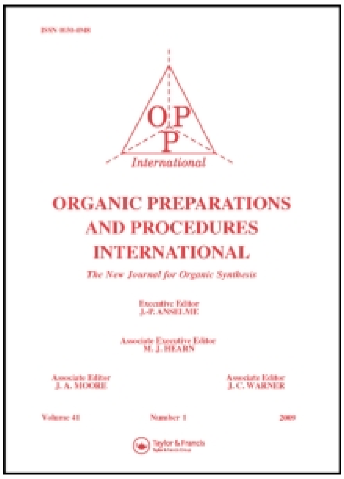

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SYNTHESIS OF CHLOROCARBONYL KETENES

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SYNTHESIS OF CHLOROCARBONYL KETENES

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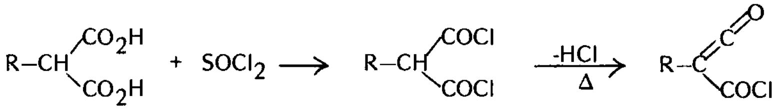
In repeating the reported synthesis[1] of phenylmalonyl dichloride (IIa), we observed the formation of phenylchlorocarbonyl ketene (IIIa) as a variable by-product. Appropriate modification of conditions has provided a simple procedure by which this novel compound may be obtained cleanly and in high yield. The method has proved to have general applicability and has been extended to the synthesis of other chlorocarbonyl ketenes.



I II III

a) R = Ph b) R = $PhCH_2$ c) R = $PhCH_2CH_2$

Sorm *et al* reported[1] the preparation of phenylmalonyl dichloride (IIa) by reaction of phenylmalonic acid (Ia) with phosphorus pentachloride in diethyl ether. Upon repeating Sorm's procedure, we found that distillation of crude phenylmalonyl dichloride (IIa) presented gassing problems and often resulted in the formation of substantial quantities of phenylchlorocarbonyl ketene (IIIa). This pyrolitic dehydrohalogenation is not altogether unprecedented, in view of the reported pyrolitic formation of α-carbethoxy ketenes[2] from the corresponding acid chlorides.

In the method described herein, variable mixtures of diacid chloride and chlorocarbonyl ketene are avoided by refluxing crude product in toluene or xylene under a slow stream of nitrogen, prior to final distillation. Through this expedient, dehydrohalogenation is clean and complete and high yields of pure chlorocarbonyl ketenes are obtained on distillation; we have observed no decarboxylation under these conditions.

EXPERIMENTAL

Phenylchlorocarbonyl Ketene (IIIa). Thionyl Chloride Procedure.-A 1 l. three-neck flask, equipped with a condenser, dropping funnel, thermometer, stirrer, and gas inlet, was charged with phenylmalonic acid (Ia), 180 g (1 mole) and toluene (250 ml). Then 218 ml (357 g, 3 moles) of thionyl chloride was added dropwise over a 15 minute period to the well stirred mixture. The mixture was heated at reflux under a slow stream of nitrogen for 18.5 hours. (The reflux temperature gradually rose from 77° to 124° during this period.) Excess thionyl chloride and most of the toluene was removed under reduced pressure at a temperature of below 35°C. The residue was distilled in vacuo to give 170.5 g (94.7% yield) of crude product, b.p. 95°-102°/1.75 mm. Redistillation gave 166.8 g (92.4% overall) of phenylchlorocarbonyl ketene (IIIa); b.p. 84-85°/0.2 mm, λ_{max}^{film} 4.70 (ketene), 5.8 (carbonyl) μ, mass spectrum M+ at m/e 180, 145 (M-Cl), 117 (M-CO), 89, 51 and 39. The compound (IIIa) solidified upon cooling to 0°. The compound (IIIa) is stable for several months when kept at 5°.

Anal. Calcd. for $C_9H_5ClO_2$: C, 59.86; H, 2.79; Cl, 19.63.
Found: C, 59.90; H, 2.81; Cl, 19.65.

