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# Hydroximoyl Fluorides as the precursors for the Generation of Nitrile Oxides: Synthesis, Stability and [3+2]-cycloaddition

Feng-Teng Gao, Zheng Fang, Rui-Rui Su, Pei-Xin Rui, Xiang-Guo Hu*

National Engineering Research Center for Carbohydrate Synthesis, Jiangxi Normal University, Nanchang, 330022, China

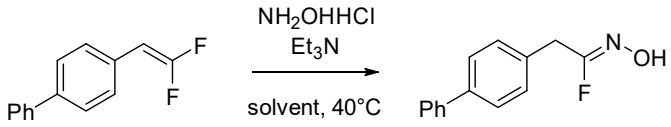
Email: huxiangg@iccas.ac.cn

# Contents

## 1. Reagents and instrumentation

All reagents were used as received from commercial sources without further purification or prepared as described in the literature. All solvents were dried over 4Å molecular sieves before use unless otherwise stated. Reactions were stirred using Teflon-coated magnetic stirring bars. Analytical TLC was performed with 0.20 mm silica gel 60F plates with 254 nm fluorescent indicator. TLC plates were visualized by ultraviolet light or by treatment with a spray of Pancaldi reagent {$(NH_4)_6MoO_4$, $Ce(SO_4)_2$, $H_2SO_4$, $H_2O$} or a solution 0.5% ninhydrin in n-butanol. Chromatographic purification of products was carried out by flash column chromatography on silica gel (230-400 mesh). Melting points were determined using a WRX-4 visual melting point apparatus. Both melting points and boiling points are uncorrected. Infrared spectra were recorded on an IR Affinity-1. NMR spectra were measured in $CDCl_3$ (with TMS as internal standard) or $D_2O$ or MeOD on a Bruker AV400 ($^1H$ at 400 MHz, $^{13}C$ at 100 MHz, $^{19}F$ at 376 MHz) magnetic resonance spectrometer. High-resolution mass spectra (HRMS) were recorded on a SYNAPT G2Si High Definition MS System. Chemical shifts ($\delta$) are reported in ppm, and coupling constants ($J$) are in Hz. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. The HRMS were measured under ESI model (specified in the section of characterization data).

## 2. Table S1. Reaction optimization of 1a to 2a

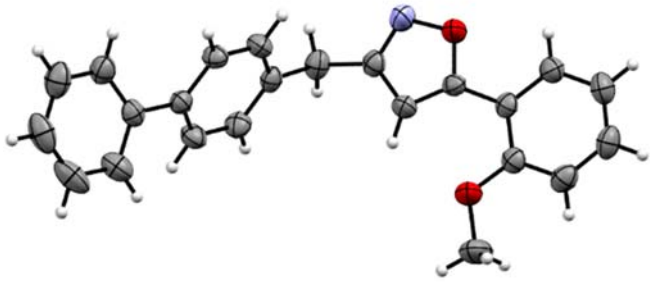



**1a** **2a**

| entry | Solvent | Conversion (%)[a] |
|---|---|---|
| 1 | $CH_2Cl_2$ | 0 |
| 2 | MeOH | 0 |
| 3 | Toluene | 7% |
| 4 | DMF | 100% |
| 5 | MeCN | 73% |

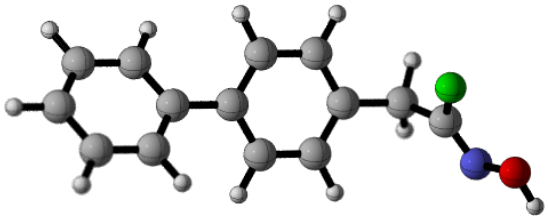
Reaction conditions: **1a** (0.1 mmol), hydroxylamine (0.35 mmol), triethylamine (0.5mmol), solvent (2 mL) at 40°C under nitrogen atmosphere for 3h. [a] As 2a is not stable, the conversion rate was used for reaction optimization.

# 3. X-ray Structure of 6d



## 4. Computational Details:

Calculations were performed using the Gaussian 09 software package.[1] Structure and energy optimizations were performed with popular DFT methods. All of geometries were optimized at B3LYP/6-31+G(d) level of theory, with the SMD solvation model[2] to account for the solvation effects of *N, N*-dimethylformamide. All of the optimized geometries were verified by frequency computations as zero imaginary frequencies. Single-point energy calculations on the optimized geometries were then evaluated at B3LYP/6-311++g (2df, 2pd) basis set within the SMD model (*N*, *N*-dimethylformamide). The thermal corrections evaluated from the unscaled vibrational frequencies at the B3LYP/6-31+G(d) level on the optimized geometries were then added to the B3LYP/6-311++g(2df,2pd) electronic energies to obtain the free energies. the structural representations were generated with CYLview.

| Entry | 3D Geometry | Relative Energy(KJ/mol) in DMF |
|---|---|---|
| (*Z*-**2a**) |  | 0 |

[1] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A.; Peralta, Jr., J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision E.01,* Gaussian, Inc., Wallingford CT, 2013.

[2] Marenich, A.V.; Cramer, C.J.; Truhlar, D.G. *J. Phys. Chem.* B 2009,113,6378.

| | | |
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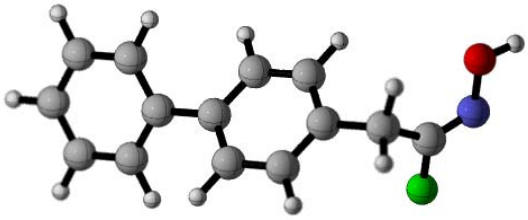
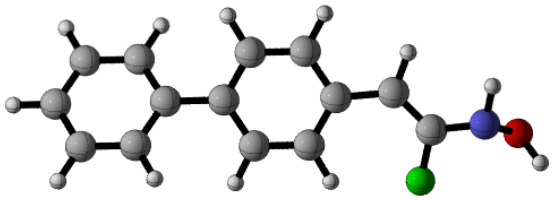
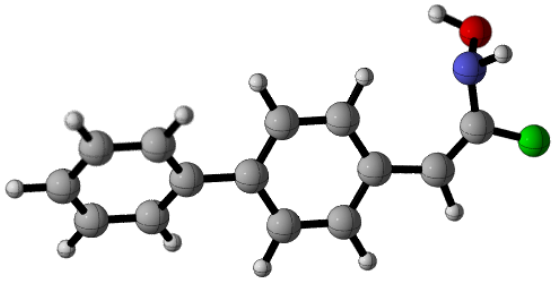
| (*E*-**2a**) |  | 6.948 |
| (Z-**5a**) |  | 40.833 |
| (*E*-**5a**) |  | 55.488 |

*Z*-**2a**

| | | | |
|---|---|---|---|
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| H | 5.69731700 | 1.58125700 | -0.14388800 |
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| C | 0.42081400 | -0.66323100 | 0.92768800 |
| C | 0.64226500 | 1.37312400 | -0.34099700 |
| C | -0.94001300 | -0.40876300 | 1.09758000 |
| H | 0.85364800 | -1.54993900 | 1.38321800 |
| C | -0.72097500 | 1.62568400 | -0.17022700 |
| H | 1.24018700 | 2.07182200 | -0.92031600 |
| C | -1.53094700 | 0.73959600 | 0.55058300 |
| H | -1.54675100 | -1.10655700 | 1.67122800 |
| H | -1.15806600 | 2.52052000 | -0.60801500 |
| C | -3.01558700 | 1.01303200 | 0.74200900 |
| H | -3.30561500 | 0.87313900 | 1.78796800 |
| H | -3.24223800 | 2.05064800 | 0.46741400 |
| C | -3.88211300 | 0.11866700 | -0.08372800 |
| N | -4.71974500 | -0.70679700 | 0.39782500 |
| F | -3.71662000 | 0.24912200 | -1.42593900 |
| O | -5.41556700 | -1.42338600 | -0.59135300 |
| H | -6.00411300 | -1.99543000 | -0.06584100 |

*E*-**2a**

| | | | |
|---|---|---|---|
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| H | -6.52861100 | 0.52139500 | -0.41323600 |
| H | -5.62593300 | -1.60241000 | 0.53188300 |
| C | -1.20150900 | -0.13496800 | 0.20880900 |
| C | -0.37579100 | 0.93914900 | 0.59206900 |
| C | -0.59199100 | -1.38455000 | -0.00482700 |
| C | 0.99967400 | 0.76954500 | 0.75236200 |
| H | -0.81354900 | 1.91393800 | 0.78991400 |
| C | 0.78488800 | -1.55271800 | 0.15717100 |
| H | -1.19336800 | -2.23381900 | -0.31802600 |
| C | 1.60031400 | -0.47916400 | 0.53676900 |
| H | 1.60975000 | 1.61634400 | 1.05979100 |
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| C | 3.10089000 | -0.65878300 | 0.71282900 |
| H | 3.45623500 | -0.11689800 | 1.59289000 |
| H | 3.33621800 | -1.72126800 | 0.85524400 |
| C | 3.88459000 | -0.18325000 | -0.46789800 |
| N | 4.80397700 | 0.68334800 | -0.59307100 |
| F | 3.56715100 | -0.80692900 | -1.63589000 |
| O | 5.11577600 | 1.30864000 | 0.63022300 |
| H | 5.81773100 | 1.93489400 | 0.37647800 |

*Z*-**5a**

| | | | |
|---|---|---|---|
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| C | 2.85503000 | 0.00584500 | 0.00745000 |
| C | 3.47231500 | -1.18051500 | -0.43492700 |
| C | 4.85952900 | -1.33431000 | -0.37610600 |
| C | 5.66355800 | -0.30555400 | 0.12639600 |
| C | 5.06497000 | 0.87879500 | 0.56943700 |
| H | 3.22854100 | 1.95067800 | 0.88029200 |
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| H | 5.31256500 | -2.25702500 | -0.73115300 |
| H | 6.74318800 | -0.42557100 | 0.17211500 |
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| C | 0.51344200 | -0.92071200 | 0.16102300 |
| C | 0.79084700 | 1.41778600 | -0.33106100 |
| C | -0.87121900 | -0.77801900 | 0.10691800 |
| H | 0.92683100 | -1.89728500 | 0.39892200 |
| C | -0.59249300 | 1.56449600 | -0.38805200 |
| H | 1.42025800 | 2.28237600 | -0.52455900 |
| C | -1.46153600 | 0.47362600 | -0.17246200 |
| H | -1.49066700 | -1.64716100 | 0.29537000 |
| H | -1.01464400 | 2.54141300 | -0.61343100 |
| C | -2.90188000 | 0.72565800 | -0.25004700 |
| H | -3.19112500 | 1.75162800 | -0.46576500 |
| C | -3.93305300 | -0.12906900 | -0.13260000 |
| N | -5.26153200 | 0.12030900 | -0.44772100 |
| H | -5.38058600 | 1.07752600 | -0.77831800 |
| O | -6.10289900 | -0.00319600 | 0.73070100 |
| H | -6.73042100 | -0.70673900 | 0.48308400 |
| F | -3.75663500 | -1.43375800 | 0.22198000 |

*E*-5a

| | | | |
|---|---|---|---|
| C | -3.59749400 | -0.90038000 | -0.65821800 |
| C | -2.74376400 | -0.00125900 | 0.01016500 |
| C | -3.32014400 | 1.12596200 | 0.62747900 |
| C | -4.69891000 | 1.34532800 | 0.57911000 |
| C | -5.53438400 | 0.44320400 | -0.08827500 |
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| H | -0.73543400 | 1.85769800 | -0.04610200 |
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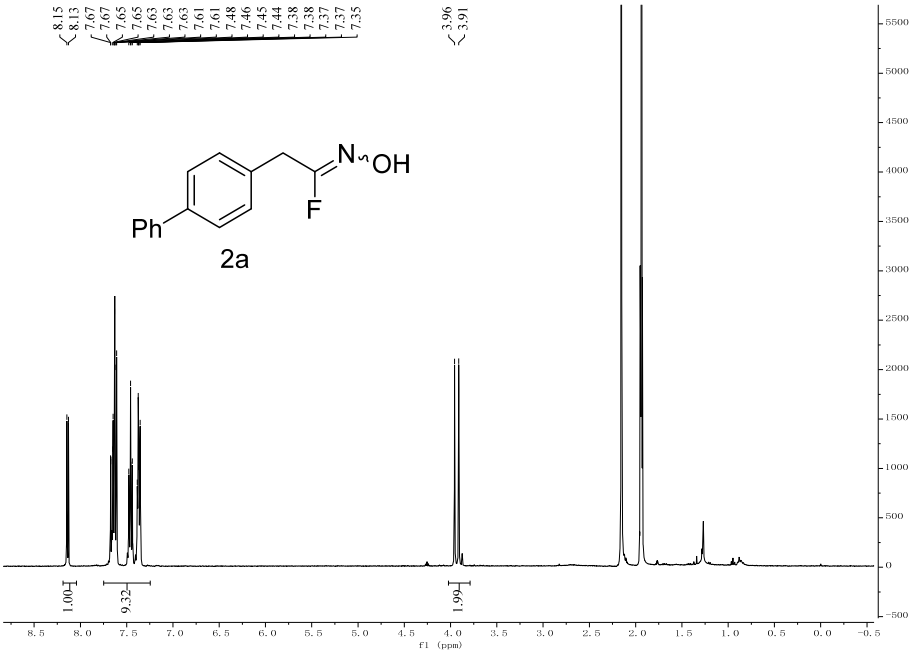
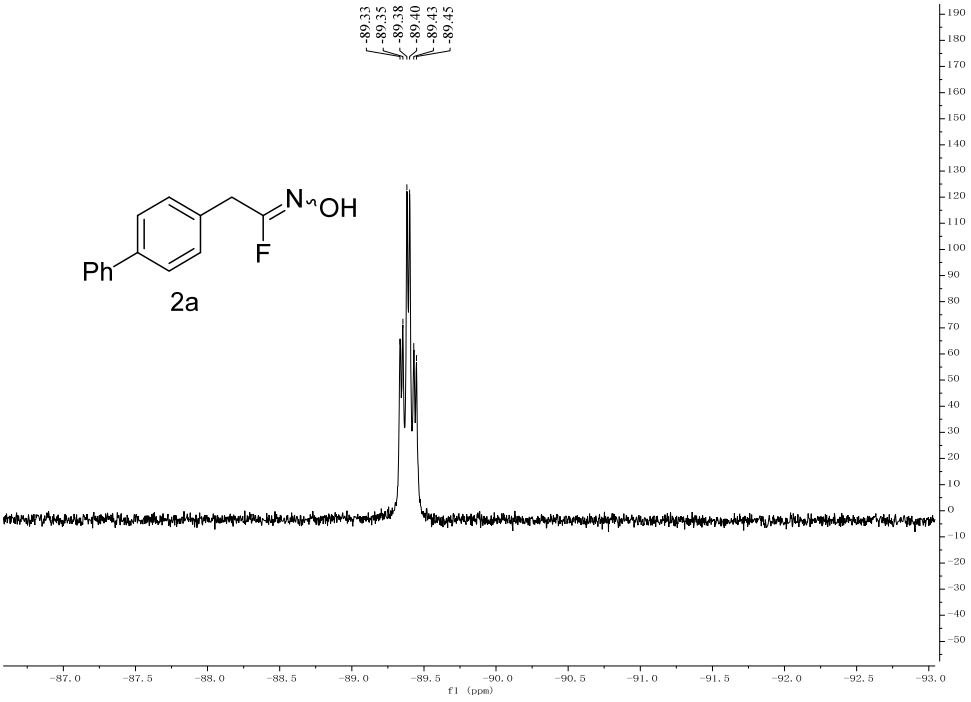
| H | -1.41209400 | -2.39161500 | 0.18804300 |
| C | 1.54302400 | -0.67289800 | 0.15885500 |
| H | 1.67871000 | 1.48467300 | 0.05122200 |
| H | 1.00849600 | -2.76449900 | 0.25791300 |
| C | 2.97184100 | -1.00368500 | 0.20918500 |
| H | 3.19729000 | -2.06740200 | 0.24513400 |
| C | 4.04109400 | -0.19578400 | 0.22345100 |
| N | 4.08797900 | 1.19366800 | 0.19212600 |
| F | 5.29251400 | -0.80363600 | 0.27519900 |
| O | 4.61841000 | 1.63478600 | -1.10014300 |
| H | 3.87253400 | 2.13965800 | -1.47423500 |
| H | 4.76696800 | 1.55069600 | 0.86635300 |

# 5 Copies of NMR Spectra

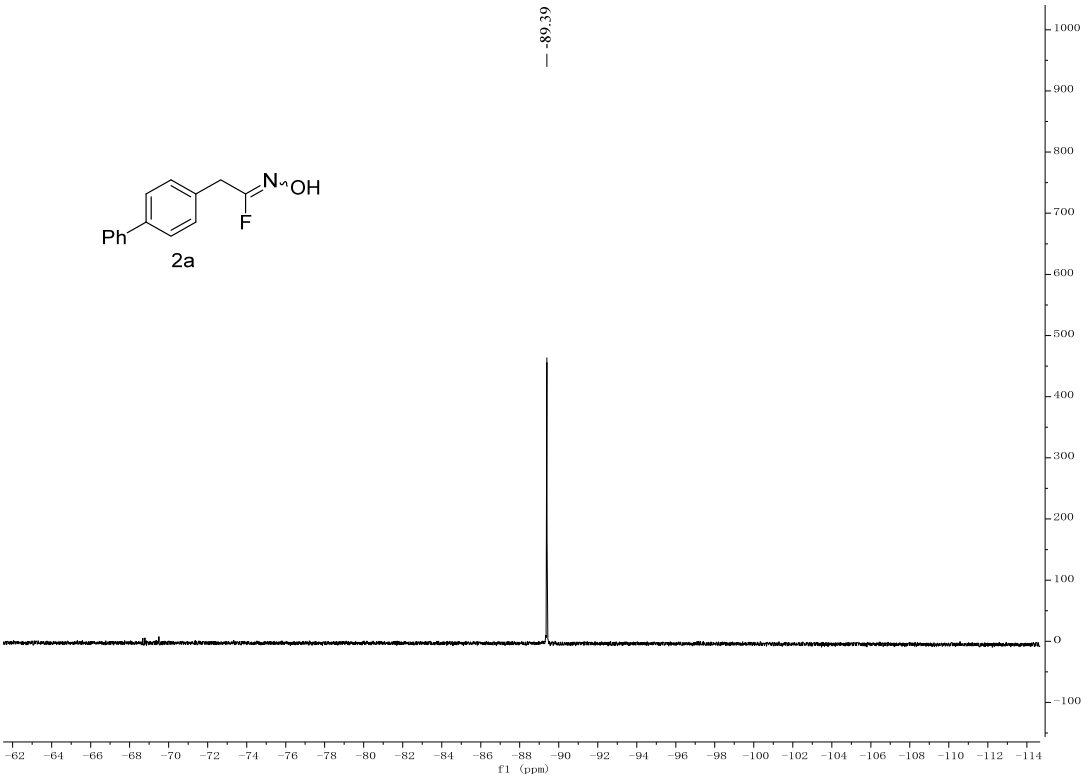
$^{1}$H NMR ($d_3$-MeCN, 400 MHz, 25 ºC) of **2a**



