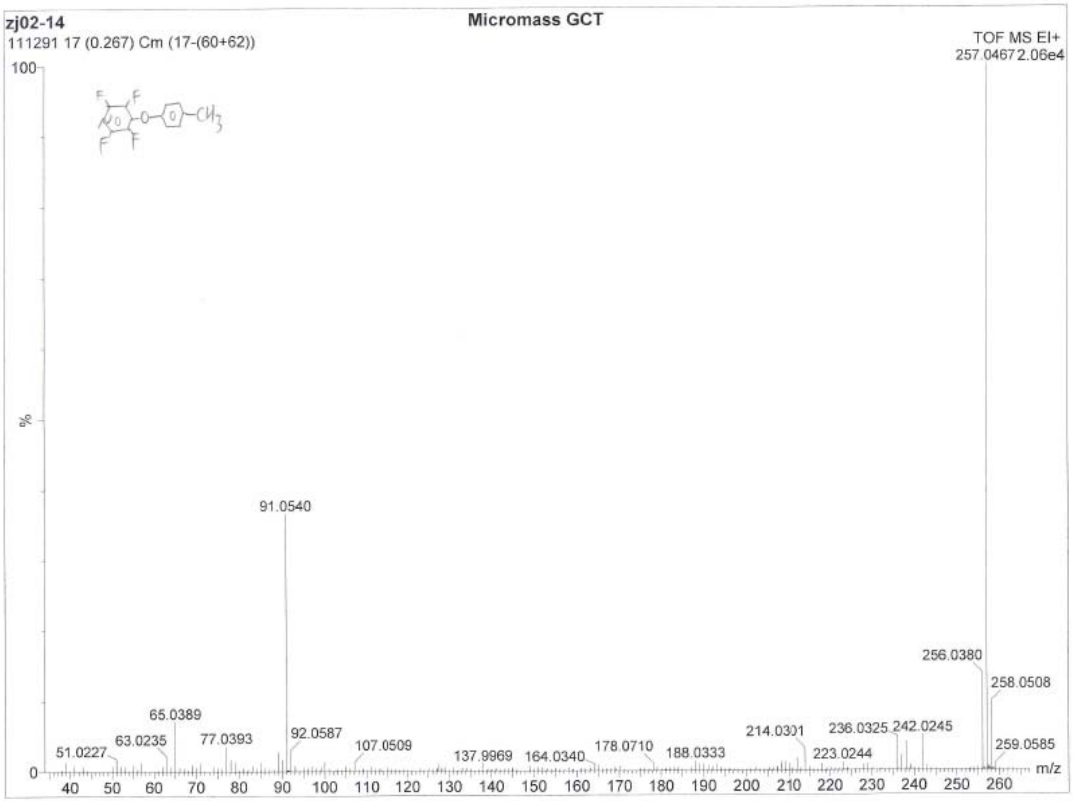
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

