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FUNCTIONALIZATION OF 18-METHYL GROUP OF C-NOR-D-HOMOSTEROID BY THE BARTON REACTION[1]

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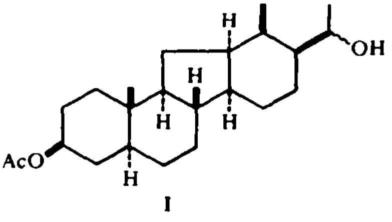
Abstract—The results of photolysis of3-O,11-O-diacetyletiojerv-5-ene-3β,11β,20α-triol nitrite (IVb) and the corresponding isomeric 20β-ol nitrite (Vb) are described. It has been found that the products from two isomeric 20-alcohol nitrites are not parallel and the nitrite of the 20α-alcohol affords the products. VII and VIII, arising from hydrogen abstraction from the 18-Me group whereas the nitrite of the corresponding 20β-alcohol gives IX, originating from β-scission, and X arising from hydrogen abstraction from the 15-position of the C-nor-D-homosteroid framework. The pronounced difference in these results from the photolysis of two isomeric nitrites is interpreted in terms of the steric factors involved in the transition states of the two reacting 20-alkoxyl radicals XV and XVI.

The structures of VII, VIII, IX and X were clarified mainly spectroscopically. The formation of alkyl nitrate IX in the photolysis of nitrites has never previously been observed. The probable sequences in the formation of the products, VII, IX and X, are discussed.

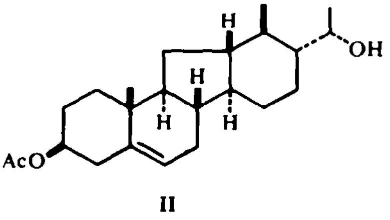
WE HAVE recently reported[2] the successful introduction of an oxygen function at the inactive 18-methyl group of a C-nor-D-homosteroid by the hypoiodite reaction.[3] In this particular case, the 20-hydroxyl on a β-ethyl side chain attached to C-17 of a *cis* C/D ring fused C-nor-D-homosteroid (I), was successfully used for the oxygenation of the 18-methyl group. Subsequently we have also observed that the analogous reaction with a *trans* C/D ring fused C-nor-D-homosteroid (II) with the 17α-substituent resulted largely in the loss of the 17α-substituent by β-scission.[4]

It was interesting to examine whether the functionalization of the inactive 18-Me groups in these systems by the Barton reaction is possible.[5] Although a number of successful functionalizations of inactive positions of steroid molecules by intramolecular radical processes have been reported, the Barton reaction on a system analogous to the present case has not been described.[6] An 18-functionalized C-nor-D-homosteroid, once synthesized, would provide useful intermediates for the preparations of the modified steroids, *e.g.*, the C-nor-D-homo-analogue of aldosterone and of certain steroidal alkaloids, such as veracevine.

In this paper, we describe the results of the photolysis of the nitrites (IVb and Vb) of 3-O,11-O-diacetyletiojerv-5-ene-3β,11β,20α-triol and the corresponding isomeric 20β-triol:



