Facile Photochemical Synthesis of Some 4-Oxoalkanoic Acids and Esters

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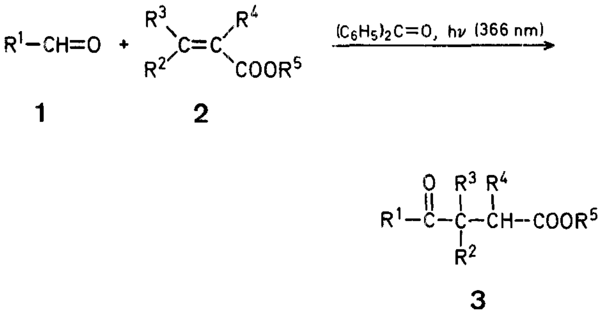
4-Oxoalkanoic acids and esters **3** (γ-ketocarboxylic acids and esters) are valuable intermediates in the synthesis of butenolides[1]. They are usually obtained by condensation of two compounds containing either the C(1)—C(2) and the C(3)—C(4)—C(5) part[2] or the (C(1)—C(2)—C(3)—C(4) and the C(5) part[3] of the desired γ-keto compound. Schlessinger et al., however, demonstrated that γ-ketocarboxylic esters can also be obtained by a *multi-step* synthesis in which the key step is the addition of a carbonyl anion equivalent in a Michael fashion to a α,β-unsaturated ester[4], which is, therefore, a coupling of a C(1)—C(2)—C(3) and C(4)—C(5) fragment.

In this paper, we describe a one-step synthesis of γ-ketocarboxylic acids and esters **3** starting with two reagents containing the C(1)—C(2)—C(3) and the C(4)—C(5) fragment, i.e. the benzophenone-initiated photochemical addition of aldehydes **1** to α,β-unsaturated carboxylic acids and esters **2**.



The present work has some analogy with, and was in fact encouraged by the radiation-induced additions of formamide to α,β-unsaturated esters[5], of aldehydes to cyclohexenones[6], and of alkanols to α,β-unsaturated esters[7]. Our results are listed in the Table.

The first step in the product formation is most likely the abstraction of the aldehydic hydrogen by photo-excited benzophenone with formation of an acyl radical. This radical then adds to the C=C-bond of the enone.

After distillation in most cases, substantial amounts of polymeric material remained as pot residue, especially for products **3a** and **3b**. Large amounts of carbon monoxide were formed on using 2-methylpropanal (**1e**; $R^1 = i\text{-}C_3H_7$) as a reagent, thus preventing the formation of substantial amounts of the γ-keto compound **3e**. In the case of ethyl sorbate (**2k**) and methyl cinnamate (**2l**) no γ-keto compounds **3** were formed, irradiation only led to (*E*/*Z*)-isomerization. This is similar to Elad's finding that aminocar-

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Table. 4-Oxoalkanoic Acids and Esters 3 prepared

