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### Monitoring the Phosphorylation of Phenol Derivatives with Diethyl Chlorophosphate in Liquid-Liquid and Solid-Liquid Phase by In Situ Fourier Transform Infrared Spectroscopy, Part II

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## MONITORING THE PHOSPHORYLATION OF PHENOL DERIVATIVES WITH DIETHYL CHLOROPHOSPHATE IN LIQUID–LIQUID AND SOLID–LIQUID PHASE BY IN SITU FOURIER TRANSFORM INFRARED SPECTROSCOPY, PART II

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*The reaction of 4-chlorophenol and 4-nitrophenol with diethyl chlorophosphate carried out in a liquid–liquid and solid–liquid two phase system, respectively, was monitored by in situ Fourier transform IR spectroscopy.*

**Keywords** Heterogeneous phase; in situ Fourier transform IR spectroscopy; monitoring; phosphorylation; substituted phenols

## INTRODUCTION

In situ Fourier transform (FT) IR spectroscopy is a simple and practical on-line method to monitor a wide variety of organic chemical reactions,<sup>1–9</sup> making optimization of the conditions possible.<sup>1</sup> Hence, in situ FT IR spectroscopy may be an important tool in environmentally friendly (“green”) chemistry. In addition, intermediates can be observed,<sup>6,7</sup> and equilibrium constants<sup>8</sup> can be determined by utilizing this up-to-date technique that is spreading in the chemical industry. Organophosphorus reactions may also be monitored by the in situ FT IR method.<sup>1,9</sup>

The React IR 1000 spectrometer equipped with an attenuated total reflexion (ATR) detector may be used in a wide temperature range (–80 to 250°C) under pressure and also for heterogeneous (solid–liquid and liquid–liquid) reactions.

This article presents new results obtained regarding the phosphorylation of phenol derivatives. Newer model reactions were studied, and heterogeneous reactions of different types were investigated.

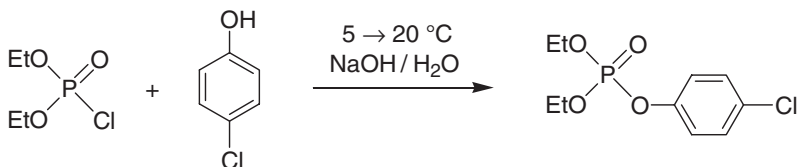
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## RESULTS AND DISCUSSION

The phosphorylation reaction of 4-chlorophenol with diethyl chlorophosphate was carried out as has been described for phenol (Scheme 1).<sup>1</sup> First, the IR spectra of the reaction components (4-chlorophenol, diethyl chlorophosphate, and diethyl 4-chlorophenyl phosphate, prepared in a separate experiment) were measured. The spectrum of the phenol derivative was obtained in water solution, while the spectra of the other two components were recorded on neat samples (Figure 1).



Scheme 1

Diethyl chlorophosphate displayed intense absorptions at 1007/1023 and 1282  $\text{cm}^{-1}$  due to  $\nu_{\text{P}-\text{O}-\text{C}}$  (alkyl) and  $\nu_{\text{P}=\text{O}}$  stretching vibrations, respectively. The IR spectrum of the diethyl aryl ester showed intense signals at 1027, 1220, and 1278  $\text{cm}^{-1}$  due to the  $\nu_{\text{P}-\text{O}-\text{C}}$  (alkyl),  $\nu_{\text{P}-\text{O}-\text{C}}$  (aryl), and  $\nu_{\text{P}=\text{O}}$  stretching vibrations, respectively. There were additional absorptions at 930 and 961  $\text{cm}^{-1}$ .

The phosphorylation, which was monitored by inserting the probe into the mixture, was carried out as follows. The solution of 4-chlorophenol in water was kept at  $\sim 2^\circ\text{C}$ , and the diethyl chlorophosphate was added with vigorous stirring during  $\sim 5$  min. Then sodium hydroxide/water was added during  $\sim 25$  min so that the temperature did not rise above  $5^\circ\text{C}$ . The cooling bath was removed, and the mixture was stirred further at  $20^\circ\text{C}$  for 4 h. The 3D diagram obtained can be seen in Figure 2.

