

## Electronic Supporting Information

### Development of an Indicator for the Direct Visualization of Radical Intermediates in Organic Reactions

Qiuli Yao<sup>ab</sup> and Chao-Jun Li<sup>\*a</sup>

<sup>a</sup>Department of Chemistry, McGill University, 801 Sherbrooke Street West, Montreal, Quebec H3A 0B8, Canada.

<sup>b</sup>School of Pharmacy, Zunyi Medical University, 6 Xuefu Road West, Zunyi, 563000, China  
E-mail: cj.li@mcgill.ca

General Information.....	S1
Experimental Part.....	S1
NMR Spectra.....	S5

#### General Information

All commercially available compounds were used without further purification. NMR spectra were recorded on a Bruker AVIIIHD 500 spectrometer. Chemical shifts are reported in parts per million (ppm) and referenced to an internal SiMe<sub>4</sub> standard (0 ppm) for <sup>1</sup>H NMR, chloroform-d (77.16 ppm) or CD<sub>3</sub>CN (118.26 ppm) for <sup>13</sup>C NMR. High-resolution mass spectrometry was conducted by using electro-spraying ionization (ESI) on a Thermo-Scientific Exactive Orbitrap. Thin-layer chromatography (TLC) was performed with Merck TLC silica gel 60 F<sub>254</sub>. Flash column chromatography was performed with E. Merck silica gel 60 (230–400 mesh).

#### Experimental Part

**Preparation of derivative A:** To a 25 mL reaction flask equipped with a condenser in argon was added Rhodamine B (1.5 mmol) and 1,2-dichloroethane (15 mL). With vigorous stirring, POCl<sub>3</sub> (4.5 mmol, 0.45 mL) was added dropwise to the mixture. After that the temperature was increased to 86 °C. The reaction mixture was cooled to r.t. after 4 h and concentrated to give the crude acid chloride, to which was directly added 1,2-dichloroethane (15 mL), BnNH<sub>2</sub> (2.25 mmol) and NEt<sub>3</sub> (4.5 mmol) dropwise. The reaction was run 2 days until it was concentrated and purified by flash column chromatography to give 587 mg pure product **A** as a white solid in 81% yield, mp 166–167 °C. <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>CN) δ 7.83 (m, 1H), 7.50 (m, 2H), 7.01–6.96 (m, 4H), 6.90 (m, 2H), 6.29 (d, *J*=3.5 Hz, 2H), 6.2 (d, *J*=5 Hz, 2H), 6.15 (dd, *J*<sub>1</sub>=10 Hz, *J*<sub>2</sub>=3 Hz, 2H), 4.18 (s, 2H), 3.3 (q, *J*=6.7 Hz, 8H), 1.09 (t, *J*=7.5 Hz, 12H). <sup>13</sup>C NMR (126 MHz, CD<sub>3</sub>CN) δ 168.3, 154.6, 154.2, 149.7, 139.0, 133.5, 132.3, 129.9, 129.18, 129.15, 128.6, 127.2, 124.5, 123.4, 109.1, 106.3, 98.2, 65.6, 45.0, 44.4, 12.8. HRMS (ESI) calc. for (M+H)<sup>+</sup> C<sub>35</sub>H<sub>38</sub>N<sub>3</sub>O<sub>2</sub>: 532.2959, found 532.2961.

**Typical experimental procedure for the reaction of derivative A with radical intermediates:** To derivative **A** and radical initiator (DTBP, BPO, AIBN, or AAPH) were added the specific solvent. The air-tight tube (10 mL) containing these reactants and solvent was evacuated by four freeze-pump-thaw cycles and back-filled with ultra-purified argon (>99.999%) prior to use. The temperature of the reaction was increased from r.t. to the specific degree and pictures were taken by camera upon change of color.

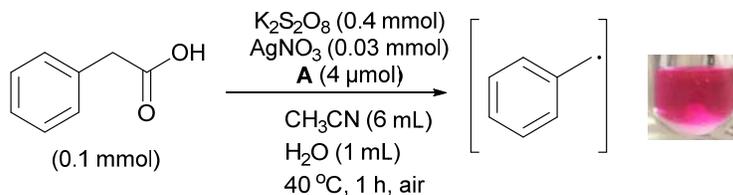
In the bromination of toluene by NBS, compounds **A**, BPO, toluene, NBS and CCl<sub>4</sub> were added to an air-tight tube (10 mL). The mixture was evacuated by four freeze-pump-thaw cycles and back-filled with ultra-purified argon (>99.999%). The temperature for the reaction was raised from r.t. to 80 °C in 10 min and then kept at this temperature for 2 h. Then the reaction mixture was cooled to room temperature. 1,3,5-Trimethoxybenzene was added as an internal standard to the solution and <sup>1</sup>HNMR spectrum was taken to determine the yields for products **1** and **2**. Further purification by TLC (n-hexane) gave a mixture of products **1** and **2** as colorless oils, which were difficult to separate. <sup>1</sup>HNMR of compound **1** (500 MHz, CDCl<sub>3</sub>) δ 7.45-7.28 (m, 5H), 4.54 (s, 2H). <sup>13</sup>CNMR of compound **1** (126 MHz, CDCl<sub>3</sub>) δ 137.8, 129.1, 128.8, 128.4, 33.6. These data were consistent with the literature report.<sup>1</sup> <sup>1</sup>HNMR of compound **2**: (500 MHz, CDCl<sub>3</sub>) δ 7.62-7.61 (m, 2H), 7.45-7.28 (m, 3H). <sup>13</sup>CNMR of compound **2**: (126 MHz, CDCl<sub>3</sub>) δ 142.0, 129.9, 128.7, 126.5, 41.1. These data were consistent with the literature report.<sup>2</sup>

