Synthesis of Dialkyl Alkoxycarbonylmethanephosphonates (Alkyl Dialkoxyphosphinylacetates) using Phase-Transfer Catalysis

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A facile method for the preparation of dialkyl alkoxycarbonylmethanephosphonates under phase-transfer catalysis is described. Phase-transfer catalysis has been used in numerous C-alkylation, O-alkylation, and N-alkylation procedures\(^1,2\), whereas its use for P-alkylation is still quite limited. It has been reported\(^3,4\) that dialkyl phosphites undergo alkylation with electrophilic alkenes or benzyl chloride in the presence of potassium carbonate and tetrabutylammonium bromide or crown ethers in a solid-liquid two-phase system. Dialkyl aminocarbonylmethanephosphonates have been obtained by alkylation of dialkyl phosphites in liquid-liquid two-phase systems\(^5\). We report here that the reaction of dialkyl phosphites (1) with alkyl chloroacetates (2) affording dialkyl alkoxycarbonylmethanephosphonates (3) may be conveniently carried out under liquid-liquid phase-transfer catalysis.

\[
\begin{align*}
\text{R}^0\text{O} & \quad \text{O} \\
\text{R}^0\text{P}^-\text{CH}_2 & \quad \text{O} \\
\text{R}^0 & \quad \text{OR}^2 \\
\end{align*}
\]

\[
\begin{align*}
\text{NaOH/H}_2\text{O/CH}_2\text{Cl}_2/\text{TEBA}, \\
0 - 5 ^\circ\text{C}, 0.3 - 5 \text{h} \\
55 - 91\% \\
\end{align*}
\]

Most of the dialkyl phosphites 1 and alkyl chloroacetates 2 are easily hydrolyzable in aqueous alkali metal hydroxide. We have found, however, that when the dichloromethane solution of dialkyl phosphites 1 and chloroacetates 2 containing a catalytic amount of quaternary ammonium salt are treated with 50% aqueous sodium hydroxide at 0 - 5 °C and the reaction is monitored by \(^1\)H-N.M.R. till disappearance of the starting material, dialkyl alkoxycarbonylmethane-
Table 1. Dialkyl Alkoxy carbonyl methanephosphonates (3, Alkyl Dialkoxyphosphinylacetates) prepared