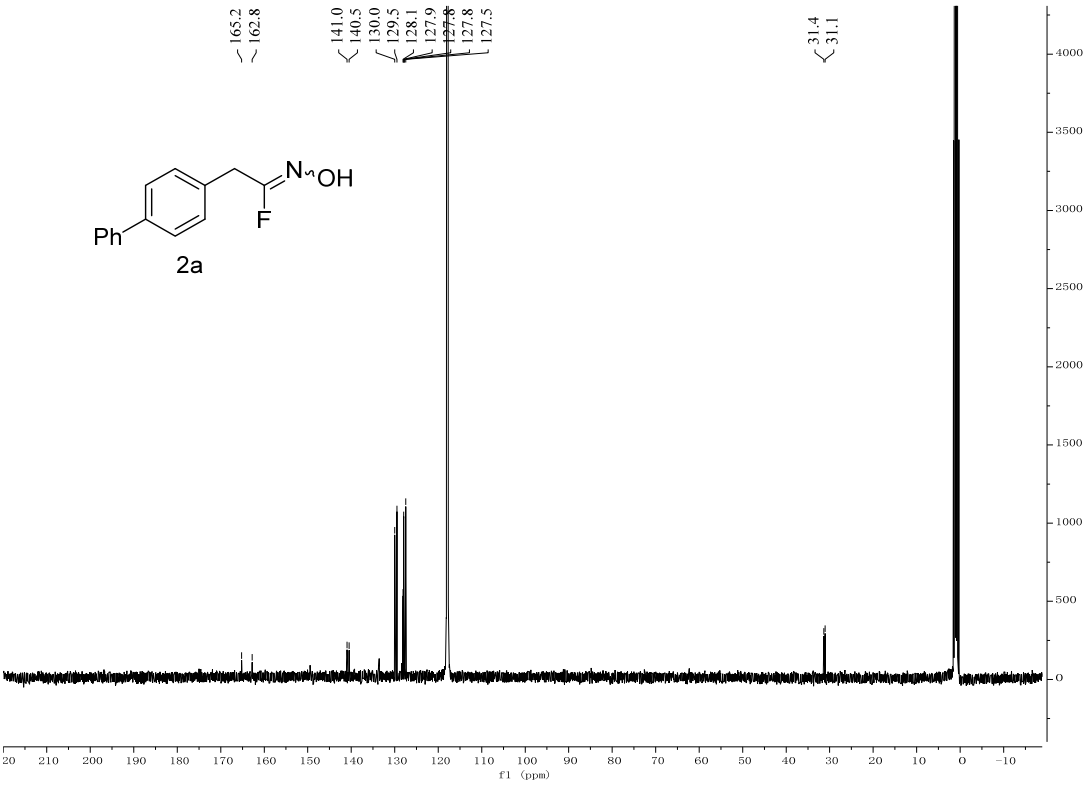

$^{19}$F NMR ($d_3$-MeCN, 376 MHz, 25 ºC) of **2a**



$^{19}F$ {$^{1}H$}NMR ($d_3$-MeCN, 376 MHz, 25 ºC) of **2a**




$^{13}C$ NMR ($d_3$-MeCN, 100 MHz, 25 ºC) of **2a**



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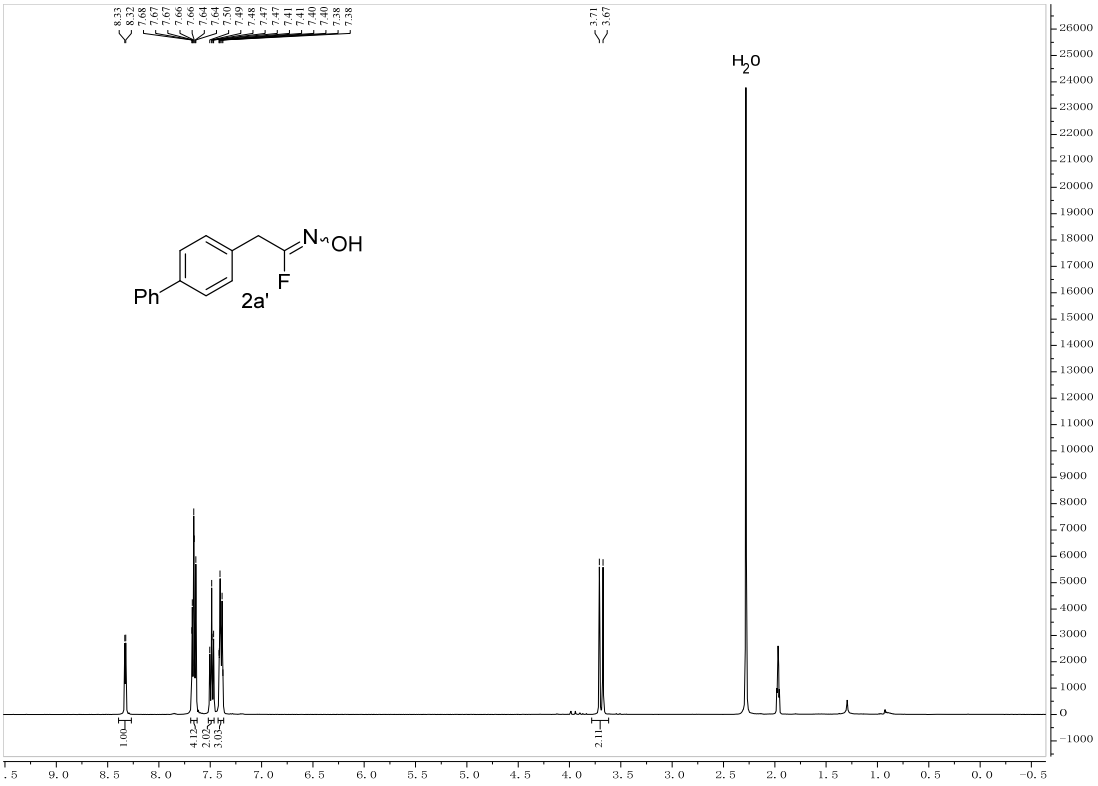


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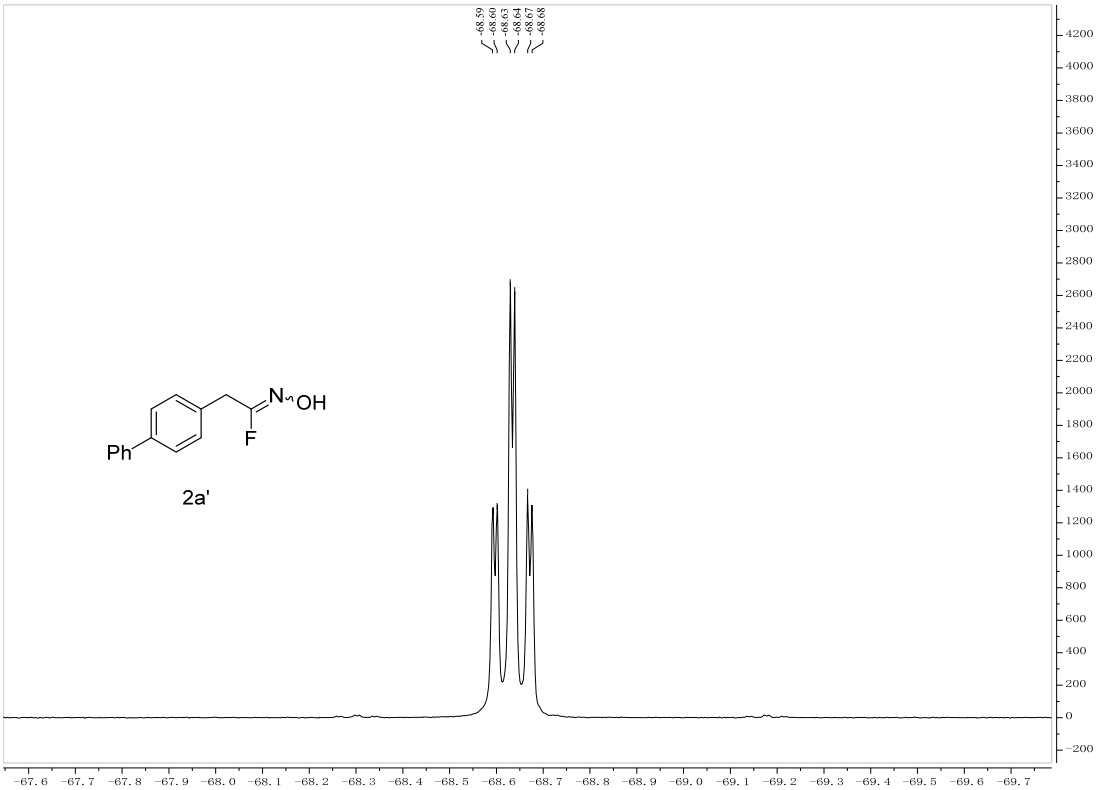

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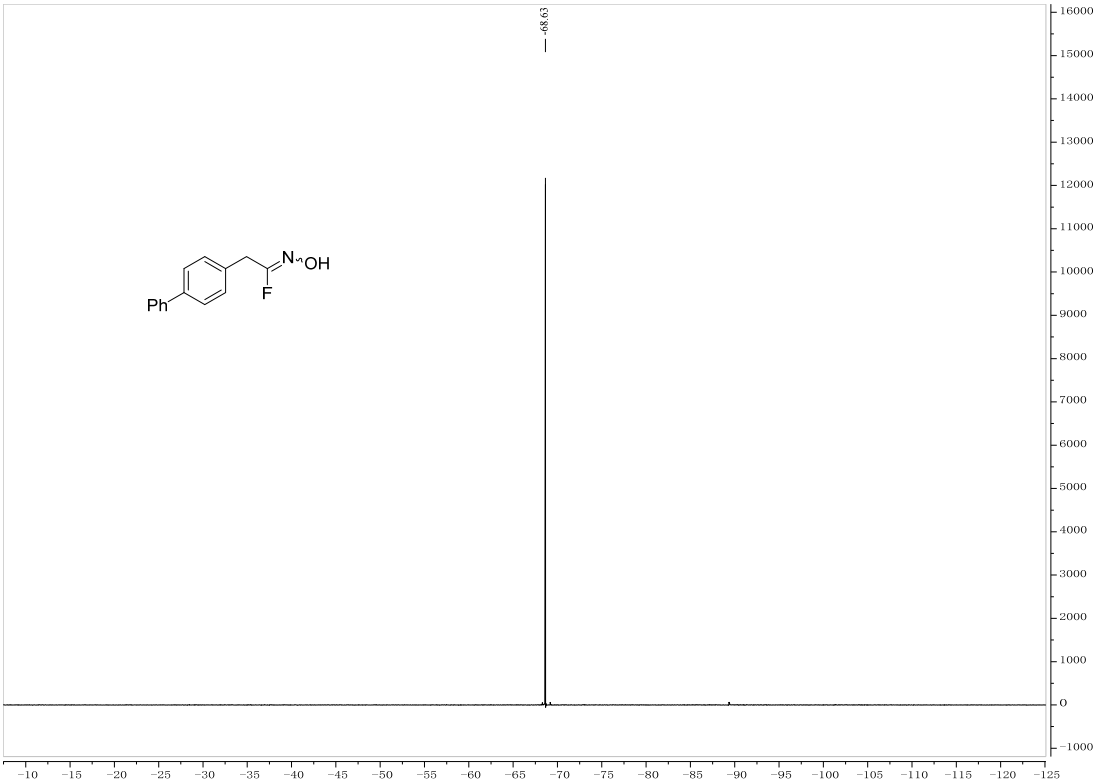


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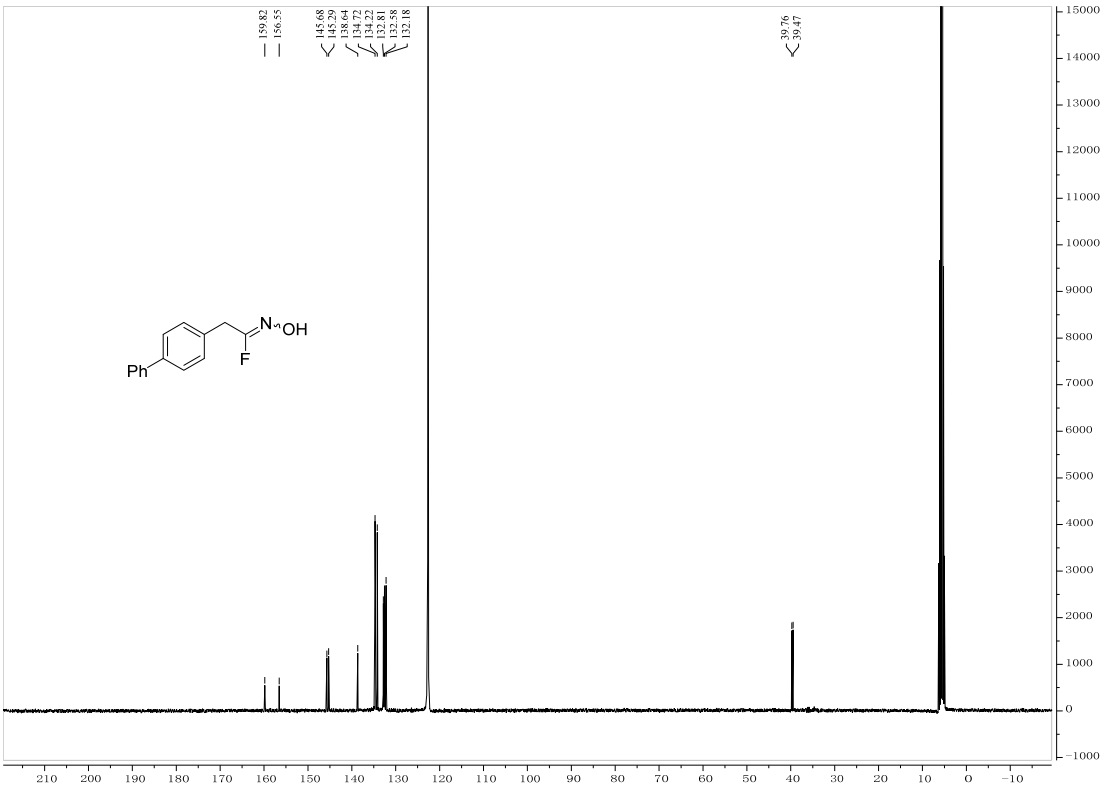

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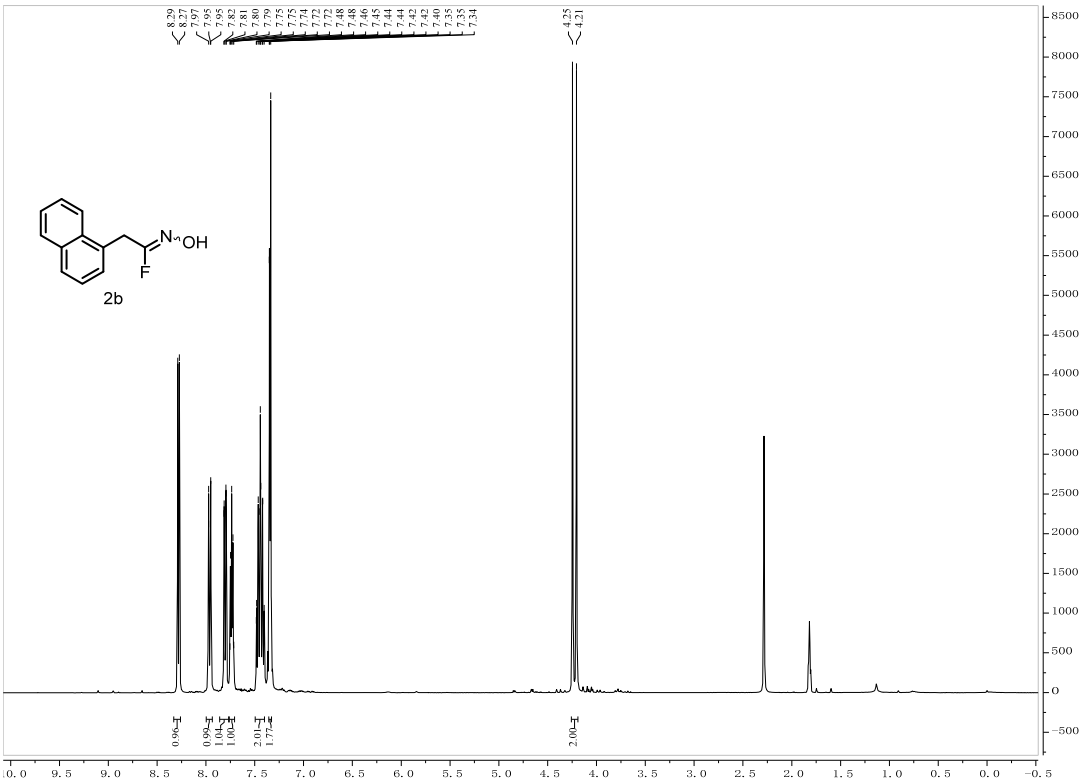