In the addition reaction of styrene to BrCCl<sub>3</sub>, compounds **A**, BPO, BrCCl<sub>3</sub> and styrene were added to an air-tight tube (10 mL) sequentially, and was evacuated by four freeze-pump-thaw cycles and back-filled with ultra-purified argon (>99.999%). The temperature for the reaction was raised from r.t. to 80 °C in 10 min and then kept at this temperature for 2 h. After that the reaction mixture was concentrated and product **3** was purified by TLC (eluent: n-hexane/EtOAc=20:1) as colorless oil. <sup>1</sup>HNMR of compound **3** (500 MHz, CDCl<sub>3</sub>): δ 7.52-7.50 (m, 2H), 7.42-7.41 (m, 2H), 7.37-7.34 (m, 1H), 5.45 (dd, *J*=7.5, 5.0 Hz, 1H), 3.82-3.81 (m, 2H); <sup>13</sup>CNMR of compound **3**: (126 MHz, CDCl<sub>3</sub>) δ 140.8, 129.0, 128.9, 127.9, 96.6, 62.7, 47.6. These data were consistent with the literature report.<sup>3</sup>

In the trifluoromethylation reaction, compounds **4**, **5**, **A** and solvent were added to an air-tight quartz tube (10 mL), evacuated by four freeze-pump-thaw cycles, and back-filled with ultra-purified argon (>99.999%). Then the solution was irradiated by using a standard LZC-4V photoreactor from Luzchem Company for 24 h. The mixture of the reaction was filtered through celite, and the solution was concentrated. Product **6** or **7** was purified by TLC (eluent: n-hexane/EtOAc 20:1) as white solid. <sup>1</sup>HNMR of compound **6**: (500 MHz, CDCl<sub>3</sub>) δ 6.14 (s, 2H), 3.85 (s, 3H), 3.83 (s, 6H); <sup>13</sup>CNMR of compound **6**: (126 MHz, CDCl<sub>3</sub>) δ 163.6, 160.5, 124.5 (q, *J*<sub>C-F</sub>=273.8 Hz, CF<sub>3</sub>), 100.5 (q, *J*<sub>C-F</sub>=30.2 Hz), 91.4, 56.4, 55.5; <sup>19</sup>FNMR of compound **6**: (471 MHz, CDCl<sub>3</sub>) δ -54.2. These data were consistent with the literature report.<sup>4</sup> <sup>1</sup>HNMR of compound **7**: (500 MHz, CDCl<sub>3</sub>) δ 6.35 (s, 1H), 3.93 (s, 6H), 3.82 (s, 3H); <sup>13</sup>CNMR of compound **7**: (126 MHz, CDCl<sub>3</sub>) δ 162.3, 160.6, 123.4 (q, *J*<sub>C-F</sub>=274.3 Hz), 106.2 (q, *J*<sub>C-F</sub>=30.2 Hz), 92.6, 64.8 (t, *J*=1.9 Hz), 56.3; <sup>19</sup>FNMR of compound **7**: (471 MHz, CDCl<sub>3</sub>) δ -55.5. These data were consistent with the literature report.<sup>4</sup>

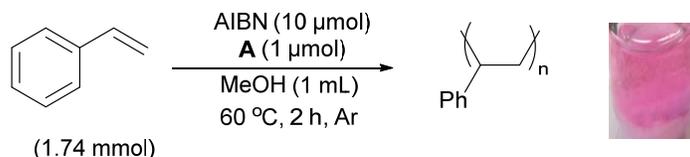
#### **Other examples for the detection of radical intermediates by derivative A**

Derivative **A** was used in the detection of benzyl radical intermediates, which were formed from the decarboxylation of phenylacetic acid by redox processes (Scheme S1).<sup>5</sup> To a 10 mL tube was added phenylacetic acid (0.1 mmol), K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (0.4 mmol), AgNO<sub>3</sub> (0.03 mmol), **A** (4 μmol), CH<sub>3</sub>CN (6 mL) and H<sub>2</sub>O (1 mL) sequentially under air. The temperature for the reaction was raised from r.t. to 40 °C. The solution turned into pink color in 5 min.



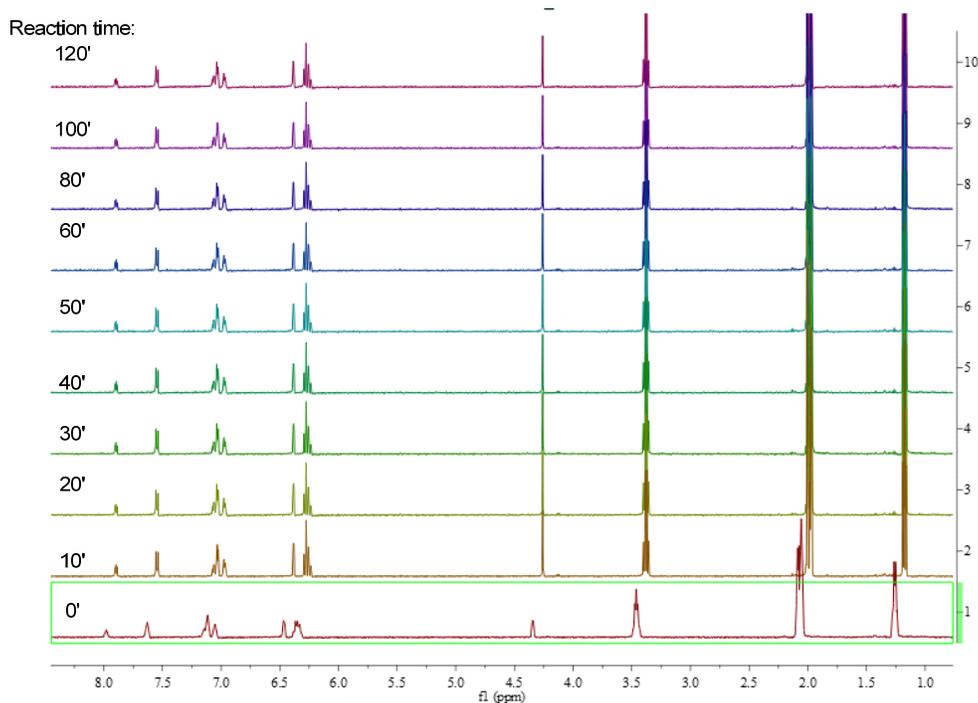
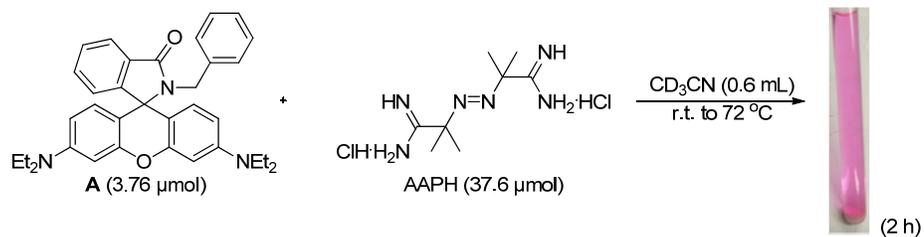
**Scheme S1.** Color change for the oxidative decarboxylation of phenylacetic acid