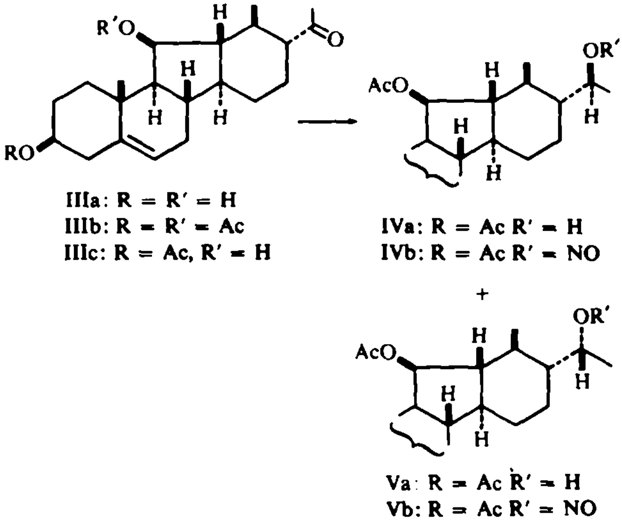
I

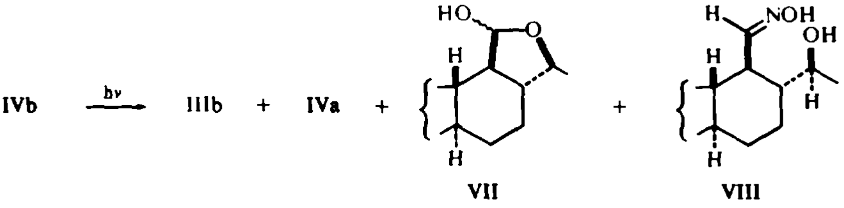


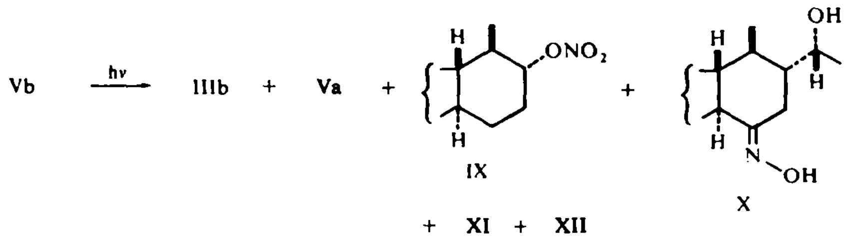
II

RESULTS

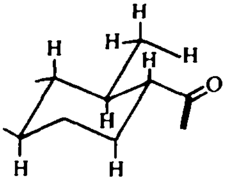
Preparation of etiojerv-5-ene-3β,11β-diol-20-one (IIIa) from jervine has already been reported.[7] Acetylation of both 3β- and 11β-hydroxyls of this compound with acetic anhydride and pyridine at 95–105° yielded the corresponding 3-O,11-O-diacetyl derivative (IIIb), m.p. 162–163°. Acetylation at room temperature afforded the corresponding 3-O-monoacetyl derivative (IIIc) m.p. 182–184°.







Reduction of IIIb with $NaBH_4$ in ethanol containing a small amount of ethylacetate readily afforded a mixture of two epimeric 20-ols. This pair of 20-epimers was separated by preparative TLC to the two pure 20-ols IVa, m.p. 205–207° (18 %) and Va, m.p. 177–179° (54 %). The mass spectra of IVa and Va showed nearly superimposable fragmentation patterns, with base peaks at m/e 358. The configurations at C-20 in IVa and Va were assigned on the basis of conformational considerations for the course of the reduction of the ketone (IIIb) with complex metal hydride as well as NMR spectra of the epimeric 20-ols. In normal steroids, reduction of 20-keto-pregnanes with complex metal hydrides leads invariably to the predominant formation of the 20β-isomer.[8, 9] This has been explained as the consequence of "steric approach" control in the hydride reduction.[9, 10] The product composition in the hydride reduction of 20-ketones of C-nor-D-homosteroids, particularly with bulky $NaBH_4$, would be similarly governed mainly by steric approach control. Examination of the model of IIIb reveals that the chair form having the equatorial 13β-Me and 17α-substituent should be the stable conformation of the D-ring and that the preferred conformation of the side chain† at C-17 of the ketone IIIb would be VI in which the C-20—C-21 bond would lie by almost eclipsing with C-16—C-17 bond. The attack by the hydride from the least hindered side (β-side, would lead to the 20β-epimer as the major product.



VI

Thus, the configuration at C-20 of IVa is probably α and that of Va β. The probable configurations at C-20 of IVa and Va may be obtained by comparison of the coupling constants between the 17β-hydrogen and the 20-hydrogen of IVa and Va in conjunction with comparison of chemical shifts of the 18-Me groups of IVa and Va.

In the 100 MHz NMR spectrum of IVa and Va, the protons attached to C-20 have appeared as the X part of A_3BX system where A_3 denotes protons at the 21-Me and B is the 17β-proton. Each peak in the quartet signal of the C-20 proton of IVa and Va revealed small splittings of 1 Hz and 2 Hz of J_{BX}, respectively (see Figs.).

Conroy's graph[12] affords two dihedral angles between the 17β-hydrogen and C-20-hydrogen for each J_{BX} of IVa and Va. (Approx. 70° or 100° for IVa and approx. 60° or 105° for Va.)

