

## Remarkable effect of phosphine on the reactivity of *O,P*-acetal –Efficient substitution reaction of *O,P*-acetal

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### General

The  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  and  $^{31}\text{P}$  NMR spectra were measured by JEOL JNM-ECS 400 or JEOL JNM-AL 300 spectrometers with tetramethylsilane as an internal standard at 20-25 °C. IR spectra were recorded by SHIMADZU FTIR-8400 using a diffuse reflectance measurement of samples dispersed in KBr powder. HRMS spectra were recorded by JEOL LMS-D 300 spectrometers. Merck silica gel 60 (230-400 mesh) was used for column chromatography.

### Materials

Acetals **1a**, **1b** and **1d** were synthesized from commercially available corresponding aldehydes and alcohols. (*o*-CF<sub>3</sub>Ph)<sub>3</sub>P was prepared according to the literature.<sup>1</sup> Other reagents were commercially available and used without further purification.

### General procedure for the preparation of acetals **1a**, **1b** and **1d**.<sup>2</sup>

A solution of aldehyde (1 equiv.), 10-camphorsulfonic acid (0.15 equiv.) and alcohol (100 equiv.) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.1 M) was stirred at room temperature. After checking for the disappearance of the aldehyde on TLC, sat. NaHCO<sub>3</sub> aq. was added to the reaction mixture and the solution was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and filtered, then evaporated under vacuum. The residue was purified by flash column chromatography on SiO<sub>2</sub> to give the acetal.

***n*-Dodecanal dimethyl acetal (1a)**<sup>2</sup>: colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.88 (3H, t, *J* = 6.7 Hz), 1.26 (18H, brm), 1.56-1.61 (2H, m), 3.31 (6H, s), 4.36 (1H, t, *J* = 5.7 Hz).

**3-Phenylpropionaldehyde dimethyl acetal (1b)**<sup>2</sup>: colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.89-1.96 (2H, m), 2.68 (2H, t, *J* = 8.0 Hz), 3.33 (6H, s), 4.37 (1H, t, *J* = 5.8 Hz), 7.16-7.31 (5H, m).

***n*-Dodecanal diisopropyl acetal (1d)**: colorless oil; IR (KBr, cm<sup>-1</sup>): 2972, 2926, 2855, 1266, 1381, 1111, 1015; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.88 (3H, t, *J* = 6.7 Hz), 1.14 (6H, d, *J* = 6.2 Hz), 1.19 (6H, d, *J* = 6.0 Hz), 1.26-1.39 (18H, brm), 1.53-1.58 (2H, m), 3.86 (2H, sept, *J* = 6.2 Hz), 4.54 (1H, t, *J* = 5.5 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.1, 22.6, 22.7, 23.5, 24.9, 29.3, 29.5, 29.6 (3C), 31.9, 35.4, 67.4, 100.4; HRFABMS calcd for C<sub>18</sub>H<sub>38</sub>O<sub>2</sub> (M+Na<sup>+</sup>): 309.2770, found: 309.2780.

### General procedure for the substitution reaction of *O,P*-acetal with nucleophiles (Table 2)

In a flame-dried two-necked Schrenk tube with nitrogen, TESOTf (2 equiv.) was added slowly to a stirred solution of acetal **1** (1 equiv.) and (*o*-tol)<sub>3</sub>P (3 equiv.) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.1 M) at -5 °C and the resulting solution was stirred for 0.5 h at the same temperature. After checking for the disappearance of **1** and the formation of *O,P*-acetal on TLC, H<sub>2</sub>O (10 ml/mmol) or nucleophile (1.2 or 3.0 equiv.) was added to the mixture, and the solution was then stirred at rt. After checking for the disappearance of *O,P*-acetal on TLC, sat. NaHCO<sub>3</sub> aq. was added to the reaction mixture. The resulting solution was extracted with CH<sub>2</sub>Cl<sub>2</sub> and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was subjected to silica-gel column chromatography to give the products **2-6**. Compounds **2a-2c** are commercially available and **3b**<sup>3</sup>, **3c**<sup>6</sup>, **4b**<sup>4</sup>, **4c**<sup>4</sup>, **5b**<sup>5</sup>, **5c**<sup>7</sup> are known compounds.