<table>
<thead>
<tr>
<th>3</th>
<th>R¹</th>
<th>R²</th>
<th>Reaction Time [min]</th>
<th>Yield [%]</th>
<th>b.p. [°C]/torr</th>
<th>Molecular Formula or Lit. b.p. [°C]/torr</th>
<th>M.S. [m/e (M⁺ + 1)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>C₂H₅</td>
<td>C₂H₅</td>
<td>20</td>
<td>55</td>
<td>90-93/0.3</td>
<td>C₆H₁₂O₈P (238.2)</td>
<td>225</td>
</tr>
<tr>
<td>b</td>
<td>C₂H₅</td>
<td>i-C₃H₇</td>
<td>20</td>
<td>71</td>
<td>87-89/0.3</td>
<td>C₆H₁₄O₈P (239.2)</td>
<td>239</td>
</tr>
<tr>
<td>c</td>
<td>C₂H₅</td>
<td>t-C₃H₇</td>
<td>50</td>
<td>70</td>
<td>93-95/0.3</td>
<td>C₆H₁₂O₈P (238.3)</td>
<td>253</td>
</tr>
<tr>
<td>d</td>
<td>C₃H₇</td>
<td>C₆H₁₄</td>
<td>35</td>
<td>67</td>
<td>114-116/0.2</td>
<td>C₇H₁₄O₈P (278.3)</td>
<td>279</td>
</tr>
<tr>
<td>e</td>
<td>C₆H₁₄</td>
<td>i-C₃H₇</td>
<td>30</td>
<td>60</td>
<td>130-132/0.3</td>
<td>C₇H₁₂O₈P (308.3)</td>
<td>309</td>
</tr>
<tr>
<td>f</td>
<td>i-C₃H₇</td>
<td>i-C₃H₇</td>
<td>90</td>
<td>78</td>
<td>89-91/0.3</td>
<td>C₇H₁₂O₈P (280.3)</td>
<td>267</td>
</tr>
<tr>
<td>g</td>
<td>i-C₃H₇</td>
<td>t-C₃H₇</td>
<td>110</td>
<td>83</td>
<td>90-92/0.3</td>
<td>C₇H₁₄O₈P (306.4)</td>
<td>281</td>
</tr>
<tr>
<td>h</td>
<td>i-C₃H₇</td>
<td>C₆H₁₄</td>
<td>110</td>
<td>81</td>
<td>124-126/0.4</td>
<td>C₇H₁₂O₈P (334.4)</td>
<td>307</td>
</tr>
<tr>
<td>i</td>
<td>i-C₃H₇</td>
<td>i-C₆H₁₄</td>
<td>145</td>
<td>64</td>
<td>122-124/0.4</td>
<td>C₈H₁₂O₈P (364.5)</td>
<td>337</td>
</tr>
<tr>
<td>j</td>
<td>n-C₆H₁₄</td>
<td>i-C₃H₇</td>
<td>50</td>
<td>80</td>
<td>118-120/0.25</td>
<td>C₈H₁₂O₈P (394.4)</td>
<td>355</td>
</tr>
<tr>
<td>k</td>
<td>i-C₆H₁₄</td>
<td>t-C₃H₇</td>
<td>100</td>
<td>91</td>
<td>128-130/0.25</td>
<td>C₈H₁₂O₈P (388.4)</td>
<td>309</td>
</tr>
<tr>
<td>l</td>
<td>n-C₆H₁₄</td>
<td>C₆H₁₄</td>
<td>100</td>
<td>75</td>
<td>134-136/0.2</td>
<td>C₈H₁₂O₈P (334.4)</td>
<td>335</td>
</tr>
<tr>
<td>m</td>
<td>n-C₆H₁₄</td>
<td>i-C₆H₁₄</td>
<td>180</td>
<td>69</td>
<td>155-156/0.6</td>
<td>C₈H₁₂O₈P (364.5)</td>
<td>365</td>
</tr>
<tr>
<td>n</td>
<td>i-C₆H₁₄</td>
<td>i-C₆H₁₄</td>
<td>160</td>
<td>76</td>
<td>155-156/0.05*</td>
<td>C₈H₁₂O₈P (406.5)</td>
<td>407</td>
</tr>
<tr>
<td>o</td>
<td>i-C₆H₁₄</td>
<td>t-C₆H₁₄</td>
<td>300</td>
<td>79</td>
<td>158-160/0.05*</td>
<td>C₈H₁₂O₈P (420.6)</td>
<td>421</td>
</tr>
<tr>
<td>p</td>
<td>i-C₆H₁₄</td>
<td>C₆H₁₄</td>
<td>120</td>
<td>75</td>
<td>163-165/0.05*</td>
<td>C₈H₁₂O₂₆P (446.6)</td>
<td>447</td>
</tr>
<tr>
<td>q</td>
<td>i-C₆H₁₄</td>
<td>i-C₆H₁₄</td>
<td>200</td>
<td>65</td>
<td>173-175/0.05*</td>
<td>C₈H₁₂O₂₆P (476.7)</td>
<td>477</td>
</tr>
</tbody>
</table>

a) Yield of distilled product.
b) Satisfactory microanalysis obtained: C = 0.36, H = 0.30, P = 0.24; exceptions: 3l (C = 0.55), 3q (C = 0.61).
c) Recorded with a Finnigan 4021 spectrometer.

