*Triterpenoids. Part XXXII.** cyclo*Laudenol, a Triterpenoid Alcohol from Opium.*

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From the alkaloid-free fraction of opium (+)-*n*-nonacosan-10-ol and a new triterpenoid alcohol, named *cyclo*laudenol, have been isolated. *cyclo*-Laudenol contains a vinylidene group and a *cyclo*propane ring. The reactions of the dihydro-derivative, *cyclo*laudanol, are very similar to those of *cyclo*-artanol, this similarity extending to molecular-rotation relations. It is concluded that *cyclo*laudenol and *cyclo*artenol have the same nuclear structure and differ only in the nature of their side chains.

Opium has been the subject of chemical examination since the beginning of the eighteenth century and approximately thirty different alkaloids have been isolated from this source and their structures elucidated. The commercial extraction of alkaloids from opium has achieved a high level of efficiency although the method employed is believed to be essentially that described in 1833 by Gregory (*Annalen*, **7**, 261; cf. Anderson, *ibid.*, 1853, **86**, 180). The opium is stirred with water, the mixture treated with a hot solution of calcium chloride and filtered, and the press-cake washed. The filtrate and washings are combined and processed for alkaloids. The press-cake has been shown to contain the calcium salts of meconic, lactic, and sulphuric acids, but apart from this observation there is no record of an examination of the non-alkaloidal constituents of opium.

Through the courtesy of the Directors of Messrs. T. and H. Smith Ltd., Edinburgh, we have been able to examine the press-cake or marc from opium. Extraction of the marc with chloroform gave a fat (18%), which was saponified by using alcoholic potassium hydroxide. The non-saponifiable fraction was obtained as an orange-coloured gum which, not without difficulty, was crystallised from acetone. The crystalline solid was chromatographed on alumina, the most easily eluted fraction being a gum which has not been examined. The next fraction was a crystalline, optically inactive alcohol, $C_{29}H_{60}O$, m. p. 81—82°, which gave negative reactions in the Liebermann–Burchard test and with the tetranitromethane reagent. The alcohol was characterised as its acetate, and was oxidised to the corresponding ketone, reduction of which by the Wolff–Kishner method gave a hydrocarbon, $C_{29}H_{60}$. The analytical data and physical constants of the alcohol and its derivatives suggested that it is (+)-*n*-nonacosan-10-ol. This alcohol was isolated by Chibnall, Piper, Pollard, Smith, and Williams (*Biochem. J.*, 1931, **25**, 2095) from apple cuticle wax; it does not show any appreciable optical rotation although the hydrogen phthalate has a very slight dextrorotation. (+)-*n*-Nonacosan-10-ol has also been isolated from the fruit of *Ginkgo bilboa* (Kawamura, *Jap. J. Chem.*, 1928, **3**, 89; Chibnall and Piper, *Biochem. J.*, 1934, **28**, 2209). A comparison of the m. p.s of the alcohol and its derivatives isolated from the three sources is shown below:

	Opium	Apple cuticle	*Ginkgo bilboa*
(+)-*n*-Nonacosan-10-ol	81—82°	81·9—82·2°	82·5°
(+)-*n*-Nonacosan-10-yl acetate	44·5—45·5	44·5—45	43—43·5
n-Nonacosan-10-one	74·5—75·5	74·7—74·9	74
n-Nonacosane	63—64	62·7—63	—

The alcohol obtained from opium and its acetate and ketone were undepressed in m. p. when mixed with the corresponding compounds derived from apple cuticle wax and kindly given to us by Professor A. C. Chibnall, F.R.S., to whom we express our best thanks. The infra-red absorption spectra of the alcohols from the two sources were identical.

Continued elution of the alumina column gave a principal fraction from which an alcohol was readily isolated and characterised by preparation of a number of derivatives.

* The Paper by McKean and Spring, *J.*, 1954, 1989, is considered to be Part XXXI.

In the Liebermann–Burchard test the alcohol gives a deep red solution with a strong green fluorescence. Because of its origin and for reasons which emerge below, we name this alcohol *cyclo*laudenol. Analyses of the alcohol and its derivatives did not allow a firm decision to be made between the formulæ $C_{30}H_{50}O$, $C_{31}H_{52}O$, and $C_{32}H_{54}O$ for the parent.

