Triterpenoids. Part XXXIV. The Constitution of* cyclo*Laudenol.*

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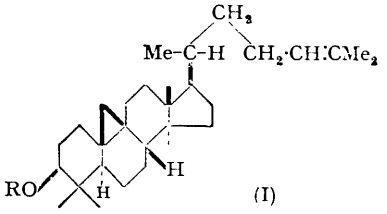
*cyclo*Laudenol, a pentacyclic alcohol obtained from opium, is a C_{31} triterpenoid. Its structure (XXIV) has been elucidated and its stereochemistry defined.

The isolation of a triterpenoid alcohol, *cyclo*laudenol, from opium was recently described by Bentley, Henry, Irvine, Mukerji, and Spring (*J.*, 1955, 596). *cyclo*Laudenol contains a *cyclo*propane ring and a vinylidene group; the reactions of the dihydro-derivative, *cyclo*laudanol, are very similar to those of *cyclo*artanol. Bentley *et al.* concluded that *cyclo*laudenol and *cyclo*artenol (I; R = H) (Bentley, Henry, Irvine, and Spring, *J.*, 1953, 3673; Barton, Page, and Warnhoff, *J.*, 1954, 2715; Irvine, Henry, and Spring, *J.*, 1955, 1316) have the same nuclear structure and differ only in the nature of the side chain. This

* Part XXXIII, *J.*, 1955, 1316

paper describes experiments which show that this view is correct and that the constitution of *cyclo*laudenol is represented by (XXIV).



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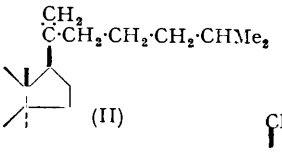

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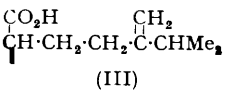

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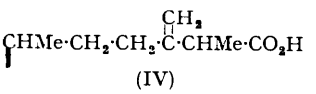

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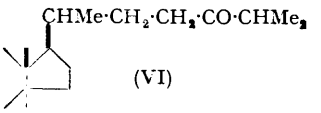

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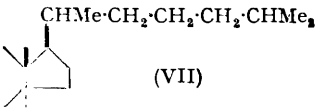

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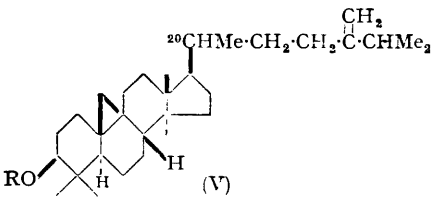


(V)

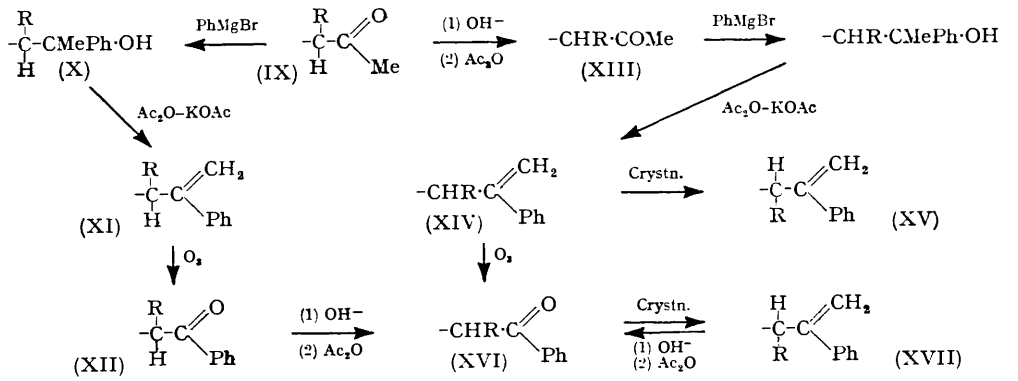
Since *cyclo*laudanol is not identical with *cyclo*artanol, it is unlikely that *cyclo*laudenol differs from *cyclo*artenol simply in the location of the double bond in the side chain. The only structure which would accommodate this view is (II) and this was considered by Bentley *et al.* to be unlikely as it would require that *cyclo*artanol and *cyclo*laudanol differ in configuration around $C_{(20)}$, *i.e.*, that the hydrogenation of the double bond in (II) has proceeded quantitatively to give the unnatural $C_{(20)}$ configuration. The formula (II) for *cyclo*laudenol has been shown to be inadmissible by considerations which emerge below.