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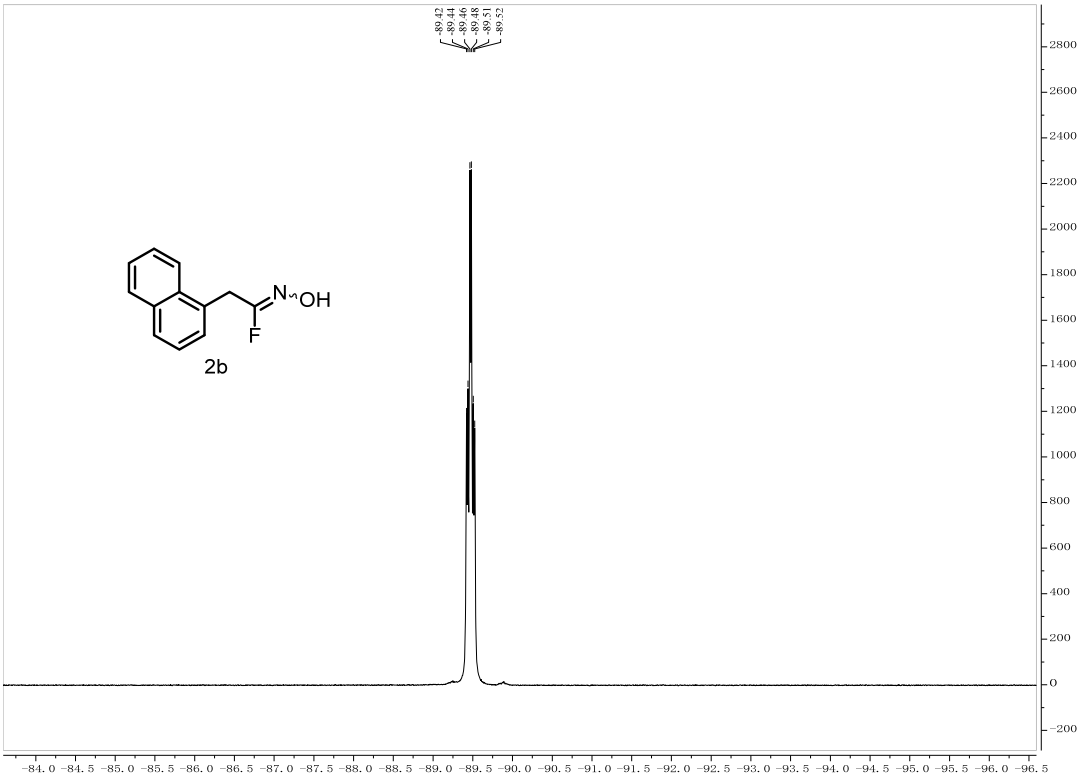
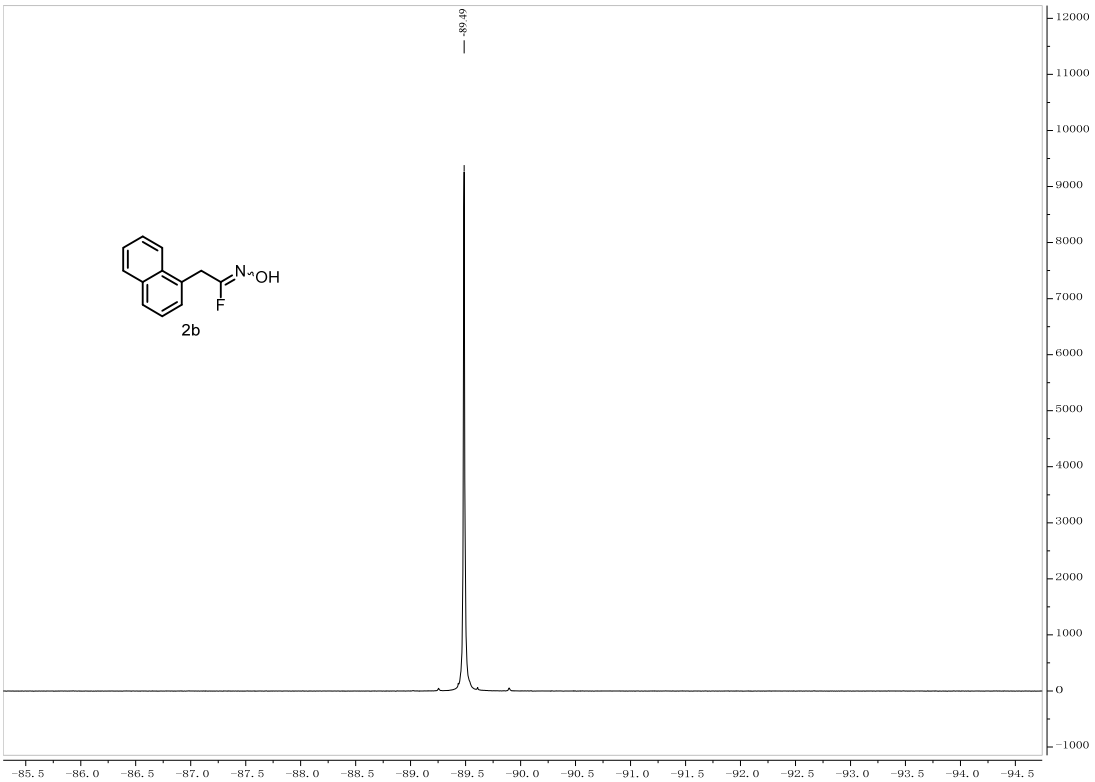


$^{19}F$ {$^{1}H$}NMR ($d_3$-MeCN, 376 MHz, 25 ºC) of **2b**

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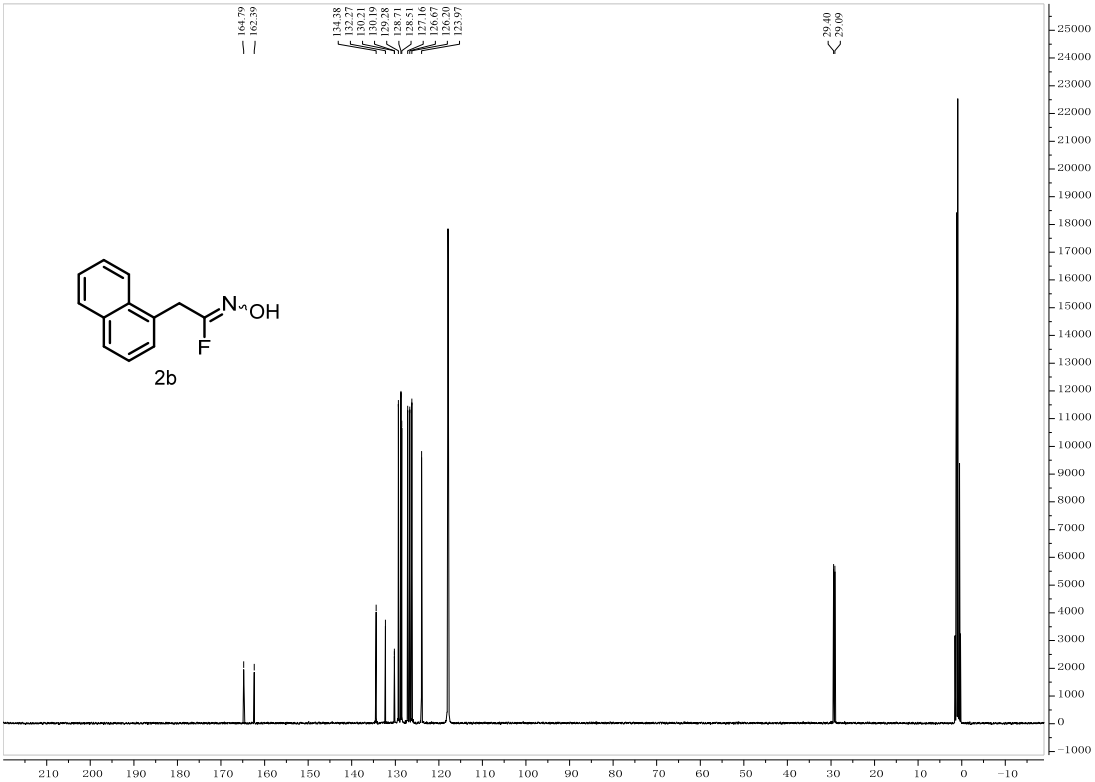

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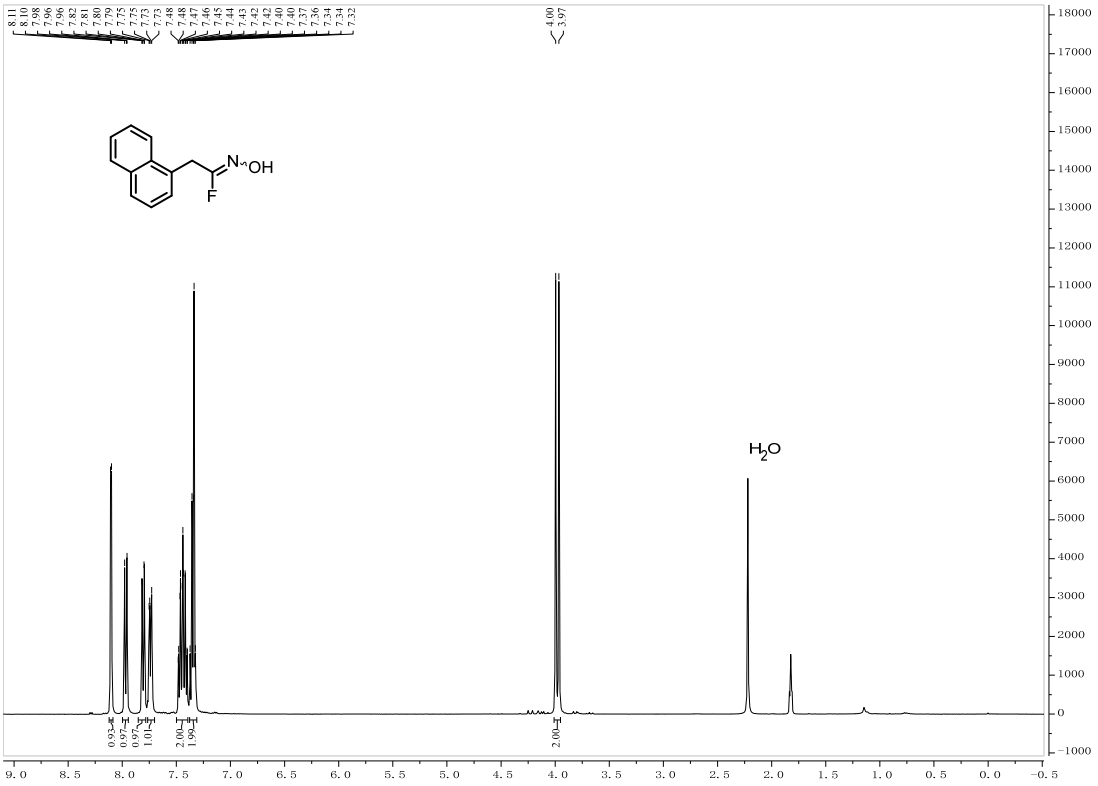


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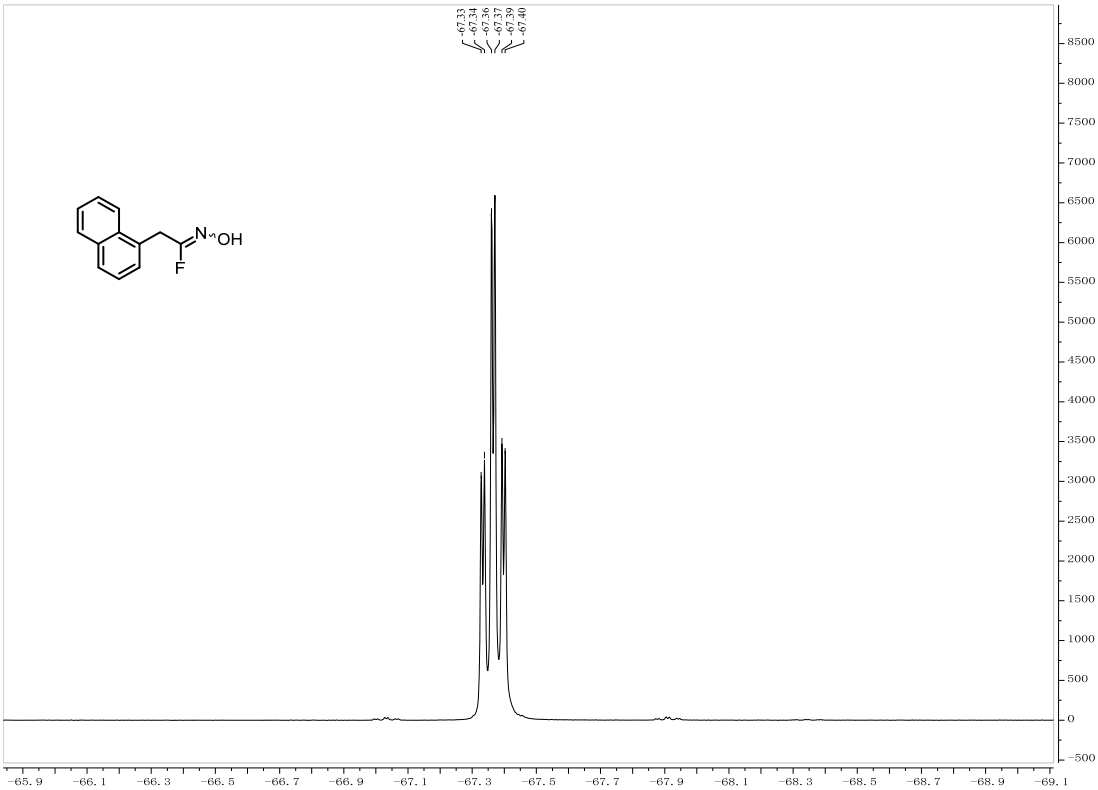
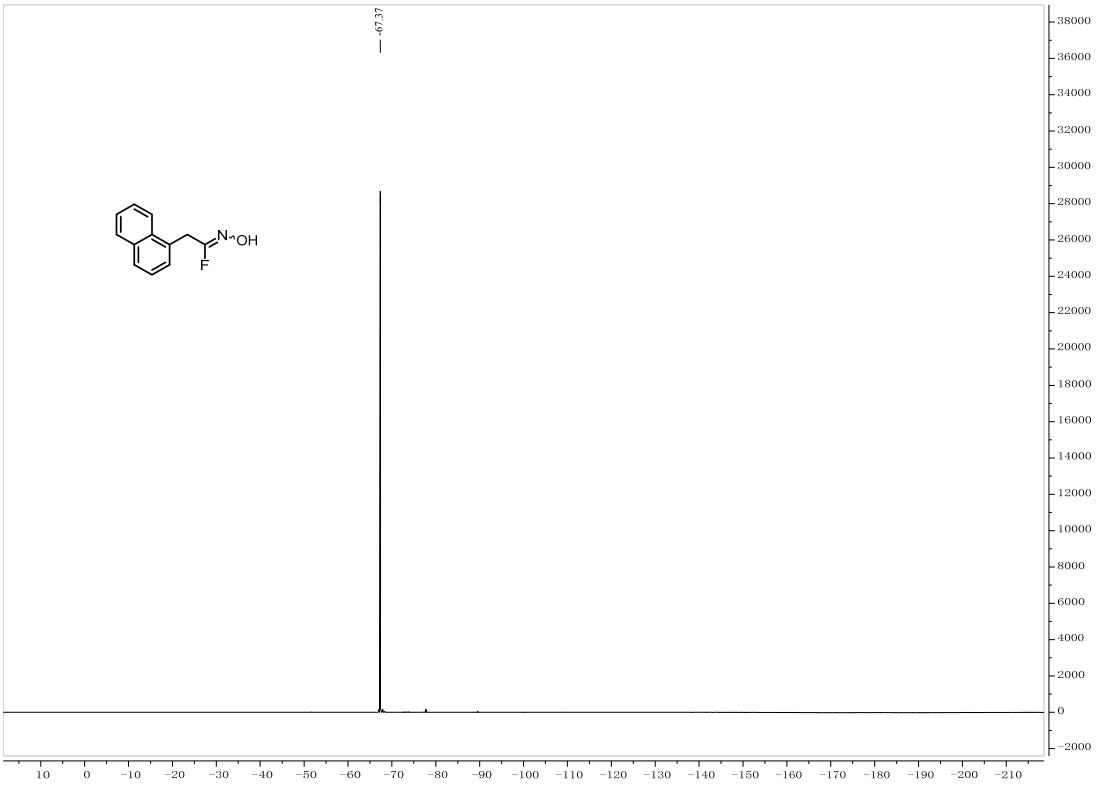


