

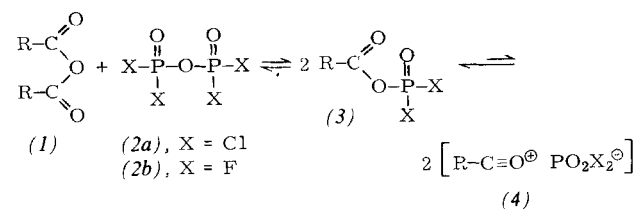
## Mixed Carboxylic-Dichlorophosphoric Anhydrides— Reactive Intermediates in Acyl Chloride Synthesis with POCl<sub>3</sub><sup>[\*\*]</sup>

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The intermediacy of mixed anhydrides (3), X=Cl, has been proposed<sup>[1]</sup> in the preparation of acyl chlorides from salts of carboxylic acids and phosphoryl chloride. Acyl dichlorophosphates have likewise been advanced as the actual acylating agents in the "phosphoryl chloride method" developed by Th. Wieland *et al.* for the acylation of amino acids<sup>[2]</sup>. That no such intermediates (3) have yet been isolated or directly identified, is probably due to instantaneous reaction of the mixed anhydrides with nucleophiles still present in the mixture (carboxylate) or being formed in the course of the reaction (chloride).

We have now succeeded in preparing compounds (3) by reaction of carboxylic anhydrides (1) with dichloro- (2a) or difluorophosphoric anhydride (2b). They are characterized by definite boiling points and correct elemental analyses; their structure is confirmed by <sup>31</sup>P- and <sup>13</sup>C-NMR spectra [*e.g.* (3a): <sup>31</sup>P- (85% H<sub>3</sub>PO<sub>4</sub>, ext.) δ = +1.66; <sup>13</sup>C-NMR (CDCl<sub>3</sub>) benzoyl carbon δ = 158.3, <sup>2</sup>J<sub>O-C-O-P</sub> = -11.5 Hz].

In the case of anhydrides containing aliphatic acyl moieties, *e.g.* (3e) and (3f), secondary processes such as ketene formation or condensation reactions prevent product isolation; however, these compounds can be prepared in dichloromethane solution. The NMR spectra provide unequivocal proof of both the presence and the structure of compounds (3).



	R	X	Yield [%]	B.p. [°C/torr]
(3a)	C <sub>6</sub> H <sub>5</sub>	Cl	61	77/10 <sup>-3</sup>
(3b)	C <sub>6</sub> H <sub>5</sub>	F	80	52/10 <sup>-2</sup>
(3c)	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	Cl	60	97/10 <sup>-3</sup>
(3d)	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	F	75	54/10 <sup>-3</sup>
(3e)	CH <sub>3</sub>	Cl	≈ 60 [a]	—
(3f)	CH <sub>3</sub>	F	≈ 90 [a]	—

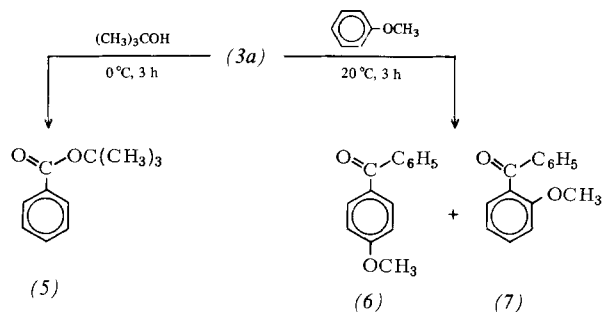
[a] Determined spectroscopically in CH<sub>2</sub>Cl<sub>2</sub> solution.

Neither <sup>31</sup>P- nor <sup>13</sup>C-NMR shows any evidence of dissociation of the anhydrides (3) into acylium ions (4) which might be expected from the high leaving tendency of the dihalophosphate anion<sup>[3]</sup>. The IR spectrum also displays only a C=O vibration at 1780 cm<sup>-1</sup> and no band at higher frequencies that could be attributed to stretching of the acylium function.

As expected, the anhydrides (3) are highly reactive. Unlike the corresponding acyl chlorides, they form esters of tertiary alcohols under mild conditions [*e.g.* (5), 68%]; with arenes, aryl ketones are produced *without* any Friedel-Crafts catalyst [*e.g.* (6) and (7), 73% (93:7)].

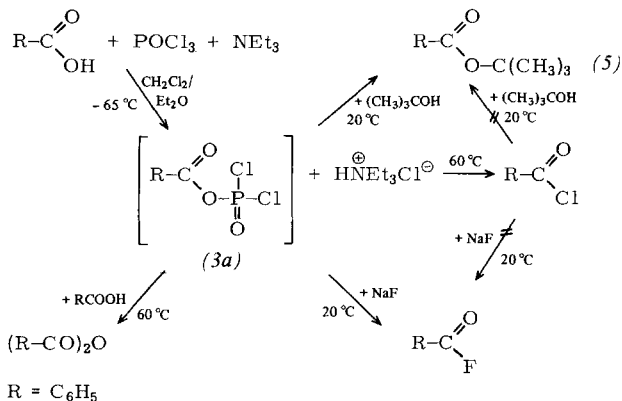
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As we were able to establish by  $^{31}\text{P}$ -NMR and by chemical reactions, the formation of acyl chlorides from carboxylic acids and  $\text{POCl}_3$  proceeds *via* acyl dichlorophosphates (3). When benzoic acid, triethylamine, and  $\text{POCl}_3$  are reacted in dichloromethane/ether at  $-65^\circ\text{C}$ , triethylammonium hydrochloride is precipitated. The presence of (3a) in the filtrate is demonstrated by the  $^{31}\text{P}$ -NMR spectrum which remains unchanged upon admixture of authentic (3a).

If the solution is warmed to  $60^\circ\text{C}$ , benzoyl chloride and benzoic anhydride are formed; addition of alkali chlorides increases the percentage of acyl chloride. Apart from these two compounds, *tert*-butyl benzoate (5) is formed in the presence of *tert*-butanol at room temperature; benzoyl fluoride is produced upon addition of sodium fluoride and catalytic amounts of crown ether. Under these conditions, neither benzoyl chloride nor benzoic anhydride react with *tert*-butanol or NaF. Leaving group in each case is the dichlorophosphate ion,  $\text{Cl}_2\text{P}(\text{O})\text{O}^-$ .



The above evidence definitely establishes the acyl dichlorophosphates (3) as true intermediates in the acyl chloride synthesis with  $\text{POCl}_3$ ; at the same time, the high acylating potential of the mixed anhydrides (3) is demonstrated.

#### Procedure

Synthesis of (3a): (2a) $^{[4]}$  (9.80 g, 38.8 mmol) and benzoic anhydride (1), R =  $\text{C}_6\text{H}_5$ , (8.78 g, 38.8 mmol), are heated to  $95^\circ\text{C}$  for 8 h, with strict exclusion of moisture. Fractional distillation of the reaction mixture yields 1.7 g (17%) of (2a), b. p.  $30^\circ\text{C}/10^{-3}$  torr, and 11.3 g (61%) of (3a), b. p.  $77^\circ\text{C}/10^{-3}$  torr.

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#### CAS Registry numbers:

(1) (R =  $\text{C}_6\text{H}_5$ ), 93-97-0; (2a), 13498-14-1; (2b), 14456-60-1; (3a), 67598-46-3; (3b), 67598-47-4; (3c), 67598-48-5; (3d), 67598-49-6; (3e), 67598-50-9; (3f), 67598-51-0; (5), 774-65-2; (6), 611-94-9; (7), 2553-04-0; *tert*-butyl alcohol, 75-65-0

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