Preparation of ω-Formylalkenoates from Cyclic β-Ketoesters[1]

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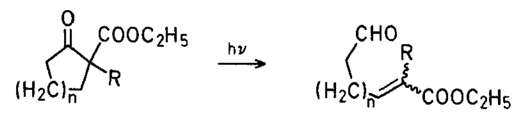
Dieckmann esters alkylated between the two functional groups are easily accessible by direct alkylation of the sodium salt of the β-ketoester[2]. Their six-membered ring homologues also can be obtained without difficulties[3]. The photochemical α-cleavage of these alkylated β-ketoesters is a simple approach to difunctional synthons and one of them has already been shown to be a useful starting material in the synthesis of natural compounds[4]. The present article describes the photochemical preparation of ω-formylalkenoates **3** or **4**, respectively, from cyclopentanones **1a–e** and cyclohexanones **2a–e**.



1 or 2

3a-e or **4a-e**
(n = 1) (n = 2)

1	n	R	2	n	R
a	1	H	**a**	2	H
b	1	CH_3	**b**	2	CH_3
c	1	C_2H_5	**c**	2	C_2H_5
d	1	n-C_3H_7	**d**	2	n-C_3H_7
e	1	i-C_3H_7—CH_2	**e**	2	i-C_3H_7—CH_2

Scheme A

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Table 1. Photoconversion of Cyclic Ketones **1a–e** and **2a–e** to the (*E*)- and (*Z*)-ω-Formylalkenoates **3a–e** and **4a–e**, Respectively

Substrate	Amounts used substrate (g)/C_6H_6 (ml)	Irradiation time	Conversion [%]	Yield [%]		Yield [%] of diene **6**
				(*E*)	(*Z*)	
1a	12/110	4h	95	36	24	—
1b	10/125	8h	95	49	31	—
1c	8.4/400	6h	87	50	21	—
1d	10/400	14h	95	51	24	—
1e	4.2/125	4h	98	33	33	—
2a	10/125	25h	54	4	1.5[a]	4.5
2b	6/125	3h	92	22	18	28
2c	3.7/125	4.5h	82	8	12	20
2d	8.5/125	11h	85	6.5	12	27
2e	8.5/125	9h	84	7	12	33

[a] Including 0.5% of the non-conjugated isomer corresponding to (*Z*)-**4a**.