$^{19}F$ {$^{1}H$} NMR ($d_3$-MeCN, 376 MHz, 25 ºC) of **2b'**

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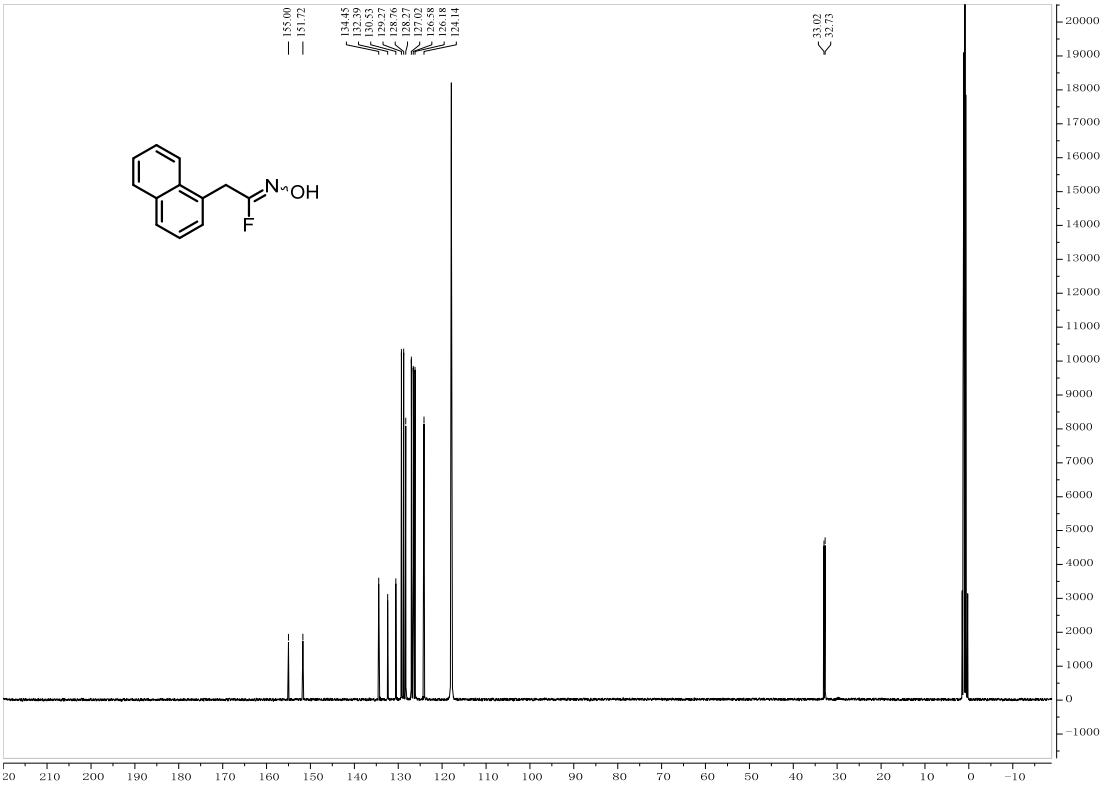
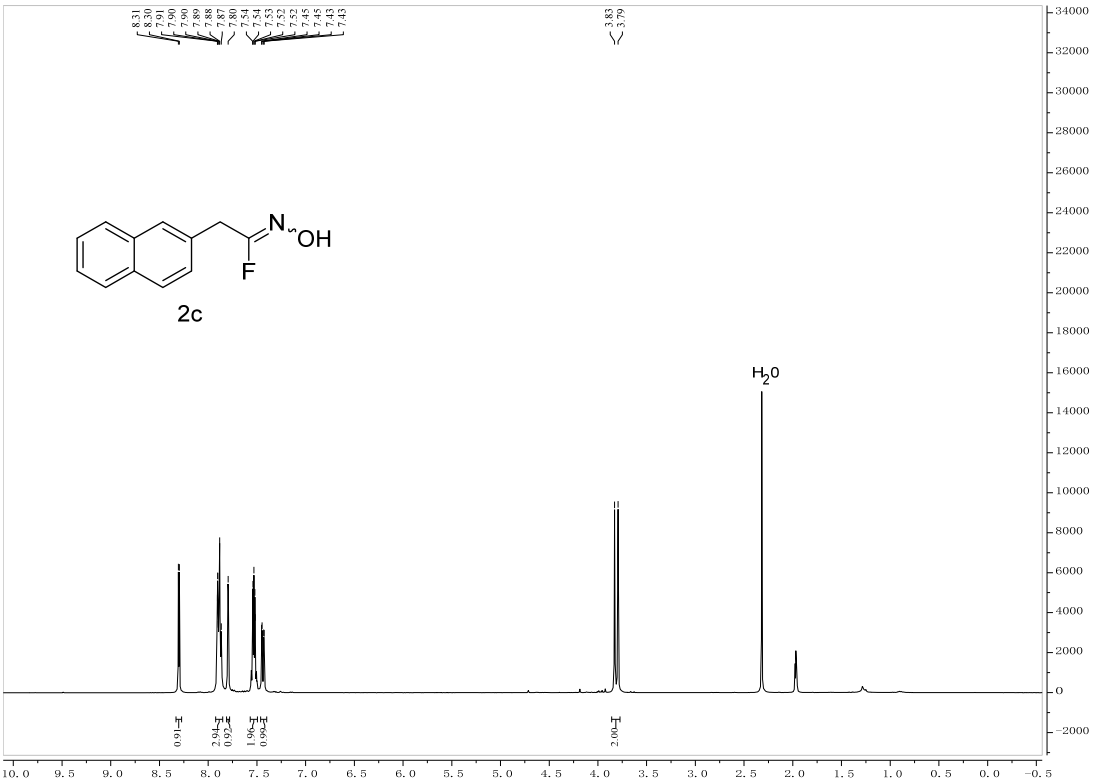
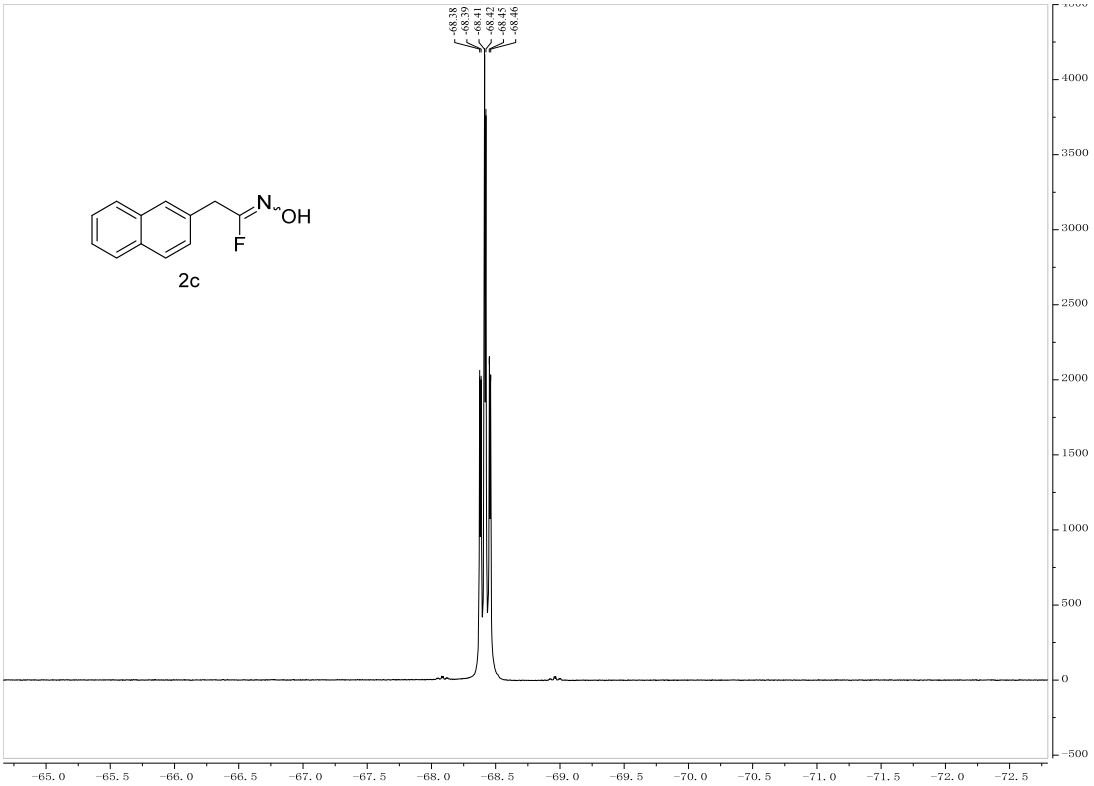


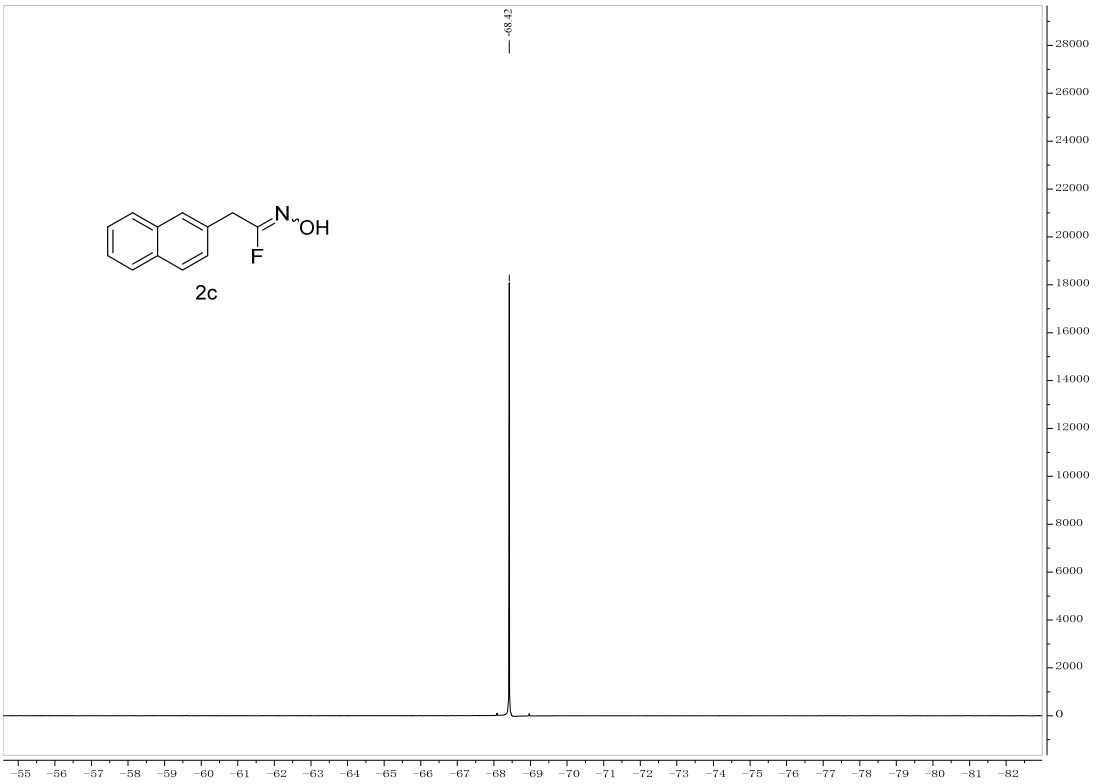
$^{1}$H NMR ($d_3$-MeCN, 400 MHz, 25 ºC) of **2c**



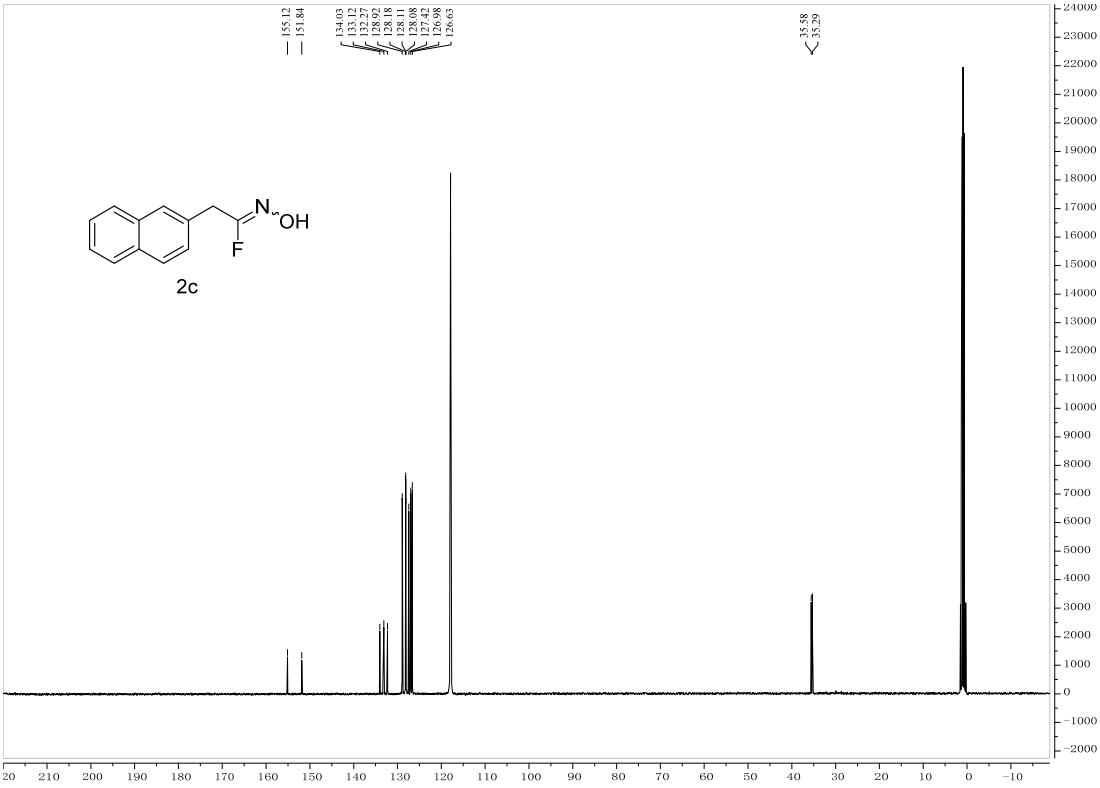

$^{19}$F NMR ($d_3$-MeCN, 376 MHz, 25 ºC) of **2c**



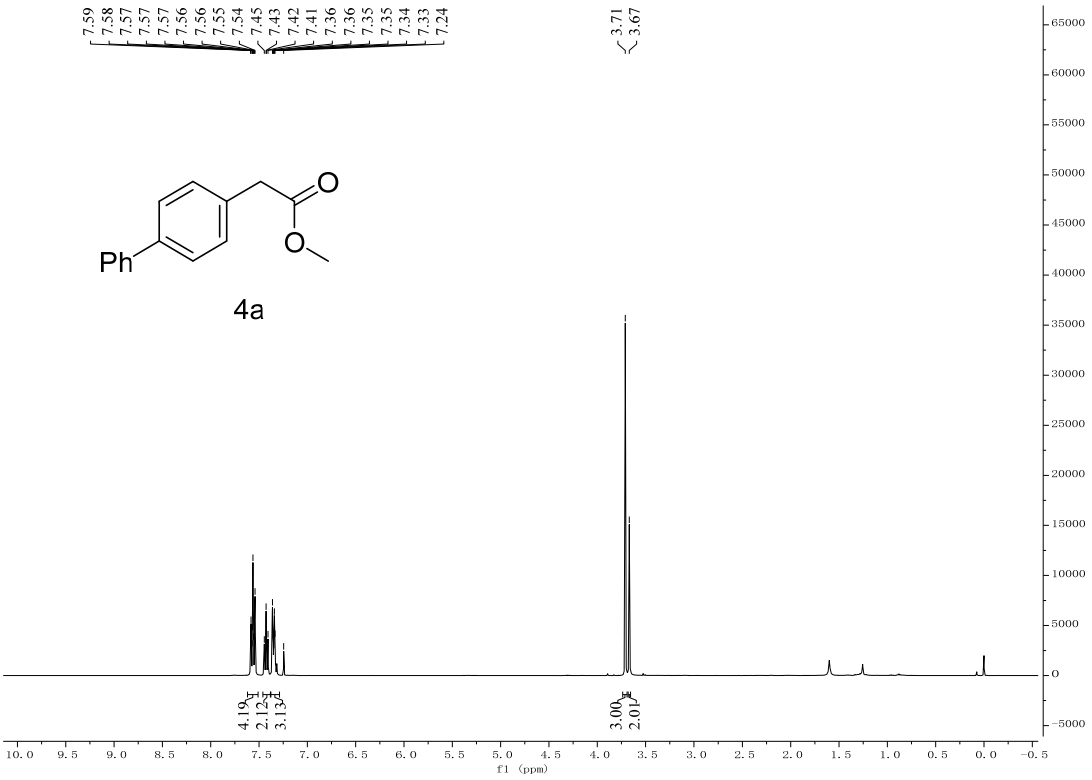
$^{19}F$ {$^{1}H$}NMR ($d_3$-MeCN, 376 MHz, 25 ºC) of **2c**



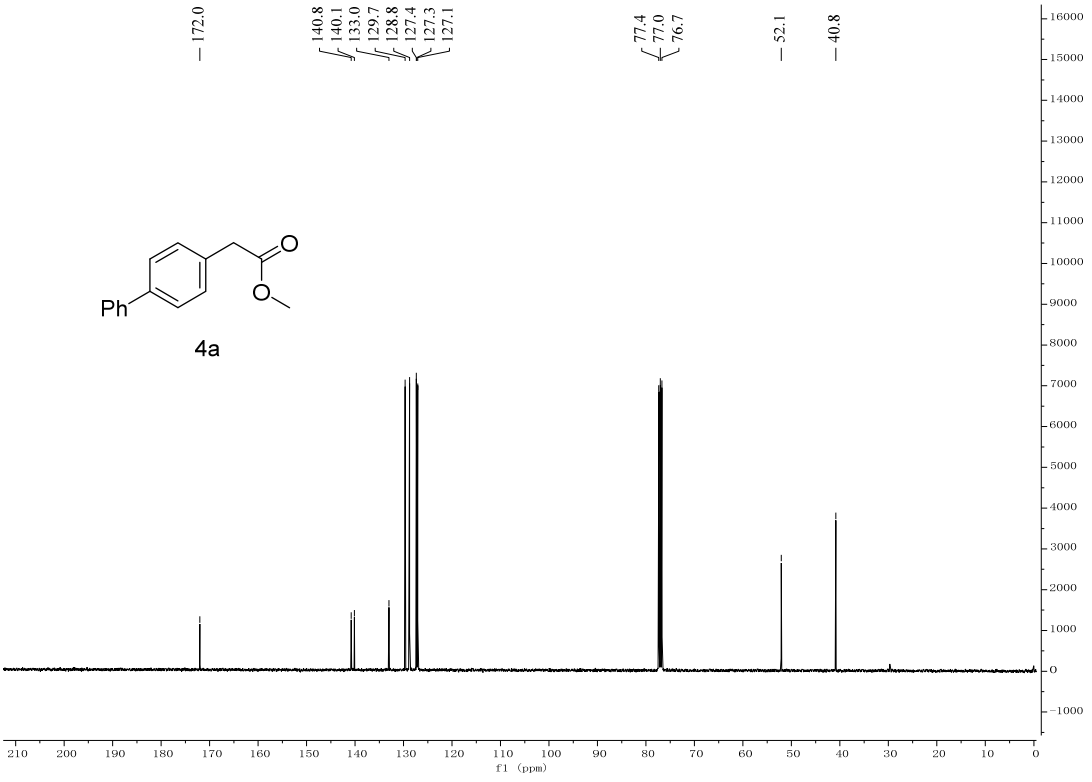

$^{13}C$ NMR ($d_3$-MeCN, 100 MHz, 25 ºC) of **2c**



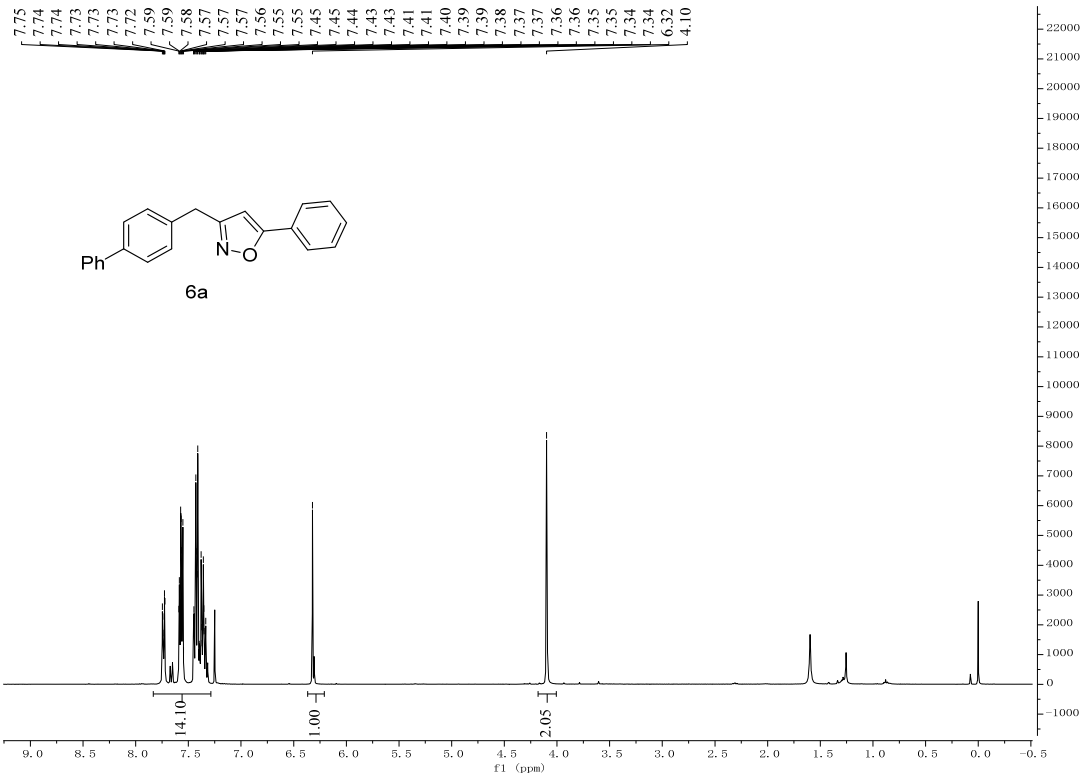
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **4a**



