Syntheses of α-Keto Acid Chlorides

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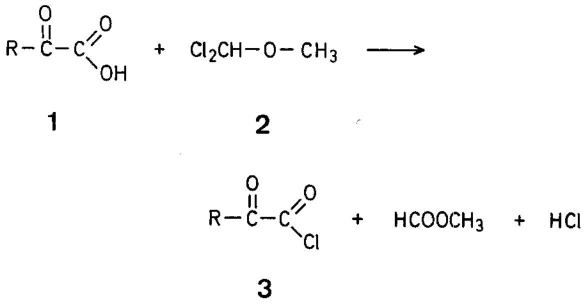
Most of the conventional reagents for the synthesis of acid chlorides from carboxylic acids have appeared rather unfit for use in the preparation of acid chlorides from α-keto acids. Treatment of pyruvic acid (**1**, $R=CH_3$) with phosphorous halides does not yield pyruvic acid chlorides **3** ($R=CH_3$) at all[1-4]; with phosgene, thionyl chloride, or oxalyl chloride, **3** ($R=CH_3$) is obtained in low yield only[5,6,7]. A first useful synthesis of this product, starting from trimethylsilyl pyruvate, was reported only very recently[8].



For the preparation of acid chlorides α,α-dichloromethyl alkyl ethers have been used[9,10]. It is surprising that dichloromethyl methyl ether **2** did not find wider use after this reagent had become well accessible[11]. We found that several α-keto acid chlorides **3** could be obtained, sometimes with good yields, by treatment of the corresponding acids **1** with **2** (see table). The reaction of phenylpyruvic acid **1**

Table. Preparation of α-Keto Acid Chlorides (**3**)

R	Yield (%)	B.p.	¹H-N.M.R. δ(CDCl₃, TMS)	*p*-Nitroanilides M.p.	Elemental Analysis			
CH_3	54	53°/126 torr	2.59 (s)	197–199°	calc.	C 51.92	H 3.87	N 13.46
					found	51.94	3.85	13.41
C_2H_5	32	51°/ 72 torr	3.84 (q, 2H), 1.15 (t, 3H)	210–211°	calc.	C 54.05	H 4.54	N 12.61
					found	53.97	5.56	12.42
$i\text{-}C_3H_7$	9.8	35°/ 45 torr	3.25 (m, 1H), 1.18, 1.09 (2 × s, 6H)	141–142°	calc.	C 55.93	H 5.12	N 11.90
					found	56.06	5.13	11.93
C_6H_5	78	80°/ 3 torr	7.75 (m, 2H), 7.36 (m, 3H)	209–210°	calc.	C 62.22	H 3.73	N 10.37
					found	62.18	3.72	10.41

($R = C_6H_5CH_2$) with **2** yielded unidentified products. Phenylpyruvic acid exists mainly in the enol form which might explain this failure.

General Procedure for the Preparation of α-Keto Acid Chlorides (3):

One equivalent of **2** was added dropwise to the stirred α-keto acid **1** at room temperature; soon the evolution of hydrogen chloride started. The mixture was heated at an oil bath temperature of 50° for 30 min, and then destilled under reduced pressure through a 15 cm Vigreux column. No attempts were made to collected the methyl formate (b.p. 31°/760 torr). The acid chlorides thus obtained were found to be stable if stored in sealed tubes at −20°. The nitroanilides used for identification were prepared in dry ether and recrystallised from ethanol/hexane.

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