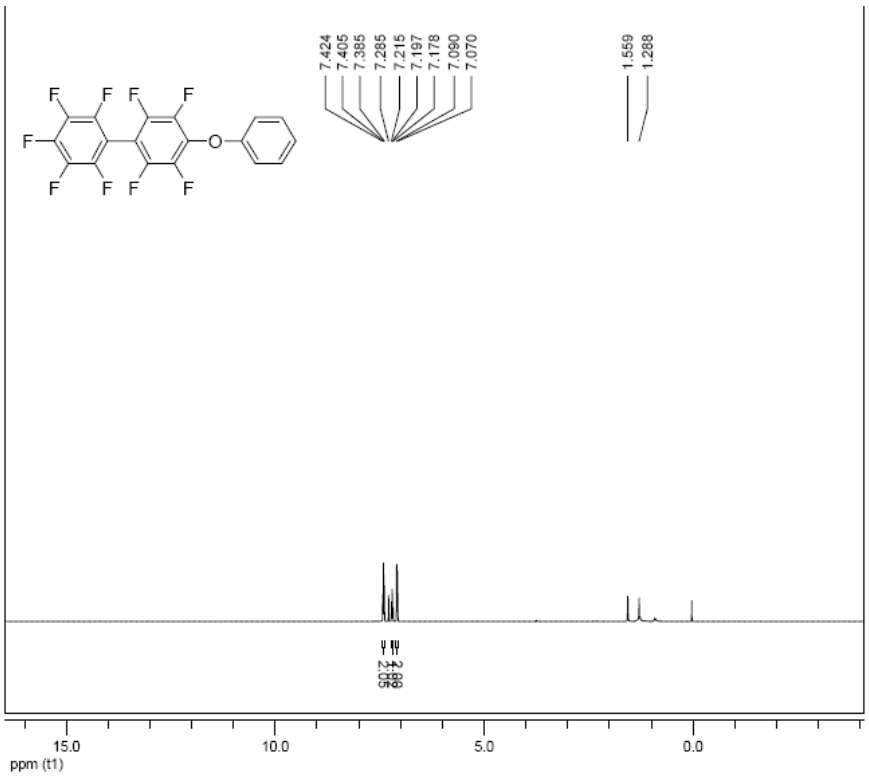
^{13}C NMR spectra of **3l**



HRMS (EI) spectra of **3l**



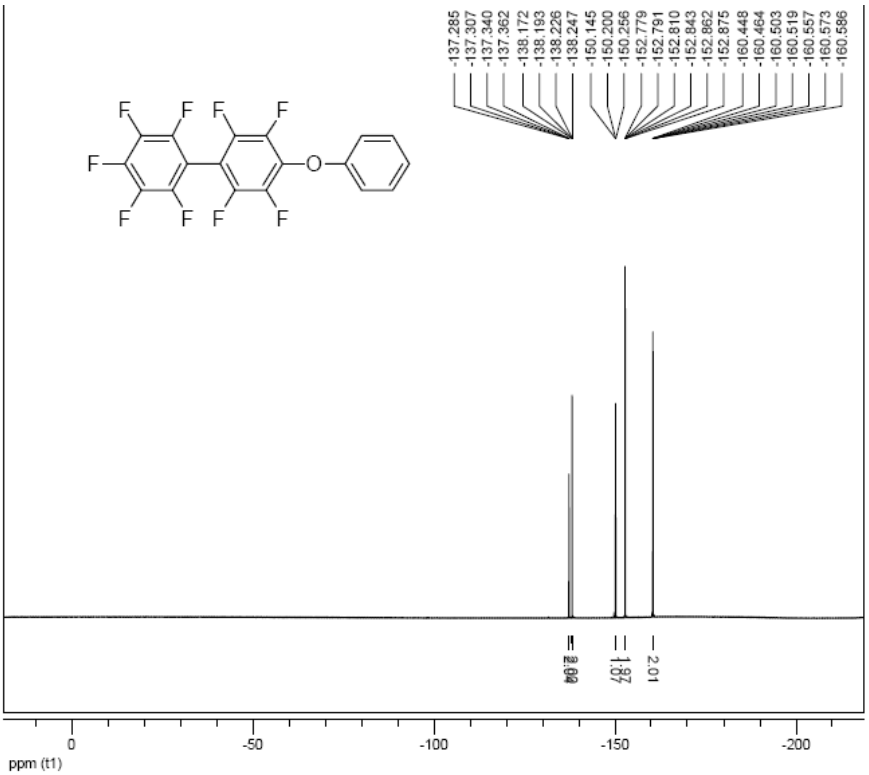
^{1}H NMR spectra of **3m**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