Derivative **A** was used in the detection of radical intermediate in the polymerization of styrene initiated by AIBN in the solvent of methanol (Scheme S2).<sup>6</sup> To a 10 mL tube was added **A** (1  $\mu\text{mol}$ ), AIBN (10  $\mu\text{mol}$ ), MeOH (1 mL) and styrene (1.74 mmol, 0.2 mL) sequentially, and was evacuated by four freeze-pump-thaw cycles and back-filled with ultra-purified argon (>99.999%). The temperature for the reaction was raised from r.t. to 80  $^\circ\text{C}$  and then kept at this temperature for 2 h. The solution turned into pink color in 1 h.



**Scheme S2.** Color change for the polymerization of styrene

**The reaction of derivative A with AAPH followed by  $^1\text{H}$ NMR (Figure S1):** To an NMR tube with an air-tight cap was added derivative **A** (3.76  $\mu\text{mol}$ ), AAPH (37.6  $\mu\text{mol}$ ) and  $\text{CD}_3\text{CN}$  (0.6 mL). The NMR tube containing these reactants and solvent was evacuated by four freeze-pump-thaw cycles and back-filled with ultra-purified argon (>99.999%) prior to use. The temperature of the reaction was raised from r.t. to 72  $^\circ\text{C}$  in 10 min, and  $^1\text{H}$ NMR spectra were taken by a Varian VNMRS 500 spectrometer at the time indicated in Figure S1.



Conditions: A (3.76  $\mu\text{mol}$ ), AAPH (37.6  $\mu\text{mol}$ ),  $\text{CD}_3\text{CN}$  (0.6 mL), heated from r.t. to 72  $^\circ\text{C}$  in 10 min. The spectra were taken at (1) 0 min at 25  $^\circ\text{C}$ , (2) 10 min when the temperature reached 72  $^\circ\text{C}$ , (3) 20 min, (4) 30 min, (5) 40 min, (6) 50 min, (7) 60 min, (8) 80 min, (9) 100 min, and (10) 120 min.

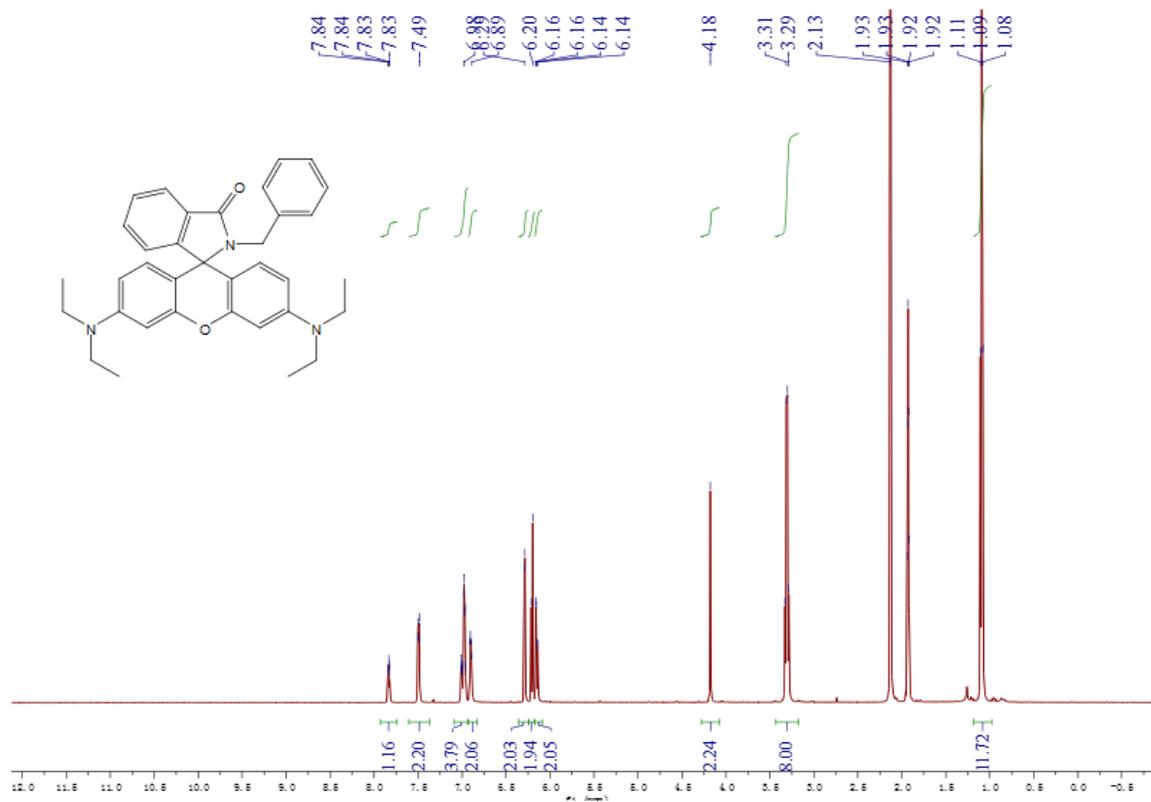
**Figure S1.** The reaction of derivative **A** with AAPH followed by  $^1\text{H}$ NMR in  $\text{CD}_3\text{CN}$

