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A PHOTOCHEMICAL REARRANGEMENT OF β,γ-UNSATURATED CYCLIC KETONES

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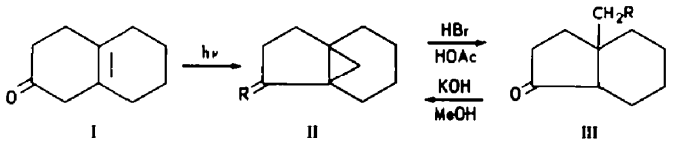
Abstract—Irradiation of the β,γ-unsaturated cyclic ketones I and IV results in an unusual rearrangement yielding the conjugated cyclopropyl ketones IIa and Va. The structures of the photoproducts were deduced from their spectroscopic properties and proved by converting the photoproducts to compounds of known structure. The photoproduct Va has been converted to a 10α methyl A-nor steroid. A possible mechanism for the reaction is discussed.

SEVERAL investigations of β,γ-unsaturated cyclic ketones have shown that the spectroscopic properties of these compounds are quite different from those of other unsaturated ketones.[1] The differences arise from interaction between the carbonyl group and the double bond, this coupling being strongly dependent on the orientation of the two groups. Since varying degrees of interaction between the carbonyl and the double bond are possible, one could expect to see, on irradiation, the characteristic photochemical reactions of the carbonyl, those of the double bond, and possibly a new or unusual reaction of the composite system.

Looking for such new or unusual reactions of β,γ-unsaturated cyclic ketones, we have examined the irradiation of 3,4,5,6,7,8-hexahydronaphthalene-2(1*H*)-one (I).[2] On the basis of literature reports[3–10] the reaction most likely to occur would involve cleavage of the carbon–carbon bond which is α to the carbonyl and allylic to the double bond. The resulting ionic or radical intermediate could then (a) decarbonylate, or (b) recombine at the other end of the allylic system to form a new β,γ-unsaturated cyclic ketone. We find that although the expected carbon-to-carbon bond was broken in forming the major reaction product (>50% yield) *neither* of the expected paths was followed.

RESULTS

Irradiation of I in t-butanol with a high pressure mercury arc (Hanovia), using a Pyrex filter, yielded the photoproduct IIa in greater than 50% yield. The structure of IIa has been established in the following manner. Analysis of the photoproduct showed it to have the same empirical formula, $C_{10}H_{14}O$, and molecular weight as the starting ketone, indicating that a rearrangement had taken place. The NMR spectrum of IIa showed the absence of olefinic protons and a general shift of the spectrum to higher field when compared with that of the starting ketone. The IR spectrum showed absorption at ν 3065 and 1715 cm^{-1} and the ultraviolet absorption



I II III
(a) R=O (a) R=Br
(b) R=H2 (b) R=H

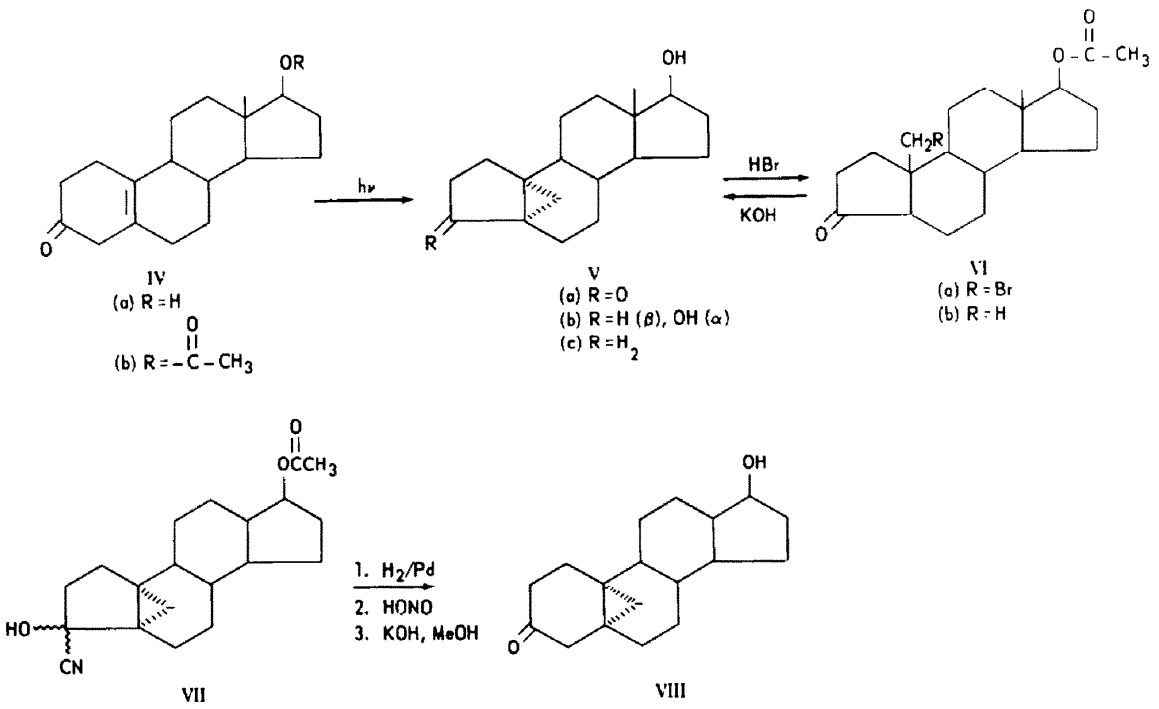
spectrum exhibited maxima at 277 mμ (ε 138) and 208 mμ (ε 5200). These measurements suggested the presence of a cyclo-propyl conjugated cyclopentanone". Treatment of IIa with hydrobromic acid in glacial acetic acid afforded the bromo compound IIIa. The NMR spectrum of IIIa indicated the presence of an AB system at δ 3·62 ($\Delta\nu$ 5·4 Hz, J = 10·3 Hz) characteristic of a —CH_2Br grouping on a quaternary carbon. On treatment with alkali, IIIa regenerated the photoproduct IIa demonstrating that the acid treatment did not result in a rearrangement and that IIIa was a γ-bromo-ketone. Hydrogenolysis of IIIa yielded IIIb, whose NMR spectrum now showed a methyl group singlet confirming the presence of a —CH_2Br on a quaternary carbon. Furthermore, the IR spectrum of IIIa and IIIb showed carbonyl absorption at 1742 cm^{-1} and 1740 cm^{-1} respectively, as would be expected from a cyclopentanone derivative. The proof for structure IIa was completed by Wolff–Kishner reduction of IIa to the known hydrocarbon, tricyclo[4.3.1.$0^{1,6}$]-decane, IIb.[12,13]

