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# A Convenient Method for the Phosphorylation of Phenols with Diethyl Cyanophosphonate

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### SYNTHETIC COMMUNICATIONS, 27(17), 3035-3038 (1997)

### A CONVENIENT METHOD FOR THE PHOSPHORYLATION OF PHENOLS WITH DIETHYL CYANOPHOSPHONATE Angel Guzmán\* and Eduardo Díaz Instituto de Química , Universidad Nacional Autónoma de México

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Abstract: Phosphorylation of phenols with diethyl cyanophosphonate in methylene chloride solution at 0°C is an easy, rapid and good yielding reaction.

The synthesis of phosphate esters is an important objective in organic synthesis, because they have found wide use in the preparation of biologically active molecules<sup>1</sup> as well as in the reduction of phenols to aromatic hydrocarbons<sup>2</sup>. Mixed phosphate esters have been prepared by several methods<sup>3-6</sup>; one of the best involves the reaction of a dialkyl phosphite with an alcohol or phenol in presence of triethyl amine in carbon tetrachloride<sup>6,7</sup>. Other variations have been reported<sup>8-11</sup>, including phase transfer<sup>9</sup> and the high yielding method based on the activation of trialkyl phosphites with molecular iodine<sup>11</sup>. In this communication we report a protocol for the phosphorylation of phenols with diethyl cyanophosphonate, which proceeds rapidly, under mild conditions and in high yield. We have found that the reaction of a phenol in methylene chloride with 1.1 equivalents of diethyl cyanophosphonate and 2.0 equivalents of triethylamine at 0°C was complete within 30 minutes, (Eq. 1) with the exception of ortho-disubstituted phenols (entry 7). The reaction works satisfactorily with phenols which contain electron-withdrawing or electron-releasing groups (Table 1),

$$H$$
 + (EtO)<sub>2</sub>-PO-CN  $H$  =  $Et_3 N$   $V$  =  $Et_3 N$  =

3035

TABLE 1 а bp Reaction Entry Phenol %yield Conditions 0°C/Torr 0°/30 min 98-102/1.0 91 1 122-123/0.6 0°C/30min. 90 2 91 0°C/30min. 91-93/2.5 Э 92 соосн3 0°C/30min 136-138/1.8 4 b Heavy oil 0°C/30min. 96 5 NHCOCH₃ OH 6 93 0°C/30min. 139-141/1.5 сн₃ сн₃ QН 7 20°C/3h 120-122/2.0 93 он 0°C/30min. 98/0.6 89 8 ٢н QН NO2 9 0°C/30min 136-138/1.2 88 ЮH 87 0°C/30min 150-152/1.4 10

<sup>a</sup> uncorrected; <sup>b</sup> purified by flash column chromatography

### PHOSPHORYLATION OF PHENOLS

### **EXPERIMENTAL**

IR spectra were recorded on a Nicolet Magna 750 spectrometer. NMR spectra were determinated in CDCl<sub>3</sub> solution with a Varian Gemini 200 using tetramethylsilane as an internal standard. Mass and High resolution mass spectra were determinated on a Jeol-SX 102A instrument, using PEG as internal reference for FAB technique.

### General procedure:

1.58 g (10 mmol) of methyl salicylate were dissolved in 8 mL of dried methylene chloride.

The solution was cooled to 0°C and then 1.79 g (11 mmol) of diethyl cyanophosphonate,

followed by triethyl amine (2.02 g, 20 mmol) were added. After stirring at 0°C for 30 minutes, the mixture was diluted with methylene chloride (10 mL), the mixture washed with water (2x10 mL), dried with anhydrous sodium sulfate and concentrated. Distillation under vacuum afforded the pure phosphate ester in 88-93 % yield.

In view of the easily available starting materials, satisfactory yield, and simple experimental procedure the present method offers an attractive alternative to the procedures for the preparation of phosphate esters.

1: bp 98-102°/0.35. Torr (Lit <sup>8</sup> 102°/0.1 );. IR (neat) 3097, 2985, 1591, 1489, 1282, 1220, 1031, 959, 931 cm <sup>-1</sup>. <sup>1</sup> H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>): 7.3 (2H,d ), 7.17 (2H, d), 4.21 (4H, q), 1.35 (6H,dt, J<sub>1</sub> = 1.1, J<sub>2</sub> = 7.0). EI-MS m/z : 230 (M+).

**2**: bp 122.123°/0.6 Torr.( Lit<sup>12</sup> 105<sup>0</sup>/ 0.001) .IR (neat ) 2987, 2230, 1604, 1502, 1280, 1234,1030, 959, 930 cm<sup>-1</sup>. <sup>1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>) : 7.66 (2H, d), 7.37 (2H, d), 4.25 (4H,dq, J<sub>1</sub>= 7.3, J<sub>2</sub> = 8.4), 1.37 (6H, dt, J<sub>1</sub> = 7.3, J<sub>2</sub> = 1.1). HRMS: calcd for C<sub>11</sub> H<sub>14</sub> N O<sub>4</sub> P 255.0737; found 255.0737

3: bp 91-93°/2.5 Torr.(Lit<sup>13</sup>. 108-110<sup>0</sup>/3.0) . IR (neat) 1522, 1302,1024, 1009, 997 cm <sup>-1</sup>; <sup>1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>) : 4.26 (4H, m), 1.37 (6H, dt). <sup>13</sup>C-NMR (CDCl<sub>3</sub>) : 15.8, (CH<sub>3</sub>), 65.6, (CH<sub>2</sub>) 126.0(C-1); 138.0 (C-3); 139.0 (C-4); 141.8 (C-2). HRMS calcld for C<sub>10</sub>H<sub>10</sub>F<sub>5</sub>O<sub>4</sub>P 321.0315, found 321.0327.