**(1-Methoxydodecyl)phenylsulfide (3a) (entry 2)**: colorless oil; IR (KBr, cm<sup>-1</sup>): 2926, 2855, 2253, 1468, 1379, 1098; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.88 (3H, t, *J* = 6.7 Hz), 1.24 (16H, brm), 1.44 (2H, brm), 1.69-1.78 (2H, m), 3.47 (3H, s), 4.62 (1H, t, *J* = 6.6 Hz), 7.26-7.33 (3H, m), 7.46-7.49 (2H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.1, 22.7, 26.2, 29.1, 29.3, 29.5 (2C), 29.6 (2C), 31.9, 35.6, 55.3, 91.0, 127.4, 128.7, 133.4, 133.5; HREIMS calcd

for C<sub>19</sub>H<sub>32</sub>OS: 308.2174, found: 308.2193.

**2-Methoxytridecanonitrile (4a) (entry 3):** colorless oil; IR (KBr, cm<sup>-1</sup>): 2928, 2855, 2255, 1462, 1109; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.88 (3H, t, *J* = 6.7 Hz), 1.26-1.29 (16H, brm), 1.43-1.50 (2H, m), 1.79-1.87 (2H, m), 3.49 (3H, s), 4.04 (1H, t, *J* = 6.6 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.1, 22.7, 24.7, 29.0, 29.3 (2C), 29.4, 29.6 (2C), 31.9, 33.3, 57.9, 70.7, 118.2; HRFABMS calcd for C<sub>14</sub>H<sub>27</sub>NO (M+Na<sup>+</sup>): 248.1990, found: 248.1968.

**1-Methoxydodecylbenzene (5a) (entry 4):** colorless oil; IR (KBr, cm<sup>-1</sup>): 2926, 2853, 1454, 1263, 1099; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.87 (3H, t, *J* = 6.8 Hz), 1.24-1.38 (18H, brm), 1.60-1.65 (1H, m), 1.75-1.81 (1H, m), 3.20 (3H, s), 4.07 (1H, t, *J* = 6.6 Hz), 7.24-7.37 (5H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.1, 22.7, 25.8, 29.3, 29.5, 29.6 (4C), 31.9, 38.2, 56.6, 84.2, 126.7, 127.4, 128.3, 142.5; HREIMS calcd for C<sub>19</sub>H<sub>32</sub>O: 276.2445, found: 276.2453.

**2-Methoxytridecane (6a) (entry 5):** colorless oil; IR (KBr, cm<sup>-1</sup>): 2959, 2924, 2855, 2820, 1464, 1373, 1261, 1142, 1123, 1092; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.88 (3H, t, *J* = 6.6 Hz), 1.12 (3H, d, *J* = 6.0 Hz), 1.26-1.38 (20H, brm), 3.25-3.31 (1H, m), 3.31 (3H, s); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.1, 19.0, 22.7, 25.4, 29.3, 29.6 (2C), 29.7, 29.8, 29.9, 31.9, 36.3, 55.9, 76.9;

**(1-Methoxy-3-phenylpropyl)phenylsulfide (3b)<sup>3</sup> (entry 7):** colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.98-2.12 (2H, m), 2.76 (2H, t, *J* = 7.6 Hz), 3.48 (3H, s), 4.54 (1H, t, *J* = 6.6 Hz), 7.13-7.31 (8H, m), 7.45-7.48 (2H, m).

**2-Methoxy-4-phenylbutyronitrile (4b)<sup>4</sup> (entry 8):** colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.05-2.25 (2H, m), 2.82 (2H, t, *J* = 7.6 Hz), 3.48 (3H, s), 3.96 (1H, t, *J* = 6.7 Hz), 7.17-7.26 (3H, m), 7.29-7.34 (2H, m).

**1,3-Diphenyl-1-methoxypropane (5b)<sup>5</sup> (entry 9):** colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.92-2.14 (2H, m), 2.63-2.73 (2H, m), 3.21 (3H, s), 4.08 (1H, t, *J* = 6.6 Hz), 7.16-7.34 (10H, m).

**[Methoxy(4-methoxyphenyl)methyl]phenylsulfide (3c)<sup>6</sup> (entry 11):** colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 3.48 (3H, s), 3.78 (3H, s), 5.69 (1H, s), 6.78-6.83 (2H, m), 7.20-7.26 (5H, m), 7.31-7.36 (2H, m).

**2-Methoxy-2-(4-methoxyphenyl)acetonitrile (4c)<sup>4</sup> (entry 12)**; colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 3.42 (3H, s), 3.75 (3H, s), 5.06 (1H, s), 6.86 (2H, d, *J* = 8.6 Hz), 7.33 (2H, d, *J* = 8.4 Hz).

