

NEW PHOTOCYCLIZATION OF CYCLOHEXENONES IN
THE PHOTOLYSIS OF 4-METHOXY CHOLEST-4-ENE-3-ONE

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Recently there has been considerable interest in the photochemical reactivity of cyclohexenones. However not all the aspects of the mechanism of these transformations are well understood. It is usually accepted that the triplet states $^3(n, \pi^*)$ or $^3(\pi, \pi^*)$ are involved in the photochemical conversions of cyclohexenones, although it is difficult to distinguish between these pathways (1).

Because of the weak splitting between the $^3(n, \pi^*)$ and $^3(\pi, \pi^*)$ excited states, the ordering of the energy levels may be easily reversed by structural modifications (2) or by use of different experimental conditions (3). Moreover, it has recently been shown that the potential energy surfaces for the $^3(n, \pi^*)$ and $^3(\pi, \pi^*)$ triplet states of acrolein intersect.

It appeared particularly desirable to collect new information on the reactivity of the triplet states and we began to study the influence of substitution on the photoreactivity of cyclohexenones. We describe here the unusual photochemical cyclization of 4-methoxy cholest-4-ene-3-one 1.

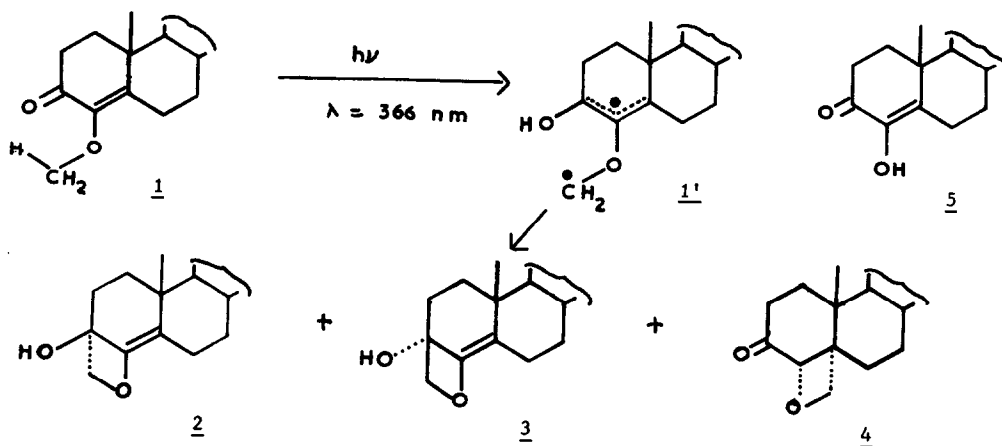
A solution of 1 (10^{-3} M) in dioxane or methanol, carefully deoxygenated is irradiated for 8 hours with an HPW 125 W Philips lamp ($\lambda = 360$ nm). By silica gel chromatography we isolated three new products 2, 3 and 4 in yields of 30, 50 and 8 % respectively for 90 % conversion (5), (6). The results are shown in scheme I.

We have attributed methylene oxetanols structures (2 and 3) to both major compounds from the reaction, from the evidence of their spectral properties and a chemical correlation.

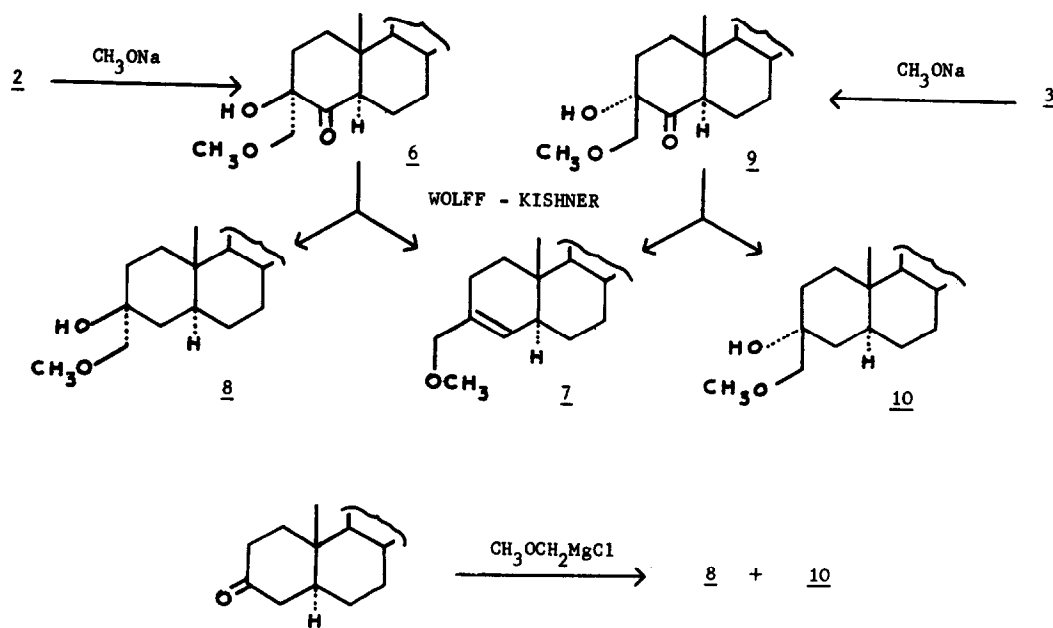
2 [F = 190-191°; I.R. (CHCl_3): 3600, 3430 (OH); 1730 (C = C) (7); 892, 878 cm^{-1} (C-O-C); U.V.: a single maximum $\lambda_{\text{max}}^{\text{C}_6\text{H}_{12}} = 205$ nm, $\epsilon_{\text{max}} = 11.250$. N.M.R. (CDCl_3) AB spectrum: (2H oxetane ring) $\delta_{\text{A}} = 4.50$; $\delta_{\text{B}} = 4.66$ ppm; $J_{\text{AB}} = 6$ Hz; neither vinylic hydrogen, nor methoxy group. Mass: Parent: 414 (100%), 384 (15%), 371 (40%)].