Since the photorearrangement of a β,γ-unsaturated ketone to a cyclopropyl conjugated ketone has only been reported once previously[10], the generality as well as the requirements of this reaction were investigated. The steroid 17β-hydroxyoestren-5(10)-en-3-one (IVa) was irradiated under the same conditions as I in t-butanol, yielding the photoproduct Va. Mass spectroscopic and analytical data established that the photoproduct was isomeric with the starting material and its structure was established by a series of reactions similar to those employed for IIa. The NMR spectrum of Va showed a general shift to higher field compared to that of the starting ketone IVa and no absorption in the region where olefinic protons absorb.

Treatment of Va with hydrobromic acid in glacial acetic acid yielded the γ-bromo-ketone VIa, whose NMR spectrum contained an AB quartet centered at δ 3·42 ($\Delta\nu$ 24·0 Hz, J_{AB} = 11·0 Hz). The bromo compound VIa could be recyclized to Va with alkali and on hydrogenolysis with $Pd/CaCO_3$ yielded a keto-acetate (VIb) whose NMR spectrum showed the presence of a new Me group (singlet) at C-10 (δ 0·83). The IR spectra of VIa and VIb showed absorption at 1742 cm^{-1} and 1735 cm^{-1} respectively, characteristic of cyclopentanone derivatives.

The above spectroscopic and analytical data show that the structure of the photoproduct is quite analogous to that obtained from I (i.e. IIa) and we can now focus our attention on determining the stereochemistry of the cyclopropyl group. Its stereochemistry was first deduced as α from physical measurements and then proven to be so by chemical transformation.

It has been shown that the sign of the ORD of a conjugated cyclopropyl ketone is governed by a modified octant rule in which the cyclopropane ring outweighs all the other substituents.[14] The ORD curve of Va shows a large negative Cotton effect (amplitude −462) from which one would conclude that the cyclopropane ring was α. Furthermore, if the cyclopropane ring were β then VIb obtained by hydrogenolysis

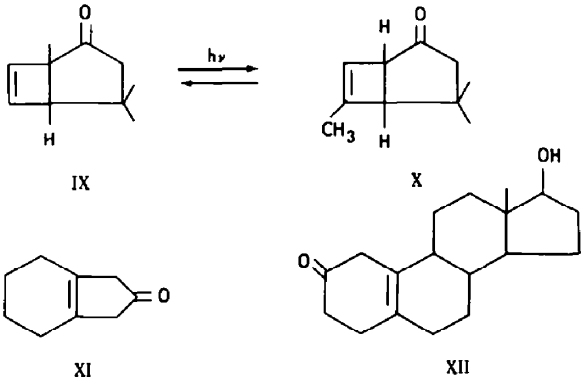


of the bromo ketone would be expected to be identical to 17β-acetoxy-A-nor-5β,10β-androstan-3-one previously reported by Rull and Ourisson.[15] The melting point of VIb as well as that of the 17β alcohol were different from those reported by Rull and Ourisson. In addition, the ORD curve of VIb was opposite in sign to that reported for the 5β,10β steroid by later investigators.[16]

In order to establish unequivocally the configuration of the cyclopropyl group, Va was transformed to a compound of known and established stereochemistry. This was accomplished by reducing the cyanohydrin VII of Va to the amino alcohol. Treatment of the amino alcohol with nitrous acid resulted in expansion of ring A into a 6-membered ring. The 3-keto steroid was separated by chromatography and found to be identical with 17β-hydroxy-5α,19-cyclo-10α-androstan-3-one (VIII) prepared by Ginsig and Cross[17] from 17β-hydroxy-5(10)-oestran-3α-ol, using a Simmons-Smith methylenation reaction. Therefore the photoproduct has the structure Va.