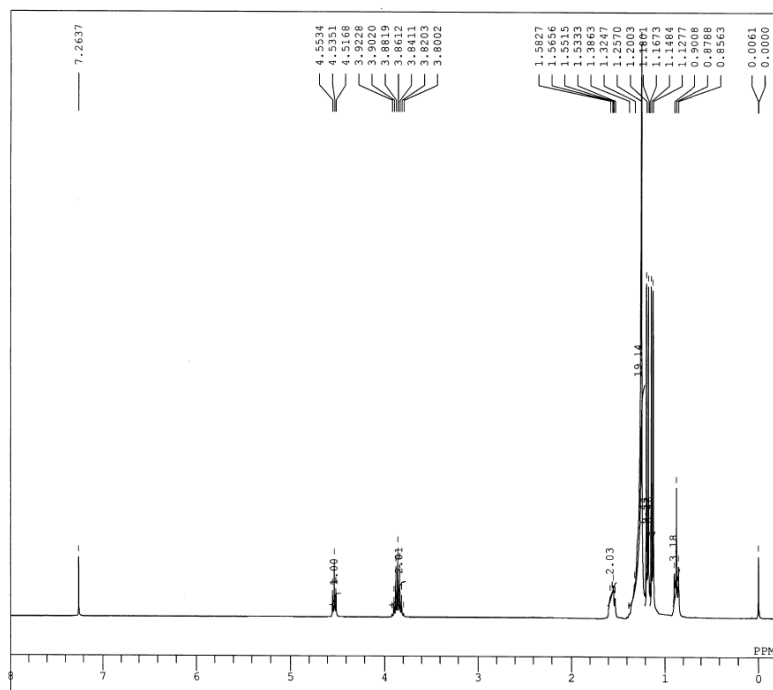
**1-Methoxy-4-[methoxy(phenyl)methyl]benzene (5c)<sup>7</sup> (entry 13)**; colorless oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 3.28 (3H, s), 3.69 (3H, s), 5.12 (1H, s), 6.77 (2H, d, *J* = 8.6 Hz), 7.16-7.25 (7H, m).

### **Isolation and characterization of the stable *O,P*-acetal generated from **1a** and (*p*-tol)<sub>3</sub>P**

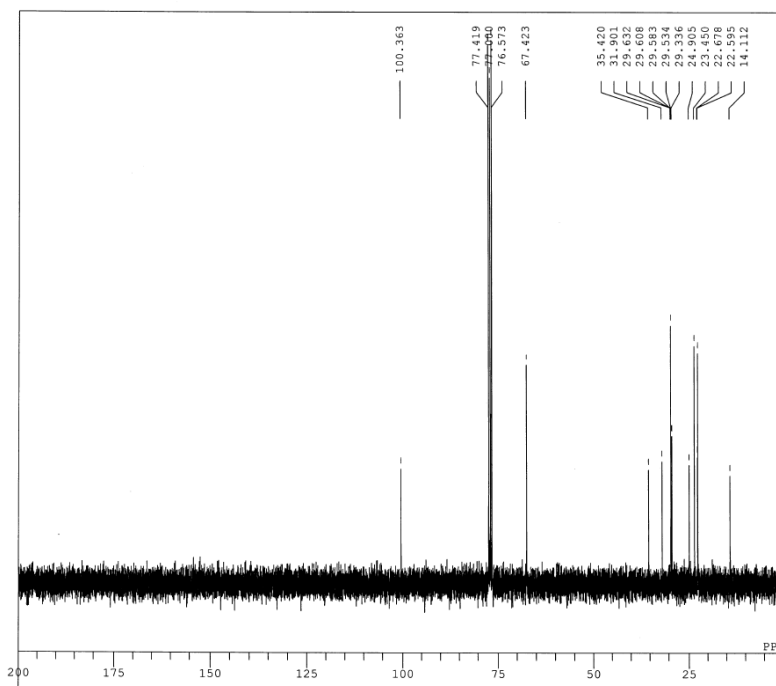
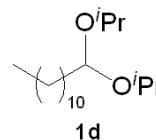
In a flame-dried two-necked Schrenk tube with nitrogen, TESOTf (2 equiv.) was added slowly to a stirred solution of acetal **1a** (1 equiv.) and (*p*-tol)<sub>3</sub>P (3 equiv.) in dry CH<sub>2</sub>Cl<sub>2</sub> (0.1 M) at 0 °C and the reaction mixture was stirred for 0.5 h at the same temperature. After checking for the disappearance of **1** and the formation of *O,P*-acetal on TLC, sat. NaHCO<sub>3</sub> aq. was added to the reaction mixture. The resulting solution was extracted with CH<sub>2</sub>Cl<sub>2</sub> and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the residue was subjected to silica-gel column chromatography to give the stable *O,P*-acetal.