The NMR spectrum of IVa shows the 18-Me at τ 9·16 (W_H 6·0Hz.) and the 21-Me at τ 8·95 as a doublet with J_{A_3X} 6·6 Hz. On the other hand, the spectrum of Va shows the 18-Me at τ 910 (J = 5·5 Hz) and the 21-Me τ 8·83 (J = 6·6 Hz). The 18-Me and 21-Me resonance frequencies of Va appear downfield of those of IVa.‡

Taking these dihedral angles and chemical shifts of 18- and 21-Me of IVa and Va into consideration, a brief assessment of the stability of possible conformations by examination of the Dreiding model led to the conclusion that the most plausible pair

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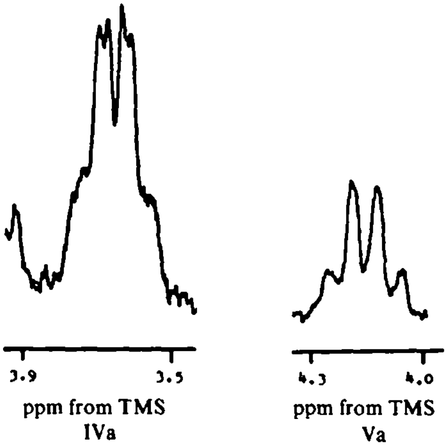
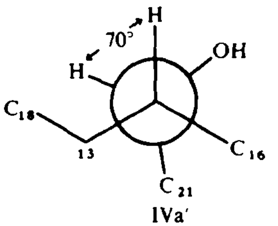
† The preferred conformation of the 17β-acetyl side chain in the steroid molecule was suggested from the optical rotatory dispersion studies and dipole moment measurements etc.[11] Although the optical rotatory dispersion of 20-ketone (IIIa) has shown the negative Cotton effect (a = − 12) deduction of the preferred conformation from this single value was not convincing.

‡ Chemical shifts of the 18-Me of these compounds would be greatly affected by deshielding due to the 20-hydroxyl groups.

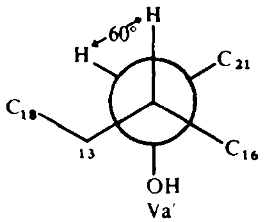
for the conformations of IVa and Va would be IVa′ and Va′.† IVa seems α at C-20 and Va would be β. This assignment is consistent with the mode of the reactions of the corresponding nitrite esters which will be discussed later.



Signals of C-20 protons of IVa and Va (100 MHz)



IVa′



Va′

The respective nitrite esters (IVb) and (Vb) were prepared from these two isomeric 20-ols by the usual method and these nitrites in benzene were immediately subjected to photolysis by a 150W high pressure Hg arc lamp. A nitrite ester (IVb) of the less polar 20α-isomer was irradiated for 12 hours and the crude product was submitted to column chromatography. Four compounds were obtained and two of these were identified as the 20α-alcohol (IVa) (22 %) and the 20-one (IIIb) (9 %). Two new compounds VII, m.p. 239–243° (5 %) and VIII, m.p. 225–227° (15 %) were obtained. The structure of VIII has been proved to be that of a 18-oximino-derivative arising from the Barton reaction. The molecular formula of VIII was determined as $C_{25}H_{37}O_6N$ from the elemental analysis and the mass spectrum (M^+ −60 peak at 387). The NMR spectrum of VIII has shown the 19-Me protons at τ 8·85 and the absence of the doublet expected for the 18-Me protons. Moreover, a proton doublet due to the 18-oximino-hydrogen appeared at τ 2·86 (J = 7·8 Hz). These data are in good agreement with the 18-oximino-structure for VIII.

The absence of a signal due to 18-Me protons in the NMR spectrum of the minor compound VII suggested that the compound arises by hydrogen abstraction from the 18-Me protons by a 20-alkoxyl radical. Analytical results on VII agreed with the

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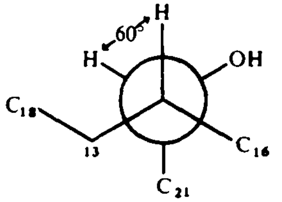
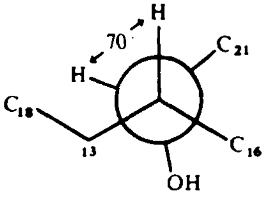
† In these conformations, IVa′ and Va′, the respective 21-Me group is in quite a different environment and this may explain the significant difference in its chemical shift (Δ = 0·12 PPM) between IVa and Va. Another plausible pair of conformers would be IVa″ and Va″, but this is precluded as the chemical shift of 18-Me of Va″ would have a more shielded value than that of IVa″.