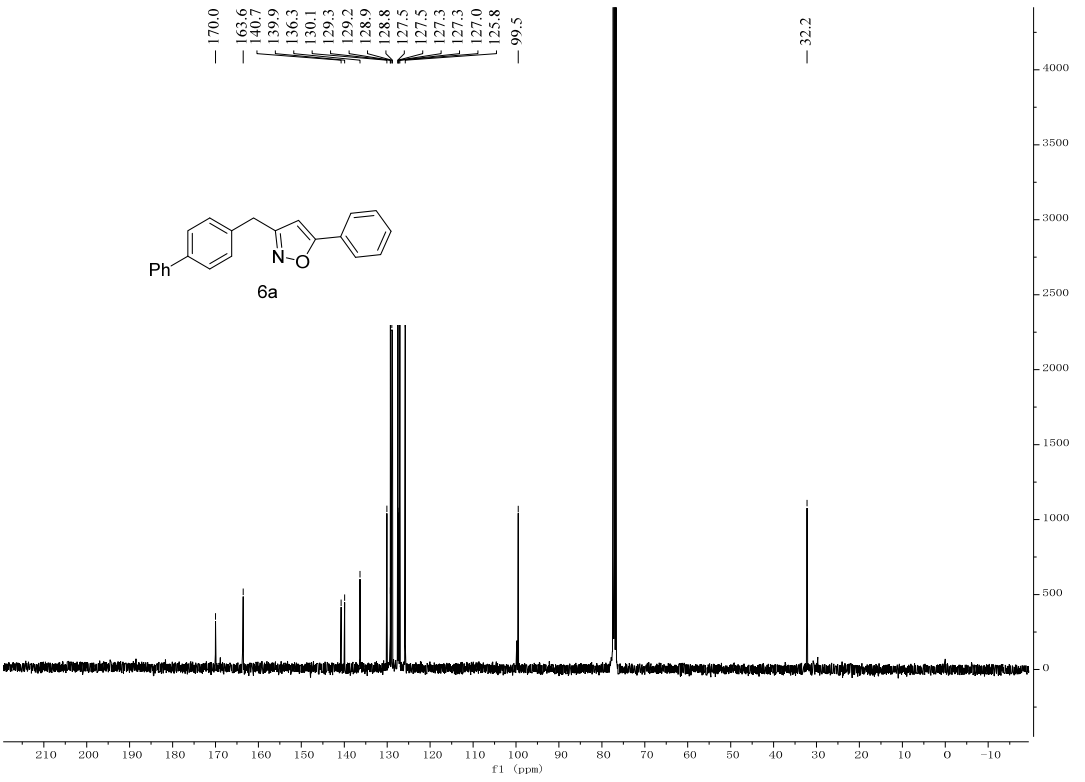

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **4a**



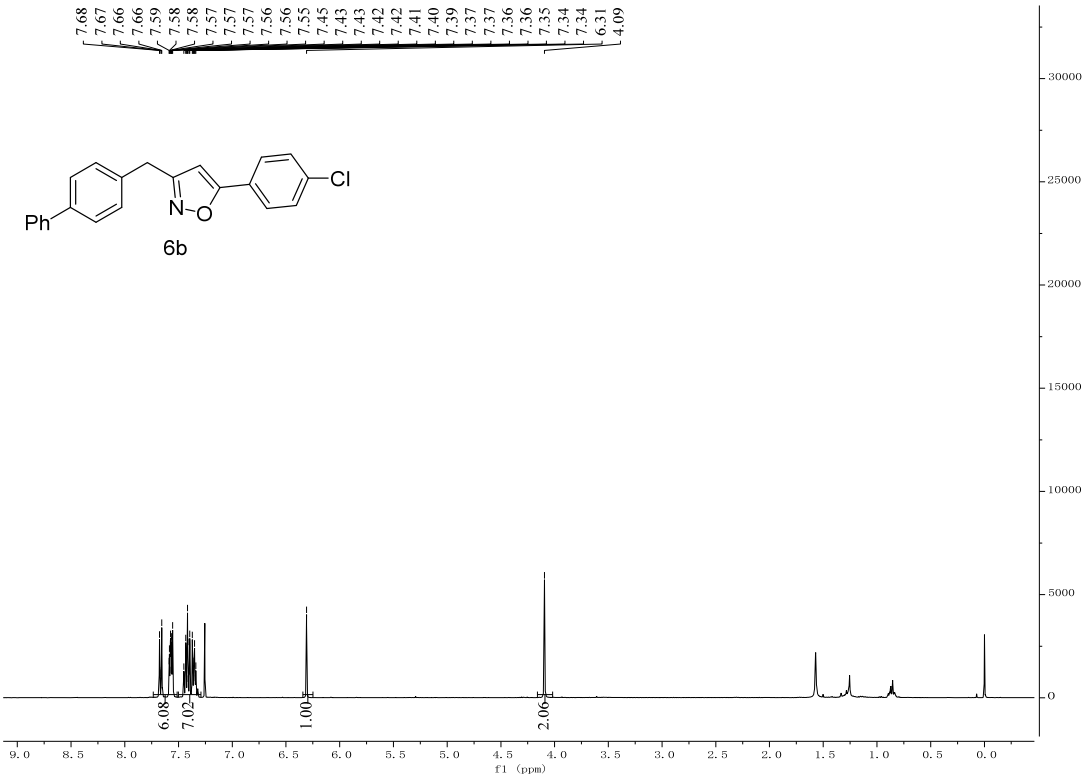
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6a**



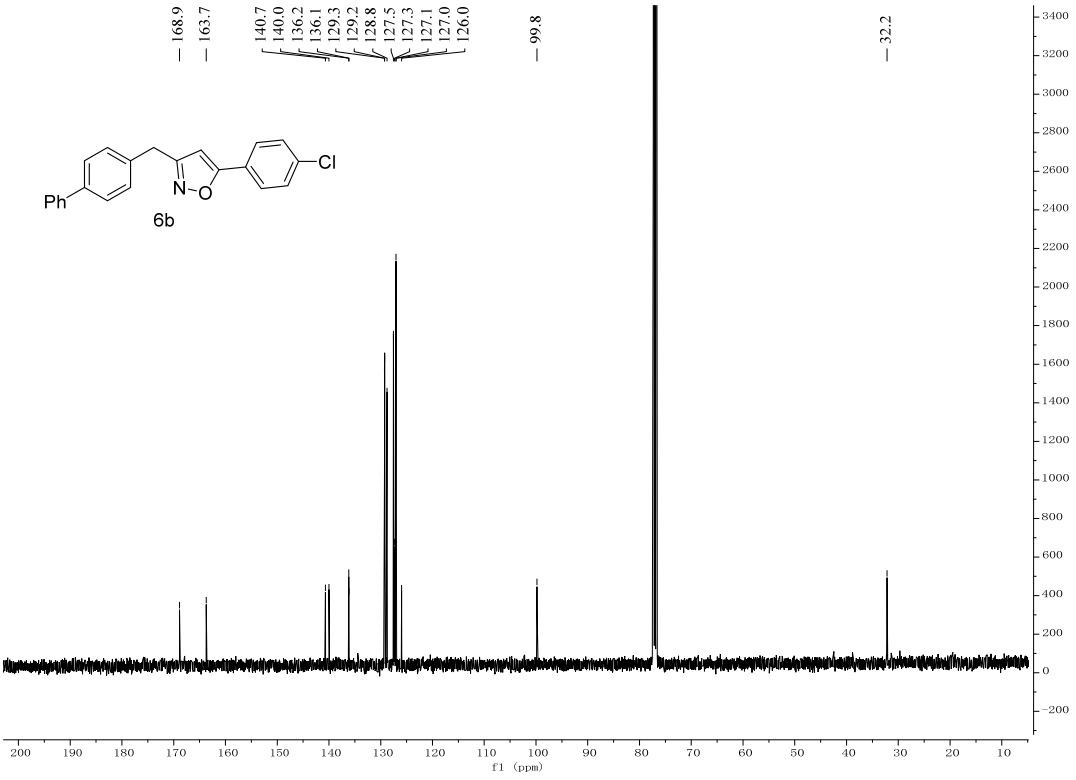

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6a**



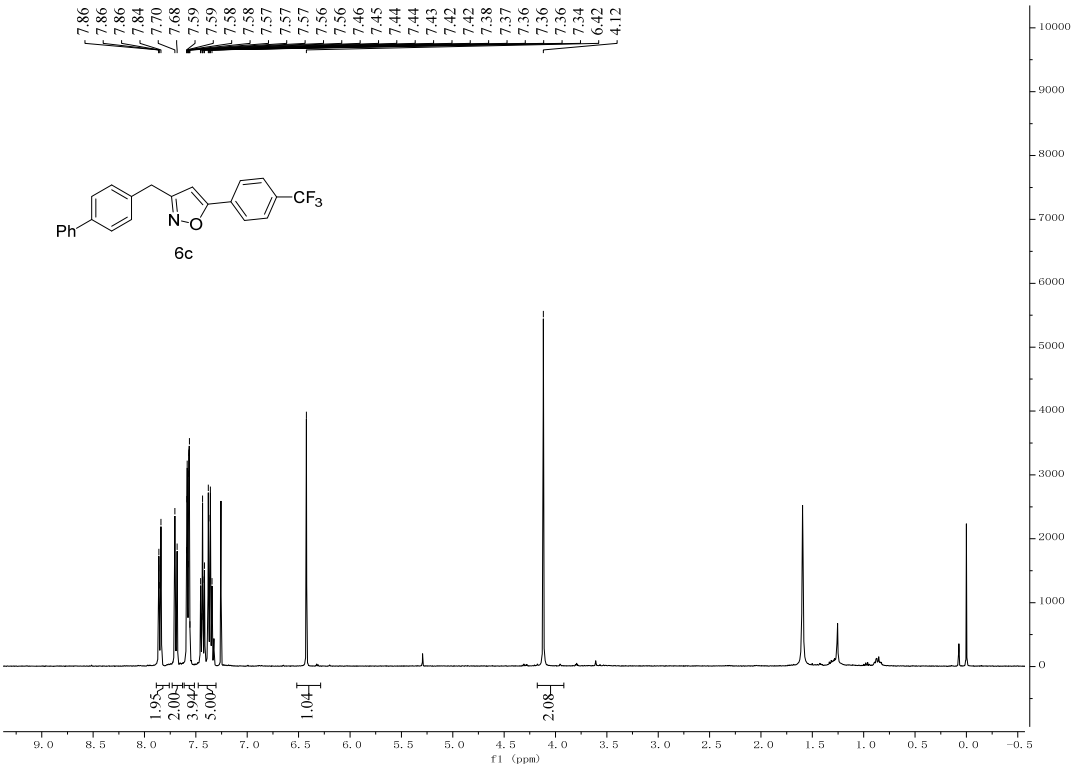
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6b**



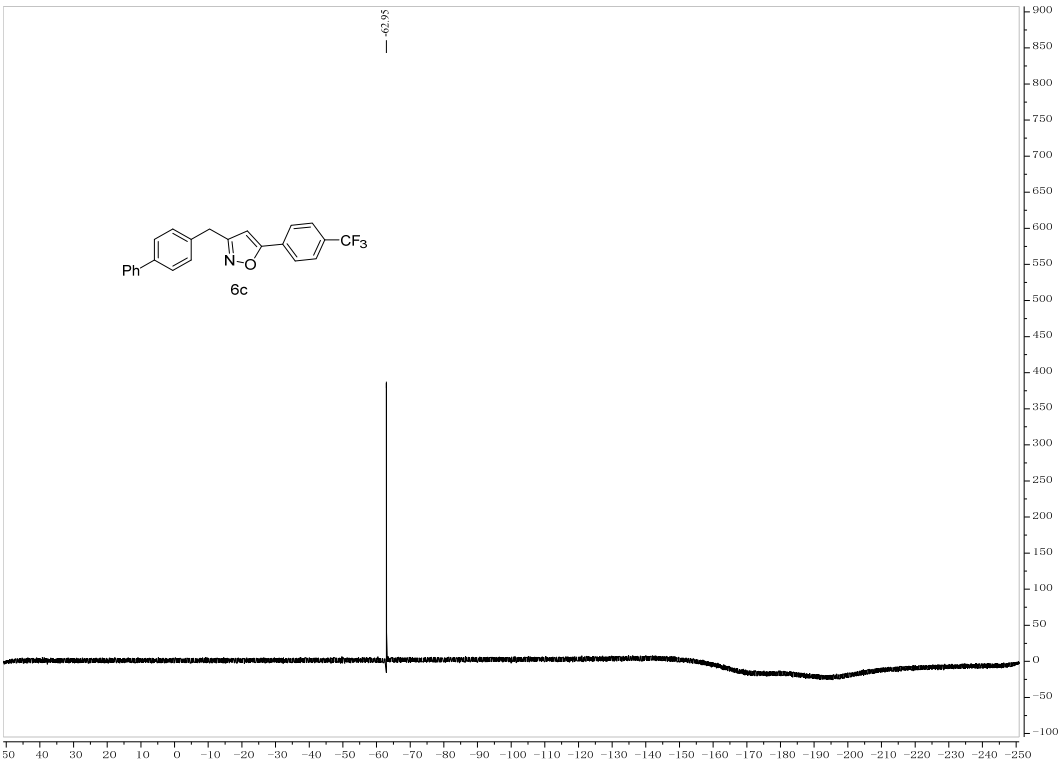

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6b**



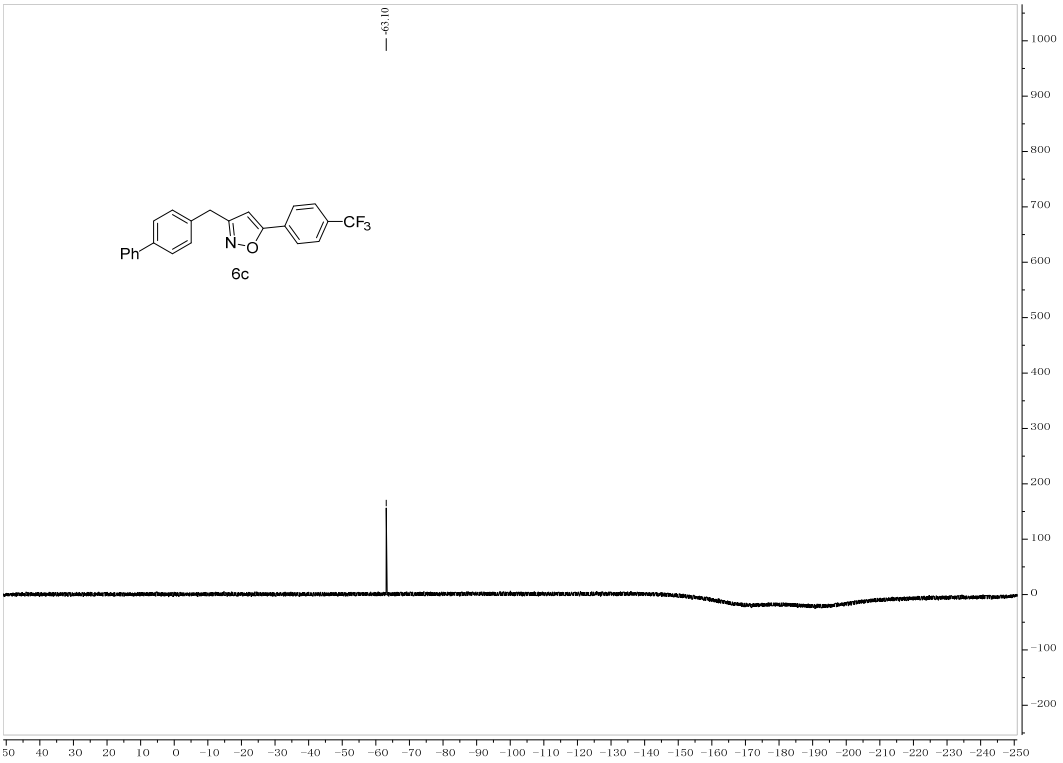
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6c**



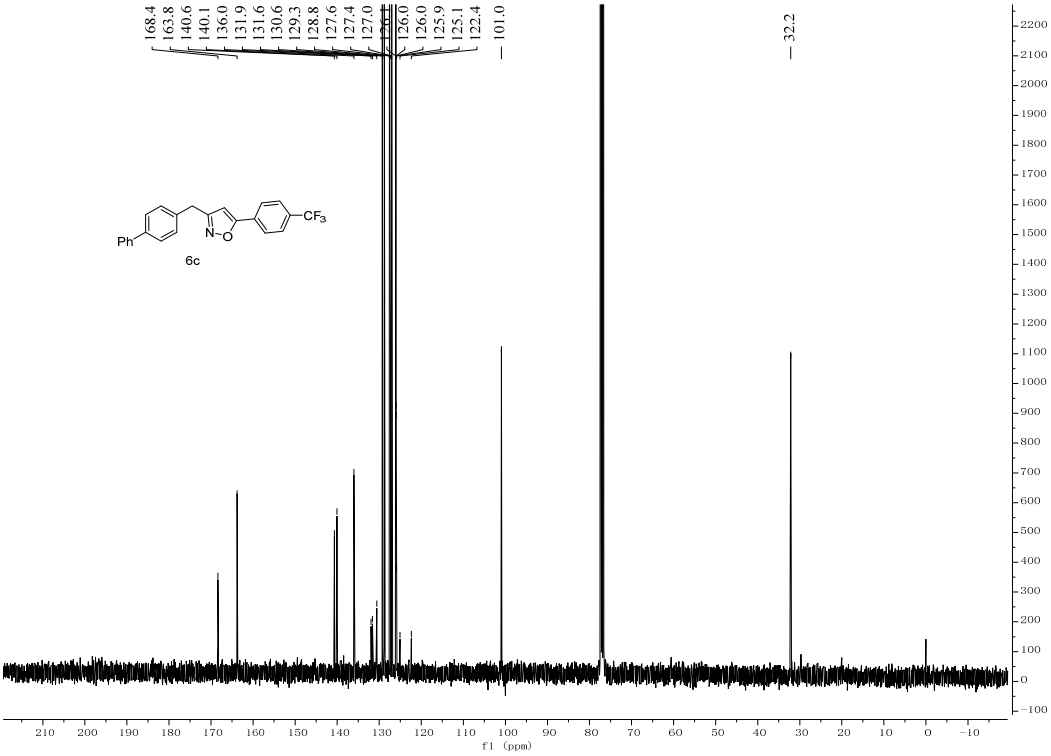

$^{19}$F NMR ($CDCl_3$, 376 MHz, 25 ºC) of **6c**



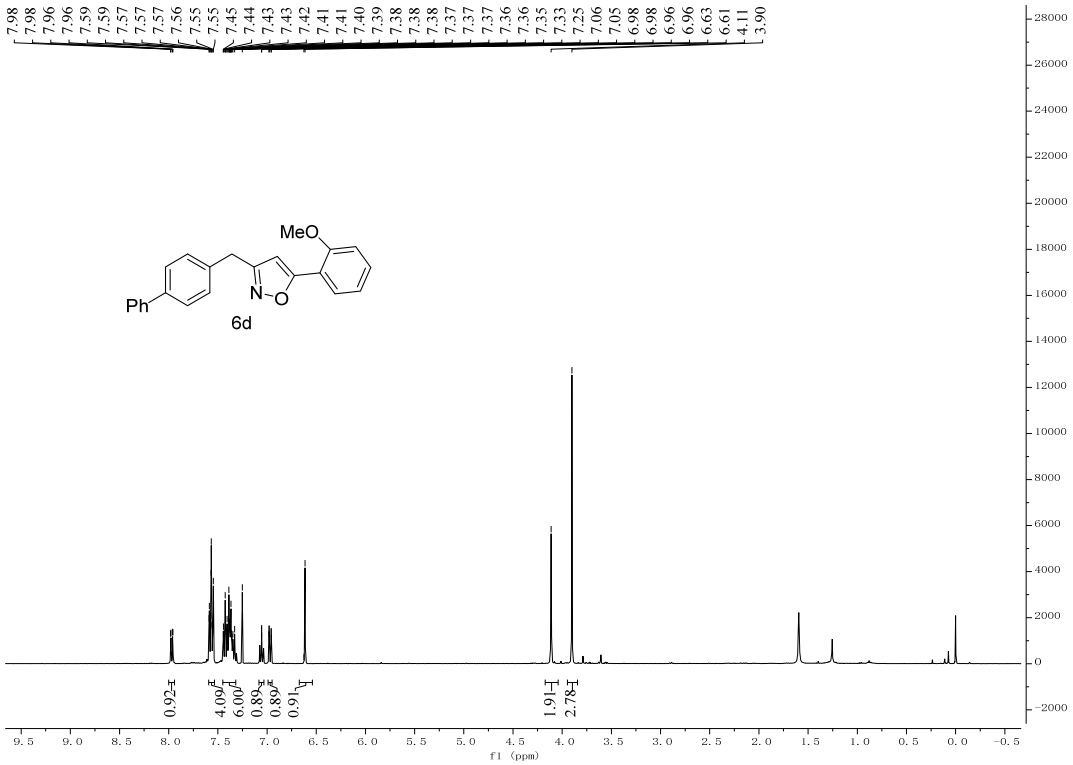
$^{19}F$ {$^{1}H$} NMR ($d_3$-MeCN, 376 MHz, 25 ºC) of **2 c'**