Our first approach to the elucidation of the structure of *cyclo*laudenol was to consider the possibility that *cyclo*laudenol is related to a higher homologue of *cyclo*artenol, *i.e.*, that it is a C_{31} or a C_{32} triterpenoid. Eburicoic acid (Holker, Powell, Robertson, Simes, Wright, and Gascoigne, *J.*, 1953, 2422) and the polyporenic acids B and C (Guider, Halsall, Hodges, and Jones, *J.*, 1954, 3234; Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548) are C_{31} triterpenoids of the lanostane group, the C_9 side chains in which have the structure (III); the side chain of the related polyporenic acid A (Halsall and Hodges, *J.*, 1954, 2385; Halsall, Hodges, and Jones, *J.*, 1953, 3019; Roth, Saucy, Anliker, Jeger, and Heusser, *Helv. Chim. Acta*, 1953, **36**, 1908) is represented by (IV). An attractive hypothesis was that *cyclo*laudenol is a C_{31} triterpenoid, and that the double bond has the same position as in the C_{31} triterpenoids named above, *i.e.*, that *cyclo*laudenol is (V; R = H). The latter part of this suggestion was shown to be untenable by the following experiments. Ozonisation of *cyclo*laudenyl acetate yields formaldehyde and a ketone, oxonor*cyclo*laudanyl acetate (Bentley *et al.*, *loc. cit.*, 1955), which we find is reduced, by the Wolff–Kishner method, to nor*cyclo*laudanyl acetate, characterised by its conversion by standard methods into nor*cyclo*laudanol and nor*cyclo*laudanone. If (V; R = Ac) represented *cyclo*laudenyl acetate, oxonor*cyclo*laudanyl acetate would be (VI) and nor*cyclo*laudanyl acetate (VII), *i.e.* nor*cyclo*laudanyl acetate, would be identical with *cyclo*artanyl acetate. However, the last two compounds are distinct, as are the two corresponding alcohols. That nor*cyclo*laudanol differs from *cyclo*artanol simply in configuration round $C_{(3)}$ was considered unlikely because of molecular-rotation considerations and was excluded by the fact that nor*cyclo*laudanone differs from *cyclo*artanone.

We next examined oxonor*cyclo*laudanyl acetate more closely. When treated with potassium hypobromite, this ketone is slowly oxidised to an acid characterised as its methyl ester (methyl 3β-acetoxybisnor*cyclo*laudanoate), thus showing that oxonor*cyclo*laudanyl acetate is a methyl ketone and that the side chain in *cyclo*laudenol is terminated by an *iso*propenyl group. The conversion of *cyclo*laudenyl acetate into oxonor*cyclo*laudanyl acetate and thence into methyl 3β-acetoxybisnor*cyclo*laudanoate is represented as follows: $-CMe{:}CH_2 \longrightarrow -COMe \longrightarrow CO_2Me$. The hypobromite oxidation of the methyl ketone is

very slow, the acid produced is not obtained crystalline, and the ester is isolated in low yield after a tedious purification. Consequently we did not attempt Barbier–Wieland degradation of this ester for elucidation of the nature of the side chain. Instead we attempted to isomerise the side-chain double bond in *cyclo*laudenyl acetate by addition and elimination of hydrogen chloride in the hope that it would be converted into the *iso*propylidene isomer. It was evident that this reaction, even if successful, would be accompanied by fission of the *cyclo*propane ring and formation of a mixture of isomers with nuclear unsaturation but, in spite of this, we hoped that careful ozonolysis of the product would preferentially attack the side-chain double bond. Treatment of *cyclo*laudenyl acetate with dry hydrogen chloride yielded a well-crystalline " hydrochloride " of relatively sharp melting point, undergoing dehydrohalogenation with acetic anhydride to give an acetate, again having a remarkably sharp melting point. Ozonolysis of this gave formaldehyde as the only volatile product. So far as the side chain is concerned the reactions described above have followed the course: $-CHR\cdot CMe{:}CH_2 \rightleftharpoons -CHR\cdot CClMe_2$. An attempt was made to isolate a homogeneous product from the non-volatile fraction of the product obtained from the ozonolysis, but this was unsuccessful, no doubt owing to simultaneous nuclear and side-chain attack by the oxidising agent on the mixture of double-bond isomers resulting from acid fission of the *cyclo*propane ring.

We next turned to a stepwise degradation of oxonor*cyclo*laudanyl acetate. A preliminary examination of this ketone led to a proof that $C_{(24)}$ in *cyclo*laudenol carries an alkyl substituent. Attempts were made to prepare an enol-acetate of oxonor*cyclo*laudanyl acetate to serve as a starting point for side-chain degradations. Using two different methods (see Experimental section) these attempts led instead to a keto-acetate, m. p. 123—125°, $[\alpha]_D$ +52°, different from, and isomeric with oxonor*cyclo*laudanyl acetate, m. p. 140—141°, $[\alpha]_D$ +61°. Hydrolysis of oxonor*cyclo*laudanyl acetate with alkali, followed by reacetylation, gives the same isomer, which is also produced by treatment of the ketone with chromic acid at room temperature. Assuming the designation *b* for the configuration at $C_{(24)}$ in *cyclo*laudenol (and consequently in *oxo*nor*cyclo*laudanyl acetate) (see below), this isomer is named oxonor*cyclo*-24*ab*-laudanyl acetate since, for reasons given in the sequel, we believe it to be a difficulty separable mixture of the 24*a*- and 24*b*-epimers. Reaction of *oxo*nor*cyclo*laudanyl acetate (IX) with phenylmagnesium bromide followed by acetylation yields 25-hydroxy-25-phenylnor*cyclo*laudanyl acetate (X); with acetic anhydride and



		24*b*-Series			24*ab*-Series			24*a*-Series	
		M. p.	$[\alpha]_D$		M. p.	$[\alpha]_D$		M. p.	$[\alpha]_D$
Norketone	(IX)	140—141°	+61°	(XIII)	123—125°	+52°		—	—
Alcohol	(X)	152—154	+37	—	—	—	—	—	—
Styryl compound	(XI)	101—102	+56	(XIV)	99—114	+50	(XV)	138—139°	+44°
Phenyl ketone ...	(XII)	112—114	+58	(XVI)	99—102	+49	(XVII)	110—111	+44