Va''

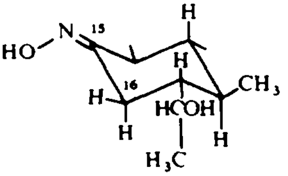


IVa''

molecular formula $C_{23}H_{34}O_4$ and it was found that treatment of VIII with acetone containing aqueous hydrochloric acid afforded needles which were identical with VII. Thus, VII should be formulated either as a 13β-formyl compound generated from the hydrolysis of the oximino-group of VIII, or a product transformed therefrom. Although, due to solubility problems, a clear NMR spectrum could not be obtained, VII lacked an aldehydic proton signal and the 13-formyl structure is thus excluded; the compound should be a hemi-acetal.

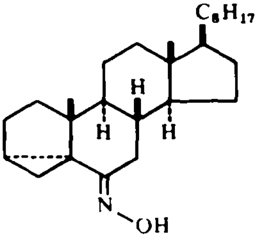
Photolysis of the nitrite ester Vb was then undertaken. The mixture of products obtained was subjected to column chromatography. Six compounds were isolated in this case. These were the 20-one (IIIb) (7 %), the 20α-alcohol (Va) (21 %), IX, m.p. 144–148° (2%), X, m.p. 174–176°, XI, m.p. 205–207° and XII, m.p. 212–222°. The molecular formula of IX was found to be $C_{23}H_{33}O_7N$ by elemental analysis and by the mass spectrum (M^+ – 60 at 375). In the NMR spectrum of this compound, the signals due to the 18- and 19-Me protons were apparently intact [18-Me at τ 9·08 (d, J = 6·0 Hz) and 19-Me at τ 8·83] but a doublet expected from the 21-Me had vanished. This spectrum indicated that IX was the compound arising from β-scission[13] of the 20-alkoxyl radical. Convincing evidence for the structure was obtained from the IR spectrum which showed strong bands at 1623 cm^{-1} and 1277 cm^{-1} attributable to NO_2 asymmetric and symmetric stretching of the ONO_2 group respectively.[14] Nitrate structure arising from β-scission of the 20-alkoxyl radical followed by the combination of the resultant 17-carbon radical with oxides of nitrogen, accommodates all these results. The configuration of ONO_2 should be α, since the NMR spectrum of IX showed the 17-hydrogen as a broad signal at τ 5·4 coinciding with 3α-hydrogen and the half-band width (15–20 Hz) requires β-assignment of the C-17 hydrogen.

The mass spectrum of X has revealed (M^+-60) peak at 387 which is in agreement with the molecular formula $C_{25}H_{37}O_6N$. This suggested X to be an oximino-compound arising from hydrogen abstraction by the 20-alkoxyl radical. The NMR spectrum demonstrated that the 20-Me, the 18-Me and the 19-Me were still intact as revealed by signals at τ 8·77 (d, J = 5·2 Hz), τ 8·97 (d, J = 6·6 Hz) and τ 8·82 respectively. Therefore, the 20-alkoxyl radical must have abstracted hydrogen from other than the 18-Me. Examination of a model of Vb shows that the 15α-hydrogen of Vb may also be abstracted by a 20-alkoxyl radical (*vide infra*) and if so, an 15-oximino-compound (X), in which the conformation of the D-ring is depicted as XIII, may be formed. The NMR spectrum has proved that this hypothetical formula for X is correct. Thus, apart from the signal due to olefinic C-6 hydrogen, 3α-hydrogen and 11α-hydrogen, a distinct single proton doublet appeared at τ 6·48 (J = 12 Hz) in the NMR spectrum of X. This doublet can only be explicable in terms of the structure X. Hydrogens attached to carbon α- to oximino-group are known to appear downfield[15] and in the present case, this doublet is assignable to either 14α-hydrogen or C-16 methylene hydrogen deshielded by the 15-oximino function. However, the observed coupling constant requires that this deshielded hydrogen should be 16-equatorial hydrogen.