The presence of a secondary hydroxyl group in *cyclo*laudenol follows from the preparation of an acetate and a benzoate and from its oxidation to a ketone, *cyclo*laudenone, which is stable to chromic acid at room temperature. A number of observations show that *cyclo*laudenol contains one double bond which is reactive. First, when shaken over a platinum catalyst, *cyclo*laudenyl acetate absorbs one mol. of hydrogen to yield *cyclo*laudanyl acetate. Secondly, the first acetate absorbs one mol. of bromine to yield its dibromide, and finally, oxidation of *cyclo*laudenyl acetate with perbenzoic acid yields a monoxide. As expected from this behaviour, *cyclo*laudenyl acetate shows an apparent absorption maximum at 2060 Å ($\varepsilon = 1500$) whereas *cyclo*laudanyl acetate and *cyclo*laudenyl acetate oxide do not show any appreciable absorption in the ethylenic region. In contrast to their apparently saturated nature, however, *cyclo*laudanyl acetate, the derived *cyclo*laudanol, *cyclo*laudenyl acetate oxide, and *cyclo*laudenyl acetate dibromide each give a faint but distinct colour with tetranitromethane.

A close relation between *cyclo*laudenol and *cyclo*artenol (I) (Bentley, Henry, Irvine, and Spring, *J.*, 1953, 3673; Henry and Spring, *Chem. and Ind.*, 1954, 189; Barton, Page, and Warnhoff, *J.*, 1954, 2715) was suggested at an early stage in this work by a number of considerations. First, dihydro-derivatives of both compounds do not show light absorption in the ethylenic region but do give a positive reaction with the tetranitromethane reagent. Secondly, molecular-rotation differences between corresponding compounds of both series are similar, as shown in the following Table, and in particular

	M_D *						
	Alcohol	Acetate	Benzoate	Ketone	Δ_1	Δ_2	Δ_3
*cyclo*Artenol	+230°	+280°	+400°	+ 93°	+50°	+170°	−137°
*cyclo*Laudenol	+206	+265	+343	+ 83	+59	+137	−123
*cyclo*Artanol	+214	+277	—	+102	+63	—	−112
*cyclo*Laudanol	+190	+242	—	—	+52	—	—

* The M_D values for *cyclo*laudenol and its derivatives given in this paper are based on the molecular formula $C_{31}H_{52}O$, as are the theoretical values for carbon and hydrogen analyses.

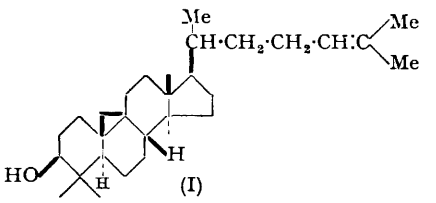
the change in molecular rotation accompanying oxidation of *cyclo*laudenol to *cyclo*laudenone is strongly negative, whereas with many naturally occurring triterpenoid alcohols it is positive. Members of the tetracyclic triterpenoid group containing a reactive double bond show little change in molecular rotation on hydrogenation (Barton and Jones, *J.*, 1944, 659; Jones and Woods, *J.*, 1953, 464). In this respect, *cyclo*laudenol, like *cyclo*artenol, is related to this group. Again, the molecular-rotation change accompanying acetylation of a 3β-hydroxy-triterpenoid is positive, whereas the corresponding change for a 3α-hydroxy-compound is strongly negative (Halsall, Meakins, and Swayne, *J.*, 1953, 4139). The molecular-rotation changes on acetylation of *cyclo*laudenol and *cyclo*laudanol are positive and roughly equal to those observed for *cyclo*artenol and *cyclo*artanol, from which it is inferred that if *cyclo*laudenol resembles *cyclo*artenol in being a 3-hydroxy-triterpenoid, the hydroxyl group has the β-configuration.