**(1-Methoxydodecyl)tris(*p*-tolyl)phosphonium trifluoromethanesulfonate**; colorless gummy oil; IR (KBr, cm<sup>-1</sup>): 3061, 3032, 2926, 2853, 2249, 1599, 1503, 1454, 1435, 1402, 1379, 1316, 1261, 1225, 1194, 1157, 1111, 1032; <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.87 (3H, t, *J* = 6.9 Hz), 1.22-1.30 (16H, brm), 1.61-1.62 (2H, brm), 1.70-1.88 (2H, m), 2.49 (9H, s), 3.49 (3H, s), 5.45 (1H, dt, *J* = 9.9, 2.9 Hz), 7.49 (6H, dd, *J* = 8.0, 3.0 Hz), 7.67 (6H, dd, *J* = 11.9, 8.2 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 14.0, 21.7, 22.5, 26.0, 26.2, 29.2, 29.3, 29.4 (2C), 31.7, 32.1 (2C), 62.9 (d, *J*<sub>C-P</sub> = 6.7 Hz), 78.4 (d, *J*<sub>C-P</sub> = 61.3 Hz), 113.5 (d, *J*<sub>C-P</sub> = 84.3 Hz), 120.8 (d, *J*<sub>C-F</sub> = 321.1 Hz), 130.9 (d, *J*<sub>C-P</sub> = 12.5 Hz), 134.1 (d, *J*<sub>C-P</sub> = 10.5 Hz), 146.2 (d, *J*<sub>C-P</sub> = 2.9 Hz); <sup>19</sup>F NMR (CDCl<sub>3</sub>): δ -78.1; <sup>31</sup>P NMR (CDCl<sub>3</sub>): δ 21.1; HRFABMS (positive) calcd for C<sub>34</sub>H<sub>48</sub>OP (M<sup>+</sup>): 503.3437, found: 503.3423; HRFABMS (negative) calcd for CO<sub>3</sub>F<sub>3</sub>S (M<sup>-</sup>): 148.9520, found: 148.9521.

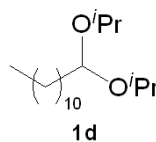
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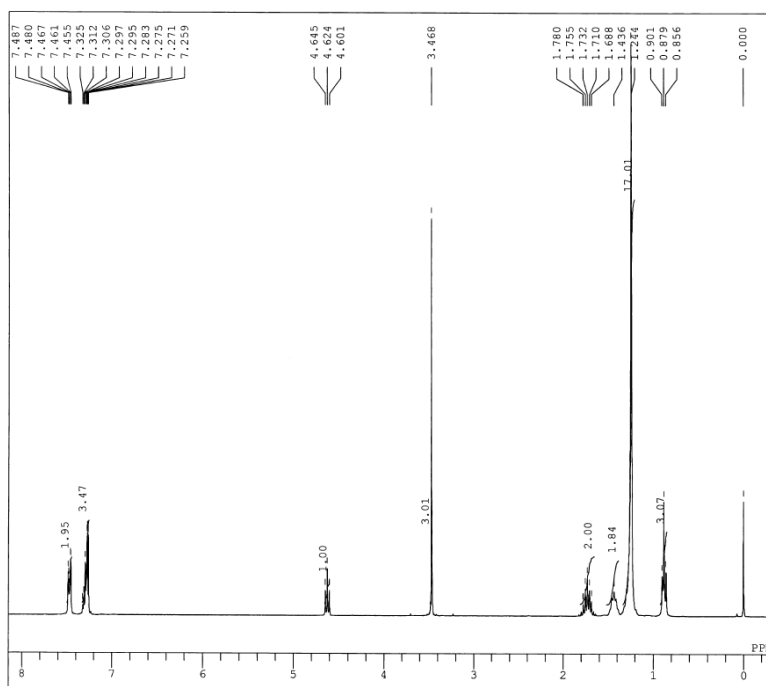
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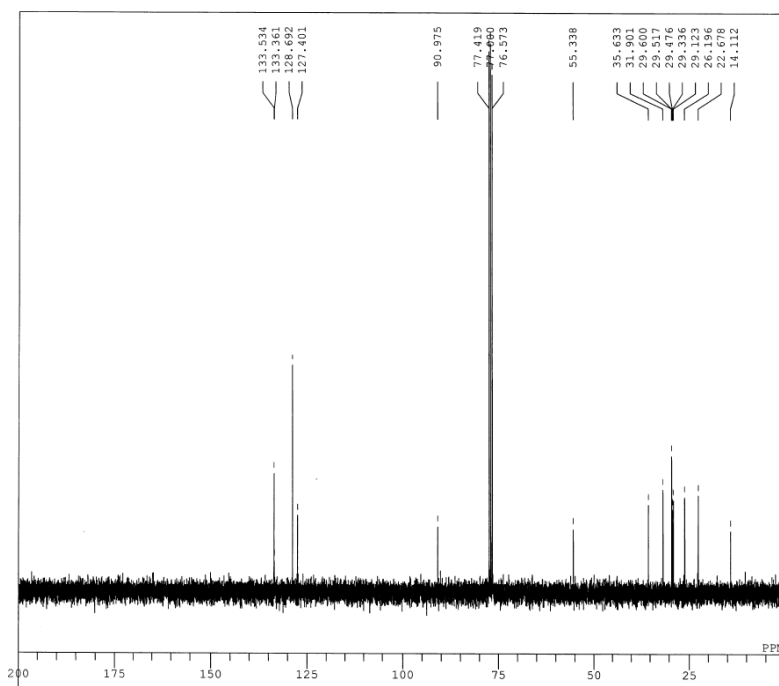
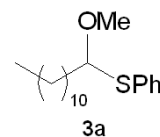
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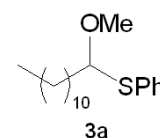
$^1\text{H}$  and  $^{13}\text{C}$  NMR of **3a**