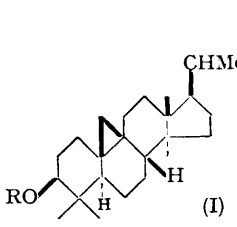
potassium acetate this gives 25-phenylnor*cyclo*laud-25(27)-enyl acetate (XI) which we consider to be the sterically pure 24*b*-epimer. That the dehydration had proceeded in the direction indicated was established by ozonolysis of the styryl compound (XI), formaldehyde (in high yield) and the 24*b*-phenyl ketone (XII) being isolated. The last

compound is also considered to be sterically homogeneous. Similar treatment of oxonor-*cyclo*-24*ab*-laudanyl acetate (XIII) with phenylmagnesium bromide and of the resultant alcohol with acetic anhydride and potassium acetate gives a difficulty separable mixture which we designate 25-phenylnor*cyclo*-24*ab*-laud-25(27)-enyl acetate (XIV). It shows the same ultra-violet absorption spectrum as the 24*b*-isomer (XI). After many crystallisations this gave pure 25-phenylnor*cyclo*-24*a*-laud-25(27)-enyl acetate (XV). Ozonisation of the 24*ab*-styryl compound (XIV) again gave a high yield of formaldehyde together with a ketone considered to be the 24*ab*-phenyl ketone (XVI), the ultra-violet absorption of which was identical with that of the 24*b*-isomer (XII). After many crystallisations this gave the pure 24*a*-phenyl ketone (XVII). Treatment of the 24*a*-phenyl ketone or its 24*b*-isomer with alkali followed by reacetylation gave in each case the 24*ab*-phenyl ketone (XVI) obtained previously from the 24*ab*-methyl ketone (XIII).

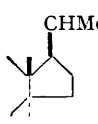
Further identification of the 24-alkyl substituent was attempted by treatment of the 24*ab*-phenyl ketone (XVI) with phenylmagnesium bromide. The crude product (XVIII) with acetic anhydride and potassium acetate gave the pure diphenylethylene (XIX) (max. at 2050 and 2430 Å; ε 29,300 and 13,400). Ozonolysis then yielded benzophenone and a ketone (XX) characterised by its oxime.

$$\underset{\text{(XVI)}}{\text{-CHR·COPh}} \longrightarrow \underset{\text{(XVIII)}}{\text{-CHR·CPh}_2\text{·OH}} \longrightarrow \underset{\text{(XIX)}}{\text{-CR:CPh}_2} \longrightarrow \underset{\text{(XX)}}{\text{-COR}}$$

It being established that *cyclo*laudenol and the ketone are related as $-CHR\cdot CMe{:}CH_2$ to –COR, identification of R could have been attempted by repetition of the Barbier–Wieland degradation or by conversion of *cyclo*artenol (I; R = H) into 24-oxotrisnor*cyclo*laudanyl acetate, the second method depending on the hypothesis that *cyclo*laudenol and *cyclo*artenol differ solely in the nature of the side chain. Since supplies of *cyclo*laudenol were very limited we examined the second method by reactions chosen, as in the degradation of *cyclo*laudenol, to leave the labile *cyclo*propane bridge intact. Careful treatment of *cyclo*artenyl acetate with ozone gave, in 70% yield, 3β-acetoxytrisnor*cyclo*artan-24-al (XXI), characterised as its dimethyl acetal and oxime. Reaction of the aldehyde (XXI) with diazoethane yielded the ethyl ketone (XXII) (24-oxonor*cyclo*artanyl acetate) characterised by its oxime and by its stability to chromic acid at room temperature; it is different from 24-oxotrisnor*cyclo*laudanyl acetate. The aldehyde was converted by diazomethane into the methyl ketone (XXIII) (24-oxobisnor*cyclo*artanyl acetate; characterised by its oxime and stability to chromic acid at room temperatur), which is identical with 24-oxotrisnor-*cyclo*laudanyl acetate; identity was confirmed by a comparison of their infra-red absorption spectra for which we express our best thanks to Professor E. R. H. Jones, F.R.S., and Dr. G. D. Meakins.

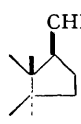


(I)



(XXI)

(XXII)

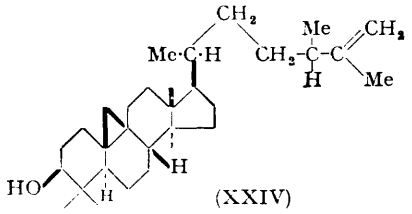


(XXIII)

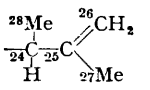
The constitution of *cyclo*laudenol is therefore represented by (XXIV). The one feature of the sterochemistry of *cyclo*laudenol which remains to be defined, namely, the configuration at $C_{(24)}$, was established by molecular-rotation relations. The two possible configurations for the terminal carbon atoms in the side chain of *cyclo*laudenol are represented by (XXV; 24*b* on the current convention) and (XXVI; 24*a*). Bergmann and Low (*J. Org. Chem.*, 1947, **12**, 67) have shown that the introduction of a 24*a*-methyl group * into cholestanol and cholesterol and their esters causes a substantial positive

* The configurational indices used by Bergmann and Low should be interchanged to conform with presently accepted nomenclature.