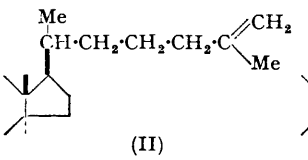
The suspected presence of a *cyclo*propane ring in *cyclo*laudenol was confirmed as follows. Treatment of *cyclo*laudanyl acetate with hydrogen chloride gave an acetate mixture, m. p. 145—155°, which in contrast to *cyclo*laudanyl acetate gives a strong yellow colour with tetranitromethane and shows ethylenic absorption between 2000 and 2200 Å. From this mixture, by a tedious crystallisation procedure, a homogeneous compound, laudenyl acetate, m. p. 173—174°, was isolated which shows an apparent absorption maximum at 2080 Å ($\varepsilon = 3000$) and gives a strong yellow colour with the tetranitromethane reagent. The infra-red absorption spectra of *cyclo*laudenol and its derivatives were kindly examined by Dr. A. R. H. Cole, of the University of Western Australia, to whom we express our best thanks. In carbon tetrachloride solution, *cyclo*laudenol, its

acetate, and *cyclo*laudanyl acetate all show a band at 3040 cm.$^{-1}$ characteristic of a methylene group included in a *cyclo*propane ring (Cole, *Chem. and Ind.*, 1953, 946).

Ozonolysis of *cyclo*laudenyl acetate gives formaldehyde and a ketone oxonor*cyclo*laudanyl acetate; thus in contrast to *cyclo*artenol which contains an *iso*propylidene group, *cyclo*laudenol contains a vinylidene group. The presence of a vinylidene group was confirmed by Dr. Cole's infra-red measurements; the spectra of *cyclo*laudenol and its acetate include bands at 3071 cm.$^{-1}$ (in carbon tetrachloride) and at 887 cm.$^{-1}$ (in carbon disulphide) and these bands are absent from the spectrum of *cyclo*laudanyl acetate.

The possibility that *cyclo*laudenol differs from *cyclo*artenol simply in the position of the double bond in the side chain was next considered. If *cyclo*laudenol is (II), *cyclo*laudanyl acetate should be identical with *cyclo*artanyl acetate (VII; R = C_8H_{17}) whereas the two are distinct. If *cyclo*laudenol is (III), the non-identity of *cyclo*artanyl acetate (VII; R = C_8H_{17}) and *cyclo*laudanyl acetate requires that hydrogenation of the $\Delta^{20\,(21)}$-bond in *cyclo*laudenyl acetate has proceeded quantitatively to give the unnatural configuration at $C_{(20)}$. This point will be further discussed in a later paper dealing with a closer investigation of the side chain of *cyclo*laudenol.


(I)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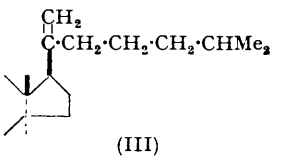
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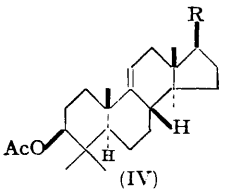
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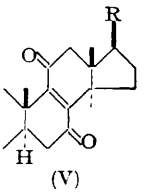
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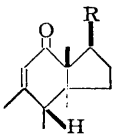
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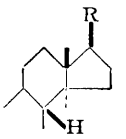
(VII)