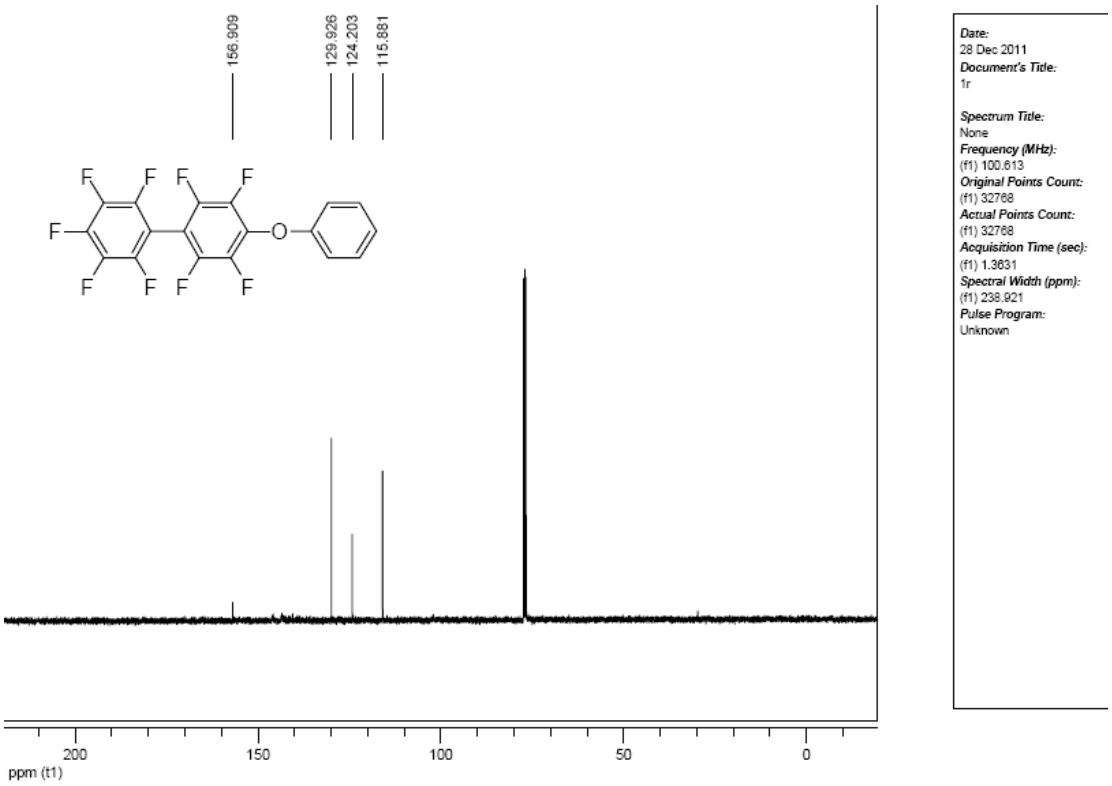
^{19}F NMR spectra of **3m**



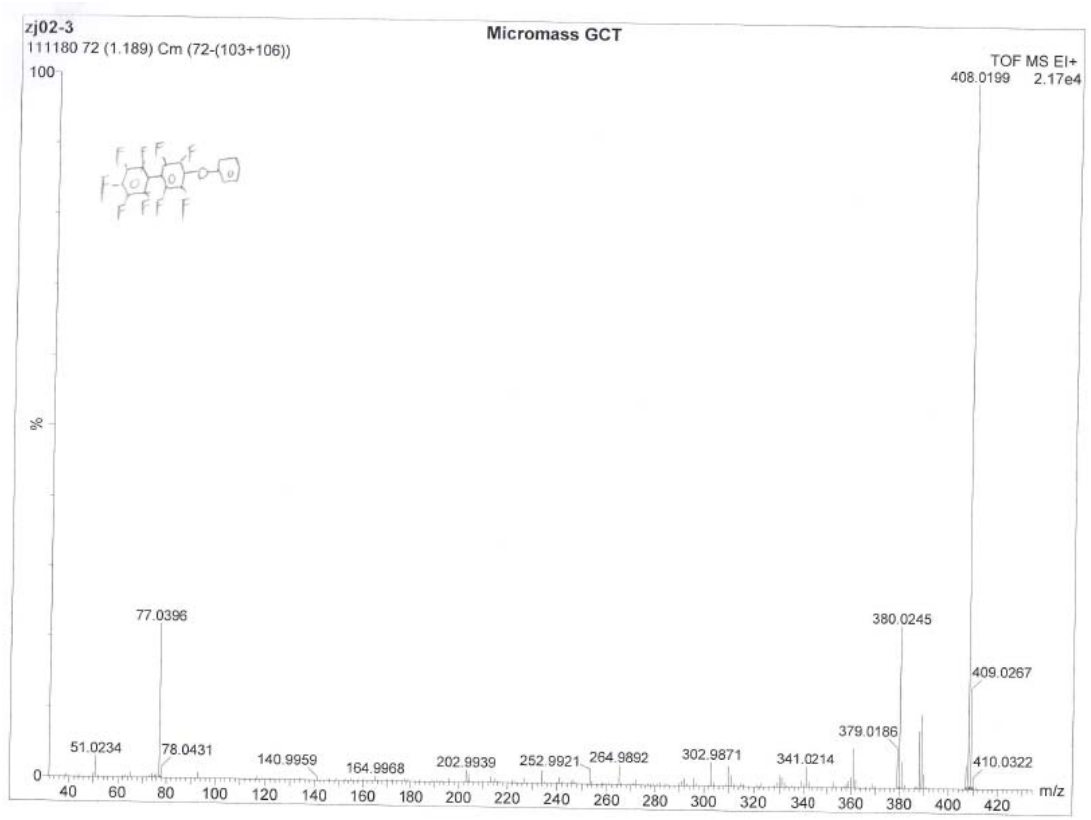
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