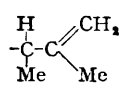
increment (Δ *ca.* +22°) in molecular rotation, whereas a negative change (Δ *ca.* −29°) accompanies the introduction of a 24*b*-methyl group. A comparison of the molecular rotations of lanostane derivatives with those of the corresponding laudane derivatives is



(XXIV)



(XXV)



(XXVI)

shown below; in all cases the Δ value ($[M]_D$ laudane $-[M]_D$ lanostane derivative) is negative, from which we conclude that *cyclo*laudenol is 24*b*-methyl-9 : 19-*cyclo*lanost-25-en-3β-ol (24*b*-methyl*cyclo*art-25-enol) (XXV).

	$[M]_D$		$[M]_D$ [3]	Δ
Lanostane [1]	+145°	Laudane	+107°	−38°
Lanostanol [1]	+150	Laudanol	+ 93	−57
Lanostanyl acetate [1]	+193	Laudanyl acetate	+155	−38
Lanostanone [1]	+116	Laudanone	+ 62	−54
*cyclo*Artanol [2]	+214	*cyclo*Laudanol	+191	−23
*cyclo*Artanyl acetate [2]	+277	*cyclo*Laudanyl acetate	+242	−35

	$[M]_D$ [1]		$[M]_D$ [4]	Δ
Lanost-8-enol	+261°	Eburic-8-enol	+238°	−23°
Lanost-8-enyl acetate	+275	Eburic-8-enyl acetate	+271	− 4
Lanost-8-ene	+272	Eburic-8-ene I	+234	−38
		Eburic-8-ene II	+218	−54

[1] From Elsevier's " Encyclopaedia of Organic Chemistry," Vol. 14S. [2] From Bentley, Henry, Irvine and Spring, *J.*, 1953, 3673. [3] From Bentley, Henry, Irvine, Mukerji and Spring, *J.*, 1955, 596. [4] From Robertson *et al.*, *J.*, 1951, 2346; 1953, 2414.

The Table also includes a comparison of the molecular rotations of lanost-8-enol and eburic-8-enol derivatives. Although the data are more limited than those available in the laudane series, we conclude from the negative value of Δ that eburic-8-enol is 24*b*-methyllanost-8-enol. It follows that the saturated parent of the eburicoic acid group, eburicane (which has not been prepared), will prove to be identical with laudane.

Experimental

Specific rotations were measured in chloroform solution in a 1-dm. tube at room temperature, and ultraviolet absorption spectra in ethanol using a Unicam SP 500 spectrophotometer. Grade II alumina and light petroleum of b. p. 60—80° were used for chromatography unless otherwise specified.

Wolff–Kishner Reduction of 25-*Oxo*-26-*nor*cyclo*laudanyl Acetate.*—A mixture of 25-oxo-26-nor*cyclo*laudanyl acetate (250 mg.), 100% hydrazine hydrate (2·5 ml.), and sodium ethoxide (from 312 mg. of sodium) in ethanol (15 ml.) was kept at 200° for 12 hr. The product was isolated in the usual manner and treated on the steam-bath for 3 hr. with acetic anhydride (5 ml.) and pyridine (5 ml.). A dry solution of the acetylated product (236 mg.) in light petroleum (25 ml.) was filtered through a column (1 × 8 cm.) of alumina (6 g.). The fraction eluted with light petroleum (125 ml.) was crystallised from methanol to give 26-*nor*cyclo*laudanyl acetate* as needles (134 mg.), m. p. 118—120°, $[\alpha]_D$ +58° (*c*, 1·1) (Found : C, 81·3; H, 11·6. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%). A mixture with *cyclo*artanyl acetate had m. p. 117—128°. Hydrolysis of the acetate with 3% methanolic potassium hydroxide gave 26-*nor*cyclo*laudanol*, needles (from methanol), m. p. 114—115°, $[\alpha]_D$ +49° (*c*, 1·6) (Found : C, 83·9; H, 12·2. $C_{30}H_{52}O$ requires C, 84·0; H, 12·2%). A mixture of 26-nor*cyclo*laudanol and *cyclo*artanol had m. p. 98—110°. Oxidation of 26-nor*cyclo*laudanol with chromic acid in acetic acid for 12 hr. at room temperature and isolation of the product in the usual manner, gave 26-*nor*cyclo*laudan*-3-*one* which separates from methanol as blades, m. p. 100—101°, depressed to 92—97° when mixed with *cyclo*artanone, $[\alpha]_D$ +22° (*c*, 2·2) (Found : C, 84·0; H, 11·9. $C_{30}H_{50}O$ requires C, 84·4; H, 11·8%). The *oxime* separates as needles, m. p. 203°, from chloroform–methanol (Found : C, 81·7; H, 11·3. $C_{30}H_{51}ON$ requires C, 81·6; H, 11·6%).

