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THE PHOTOSENSITIZED REARRANGEMENT OF β,γ-UNSATURATED KETOSTEROIDS

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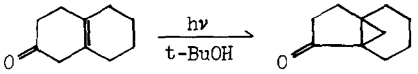
The photochemical transformations of cyclic-β,γ-unsaturated ketones have been described by several workers[1] involving cleavage of the carbon-carbon bond situated at allyl to the double bond and α to the carbonyl with subsequent decarbonylation or with subsequent double bond migration and recyclization to form a new β,γ-unsaturated ketone. On the other hand direct irradiation of β,γ-unsaturated ketone such as 3,4,5,6,7,8-hexahydronaphthalen-2(IH)-one (I)[2] in t-BuOH was reported to afford the corresponding conjugated cyclopropyl ketone(II).

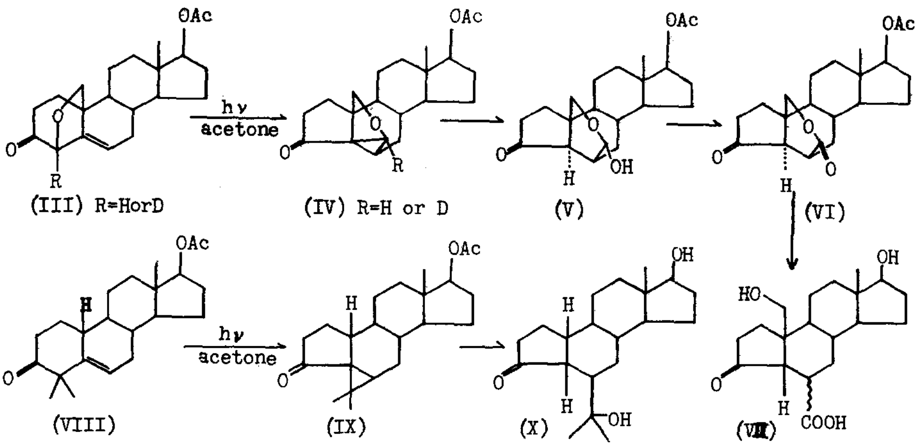


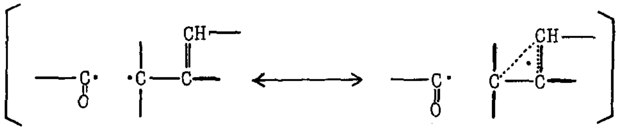
(I) (II)

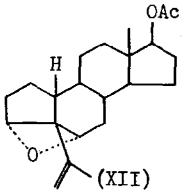
We want to report the photochemical isomerization of 17β-acetoxy-4β,19-oxidoandrost-5-en-3-one(III:R=H)[3] and 17β-acetoxy-4,4-dimethyl-19-norandrost-5-en-3-one(VIII)[4] into the corresponding conjugated cyclopropyl ketones (IV:R=H and IX), and the multiplicity of this isomerization is also described.

Irradiation[5] of 0.26 M. solution of the compound (III:R=H) λ_{max}^{EtOH} 313 mμ (ε 260) in acetone under argon gas with a high pressure mercury arc (Hanovia 200 w) for two hours yielded the photoproduct[6] (IV; R=H, mp 191-3°C) in 80% yield: UV; λ_{max}^{EtOH} 204 mμ (ε 4300), IR; ν_{max}^{KBr} 1728 (five membered ring ketone), 1740, 1248 (acetate) cm^{-1}, NMR[7] τ ; 9.18 (3H, s, 18-CH_3), 7.97 (3H, s, OAc), 5.76(2H, AB q, $\Delta\nu$=14.5 cps, J=9 cps, 19-methylene proton), 5.64 (1H, d, J=5.5 cps, alkoxy-substituted cyclopropane proton[8]), 5.36 (1H, t, J=9 cps, 17α-H). No vinyl proton was observed in the NMR spectrum. Mass spectrum of the compound (IV;R=H) showed the molecular ion peak at m/e = 344. These spectral data suggested the presence of an alkoxy - substituted cyclopropane ring conjugated with a five membered ring ketone.

