679. *The Chemistry of Santonin. Part IV.* Some Irradiation Products of the Santonins.*

By WESLEY COCKER, K. CROWLEY, J. T. EDWARD, T. B. H. MCMURRY, and E. R. STUART.

The chemistry of the compounds obtained by the irradiation of aqueous solutions of potassium santoninate and potassium 11β(H)-santoninate with ultraviolet light is discussed.

THE action of sunlight on santonin (I) has been the subject of considerable study. Francesconi and Maggi [1] isolated photosantonic acid, $C_{15}H_{22}O_5$, a dibasic acid, from a solution of santonin containing one equivalent of potassium hydroxide, which had been exposed to sunlight. The corresponding lactone, photosantonolactonic acid, $C_{15}H_{20}O_4$, was obtained when photosantonic acid was heated. When, however, a solution of santonin containing three equivalents of potassium hydroxide was exposed to sunlight, photosantoninic acid, $C_{30}H_{42}O_9$, was obtained. Irradiation of an ethanolic solution of santonin gave [2] photosantonin, the ethyl ester of photosantonolactonic acid, as well as photosantonic acid, and a further compound, $C_{17}H_{24}O_4$, whilst irradiation of an acetic acid solution of santonin gave yet another compound, $C_{30}H_{38}O_7$, photosantonic acid, and *iso*photosantonic acid. The lactone of the latter acid has recently been shown [3] to have structure (II), which has been assigned by Perold [4] to geigerin, the bitter principle of the so-called vomiting bush.

We have found that when potassium santoninate in neutral aqueous solution is subjected to the light from a 500 watt ultraviolet lamp, and the product acidified, a monobasic acid, $C_{15}H_{20}O_4,H_2O$ is obtained as the main crystalline product. We propose to name it lumisantoninic acid, and on the basis of evidence described below, assign to it structure (III).

The acid displays ultraviolet absorption maxima at 2480 (log ε 3·7) and 3350 Å (log ε 2·37), indicative of a trisubstituted C=C conjugated with a C=O grouping. The intensity of absorption at the higher wavelength is unusually high although a somewhat similar intensity (log ε 2·59 and 2·32 at 2930 Å) was encountered by Herout and Šorm [5] in the case of the unsaturated, but not conjugated lactones, oxopelenolide-a and -b. Peaks in the infrared spectrum (in Nujol) which occur at 3550 (OH), 2600 (CO_2H), 1728 (CO_2H), 1695 (αβ-unsaturated ketone), and 1576 cm.$^{-1}$ (ethylenic linkage of αβ-unsaturated ketone) are in agreement with structure (III).

Whilst the acid readily affords its lactone, lumisantonin, $C_{15}H_{18}O_3$ (IV), when heated

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* Part II, *J. Pharm. Pharmacol.*, 1956, **8**, 1097; Part III, *J.*, 1956, 4549.

[1] Francesconi and Maggi, *Gazetta*, 1903, **33**, II, 65.

[2] Villauechia, *Atti R. Accad. Lincei*, 1885, IV, **1**, 723; *Ber.*, 1885, **18**, 2861.

[3] Barton, de Mayo, and Shafiq, *J.*, 1957, 929.

[4] Perold, *J.*, 1957, 47.

[5] Herout and Šorm, *Chem. Listy*, 1956, **50**, 586; *Coll. Czech. Chem. Comm.*, 1956, **21**, 1494.

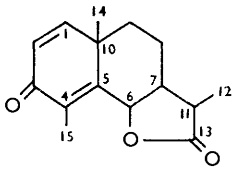
alone or with acetic anhydride, lactonisation also takes place quantitatively with cold ethereal diazomethane. The presence of a γ-hydroxyl group is thus established. Lactonisation of the acid involves loss of two molecules of water, the second of which is present in the acid as hydrate. The lactone has ultraviolet and infrared spectra similar to those of its acid. Thus it shows maxima (in EtOH) at 2400 (log ε 3·67) and 3380 Å (log ε 2·41) and (in $CHCl_3$) at 1772 (butanolide), 1696 (keto), and 1572 cm.$^{-1}$ (C=C).

Ozonolysis of the lactone (IV) gives a gum which rapidly reduces Tollens's reagent, and gives a positive iodoform reaction. Tests for aldehyde were negative.

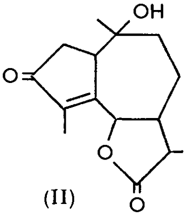
Reduction of lumisantoninic acid (III) and its lactone (IV) over palladised charcoal or Adams catalyst affords dihydrolumisantoninic acid (V) and dihydrolumisantonin (VI). The keto-group is reduced in small yield by the latter catalyst, but only after very long periods. This fact indicates distortion in the molecule and is reminiscent of the chemistry of santonic acid,[6] a contrast to the case of santonin itself which readily yields hexahydro-derivatives with the platinum catalyst.[7] Dihydrolumisantonin (VI) can also be obtained from dihydrolumisantoninic acid (V) by heating it alone or with acetic anhydride or by treating it with ethereal diazomethane.