Methyl 3β-*Acetoxy*-26 : 27-*bisnor*cyclo*laudan*-25-*oate*.—25-Oxo-26-nor*cyclo*laudanyl acetate (375 mg.) in dioxan (15 ml.) was shaken with bromine (1 ml.), potassium hydroxide (15 g.), and water (20 ml.) at room temperature for 14 days. The acidic fraction (284 mg.) isolated in the usual manner (insoluble potassium salt) was treated on the steam-bath for 2½ hr. with acetic anhydride (5 ml.) and pyridine (5 ml.). The acetylated acid, which could not be obtained crystalline, was esterified with ethereal diazomethane, and a solution of the methyl ester in light petroleum (25 ml.) was percolated through a column (1·75 × 5 cm.) of alumina (9 g.). Elution with light petroleum–benzene gave a fraction (62 mg.) which, on crystallisation from methanol, yielded *methyl* 3β-*acetoxy*-26 : 27-*bisnor*cyclo*laudan*-25-*oate* as needles, m. p. 115—116°, $[\alpha]_D$ +57° (*c*, 1·1) (Found : C, 76·8; H, 10·5. $C_{32}H_{52}O_4$ requires C, 76·8; H, 10·5%).

Treatment of cyclo*Laudenyl Acetate with Hydrogen Chloride*.—*cyclo*Laudenyl acetate (2 g.) in dry chloroform (40 ml.) was treated with a stream of dry hydrogen chloride at 0° for 3 hr. The solid obtained on removal of the solvent crystallised from methanol, giving a "*hydrochloride*" (1·7 g.) as needles, m. p. 166—170° (decomp.), $[\alpha]_D$ +64° (*c*, 1·3) (Found : C, 76·0; H, 10·8. $C_{33}H_{55}O_2Cl$ requires C, 76·3; H, 10·7%). The compound gives a strong yellow colour with tetranitromethane. A solution of the "hydrochloride" in acetic anhydride (15 ml.) was refluxed for 15 hr., then diluted with water. The product, isolated in the usual manner, separated from chloroform–methanol as needles (1·1 g.), m. p. 152—156°, $[\alpha]_D$ +61° (*c*, 1·1) (Found : C, 81·8; H, 11·0. $C_{33}H_{54}O_2$ requires C, 82·1; H, 11·3%). Ozonised oxygen was then passed through a solution of this product (1·3 g.) in acetic acid (170 ml.) at room temperature for 1 hr. The solution was diluted with water (1 l.), treated with 10% ferrous sulphate solution (20 ml.), and steam-distilled. From the distillate (500 ml.), formaldehyde (22%) was isolated as its dimethone, needles (from ethanol), m. p. and mixed m. p. 190—191° (Found : C, 69·7; H, 8·2. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%). The filtrate from the dimethone derivative was again steam-distilled and the distillate (250 ml.) treated with aqueous 2 : 4-dinitrophenylhydazine hydrochloride; no hydrazone separated. The non-volatile product was treated with chromic acid by the method (Bentley *et al.*, *loc. cit.*, 1953) used for the preparation of laud-9(11)-enyl acetate from the mixture obtained by treatment of *cyclo*laudanyl acetate with hydrogen chloride, but no crystalline product was isolated.

Treatment of 25-*Oxo*-26-*nor*cyclo*laudanyl Acetate with Alkali*.—25-Oxo-26-nor*cyclo*laudanyl acetate (m. p. 140—141°, $[\alpha]_D$ +61°; 200 mg.) was refluxed with 5% methanolic potassium hydroxide (150 ml.) for 5 hr. to yield 25-*oxo*-26-*nor*cyclo-24ab-*laudanol* (138 mg.), separating from aqueous methanol as short, thick needles, m. p. 139—141°, $[\alpha]_D$ +43° (*c*, 1·4) (Found : C, 81·0; H, 11·4. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Acetylation of this alcohol (110 mg.) at room temperature for 12 hr. with acetic anhydride (5 ml.) and pyridine (5 ml.) and two crystallisations from methanol gave 25-*oxo*-26-*nor*cyclo-24ab-*laudanyl acetate* as needles (60 mg.), m. p. 123—125° unchanged on further crystallisation, $[\alpha]_D$ +52° (*c*, 1·5) (a mixture with 25-oxo-26-nor*cyclo*laudanyl acetate had m. p. 123—135°) (Found : C, 79·3; H, 10·7. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The *oxime* separated from methanol as needles, m. p. 153—154°, $[\alpha]_D$ +50° (*c*, 1·5) (Found : C, 76·6; H, 10·5. $C_{32}H_{53}O_3N$ requires C, 76·9; H, 10·7%). Treatment of 25-oxo-26-nor*cyclo*laudanyl acetate (100 mg.) in acetic acid (25 ml.) with chromic acid (18 mg.) for 12 hr. at room temperature did not give an acidic product. The neutral product furnished 25-oxo-26-nor*cyclo*-24*ab*-laudanyl acetate, separating from methanol as needles (72 mg.), m. p. 123—125° alone or mixed with the specimen described above, $[\alpha]_D$ +53° (*c*, 1·2).

25-Oxo-26-nor*cyclo*-24*ab*-laudanyl acetate was also obtained as follows : (i) A mixture of 25-oxo-26-nor*cyclo*laudanyl acetate (100 mg.), acetic anhydride (2 ml.), and freshly fused potassium acetate (100 mg.) was kept at 132° for 10 hr. The product, isolated in the normal manner, gave 25-oxo-26-nor*cyclo*-24*ab*-laudanyl acetate which, twice crystallised from methanol, gave needles (87 mg.), m. p. 123—125°, $[\alpha]_D$ +51° (*c*, 1·2).