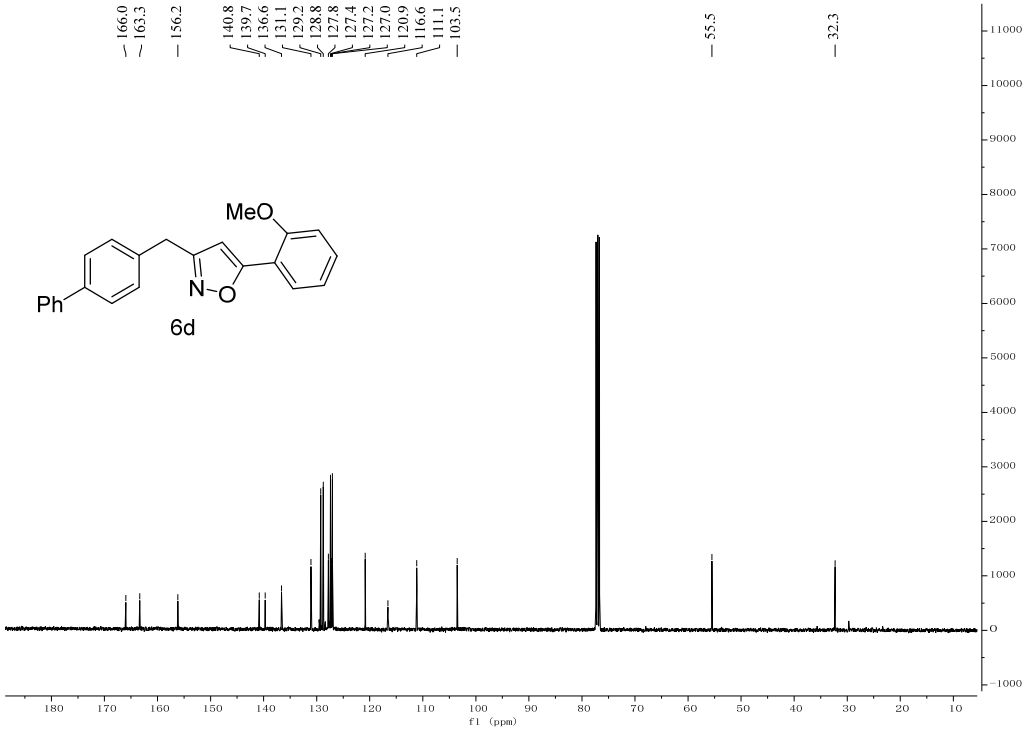

$^{13}C$ NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6c**



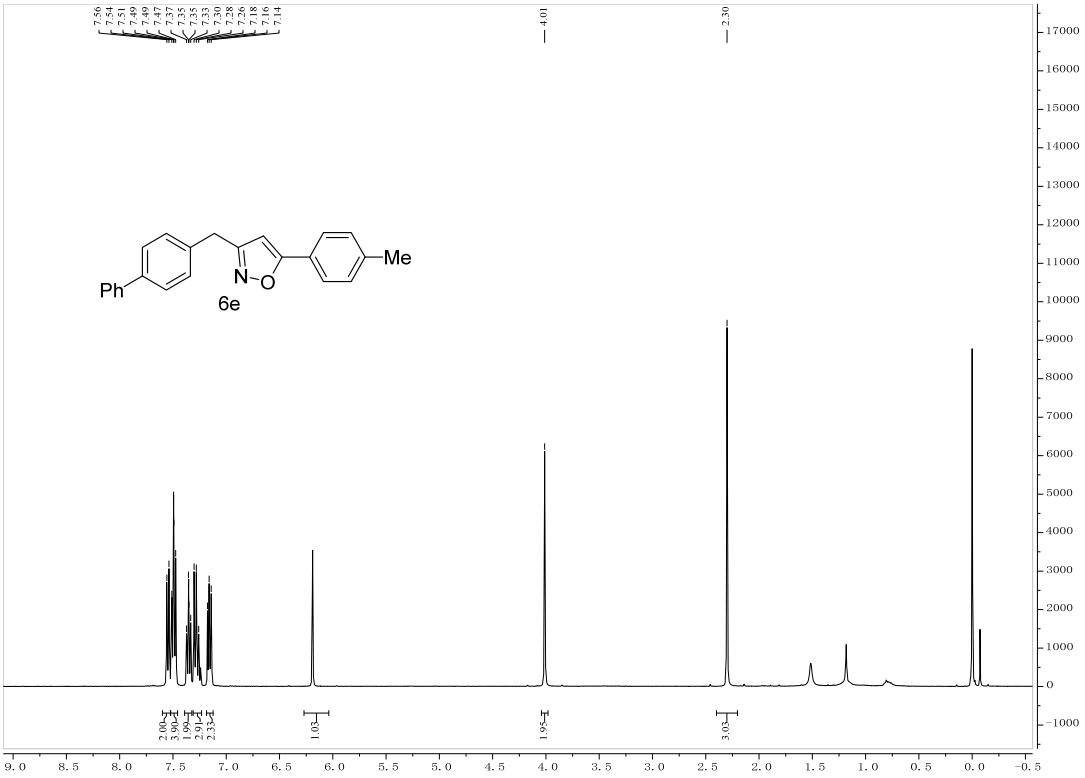
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6d**



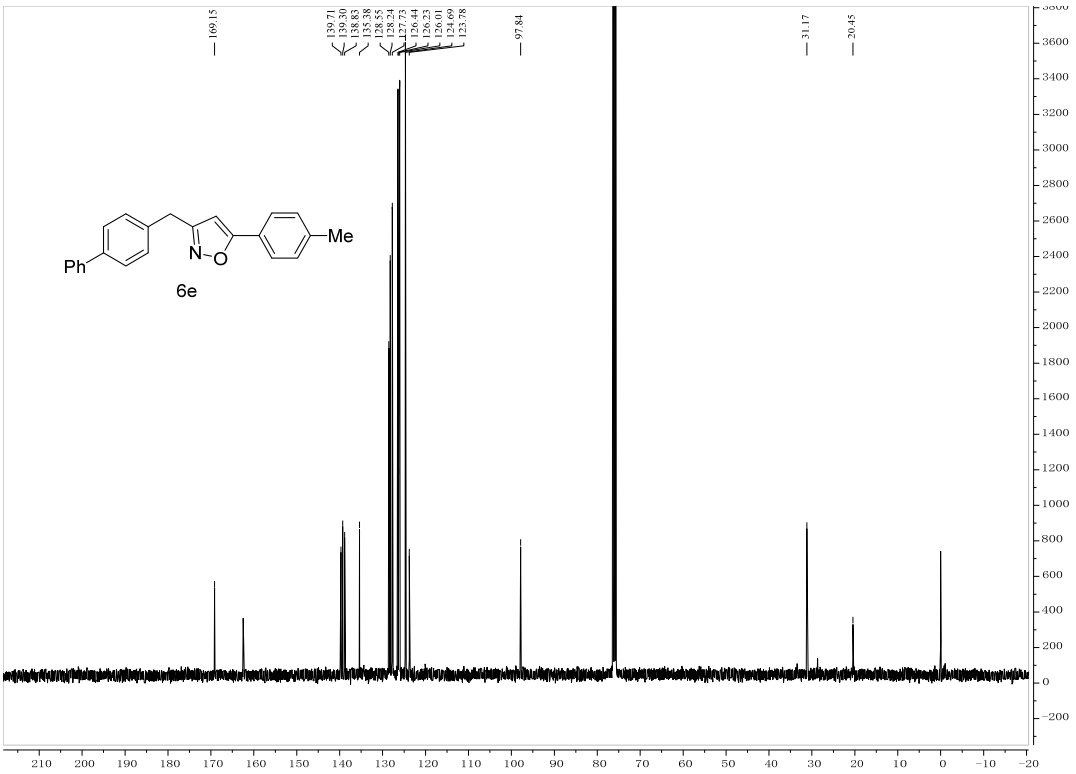

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6d**



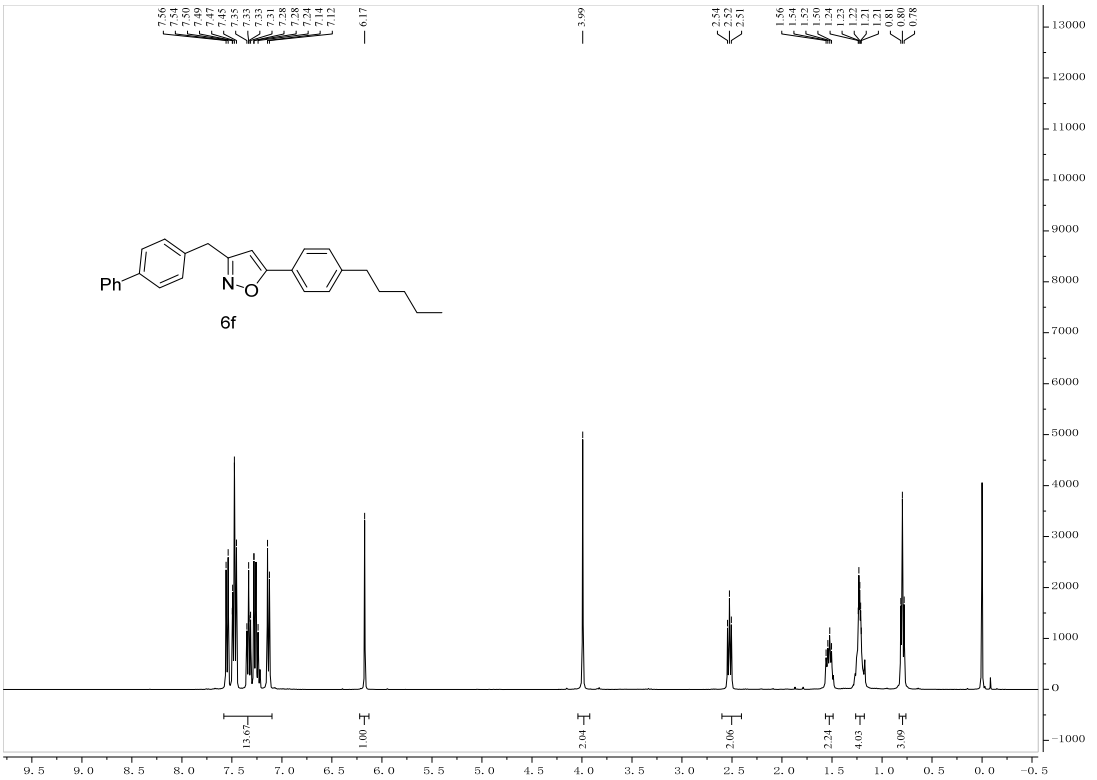
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6e**



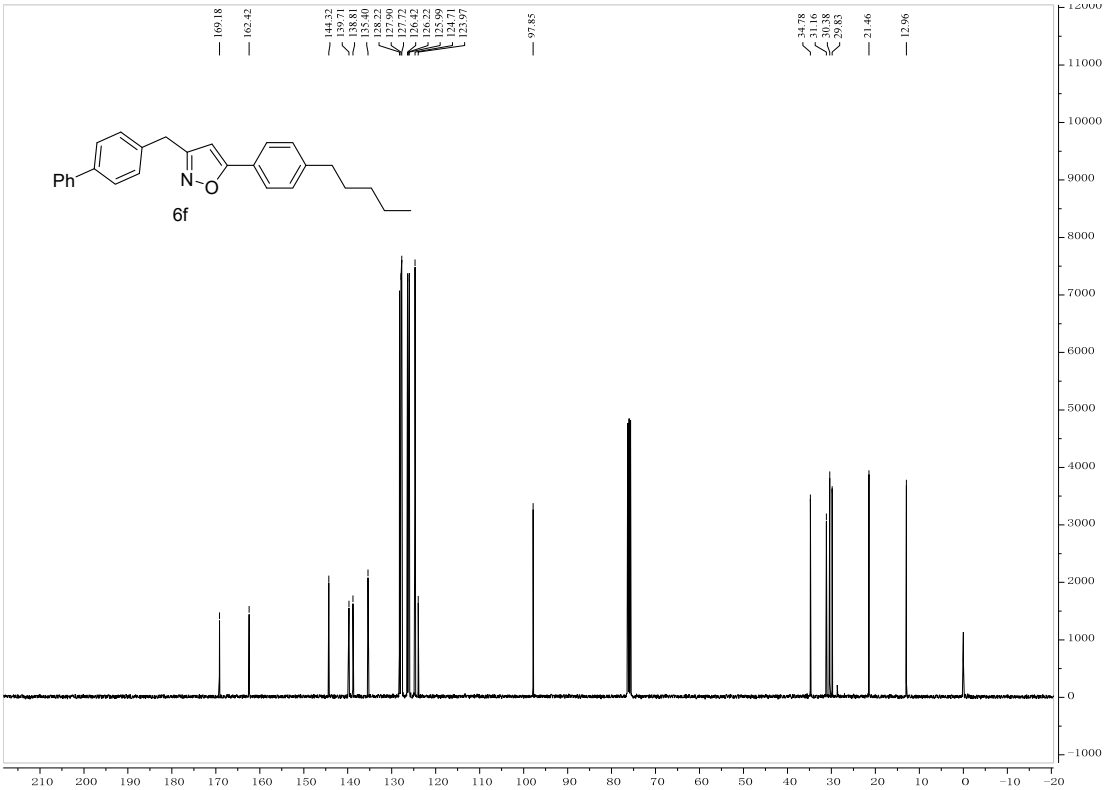

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6e**



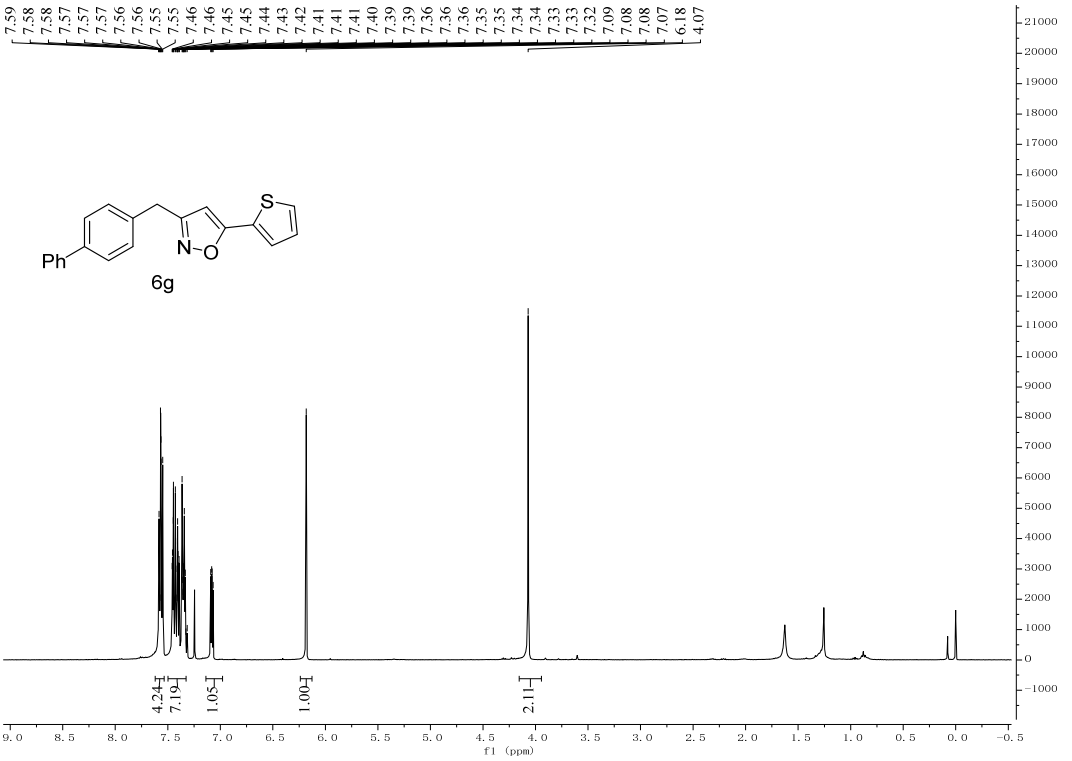
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6f**