The large downfield shift of the cyclopropyl protons in IIa and Va prompted us to examine the position of these protons when the carbonyl is reduced to a hydrocarbon and to an alcohol. Wolff-Kishner reduction of the keto alcohol Va gave the alcohol Vc which showed cyclopropyl protons as an AB quartet with centers at δ 0·52 and δ 0·02 (J_{AB} = 4·5 Hz). Reduction with LAH of Va, however, yielded only Vb, one of the two possible diols, the cyclopropyl protons of which had centers at δ 0·90 and δ 0·10 (J_{AB} = 5·4 Hz). The chemical shifts of the cyclopropyl protons in Vc and Vb show that one of the cyclopropyl protons in Vb has shifted 23 Hz (δ 0·52 vs 0·90). This shift can be used in determining the configuration (α or β) of the hydroxyl group.

It has been established that the presence of an electronegative substituent such as a hydroxyl group results in a paramagnetic shift in the absorption of a neighboring proton.[18,19] The C_{19}-methylene proton of the cyclopropyl ring lies under the A ring of the molecule and, for the hydroxyl group to be close by, it must be α since if β it would be on the opposite side of the molecule, too far away to influence either of the cyclopropyl protons. Therefore the diol has the structure Vb. Also, catalytic and metal hydride reduction of conjugated cyclopropyl ketones have been shown previously to give (in greater than 90% yield) the isomer in which the hydroxyl and cyclopropane groups are *cis*.[20]



IX X

XI XII

Although two possible cyclopropyl compounds could have formed in the photorearrangement of IV, the reaction proceeded in a sterospecific manner to yield only one. In an attempt to learn more about the stereochemical requirements of the rearrangement, 17β-hydroxy-oestren-5(10)-en-2-one (XII) was prepared from 2-methoxyoestradiol[21] and its photochemistry was examined under the same conditions as IVa. The CD curve of XII showed a negative Cotton effect whereas the CD curve of IVa showed a positive Cotton effect (Fig. 1). It was hoped that the stereochemistry of the rearranged product could be related to the sign of the Cotton effect. Unexpectedly, the principal photoproduct obtained from XII had incorporated the elements of t-butanol rather than having undergone the expected isomerization. Similar photoproducts were observed as minor products in the irradiation of IVa; however, the structure of these products has not been elucidated.

In investigating the photochemistry of less substituted β,γ-unsaturated ketones as well as the effect of ring size, the irradiation of cyclohex-3-enone and 4,5,6,7-tetrahydro-2-indanone (XI) were studied. Neither of these compounds rearranged under the conditions employed.

DISCUSSION

Most of the photochemical rearrangements of β,γ-unsaturated ketones involve cleavage of the carbon-to-carbon bond α to the carbonyl group and allylic to the carbon-to-carbon double bond, followed by reaction at either end of the allylic system regenerating the starting material or producing the kind of isomerization noted by Büchi *et al.*[3] and Erman.[9] The rearrangement reported here is quite different: cleavage of the same carbon-to-carbon bond occurs but subsequent reaction takes

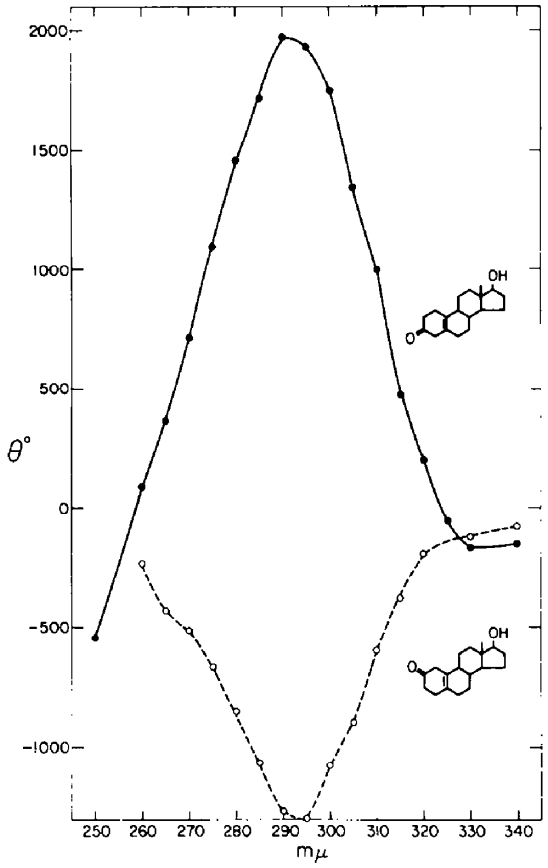


FIG. 1 CD curves of IVa ———— and XII - - - - -.

