Triterpenoids. Part XXXIII. The Constitution of* cyclo*Artenol.*

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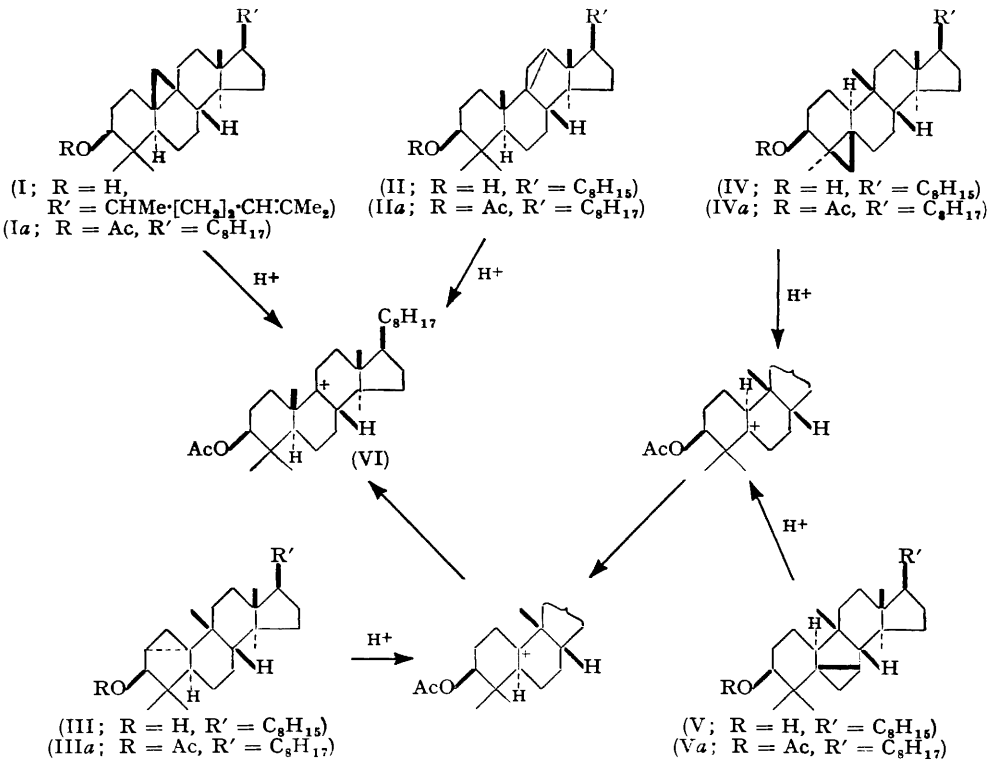
*cyclo*Artenol is shown to be 9 : 19-*cyclo*lanost-24-en-3β-ol (I).

In Part XXVIII of this Series (Bentley, Henry, Irvine, and Spring, *J.*, 1953, 3673) it was shown that *cyclo*artenol is a *cyclo*lanost-24-en-3β-ol. A limitation to the number of positions available for the *cyclo*propane ring in *cyclo*artenol was imposed by the observation that although treatment of *cyclo*artanyl acetate with hydrogen chloride gives a mixture of double-bond isomers consisting of a preponderating amount of lanost-9(11)-enyl acetate together with a smaller proportion of an equilibrium mixture of lanost-8- and lanost-7-enyl acetates, lanost-9(11)-enyl acetate is recovered unchanged after the same acid treatment and, further, that this acid treatment does not convert either the 7- or the 8-enyl acetate into lanost-9(11)-enyl acetate. Bentley *et al.* concluded that these observations prove that during the acid rearrangement of *cyclo*artanyl acetate, lanost-9(11)- and -8-enyl acetate are formed *simultaneously* by the loss of a proton from the carbonium ion (VI) and that the 8-enyl acetate subsequently equilibrates to a mixture with the 7-enyl acetate. These facts

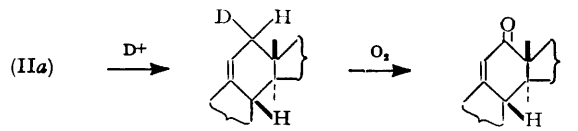
* Part XXXII, *J.*, 1955, 596.