d) i-C₃H₇ = \text{CH₃CH₂CH}_2- \text{CH₂CH₃}

Table 2. Spectral Data of Compounds 3

<table>
<thead>
<tr>
<th>3</th>
<th>I.R. (film)*, v [cm⁻¹]</th>
<th>1H-N.M.R. (CDCl₃/TMS) b</th>
<th>3</th>
<th>I.R. (film)*, v [cm⁻¹]</th>
<th>1H-N.M.R. (CDCl₃/TMS) b</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>970, 1030</td>
<td>1270 1740</td>
<td>b</td>
<td>970, 1030</td>
<td>1275 1735</td>
</tr>
<tr>
<td></td>
<td>4.1 (m, 6H, 3O—CH₂)</td>
<td>2.82 (d, 2H, P—CH₂)</td>
<td></td>
<td>4.0 (q, 4H, 2O—CH₂)</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
<tr>
<td></td>
<td>1.35 (m, 9H, 3CH₃)</td>
<td></td>
<td></td>
<td>1.45 [m, 17H, 2CH(OH)]</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.95 (m, 1H, O—CH)</td>
<td>2.81 (d, 2H, P—CH₂)</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
<tr>
<td></td>
<td>4.1 (m, 4H, 2O—CH₂)</td>
<td>1.45 [s, 9H, C(CH₃)₃]</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
<tr>
<td></td>
<td>4.68 (m, 1H, O—CH)</td>
<td>2.74 (d, 2H, P—CH₂)</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
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<tr>
<td></td>
<td>4.78 (m, 3H, 3O—CH₂)</td>
<td>1.29 [m, 18H, 3CH(C₂H₅)]</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
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<tr>
<td></td>
<td>4.15 (m, 1H, O—CH)</td>
<td>1.31 [d, 12H, 2CH(CH₃)₂]</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
<tr>
<td></td>
<td>4.65 (m, 2H, 2O—CH₂)</td>
<td>1.54 [m, 10H, (CH₂)₂]</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
<tr>
<td></td>
<td>4.7 (m, 3H, 3O—CH₂)</td>
<td>1.33 [d, 12H, 2CH(CH₃)₂]</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
<tr>
<td></td>
<td>4.62 (m, 2H, 2O—CH₂)</td>
<td>2.77 (d, 2H, P—CH₂)</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
<tr>
<td></td>
<td>4.95 (m, 1H, O—CH)</td>
<td>1.2 [m, 27H, CH + 4CH₂ + 6CH₃]</td>
<td></td>
<td>4.0, 4H, 2O—CH₂</td>
<td>2.75 (d, 2H, P—CH₂)</td>
</tr>
</tbody>
</table>

a) Recorded with a Specord 75-IR spectrometer.
b) Recorded with a 60 MHz Varian EM-360L spectrometer.
phosphonates (3) are obtained as the products. Triethylbenzylammonium chloride (TEBA) is more effective than tetrabutylammonium bromide (TBAB) and trioctylmethy lammonium chloride in catalyzing the reaction. It should be mentioned that changes of the reaction temperature and of the order of mixing the reagents as well as the use of sodium hydroxide solution of lower concentration leads to the formation of complex hydrolysis products and low yields of products 3. The present paper describes a mild and convenient method for the preparation of dialkyl alkoxy carbonylmethane phosphonate.

Preparation of Dialkyl Alkoxy carbonylmethane phosphonates (3) using Phase-Transfer Catalysis; General Procedure:
To a stirred mixture of a dialkyl phosphite (1; 0.03 mol), an alkyl chloroacetate (2; 0.03 mol), and triethylbenzylammonium chloride (411 mg, 1.8 mmol) in dichloromethane (20 ml) at 0°C, 50% aqueous sodium hydroxide (7.5 ml) is added dropwise. The temperature of the exothermic reaction is kept at 0–5°C by external cooling for the appropriate reaction time (Table 1). The mixture is then diluted with dichloromethane (30 ml) and water (30 ml), the organic layer is separated, washed with water (2 x 30 ml), and dried with sodium sulfate. The residue obtained after removal of the solvent is purified by distillation.

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