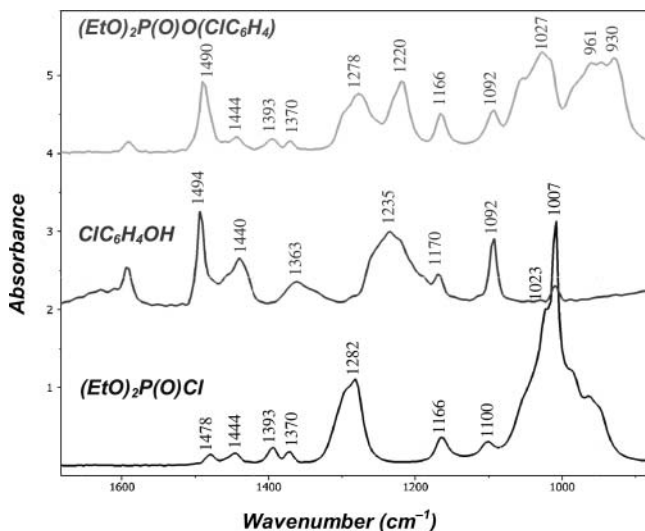
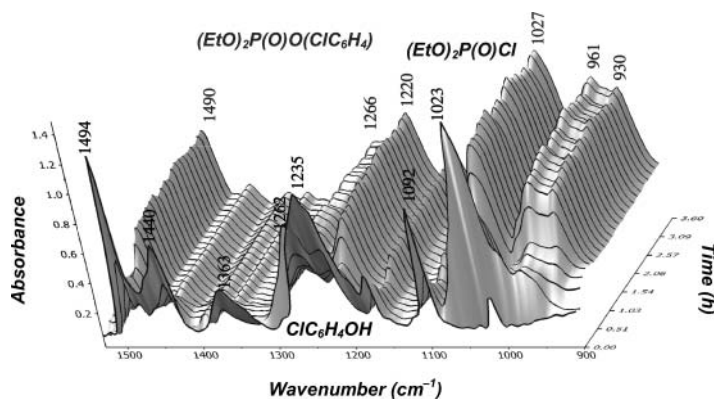


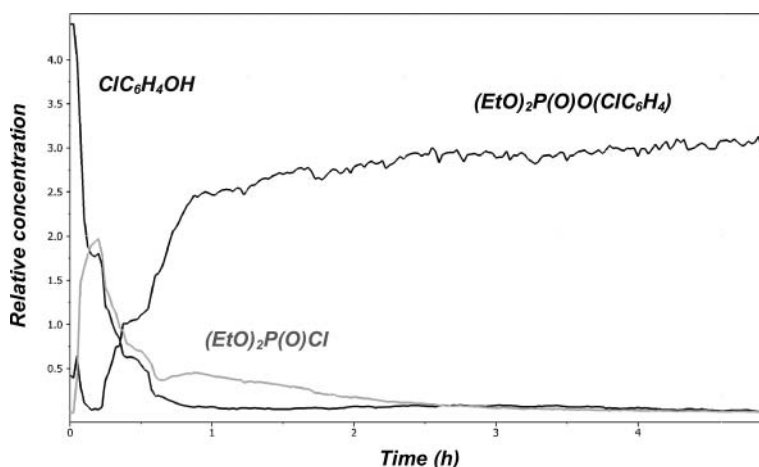
Figure 1 IR spectra of the reaction components.



**Figure 2** A segment of the 3D IR spectrum for the phosphorylation of 4-chlorophenol with diethyl chlorophosphate in water in the presence of sodium hydroxide at  $5 \rightarrow 20^\circ\text{C}$ .

Decrease of the concentration of the phosphorylating agent can be followed by monitoring the peak at  $1023\text{ cm}^{-1}$ . At the same time, formation of the diethyl aryl phosphate can be monitored by the absorptions at 1220, 1027, 961, and  $930\text{ cm}^{-1}$ . Formation of the diethyl phenyl phosphate was controlled by the appearance of the peaks at 1208, 961, and  $942\text{ cm}^{-1}$ , where 1208 is a broad peak as a result of the overlap of two absorptions.<sup>1</sup> Formation of the hydrolyzed byproduct  $(\text{EtO})_2\text{P}(\text{O})\text{OH}$  could not be detected in the 3D diagram. As a matter of fact, its quantity was  $<5\%$  according to GC. The phosphorylation was complete after 3 h. The absorbance—time diagram obtained after deconvolution (that is, the separation of the absorption bands of the reaction components) and a few iterations by a suitable computer program (belonging to the React IR equipment) is shown in Figure 3, while the reproduction of the IR spectra from the 3D diagram can be seen in Figure 4.

Table I contains the comparison of the measured IR spectra and those obtained after deconvolution. It can be seen that the agreement is quite good for all three components.