eliminate structures from which the carbonium ion (VI) is developed by rearrangement of intermediate cations in which either $C_{(8)}$ or $C_{(11)}$ is the electron-deficient centre. Subsequently, a second limitation to the number of possible structures for *cyclo*artenol was imposed by Cole (*Chem. and Ind.*, 1953, 946; *J.*, 1954, 3810). In a valuable contribution to the chemistry of *cyclo*propane compounds, Cole showed that an infra-red absorption band at about 3042—3052 cm.$^{-1}$ is characteristic of an unsubstituted methylene group included in a *cyclo*propane ring and that such a band is present in the spectrum of *cyclo*artenol. If it is assumed that the *cyclo*propane ring in *cyclo*artenol extends from $C_{(9)}$, these considerations lead to the conclusion that the triterpenoid alcohol is either (I) or (II). When the work described in this paper was commenced, it was clear that this assumption was not justified, and that three additional formulæ (III), (IV), and (V) qualified for consideration as representing *cyclo*artenol in that each conformed to the specifications outlined above. The path to the ion (VI) by the proton-induced rearrangement of *cyclo*artanyl acetate [(I*a*), (II*a*), (III*a*), (IV*a*), or (V*a*)] is shown in each case. The experiments now described prove that (II), (III), and (IV) cannot represent *cyclo*artenol from which we conclude by negation that (I) or (V) represents the triterpenoid alcohol. However, in addition we also offer positive evidence which in our view establishes that (I) truly reflects the structure of *cyclo*artenol.



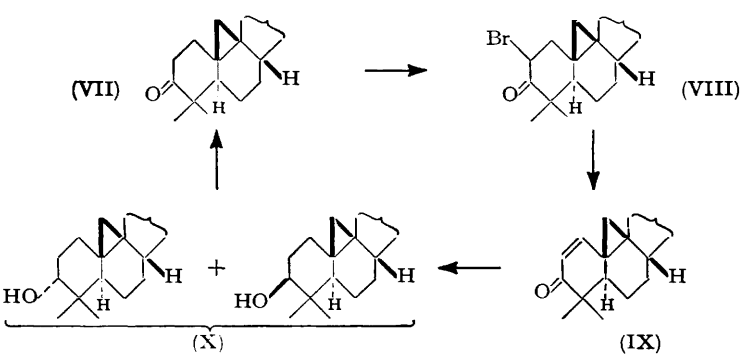
The formulæ (III) and (IV) for *cyclo*artenol were shown to be untenable on two counts. First, *cyclo*artanone and its semicarbazone show the ultra-violet absorption spectrum of a compound containing an isolated carbonyl and semicarbazone group respectively; no exaltation attributable to conjugation between a carbonyl group and a *cyclo*propane ring is observed. Secondly, *cyclo*artanone readily forms an enol acetate which shows the normal ultra-violet absorption spectrum of a simple enol acetate, *i.e.*, it does not show an exaltation attributable to conjugation between a *cyclo*propane ring and an ethylenic bond. Hydrolysis of the enol acetate regenerates *cyclo*artanone.

A method for testing the validity of structure (II) was suggested by the treatment of a similar structural problem by Barton and de Mayo (*J.*, 1953, 2178) in a study of the *cyclo*propane ring in phyllanthol. Reaction of *cyclo*artanyl acetate with deuterium chloride and a trace of deuterium oxide gave a mixture of deuterated double-bond isomers. Applying to this the partial oxidation technique successfully used for the preparation of lanost-9(11)-enyl acetate from *cyclo*artanyl acetate (Bentley *et al.*, *loc. cit.*) an *x*-deuterolanost-9(11)-enyl acetate was obtained; the m. p., rotation, and ultra-violet absorption spectrum of the deuterated compound were identical with those of lanost-9(11)-enyl acetate within the limits of experimental accuracy. Analysis of the deuterated compound showed the presence of approximately 0·8 gram-atom of deuterium per mole. If *cyclo*artenol is correctly represented by (II), the deuterated compound must be 12-deuterolanost-9(11)-enyl acetate and oxidation with chromic acid should eliminate the deuterium to yield 12-oxolanost-9(11)-enyl acetate, as follows:



