

PHOTOCHEMICAL TYPE I FRAGMENTATION OF THE A RING IN METHYL-7 α ,12 α -DIHYDROXY-3-OXO-5 β -CHOLAN-24-OATE[†]

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(Received August 24, 1984; in revised form October 25, 1984)

Summary

Irradiation of methyl-7 α ,12 α -dihydroxy-3-oxo-5 β -cholan-24-oate in benzene or acetonitrile yields 7 α ,12 α -dihydroxy-2,3-*seco*-5 β -cholan-3,24-dioic-24-methylester (3 \rightarrow 7)-lactone, whereas in methanol 7 α ,12 α -dihydroxy-3,4-*seco*-5 β -cholan-3,24-dioic dimethyl ester is formed in addition to the lactone. The lactone is formed as a result of intramolecular trapping of the ketene intermediate by the 7 α -OH group.

1. Introduction

The formation of a biradical intermediate via Norrish type I fragmentation is a probable initial step in the photolysis of cycloalkanones [1]. The biradical first observed by Caldwell *et al.* [2] can eliminate CO and/or shift hydrogen which results in the formation of an unsaturated aldehyde and/or ketene depending on structural factors [3, 4]. In protic solvents like alcohols or water the ketene intermediate usually forms an ester or a carboxylic acid [5]. If free OH groups exist, the ketene intermediate is found in some cases to undergo an intramolecular reaction to form lactones [6, 7]. Therefore photolysis of methyl-7 α ,12 α -dihydroxy-3-oxo-5 β -cholan-24-oate (1) seemed to us to be a very good example to demonstrate the dependence of the intermediate ketene reaction on the structure and on the choice of solvent.

2. Results

According to Jones *et al.* [8] 1 can be prepared in good yields from methyl cholate by Oppenauer oxidation with aluminium isopropylate-acetone. The irradiation of 1 in benzene yields 7 α ,12 α -dihydroxy-2,3-*seco*-

[†] Dedicated to Professor Dr. Dietrich Schulte-Frohlinde on the occasion of his 60th birthday.

5 β -cholan-3,24-dioic-24-methylester (3 \rightarrow 7)-lactone (8) (49%), whereas in methanol a mixture of 8 (45%) and 7 α ,12 α -dihydroxy-3,4-seco-5 β -cholan-3,24-dioic dimethyl ester (6) (47%) is obtained (Fig. 1). When acetonitrile is used as solvent the same results are obtained as with benzene.

These results show that both α fragmentations in the A ring of ketone 1 occur with equal probability under formation of the intermediate biradicals 2 $\cdot\cdot$ and 3 $\cdot\cdot$. The subsequent stabilization of 2 $\cdot\cdot$ and 3 $\cdot\cdot$ by hydrogen shifting results in the formation of the ketenes 4 and 5 which are trapped either intermolecularly to form 6 or intramolecularly to form 8. Neither the formation of 7 from 4 nor the formation of 9 from 5 are observed. In benzene only some unidentified high molecular weight products are found in addition to 8 (the unsaturated aldehyde (5-exomethylene compound) from 3,4-fragmentation via 2 was not obtained (see also ref. 9)). This seems to be a clear-cut demonstration of a sterically controlled reaction. Reduction products observed when similar ketones were photolysed in acetic acid-water [9] were not detected.

3. Experimental details

The melting points were determined using a Büchi model 510 melting point apparatus and are uncorrected. The optical rotations were measured using a Perkin-Elmer model 241 polarimeter. IR spectra were recorded on dispersions in KBr using a Perkin-Elmer model 377 spectrometer. The nuclear magnetic resonance (NMR) spectra were recorded using Varian T 60 (60 MHz ^1H NMR), Varian EM 390 (90 MHz ^1H NMR) and CFT 20 (^{13}C NMR) spectrometers with tetramethylsilane as the internal standard. Column chromatography was carried out on Silica Woelm 32-100 (32 - 100 mesh).