(ii) A solution of the same acetate (100 mg.) in *iso*propenyl acetate (20 ml.) and one drop of concentrated sulphuric acid was kept at 100° for 3 hr. The product was twice crystallised from methanol, to give 25-oxo-26-nor*cyclo*-24*ab*-laudanyl acetate as needles (82 mg.), m. p. 123—125°, $[\alpha]_D$ +52° (*c*, 1·4).

Treatment of 25-*Oxo*-26-*nor*cyclo*laudanyl Acetate with Phenylmagnesium Bromide*.—The acetate (2 g., 1 mol.) in ether (80 ml.) was added during 45 min. to a solution of phenylmagnesium bromide (6 mols.) in ether (100 ml.), and the mixture refluxed for 30 min. The product was steam-distilled for 1 hr. and a solution of the non-volatile fraction (2·4 g.) in acetic anhydride (15 ml.) refluxed with freshly fused potassium acetate (0·5 g.) for 1 hr. A solution of the product in light petroleum (100 ml.) was percolated through a column (2·75 × 15 cm.) of alumina (75 g.), and the fraction (0·6 g.) eluted by light petroleum (900 ml.) crystallised from methanol to give

25-*phenyl*-26-*nor*cyclo*laud*-25(27)-*enyl acetate* as plates, m. p. 101—102°, $[\alpha]_D$ +56° (*c*, 1·2) (Found: C, 83·9; H, 10·4. $C_{38}H_{56}O_2$ requires C, 83·8; H, 10·4%). The styryl compound gives a strong yellow colour with tetranitromethane. Light absorption: max. at 2080 and 2360 Å (ε 12,200 and 8100). The fractions eluted by light petroleum–benzene (1 : 4, 1050 ml.; 1 : 1, 1350 ml.) were combined (1·5 g.) and twice crystallised from acetone–water to give the 25-*hydroxy*-25-*phenyl*-26-*nor*cyclo*laudanyl acetate* as small needles (0·7 g.), m. p. 152—154°, $[\alpha]_D$ +37° (*c*, 1·1) (Found: C, 81·0; H, 10·4. $C_{38}H_{58}O_3$ requires C, 81·1; H, 10·4%). It gives a pale yellow colour with tetranitromethane. Light absorption: max. at 2080 Å (ε 7250). A solution of the alcohol and potassium acetate (0·5 g.) in acetic anhydride (15 ml.) was heated under reflux for 4 hr. and left overnight. The product in light petroleum (80 ml.) was chromatographed on alumina (40 g.), and the fraction eluted by light petroleum (880 ml.) crystallised from methanol to give the styryl compound described above as needles (0·7 g.), m. p. and mixed m. p. 101—102°, $[\alpha]_D$ +55·6° (*c*, 1·1).

Ozonolysis of 25-*Phenyl*-26-*nor*cyclo*laud*-25(27)-*enyl Acetate*.—A solution of the styryl compound (1 g.) in dry chloroform (150 ml.) was treated with ozonised oxygen at −45°. The ozonide was decomposed with zinc and acetic acid, and after filtration the solution was washed with water, and the washings were retained. The product was steam-distilled and a solution of the residue (0·9 g.) in light petroleum (70 ml.) chromatographed on a column (2·25 × 8 cm.) of alumina (30 g.). The fraction (0·5 g.) eluted by light petroleum–benzene (4 : 1, 640 ml.) gave 25-*oxo*-25-*phenyl*-26 : 27-*bisnor*cyclo*laudanyl acetate*, which separates from methanol as needles, m. p. 112—114°, $[\alpha]_D$ +57·5° (*c*, 1·2) (Found: C, 81·1; H, 10·0. $C_{37}H_{54}O_3$ requires C, 81·3; H, 10·0%). The ketone gives a pale yellow colour with tetranitromethane. Light absorption: max. at 2050 and 2420 Å (ε 13,000 and 11,750). The *oxime* separated from methanol as short thick needles, m. p. 177—179°, $[\alpha]_D$ +55° (*c*, 1·3) (Found: C, 78·8; H, 9·7. $C_{37}H_{55}O_3N$ requires C, 79·1; H, 9·9%). From the aqueous washings, formaldehyde was isolated as its dimethone (0·24 g., 44%), needles (from ethanol), m. p. and mixed m. p. 190—191° (Found: C, 69·7; H, 8·4. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%).

Treatment of 25-*Oxo*-26-*nor*cyclo-24ab-*laudanyl Acetate with Phenylmagnesium Bromide*.—25-Oxo-26-nor*cyclo*-24*ab*-laudanyl acetate (3·7 g.) was treated with phenylmagnesium bromide (8·2 g.) as described above. The crude alcohol (4·5 g.) was readily dehydrated by refluxing for 4 hr. with acetic anhydride (30 ml.) and potassium acetate (1 g.). A solution of the product (4·4 g.) in light petroleum (150 ml.) was filtered through a column (4 × 12·5 cm.) of alumina (130 g.). The fractions (2·3 g.) eluted by light petroleum (600 ml.) and light petroleum–benzene (4 : 1, 3 l.) were combined and crystallised from ethanol, from which 25-phenyl-26-nor*cyclo*-24*ab*-laud-25(27)-enyl acetate separated as fine needles (2 g.), m. p. 99—114°, $[\alpha]_D$ +49·8° (*c*, 1·2), which gave a strong yellow colour with tetranitromethane. Light absorption: max. at 2080 and 2360 Å (ε 13,000 and 8700). Nine recrystallisations from ethanol gave 25-*phenyl*-26-*nor*cyclo-24a-*laud*-25(27)-*enyl acetate* as fine needles, m. p. 138—139°, $[\alpha]_D$ +44° (*c*, 1·1) (Found: C, 83·7; H, 10·2. $C_{38}H_{56}O_2$ requires C, 83·8; H, 10·4%).