Attention was next directed to the preparation of the parent tetracyclic alcohol, laudanol, and its derivatives. The preparation of laudenyl acetate by direct crystallisation of the mixture obtained by hydrogen chloride isomerisation of *cyclo*laudanyl acetate is accompanied by considerable losses. Application of the method previously described for the preparation of lanost-9(11)-enyl acetate (IV; R = C_8H_{17}) from the mixture obtained by treatment of *cyclo*artanyl acetate with hydrogen chloride (Bentley, Henry, Irvine, and Spring, *loc. cit.*) was more efficient. Treatment of the acetate mixture, m. p. 145—155°, with chromic acid under mild conditions, followed by chromatography, gave three homogeneous compounds. The most easily eluted was laudenyl acetate identical with that obtained by direct crystallisation of the mixture, m. p. 145—155°. A second product is a yellow acetate, m. p. 186°, analysis of which agrees with the molecular formula $C_{33}H_{52}O_4$ (or a near homologue). It does not give a colour with tetranitromethane and shows the characteristic ultra-violet absorption spectrum of a fully transoid $\overset{|}{CO}\text{–}\overset{|}{C}\text{=}\overset{|}{C}\text{–}\overset{|}{CO}$ system, with a maximum at 2700 Å (ε = 7400). This compound is an analogue of 7 : 11-dioxolanost-8-enyl acetate (V; R = C_8H_{17}) and, like the latter, it is reduced by zinc dust and acetic acid to a saturated diketone. The third product of the reaction was isolated in only small yield; analysis supported the formula $C_{33}H_{54}O_3$ (or a near homologue). It does not give a colour with tetranitromethane and shows the ultra-violet absorption spectrum of an $\alpha\beta$-unsaturated ketone with a maximum at 2410 Å (ε = 11,400). It is an analogue of 12-oxolanost-9(11)-enyl acetate (VI; R = C_8H_{17}) and it is obtained in high yield by oxidation of laudenyl acetate with chromic acid.

Catalytic hydrogenation of the acetate mixture, m. p. 145—155°, obtained from *cyclo*laudanyl acetate by treatment with hydrochloric acid, and treatment of the mixture

with chromic acid, followed by chromatography, gave the saturated laudanyl acetate as major product and dioxolaudenyl acetate as minor product. From laudanyl acetate, laudanol, laudanone, and laudane were prepared by standard methods.

The reactions of *cyclo*laudanol described above exactly parallel those of *cyclo*artanol and this striking similarity extends to the molecular-rotation relations of corresponding derivatives, as shown in the following Table. As a consequence of this exact parallelism,

	M_D			Δ_1	Δ_2
	Alcohol	Acetate	Ketone		
Laudanol	+ 93°	+155°	+ 62°	+62°	−31°
Lanostanol (artanol)	+150	+193	+116	+43	−34

Acetate	M_D	Δ [a]	Acetate	M_D	Δ [b]
Laudanyl	+155°	—	Lanostanyl	+193°	—
*cyclo*Laudanyl	+242	+ 87°	*cyclo*Artanyl	+247	+ 54°
Laudenyl	+387	+232	Lanost-9(11)-enyl	+400	+207
Oxolaudenyl	+434	+279	12-Oxolanost-9(11)-enyl	+440	+247
Dioxolaudenyl	+364	+209	7 : 11-Dioxolanost-8-enyl	+460	+267
Dioxolaudanyl	+257	+102	7 : 11-Dioxolanostanyl	+320	+127

[a] Δ Value is M_D (derivative)—M_D (laudanyl acetate). [b] Δ Value is M_D (derivative)—M_D (lanostanyl acetate).

we provisionally conclude that *cyclo*laudenol has the same nuclear structure as *cyclo*artenol and that the two alcohols differ solely in the nature of the side chain.

Experimental

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

Non-saponifiable Fraction of Opium Marc.—Opium marc (1 kg.) was extracted with boiling chloroform (2 × 4 l.), the combined extracts were evaporated, and the residue was dissolved in ether (4 l.) and washed with 3N-hydrochloric acid. The brown gum (180 g.), obtained on removal of solvent, was extracted with a mixture of boiling benzene (300 ml.) and ethanol (2 l.), and the extract decanted from a rubber-like material (10 g.). The extract was refluxed with a saturated solution of potassium hydroxide (120 g.) for 3 hr. The non-saponifiable fraction (43 g.) was isolated by means of ether in the usual manner. A solution of the non-saponifiable fraction in acetone (100 ml.) was kept at room temperature, and the crystalline solid separating (18·5 g.) was collected. A second crop (2·5 g.) was obtained by keeping the mother-liquor at room temperature. The acetone-soluble fraction of the non-saponifiable fraction of opium has not been examined in detail.