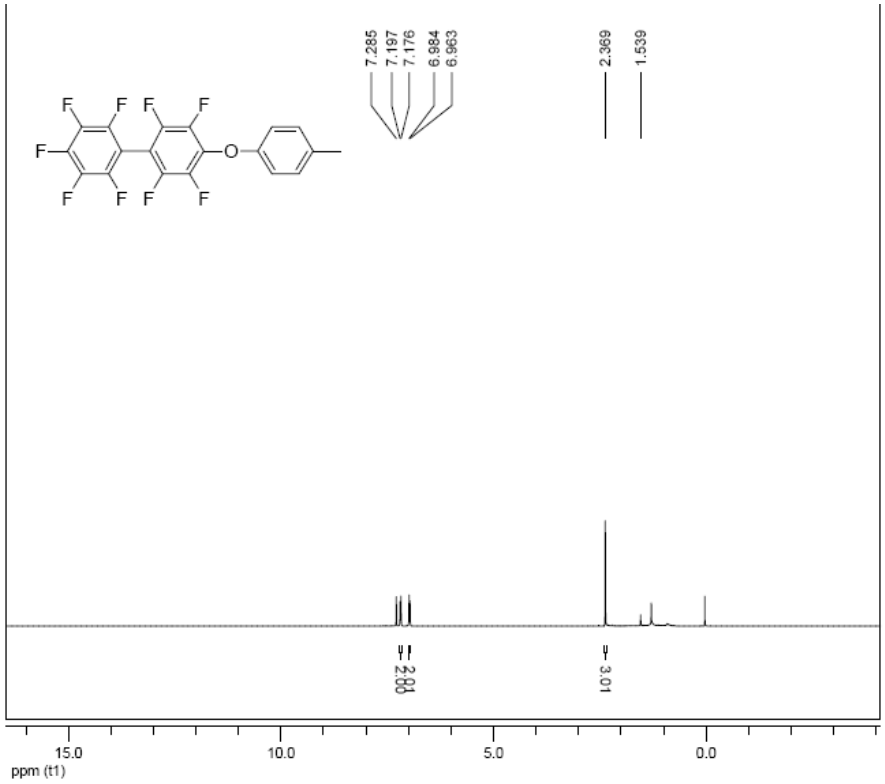
^{13}C NMR spectra of **3m**



HRMS (EI) spectra of **3m**



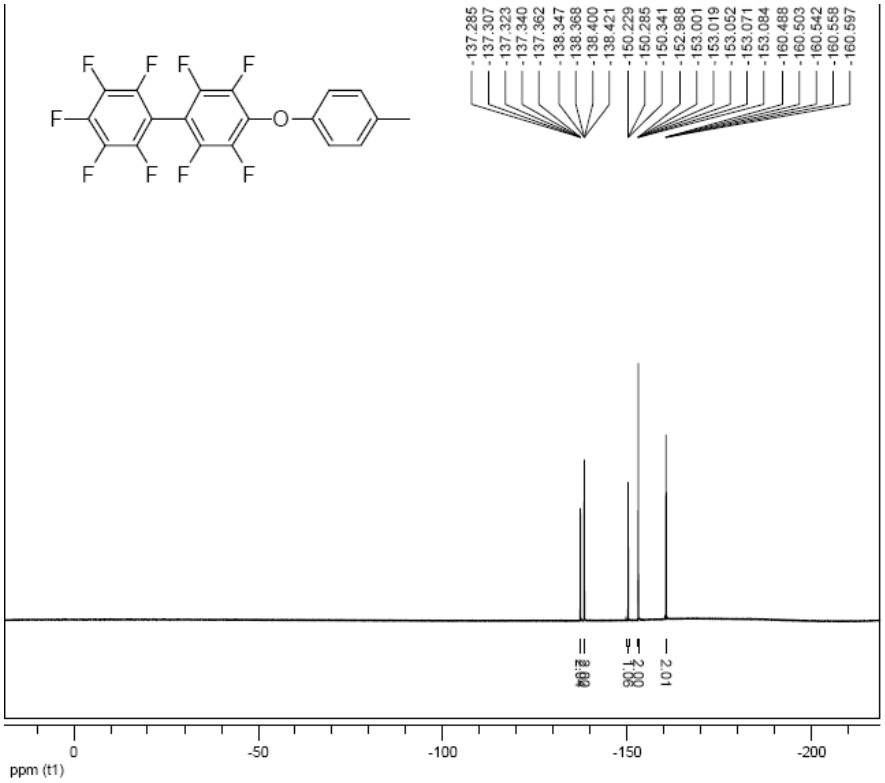
^{1}H NMR spectra of **3n**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