3.1. 7 α ,12 α -Dihydroxy-2,3-seco-5 β -cholan-3,24-dioic-24-methylester (3 \rightarrow 7)-lactone: irradiation of methyl-7 α ,12 α -dihydroxy-3-oxo-5 β -cholan-24-oate in benzene

1.68 g (4 mmol) of 1 were dissolved in 200 ml of absolute benzene and irradiated in a Pyrex vessel for 120 h under a nitrogen atmosphere (Philips HPK 125 high pressure mercury lamp). The solution was then concentrated and the residue was subjected to column chromatography (elution with a 10:1 petroleum ether-acetone mixture) to yield 0.82 g (49%) of 8: melting point, 156 - 158 $^{\circ}\text{C}$; $\alpha_{\text{D}}^{25} = -26.4^{\circ}$ ($c = 1.04$ in CHCl_3). The δ values for ^1H NMR (d_6 -dimethyl sulphoxide) were as follows: 0.62 (singlet, 3H, 18- CH_3), 0.88 (singlet, 3H, 19- CH_3), 3.58 (singlet, 3H, OCH_3), 3.78 (doublet, 1H, C-12 β H, $J = 3$ Hz), 4.18 (doublet, 1H, OH, $J = 3$ Hz) and 4.33 (singlet, 1H, C-7 β H). The δ values for ^{13}C NMR (CDCl_3) were as follows: 7.16 (C-2), 12.52 (C-18), 17.16 (C-21), 18.41 (C-19), 22.92 (C-15), 27.34 (C-9, C-16), 28.80 (C-11), 30.89 (C-22, C-23), 31.01 (C-1), 32.56 (C-4), 33.65 (C-6), 35.19 (C-20), 35.91 (C-8), 37.07 (C-10), 41.08 (C-14), 42.19 (C-5), 46.64 (C-13), 47.03 (C-17), 51.37 (OCH_3), 72.26 (C-7), 76.51 (C-12), 171.79 (C-3) and