Ozonolysis of the 24ab-*Styryl Compound*.—Ozonised oxygen (2 mols.) was passed through a solution of the 24*ab*-styryl compound (2 g.; m. p. 99—114°) in dry chloroform (150 ml.) at −45°, and the ozonide treated with zinc and acetic acid. The product (1·9 g.) was isolated by means of chloroform in the usual manner and the washings were retained. After removal of chloroform, the residue was steam-distilled for 1 hr. The non-volatile fraction was dissolved in light petroleum (150 ml.) and filtered through a column (2·75 × 11 cm.) of alumina (60 g.). The fractions (1·1 g.) eluted by light petroleum–benzene (1 : 1, 1800 ml.; 3 : 1, 500 ml.) and benzene (400 ml.) were combined and crystallised from methanol, to yield 25-oxo-25-phenyl-26 : 27-bisnor*cyclo*-24*ab*-laudanyl acetate as needles (0·7 g.), m. p. 99—102°, $[\alpha]_D$ +49° (*c*, 1·4). Light absorption: max. at 2050 and 2420 Å (ε 13,000 and 11,250). Seven crystallisation from methanol gave 25-*oxo*-25-*phenyl*-26 : 27-*bisnor*cyclo-24*a*-*laudanyl acetate*, m. p. 110—111°, $[\alpha]_D$ +44° (*c*, 1·7) (Found: C, 81·1; H, 10·0. $C_{37}H_{54}O_3$ requires C, 81·3; H, 10·0%). A mixture of 25-oxo-25-phenyl-26 : 27-bisnor*cyclo*laudanyl acetate (m. p. 112—114°) and the 24*a*-isomer had m. p. 98—103°, *i.e.* approx. the same as the 24*ab*-mixture described above. From the aqueous washings, formaldehyde (67%) was isolated as its dimethone, needles (from ethanol), m. p. and mixed m. p. 190—191° (Found: C, 69·6; H, 8·0. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%). The filtrate from the dimethone was again distilled and the distillate treated with 2 : 4-dinitrophenylhydrazine; no precipitate was obtained.

Treatment of the 24a- *and* 24b-*Phenyl Ketones with Alkali*.—(i) Hydrolysis of the 24*a*-phenyl ketone (116 mg.) with 3% methanolic potassium hydroxide and treatment of the product with acetic anhydride (5 ml.) and pyridine (5 ml.) at 95° for 1½ hr. yielded the 24*ab*-phenyl ketone

which separated from methanol as needles (84 mg.), $[\alpha]_D$ +47° (*c*, 1·2), m. p. 95—101°, alone or mixed with the specimen of m. p. 99—102°.

(ii) The 24*b*-phenyl ketone (110 mg.) was treated with 5% methanolic potassium hydroxide under reflux for 6 hr. with subsequent reacetylation. Crystallisation from methanol gave the 24*ab*-phenyl ketone (71 mg.), $[\alpha]_D$ +46° (*c*, 1·0), m. p. 96—100° alone or mixed with a specimen of m. p. 99—102°.

25 : 25-*Diphenyl*-26 : 27-*bisnor*cyclo*laud*-24-*enyl Acetate*.—The 24*ab*-phenyl ketone (1·4 g.; m. p. 98—102°) was treated with phenylmagnesium bromide (2·7 g.) as described above. The alcohol was dehydrated (without purification) by refluxing for 4 hr. with acetic anhydride (15 ml.) and potassium acetate. A solution of the product (1·4 g.) in light petroleum (100 ml.) was chromatographed on a column (3 × 8·5 cm.) of alumina (45 g.). The fraction eluted by light petroleum–benzene (4 : 1; 560 ml.) crystallised from chloroform–methanol, from which the *diphenylethylene* separated as plates (0·4 g.), m. p. 170°, $[\alpha]_D$ +53° (*c*, 1·4) (Found : C, 85·0; H, 9·5. $C_{43}H_{58}O_2$ requires C, 85·1; H, 9·6%). It gives a strong yellow colour with tetranitromethane. Light absorption : max. at 2050 and 2430 Å (ε 29,300 and 13,400).