Table 2. Characterization of ω-Formylalkenoates **3a–e** and **4a–e**

Product	b.p./torr (Lit.[10] b.p./torr)	Molecular formula[a]	U.V. λ [nm] (ε)	I.R. (neat) ν [cm^{-1}]			^{1}H-N.M.R. (CDCl$_3$) δ [ppm]	
				(C—H$_{ald}$)	(C—O)	(C—C)	(H$_{ald}$)	(H$_{olefin}$)
(*Z*)-**3a**	68°/1	$C_8H_{12}O_3$ (156.2)	210 (10400), 300 (sh)	2720	1720	1660	9.83 (t)	6.25 (dt, *J* = 11.5, 6.5 Hz); 5.83 (d, *J* = 11.5 Hz)
(*E*)-**3a**	78°/1 (78–79°/1.5)	$C_8H_{12}O_3$ (156.2)	208 (12400), 300 (sh)	2710	1720	1640	9.83 (t)	7.0 (dt, *J* = 16, 6.5 Hz); 5.83 (d, *J* = 16 Hz)
(*Z*)-**3b**	97–98°/12	$C_9H_{14}O_3$ (170.2)	217 (9000), 290 (33)	2720	1720	1650	9.80 (t)	5.95 (t, *J* = 6 Hz)
(*E*)-**3b**	116°/12	$C_9H_{14}O_3$ (70.2)	215 (11500), 290 (38)	2730	1720	1650	9.82 (t)	6.63 (t, *J* = 6 Hz)
(*Z*)-**3c**	66°/0.3	$C_{10}H_{16}O_3$ (184.2)	215 (10600), 290 (43)	2710	1720	1650	9.86 (t)	5.90 (t, *J* = 6 Hz)
(*E*)-**3c**	73°/0.3	$C_{10}H_{16}O_3$ (184.2)	216 (11500), 290 (41)	2720	1720	1650	9.93 (t)	6.60 (t, *J* = 6 Hz)
(*Z*)-**3d**	78°/0.4	$C_{11}H_{18}O_3$ (198.2)	216 (9500), 290 (66)	2740	1720	1640	9.85 (t)	5.90 (t, *J* = 6 Hz)
(*E*)-**3d**	83°/0.4	$C_{11}H_{18}O_3$ (198.2)	217 (12100), 290 (50)	2740	1720	1630	9.80 (t)	6.70 (t, *J* = 6 Hz)
(*Z*)-**3e**	81°/0.3	$C_{12}H_{20}O_3$ (212.3)	217 (9000), 290 (47)	2720	1720	1640	9.90 (t)	5.86 (t, *J* = 7 Hz)
(*E*)-**3e**	85°/0.3	$C_{12}H_{20}O_3$ (212.3)	217 (11600), 290 (44)	2720	1720	1640	9.97 (t)	6.80 (t, *J* = 7 Hz)
(*Z*)-**4a**	125–135°/22 (90–94°/2)	$C_9H_{14}O_3$ (170.2)	214 (7600), 290 (27)	2725	1720	1640	9.80 (t)	6.23 (dt, *J* = 12, 7 Hz); 5.8 (d, *J* = 12 Hz)
(*E*)-**4a**	110–115°/22[b]	$C_9H_{14}O_3$ (170.2)	212 (8800), 290 (30)	2725	1720	1640	9.78 (t)	6.97 (dt, *J* = 16, 7 Hz); 5.8 (d, *J* = 16 Hz)
(*Z*)-**4b**	120–135°/15 (110–115°/2)	$C_{10}H_{16}O_3$ (184.2)	217 (7300), 290 (35)	2715	1705	1640	9.79 (t)	5.75 (t, *J* = 7 Hz)
(*E*)-**4b**	105–110°/15[b]	$C_{10}H_{16}O_3$ (184.2)	217 (8600), 290 (sh)	2715	1710	1640	9.75 (t)	6.55 (t, *J* = 7 Hz)
(*Z*)-**4c**	120–135°/12	$C_{11}H_{18}O_3$ (198.2)	217 (8200), 290 (sh)	2730	1710	1640	9.82 (t)	5.80 (t, *J* = 7 Hz)
(*E*)-**4c**	110–115°/12[b]	$C_{11}H_{18}O_3$ (198.2)	217 (9300), 290 (sh)	2730	1710	1640	9.82 (t)	6.72 (t, *J* = 7 Hz)
(*Z*)-**4d**	140–160°/15	$C_{12}H_{20}O_3$ (212.3)	217 (8600), 290 (sh)	2730	1705	1640	9.90 (t)	5.82 (t, *J* = 7 Hz)
(*E*)-**4d**	130–140°/15[b]	$C_{12}H_{20}O_3$ (212.3)	217 (9600), 290 (sh)	2730	1710	1640	9.82 (t)	6.70 (t, *J* = 7 Hz)
(*Z*)-**4e**	145–165°/15	$C_{13}H_{22}O_3$ (226.3)	217 (7300), 290 (sh)	2720	1720	1655	9.83 (t)	5.77 (t, *J* = 7.5 Hz)
(*E*)-**4e**	130–140°/15[b]	$C_{13}H_{22}O_3$ (226.3)	217 (8800), 290 (sh)	2720	1710	1645	9.90 (t)	6.73 (t, *J* = 7 Hz)

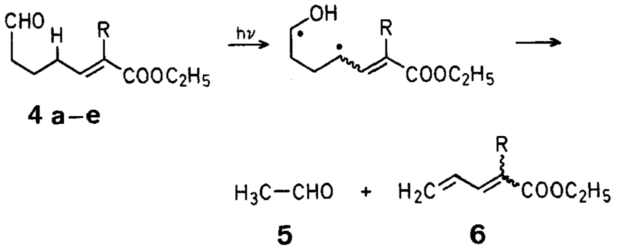
[a] All new products gave satisfactory microanalyses (C ±0.35, H ±0.28); exception (*E*)-**4a**: C −0.6.

[b] Dienoate **6**.

Irradiation of a benzene solution of these cyclanones **1** or **2** in the absorption region of the ketone, gives, as principal photoproducts, two formylalkenoates as a result of the Norrish type I reaction (Scheme **A**). The two compounds vary from each other by the (*E*)- and (*Z*)-conformation of the double bond conjugated to the ester function.

The photoproducts have two different functional groups which may react selectively with various reagents. The five-membered ring series is of interest from the synthetic point of view since the mixture of the two formylalkenoates is obtained with yields which vary from 68 to 85% (see Table 1). The (*E*)- and (*Z*)-isomers are distinguished from each other by their N.M.R. spectra which show a significant deshielding (~0.8 ppm) of the vinyl proton *cis* to the ethoxycarbonyl group compared to its value when in the *trans* position[5]. The principal spectral characteristics of the obtained aldehydes are given in Table 2. For all the aldehydes, the (*E*)-isomers show a higher boiling point and a longer retention time (whatever the column of the G.L.C.) than the corresponding (*Z*)-isomers.