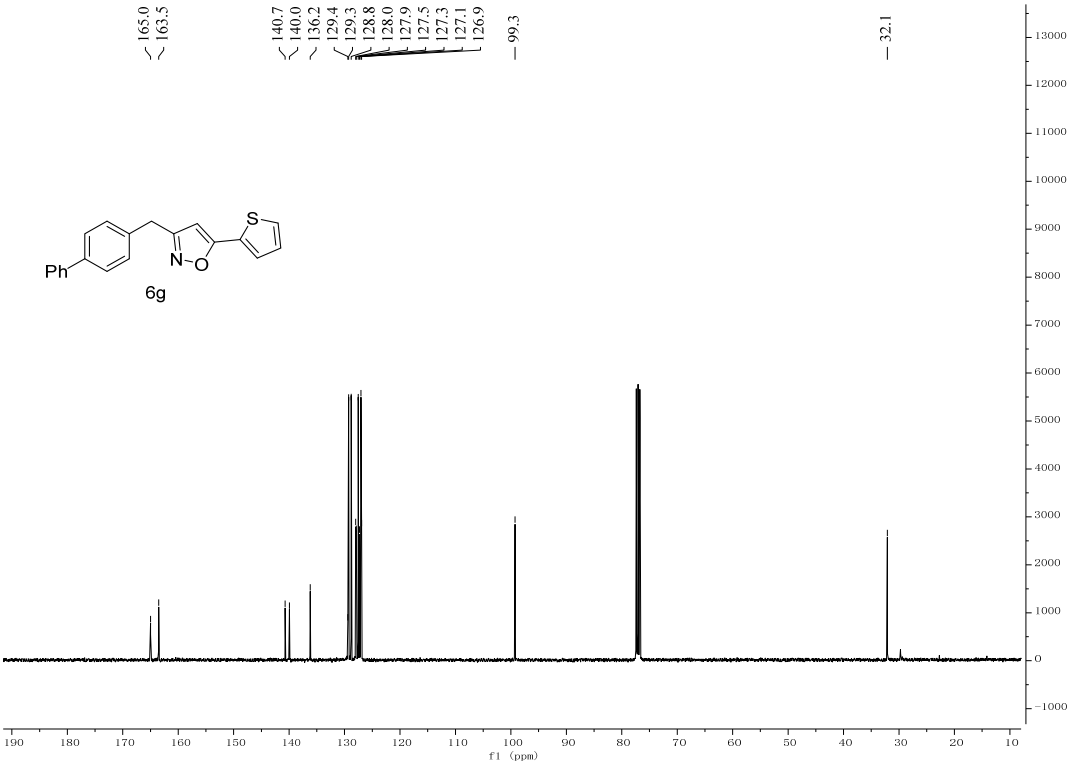

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6f**



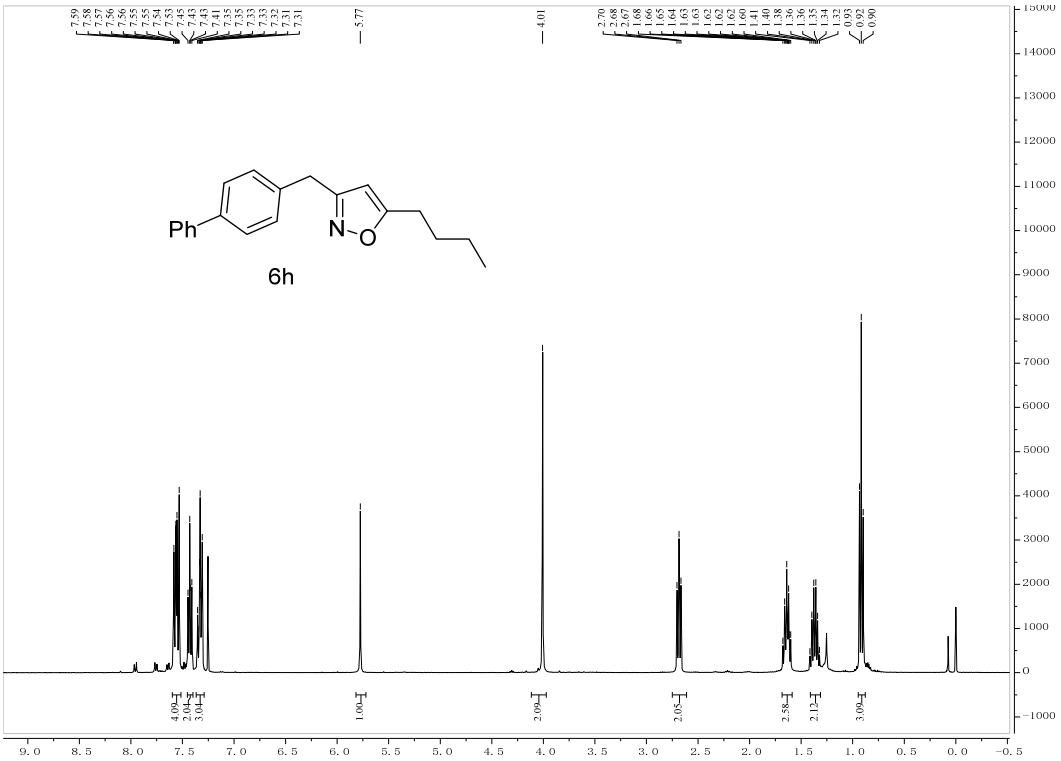
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6g**



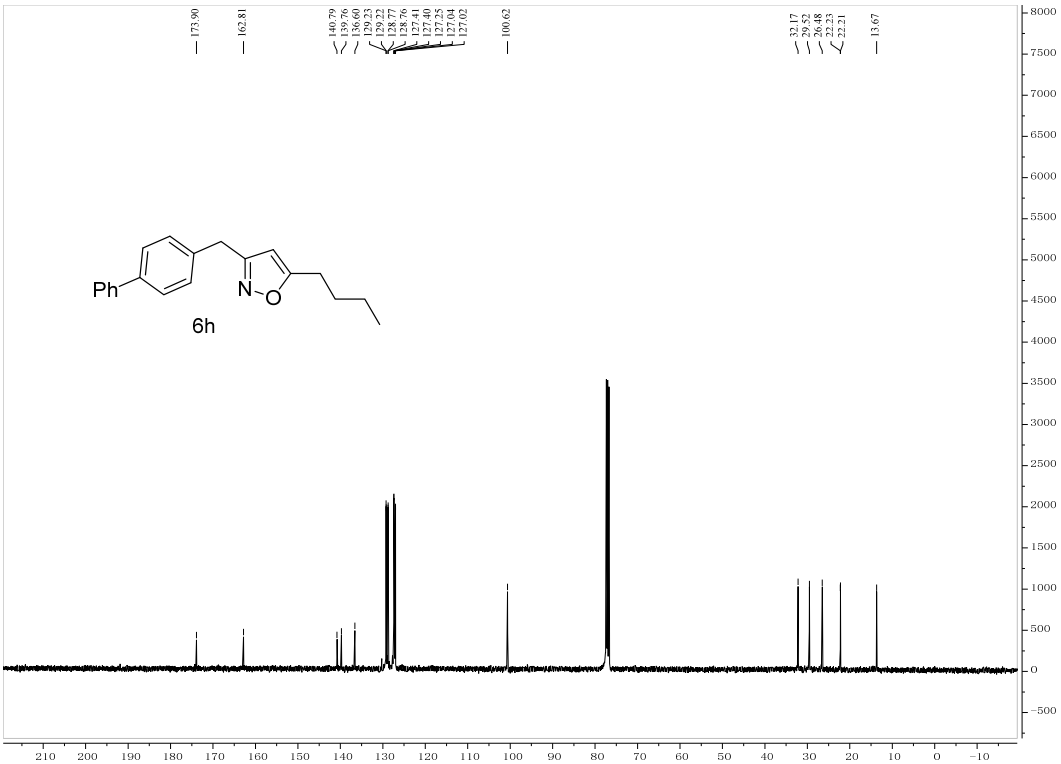

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6g**



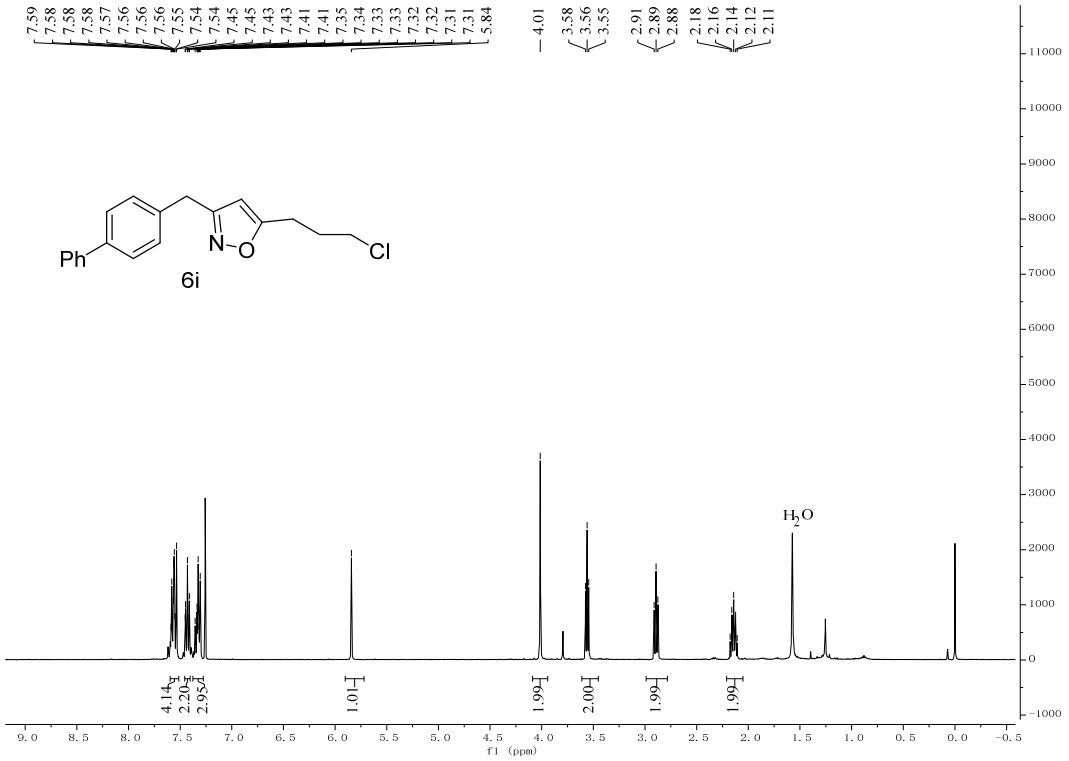
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6h**



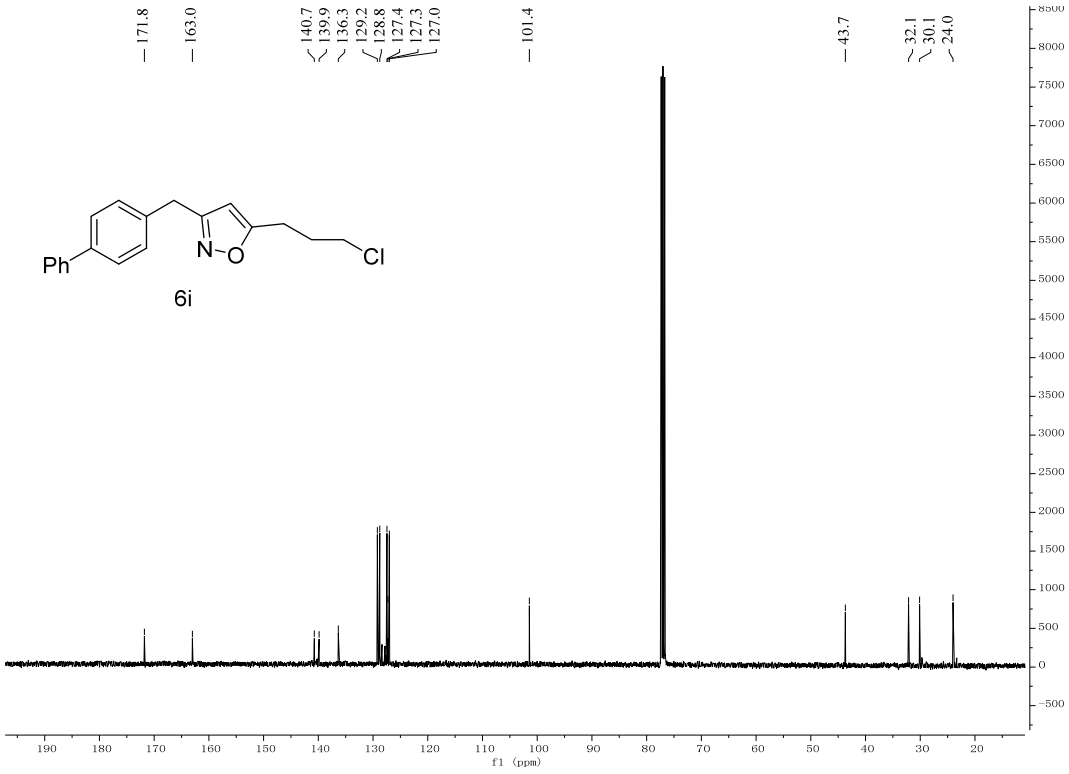

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of 6**h**



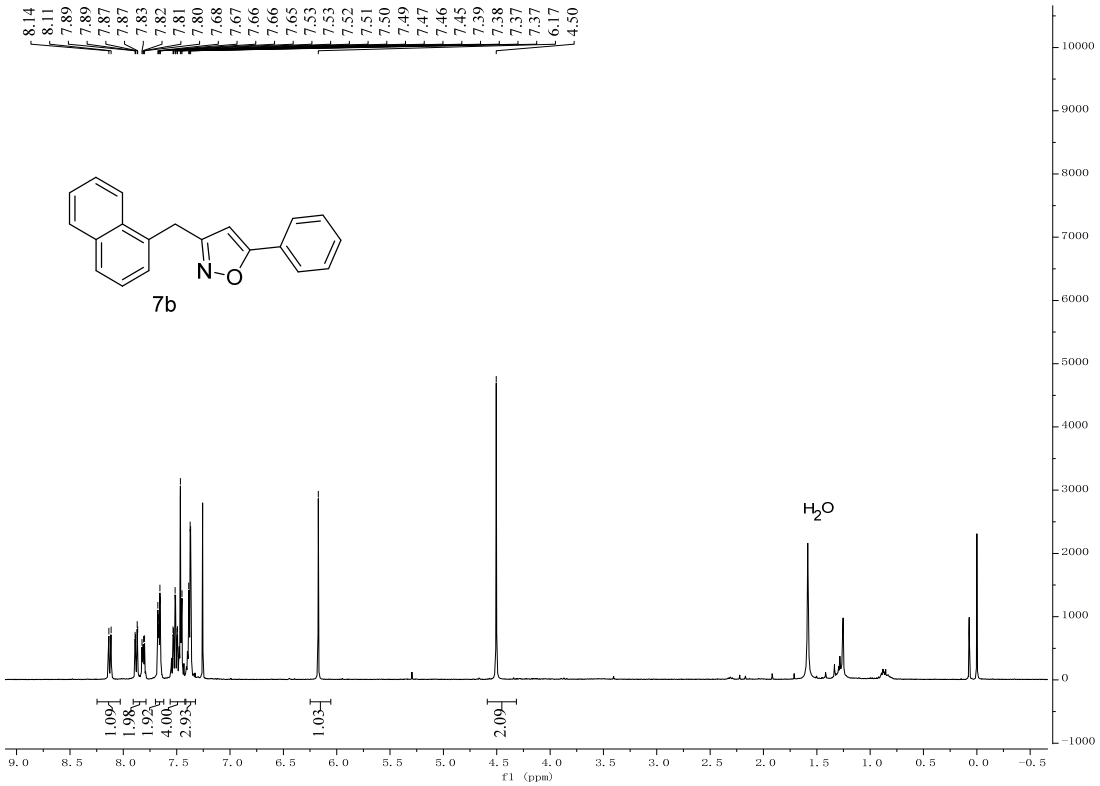
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **6i**



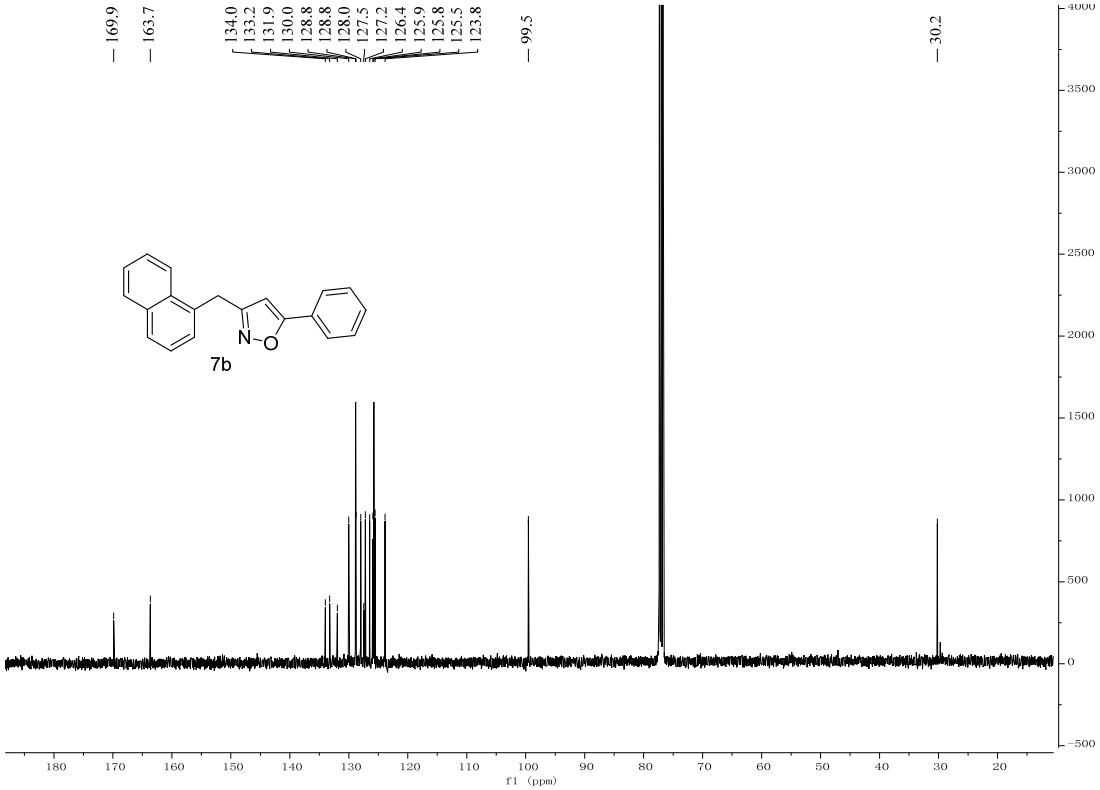

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **6i**



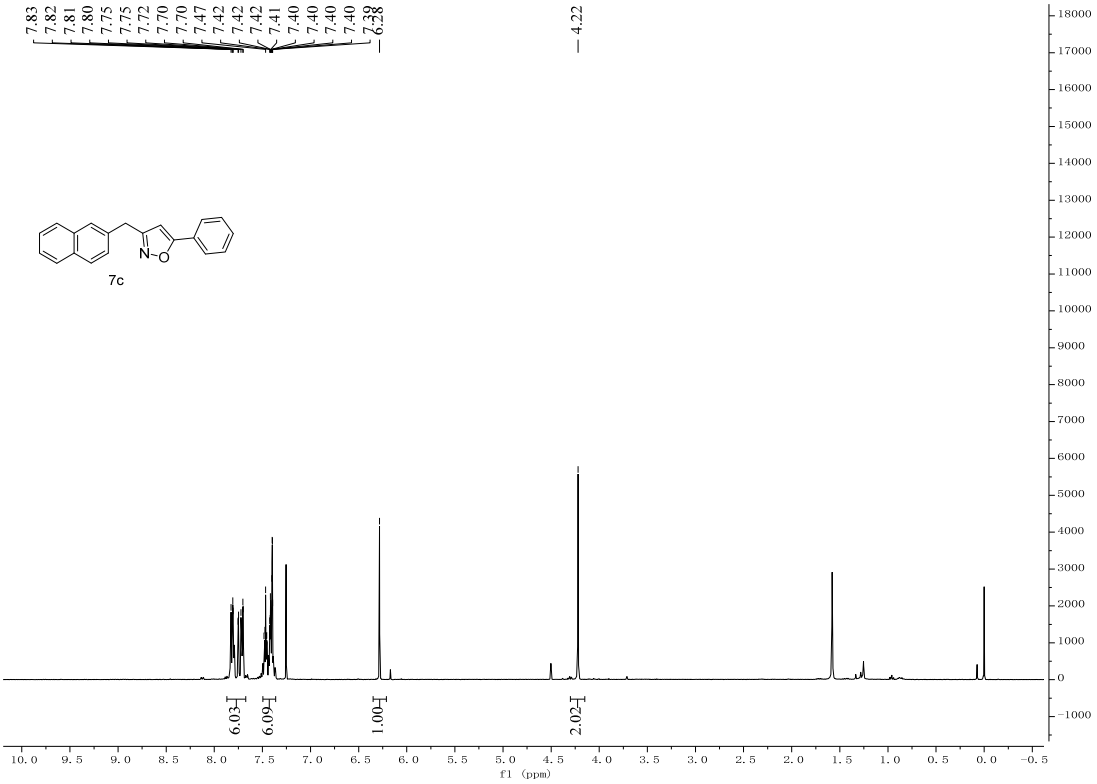
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **7b**