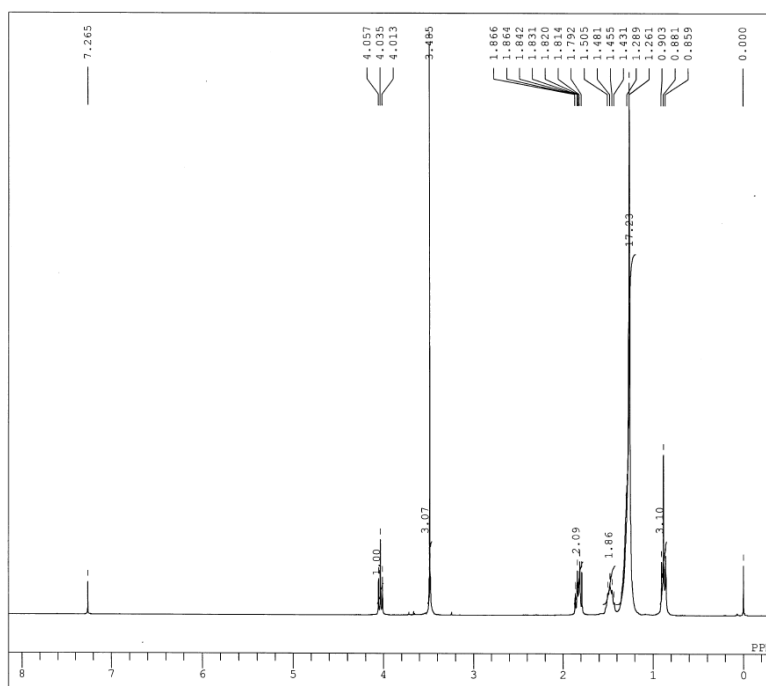
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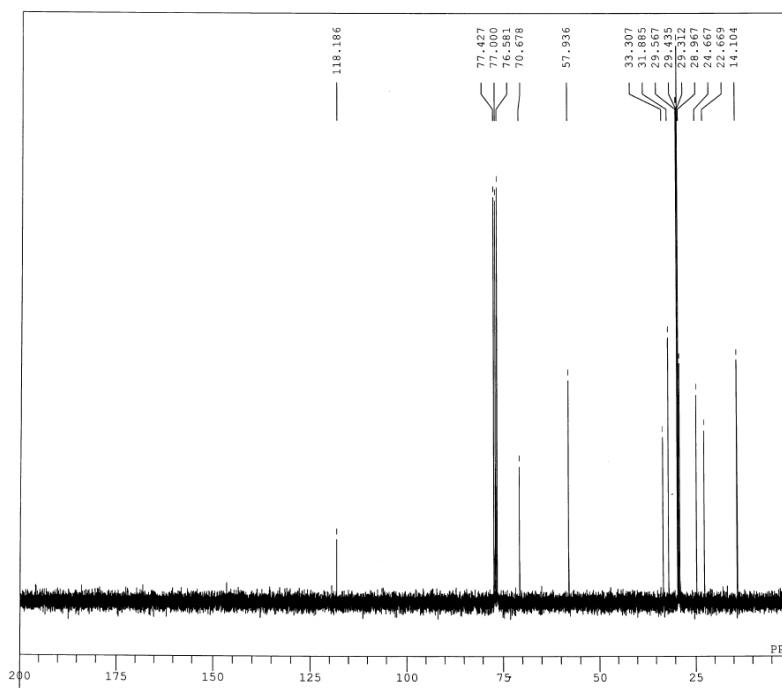
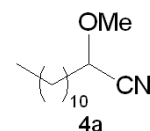
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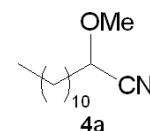
$^1\text{H}$  and  $^{13}\text{C}$  NMR of **4a**