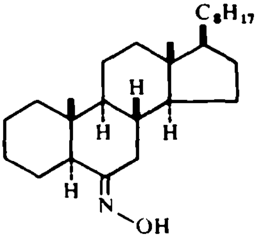


XIII

The configuration of the oximino-group of X was deduced from the results of a study of the NMR spectra of some model compounds.[16] Examination of the Dreiding model reveals that the 7-hydrogens of 3α,5-cyclo-5α-cholestan-6-one oxime (XIVa) and 5α-cholestan-6-one oxime (XIVb), in which the configuration of their oximino groups have been deduced as *anti*-C_5-C_6 bond configuration by Beckmann rearrangement,[16] may sterically be comparable with the 16-hydrogens of X. The NMR spectrum of XIVa, having no 5α-hydrogen, revealed a doublet at τ 6·67 with $J = 10$ Hz and that of XIVb a doublet at τ 6·68 with $J = 10$Hz both closely analogous to X and assignable to hydrogens deshielded by their 6-oximino-functions. The coupling constants require that these deshielded hydrogens should be the respective 7β-equatorial hydrogens. Thus the α-protons *syn* to oxime hydroxyl appear downfield of their *anti* counterparts. Therefore, the configuration of the oximino-group of X should be an *anti*-C_{14}-C_{15} bond configuration.



XIVa



XIVb

Structures of minor compounds XI† and XII have not been deduced due to the lack of material.

DISCUSSION

Involvement of a six-membered transition state in the Barton reaction has been well established.[6, 17, 18] The present investigation has shown that the products from two isomeric 20-alcohol nitrites (IVb and Vb) are not parallel and that the nitrite of the 20α-alcohol gave the products derived from hydrogen abstraction from the 18-Me protons, whereas the nitrite of the corresponding 20β-alcohol did not yield these as the major products. This pronounced difference in the results of the photolysis in two isomeric nitrites may be accounted for by considering the difference between

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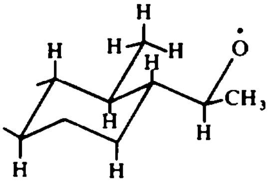
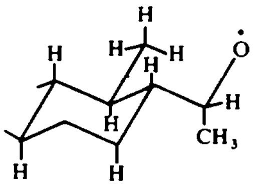
† Mass spectrum of XI showed *m/e* at 387 which corresponds to (M^+-60) peak of oxime X.

the respective conformations of the transition states of the two reacting 20-alkoxyl radicals.

Examination of models of the two nitrites reveals that the required conformations in the transition states in order to allow hydrogen abstraction from the 18-Me by alkoxyl radicals are XV and XVI for the 20α and 20β-isomers respectively.



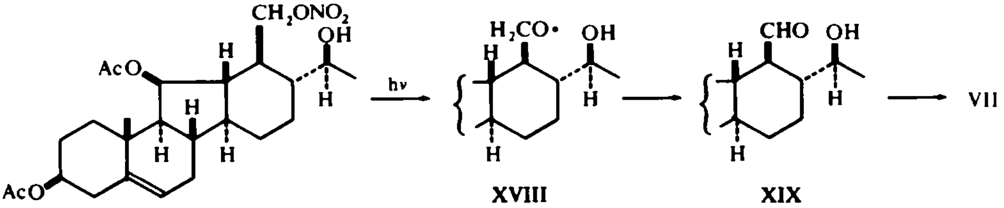
XV



XVI

Comparison between these two chair-like conformations shows that in the radical XV derived from the α-isomer the steric interference between 13α- and 16α-hydrogens and the 21-Me would be less than that in the radical XVI derived from the β-isomer. Therefore, the six-membered transition state for hydrogen abstraction from 18-Me may be more readily achieved in the α-isomer. This steric factor in the respective 6-membered transition states may explain the observed difference in the results from photolysis of the two nitrites.†

The formation of hemi-acetal VII is not readily understandable. The formation of VII via the oxime VIII under the conditions of the Barton reaction would be very unlikely. The following mechanistic processes perhaps account for the formation of VII. As has been described, the nitrate IX is formed in the present photolysis and thus it would not be unreasonable to assume the formation of the 18-nitrate (XVII) by the combination of oxides of nitrogen (*vide infra*) with the 18-carbon radical after abstraction of a hydrogen from the 18-Me group by a radical generated from Vb. Once the nitrate is formed, it could generate a 18-alkoxyl radical (XVIII) and this might afford a 13-formyl compound (XIX) either by disproportionation or α-hydrogen fission. Alternatively XIX may be produced by the elimination of nitrous acid from XVII.[20] The 13-formyl compound thus formed will readily produce hemi-acetal VII by cyclization with the 20-hydroxyl group.