Dihydrolumisantoninic acid (V) exhibits an ultraviolet maximum at 2825 Å (log ε 1·96) which is characteristic of an isolated keto-group. A second peak at 2220 Å (log ε 3·74) indicates some measure of conjugation. The fact that the acid is inert to ozone, osmium tetroxide, and catalytic reduction eliminates an $\alpha\beta$-unsaturated acid structure. Dihydrolumisantonin (VI), also inert to the reagents mentioned, shows no peak at 2220 Å, but the intensity at this wavelength is high (log ε 3·74). It is not an $\alpha\beta$-butenolide which would show a peak with higher intensity and at a higher wavelength.[8] The infrared spectrum of the acid (V) includes maxima at 3600, 1725, and 1690 cm.$^{-1}$ (CO_2H and CO), but no ethylenic absorption, whilst the lactone (VI) show strong bands at 1778 (butanolide) and 1712 cm.$^{-1}$ (isolated keto-group in a six-membered ring), and no unsaturation.

The analytical data for lumisantonin and its acid require, however, that there should be either a second carbon–carbon double bond or a further ring system, but lumisantonin gives only a dihydroxy-derivative with osmium tetroxide.



(I)



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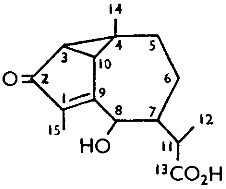

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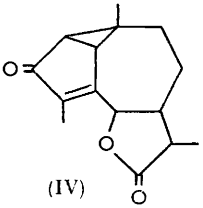

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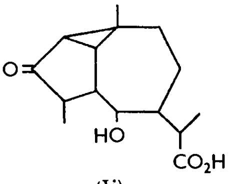

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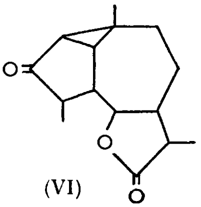

(VI)

The facts detailed above strongly suggest that lumisantonin and its dihydro-derivative, and the corresponding acids, have a *cyclo*propane system conjugated with the keto-group, as portrayed in the formulæ (III), (IV), (V), and (VI). This idea is reinforced by the fact that dihydrolumisantonin and its acid have spectra similar to that of dihydroumbellulone,[9]

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[6] Simonsen, " The Terpenes," Cambridge Univ. Press, 1952, Vol. III, p. 292.

[7] Cocker and McMurry, *J.*, 1956, 4549.

[8] Dauben and Hance, *J. Amer. Chem. Soc.*, 1955, **77**, 606.

[9] Eastman, *J. Amer. Chem. Soc.*, 1954, **76**, 4115; Eastman and Freeman, *ibid.*, 1955, **77**, 6642; Hawthorne, *J. Org. Chem.*, 1956, **21**, 1523.

a similarity which is absent from the spectra of the isomerisation products (XIV) and (XIX) (see below). Again dihydrolumisantonin semicarbazone ($\lambda_{max.}$ 2380 Å, log ε 4·38) and the semicarbazones of carone ($\lambda_{max.}$ 2355 Å, log ε 4·14) and dihydroumbellulone [9] have similar spectra which are characteristic of a ketone semicarbazone group conjugated with the *cyclo*propane system. The semicarbazone of the isomerisation product (XIX) shows the absorption ($\lambda_{max.}$ 2280 Å, log ε 4·25) of an isolated ketone semicarbazone. Further evidence suggesting the presence of the conjugated *cyclo*propane system comes from the spectrum of the 2 : 4-dinitrophenylhydrazone of dihydrolumi-11β(H)-santoninic acid (Vβ; see below) whose maximum absorption is at 3725 Å (log ε 4·28) (cf. Hawthorne [9]).

As mentioned above, extended reduction of lumisantoninic acid (III) over Adams catalyst affords an acid, $C_{15}H_{24}O_4$, probably the acid of the lactone (VII), in very small yield. It shows no maximum in the ultraviolet region (log ε 2·32 at 2210 Å). By contrast, treatment of dihydrolumisantonin (VI) with potassium borohydride readily gives the olefin (VIII) in good yield, formed presumably from the alcohol (VII). The structure of the olefin is demonstrated by ozonolysis to a product possessing the properties of a methyl ketone (positive iodoform reaction) and aldehyde (positive Schiff's test), and showing infrared maxima (in $CHCl_3$) at 1720 (ketone), 1770 (lactone), and 2750 cm.$^{-1}$ (aldehyde). Such dehydration is unusual but may result from release of strain in the molecule

Reduction of lumisantoninic acid (III) over Raney nickel in an autoclave, followed by dehydrogenation of the product, afforded 7-ethyl-1-methylnaphthalene in high yield. Traces of azulene were also formed but not characterised.

