A New Simple Synthesis of a Prostanoid Synthon*

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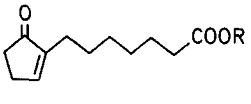
The 2-substituted cyclopentenone **1**, first synthesised by Bagli et al.[1] has served as a valuable intermediate in the synthesis of a variety of 11-deoxyprostanoids, as for example, PGB_1[2,3], 11-deoxy-PGE_1[4,5], 11-deoxy-PGE_2[4], 11,15-bis-deoxy-PGE_1[5] (and -PGE_2, -PGF_1)[6] and 11-deoxy-13-dihydro-PGE_1[7]. The intermediate **1** has also been converted[8,9] into the hydroxy-keto ester **2**, which has been successfully elaborated into (+)-PGE_1[9,10] and (−)-PGE_1[11]. Thus, the utility of the cyclopentenone **1** as a useful prostanoid synthon is well-secured.



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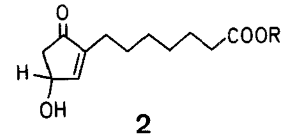

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At present three distinct routes are available for the preparation of **1** (R = H, CH_3, C_2H_5)[12] *starting with* 2-ethoxycarbonylcyclopentanone[1,4,9], 2-methoxycyclopent-2-en-1-one[5], or cyclopentanone[13]. All these methods involve several steps and the overall yields, wherever reported, are not satisfactory. We *now report a simple practical route starting* with the readily available methyl undec-10-enoate (**3**).

$$H_3COOC-CH_2-(CH_2)_6-CH_2-R$$

3: $R = -CH{=}CH_2$

4: $R = -CH{=}O$

5: $R = -CH{=}CH-COOC_2H_5$

The olefin ester **3** gave, in 83% yield, the aldehyde ester **4**[14] on ozonolysis (chloroform/methanol) followed by reductive workup (zinc/acetic acid). Condensation of **4** with methoxycarbonylmethylenetriphenylphosphorane furnished in 86% yield, the diester **5**[16]. This material was exposed to polyphosphoric acid (120°/1 h), the product esterified and after chromatography gave, as expected, 2-(6-methoxycarbonylhexyl)-cyclopent-2-en-1-one (**1**: $R = CH_3$) in 35% yield. This product was identical (G.L.C., I.R., U.V., N.M.R. and mass spectrum: semicarbazone m.p. and mixture m.p. 176 to 177°) with an authentic sample of **1** ($R = CH_3$) prepared by a known procedure[4].

All m.p.s and b.p.s are uncorrected. Light petroleum refers to the fraction b.p. 60—80°. All solvent extracts were dried over anhydrous sodium sulfate.

Methyl 9-Formylnonanoate (4):
This compound was prepared[14] in a superior yield (83%) by changing the solvent (chloroform/methanol instead of glacial acetic acid) for ozonolysis of methyl undec-10-enoate (**3**). The ester **3** (10.0 g) dissolved in chloroform/methanol (1:1, 150 ml) was cooled in an ice-salt bath (~ −10°) and a stream of ozonised oxygen (1.2 g/h) was passed for 135 min (starch/potassium iodide test). The reaction solution was added dropwise (10 min.) to a stirred mixture of zinc dust (freshly activated, 24.0 g) and 30% acetic acid (210 ml) cooled in ice water. After an additional stirring for 1 h, the mixture was refluxed on a water bath for 1/2 h. Most of the chloroform was then distilled off on a steam bath. Water (200 ml) was then added, the mixture acidified with concentrated hydrochloric acid (Congo red), extracted with chloroform (3 × 100 ml), washed with water, brine, dried, solvent removed, and the residue distilled to furnish the ester **4** as a colourless liquid; yield: 8.4 g (83%); b.p. 119—121°/2 torr (Lit.[14]: b.p. 120—121°/3 torr; yield: 55—60%).

$C_{11}H_{20}O_3$	calc.	C 65.97	H 10.07	
(200.1)	found	66.09	10.35	

2,4-Dinitrophenylhydrazone (aqueous methanol/sulfuric acid method): orange prisms; m.p. 86—87° (from methanol):

$C_{17}H_{24}O_6N_4$	calc.	C 53.67	H 6.36	N 14.73
(380.39)	found	53.00	6.62	15.14

Mass spectrum: $m/e = 380$ (M^+).

Methyl 11-Ethoxycarbonylundec-10-enoate (5):
This compound was prepared from the ester **4** (8.6 g) by the method[16] of Truscheit and Eiter using ethoxycarbonylmethylenetriphenylphosphorane[17] (15 g) instead of the methoxycarbonyl derivative. The resulting crude diester **5** was obtained as a colourless liquid by distillation; yield: 10.0 g (86%); b.p. 150—152°/0.5 torr.

$C_{15}H_{26}O_4$	calc.	C 66.63	H 9.69	
(270.36)	found	66.18	9.93	

2-(6′-Methoxycarbonylhexyl)-cyclopent-2-ene-1-one (1):
Polyphosphoric acid [prepared from phosphorus pentoxide (60 g) and 85% orthophosphoric acid, d = 1.75 (30 ml)] was treated with the diester **5** (5.0 g) and the mixture was heated on an oil bath at 120° for 1 h. The dark red reaction product was poured onto crushed ice, extracted with ether (3 × 100 ml), washed with water, brine, dried and the solvent removed. The residue (3.5 g) was esterified by treatment with 3% hydrochloric acid in methanol (30 ml) at 28° for 16 h. The product, isolated in the usual manner, was distilled to give a pale yellow liquid; yield: 2.0 g; b.p. 160—170° (bath)/0.5 torr.

This material, rich in the keto ester **1** (T.L.C.: one major and two faster-moving minor spots; solvent, 10% ethyl acetate in benzene) was purified by chromatography on silica gel (IIa, 100 g, 45 cm × 2.5 cm) with T.L.C. monitoring. The material eluted with light petroleum and 1:1 light petroleum/benzene was rejected.

A pure fraction (1.4 g, 35%) eluted with neat benzene was distilled at 160—170° (bath)/0.5 torr to furnish a colourless liquid identical (G.L.C., U.V., I.R., N.M.R., and Mass) with an authentic sample of the keto ester **1** prepared by the method[4] of Bagli and Bogri.

$C_{13}H_{20}O_3$	calc.	C 69.61	H 8.99	
(224.29)	found	69.61	9.03	

Semicarbazone (pyridine method): silky white crystals; m.p. 176—177° (ethanol); mixture m.p. with the semicarbazone of authentic sample (m.p. 176—177°) was undepressed.

$C_{14}H_{23}O_3N_3$	calc.	C 59.76	H 8.24	N 14.94
(281.35)	found	60.06	8.38	14.66

2,4-Dinitrophenylhydrazone (aqueous methanol/sulfuric acid method): brick-red silky needles; m.p. 103—104° (ethyl acetate).

$C_{19}H_{24}O_6N_4$	calc.	C 56.43	H 5.98	N 13.86
(404.41)	found	56.07	5.97	13.76

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