XVII

The formation of the 15-oximino-derivative X in the photolysis of Vb is of interest. We have already reported[4] that $Pb(OAc)_4$ oxidation of 3-O-acetyletiojerv-5-en-3β-20β-ol (XX) afforded a five-membered ether (XXI) in which the D-ring should be in the boat conformation.

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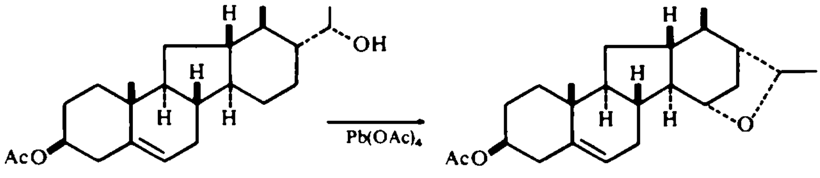
† The steric factors involved in intramolecular hydrogen abstraction have been observed in isomeric 20-ol nitrites in normal steroids. Barton *et al.*[19] have found that 20β-hydroxy-4-pregnen-3-one nitrite afforded a greater yield of the corresponding 18-oxime than that from 20α-ol nitrite.

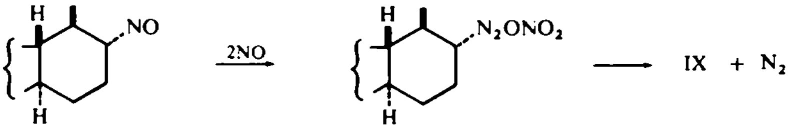
In this example, the stable chair form of the D-ring of XX, with the equatorial 13β-methyl and the equatorial C-17 substituent, inverts to a boat form in which the C-17 substituent is axial and 12β-hydrogen and 16β-hydrogen are in bow-stern relationship. Thus, the 20-alkoxyl radical is able to abstract a hydrogen from the C-15 to give the observed ether XXI. In the present investigation an exactly analogous explanation for the formation of the 15-oxime (X) would be possible. It should be noted that although examination of models indicates that a 20-alkoxyl radical seems to be able to abstract a hydrogen attached to either the C-14 or the C-15, formation of neither a 13-nitrosodimer nor a 6-membered ring ether were observed in either the Barton or the hypoiodite reaction.



XX XXI

Finally, formation of nitrate IX from Vb as the result of β-scission demands explanation. The formation of alkyl nitrates in the photolysis of nitrites has never been observed and the present case seems to be the first example.[20]

Several pathways leading to this nitrate are available. It is known that although NO is relatively stable[21] it disproportionates to afford several oxides of nitrogen. It also reacts instantly with oxygen to afford NO_2. It has been observed[22] that in the presence of a catalytic amount of NO_2, NO seems to afford several species such as N_2O_4,† N_2O, N_2O_3 and NO_2 by disproportionation. A rationale for the formation of the nitrate would be combination of the C-17 carbon radical with the NO_3 species formed by the disproportionation of NO.† Another possibility is the initial formation of a 17-nitroso-compound (XXII) followed by the formation of diazonitrate (XXIII)[24] and decomposition of this into the observed nitrate and N_2.



XXII XXIII

EXPERIMENTAL

All m.ps were taken by Yanagimoto micro-melting point apparatus and are uncorrected. IR spectra were taken by Jasco Model IR-E spectrophotometer in Nujol. The NMR spectra were recorded on a Hitachi H-60 high resolution NMR spectrometer in $CDCl_3$ soln. using TMS as an internal reference. The courses of reactions were followed by TLC (Wako gel B5).

Acetylation of Etiojerv-5-ene-3β,11β-diol-20-one. Ac_2O (4 ml) and IIIa (500 mg) in pyridine (5 ml) were warmed at 95–105° for 24 hr. After the usual working up, the residue (626 mg) was recrystallized from MeOH

† At room or liquid-helium temp, NO_2, which may be formed by the oxidation or disproportionation of NO, is known to exist as dimers in the equilibrium $2NO_2 \rightleftharpoons N_2O_4$. N_2O_4 is known to exist in three isomeric forms[14, 21a] one of which is the unsymmetrical nitro-nitrito structure $ONONO_2$, although its equilibrium concentration may be very small. $ONONO_2$ would provide several reacting species such as $\cdot NO$, NO^+, $\cdot NO_3$ and NO_3^-. Many reactions of the gas and liquid were explained by assuming these species.

to yield 565 mg of IIIb, m.p. 161–163°. The pure sample from MeOH melted at 162–163°. (Found: C, 72·09; H, 8·95. $C_{25}H_{36}O_5$ requires: C, 72·08, H, 8·71 %). IR (1717 cm^{-1}, OAc and 20-ketone) NMR (18-Me, τ 9·22, *J* = 6·0; 19-Me, τ 8·81; OAc τ 7·86, τ 7·96) MS. *m/e* 28, 43, 145, 253, 281, 356 (M$^+$-60).