The experiments described above indicate that lumisantoninic acid (III) and lumisantonin (IV) possess either the original eudesmane skeleton of santonin or a closely related ring system, together with the 4-en-3-one system.

Lumisantonin has three methyl groups. This is shown by a comparison of the intensity of the methyl bands [10] at 1383 cm.$^{-1}$ in a number of santonin derivatives (see Table). Further, the products formed by rearrangement of lumisantonin with hydrogen chloride and with deuterium chloride have identical intensities in the 1456 cm.$^{-1}$ (CH_2) band and in the 1383 cm.$^{-1}$ (CH_3) band, thus showing that no new methyl or " unperturbed " [11] methylene group has been produced during the rearrangement. However, the information to be gained from intensity measurements of the 1456 cm.$^{-1}$ band is of limited value, since it is probable that groups other than CH_2 contribute to this complex peak.[11]

Compound	Infrared max. (cm.$^{-1}$) (Me ~1383)	ε_0	No. of Me	ε_0/Me
Santonin	1382	64	3	21
,,	1385	67·5	3	22·5
,,	1383	66	3	22
,,	1382	69	3	23
Lumisantonin (IV)	1383	63	3	21
Dihydrolumisantonin (VI)	1382	50	3	17
(XIV); HCl rearrangement product of (IV)	1384	81	3	27
DCl rearrangement product of (IV)	1384	81	3	27
(XIX); HCl rearrangement product of (VI)	1383	50	3	17
DCl rearrangement product of (VI)	1383	50	3	17
(XVII)	1382	38	2	19
Limonene	1373	35	2	17·5
Marrubiin [12]	1386	54	3	18

Several rational formulæ may be suggested for lumisantonin. Thus the *cyclo*propane (IX), which could arise from santonin by a light-catalysed Michael-type addition of the $C_{(14)}$-anion to the 1 : 2-double bond might show some transannular conjugation. This, however, has only two methyl groups. Models show that (X), a structure related to

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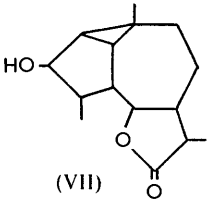
[10] Barton, Page, and Warnhoff, *J.*, 1954, 2715.

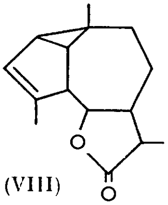
[11] Jones and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 5648; Jones, Cole, and Nolin, *ibid.*, p. 5662.

[12] Cocker, Cross, Duff, Edward, and Holley, *J.*, 1953, 2540; Burn and Rigby, *Chem. and Ind.*, 1955, 386.

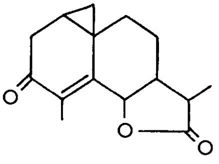
santonic acid (XI),[13] is sterically impossible. The same objection applies to (XII).[13] Further, the lactone (XIII) formed by reduction of santonic acid with borohydride is unaffected by the acidic conditions under which lumisantonin is rearranged.



(VII)



(VIII)



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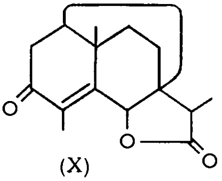

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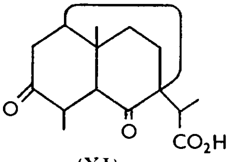

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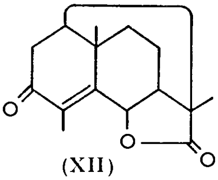
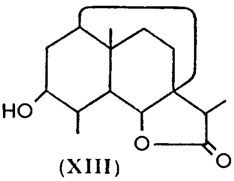


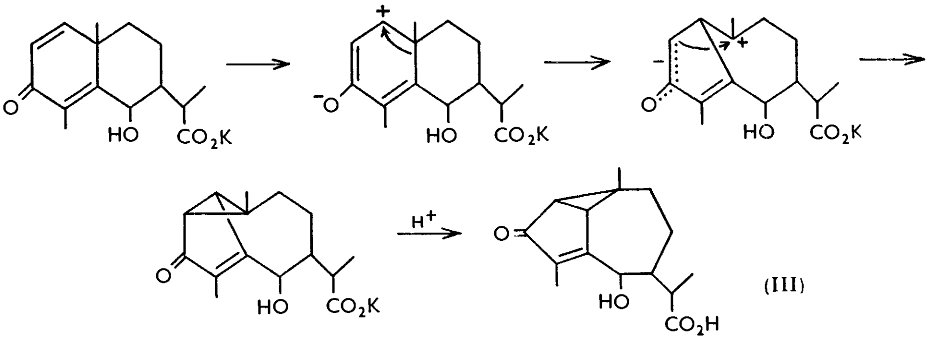
(XII)