(+)-n-*Nonacosan*-10-*ol*.—A solution of the crystalline solid (21 g.) in benzene (500 ml.) was percolated through a column (4·5 × 32 cm.) of alumina (520 g.), and the chromatogram eluted with (*a*) benzene (4·1), (*b*) benzene–ether (19 : 1; 6 l.), (*c*) benzene–ether (19 : 1; 2·5 l.), (*d*) benzene–ether (9 : 1; 9 l.), (*e*) benzene–ether (4 : 1; 4·5 l.), (*f*) benzene–ether (1 : 1; 3 l.), (*g*) benzene–ether (1 : 1; 4·5 l.), and (*h*) benzene–methanol (9 : 1; 1·5 l.). Evaporation of solution (*b*) gave a solid (3·2 g.) which when crystallised from ethyl acetate yielded (+)-*n*-nonacosan-10-ol as prisms, m. p. 81—82°, $[\alpha]_D$ ±0° (*c*, 2·5) (Found : C, 81·8; H, 14·2. Calc. for $C_{29}H_{60}O$: C, 82·0; H, 14·2%).

(+)-*n*-Nonacosan-10-yl acetate, prepared from the alcohol by using acetic anhydride and pyridine, separated from ethyl acetate as plates, m. p. 44·5—45·5° (Found : C, 79·6; H, 13·3. Calc. for $C_{31}H_{62}O_2$: C, 79·8; H, 13·4%).

n-*Nonacosan*-10-*one*.—A solution of (+)-*n*-nonacosan-10-ol (500 mg.) in acetic acid (100 ml.) was treated at 50° with a solution of chromic acid (110 mg.) in acetic acid (25 ml.), during 30 min. After 16 hr. at room temperature, methanol (5 ml.) was added, and the product isolated by means of ether. Crystallisation from ethyl acetate gave *n*-nonacosan-10-one as plates (427 mg.), m. p. 74·5—75·5° (Found : C, 82·4; H, 14·0. Calc. for $C_{29}H_{58}O$: C, 82·4; H, 13·8%).

n-*Nonacosane*.—A mixture of *n*-nonacosan-10-one (225 mg.), hydrazine hydrate (100%, 2 ml.), and a solution of sodium ethoxide (from 250 mg. of sodium) in absolute ethanol (15 ml.)

was kept at 200—210° for 18 hr. The product, isolated in the usual manner, crystallised from ethyl acetate as plates (186 mg.), m. p. 63—64° (Found: C, 84·8; H, 14·8. Calc. for $C_{29}H_{60}$: C, 85·2; H, 14·8%).

cyclo*Laudenol*.—Evaporation of the combined fractions (*c*)—(*f*) from the chromatogram gave a gum (12·4 g.) which readily crystallised from methanol to yield cyclo*laudenol* as needles (6 g.), m. p. 125°, $[\alpha]_D$ +46° (*c*, 1·5) (Found: C, 84·6, 84·4; H, 11·9, 12·1. $C_{31}H_{52}O$ requires C, 84·5; H, 11·9%). The alcohol gives a pale yellow colour with the tetranitromethane reagent. Light absorption: Max. at 2050 Å (ε = 1145). In the Liebermann–Burchard test *cyclo*laudenol gives a blood-red solution with a strong green fluorescence.

*cyclo*Laudenol (250 mg.), acetic anhydride (5 ml.), and pyridine (10 ml.) for 12 hr. at room temperature gave the *acetate*, which separates from chloroform–methanol as blades, m. p. 120—121°, $[\alpha]_D$ +55° (*c*, 1·5) (Found: C, 82·3; H, 11·5. $C_{33}H_{54}O_2$ requires C, 82·1; H, 11·3%).

*cyclo*Laudenol (400 mg.) in pyridine (5 ml.) was heated with benzoyl chloride (1 ml.) for 1½ hr. The *benzoate* crystallised from chloroform–methanol as needles, m. p. 194—195°, $[\alpha]_D$ +63° (*c*, 0·9) (Found: C, 83·5; H, 10·5. $C_{38}H_{56}O_2$ requires C, 83·8; H, 10·4%). Hydrolysis with 5% ethanolic potassium hydroxide gave *cyclo*laudenol, m. p. and mixed m. p. 125°, $[\alpha]_D$ +45° (*c*, 1·0).