place at the center of the allylic system. Lutz *et al.*[10] have reported a similar reaction involving the formation of 1-benzoyl-2,3,3-triphenyl-cyclopropane in low yield (7%) in the photolysis of 1,3,4,4-tetraphenyl-3-buten-1-one. The other products of the reaction were biphenyl and a $C_{42}H_{34}$ dimeric hydrocarbon which could have formed from benzoyl and triphenylally radicals. The two kinds of products (cyclopropane derivative and dimeric products) may have come from a single intermediate or may have formed via alternative paths. In order to intercept possible radical intermediates formed in the photolysis of IVa the irradiation was carried out in the presence of an olefin (cyclohexene or 2-methyl-but-1-ene). The reaction was followed by VPC and TLC, but neither technique showed the presence of a new photoproduct. The usual rearrangement did occur. The intermediate does not appear to have the characteristics of a long lived radical.

The formation of only one of the two possible cyclopropane derivatives in the photolysis of IVa and in that of 1,3,4,4-tetraphenyl-3-buten-1-one reported by Lutz *et al.* suggest that the reaction may proceed in a concerted manner. The proposal that in the photoisomerization of a β,γ-unsaturated ketone "bond breaking occurred as the new bond was being formed," has been made by Büchi and Burgess[3] in their

study of the isomerization of 1,4,4-trimethyl-bicyclo-[3.2.0]-hept-6-en-2-one (IX) to 1,4,4-trimethylbicyclo-[3.2.0]-heptan-2-one (X). Since the rearrangement observed by Büchi and Burgess was reversible and as the conversion of IV to Va in these irradiations was not complete, it was of interest to determine if the isomerization is reversible. This was accomplished by irradiating a sample of Va. Under the conditions of the irradiation no IV could be detected, indicating the isomerization was not reversible.

Although it has not been possible to prove that this isomerization proceeds in a concerted manner, it can be shown that those conformations of IVa that lead to the product are not inconsistent with conformations of IVa deduced from ORD or NMR data. Moscowitz, Mislow *et al.*[1] have shown that it is possible to determine the stereochemistry of β,γ-unsaturated ketones from ORD or CD data by considering this system as a dissymmetric chromophore. If VIa is treated in this manner the observed positive Cotton effect requires the carbonyl group to be below the plane formed by carbons 4, 5, and 10 of the steroid. From the Frank–Condon principle, it would be reasonable to assume that the position of the carbonyl relative to the other carbon atoms in the cyclohexenone ring would not be different in the excited state, and rapid collapse to product would yield a β-cyclopropyl ring rather than α as observed.

There is however, some question as to the validity of considering these β,γ-unsaturated systems as dissymmetric chromophores: (a) Since the observed ε values are not significantly greater than those of cyclohexenones, the system does not exhibit enhancement of the $n \rightarrow \pi^*$ transition characteristic of such a coupled system nor does the CD curve of IVa display a strong Cotton effect ($A = 24{\cdot}4$) characteristic of a dissymmetric chromophore. The Cotton effect is considerably weaker than in 3-keto steroids and is probably most easily rationalized by assuming conformational equilibrium between species giving positive and negative Cotton effects (see below). (b) Levine *et al.*[22] have evidence that the ring A of 5(10)-unsaturated steroids prefers a half-chair conformation. This conformation places the carbonyl group above the plane formed by carbons 4, 5 and 10 and makes it easier to understand the fact that the cyclopropyl group in Va is α.

Another source of information on the preferred conformation of IVa could come from its NMR spectrum. Unfortunately, the spectrum of IVa shows a singlet at δ 2·73 with a half band width 5 of Hz attributable to the two C-4 protons and a singlet at δ 2·45 with a half band width of 3·5 Hz due to the C-1 and C-2 protons. At least two interpretations of the spectrum are possible: (a) A facile equilibrium can exist for two or more conformations of the molecule such that only an average absorption band for the two C-4 and the four C_1 and C_2 protons is seen. A Dreiding model of IV indicates an easy conversion betwen half-chair and half-boat conformations consistent with this interpretation. (b) The chemical shifts of the protons in question may accidentally be nearly identical, resulting in a broadened absorption band rather than in an interpretable splitting pattern. The CD and NMR data therefore do not permit a determination of a preferred conformation of IVa. It should be noted, however, that the CD curve of XII is opposite in sign to that of IVa and the former does not appear to react under these conditions. Normal 2- and 3-keto steroids have very similar CD curves and special techniques are required to distinguish between them. Although additional work is required to learn more about this photorearrangement, it appears at present that a special geometry for the transition state is required.

