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PHOTOCHEMICAL REARRANGEMENTS OF 2-CYCLOHEXENONES[1]

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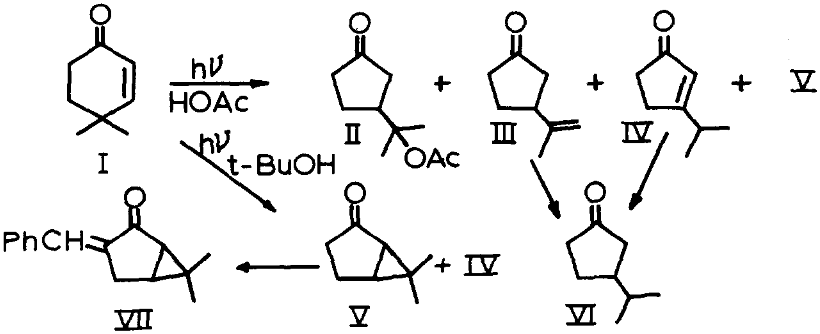
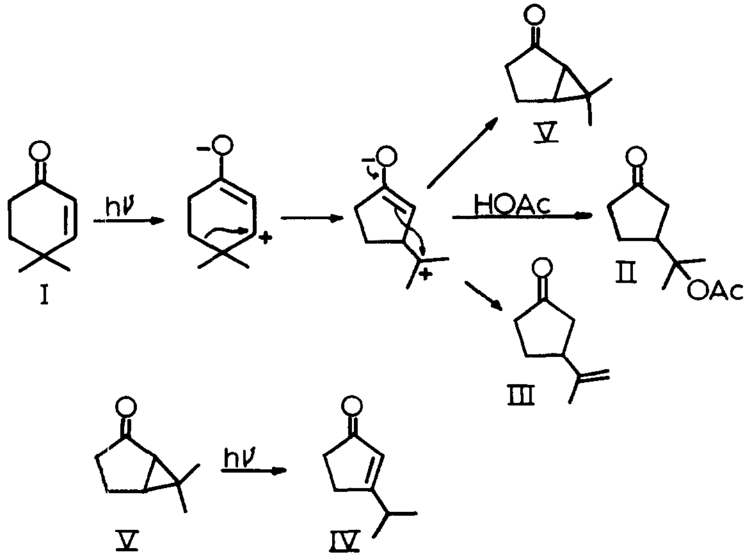
The dramatic photochemical rearrangements of santonin and other 2,5-cyclohexadienones[3] contrast sharply with the reported photodimerizations of 2-cyclohexenones. It has been generally assumed that the complex photochemical rearrangements of the 2,5-cyclohexadienones are not possible with simple 2-cyclohexenones. Kwie, Shoulders and Gardner[4] have recently shown that 4-cholesten-3-one undergoes a photoisomerization of the santonin to lumi-



santonin type. We wish to present evidence that a variety of photochemical rearrangements are possible with appropriately substituted 2-cyclohexenones. Irradiation[5] of 4,4-dimethyl-2-cyclohexenone (I) in acetic acid for 25 hours gives a mixture of products which contains an acetate (II, 30-40%), two isomeric olefins (III, 20-25%; IV, 5-10%) and a saturated ketone (V, 5%).[6] The products were separated by preparative scale vapor phase chromatography. The acetate (II) shows a single, intense carbonyl absorption at 5.75 μ (cyclopentanone and acetate carbonyl groups). The NMR spectrum of II shows a singlet six proton resonance at 8.52 τ (two identical methyl groups) and a three proton singlet at 8.07 τ (acetate methyl group) and no absorption below 7.0 τ. The acetate exchanges four protons in D_2O-Na_2CO_3, and the acetoxyl group is not lost in the base treatment. The infrared spectrum of III shows cyclopentanone carbonyl absorption at 5.73 μ and terminal methylene ($-\overset{|}{C}=CH_2$) absorption at 3.23, 6.07 and 11.19 μ. The NMR spectrum of III shows a slightly split three proton resonance at 8.07 τ, (allylic methyl protons), a single methine at 7.35 τ, two olefinic protons as a slightly split signal at 5.24 τ and methylene absorption as a complex multiplet at 7.85 τ. Catalytic reduction of III gives 3-isopropylcyclopentanone. The olefin IV shows infrared absorption at 5.83 μ (conjugated cyclopentenone carbonyl group) and 6.18 μ (conjugated double bond) and an ultraviolet maximum at 227 mμ (4.20). The NMR spectrum of IV shows a single olefinic proton as a triplet at 4.16 τ, a complex multiplet (7.18-7.94 τ) due to the methylene and methine protons and a doublet (J=6.7 c.p.s.) at 8.80 τ due to the isopropyl methyl groups. It has been established that the high field doublet is due to an isopropyl group rather than two non-equivalent methyl groups by a double resonance experiment. Saturation of the isopropyl methine resonance (70 c.p.s. down field from the 8.80 τ doublet) collapsed the high field doublet to a singlet. Catalytic reduction of IV gives 3-isopropylcyclopentanone.