cyclo*Laudenone*.—A solution of *cyclo*laudenol (460 mg). in acetic acid (100 ml.) was stirred at room temperature, and chromic acid (95 mg.) in acetic acid (20 ml.) added during 30 min. Next morning the neutral product was isolated in the usual way, and crystallised from methanol to yield cyclo*laudenone* as blades (285 mg.), m. p. 115°, $[\alpha]_D$ +19° (*c*, 1·3) (Found: C, 84·3; H, 11·6. $C_{31}H_{50}O$ requires C, 84·9; H, 11·5%).

cyclo*Laudanyl Acetate*.—*cyclo*Laudenyl acetate (500 mg.) in glacial acetic acid (150 ml.) was shaken with hydrogen and platinum (from 300 mg. of platinum oxide) for 30 min., absorption of hydrogen then having ceased. The product was crystallised from chloroform–methanol to give cyclo*laudanyl acetate* as needles (440 mg.), m. p. 132—133°, $[\alpha]_D$ +50° (*c*, 0·8) (Found: C, 81·8; H, 11·7. $C_{33}H_{56}O_2$ requires C, 81·8; H, 11·6%). It gives a pale yellow colour with tetranitromethane and shows no selective light absorption between 2000 and 2250 Å. Hydrolysis of *cyclo*laudanyl acetate with 3% ethanolic potassium hydroxide gave cyclo*laudanol*, which separates from methanol as needles, m. p. 133—134°, $[\alpha]_D$ +43° (*c*, 0·9) (Found: C, 83·9; H, 12·1. $C_{31}H_{54}O$ requires C, 84·1; H, 12·3%).

*Epoxy*cyclo*laudanyl Acetate*.—*cyclo*Laudenyl acetate (500 mg.) in chloroform (10 ml.) was treated at 0° with a chloroform solution of perbenzoic acid (1·7 ml., 106 mg./ml., 1·2 mol.). After 24 hr. at 0°, the product was isolated and twice crystallised from methanol to yield *epoxy*cyclo*laudanyl acetate*, as needles (336 mg.), m. p. 153—154°, $[\alpha]_D$ +54° (*c*, 1·8) (Found: C, 79·0; H, 10·9. $C_{33}H_{54}O_3$ requires C, 79·5; H, 10·9%).

cyclo*Laudenyl Acetate Dibromide*.—A solution of bromine in acetic acid (7·5 ml.; 15·1 mg./ml.; 1·1 mol.) was added to *cyclo*laudenyl acetate (300 mg.) in acetic acid at room temperature. The product separated as needles (210 mg.), m. p. 170—171° (decomp.). Crystallisation from chloroform–methanol gave the *dibromide* as needles, m. p. 179—180° (decomp.), $[\alpha]_D$ +38° (*c*, 1·0); the analysis was not satisfactory (Found: C, 62·7; H, 8·7. $C_{33}H_{54}O_2Br_2$ requires C, 61·7; H, 8·5%).

Ozonolysis of cyclo*Laudenyl Acetate*.—*cyclo*Laudenyl acetate (3 g.) in dry chloroform (150 ml.) was treated at −45° with ozonised oxygen (2 mols. of ozone) for 30 min. After attaining room temperature, the solution was treated with acetic acid (25 ml.), and portionwise with zinc dust (6 g.) during 30 min. with stirring. After 1 hour's stirring, the filtered solution was washed with water. The aqueous washings were combined, adjusted to pH 7·0, and treated with a saturated aqueous solution of dimedone (200 ml.). After 24 hr. at 0° the separated formaldehyde–dimedone compound (0·64 g., 35%) was collected and crystallised from ethanol, from which it separated as needles, m. p. and mixed m. p. 189—190° (Found: C, 69·5; H, 8·4. Calc. for $C_{17}H_{24}O_4$: C, 69·8; H, 8·3%). Evaporation of the dried chloroform solution gave a solid which was dissolved in light petroleum (200 ml.) and percolated through a column (2·75 × 18 cm.) of alumina (90 g.). Elution with light petroleum (1000 ml.) and light petroleum–benzene (3 : 1; 1400 ml.) gave a fraction (2·0 g.) which, after crystallisation from methanol, gave *oxonor*cyclo*laudanyl acetate* as needles, m. p. 140—141°, $[\alpha]_D$ +61° (*c*, 1·3) (Found: C, 79·2; H, 10·8. $C_{32}H_{52}O_3$ requires C, 79·3; H, 10·8%). The *oxime* separated from methanol as needles, m. p. 160—161°, $[\alpha]_D$ +54° (*c*, 0·8) (Found: C, 77·0; H, 10·6. $C_{32}H_{53}O_3N$ requires C, 76·9; H, 10·7%).