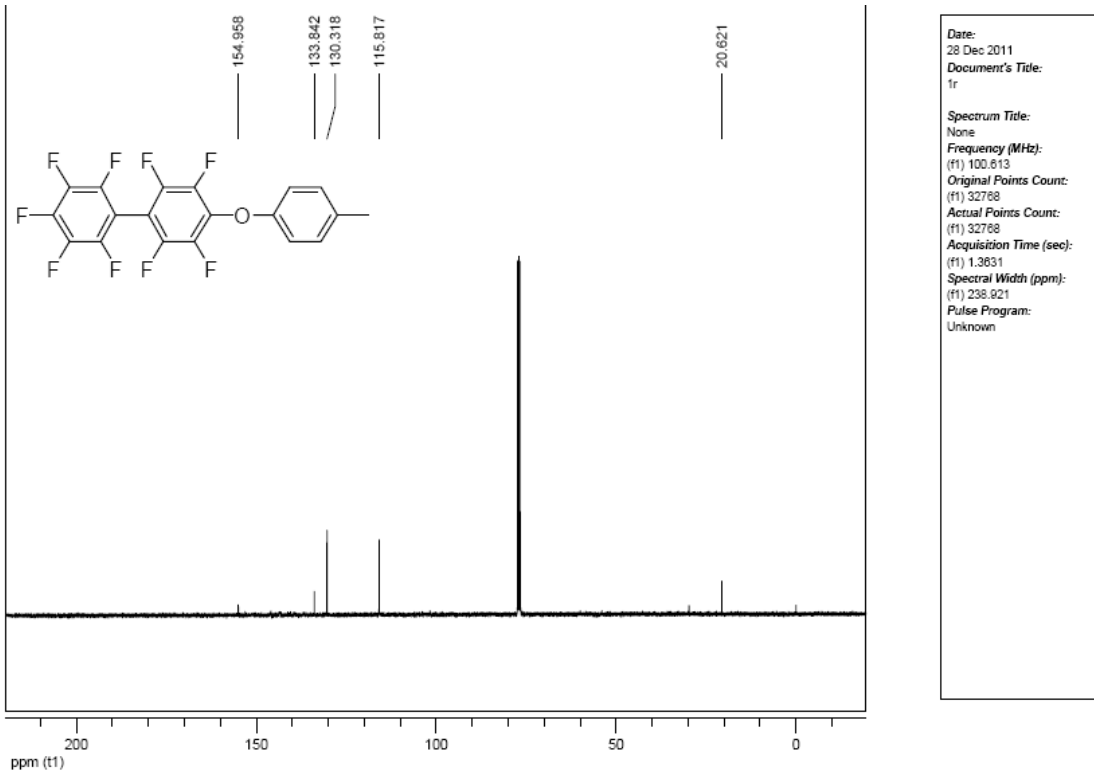
^{19}F NMR spectra of **3n**



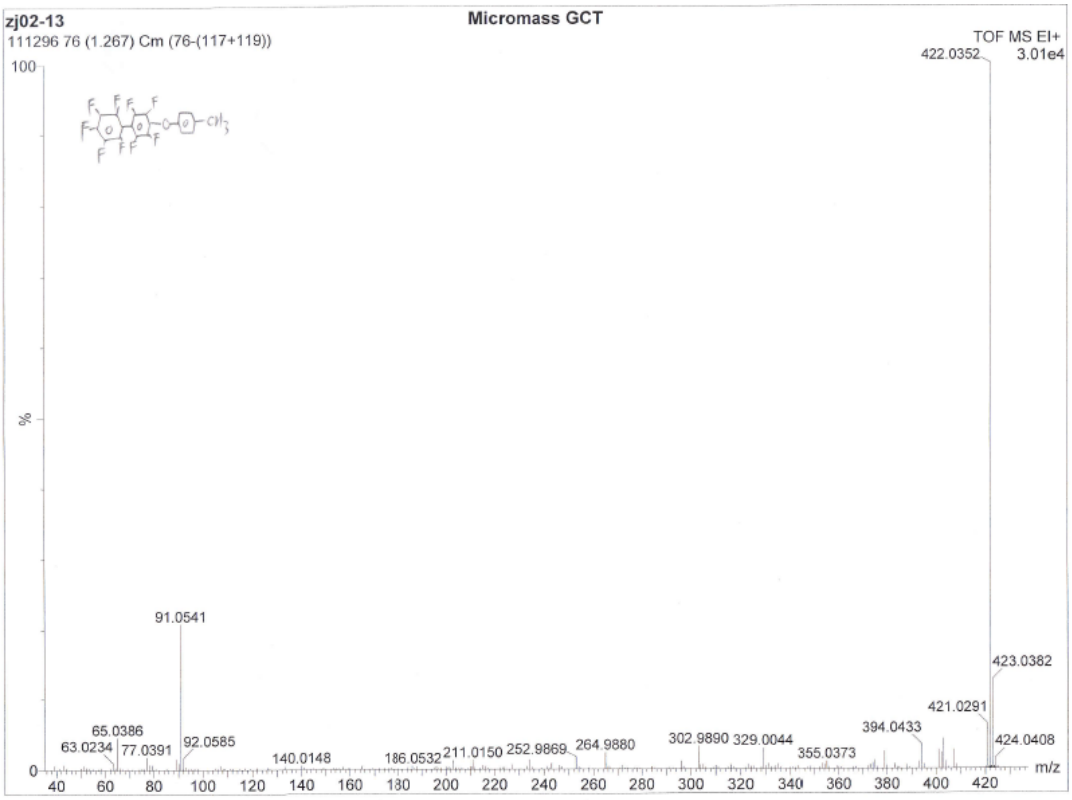
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 376.498
Original Points Count:
(f1) 65536
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 0.7340
Spectral Width (ppm):
(f1) 237.148
Pulse Program:
Unknown

