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# THE PHOTOISOMERIZATION OF β,γ-UNSATURATED KETOSTEROIDS

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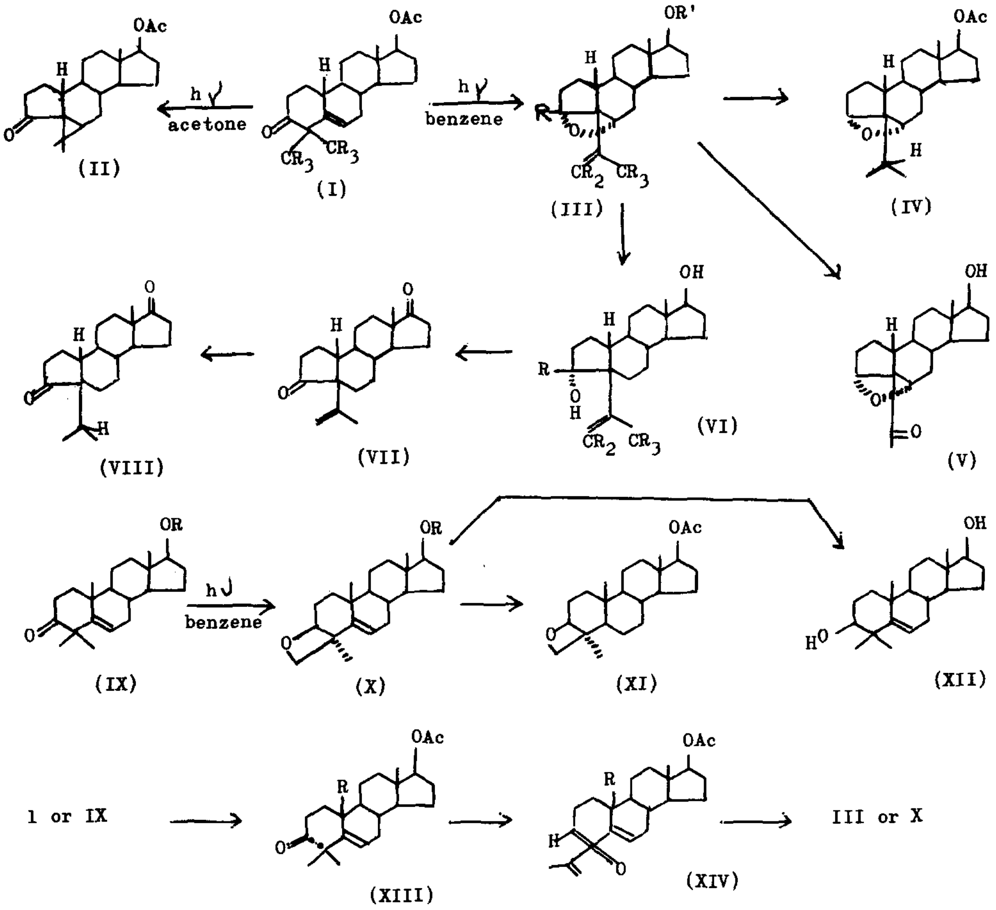
In our previous communication$^{1)}$ the photolysis of 4,4-dimethyl-19-norandrost-5-en-3-one (I; R=H) in acetone solution has been described affording a conjugated cyclopropyl ketone (II). We now wish to report the photochemistry of the same β,γ-unsaturated ketosteroid (I) and its 19-methyl analogue (IX; R=Ac) in benzene solution. In this case the photoreaction was found to proceed through a different mechanism from that observed in acetone, yielding the corresponding oxetane derivatives III (R=H, R'=Ac) and X (R=Ac) respectively.

Irradiation of the β,γ-unsaturated ketone (I; R=H: 1.5 g) in dry benzene (200 ml) under the atmosphere of argon using Hanovia high pressure mercury lamp (450 W) for ca. 14 hrs yielded an oxetane derivative (III; R=H, R'=Ac)$^{2)}$ in 30% yield: mp 94-5°C; IR:$^{3)}$ 1733 (OAc), 1650 (C=C), 965, 910 (oxetane), 892 (=$CH_2$) $cm^{-1}$; NMR $\tau$:$^{3)}$ 9.21 (3H, s, 18-$CH_3$), 8.31 (3H, d, J=1 cps, $=\overset{|}{C}-CH_3$), 7.79 (3H, s, Ac), 5.0-5.5 (5H, complex, 3β-H, 6β-H, $-\overset{|}{C}=CH_2$, 17α-H). The mass spectrum of the product ($M^+$ at m/e=344) indicates that the oxetane (III; R=H, R'=Ac) has the same molecular formula, $C_{22}H_{32}O_3$, as the starting material (I; R=H). Alkaline hydrolysis of the oxetane (III; R=H, R'=Ac) gave an oily 17β-ol (III; R=R'=H): IR ($CHCl_3$): 3610 (OH), 1648 (C=C) $cm^{-1}$; NMR $\tau$: 9.32 (3H, s, 18-$CH_3$), 8.41 (3H, br, $=\overset{|}{C}-CH_3$), 6.47 (1H, t, J=8.5 cps, 17α-H), 5.0-5.5 (4H, complex, 3β-H, 6β-H, $-\overset{|}{C}=CH_2$). These spectral data suggest that the carbonyl function in the starting ketosteroid disappeared and both an oxetane and an exomethylene moiety were newly generated in this photoisomerization.