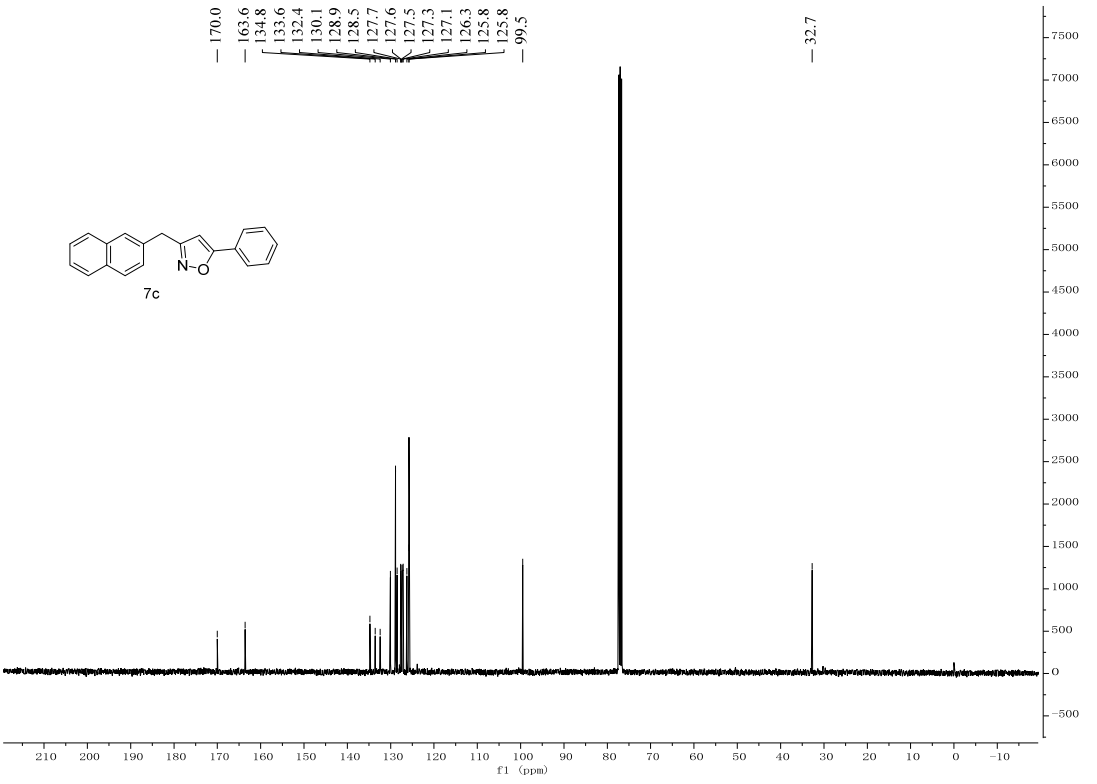

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **7b**



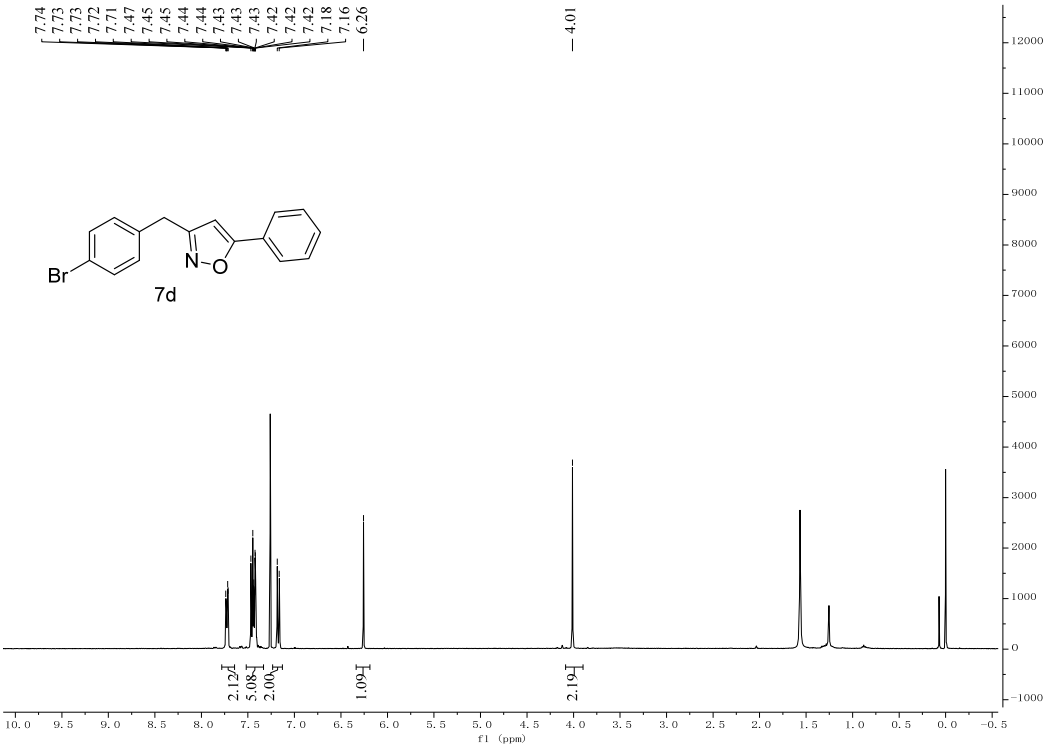
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **7c**



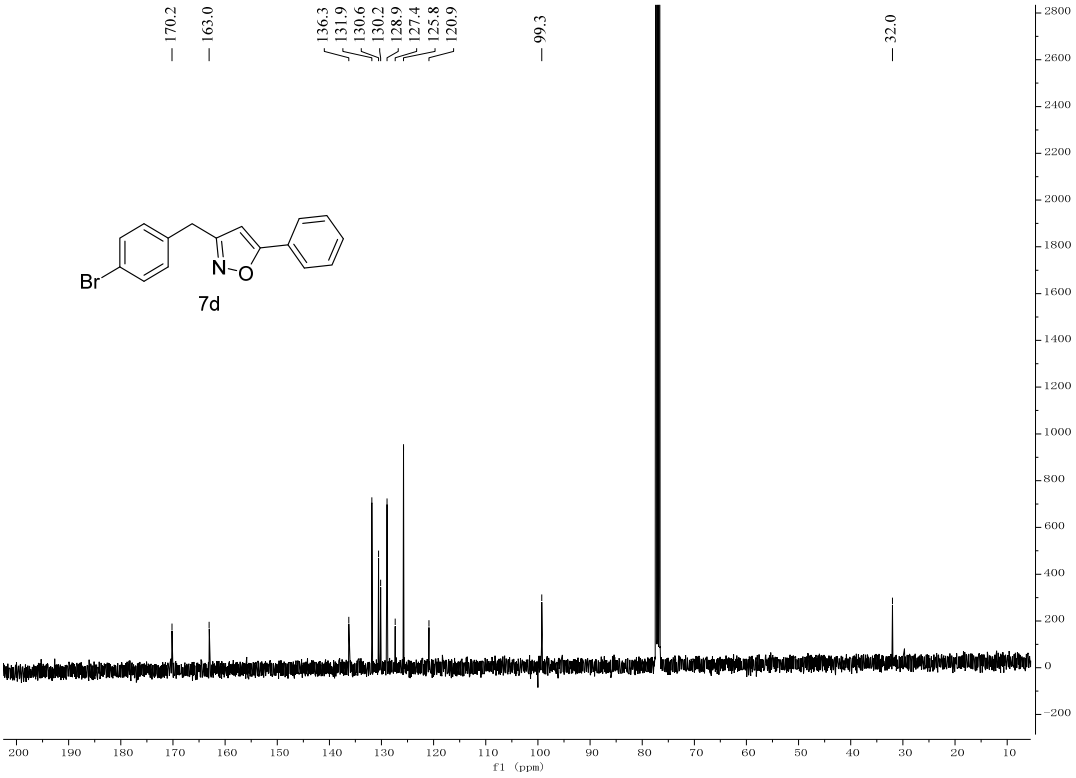

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **7c**



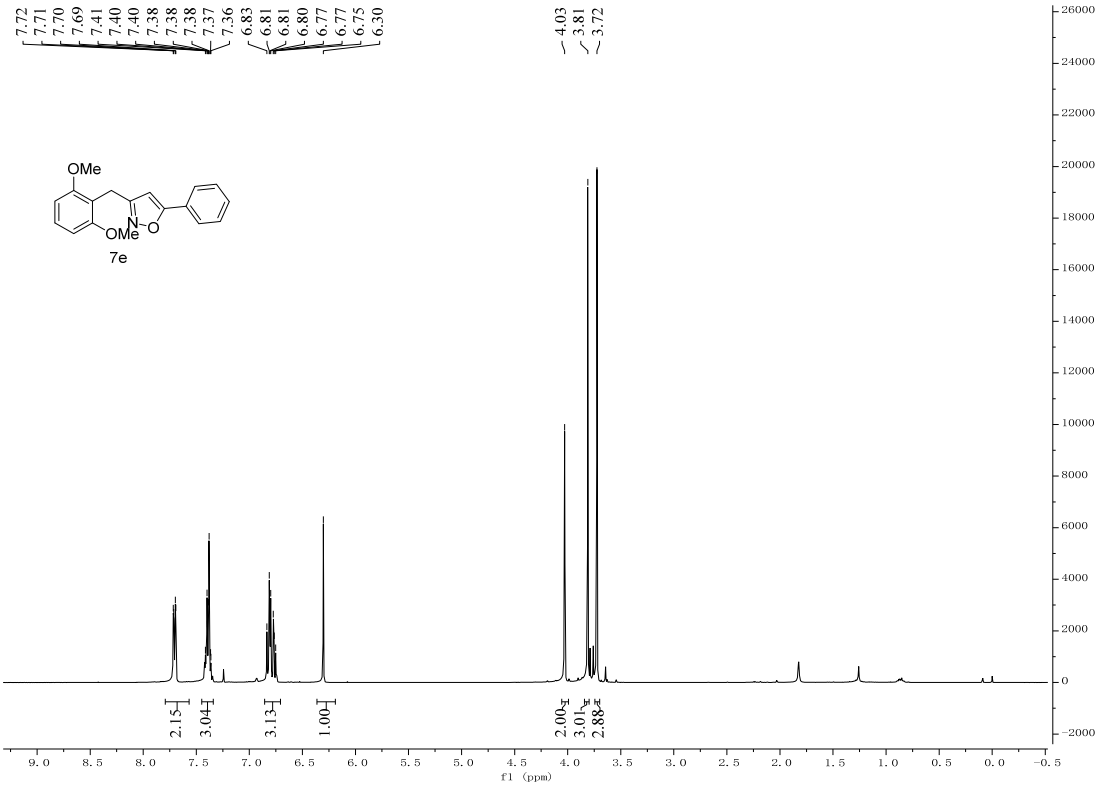
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **7d**



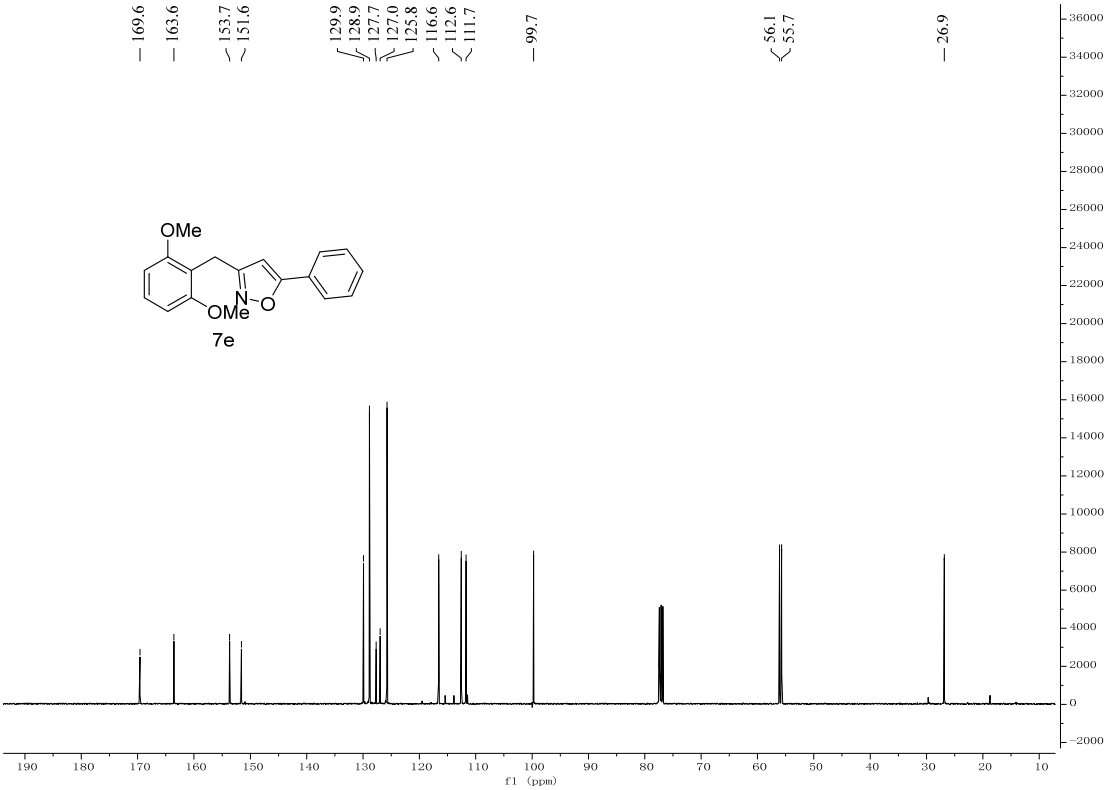

$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **7d**



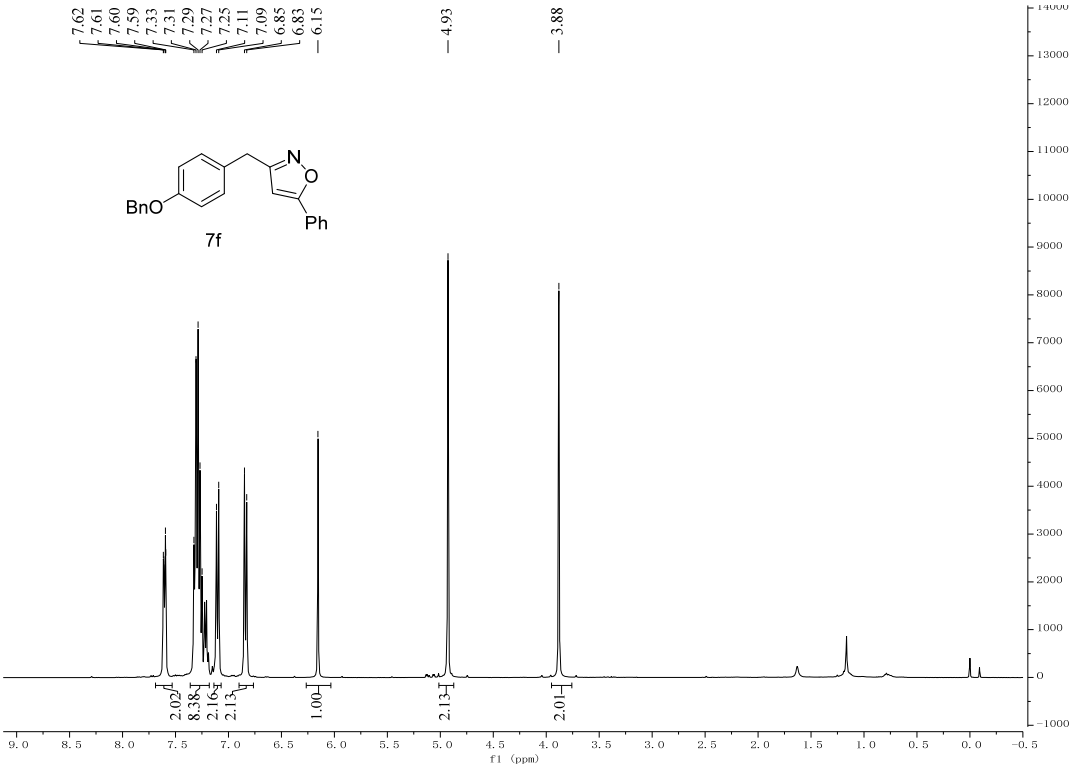
$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **7e**




$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **7e**



$^{1}$H NMR ($CDCl_3$, 400 MHz, 25 ºC) of **7f**




$^{13}$C NMR ($CDCl_3$, 100 MHz, 25 ºC) of **7f**