In the six membered-ring series, two side-reactions decrease the yields of the aldehydes. One is the elimination of the side chain which forms keto-ester **2a** when R is ethyl, propyl or isobutyl; this reaction (Norrish type II) involves γ-hydrogen abstraction by the excited carbonyl group and implies that the substituent R is in an equatorial position[6] in order to bring the hydrogen atom to be abstracted in the plane of the carbonyl group[7]. The other one results from the absorption of light by the formed aldehydes in the same region as the starting cyclic ketoesters; the reaction which then occurs is also a Norrish type II reaction with abstraction of an allylic γ-hydrogen by the excited aldehyde group; consequently, the irradiation forms a mixture of acetaldehyde (**5**) and of two dienic esters **6** (see Scheme **B**).



Scheme **B**

The efficiency of the reaction is higher for the cyclopentanones **1a–e** than for the cyclohexanones **2a–e**, as can be expected from the already known photochemical behaviour of the two homologuous series[8]. The cyclohexanones form also a ketene in moderate yields (10–20%) as a side reaction. This ketene can be trapped by compounds with mobile hydrogen atoms such as water, alcohols, or amines. 2-Ethoxycarbonylcyclohexanone (**2a**) gives poor yields of aldehyde **4a** (see Table 1) as it has a high enol content: 57% in alcohol solution[9] and more when the polarity of the solvent is decreased[3]. This enol form acts undoubtedly as an efficient triplet quencher and, as a consequence, inhibits the normal course of the reaction. The enol content in 2-ethoxycarbonylcyclopentanone (**1a**) is less than 5%[9] and when freshly distilled almost no enol can be detected.

Alkylation of 2-Ethoxycarbonylcyclopentanone (1a):

Compounds **1b–e** are prepared by alkylation of the sodium salt of Dieckmann ester **1a** with alkyl halides following the general procedure[2]. The use of the sodium salt of **1a** has the advantage of eliminating dimethyl adipate which always contaminates **1a**.

Alkylation of 2-Ethoxycarbonylcyclohexanone (2a):

Alkylation of keto-ester **2a** is performed with sodium hydride following the reported procedure[3]. All the substituted cyclohexanones are purified by distillation before use.

Irradiation of Esters 1 and 2; General Procedure:

A solution (0.11 to 0.45 molar) of the unsubstituted or 2-alkyl-2-ethoxycarbonylcyclanone is placed in a cylindrical three-necked flask fitted with a condenser and a nitrogen inlet at the bottom. The central neck of the flask is fitted with a double envelope cylindrical immersion apparatus in Vycor glass and equiped with a 400 W medium-pressure mercury lamp (taken from a highway light Philips HPLN-400 bulb after taking away the external fluorescent envelope). The irradiation is carried out at room temperature and dry nitrogen is bubbled through the solution during the irradiation. The progress of the reaction is determined by G.L.C. (SE 30 column supported on Chromosorb W for **1b–e** and **2b–e**; XF 1150 on Chromosorb W for **1a** and **2a**); tridecane is added to the reaction mixture as internal standard for the irradiation of **1a** and **2a** as they are difficultly characterized by G.L.C. After irradiation, the solvent is removed by distillation or by means of a rotatory evaporator. The residue is then distilled in two steps: a rapid distillation to eliminate the polymers and the distillate is fractionated with a spinning band column. When starting from **2a–e** the first distillation fraction is the mixture of the dienic esters **6**.

Ethyl 6-Oxo-2-hexenoate (3a):

Compound **1a** (12 g) in benzene (110 ml) is irradiated for 4 h. After elimination of the solvent, the residue is distilled rapidly to give a mixture of aldehydes (*E*)-**3a** + (*Z*)-**3a** containing 9% of the starting material; yield: 7.8 g; b.p. 95–120°/16 torr. Distillation with a spinning band (Nester and Faust) affords (a) compound **1a** (0.5 g, b.p. 59–64°/1 torr), (b) an intermediate fraction containing **1a** and (*Z*)-**3a** (0.01 g), (c) product (*Z*)-**3a** (2.7 g; b.p. 68°/1 torr), (d) an intermediate fraction containing a mixture of (*E*)-**3a** + (*Z*)-**3a** (0.2 g), and (e) product (*E*)-**3a** (4.1 g, ; b.p. 78°/1 torr). The residue can be distilled in a small distillation column to give further (*E*)-**3a** (0.1 g).

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[1] Part 13 in the photochemistry in solution series. For Part 12 see B. Furth, P. Jost, S. Sabbah, J. Kossanyi, *Nouveau J. de Chimie*, in press.

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