Aldehyde 1 R^1	Alkenoic Acid or Ester 2 R^2	R^3	R^4	R^5	Product	Yield [%]	b.p. [°C]/torr	Molecular formula[a] or Lit. b.p. [°C]/torr	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]	Purity [%] by G.L.C.[b]
CH_3	H	H	H	CH_3	**3a**	10	82–85°/15	191–191.5°/743[10]	2.15 (s, 3H); 2.3–2.9 (m, 4H); 3.67 (s, 3H)	95
CH_3	H	H	CH_3	CH_3	**3b**	0	—	—	—	—
CH_3	H	CH_3	H	CH_3	**3c**	53	98–99°/18	82–83°/10[11]	1.10 (d, 3H); 2.14 (s, 3H); 2.2–3.1 (m, 3H); 3.63 (s, 3H)	98
n-C_3H_7	H	CH_3	H	CH_3	**3d**	63	86–88°/2	81–82°/2[12]	1.00 (d, 3H); 1.10 (t, 3H); 1.6 (m, 2H); 2.50 (t, 2H); 2.5 (m, 2H); 2.90 (m, 1H); 3.65 (s, 3H)	99
i-C_3H_7	H	CH_3	H	CH_3	**3e**	7	95–100°/2	$C_9H_{16}O_3$ (172.2)	1.05 (d, 3H); 1.07 (d, 6H); 2.0–3.2 (m, 4H); 3.62 (s, 3H)	94
C_6H_5	H	CH_3	H	CH_3	**3f**	32	155–160°/0.2	180–182°/16[13]	1.15 (d, 3H); 2.1–3.1 (m, 2H); 3.60 (s, 3H); 3.65–4.2 (m, 1H); 7.6 (m, 5H)	98
CH_3	H	CH_3	H	H	**3g**	60	120–125°/2	95°/0.1[14]	1.06 (d, 3H); 2.22 (s, 3H); 2.6–3.2 (m, 3H); 10.5 (br s, 1H)	99
CH_3	CH_3	CH_3	H	C_2H_5	**3h**	50	112–115°/20	99–100°/15[15]	1.18 (s, 6H); 1.21 (t, 3H); 2.13 (s, 3H); 2.50 (s, 2H); 4.10 (q, 2H)	99
CH_3	CH_3	CH_3	H	H	**3i**	55	95–100°/1	102°/2[15]	1.23 (s, 6H); 2.15 (s, 3H); 2.61 (s, 2H); 10.5 (br s, 1H)	99
CH_3	H	i-C_3H_7	$COOC_2H_5$	C_2H_5	**3j**	81	110–115°/0.1	$C_{13}H_{22}O_5$ (258.3)	0.86 (d, 3H); 1.04 (d, 3H); 1.20 (t, 3H); 1.25 (t, 3H); 1.8 (m, 1H); 2.20 (s, 3H); 3.20 (dd, 1H); 3.75 (d, 1H); 4.11 (q, 2H); 4.16 (q, 2H)	99
CH_3	H	$CH{=}CH{-}CH_3$	H	C_2H_5	**3k**	0	—	—	—	—
CH_3	H	C_6H_5	H	CH_3	**3l**	0	—	—	—	—

[a] The microanalyses were in satisfactory agreement with the calculated values (C ±0.21, H ±0.09, O ±0.26).

[b] G.L.C. conditions: ⅛ inch stainless steel column, 15% SE-30 on Chromosorb WHP 100–120 mesh, 85 °C, +6°/min, 15 ml He/min.

bonyl radicals are more reactive towards aliphatic α,β-unsaturated esters than towards ethyl cinnamate[5]. The high yield obtained of product **3j** as compared with products **3c, d, f, g, h, i** may be explained in terms of a relatively low rate of polymer formation for the unsaturated malonate as a result of steric hindrance.

In conclusion, our results show that the photo-induced addition of aldehydes **1** to α,β-unsaturated carboxylic acids and esters **2** gives γ-keto compounds **3** in fair to good yields for those substrates which contain a β-substituent which does not conjugate with the enone moiety. The present photochemical synthesis of γ-ketocarboxylic acids and esters proves to be a valuable alternative to the already existing syntheses and is, in fact, in a number of cases more advantageous. For example, 3-methyl-4-oxopentanoic acid (**3g**) which we obtained in one step in a yield of 60% is usually prepared in a three step synthesis in a similar overall yield starting with ethyl acetoacetate and ethyl chloroacetate[8].

4-Oxoalkanoic Acids and Esters 3; General Procedure:

A pyrex vessel containing a solution of the ester **2** (0.15 mol) and benzophenone (0.015 mol) in a mixture of the aldehyde **1** (150 ml) and benzene (350 ml) is irradiated at $\lambda = 366$ nm[9] for 24 h. At that time the ester conversion is complete (G.L.C., ^{1}H-N.M.R.). The solvent is evaporated and the residue distilled at reduced pressure through a 10 cm Vigreux column. The results are listed in the Table.

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