**4:** bp 136-138°/1.8 Torr.; IR (neat) 2987, 1732, 1604, 1301, 1259, 1032, 970, 935 cm<sup>-1</sup>.<sup>1</sup>H-NMR  $\delta_{ppim}$  (CDCl<sub>3</sub>): 7.81 (1H, bd), 7.75 (1H, bd), 7.40 (1H, dt), 6.72 (1H, bt), 4.20 (4H, q), 3.84 (3H, s), 1.29 (6H, dt, J<sub>1</sub>=1.1, J<sub>2</sub>=7.0). HRMS calcd for C<sub>12</sub>H<sub>17</sub>O<sub>6</sub> P 288.0763, found 288.0766

5: Oil; IR (neat) 3087, 1675, 1602, 1550, 1255, 1031, 985, 958 cm<sup>-1. 1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>):8.48 (1H, bs), 7.57 (1H, bs), 7.2 (2H, m), 6.85 (1H, bd),4.23 (4H, quint ),2.10 (3H, s),1.37 (6H, dt). HRMS calcd for C<sub>12</sub> H<sub>18</sub> N O<sub>5</sub>P 288.1001, found 288.1008

6: bp 139-141°/1.5 Torr.(Lit<sup>14</sup>. 142°/0.15) IR (neat) 3087, 1612, 1504, 1273, 1033, 1004, 988, 954 cm<sup>-1</sup>. <sup>1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>): 7.15(1H, t), 6.55 (3H, m), 4.21 (4H, quint), 2.94 (6H, s), 1.35 (6H, dt, J<sub>1</sub>=7.0, J<sub>2</sub>=1.0). HRMS calcd for C<sub>12</sub> H<sub>20</sub> N O<sub>4</sub> P 273.1208, found: 273.1206.

7: bp 120-122°/2.0 Torr. IR (neat ) 3066,2968, 1442, 1273, 1031, 966 cm<sup>-1</sup>. <sup>1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>) : 7.13 (3H,s), 4.19 (4H, m), 3.5 (2H, h), 1.33 (6H, dt, J<sub>1</sub> = 7.1, J<sub>2</sub>= 1.1), 1.22 (6H, d, J=6.8). HRMS calcd for C<sub>16</sub> H<sub>27</sub> O<sub>4</sub> P 314.1647, found: 314.1651.

**8**: bp 98°/0.6 Torr (Lit<sup>15</sup> 98-99°/0.1). IR (neat ) 3033, 1608, 1508, 1279, 1219, 1032, 966 cm<sup>-1</sup>. <sup>1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>): 7.1 (4H, s),4.2 (4H, quint), 2.31 (3H, s), 1.34 (6H, dt J<sub>1</sub>=7.0, J<sub>2</sub>=1.1). HRMS calcd for C<sub>11</sub>H<sub>17</sub>O<sub>4</sub>P 244.0943, found 244.0953.

9: bp 136-138°/1.2 Torr.(Lit<sup>14</sup> 145<sup>0</sup>/0.45). IR (neat ) 1605, 1533, 1356, 1288, 1032, 971, 931cm<sup>-1</sup>. <sup>1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>): 7.93 (1H, bd), 7.60 (2H, m), 7.30 (1H, m), 4.28 (4H, q), 1.34 (6H, dt ). HRMS calcd for C<sub>10</sub> H<sub>14</sub> N O<sub>6</sub> P 275.0634, found 275.0634.

**10**:bp 150-152°/1.4 Torr. (Lit<sup>15</sup> 150-152<sup>9</sup>/0.1). IR (neat) 3057, 1633, 1279, 1031, 974, 935 cm<sup>-1</sup>; <sup>1</sup>H-NMR  $\delta_{ppm}$  (CDCl<sub>3</sub>): 7.77 (3H, m), 7.67 (1H, bt ), 7.45 (2H, m), 7.35 (1H, m).. HRMS calcd. for C<sub>14</sub>H<sub>17</sub>O<sub>4</sub>P 280.0943, found 280.0951.

#### REFERENCES

- 1. Reese, C. B., Tetrahedron, 1978, 34, 3143
- 2. Kenner, G. W, Williams, N. R., J. Chem. Soc., 1955, 522
- 3. Gerrard, W., J. Chem. Soc., 1940, 1464
- 4. Ruggeberg, W. H. C., Chernack, J., J. Am. Chem. Soc., 1948, 70, 1802
- 5. Atherthon, F. R., Todd, A. R., J. Chem. Soc., 1947, 674
- 6. Steinberg, G. M., J. Org. Chem., 1950, 15, 637
- 7. Silverberg, L. J., Dillon, J. L., Vemishetti, P., Tetrahedron Lett., 1996, 37, 771
- 8. Purnanand, Batra, B. S., Pant, B. P., Tetrahedron Lett., 1989, 30, 1687
- 9. Zwierzak, A., Synthesis, 1976, 305
- 10. Watanabe, Y., Inada, E., Jinno, M., Ozaki, S., Tetrahedron Lett., 1993, 34, 497
- 11. Stowell, J. K., Widlanski, T. S., Tetrahedron Lett., 1995, 36, 1825
- 12. Van Hooidonk, C., Ginjaar, L., Rec. Trav. Chim., 1967, 86, 449
- 13. Degterer, E.V., Nikolenko, L.N., Zh. Obshch. Khim., 1970, 40, 2262. CA, 74, 141637c, 1971.
- 14 Boter, H.L., Toet, H.J., Rec. Trav. Chim., 1965, 84, 1279
- 15. Batra, B.S., Purnanand, Ind. J. Chem., 1991, Sec 30B, 57

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