## References

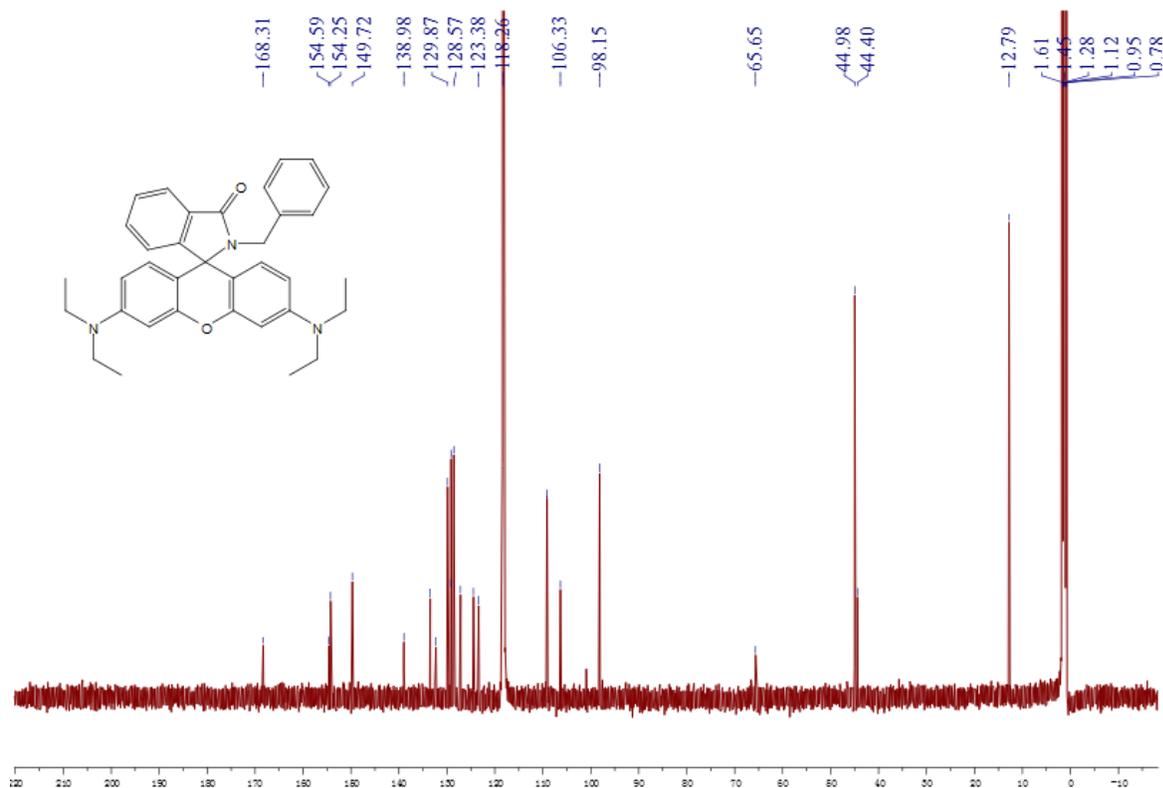
1. M. Bullpitt, W. Kitching, D. Doddrell and W. Adcock, *J. Org. Chem.*, 1976, **41**, 760.
2. R. W. Hoffmann and P. Bovicelli, *Synthesis*, 1990, **1990**, 657.
3. J. R. Khusnutdinova, N. P. Rath and L. M. Mirica, *Angew. Chem. Int. Ed.*, 2011, **50**, 5532.
4. L. Li, X. Mu, W. Liu, Y. Wang, Z. Mi and C.-J. Li, *J. Am. Chem. Soc.*, 2016, **138**, 5809.
5. X. Tan, Z. Liu, H. Shen, P. Zhang, Z. Zhang and C. Li, *J. Am. Chem. Soc.*, 2017, **139**, 12430.
6. H. Inoue, M. Helbig and O. Vogl, *Macromolecules*, 1977, **10**, 1331.

