5-(6-Methoxycarbonylhexyl)- and 5-(6-Methoxycarbonylhex-2-enyl)-cyclopent-2-enone, Prostaglandin Precursors†

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Summary The title cyclopentenones can be prepared on a large scale by thermolysis of compounds derived from dicyclopentadiene; the sequence is of possible interest in the prostaglandin field.

PREVIOUSLY we have shown that retro Diels–Alder reactions may be used to prepare various cyclopentenones.[1] We have now prepared ketones which are possible precursors of modified prostaglandins.

endo-Dicyclopentadiene smoothly underwent cyclo-addition with dichloroketen[2] (generated *in situ* from dichloracetyl chloride in refluxing pentane by dehydrohalogenation with NEt_3) to give (86%) two cycloadducts (**1a**) and (**1b**) (ratio 3 : 1) which, upon treatment with Zn–AcOH, then by Baeyer–Villiger oxidation (H_2O_2–AcOH; 0 °C) were converted into the lactones (**2a**) and (**2b**) [89% from (**1a**)–(**1b**) mixture]. Compound (**2a**), m.p. 62·5 °C, was readily obtained crystalline. The identity of the lactones (**2a**) and

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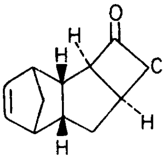
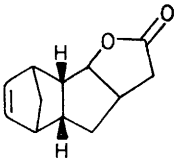
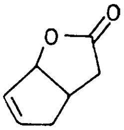
(**2b**) was proved by thermolysis at 300 °C. Thus, (**2a**) led to the known bicyclic lactone (**3a**) (nearly quantitative yield; i.r. and n.m.r. spectra identical to published values[3]). The compound (**3b**) is also described by Grieco.[4]


(1a)


(2a)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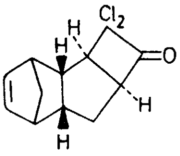
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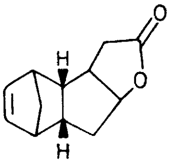
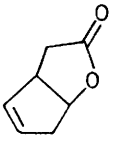
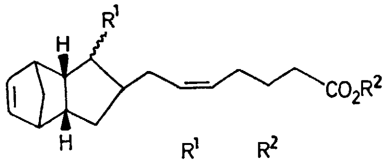

(2b)


(3b)

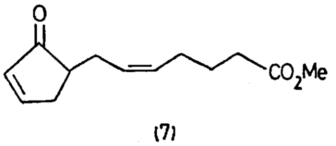
The lactol formed from (**2a**) (Bu^n_2AlH; toluene; −78 °C; 100% yield) was easily transformed by a Wittig reaction with the phosphonium salt of 5-bromopentanoic acid,[5] into the hydroxy-acid (**4**) (single *cis*-isomer, according to its ^1H n.m.r. spectrum) which in two steps (Jones oxidation and $MeOH-H_2SO_4$) led, *via* the keto-acid (**5**), to the keto-ester (**6**). Thermolysis of (**6**) (460 °C; 0·01 mmHg) provided the substituted cyclopentenone (**7**) (> 95%); δ (CCl_4) 3·6 (s, OMe), 5·4 (m, *cis*-CH=CH), and 6·1 and 7·6 (each 1H, m, cyclopentene CH=CH).

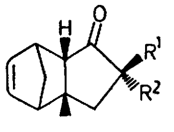
Reaction of the β-ketoester (**9**) formed (75%) from (**8**)[6] [NaH; dioxan; $OC(OMe)_2$] with methyl 7-bromoheptanoate[7] and a trace of KI led to (**10**) (*ca.* 86%) (MeONa–MeOH). The stereochemistry of (**10**) was deduced by comparison with earlier work.[1a,c]

After decarboxylation of (**10**) with $Ba(OH)_2$[8] (H_2O; reflux) then re-esterification (MeOH), compound (**12**) was obtained, which on thermolysis (500 °C; 0·01 mmHg) provided (**13**) (95%) [n.m.r. resonances for OMe and cyclopentene double bond protons similar to those for (**7**)]. The structure of (**13**) was confirmed by base-catalysed isomerization into the known ketone (**14**).[9]

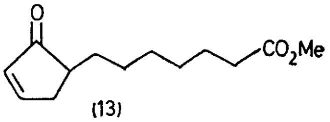


	R^1	R^2
(4)	OH,H	H
(5)	=O	H
(6)	=O	Me


(7)



	R^1	R^2
(8)	H	H
(9)	CO_2Me	H
(10)	$[CH_2]_6CO_2Me$	CO_2Me
(11)	$[CH_2]_6CO_2H$	H
(12)	$[CH_2]_6CO_2Me$	H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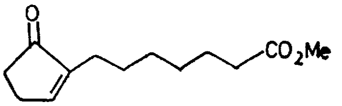
(14)

Compounds (**7**) and (**13**) may be of use in prostaglandins synthesis.

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[9] *Cf. inter alia.* F. S. Alvarez and D. Wren, *Tetrahedron Letters*, 1973, 569, and references therein.