Oxidation of deuterated lanost-9(11)-enyl acetate gave a compound indistinguishable in m. p., rotation, and absorption spectrum from 12-oxolanost-9(11)-enyl acetate (Bentley *et al.*, *loc. cit.*) which however still contains 0·8 gram-atom of deuterium per mole. Thus *cyclo*artenol cannot have the structure (II), and the only formulæ which adequately represent the triterpenoid alcohol are (I) and (V). At this stage, Barton, Warnhoff, and Page (*Chem. and Ind.*, 1954, 220; *J.*, 1954, 2715) reported that an infra-red examination of the mixture of isomeric deuterated lanostenes obtained by treatment of *cyclo*artane with deuterium chloride showed that the deuterated carbon atom is a deuterated methyl group other than one of the *gem*-methyl groups, and concluded that *cyclo*artenol is represented by (I).

Confirmation of this conclusion is offered in the following experiments: Treatment of *cyclo*artanone (VII) with *N*-bromosuccinimide in the presence of calcium carbonate gives 2-bromo*cyclo*artanone (VIII), which when refluxed with collidine gives *cyclo*art-1-en-3-one (IX). That these changes had not involved the *cyclo*propane ring was established by hydrogenation of the unsaturated ketone; this treatment saturated the double bond and also reduced the carbonyl group to a mixture of the 3α- and the 3β-alcohol (X). Oxidation of this mixture regenerated *cyclo*artanone (VII). The ultra-violet absorption spectrum of *cyclo*art-1-en-3-one (IX) shows a well-defined maximum



at 2690 Å which, we believe, proves that the αβ-unsaturated carbonyl group in *cyclo*art-1-en-3-one is directly conjugated with the *cyclo*propane ring. This observation eliminates the formula (V) and proves that *cyclo*art-1-en-3-one is (IX) and that *cyclo*artenol is correctly described as 9 : 19-*cyclo*lanost-24-en-3β-ol (I).

Experimental

Rotations were measured in chloroform solution at room temperature, with a 1-dm. tube, and ultra-violet absorption spectra were measured in ethanol solution with a Unicam SP. 500 spectrophotometer. Grade II alumina and a light petroleum fraction, b. p. 60—80°, were used for chromatography.

Enol Acetate of cyclo*Artanone*.—A solution of *cyclo*artanone (VII) (200 mg.) in *iso*propenyl acetate (25 ml.) containing one drop of concentrated sulphuric acid was heated on the steam-bath for 3 hr. The product, isolated by means of ether, was crystallised from chloroform–methanol to give the *enol acetate* of *cyclo*artanone as needles (160 mg.), m. p. 87°, $[\alpha]_D$ +66·5° (*c*, 1·1) (Found : C, 82·0; H, 11·5. $C_{32}H_{52}O_2$ requires C, 82·0; H, 11·2%). The enol acetate gives a strong yellow colour with tetranitromethane. Light absorption : max. at 2060 Å (ε 1600). Hydrolysis of the enol acetate with 3% methanolic potassium hydroxide refurnished *cyclo*artanone, which separates from methanol as blades, m. p. and mixed m. p. 110°, $[\alpha]_D$ +22° (*c*, 2·0).

19-*Deuterolanost*-9(11)-*enyl Acetate*.—A solution of *cyclo*artanyl acetate (I*a*) (1 g.) in dry chloroform (30 ml.) to which two drops of deuterium oxide (99·95%) were added was shaken with deuterium chloride (prepared from phosphorus trichloride and deuterium oxide and isolated over mercury) for 36 hr. The residue obtained on removing the solvent crystallised from chloroform–methanol as plates (0·93 g.), m. p. 140—150°. A solution of this mixture in acetic acid (75 ml.) was stirred on the steam-bath, and chromic acid (0·28 g.) in 90% acetic acid added during 5 min. Heating was continued for 10 min. and the mixture diluted with water. A solution of the neutral product (0·96 g.), isolated by means of ether, in light petroleum (100 ml.) was percolated through a column (2 × 12 cm.) of alumina (30 g.). The fraction (0·45 g.) eluted by light petroleum (600 ml.) was twice crystallised from chloroform–methanol to give 19-*deuterolanost*-9(11)-*enyl acetate* as plates, m. p. 173°, $[\alpha]_D$ +84° (*c*, 1·2) [Found : C, 81·5; H + D (as H_2O), 11·7. $C_{32}H_{53}DO_2$ requires C, 81·5; H + D, 11·8%]. It shows a strong yellow colour with tetranitromethane. Mass spectrographic analysis showed the deuterium content to be 0·815 gram-atom per mole.