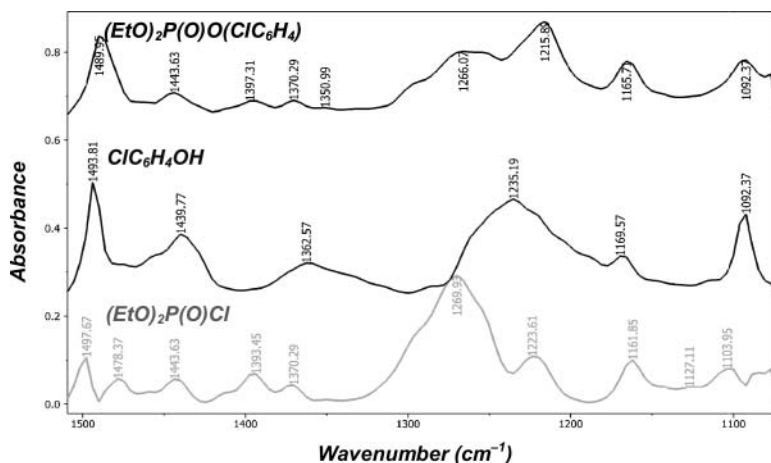
**Figure 3** Concentration profile for the reaction of 4-chlorophenol with diethyl chlorophosphate.

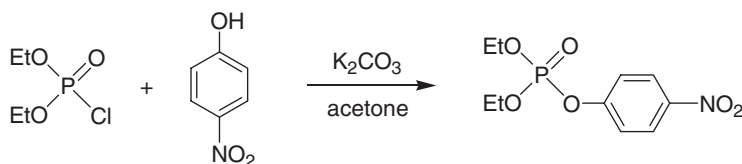
**Table I** IR absorptions measured and obtained from the 3D diagram after deconvolution (in  $\text{cm}^{-1}$ )

(EtO) <sub>2</sub> P(O)Cl		4-ClC <sub>6</sub> H <sub>4</sub> OH		(EtO) <sub>2</sub> P(O)O(4-ClC <sub>6</sub> H <sub>4</sub> )	
Obtained after deconv.	Measured	Obtained after deconv.	Measured	Obtained after deconv.	Measured
1478	1478	1494	<b>1494</b>	1490	<b>1490</b>
1444	1444	1440	<b>1440</b>	1444	1444
1393	1393			1397	1393
1370	1370	1363	1363	1370	1370
1270	<b>1282</b>	1235	<b>1235</b>	1266	<b>1278</b>
1224				1216	<b>1220</b>
1162	1166	1170	1170	1166	1166
1104	1100	1092	<b>1092</b>	1092	1092
	<b>1023</b>				<b>1027</b>
	<b>1007</b>				<b>961</b>
					<b>930</b>

According to our experience, the reaction of 4-nitrophenol with diethyl chlorophosphate was suppressed by the hydrolytic side reaction when it was carried out in water in the presence of sodium hydroxide at  $5 \rightarrow 20^\circ\text{C}$ . As much as ca. 80% of the chlorophosphate suffered hydrolysis. Most probably, the lower nucleophilicity and the low solubility of sodium 4-nitrophenolate in water are responsible for the inefficiency. Alternatively, the phosphorylation of 4-nitrophenol was carried out in acetone in the presence of potassium carbonate at  $20^\circ\text{C}$  (Scheme 2).

First the IR spectra of the components (4-nitrophenol, potassium 4-nitrophenolate, diethyl chlorophosphate, and diethyl 4-nitrophenyl phosphate, prepared in a separate experiment) were measured. The spectra of 4-nitrophenol and potassium 4-nitrophenolate were recorded in acetone solution, while those of the other components were obtained on neat samples (Figure 5).

**Figure 4** IR spectra for the reaction components obtained from the 3D diagram after deconvolution.



Scheme 2

The absorptions of the phosphorylating agent were discussed above. The presence of 4-nitrophenol is revealed by the peaks appearing at 1502, 1359, 1220, and  $\sim 1100\text{ cm}^{-1}$ . The diethyl aryl ester showed intense IR absorptions at  $1027\text{ cm}^{-1}$  ( $\nu_{P-O-C}$ , alkyl),  $1231\text{ cm}^{-1}$  ( $\nu_{P-O-C}$ , aryl),  $1282\text{ cm}^{-1}$  ( $\nu_{P=O}$ ), 950 and  $930\text{ cm}^{-1}$ .

Then the probe was inserted into the mixture of 4-nitrophenol and potassium carbonate in dry acetone. To maintain a stable temperature, the flask was immersed in a water bath at  $20^\circ\text{C}$ . Then diethyl chlorophosphate was added during 5 min, and the mixture was stirred for 1.5 h. The 3D diagram that was obtained can be seen in Figure 6.