# NMR Spectra

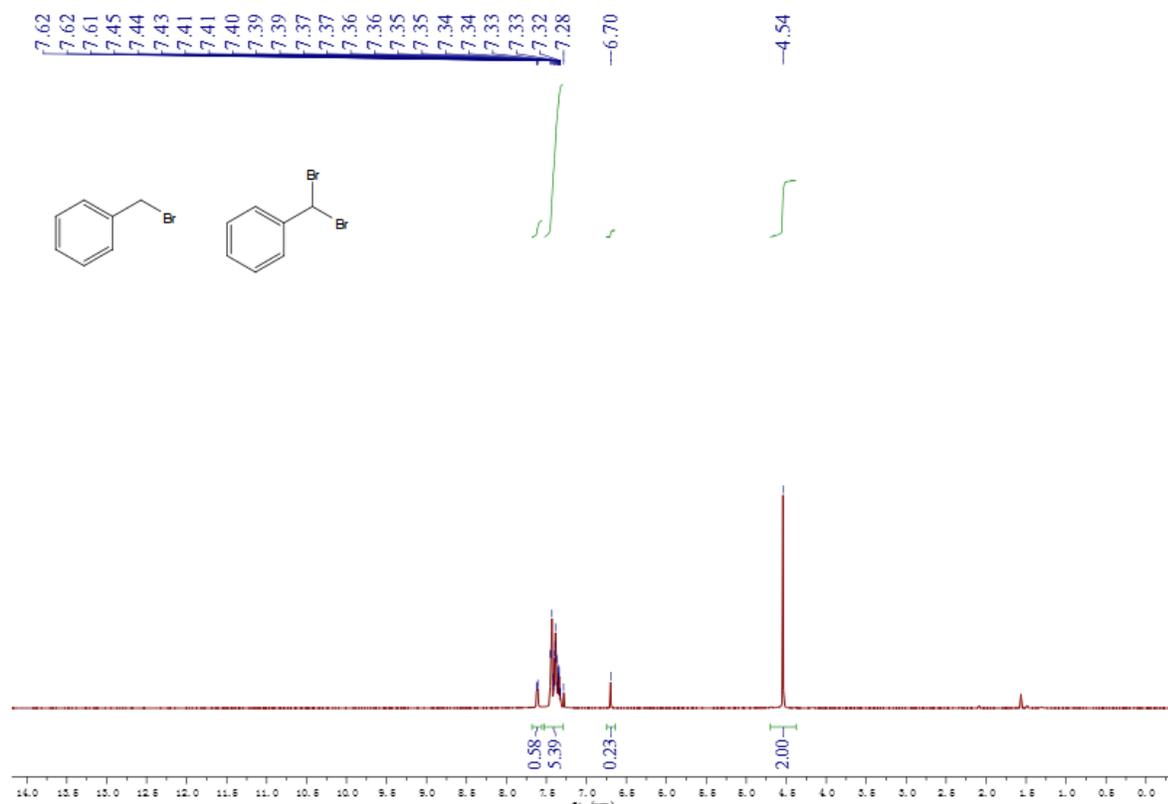
## <sup>1</sup>HNMR of compound A



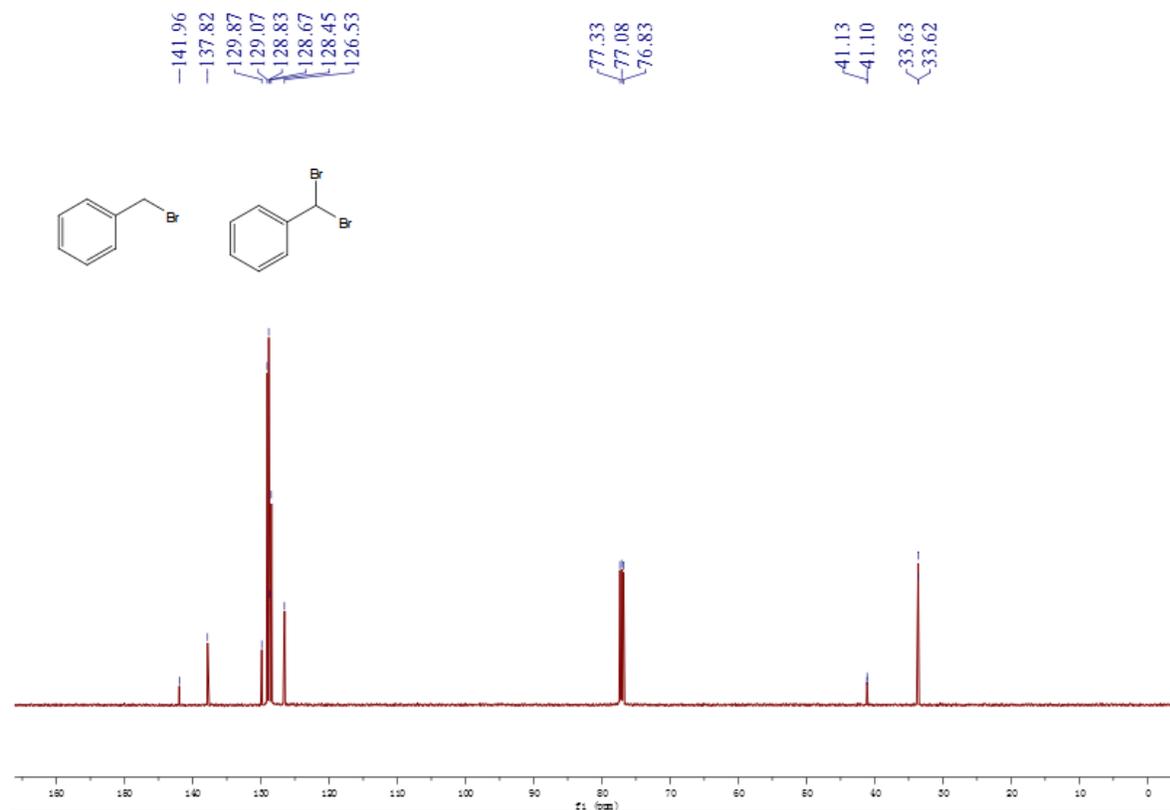
## <sup>13</sup>CNMR of compound A



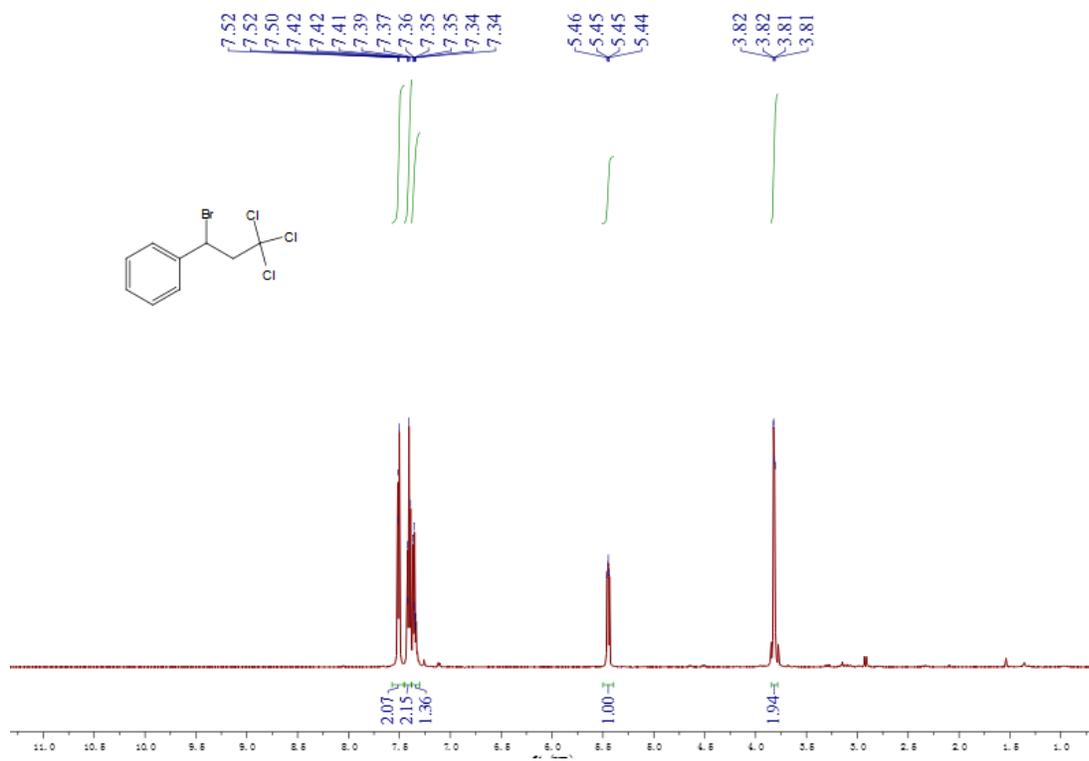