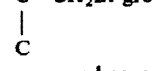
EXPERIMENTAL

The NMR spectra were obtained with a Varian A-60 spectrometer, using $CDCl_3$ solns with TMS as an internal standard. IR spectra were taken on a Beckman IR-7 spectrometer. M.ps were determined on a Kofler block and are uncorrected. UV absorption spectra were measured in EtOH solns with a Cary 14 spectrophotomer.

Silica gel H is fine silica gel used for TLC.

Photolysis of 2-*keto*-1,2,3,4,5,6,7,8-*octahydronaphthalene* (I). A soln of I[23] (450 mg) in t-BuOH (150 ml), stirred with a stream of N_2, was irradiated with a 450 W Hanovia lamp through a Pyrex filter. The reaction, which was complete in about 28 hr was monitored by VPC (disappearance of enone). Evaporation of the solvent *in vacuo* yielded an oil (400 mg). A total of 1·0 g of this oil from combined runs was chromatographed over silica gel (Merck H, 50 g). Elution with EtOAc:hexane 4:96 yielded I (120 mg) followed by *tricyclo*[4.3.1.0^{1,6}]-*decan*-7-*one* (II) as an oil (640 mg). (Found: C, 79·90; H, 9·50. $C_{10}H_{14}O$ requires: C, 79·96; H, 9·39%); ν_{max}^{film} 3065 (cyclopropyl) 1715 cm^{-1} (conj. cyclopropyl ketone) λ_{max} 208, 277 (ε 5200, 138).

3a-*Bromomethylene-indan*-1-*one* (IIIa). To tricyclo[4.3.1.0^{1,6}] decan-7-one (400 mg) in glacial AcOH was added 30% HBr in AcOH (1 ml) and the soln heated for 1 hr on a steam bath. The cooled soln was partitioned between ether and water and the ether layer, washed with $NaHCO_3$aq, water and dried. Evaporation of the solvent yielded 3a-*Bromomethylene-indan*-1-*one* (IIIa) as an oil (420 mg); ν_{max}^{film} 1742 cm^{-1} (cyclopentanone).

The NMR spectrum of IIIa showed an AB quartet centered at 3·62 ppm ($\Delta\nu$ 5·4 Hz, J = 10·3 Hz) characteristic of a  grouping.

The bromo compound gave a 2,4-*dinitrophenylhydrazone* as prisms, m.p. 167–170°. (Found: C, 46·93; H, 4·53; N, 13·60; Br, 19·13. $C_{16}H_{19}N_4O_4Br$ requires: C, 46·72; H, 4·66; N, 13·63; Br, 19·43%).

To IIIa (40 mg) in MeOH was added a 1% soln of methanolic KOH (2 ml) and the soln left overnight. The solvent was evaporated, the residue dissolved in ether, washed with water, dried and the solvent evaporated to yield an oil the IR spectrum of which was identical with that of IIa.

3a-*Methylindan*-1-*one* (IIIb). To IIIa (300 mg) in MeOH was added a large excess of 5% Pd/$CaCO_3$ and the mixture was hydrogenolyzed at atm press. After 4 hr the mixture was filtered through a small bed of celite and the filtrate evaporated. The residue was taken up in ether, washed with water, dried, and evaporated to yield 3a-*methylindan*-1-*one* (IIIb) as an oil (220 mg) m.p. 28–33°. (Found: C, 78·77; H, 10·84. $C_{10}H_{16}O$ requires: C, 78·90; H, 10·59%); ν_{max}^{film} 1737 cm^{-1} (cyclopentanone).

The NMR spectrum showed a peak at δ 1·18 ppm (3H) due to Me group.

The 2,4-*dinitrophenylhydrazone* of IIIb crystallized from MeOH as orange prisms, m.p. 140–141°. (Found: C, 57·57; H, 5·86; N, 16·82. $C_{16}H_{20}N_4O_4$ requires: C, 57·81; H, 6·01; N, 16·86%).

Tricyclo[4.3.1.0^{1,6}]*decane* (IIb). A mixture of IIa (200 mg), KOH (350 mg), diethylene glycol (3 ml) and 95% hydrazine (0·15 ml) was gently refluxed for 1 hr. Then the aqueous liquor was removed by a take-off adaptor until the temp of the liquid in the flask had reached 175–178°, when refluxing was continued for 3 hr. The reaction mixture and aqueous distillate were combined, and extracted with ether. Evaporation of the dried ether soln yielded an oil (140 mg). The oil was dissolved in low boiling petrol and passed over a small column of silica gel to yield upon evaporation of the solvent, *tricyclo*[4.3.1.0^{1,6}]*decane* IV.[11,12] (Found: C, 88·30; H, 11·60. $C_{10}H_{16}$ requires: C, 88·16; H, 11·84%); ν_{max}^{film} 3052 (cyclopropyl).