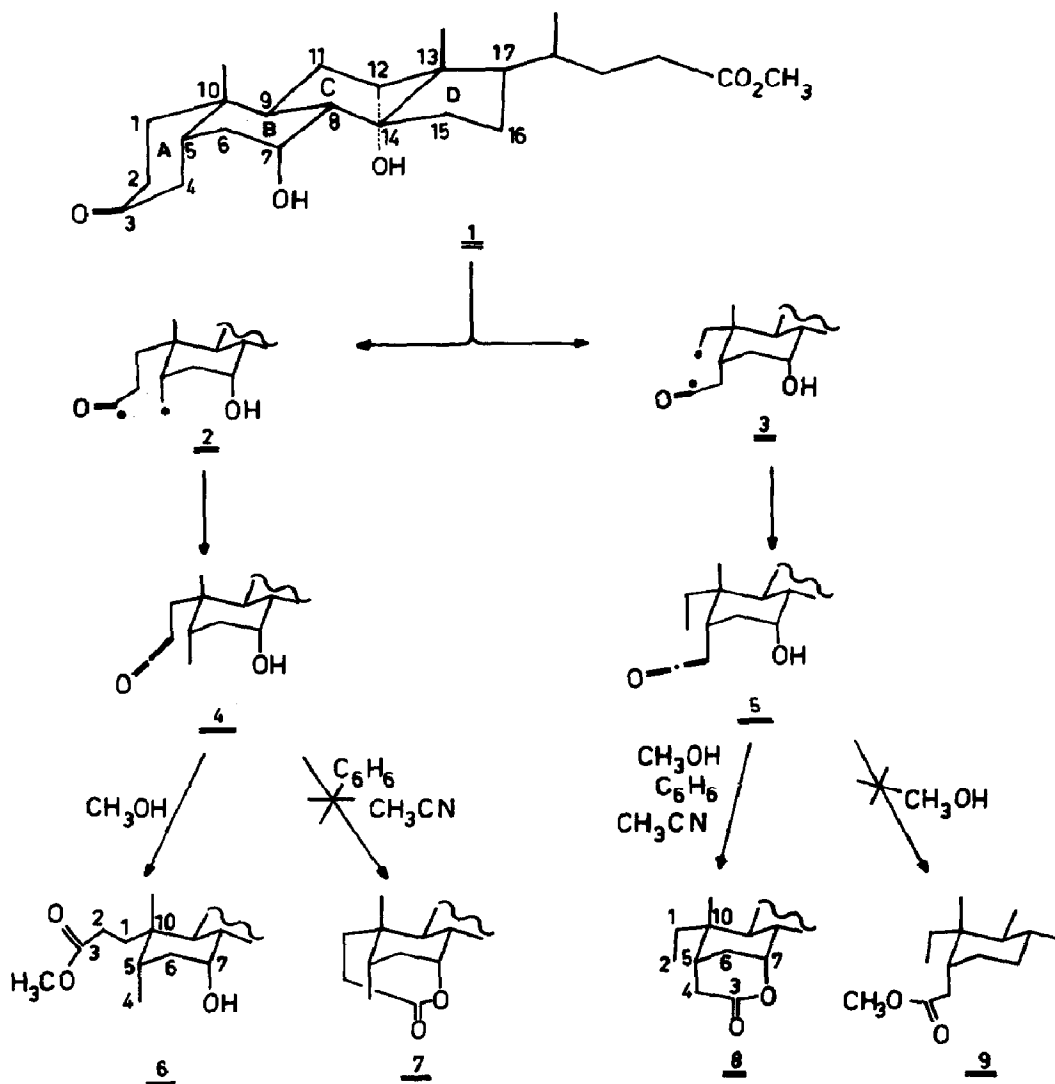


Fig. 1.

174.59 (C-24). The IR data were as follows: 3500 cm^{-1} ($\nu_{\text{O-H}}$); 1730 cm^{-1} and 1710 cm^{-1} ($\nu_{\text{C=O}}$); 1165 cm^{-1} ($\nu_{\text{C-O}}$).

$\text{C}_{25}\text{H}_{40}\text{O}_5$ contains 71.39% C and 9.59% H. The results of the analysis were as follows: 71.49% C and 9.49% H.

3.2. $7\alpha,12\alpha$ -Dihydroxy-3,4-*seco*-5 β -cholan-3,24-dioic dimethyl ester: irradiation of methyl- $7\alpha,12\alpha$ -dihydroxy-3-oxo-5 β -cholan-24-oate in methanol

1.26 g (3 mmol) of 1 were dissolved in 150 ml of absolute methanol and were irradiated as described above (see Section 3.1). Subsequent column chromatography yielded 0.57 g (45%) of 8 (elution with a 10:1 petroleum ether-acetone mixture) and 0.63 g (47%) of 6 (elution with a 7:1 petroleum ether-acetone mixture): melting point, $94 - 95\text{ }^\circ\text{C}$; $\alpha_{\text{D}}^{25} = +26.6$ ($c = 1.05$ in

CHCl₃). The δ values for ¹H NMR (CDCl₃) were as follows: 0.68 (singlet, 3H, 18-CH₃), 0.90 (singlet, 3H, 19-CH₃), 3.65 (singlet, 6H, 2 × OCH₃), 3.84 (broad singlet, 1H, C-7 β H) and 3.96 (broad singlet, 1H, C-12 β H). The δ values for ¹³C NMR (CDCl₃) were as follows: 12.54 (C-18), 17.33 (C-21), 17.76 (C-4), 18.75 (C-19), 23.26 (C-15), 27.40 (C-16), 28.47 (C-2), 28.94 (C-12), 31.06 (C-22, C-23), 31.33 (C-9), 33.49 (C-1), 35.28 (C-20), 35.45 (C-8), 35.90 (C-6), 37.05 (C-10), 39.64 (C-5), 41.47 (C-14), 46.30 (C-13), 47.07 (C-17), 51.42 (OCH₃), 51.52 (OCH₃), 68.42 (C-7), 73.07 (C-12), 174.76 and 174.98 (C-3, C-24). The IR data were as follows: 3600 - 3100 cm⁻¹ ($\nu_{\text{O-H}}$); 1725 cm⁻¹ ($\nu_{\text{C=O}}$); 1175 cm⁻¹ ($\nu_{\text{C-O}}$). C₂₆H₄₄O₆ contains 68.99% C and 9.80% H. The results of analysis were as follows: 68.94% C and 9.76% H.

Acknowledgments

We thank Dr. Jan Runsink for obtaining and discussing the ¹H and ¹³C NMR spectra. We are also grateful to the Fonds der Chemischen Industrie for supporting this work.

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