The solvent acetone displayed intense peaks at 1220 and  $1359\text{ cm}^{-1}$ . Decrease of the relative quantity of diethyl chlorophosphate cannot be followed, but that of the 4-nitrophenol can be monitored by absorptions at 1502 and  $\sim 1100\text{ cm}^{-1}$ .

Appearance of the mixed ester can be seen by the emerging peaks at 1027, 950, and  $930\text{ cm}^{-1}$ . The intense absorption of the solvent acetone at 1220 and  $1359\text{ cm}^{-1}$  suppresses other peaks in this region.

The absorbance–time diagram can be seen in Figure 7. It can be seen that the concentration of 4-nitrophenol decreases quickly, and at the same time that of potassium 4-nitrophenolate goes through a maximum. The reaction time is 1.25 h.

Reproduction of the IR spectra of the components from the 3D diagram can be seen in Figure 8.

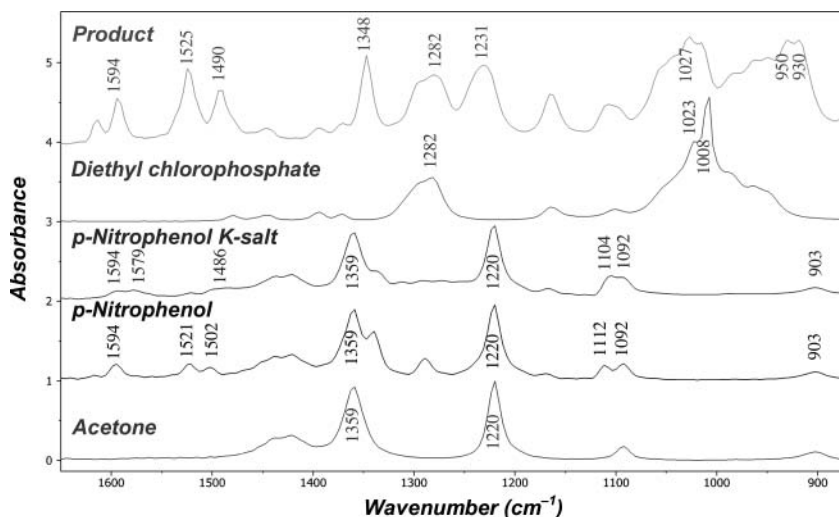
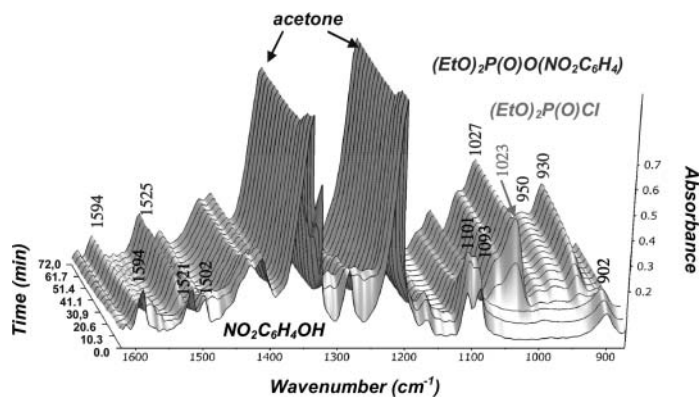
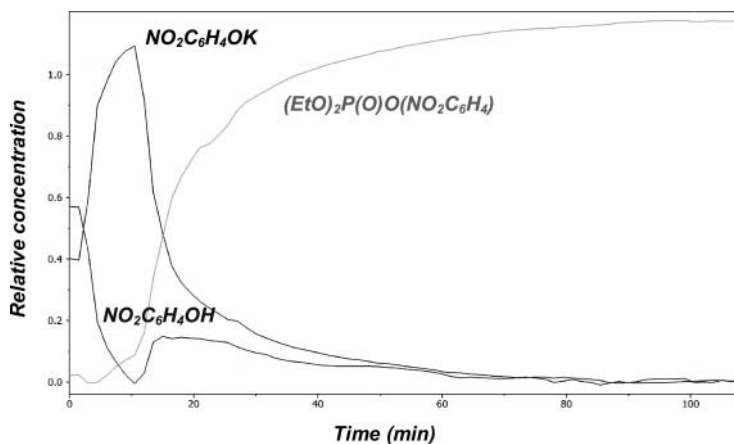