The NMR spectrum showed an AB quartet centered at δ 0·24 ppm, $\Delta\nu$ = 12·9 Hz and J = 4·5 Hz.

17β-*Hydroxy*-5(10)-*estrene*-3-*one* (IVa). Birch reduction of 3,17β-dihydroxy-estra-1,3,5(10)-triene (3-methyl ether) using the method of Wilds and Nelson[24] as modified by Dryden, Jr., *et al.*[25] yield IVa, m.p. 197·5–199·5° dec, vac (lit.,[24] m.p. 199·8–201° dec, vac); λ_{max}^{MeOH} 280–287 mμ ε 34.

Photolysis of 17β-*hydroxy*-5(10)-*estrene*-3-*one* (IVa). A soln of IVa (500 mg) in t-BuOH (150 ml), stirred with a stream of N_2, was irradiated with a 450 W Hanovia lamp through a Pyrex filter. The reaction which was complete in about 30 hr, was monitored by VPC (disappearance of enone). Evaporation of the solvent *in vacuo* yielded a gum (500 mg) which crystallized on standing. A total of 1·5 g of this crude material from combined runs was chromatographed over silica gel (Merck H, 55 g). Initial elution with EtOAc:hexane 1:4 (700 ml) afforded 380 mg of at least 3 minor products. Further elution with the same solvent yielded starting material (IVa; 150 mg) followed by 17β-*hydroxy*-5α,19-*cyclo*-*A*-*nor*-10β-androstan-3-one (Va; 830 mg) 55% yield which crystallized from EtOAc as prisms m.p. 162–163·5°. (Found: C, 78·70; H, 9·43.

$C_{18}H_{26}O_2$ requires: C, 78·79; H, 9·55%); $\nu_{max}^{CHCl_3}$ 3620, 3030 (cyclopropyl) and 1705 cm^{-1}; λ_{max} 210·5, 282 mμ (ε 4600, 120).

The NMR spectrum showed no absorption upfield from δ 0·65, absence of vinyl protons, C_{17}—H at δ3·65 (1H), C_{18}—H at δ0·77 (3H) and AB quartet centered at δ 1·05 ppm, $\Delta\nu$ = 17·0 Hz, J = 4·5 Hz.

The ORD curve of Va (MeOH) Φ_{310} −15,700, Φ_{217} +30,500.

IVa (130 mg) was irradiated in t-BuOD (44 ml) and worked up as described above. The mass spectrum of the photoproduct was identical with that of the compound prepared in t-BuOH.

Photolysis of IVa in the presence of a 5M excess of 2-methyl-but-1-ene or in cyclohexane (5M excess) gave the same distribution of photoproducts (VPC analysis) as in the absence of olefin.

Irradiation of IVa in the presence of benzophenone yields a photoproduct different from Va. The photoproduct Va is also photolabile under these conditions.

17β-*Acetoxy*-10α-*bromomethylene-A-nor*-5α-*androstan*-3-*one* (VIa). To a soln of Va (10 g) in glacial AcOH (20 ml) was added 30% HBr in AcOH (1 ml) and the soln heated on a steam bath for 30 min. The cooled soln was diluted with water and extracted with ether. The ethereal extracts were washed with water, sat $NaHCO_3$aq, water dried over $MgSO_4$ and evaporated to dryness. The residue was crystallized from hexane to yield 17β'-*acetoxy*-10α-*bromomethylene-A-nor*-5α-*androstan*-3-*one* VIa, as oblong prisms (1·29 g) m.p. 138–140°. (Found: C, 60·69; H, 7·18; Br, 20·02. $C_{20}H_{29}O_3Br$ requires: C, 60·45; H, 7·36; Br, 20·11%); $\nu_{max}^{CHCl_3}$ 1742, 1732 (sh).

The NMR spectrum showed an AB quartet centered at δ 3·42 /$\Delta\nu_{AB}$ 24·0 Hz, J = 11·0 Hz) due to a bromomethylene group on a quaternary C atom along with two singlets at δ 2·04 (3H, acetate) and δ 0·83 (3H, C-18 Me), and an apparent triplet at δ 4·45 (1 H, C-17 H).

To VIa (100 mg) in MeOH was added a 5% methanolic KOH (4 ml) and the soln refluxed for 30 min. The cooled soln was poured into water and extracted with ether. The ether extracts were washed with water, dried and the solvent evaporated to yield Va (55 mg) m.p. 162–163·5, mixed m.p. 162–163·5.