19-*Deutero*-12-*oxolanost*-9(11)-*enyl Acetate*.—Chromic acid (200 mg.) in acetic acid (30 ml.) was added during 1 hr. to a refluxing solution of 19-deuterolanost-9(11)-enyl acetate (200 mg.) in acetic acid (30 ml.). Heating was continued for a further 2 hr. and the mixture left overnight at room temperature. A solution of the neutral product (212 mg.) in light petroleum (25 ml.) was percolated through a column (1 × 10 cm.) of alumina (6 g.), and the fraction (130 mg.) eluted by light petroleum–benzene (1 : 1; 150 ml.) crystallised from methanol to give 19-*deutero*-12-*oxolanost*-9(11)-*enyl acetate* as needles, m. p. 183°, $[\alpha]_D$ +90° (*c*, 0·7) [Found : C, 79·4; H + D (as H_2O), 10·9. $C_{32}H_{51}DO_3$ requires C, 79·1; H + D, 11·0%]. Light absorption : max. at 2410 Å (ε 9000). Mass spectrographic analysis showed the deuterium content to be 0·811 gram-atom per mole.

2-*Bromo*cyclo*artanone* (VIII).—A solution of *cyclo*artanone (625 mg.) in carbontetra chloride (20 ml.) was refluxed for 5 min. with *N*-bromosuccinimide (314 mg., 1·2 mols.) in the presence of suspended calcium carbonate; the mixture was illuminated with a 250-w lamp. The mixture was diluted with carbon tetrachloride and filtered and the product crystallised from methanol to give a pale yellow solid (490 mg.), m. p. 100—110°. Further crystallisations from methanol gave 2-*bromo*cyclo*artanone* which separates as prismatic needles, m. p. 116°, $[\alpha]_D$ +43° (*c*, 1·2) (Found : C, 71·3; H, 9·7. $C_{30}H_{49}OBr$ requires C, 71·3; H, 9·8%).

Dehydrobromination of 2-*Bromo*cyclo*artanone*.—2-Bromo*cyclo*artanone (200 mg.) in collidine (3 ml.) was heated under reflux for 2 hr. and left overnight at room temperature, then filtered. A solution of the product, isolated by means of ether, was chromatographed on alumina (1·25 × 7·5 cm.; 6 g.). The fractions eluted by light petroleum (40 ml.) and light petroleum–benzene (4 : 1; 100 ml.) were combined and crystallised from methanol to give cyclo*art*-1-*en*-3-*one* (IX) as prisms, m. p. 100°, $[\alpha]_D$ −40° (*c*, 1·3) (Found : C, 85·0; H, 11·7. $C_{30}H_{48}O$ requires C, 84·8; H, 11·4%). Light absorption : maxima at 2060 (ε 5000) and at 2690 Å (ε 8700).

Reduction of cyclo*Art*-1-*en*-3-*one*.—*cyclo*Art-1-en-3-one (200 mg.) in acetic acid (125 ml.) was shaken with hydrogen and platinum (from 200 mg. of platinum oxide) for 3 hr., by which time absorption of hydrogen had ceased. The solution was filtered and evaporated and the residual gum crystallised from methanol as blades m. p. 76—87°. A solution of the crude mixture of 3α- and 3β-alcohols (X) (205 mg.) in acetic acid (125 ml.) was treated with chromic acid in acetic acid (5·85 ml., 6·4 mg./ml., 1·2 mols.) and left overnight at room temperature. The neutral product gave *cyclo*artanone which separates from methanol as blades (142 mg.), m. p. and mixed m. p. 110°, $[\alpha]_D$ +23° (*c*, 0·8) (Found : C, 84·3; H, 12·1. Calc. for $C_{30}H_{50}O$: C, 84·4; H, 11·8%).

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