Phosphorus Pentachloride Procedure. — To a stirred solution of phosphorus pentachloride, 46 g (0.22 mole) in diethyl ether (100 ml) was added 10 g (0.06 mole) of phenylmalonic acid over a two-minute period. The mixture was stirred at 20° to 25°C for four hours, refluxed for four hours, and then allowed to stand overnight at 20° to 25°. The excess phosphorus pentachloride was filtered off and the ether boiled off at atmospheric pressure. The reaction mixture gradually changed in color from dark yellow to red. The residue was distilled in vacuo to give 7.36 g (68%) of crude product, b.p. 83°-86°/1.5 mm as a yellow liquid. Redistillation gave pure (IIIa) 6.4 g (60%), b.p. 84-85°/0.2 mm.

Benzylchlorocarbonyl keten (IIIb). — Treatment of benzylmalonic acid (Ib), 194 g (1 mole), 218 ml (3 moles) of thionyl chloride, and 250 ml of toluene at reflux for 18 hrs under a slow stream of nitrogen, followed by distillation resulted in 136 g (70%) of benzylchlorocarbonyl ketene (IIIb); b.p. 110-112°/1.5 mm, λ_{max}^{film} 4.75 μ (ketene).

Anal. Calcd. for $C_{10}H_7ClO_2$: C, 61.71; H, 3.63; Cl, 18.22.
Found: C, 61.69; H, 3.65; Cl, 18.31.

Thionyl chloride is preferred over phosphorus pentachloride as the acid chloride forming reagent. For example, reaction of phenylmalonic acid (Ia) with PCl_5 gave only 34-60% yield of the ketene (IIIa), while reaction with thionyl chloride gave yields exceeding 90%.

The identity of the carbonyl ketenes was established by mass spectroscopy, infrared, n.m.r. spectra and elemental analyses. The mass spectrum of phenylchlorocarbonyl ketene (IIIa), for example, shows the molecular ion of m/e 180 and the following fragmentations which are consistent with the assigned structure. The infrared absorption spectrum shows a strong 4.7 μ ketene absorption, while no phenylmalonyl proton [Ph-C-H singlet at 5.6 ppm (δ); see Table I] signal in the n.m.r. is observed.

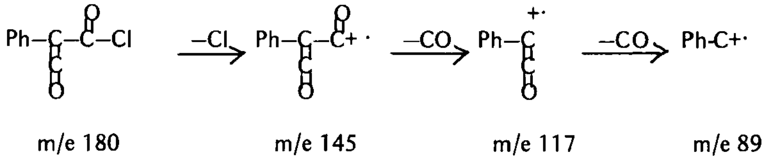
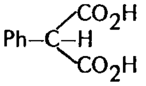
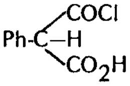
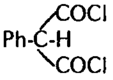


TABLE I

N.M.R. Signal for Ph-CH

Compound	Solvent	Ph-CH δ (ppm)	Ph–CH_2 δ (ppm)
	$(CD_3)_2SO$	4.64	-
Ph–CH_2CO_2H	$CDCl_3$	-	3.56
Ph–CH_2COCl	$CDCl_3$	-	4.02
	$CDCl_3$	4.95	-
	$CDCl_3$	5.60	-

The higher reactivity of ketene relative to acid chloride in phenylchlorocarbonyl ketene has been utilized in a method of synthesis of penicillins containing the phenylmalonyl side chain.

Phenylethyl chlorocarbonyl ketene (IIIc). – A mixture of β-phenylethylmalonic acid 26.4 g (0.13 mole), 21.8 ml (0.3 mole) of thionyl chloride, and 25 ml of toluene was treated in the same manner as for the preparation of (IIIa) to produce 22.5 g (85%) of (IIIc); b.p. 94-95°/0.7 mm, λ_{max}^{film} 4.75 μ (ketene).

Anal. Calcd. for $C_{11}H_9ClO_2$: C, 63.32; H, 4.35; Cl, 17.00.

Found: C, 63.24; H, 4.47; Cl, 17.13.

Mass spectrum M+ at m/e 208, 173 (M-Cl), 146, 124, 104, 91, 55.

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