On catalytic hydrogenation with Pd/c the oxetane (III; R=H, R'=Ac) yielded a saturated compound (IV): mp 56-58°C; IR: 1736 (Ac), 982, 961, 908 (oxetane) $cm^{-1}$; NMR $\tau$: 9.19 (3H, s, 18-$CH_3$), 9.26, 9.19, 9.14, 9.08 (6H, isopropylmethyl), 7.96 (3H, s, Ac), 5.17-5.50 (3H, br, 3β-H, 6β-H 17α-H); Mass spectrum: $M^+$ at m/e=346. Consecutive treatment of the photoproduct (III; R=H, R'=Ac) with osmium tetroxide, sodium periodate and alkali furnished a



methyl ketone (V): mp 108-110°C; IR: 3410 (OH), 1702 ($CH_3CO$), 990, 943, 910 (oxetane) $cm^{-1}$; NMR τ: 9.30 (3H, s, 18-$CH_3$), 7.86 (3H, s, $CH_3CO$), 6.36 (1H, 17α-H), 4.86 (2H, m, 3β-H, 6β-H). These chemical data clearly suggests the presence of an isopropenyl function in the oxetane (III; R=H, R'=Ac).

Lithium aluminum hydride reduction of the unsaturated oxetane (III; R=H, R'=Ac) in the presence of $AlCl_3$ afforded an unsaturated diol (VI: R=H); mp 159-160°C; IR; 3400, 3230 (OH), 1637 (C=C), 890 (=$CH_2$)$cm^{-1}$; NMR τ: 9.24 (3H, s, 18-$CH_3$), 8.22 (3H, br, =C-$CH_3$), 6.45 (1H, 17α-H), 5.99 (1H, br, 3β-H), 5.20 (2H, br, =$CH_2$). The diol (VI; R=H) was oxidized with Jones reagent into a 3,17-diketone (VII): mp 155-8°C; IR: 1740 (3- and 17-CO), 1632 (C=C) $cm^{-1}$. An infrared absorption band of VII at 1740 $cm^{-1}$ indicates that the two hydroxyl groups in VI had been attached to the five membered ring A and D. Catalytic hydrogenation of the diketone (VII) with Pd/C furnished a saturated diketone (VIII): mp 156-7°C; IR: 1745, 1735 (3- and 17-CO)cm$^{-1}$; NMR $\tau$: 9.10 (3H, s, 18-$CH_3$), 9.25, 9.18, 9.08, 9.00 (6H, isopropyl-methyl); Mass spectrum: $M^+$ at m/e=302.

Irradiation of the hexadeuterio compound (I; R=D)$^{4)}$ in the same photolytic conditions as for the compound (I; R=H) gave the corresponding oxetane (III; R=D, R'=Ac): mp 88-9°C; IR: 2160 ($CD_3$), 1736 (Ac), 1608 (C=C), 968, 929, 910 (oxetane)cm$^{-1}$; NMR $\tau$: 9.22 (3H, s, 18-$CH_3$), 7.98 (3H, s, Ac), 5.40 (1H, 17α-H), 5.16 (1H, q. J=8.3 and 1.5 cps, 6β-H); Mass spectrum: $M^+$ at m/e=350. The deuterated oxetane (III; R=D, R'=Ac) was analogously cleaved reductively with $LiAlH_4$ and $AlCl_3$ to yield the corresponding deuterated diol (VI; R=D): mp 119-20°C; IR: 3400, 3320 (OH), 2220 ($CD_3$), 1588 (C=C)cm$^{-1}$; NMR (d-pyridine) $\tau$: 9.03 (3H, s, 18-$CH_3$), 6.17 (1H, 17α-H); Mass spectrum: $M^+$ at m/e=310. Absence of other proton signals than a signal for one proton at $\tau$6.17 within the range $\tau$ 5-7 shows that a hydrogen (or deuterium) atom of the $C_4$ methyl group in the original compound (I; R=H or D) shifted to the $C_3$ position of the photoproduct (III). From above data coupled with photomechanistic considerations$^{5)}$ the structure of the product was deduced as III (R=H, R'=Ac).