<sup>1</sup>HNMR of unseparated compounds **1** and **2**



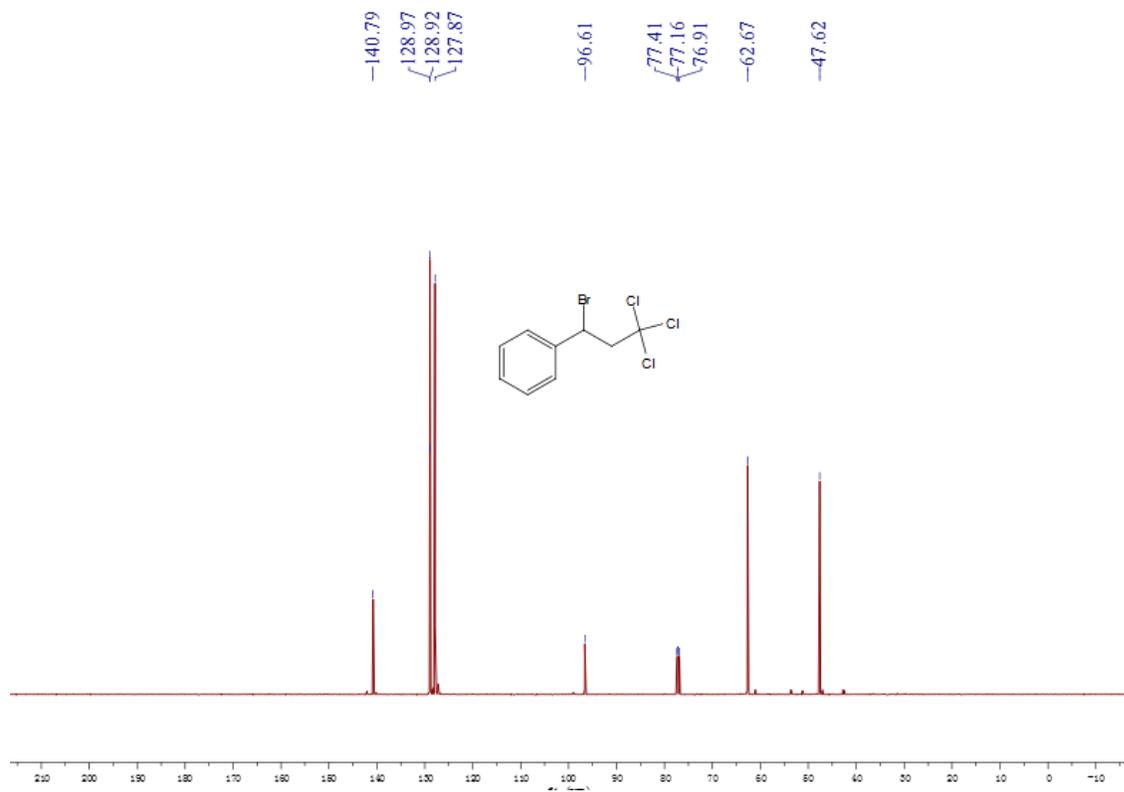
<sup>13</sup>CNMR of unseparated compounds **1** and **2**