3 [F = 133-135°; I.R. (CHCl_3): 3610, 3420 (OH); 1733 (C = C) (7); 888, 872 cm^{-1} (C-O-C). U.V.: a single maximum $\lambda_{\text{max}}^{\text{C}_6\text{H}_{12}} = 208$ nm, $\epsilon_{\text{max}} = 11.300$. N.M.R. (CDCl_3) AB spectrum (2H): $\delta_{\text{A}} = 4.70$; $\delta_{\text{B}} = 4.87$ ppm, $J_{\text{AB}} = 5.6$ Hz, neither vinylic hydrogen, nor methoxy group;

SCHEME I



SCHEME II



Mass : Parent 414 (100 %), 384 (25 %), 371 (75 %).

Confirmation of the structures and the assignment of the stereochemistry on C_3 could be achieved by the sequence of reactions presented in scheme II.

Treatment of 2 by sodium methoxide leads rapidly to 6 (10) [F = 120-121° . I.R. (CHCl₃) : 3570 (OH) ; 1712 (C = O) ; 1110 cm⁻¹ (C-O-C). U.V. : $\lambda_{\max}^{C_2H_5OH} = 280 \text{ nm}$, $\epsilon_{\max} = 59$. N.M.R. (CDCl₃) : singlet (3H : OCH₃) 3,3 ppm ; AB spectrum (2H : CH₂O) : $\delta_A = 3.65$, $\delta_B = 3.69$ ppm $J_{AB} = 10 \text{ Hz}$].

6 is then converted by WOLF-KISHNER reduction to two products which were separated by thin layer chromatography : 7 [N.M.R. (CDCl₃) : 6.6 ppm (1H) ; 4.1 ppm multiplet (2H) ; 3.4 ppm singlet (3H)] and 8 [F = 92-94° . I.R. (CHCl₃) : 3580, 3460 (OH) ; 1110 cm⁻¹ (C-O-C). N.M.R. (CDCl₃) : two singlets (5H in all) : 3.40 ppm and 3.41 ppm].

In a similar way treatment of 3 by sodium methoxide leads to 9 [F = 122-123° . I.R. (CHCl₃) : 3550 (OH) ; 1715 (C = O) ; 1115 cm⁻¹ (C-O-C). U.V. : $\lambda_{\max}^{Ether} = 295 \text{ nm}$; $\epsilon_{\max} = 33$. N.M.R. (CDCl₃) : singlet (3H) : 3.42 ppm ; AB spectrum (2H) : $\delta_A = 3.19$ ppm ; $\delta_B = 3.71$ ppm ; $J_{AB} = 9.5 \text{ Hz}$], which is reduced to a mixture of 7 and 10 [F = 101-102° . I.R. (CHCl₃) : 3570, 3460 (OH) ; 1110 cm⁻¹ (COC). N.M.R. (CDCl₃) : singlet (3H) : 3.38 ppm ; singlet (2H) : 3.17 ppm].

8 and 10 were synthesized by an independent pathway. When treated with methoxymethylmagnesium chloride 5 α -cholestane-3-one is converted into 8 and 10. The stereochemistry on C_3 is then firmly established by dehydration of these two alcohols (9).

The minor product of the reaction, 4 is a keto-oxetane [F = 142-146° . I.R. (CHCl₃) : 1710 (C = O) ; 985, 975 cm⁻¹ . U.V. : $\lambda_{\max}^{C_2H_5OH} = 307 \text{ nm}$, $\epsilon_{\max} = 28$. N.M.R. (CDCl₃) : AB spectrum (2H oxetane ring) ; $\delta_A = 4.47$ ppm, $\delta_B = 4.79$ ppm, $J_{AB} = 6.25$ ppm ; broad singlet (1H : O = C-CH-O) : 4.22 ppm. Mass : Parent : 414 (30 %), 384 (100 %)].

We assume that the most probable stereochemistry of this compound is 4 α : 5 α . This is supported by the mechanism of its formation (11). It is known that α -keto-oxetanes can be cleaved by action of light (12). When irradiated with an HOQ Philips lamp in a pyrex vessel ($\lambda > 300 \text{ nm}$), 4 is converted into cholest-4-ene-3-one as main product (13).

This noteworthy reaction of 1 which leads to a new class of compounds, the α -methylene oxetanols, and to a keto-oxetane, probably goes by a Norrish type II mechanism. One hydrogen atom of the methoxy group is abstracted by the excited triplet carbonyl (14) so as to form the biradical 1'. Cyclization at C_3 leads to 2 et 3 ; cyclization at C_5 leads to the oxetane 4.

These results are to be compared with work which has recently been described by AGOSTA and al. (16) ; they have shown that hydrogen atoms located γ to the carbonyl groups of enones can be abstracted with high efficiency, the resulting biradicals leading then to cyclization products.

Further studies are in course, in order to establish the generality and the mechanism of this reaction.

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