Treatment of cyclo*Laudanyl Acetate with Hydrogen Chloride*.—A solution of the acetate (1 g.) in dry chloroform (50 ml.) at 0° was treated with a stream of dry hydrogen chloride

for 3 hr. The product, isolated in the usual manner, crystallised from chloroform–methanol as needles (770 mg.), m. p. 145—155°, $[\alpha]_D$ +62° (*c*, 1·5), showing a strong yellow colour with tetranitromethane. Light absorption: Max. at 2080 Å (ε = 3100).

Laudenyl Acetate.—(i) Six crystallisations of the acetate mixture, m. p. 145—155° (770 mg.), described above, from chloroform–methanol gave *laudenyl acetate* as needles (60 mg.), m. p. 173—174°, $[\alpha]_D$ +81° (*c*, 0·9) (Found: C, 81·4; H, 11·5. $C_{33}H_{56}O_2$ requires C, 81·8; H, 11·6%). Light absorption: Max. at 2060 Å (ε = 3100).

(ii) Chromic acid (440 mg.) in 90% acetic acid (25 ml.) was added during 5 min. to a solution of the acetate mixture, m. p. 145—155° (1·47 g.), in acetic acid (100 ml.) at 90°. The mixture was heated for a further 10 min. and diluted with water, and the product (1·46 g.) isolated by means of ether. A solution of this solid in light petroleum (100 ml.) was filtered through a column (2 × 16 cm.) of alumina (45 g.), and the chromatogram eluted with (*a*) light petroleum (1·1 l.), (*b*) light petroleum–benzene (4 : 1; 1·3 l.), (*c*) light petroleum–benzene (1 : 1; 600 ml.), (*d*) benzene (200 ml.), and (*e*) benzene (500 ml.). Fraction (*a*) (610 mg., m. p. 171—173°) was twice crystallised from chloroform–methanol to give laudenyl acetate, m. p. 173°, $[\alpha]_D$ +80° (*c*, 1·4) (Found: C, 81·8; H, 11·9%). A mixture with the specimen obtained by method (i) was undepressed in m. p.

Dioxolaudenyl Acetate.—Fraction (*c*) from the chromatogram described above was evaporated. The yellow crystalline solid (270 mg., m. p. 184—185°) was crystallised from methanol to give *dioxolaudenyl acetate* as light yellow blades, m. p. 186°, $[\alpha]_D$ +71° (*c*, 1·1) (Found: C, 77·0; H, 10·5. $C_{33}H_{52}O_4$ requires C, 77·3; H, 10·2%). Light absorption: Max. at 2700 Å (ε = 7400).

Oxolaudenyl Acetate.—(i) Chromic acid (300 mg.) in acetic acid was added during 1 hr. to a refluxing solution of laudenyl acetate (300 mg.) in acetic acid (50 ml.), and heating continued for 2 hr. The neutral product, isolated by means of ether, in light petroleum (25 ml.) was filtered through a column (1 × 14 cm.) of alumina (9 g.). Elution with light petroleum (125 ml.) gave a fraction, crystallisation of which from methanol yielded laudenyl acetate in blades (30 mg.), m. p. and mixed m. p. 171—172°. Elution with light petroleum–benzene (1 : 1; 150 ml.), benzene (75 ml.), and benzene–ether (4 : 1; 75 ml.) gave a fraction 130 mg.), which after several crystallisations from methanol yielded *oxolaudenyl acetate* as blades, m. p. 194°, $[\alpha]_D$ +87° (*c*, 0·9) (Found: C, 80·0; H, 10·9. $C_{33}H_{54}O_3$ requires C, 79·5; H, 10·9%). Light absorption: Max. at 2410 Å (ε = 10,300).