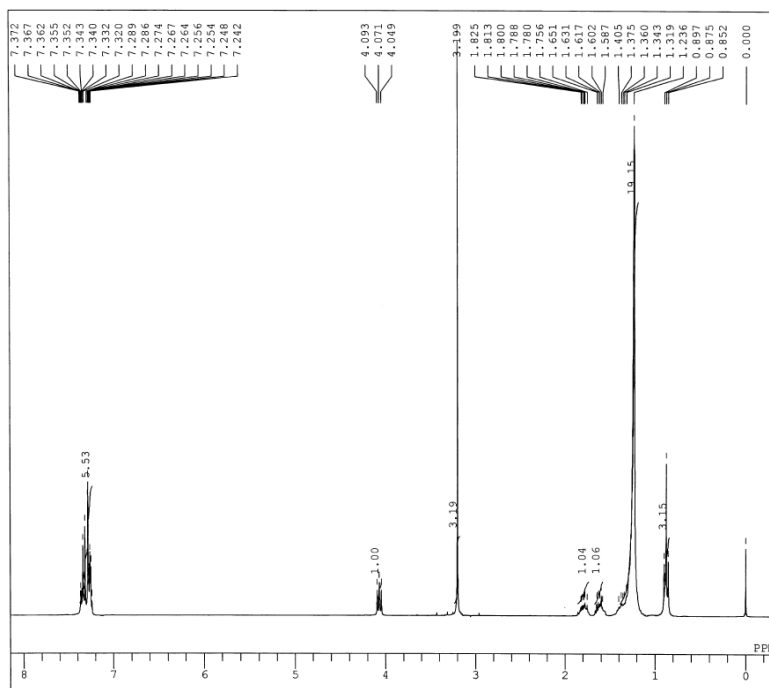
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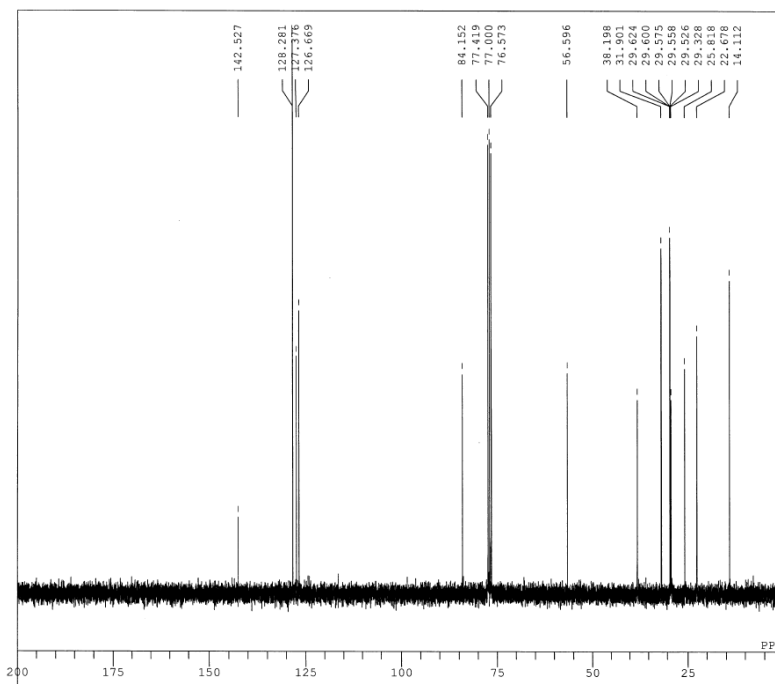
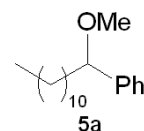
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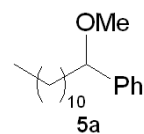
$^1\text{H}$  and  $^{13}\text{C}$  NMR of **5a**