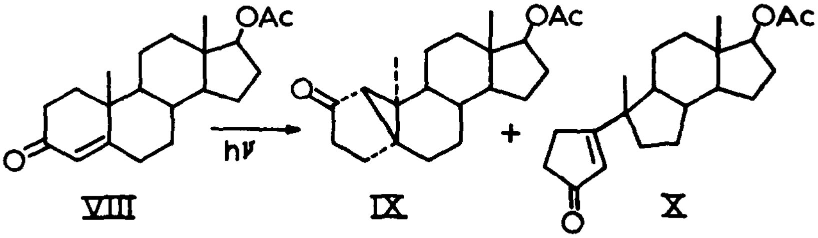
Irradiation of 4,4-dimethyl-2-cyclohexenone (I) using t-butanol as a solvent following the suggestion of Kwie, Shoulders and Gardner gives V (60%) and 3-isopropyl-2-cyclopentenone (IV, ca. 5%).[4] The bicyclic ketone (V) shows infrared absorption at 5.81 μ (carbonyl group) and 3.32 μ (cyclopropane C-H), ultraviolet absorption 207 mμ (5,430) and a maximum in the near infrared at 1.673 μ (first overtone of the cyclopropane C-H stretching vibration). The nuclear magnetic resonance spectrum of V shows a complex series of overlapping multiplets 7.46-8.58 τ (six protons) and two methyl groups as a single peak (six protons) at 8.89 τ. A slow scan of the methyl peak shows slight splitting consistent with two slightly nonequivalent methyl groups. The complete absence of absorption below 7.46 τ precludes the presence of olefinic protons. The bicyclic ketone (V) forms a monobenzal derivative (VII; 5.93, 6.18μ; 300.5 mμ (11,800)). The nuclear magnetic resonance spectrum of the monobenzal derivative (VII) shows two nonequivalent methyl groups at 8.98 and 8.85 τ, the cyclopropyl methine protons as a multiplet at 7.08 τ and the five aromatic protons and single olefinic proton as a complex multiplet at 2.65 τ .

Formation of II, III and V in the irradiation of I can easily be rationalized in terms of the polar state hypothesis. The photochemical rearrangements of I do not proceed smoothly in aprotic media thus suggesting strongly that proton donation by the solvent is important at some stage of the reaction. Irradiation of the bicyclic ketone

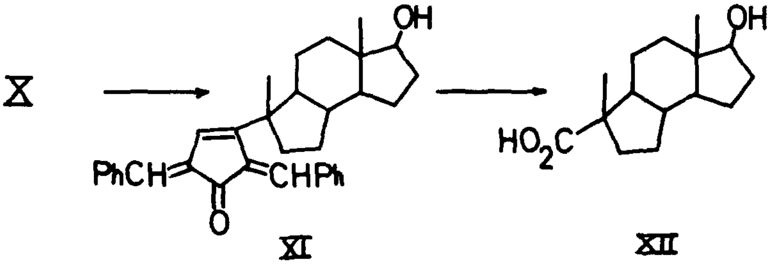


V in acetic acid gives IV but not the other photoproducts. This process is analogous to the vapor phase photoisomerization of cyclopropyl methyl ketone to 3-penten-2-one.[7] The 3-isopropylcyclopentenone disappears (presumably by dimerization) at a rate which approximates the rate of formation.

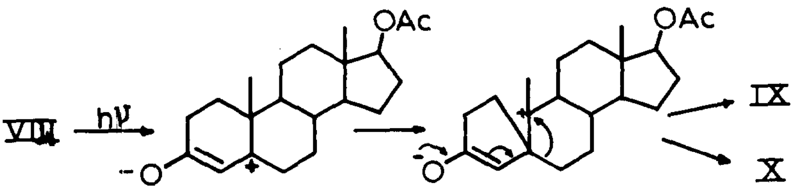
Irradiation of testosterone acetate (VIII) in _t_-butanol gives IX (m.p. 167-169°, 32%), X (m.p. 109-109.5°, 25%) and starting material (43%).



Structure IX is established by direct comparison (infrared, mixed m.p.) with an authentic sample.[8] Structure X rests on its spectral properties (5.77, 5.86, 5.96μ ; 232 mμ (18,000); 4.20μ , olefinic proton), reduction to the dihydroderivative (m.p. 84-86°, 5.75μ; dibenzalderivative, m.p. 190-192°; 231 (16,800) and 348 mμ (32,100) and conversion to the dibenzal derivative XI (m.p. 186-187.5°, 225 (15,000) and 317 mμ (31,300) which gives the acid XII[9] on ozonolysis followed by treatment with alkaline hydrogen peroxide.



Formation of IX and X in the irradiation of testosterone is most surprising in view of the recent observation that irradiation of 10α-testosterone simply gives the Δ^5-isomer[10] via a light induced enolization. The formation of IX is analogous to the formation of V. The rearrangement to X requires an additional 5,6-bond migration.



The conversion of testosterone to IX provides a practical, direct route to 10α-steroid derivatives.

Irradiation of 17α-methyltestosterone gives photoproducts analogous to IX and X.

Satisfactory elemental analyses have been obtained for all new compounds.

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5. The irradiation was carried out with a Pyrex jacketed, immersion type mercury arc lamp. The solution contained 5 g. of 4,4-dimethyl-2-cyclohexenone (I) per liter of acetic acid. I is stable in acetic acid in the dark.

6. The crude product was analyzed by vapor phase chromatography.

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