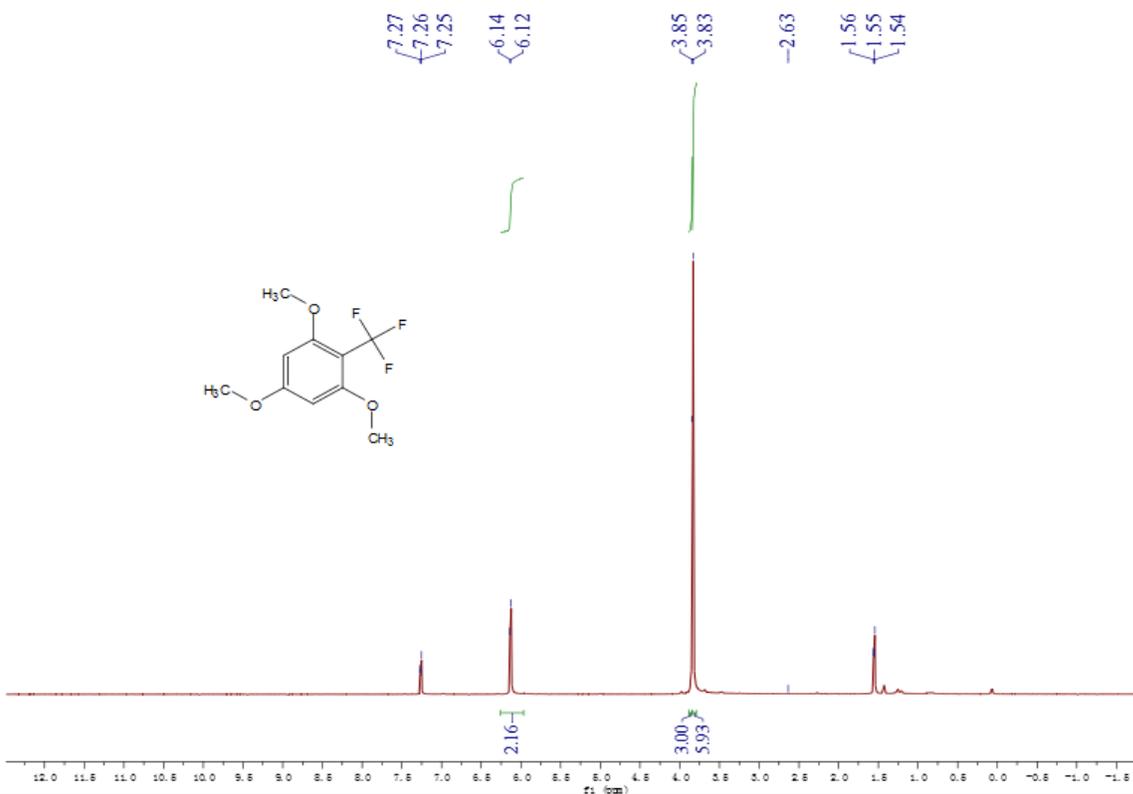
### <sup>1</sup>HNMR of compound 3



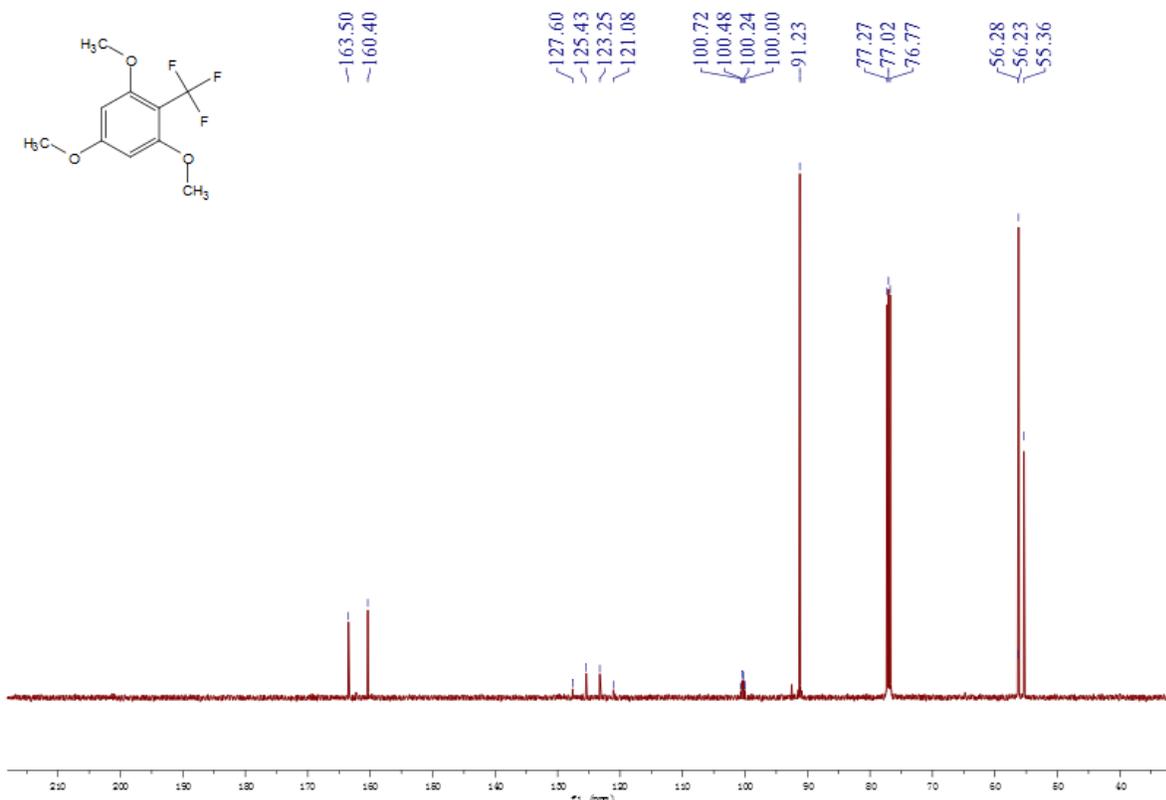
### <sup>13</sup>CNMR of compounds 3



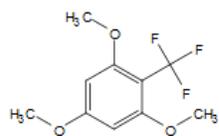
<sup>1</sup>H NMR of compound 6



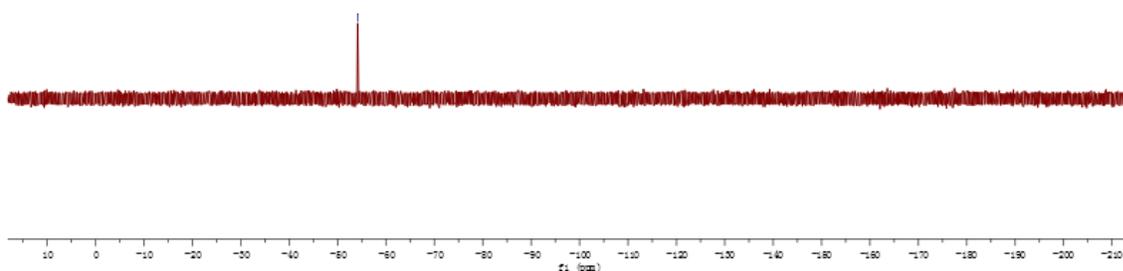
<sup>13</sup>C NMR of compound 6