An analogous photoreaction was conducted on 19-methyl β,γ-unsaturated ketone (IX: R=Ac) under the same photolytic conditions as for the 19-nor ketone (I: R=H), yielding an oxetane derivative (X: R=Ac): mp 173-4°C; IR: 1740 (Ac), 975, 965, 910 (oxetane)cm$^{-1}$; NMR $\tau$: 9.17 (3H, s, 18-$CH_3$), 8.74 (3H, s, 19-$CH_3$), 8.48 (3H, s, 4α-Me), 7.97 (3H, s, Ac), 5.51 (2H, AB q. $\Delta\nu$=19.7, J=5.6 cps, oxetane-$CH_2$-), 5.35-5.60 (2H, complex, 3α-H, 17α-H), 4.58 (1H, t, J=3.5 cps, =CH -); Mass spectrum: $M^+$ at m/e=358. Alkaline hydrolysis of X (R=Ac) gave a 17β-ol (X: R=H): mp 163-4°C; IR: 3410 (OH) 962, 934, 907 (oxetane)cm$^{-1}$; NMR $\tau$: 9.22 (3H, s, 18-$CH_3$), 8.77 (3H, s, 19-$CH_3$), 8.52 (3H, s, 4α-$CH_3$), 6.40 (1H, 17α-H), 5.56 (1H, t, J=3.5 cps, 3α-H), 5.55 (2H, AB q. $\Delta\nu$=11.8, J=5.8 cps, oxetane-$CH_2$-), 4.67 (1H, br, =CH-). NMR spectrum of the 17β-ol (X; R=H) showed one olefinic and three oxetane protons implying that the oxetane (X) should be a different type from the photoproduct III (R=H, R'=Ac).

On catalytic hydrogenation with $PtO_2$ in AcOH the oxetane (X; R=Ac) afforded a saturated compound (XI): mp 118-9°C; IR: 1740 (Ac) 969 (oxetane)cm$^{-1}$; NMR $\tau$: 9.22 (3H, s, 18-$CH_3$), 8.77 (3H, s, 19-$CH_3$), 8.72 (3H, s, 4α-$CH_3$), 8.02 (3H, s, Ac), 5.88 (2H, complex, 3α-H, 17α-H). Reductive cleavage of the oxetane ring in X (R=Ac) with $LiAlH_4$ and $AlCl_3$ yielded a diol (XII): mp 204-5°C; IR: 3410, 3260 (OH)cm$^{-1}$; NMR (d-pyridine) $\tau$: 9.10 (3H, s, 18-$CH_3$), 8.82 (3H, s, 19-$CH_3$), 8.63 (3H, s, 4-$CH_3$), 8.55 (3H, s, 4-$CH_3$), 6.48 (1H, br, 3α-H), 6.13 (1H, 17α-H), 4.32 (1H, m, =CH-); Mass spectrum $M^+$ at m/e=318. The diol thus obtained was identical with the authentic sample of 3β,17β-dihydroxy-4,4-dimethylandrost-5-ene.$^{6)}$ The structure of the oxetane (X; R=Ac) was assigned on the bases of these findings.

These photolytic oxetane formation might proceed through an intermedial diradical (XIII). The radical (XIII) is stabilized by an internal hydrogen abstraction* and forms a diene aldehyde (XIV) as in the usual ketone photolysis. Internal addition of the aldehyde function to the original ($\Delta^5$) or newly formed olefinic linkage ($-\overset{|}{C}=CH_2$) finally would afford the oxetane III (R=H, R'=Ac) or X (R=Ac), respectively. A severe steric interaction between 19-methyl and 5β-isopropenyl groups might determine the formation of the oxetane (X; R=Ac) in the case of 19-methyl ketone (IX; R=Ac).

## REFERENCES

1) K. Kojima, K. Sakai and K. Tanabe; Tetrahedron Letters 1969 1925.

2) General references for oxetane; A. Weisberger, "Heterocyclic compounds with three and four-membered rings", Part II, p 983.
Interscience Pub., Inc., New York: W.A. Noyes Jr., G.S. Hammond and J.N. Pitts, Jr., "Advances in Photochemistry", Vol. VI, p 301, J. Wiley & Sons Inc.

3) All compounds described here gave expected elemental analysis. The IR spectra were taken with nujol. The NMR spectra were measured in $CDCl_3$ solution unless specified otherwise. s=singlet d=doublet t=triplet q=quartet br=broad.

4) Treatment of 19-nortestosterone with $CD_3I$ in the presence of t-BuOK, followed by acetylation yielded the hexadeuteriocompound (I:R=D). cf. H.J. Ringold and G. Rosenkranz; J. Org. Chem. 22, 602 (1957).

5) The formation of a 3β,6β-oxetane from an intermediate (XIV) would be improbable by inspection of the molecular model.

6) Authentic sample was synthesized by reduction of the ketone (IX: R=H) with $LiAlH_4$. cf. R.B. Woodward, A.A. Patchett, D.H.R. Barton, D.A.J. Ives and R.B. Kelly; J. Chem. Soc. 1957, 1131.

* **1-8 hydrogen abstraction**