17β-*Acetoxy-A-nor*-5α,10α-*androstan*-3-*one* (VIb). The compound VIa (300 mg) was dissolved in MeOH (15 ml), 5% Pd/$CaCO_3$ (300 mg) added, and the mixture was hydrogenated at atm press. After the uptake of H_2 ceased, the catalyst was removed by filtration through a small bed of celite. The filtrate was evaporated, the residue taken up in ether, washed with water, dried, and evaporated to yield a gum which crystallized on standing. The gum was chromatographed over silica gel (Merck 0·05–0·20 mm; 10 g) and elution with EtOAc:hexane 1:4 afforded unreacted VIa (20 mg), and 17β-*acetoxy-A-nor*-5α,10α-*androstan*-3-*one* VIb, as chunky prisms (180 mg) m.p. 114·5–115·5° from hexane. (Found: C, 75·66; H, 9·35. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%); $\nu_{max}^{CHCl_3}$ 1735, 1727 cm^{-1}.

The NMR spectrum showed the presence of a new Me group on C-10 at δ 0·99 along with the C-18 Me at δ 0·83, and acetyl at δ 2·06 and C_{17}—H apparent triplet δ 4·65. The ORD of VIb (MeOH) Φ_{304} −715, Φ_{264} +639.

Hydrolysis of the acetate VIb with 5% methanolic KOH furnished 17β-*hydroxy-A-nor*-5α,10α-*androstan*-3-*one* as rosettes from hexane, m.p. 127–128·5°. (Found: C, 78·01, H, 10·06. $C_{18}H_{28}O_2$ requires: C, 78·21; H, 10·21%); $\nu_{max}^{CHCl_3}$ 3620, 1734 cm^{-1} (cyclopentanone). The NMR showed C-18 Me at δ 0·77 and C-19 Me at δ 0·97.

17β-*Hydroxy*-5α,19-*cyclo-A-nor*-10α-*androstane* (Vc). A mixture of Va (200 mg), KOH (350 mg) diethylene glycol (5 ml) and 95% hydrazine hydrate (0·15 ml) was gently refluxed for 1 hr. The soln was then concentrated to an internal temp of 210° and heated under reflux for 4 hr. The reaction mixture was extracted with ether and the extracts washed with water, dried and evaporated to yield a pale brown gum. The gum was dissolved in benzene and filtered through alumina. Crystallization from hexane afforded 17β-*hydroxy*-5α,19-*cyclo-A-nor*-10α-*androstane* Vc (125 mg) as fine, silky needles m.p. 137–138°. (Found: C, 82·77; H, 11·00. $C_{18}H_{28}O$ requires: C, 83·02; H, 10·84%); ν_{max} 3620 cm^{-1}. The NMR spectrum showed an AB quartet centered at δ 0·27 (Δν 29·5 Hz, J = 4·5 Hz) due to the non-equivalent protons of the cyclopropyl methylene group. C_{18}—methyl group δ 0·76 and C_{17}—H apparent triplet at 3·60.

17β-*Acetoxy*-5α,19-*cyclo-A-nor*-10α-*androstan*-3-*one* (Vd). To Va (1 g) in pyridine (5 ml) was added Ac_2O (25 ml) and the solution left overnight. The soln was poured into cold dil HCl and extracted with ether. The ether extracts were washed with 1% HCl, water and sat $NaHCO_3$aq, dried and evaporated to give 17β-*acetoxy*-5α,19-*cyclo-A-nor*-10α-*androstan*-3-one Vd (1·05 g) oblong prisms m.p. 117–119 and 126–127 from hexane. (Found: C, 76·11; H, 9·14. $C_{20}H_{25}O_3$ requires: C, 75·91; H, 8·92%); ν_{max} 1735 and 1724 cm^{-1}.

Tiffenau–Demjanov ring enlargement of 17β-*acetoxy-A-nor*-5α,19-*cyclo*-10α-*androstan*-3-*one* (Vd). A soln of 17β-acetoxy-5α,19-cyclo-A-nor-10α-androstan-3-one (1·26 g) in EtOH (25 ml) was cooled to −5°. KCN (7·68 g) was added and then glacial AcOH (5·76 ml) was added dropwise during 45 min, the temp being

maintained at −5° during this addition and for 1 hr thereafter. After standing overnight, at room temp, the resulting fawn colored mixture was poured into water and extracted with EtOAc. The organic phase was separated, filtered, treated with charcoal, and the solvent was evaporated. The residue was dissolved in glacial AcOH (25 ml), PtO_2 (250 mg) added, and the nitrile was hydrogenated at atm press. The uptake of H_2 ceased at the theoretical point and the catalyst was filtered off. The filtrate was evaporated to dryness and the residue dissolved in glacial AcOH (1 ml). The soln was cooled in ice, and ice cold $NaNO_2$aq (600 mg) added. The mixture, which tended to foam, was thoroughly stirred and allowed to stand overnight. The ether extracts of the resulting mixture were washed with water, sat $NaHCO_3$aq and again with water, dried and evaporated to yield a crystalline residue (40 mg). The residue was recrystallized from EtOAc and acetone to yield fine needles m.p. 279–280. M > 600° (mass spec).