(ii) Fraction (*e*) from the chromatogram used in the preparation of laudenyl acetate was evaporated, and the solid (m. p. 188—189°, 120 mg.) twice crystallised from methanol to give oxolaudenyl acetate as blades, m. p. 188—189°, $[\alpha]_D$ +85° (*c*, 1·4), undepressed in m. p. when mixed with the specimen described above.

Dioxolaudanyl Acetate.—Zinc dust (1 g.) was added portionwise to a refluxing solution of dioxolaudenyl acetate (50 mg.) in acetic acid (10 ml.), and refluxing continued for 1 hr. The product, isolated by means of ether, crystallised from methanol to give *dioxolaudanyl acetate* as plates (34 mg.), m. p. 241°, $[\alpha]_D$ +50·5° (*c*, 1·5) (Found: C, 77·2; H, 10·7. $C_{33}H_{54}O_4$ requires C, 77·0; H, 10·6%).

Laudanyl Acetate.—A solution of the acid-isomerisation mixture from *cyclo*laudanyl acetate (m. p. 145—155°, 3·2 g.) in glacial acetic acid (300 ml.) was shaken at 80° for 7 hr. with hydrogen and platinum (1·5 g.). The product crystallised from chloroform–methanol as needles (2·1 g.), m. p. 153—156°, $[\alpha]_D$ +35° (*c*, 1·3). A solution of this mixture in acetic acid (300 ml.) was treated on the steam-bath with a solution of chromic acid (1·2 g.) in acetic acid (75 ml.) added during 30 min. The mixture was heated for 1 hr., the neutral product (2·0 g.) isolated in the usual manner and dissolved in light petroleum (150 ml.), and the solution percolated through a column (2·25 × 16 cm.) of alumina (60 g.). Elution with light petroleum (1500 ml.) gave *laudanyl acetate* (600 mg.) which separated as needles from chloroform–methanol, m. p. 171°, $[\alpha]_D$ +32° (*c*, 1·2) (Found: C, 81·2; H, 12·3. $C_{33}H_{58}O_2$ requires C, 81·4; H, 12·0%). Elution with light petroleum–benzene (4 : 1; 450 ml.) yielded a fraction (170 mg.) which separated as pale yellow needles from methanol, m. p. 183—184°, alone or mixed with dioxolaudenyl acetate, $[\alpha]_D$ +67·5° (*c*, 0·6). Light absorption: Max. at 2720 Å (ε = 6900).

Laudanol.—Hydrolysis of laudanyl acetate in 3% ethanolic potassium hydroxide followed by crystallisation of the product from chloroform–methanol yielded *laudanol* as fine needles, m. p. 200—201°, $[\alpha]_D$ +21° (*c*, 0·9) (Found: C, 84·0; H, 12·8. $C_{31}H_{56}O$ requires C, 83·7; H, 12·7%).

Laudanone.—Oxidation of laudanol (500 mg.) with chromic acid (100 mg.) in acetic acid (20 ml.) for 12 hr. at room temperature and isolation of the neutral product in the usual

manner, gave *laudanone* (360 mg.), which separated as plates from chloroform–methanol, m. p. 131—132°, $[\alpha]_D$ +14° (*c*, 1·0) (Found: C, 84·1; H, 12·5. $C_{31}H_{54}O$ requires C, 84·1; H, 12·3%).

Laudane.—A mixture of laudanone (200 mg.), hydrazine hydrate (100%, 2 ml.), and sodium ethoxide (from 250 mg. of sodium) in ethanol (10 ml.) was kept at 200° for 18 hr. A solution of the dried product, isolated by means of ether, in light petroleum (25 ml.) was filtered through a column (1 × 9 cm.) of alumina (6 g.). Elution with light petroleum (50 ml.) gave a fraction (145 mg.) which after crystallisation from chloroform–methanol yielded *laudane* as plates, m. p. 142—143°, $[\alpha]_D$ +25° (*c*, 1·7) (Found: C, 87·0; H, 13·2. $C_{31}H_{56}$ requires C, 86·8; H, 13·2%).

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