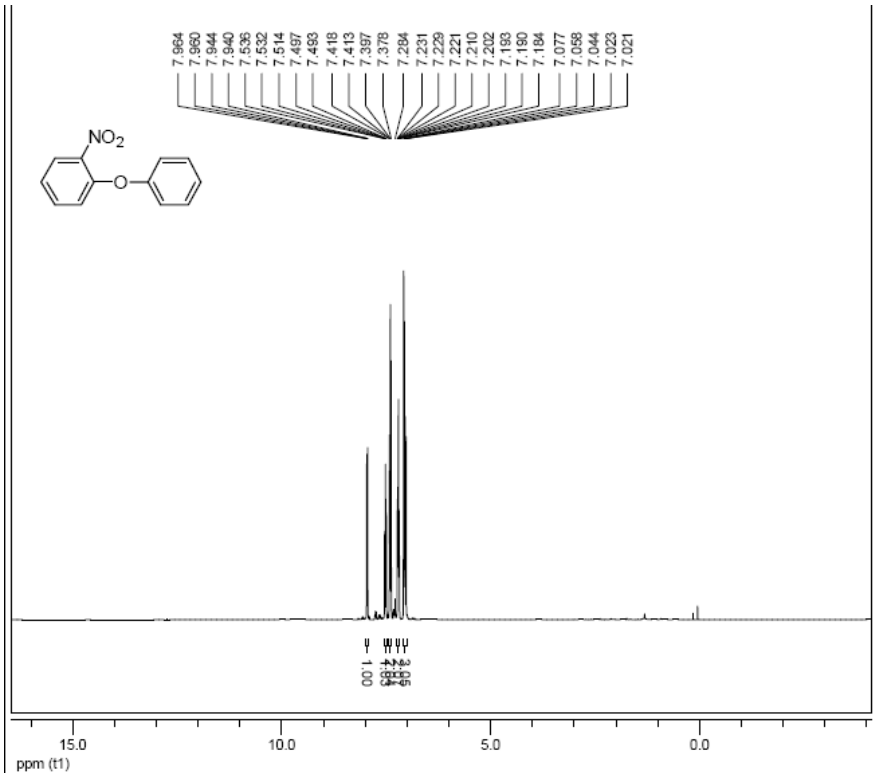
^{13}C NMR spectra of **3n**



HRMS (EI) spectra of **3n**



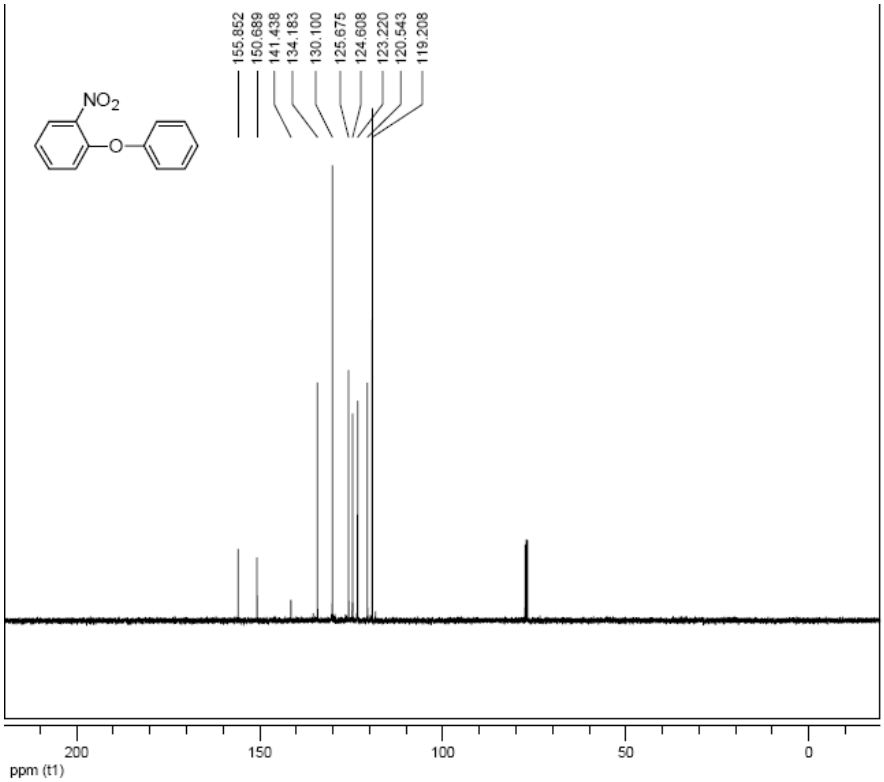
^{1}H NMR spectra of **3o**



Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9846
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
Unknown