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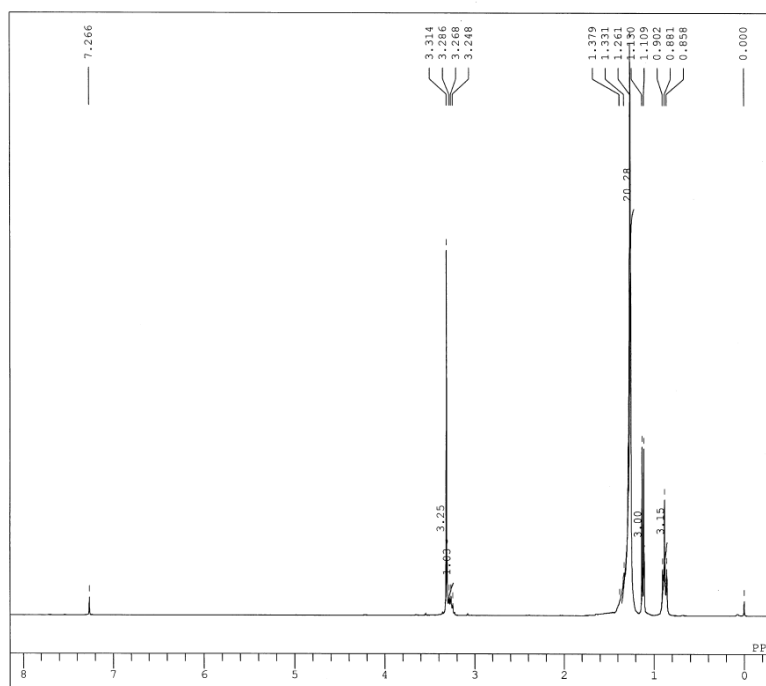


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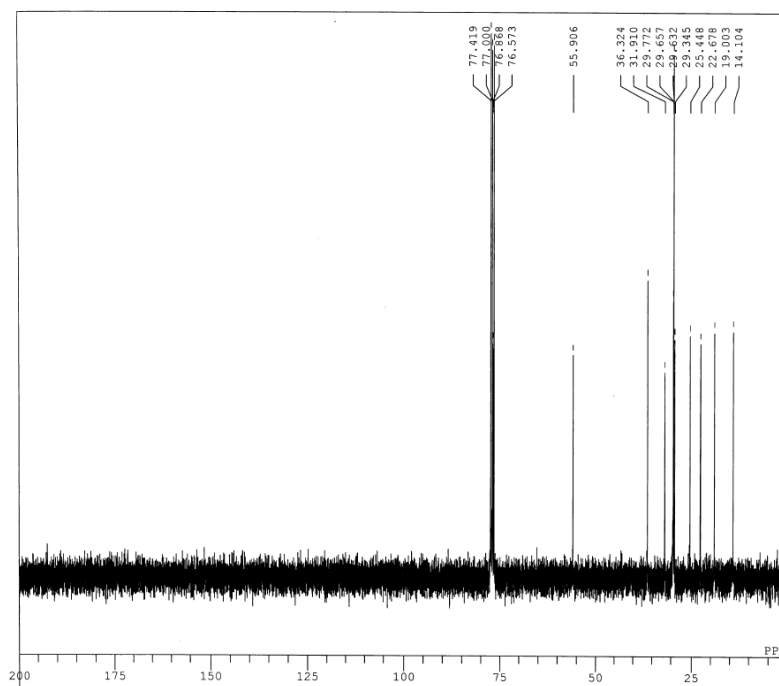
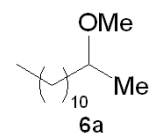




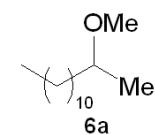
$^1\text{H}$  and  $^{13}\text{C}$  NMR of **6a**