Reduction of 3-O,11-O-*diacetyletiojerv-5-en*-3β,11β-*ol-20-one* (IIIb) *with* $NaBH_4$. EtOAc (0·5 ml), $NaBH_4$ (272 mg) and the IIIb (300 mg) in EtOH (25 ml) were stirred for 4 hr at room temp. After decomposition of excess $NaBH_4$ with AcOH, the soln was treated by the usual method. The residue (315 mg) revealed two main spots on TLC. It was then submitted to preparative TLC (solvent, $CHCl_3$–ether: 5:1) to yield two crude 20-ols. Recrystallization of the less-polar comp (71 mg) from acetone–ether afforded pure 20α-alcohol (IVa) (53 mg), m.p. 207-209°. (Found: C, 71·58; H, 9·05. $C_{25}H_{38}O_5$ requires: C, 71·74; H, 9·15 %). IR (1726, 1706 cm^{-1}, OAc) (3460 cm^{-1}, OH) NMR (18-Me, τ 9·16) (W½h, 6·0 Hz); 19-Me, τ 8·83; 21-Me τ 8·95, (*J* = 6·6 Hz)]. MS. 28, 43, 145, 160, 265, 283, 358 (M$^+$-60).

Recrystallization of the polar compound (218 mg) from acetone–ether afforded 162 mg of pure 20β-alcohol (Va), m.p. 177–179°. (Found: C, 71·74; H, 9·15. $C_{25}H_{38}O_5$ requires: C, 71·74; H, 9·15 %). IR (1728 and 1712 cm^{-1}, OAc) (3456 cm^{-1}, OH) NMR [18-Me, τ 9·10 (*J* = 5·5 Hz); 19-Me, τ 8·82; 21-Me, τ 8·83 (*J* = 6·6 Hz)]. MS. 18, 28, 43, 145, 160, 265, 283, 358 (M$^+$-60).

The preparation and photolysis of nitrite (IVb) *of* 3-O,11-O-*diacetyletiojerv-5-ene*-3β,11β,20α-*triol*. The less polar 20α-alcohol (543 mg) in pyridine (6 ml) was nitrosated by the usual procedure at −25 – −30°. The nitrite (IR 1729 cm^{-1}, OAc, 1625, 792 cm^{-1}, -ONO) (566 mg) obtained in dry benzene (18 ml) was irradiated under N_2. At the end of 12 hr, nearly all the nitrite was decomposed, as shown by TLC. After evaporation of the solvent under reduced pressure the residue was extracted with $CHCl_3$ (25 ml × 2), washed with water, dried and evaporated. The residue (603 mg) was submitted to column chromatography (Merck silica gel 0·08 mm, 12 g). Elution with light petroleum, light petroleum–benzene (10:1), (5:1), (3:1), benzene, benzene–ether (10:1), (5:1), (3:1) and finally ether afforded four fractions. Recrystallization of the least polar fraction (58 mg) from MeOH afforded IIIb (40 mg). Recrystallization of the third polar fraction (128 mg) from acetone–ether yielded IVa (104 mg). Recrystallization of the second polar comp (48 mg) from acetone–ether afforded the crystals of hemi-acetal VII (25 mg), m.p. 239–243°. (Found: C, 68·74; H, 8·32. $C_{25}H_{36}O_6$ requires: C, 69·42; H, 8·39%) IR (3340 cm^{-1}, OH) (1724 cm^{-1}, OAc). MS. *m/e* 28, 43, 145, 150, 174, 187, 354 (M$^+$-60-18). Recrystallization of the most polar fraction (155 mg) from acetone–ether afforded the 18-oximino-deriv VIII m.p. 225–227° (87 mg). (Found: C, 67·08; H, 8·39; N, 3·24. $C_{25}H_{37}O_6N$ requires: C, 67·09; H, 8·33; N, 3·13 %). IR (1720, 1745 cm^{-1}, OAc) (3200, 3400 and 3500 cm^{-1}, OH). NMR (21-Me, τ 8·90; 19-Me, τ 8·85; OAc, τ 8·00, τ 7·99; C-20-H, τ 6·22; C-3-H, τ 5·36; C-18-H, τ 2·86 (d, *J* = 7·6 Hz). MS. *m/e* 28, 32, 43, 58, 91, 145, 171, 174, 187, 353, 369, 387 (M$^+$-60).