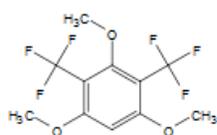
$^{19}\text{F}$ NMR of compound 6



-54.17



$^1\text{H}$ NMR of compound 7

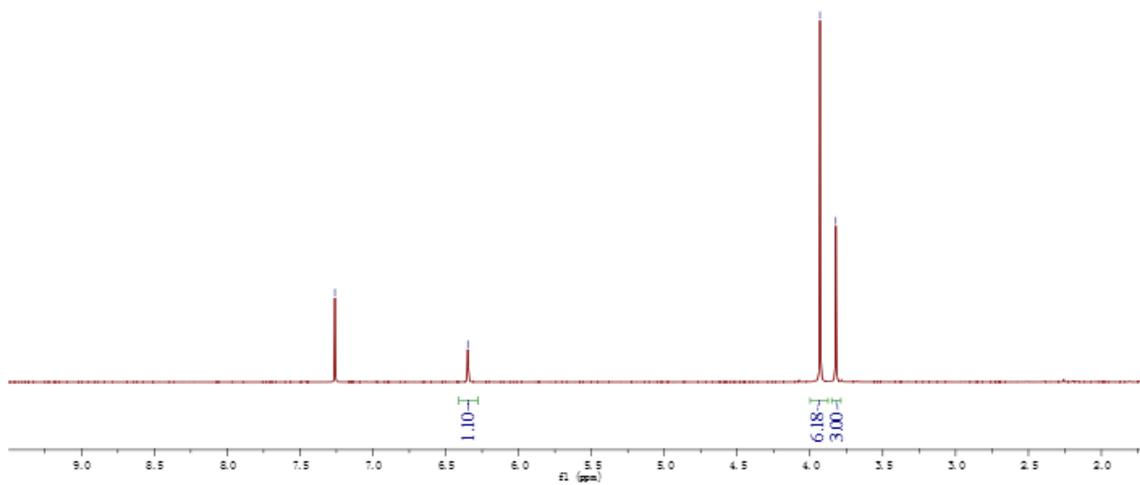


-7.26

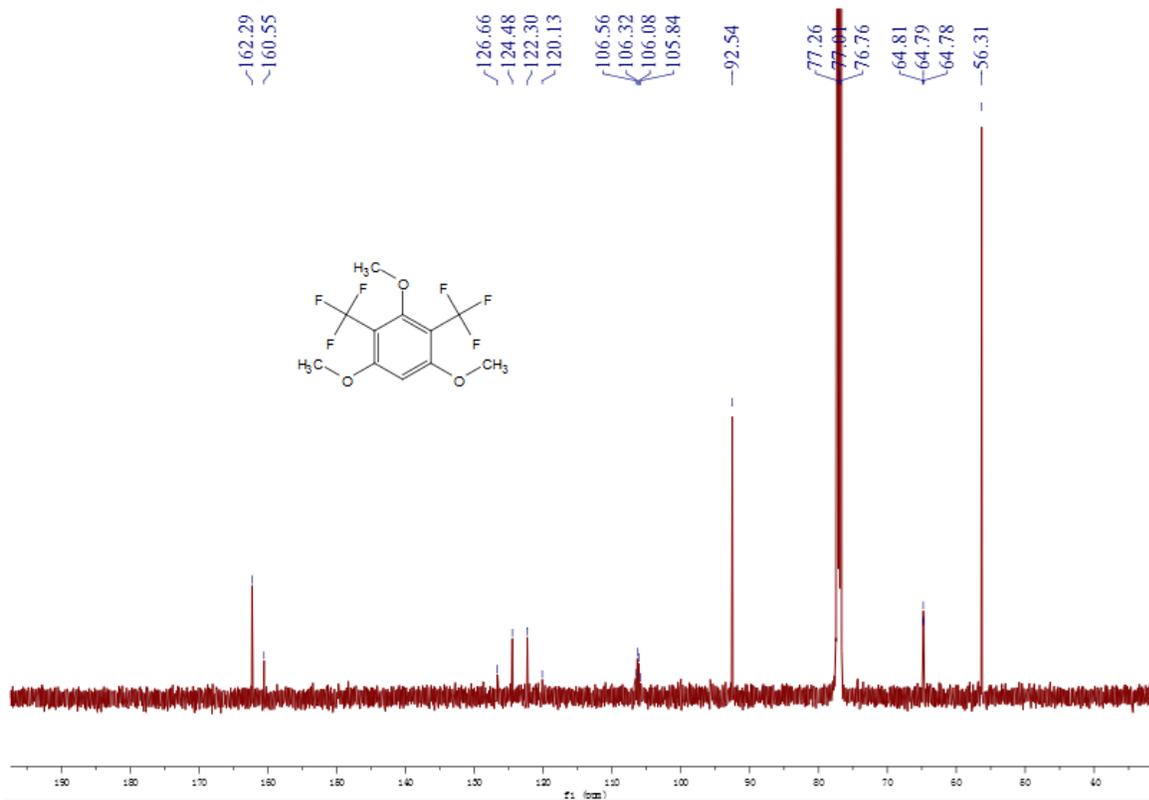
-6.35

-3.93

-3.82



<sup>13</sup>CNMR of compound 7



<sup>19</sup>F NMR of compound 7