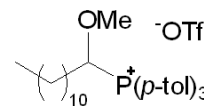
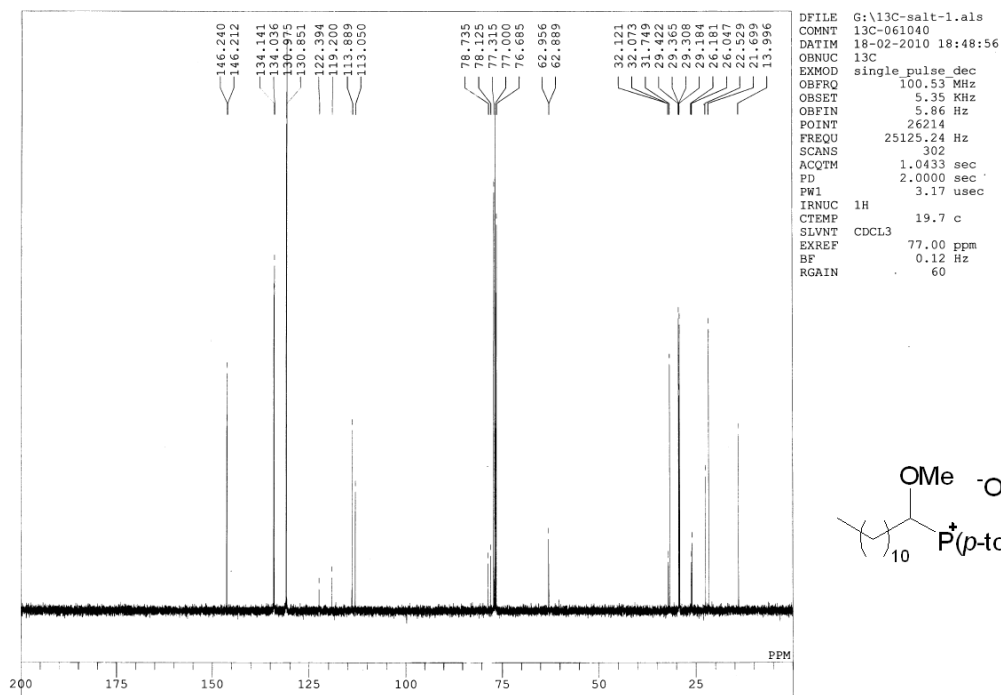
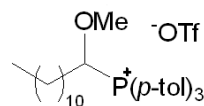
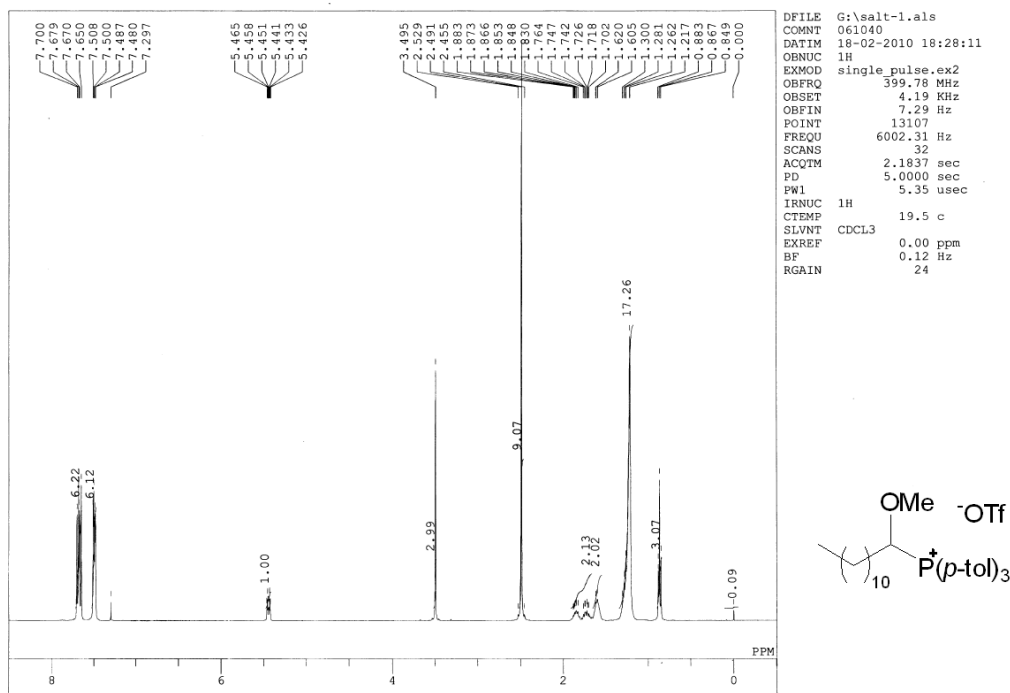
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 COMNT 090232 C  
 DATIM Thu Dec 17 21:37:07 2009  
 OBNUC 13C  
 EXMOD BCM  
 OBFRQ 75.45 MHz  
 OBSST 124.00 KHz  
 OBFIN 1840.00 Hz  
 POINT 32768  
 FREQU 20356.23 Hz  
 SCANS 400  
 ACQTM 1.6097 sec  
 PD 1.3900 sec  
 PW1 4.50 usec  
 IRNUC 1H  
 CTEMP 21.1 c  
 SLVNT CDCL3  
 EXREF 77.00 ppm  
 BF 0.12 Hz  
 RGAIN 25



$^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  and  $^{31}\text{P}$  NMR of *O*, *P*-acetal generated from **1a** and (*p*-tol) $_3\text{P}$





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