The preparation and photolysis of 3-O,11-O-*diacetyletiojerv-5-ene*-3β,11β,20β-*triol nitrite* (Vb). 20β-Alcohol (648 mg) in pyridine (6·5 ml) was nitrosated in the usual way to afford Vb. (IR 1734 cm^{-1}, OAc, 1636, 786 cm^{-1}, ONO) (675 mg). This nitrite was dissolved in benzene (18 ml) and was irradiated by a high pressure Hg arc lamp for 30 hr under N_2. The soln was washed with water (20 ml × 3). After removal of the solvent under reduced pressure, the residue (663 mg) was submitted to column chromatography on silica gel (13 g) to give five fractions. The composition and order of solvents used for the elution were the same as previously. (Fractions I to V, in the order of increasing polarity). Recrystallization of fraction I (34 mg) from MeOH yielded crystals of IX (16 mg) m.p. 144–148°. (Found: C, 64·26; H, 7·67; N, 3·14. $C_{23}H_{33}O_7N$ requires: C, 63·43; H, 7·64; N, 3·22 %) IR (1742 cm^{-1}, OAc; 1623 cm^{-1}, 1277 cm^{-1}, ONO_2) NMR [18-Me, τ 9·08, d, *J* = 6·0 Hz; 19-Me, τ 8·83; OAc, τ 7·99, τ 8·00; 17-αH, τ 4·48 (W½h 15–20 Hz); C-6H, τ 4·70]. MS. *m/e* 29, 41, 43, 55, 69, 81, 91, 93, 95, 105, 120, 129, 131, 133, 145, 157, 169, 183, 197, 211, 225, 237, 253, 255, 269, 300, 312, 330, 375 (M$^+$-60). Recrystallization of fraction II (82 mg) afforded IIIb (47 mg). Recrystallization of the fraction III (45 mg) from MeOH yielded crystals of XI, m.p. 205–207°. (Found: C, 69·35; H, 8·37; N, 2·72%) IR (1735 cm^{-1}, weak absorption around 3400–3600 cm^{-1}). MS. *m/e* 27, 30, 43, 55, 67, 79, 91, 105, 120, 145, 239, 252, 268, 314, 327, 342, 368, 387. The mother liquor from this crystallization afforded the residue which was submitted to preparative TLC ($CHCl_3$–ether: 5:1) to yield the residue (26 mg) which was recrystallized from acetone–ether to yield crystals of X (16 mg), m.p. 174–176°. MS. *m/e* 29, 43, 55, 67, 79, 91, 93, 105, 131, 143, 145, 157, 178, 195, 252, 268, 327, 343, 387 (M$^+$-60). IR (1703; 1737 cm^{-1}, OAc, 3360 cm^{-1}, OH) NMR (C-6H 4·40; 11-αH, τ 4·69 (d, *J* = 3·4 Hz); 3-αH, τ 5·41; 16-βH, τ 6·48 (d, *J* = 12·0 Hz); 3- and 11-OAc τ 7·99; 19-Me, τ 8·82; 21-Me, τ 8·78 (d, *J* = 5·2 Hz); 18-Me, τ 8·98 (*J* = 6·6 c/s). Fraction IV (185 mg) was recrystallized from acetone–ether to yield pure 20β-alcohol (134 mg). Fraction V (37 mg) was recrystallized from acetone–ether to afford crystals (11 mg) of XII, m.p. 212–222°. IR (3360, 1731, 1724, 1244 cm^{-1}).

Hydrolysis of the oxime (VIII). VIII (20 mg) in aqueous acetone (acetone–water: 5:1 in volume) (1 ml) containing 2% HCl was set aside at room temp. After 2 hr, needles appeared in the soln and it was set aside overnight. The crystals (10 mg) were collected by filtration. This gave an IR spectrum identical to VII which was obtained by photolysis.

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