The filtrate was evaporated to dryness and the resulting gum chromatographed over silica gel (H, 60 g). Elution with EtOAc:hexane (1:9) afforded 17β-*acetoxy*-5α,19-*cyclo*-10α-*androstan*-3-*one* (VIIIa) (70 mg) and with EtOAc:hexane (1:3) yielded the starting A-nor-keto-acetate (560 mg), m.p. and mixed m.p. 117–119 and 126–127°.

The keto-acetate was recrystallized from hexane as needles, m.p. 111–112·5. A mol wt of 330 was confirmed by mass spectroscopy. ν_{max} 1715 cm^{-1}.

VIIIa in MeOH was added to 1% methanolic KOH (6 ml) and the soln refluxed for 30 min. The solvent was evaporated, water added and the residue extracted with ether. The ether extracts were washed with water, dried and the solvent evaporated to yield 17β-*Hydroxy*-5α,19-*cyclo*-10α-*androstane*-3-*one* mixed m.p. 127–134°. The IR spectrum was identical with that of an authentic specimen. The NMR spectrum showed peaks at 15·5, 21·5 (geminal cyclopropyl protons), 46·5 (18H, singlet), 218 Hz (17αH) in agreement with those reported.[16] The compound also had the same R_f on TLC and retention time on VPC as the authentic sample.

3α,17β-*Dihydroxy*-5α,19-*cyclo*-*A*-*nor*-10α-*androstane* (Vb). LAH (30 mg) in ether (20 ml) was added dropwise with vigorous stirring to a soln of Va (200 mg) in ether (70 ml). After stirring for 2 hr the flask was cooled in ice and the excess hydride decomposed with cold, dil H_2SO_4. The ether layer was separated, washed with water, sat $NaHCO_3$aq, water and dried. After evaporation of the solvent, the residue was recrystallized from ether to yield Vb as needles m.p. 173–177° from ether. (Found: C, 78–48; H, 10·20. $C_{18}H_{28}O_2$ requires: C, 78·21; H, 10·21%).

TLC on silica gel indicated traces of a second compound, probably the C-3 epimer. The NMR spectrum of Vb showed an AB quartet centered at δ 0·50 (Δ 47 Hz, J = 5·4 Hz).

17β-*Hydroxy*-5(10)*estrene*-2-*one* (XII). Birch reduction of 2,17β-dihydroxy-estra-1,3,5(10)-triene-2-methyl ether[25] and hydrolysis of the crude dihydroether with oxalic acid in aqueous MeOH[24] yielded a crude solid. Purification of the solid by chromatography over silica gel H with EtOAc–hexane (1:1) yielded 17β*Hydroxy*-*oestr*-5(10)-*en*-2-*one* which crystallized as prisms, m.p. 150° from EtOAc. (Found: C, 79·09; H, 9·33. $C_{18}H_{26}O_2$ requires: C, 78·79; H, 9·55%); $\nu_{max}^{CHCl_3}$ 1710 cm^{-1}.

Photolysis of 17β-*hydroxy*-5(10)-*estrene*-2-*one* (XII). A soln of XII (90 mg) in t-BuOH was photolyzed for 70 hr as described above, however, 50% of the starting steroid still remained. Further irradiation through a quartz filter for 8 hr reduced unreacted starting material to ca. 10%. The solvent was evaporated and the residue partially dissolved in EtOAc:hexane 1:4. This soluble material was chromatographed over silica gel (H, 4·5 g) to yield a compound M 348.

Photolysis of *cyclohex*-3-*enone*. Cyclohex-3-enone (500 mg) was dissolved in t-BuOH (170 ml) and irradiated with a 450 W Hanovia lamp as described previously. The soln was analyzed by VPC after 3·5 and 7·0 hr irradiation. The starting ketone was disappearing but no volatile products were found.

4,5,6,7-*Tetrahydro*-2-*indanone*. A soln of 4,5,6,7-tetrahydro-2-indanol (2·75 g), prepared according to the method of Starr and Eastman[27] in pyridine was allowed to stand overnight with excess CrO_3 in pyridine (2 g CrO_3 in 20 ml pyridine). The reaction product was chromatographed over silica gel yielding an oil. The mol wt determined by mass spectroscopy was 136. The NMR spectrum of the oil in $CDCl_3$ showed no absorption above δ 3·0. ν_{max}^{film} 1749 cm^{-1}.

A 2,4-dinitrophenylhydrazone was prepared according to the procedure of Wilds and Nelson[24] and recrystallized from MeOH–EtOAc, m.p. 165–166°. (Found: C, 57·37; H, 4·91. $C_{15}H_{16}N_4O_4$ requires: C, 56·96; H, 5·10%).

Photolysis of 4,5,6,7-*tetrahydro*-2-*indanone*. 4,5,6,7-tetrahydro-indan-2-one (30 mg) in t-BuOH (1 ml) was degassed and irradiated in an NMR tube next to a 450 W Hanovia lamp with a Pyrex filter. The sol was analyzed by VPC after 7·5 and 15 hr irradiation. The starting ketone was slowly decomposed and only traces of volatile products were formed.

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