Acid cleavage (70% $HClO_4$ in aq. dioxane at room temperature) of the cyclopropane ring




(XI)



(XII)

in the compound (IV; R=H) gave a hemiacetal (V; mp 168-70°C)* in good yield: IR; ν_{max}^{KBr} 3500 (OH), 1700 (broad, 3-CO and acetate) cm^{-1}, NMR (d-pyridine) τ; 4.64 (1H, s, -C<u>H</u>(OH)(OR)). Oxidation of the compound (V) with Jones reagent yielded the corresponding lactone (VI; mp 203-5°C)*: IR; ν_{max}^{KBr} 1755 (lactone and acetate) cm^{-1}, NMR τ; 5.78 (2H, AB q, $\Delta\nu$=19.5 cps, J=13.5 cps, 19-methylene proton). Lower field doublet of the AB quartet further coupled with 9α-H (J≃1.5 cps). The signal at τ 4.64 in the compound (V) was disappeared. The lactone ring of the compound (VI) was hydrolyzed with KOH-MeOH to afford a hydroxy carboxylic acid (VII; mp 241-3°C)*: IR; ν_{max}^{KBr} 3490 (OH), 1758 (five membered ring ketone), 1709 (COOH).

Irradiation of the compound (III; R=D) under the same photolytic conditions as for the compound (III; R=H) afforded the corresponding photoproduct (IV; R=D). NMR spectrum of the compound (IV; R=D) showed the same signals except the disappearance of the signal at τ 5.64 as the compound (IV ;R= H)

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* 5-H configurations of (V and VI) and (VII and X) were assigned as shown by their respective negative and positive Cotton Effect in their ORD curves.[13]

These spectral and chemical data confirmed the proposed structure of the photoproduct (IV; R=H).

This photochemical reaction proceeded more rapidly (ca 2 hr for the completion of the reaction) in acetone, 30% aq. acetone, acetophenone in t-BuOH, and acetophenone in benzene than in benzene itself (ca 13 hr for one-half completion of the reaction), but did not proceed in t-BuOH, MeOH, and dioxane. This reaction was effectively sensitized with acetone (Et=82 Kcal/mole),9) acetophenone (Et=74 Kcal/mole),10) propiophenone (Et=74 Kcal/mole)11) and xanthone (Et=74 Kcal/mole).10) Benzophenone (Et=69 Kcal/mole)10) was found to be less effective in this reaction. Complete quenching of the photoreaction was observed when piperylene (Et=ca 57 Kcal/mole)12) or naphthalene (Et=60 Kcal/mole)10) was added in the above reaction mixture.

This photochemical reaction must therefore proceed via a triplet intermediate and the lowest triplet of the compound (III; R=H) lies within the range 69-74 Kcal/mole.

Irradiation of the compound (VIII) λ_{max}^{EtOH} 296 mμ (ε=100) in acetone** under the same reaction conditions as for the compound (III; R=H) afforded an analogously rearranged photoproduct (IX; mp 125-7°C) in 18.5% yield: UV; λ_{max}^{EtOH} 216 Mμ (ε=5600), IR; ν_{max}^{KBr} 1740, 1235 (acetate), 1720 (3-CO), NMR τ: 9.23 (3H, s, 18-CH_3), 8.88 (3H, s, CH_3), 8.85 (3H, s, CH_3), 8.00 (3H, s, OAc), 5.43 (1H, 17α-H). Mass spectrum of the compound (IX) showed the molecular ion peak at m/e=344. This photoproduct (IX), after saponification with alkali, was converted by acid into the corresponding tertiary hydroxy ketone (X; mp 149-50°C)*: IR; ν_{max}^{KBr} 3450 (OH), 1730 (3-CO), NMR τ; 9.23 (3H, s, 18-CH_3), 8.72 (6H, broad s, isopropyl-CH_3). Mass spectrum of the compound (X) showed the molecular ion peak at m/e = 320. These data are in good agreement with the assigned structure (IX).

These photochemical isomerization reactions may proceed through an intermediate as shown in **XI** , and acetone was the best solvent.

** Irradiation of the compound (VIII) in benzene solution gave rise to the another isomerization product (XII). The detail will be published in near future.

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3) The compound (III; R=H or D) was synthesized by treatment of 17β-acetoxy-4-bromo-19-hydroxyandrost-4-en-3-one with KOH in MeOR and R_2O (R=H or D)

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5) Quarz immersion apparatus was used in all photolysis runs.

6) All compounds described here gave expected elemental analysis.

7) NMR spectrum was determined in $CDCl_3$ solution unless specified otherwise.

s=singlet d=doublet t=triplet q=quartet

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