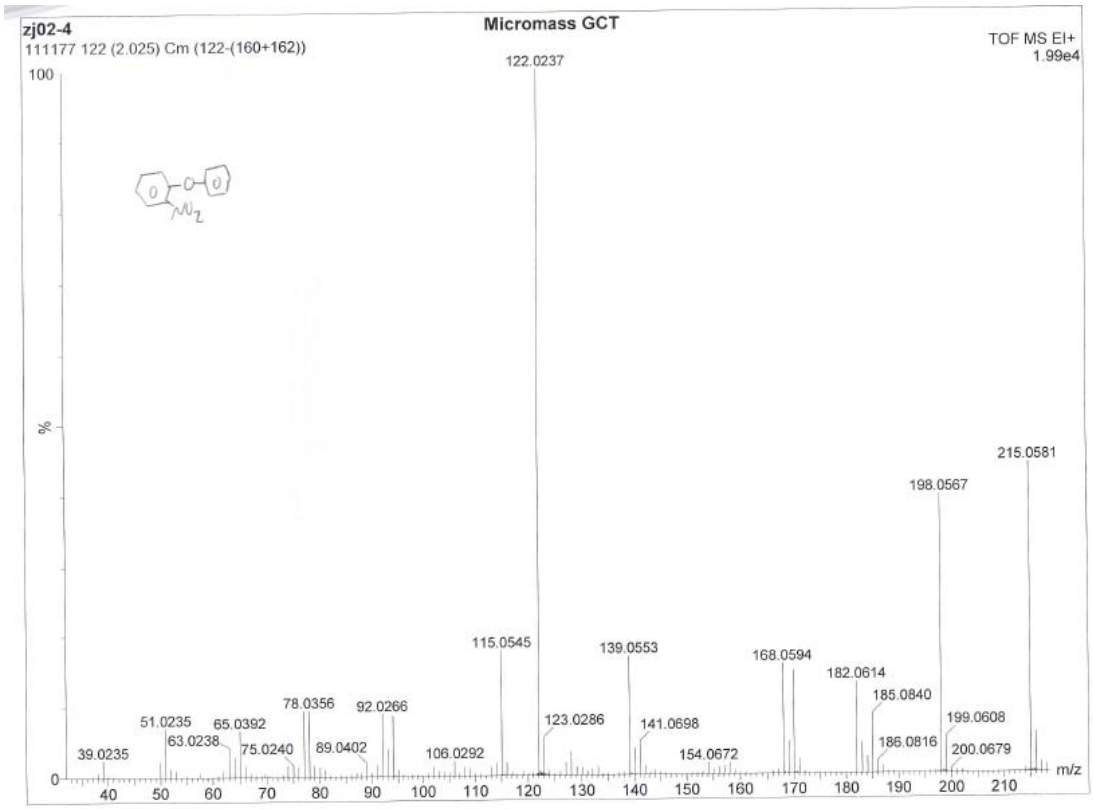
^{13}C NMR spectra of **3o**



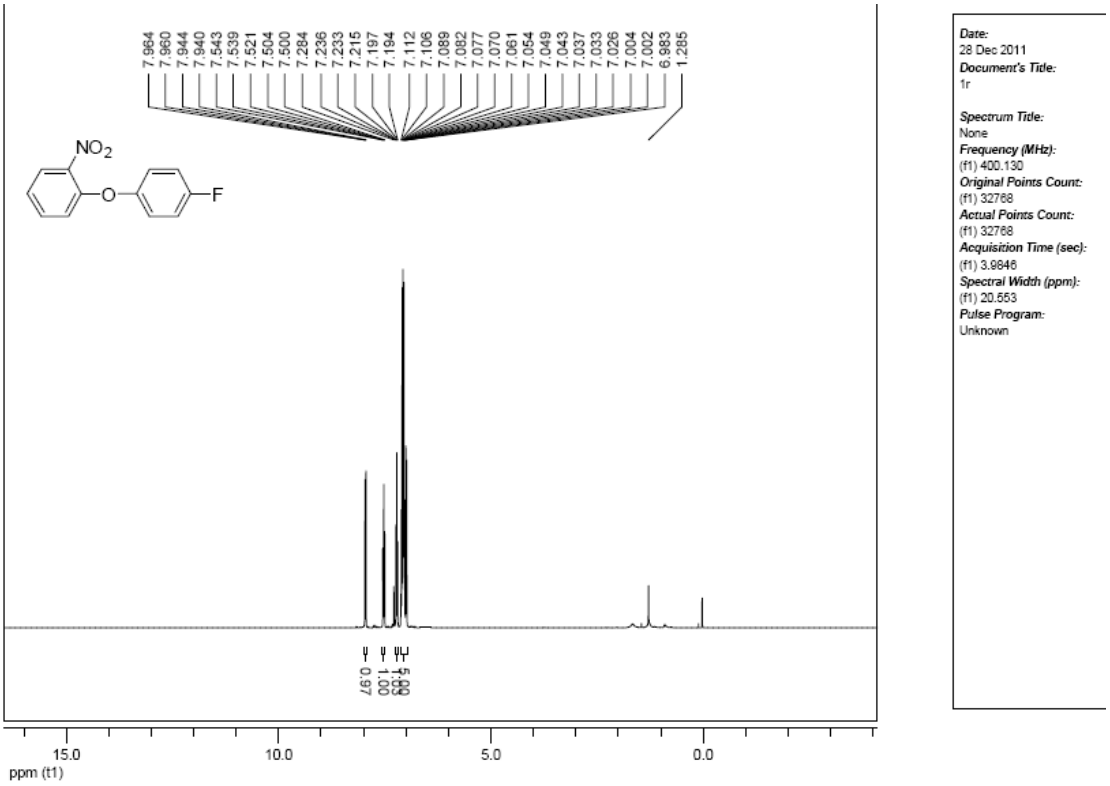
Date:
28 Dec 2011
Document's Title:
1r

Spectrum Title:
None
Frequency (MHz):
(f1) 100.613
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.3631
Spectral Width (ppm):
(f1) 238.921
Pulse Program:
Unknown

