Tetrahedron Letters No. 13, pp 1131 - 1134 , 1977. Pergamon Press. Printed in Great Britain.

A USEFUL PREPARATION OF (±) T-BUTYL 3-HYDROXY-5-OXO-1-CYCLOPENTENE-HEPTANOATE AND ITS 3-DEOXY-DERIVATIVE, IMPORTANT PROSTAGLANDIN INTERMEDIATES

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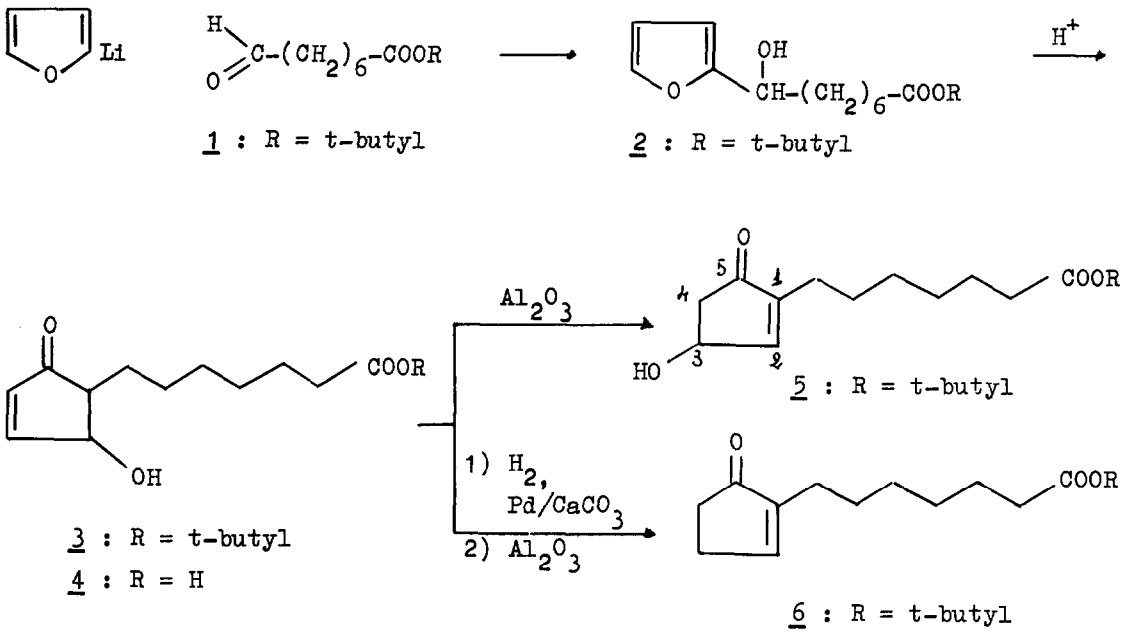
(Received in UK 4 February 1977; accepted for publication 21 February 1977)

Within the past few years, the syntheses of substituted cyclopentenones, like 5 and 6, have been the object of intensive investigations, since these compounds are major synthons for the prostaglandins assembly via conjugate addition of organometallic derivatives (1). Nevertheless, at present, only complex multi-step syntheses are available (2).

Recently we reported a new method of construction of cyclopentenone derivatives by acid-catalyzed rearrangement of suitable furylcarbinols, alkyl or aryl 2-substituted (3). In this letter we wish to report the first important extension of this method to 2-furylcarbinols possessing a second functional group in their side chain, whose applicability has rapidly and efficiently led to the synthesis of (±) t-butyl 3-hydroxy-5-oxo-1-cyclopenteneheptanoate 5, and its deoxy-derivative 6, key intermediates in the preparation of the prostanoic acid skeleton (1, 2).

The starting material, t-butyl 8-hydroxy-8-(2-furyl)-octanoate 2, was easily prepared by reaction of t-butyl 8-formyloctanoate 1 (4) with 2-furyl lithium in dry Et_2O at -20 °C for 15 minutes.



ν_{max} 3600, 1725, and 1605 cm^{-1}; δ 7.30, 6.28, and 6.20 (3 m, 3 H, relative to the furan protons; 4.55 (t, 1 H, -CH-OH), 2.30 (m,1 H, -OH) 2.10 (m, 2 H, $-CH_2-$ α to the ester function) (5).