24-*Oxo*-25 : 26 : 27-*trisnor*cyclo*laudanyl Acetate*.—A solution of the diphenylethylene (350 mg.) in dry chloroform (100 ml.) was treated with ozonised oxygen at −45°, and the ozonide treated with zinc and acetic acid. The product (320 mg.) was isolated by means of chloroform in the usual manner and the water-washings were retained. The residue obtained on removal of the solvent was steam-distilled, and a solution of the non-volatile fraction in light petroleum–benzene (1 : 1, 80 ml.) percolated through a column of alumina (1·75 × 6·75 cm., 12 g.). The fraction (77 mg.) eluted by light petroleum–benzene (1 : 3, 250 ml.) crystallised from methanol, to give 24-*oxo*-25 : 26 : 27-*trisnor*cyclo*laudanyl acetate* as plates, m. p. 170°, $[\alpha]_D$ +58° (*c*, 1·2) (Found : C, 78·7; H, 10·8. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). The *oxime* separated from chloroform–methanol as plates, m. p. 219—220°, $[\alpha]_D$ +50° (*c*, 0·8) (Found : C, 76·2; H, 10·2. $C_{30}H_{49}O_3N$ requires C, 76·4; H, 10·5%). Ether-extraction of the aqueous washings gave a clear gum (62 mg.) with a fragrant odour. A solution in methanol (2 ml.) on treatment with Brady's reagent yielded benzophenone 2 : 4-dinitrophenylhydrazone which separated from acetic acid as orange plates (89 mg., 43%), m. p. and mixed m. p. 235—236° (Found : C, 63·1; H, 3·9; N, 15·6. Calc. for $C_{19}H_{14}O_4N_4$: C, 63·0; H, 3·9; N, 15·5%). Light absorption : max. at 2060, 2240, 2500, and 3800 Å (ε 37,800, 26,400, 18,500, and 30,000).

3β-*Acetoxy*-25 : 26 : 27-*trisnor*cyclo*artan*-24-*al*.—Ozonised oxygen (2 mols.) was passed through a solution of *cyclo*artenyl acetate (4 g.) in dry chloroform (200 ml.) at −45°. Treatment of the ozonide with zinc dust and acetic acid and isolation of the product by means of chloroform gave 3β-*acetoxy*-25 : 26 : 27-*trisnor*cyclo*artan*-24-*al*, as prisms (2·8 g.) (from aqueous acetone), m. p. 155—157°, $[\alpha]_D$ +59·5° (*c*, 2·0) (Found : C, 78·7; H, 10·5. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·5%). From a hot solution of the aldehyde in methanol, 24 : 24-*dimethoxy*-25 : 26 : 27-*trisnor*cyclo*artanyl acetate* separated as prisms, m. p. 125—126°, $[\alpha]_D$ +53° (*c*, 1·1) (Found : C, 76·0; H, 10·7. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%). The *oxime* of the aldehyde separated from methanol as needles, m. p. 198° (Found : C, 75·7; H, 10·1. $C_{29}H_{47}O_3N$ requires C, 76·1; H, 10·3%).

24-*Oxo*-26-*nor*cyclo*artanyl Acetate*.—3β-Acetoxy-25 : 26 : 27-trisnor*cyclo*artan-24-al (2·8 g.) in dry ether (30 ml.) and dioxan (20 ml.) was treated with ethereal diazoethane (50 ml.; from 12 g. of nitrosoethylurea) at room temperature for 2 days. A solution of the product in light petroleum (100 ml.) was filtered through a column (2·5 × 18 cm.) of alumina (90 g.), and the fraction (1·2 g.) eluted by light petroleum–benzene (4 : 1, 1050 ml.; 1 : 1, 1350 ml.) was crystallised from aqueous methanol, to yield 24-*oxo*-26-*nor*cyclo*artanyl acetate* as blades, m. p. 118°, $[\alpha]_D$ +57° (*c*, 1·4) (Found : C, 78·9; H, 10·8. $C_{31}H_{50}O_3$ require C, 79·1; H, 10·7%). The *oxime* separated from methanol as needles, m. p. 160° (Found : C, 77·2; H, 10·4. $C_{31}H_{51}O_3N$ requires C, 76·7; H, 10·6%). The ketone was recovered unchanged after treatment with chromic acid at room temperature.

24-*Oxo*-26 : 27-*bisnor*cyclo*artanyl Acetate*.—3β-Acetoxy-25 : 26 : 27-trisnor*cyclo*artan-24-al (1·4 g.) in dry ether (20 ml.) and dioxan (10 ml.) was treated with ethereal diazomethane (50 ml.; from 5 g. of nitrosomethylurea) at room temperature for 3 days. A solution of the product (1·5 g.) in light petroleum–benzene (4 : 1; 150 ml.) was percolated through a column (2·5 × 17 cm.) of alumina (60 g.). The combined fractions (850 mg.) eluted by light petroleum–benzene (3 : 2, 1200 ml.; 2 : 3, 600 ml.) were crystallised from methanol, to give 24-*oxo*-26 : 27-*bisnor*cyclo*artanyl acetate* as plates, m. p. 170° alone or mixed with 24-oxo-25 : 26 : 27-trisnor-*cyclo*laudanyl acetate, $[\alpha]_D$ +58° (*c*, 1·2) (Found : C, 78·9; H, 10·6. $C_{30}H_{48}O_3$ requires C, 78·9; 10·6%). The *oxime* of 24-oxo-26 : 27-bisnor*cyclo*artanyl acetate separated from chloroform–

methanol as needles, m. p. 219—220°, alone or mixed with the oxime of 24-oxo-25 : 26 : 27-trisnor-*cyclo*laudanyl acetate, $[\alpha]_D$ +50° (*c*, 0·9) (Found : C, 76·2; H, 10·0. $C_{30}H_{49}O_3N$ requires C, 76·4; H, 10·5%). 24-Oxo-26 : 27-bisnor*cyclo*artanyl acetate was recovered unchanged after treatment with chromic acid at room temperature.

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