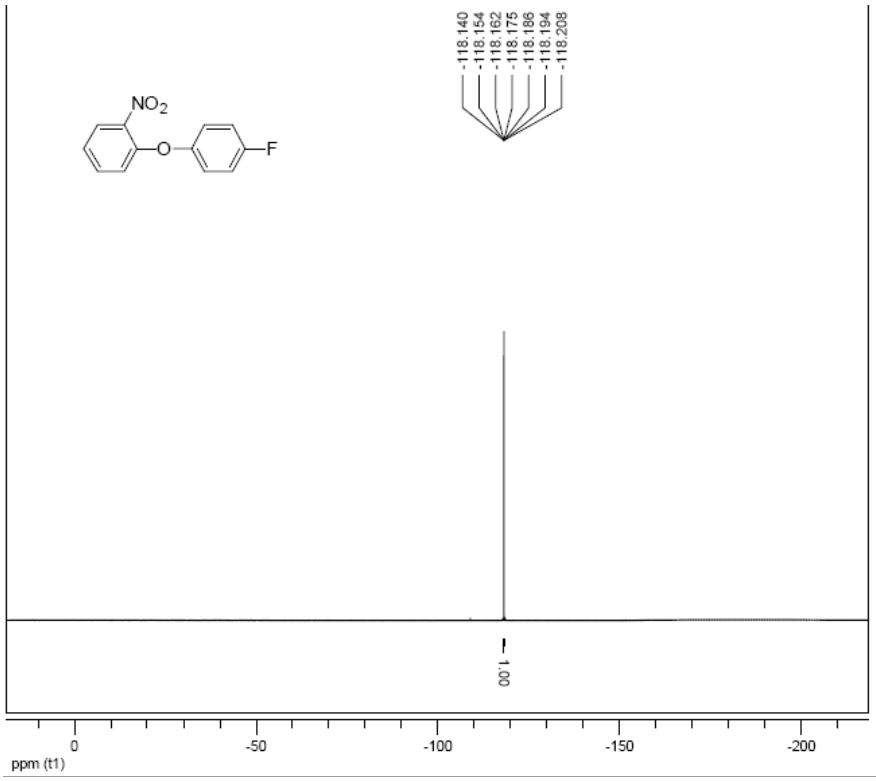
HRMS (EI) spectra of **3o**



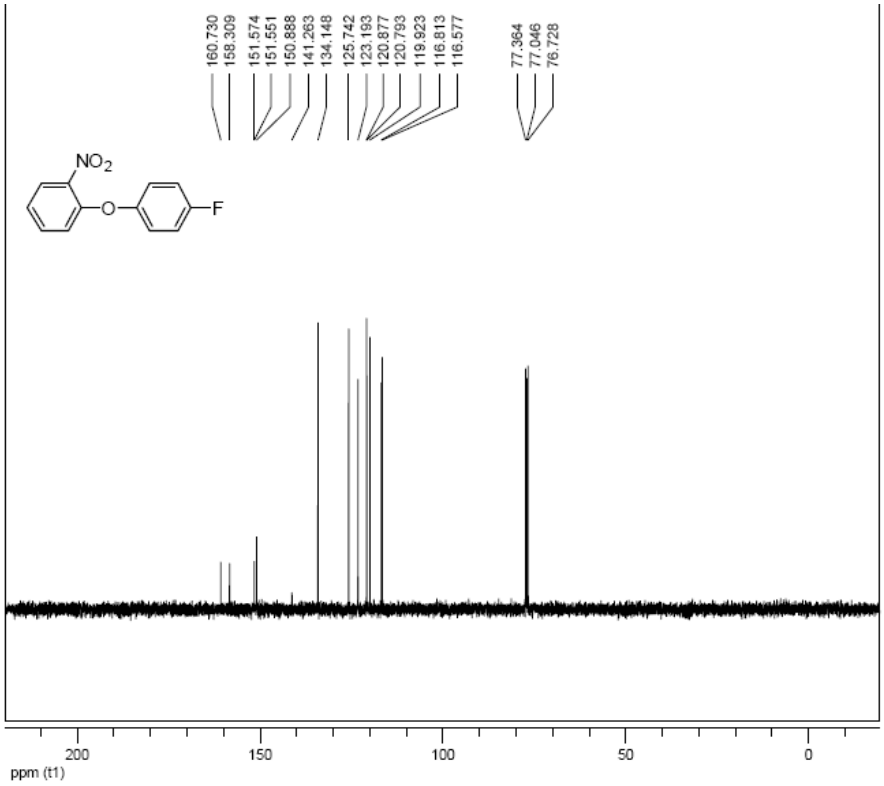
^{1}H NMR spectra of **3p**



^{19}F NMR spectra of **3p**



^{13}C NMR spectra of **3p**



HRMS (EI) spectra of **3p**