2 (1 g) was dissolved in 2:1 acetone-water mixture (20 ml), then 0.15 g of PPA were added and the solution was stirred at 50°C for 24 h. The usual work-up (3) furnished a reddish oil that was chromatographed on SiO_2 : elution with 2:1 benzene-diethyl ether yielded the pure ester 3, $C_{16}H_{26}O_4$, as oil (0.51 g, 51 %). ν_{max} 3600, 1730-1710 (broad), and 1600 cm^{-1}. δ 7.48 (dd, 1 H, J_1= 3 Hz, J_2= 6 Hz), 6.13 (dd, 1 H, J_1= 1.5 Hz, J_2= 6 Hz), 4.58 (m, 1 H, -CH-OH), 3.3 (m,1 H, -OH), 2.15 (m, 3 H, $-CH_2-$ and -CH-, α respectively to the ester and

ketone functions); elution with 9:1 CH_2Cl_2-CH_3OH afforded the hydroxy-acid 4, $C_{12}H_{18}O_4$, (0.2 g, 20 %). δ 7.50 (dd, 1 H, J_1= 3 Hz, J_2= 6 Hz), 6.20 (dd, 1 H, J_1= 1.5 Hz, J_2= 6 Hz), 5.55 (m, 2 H, -COOH and -OH), 4.7 (m, 1 H, -C<u>H</u>-OH), 2.3 (m, 3 H, -C<u>H</u>$_2$- and -C<u>H</u>-, respectively α to the acid and ketone functions) (6).

The compound 3 showed synthetic versatility: in fact, after adsorption on alumina (Brockmann grade III, basic) for 16 h, and elution with 4:1 benzene-diethyl ether, 3 underwent a conversion to (±) t-butyl 3-hydroxy-5-oxo-1-cyclopenteneheptanoate 5, $C_{16}H_{26}O_4$, (yield 95 %), a key intermediate in the PGE_1 synthesis (1). ν_{max} 3610, 1735-1710 (broad), and 1640 cm^{-1}; δ 7.05 (m, 1 H, C_2-<u>H</u>), 4.85 (m, 1 H, C_3-<u>H</u>), 4.2 (m, 1 H, -O<u>H</u>), 2.7 (dd, 1 H, C_4-<u>H</u>; J_1= 16 Hz, J_2= 6 Hz), 2.3-2.0 (m, 5 H, C_4-<u>H</u>, the allylic -C<u>H</u>$_2$-, and the -C<u>H</u>$_2$- α to the ester function) (7).

This conversion has proved to be interesting in synthetic field, but at present we have no fact that can support a possible mechanism: however, the reaction might proceed via dehydration-hydration sequence (heterogeneous catalysis being involved), with the initial formation of an unstable cyclopentadienone (8), that immediately changes into the more stable α-β unsaturated ketone 5; this assumption is supported by the fact that when the C=C double bond of 5 is reduced, only the dehydration reaction occurs, with the formation of the more stable α-β unsaturated ketone 6.

In fact, 3, by catalytic reduction on $Pd/CaCO_3$ in methanol and subsequent elution on alumina (Brockmann grade III, basic) with benzene, yielded nearly quantitatively the t-butyl 5-oxo-1-cyclopenteneheptanoate 6, $C_{16}H_{26}O_3$, as oil, a key intermediate in the synthesis of 11-deoxy $PGF_1\beta$, a pharmacologically active derivative of the prostaglandins (9). ν_{max} 1730, 1705, and 1635 cm^{-1}; δ 7.2 (m, 1 H, C_2-<u>H</u>), 2.5-2.0 (complex m, 8 H, 2 allylic -C<u>H</u>$_2$- and 2 -C<u>H</u>$_2$- α situated to the ester and ketone functions).

This synthesis represents a new and useful alternative to the routes at present employed, since the starting materials are easily available and overall yields of the products are satisfactory.

Acknowledgement: we are grateful to the Italian CNR for financial support.

References and remarks

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5) ^{1}H-NMR spectra were taken with a Perkin-Elmer R 32 spectrometer in CCl_4 solution. IR spectra were taken with a Perkin-Elmer 257 spectrometer in 1% $CHCl_3$ solution.

6) IR and ^{1}H-NMR data were completely in agreement with the ones reported for similar compounds: K. Ogura, M. Yamashita, and G. Tsuchihashi, Tetrahedron Lett., 759 (1976) and references therein.

7) 5 was pure and the starting material 3 was completely absent; the IR and ^{1}H-NMR data were consistent with the ones reported for these compounds: see ref. 1).

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