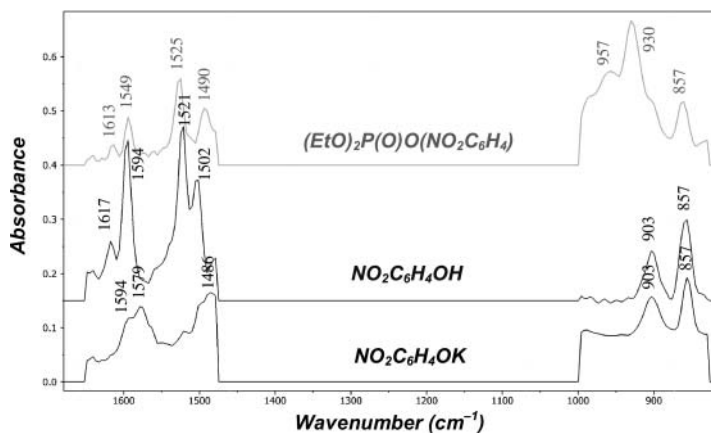
Figure 5 IR spectra for the reaction components.



**Figure 6** A segment of the 3D IR spectrum for the phosphorylation of 4-nitrophenol with diethyl chlorophosphate in acetone in the presence of  $K_2CO_3$  at  $20^\circ C$ .



**Figure 7** Concentration profile for the reaction of 4-nitrophenol with diethyl chlorophosphate.



**Figure 8** IR spectra for the reaction components obtained from the 3D diagram after deconvolution.

**Table II** IR absorptions measured and obtained from the 3D diagram after deconvolution (in  $\text{cm}^{-1}$ )

4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OH		4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> OK		(EtO) <sub>2</sub> P(O)O(4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> )	
Obtained after deconv.	Measured	Obtained after deconv.	Measured	Obtained after deconv.	Measured
1594	1594	1594	1594	1594	1594
1521	1521	1579	1579	1525	1525
1502	1502	1486	1486	1490	1490
				957	950
903	903	903	903	930	930
857	857	857	857	857	857

Comparison of the measured IR data with those obtained after deconvolution from the 3D diagram is shown in Table II.

## EXPERIMENTAL

### Equipment

In situ Fourier transform IR measurements were carried out using React IR 1000 equipment. The DiCOMP measuring head was placed in a 100 mL four-necked flask equipped with a dropping funnel, a condenser, a thermometer, and a magnetic stirrer. The temperature was maintained by using an external ice-cooling or an appropriately adjusted water bath. The <sup>31</sup>P NMR spectra were obtained with a Bruker DRX-500 spectrometer operating at 202.4 MHz using 85% H<sub>3</sub>PO<sub>3</sub> as external standard.

### Phosphorylation of 4-Chlorophenol with Diethyl Chlorophosphate in Liquid-Liquid Phases

To 14.8 g (115.0 mmol) 4-chlorophenol in 30 mL of water, 18.3 mL (126.5 mmol) of diethyl chlorophosphate was added dropwise with external ice-cooling and vigorous stirring, whereupon the temperature increased from 0 to 5°C. Then a solution of 4.8 g (120.8 mmol) of sodium hydroxide in 43.5 mL of water was added dropwise over a period of 25 min so that the temperature did not rise above 5°C. After complete addition, the cooling bath was removed, and the mixture was allowed to warm up to room temperature. The content of the flask was stirred for 4 h; then 50 mL of dichloromethane was added, and the organic phase was separated, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated in vacuo. The crude product thus obtained was purified by flash column chromatography (using 3% methanol in chloroform as eluent and silica gel as adsorbant) to afford 22.8 g (75%) of diethyl 4-chlorophenyl phosphate; <sup>31</sup>P NMR (CDCl<sub>3</sub>):  $\delta = -6.3$  ( $\delta[\text{lit}^{10}] = -6.5$ ).

### The Phosphorylation of 4-Nitrophenol with Diethyl Chlorophosphate in Solid-Liquid Phases

To a mixture of 4-nitrophenol (4.6 g, 33.3 mmol) and potassium carbonate (4.6 g, 33.3 mmol) in 50 mL of acetone, diethyl chlorophosphate (5.0 mL, 34.6 mmol) was added dropwise at 26°C during ~5 minutes. The content of the flask was stirred further for 1.5 h.

Then the mixture was filtered and the organic phase was evaporated to furnish 8.4 g (92%) of diethyl 4-nitrophenyl phosphate;  $^{31}\text{P}$  NMR ( $\text{CDCl}_3$ ):  $\delta = -7.1$  ( $\delta[\text{lit}^{11}] = -7.4$ ).

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