(XIII)

We believe that lumisantonin is best expressed by (IV) and its acid by (III).* These compounds can be produced from santonin by the series of photocatalysed reactions shown in the annexed scheme (cf. ref. 3). In structures (III) and (IV) the ring system is rather strained which is probably responsible for the unusual intensities of the ketone bands in the ultraviolet spectrum. The conjugation of the *cyclo*propane system with the ketone group accounts for the maximum at 2220 Å shown by dihydrolumisantoninic acid (V), though the degree of conjugation is susceptible to small increases in ring strain, since the peak does not appear in the corresponding lactone (VI).

*cyclo*Propanes are well known to undergo cleavage with mineral acids. It is not surprising therefore that lumisantonin (IV) and its dihydro-derivative (VI) undergo isomeric change with acid. Treatment of the former with hydrogen chloride in chloroform [14] gives the guaienolide, 4-chloro-2-oxoguai-9-en-8 : 13-olide (XIV), and a new active carbon–carbon double bond is created. This lactone (XIV) shows infrared maxima



(in $CHCl_3$) at 1778 (butanolide), 1753 (*cyclo*pentanone), and 1620 cm.$^{-1}$ (isolated C=C). In the ultraviolet spectrum there is a maximum at 2970 Å (log ε 1·48). Ozonolysis affords a gum which gives a green ferric reaction, and reduces Tollens's reagent (potential α-ketol), but fails to reduce Schiff's reagent. Conclusive evidence that this acid-catalysed isomeric

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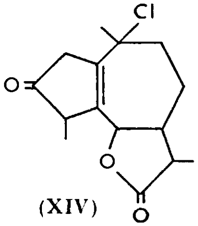
* An alternative formulation with the $C_{(14)}$ transposed from $C_{(4)}$ to $C_{(10)}$ does not account so well for the formation of the acid-catalysed isomerisation products.

[13] Woodward, Brutschy, and Baer, *J. Amer. Chem. Soc.*, 1948, **70**, 4216.

[14] Barton, *J.*, 1951, 1444; cf. Büchi and White, *J. Amer. Chem. Soc.*, 1957, **79**, 750.

change takes place, and that the product is a guaienolide comes from the fact that when boron trifluoride in acetic acid is the isomerising agent lumisantonin affords 4-acetoxy-2-oxoguai-1(9)-en-8 : 13-olide, the acetate of (II). This compound is obtained along with *iso*photosantonic acid lactone (II)[2,3] when santonin is irradiated in aqueous acetic acid (cf. Barton, de Mayo, and Shafiq[3]). The acetate shows absorption at 2370 (log ε 4·2) and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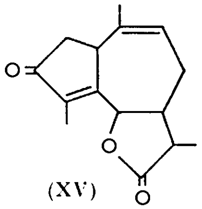
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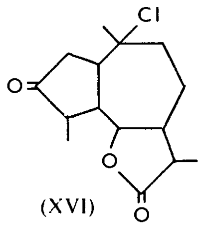
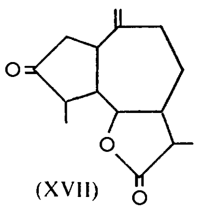

(XVI)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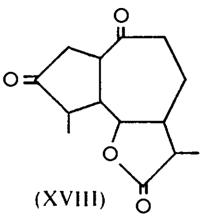
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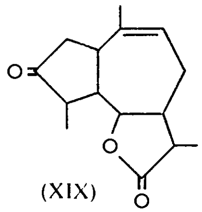
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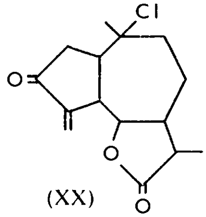
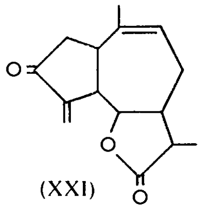

(XX)


(XXI)

3090 Å (log ε 1·73). The unsaturated compound 2-oxoguai-1(15) : 4-dien-8 : 13-olide (XXI) is also obtained in the isomerisation. The latter shows maximum absorption at 2195 (log ε 4·14) and 3245 Å (log ε 1·91) in the ultraviolet and at 1775 (lactone), 1716 (*cyclo*-pentenone), 1647 and 1602 (C=C), 925(>C=CH_2), and 832 cm.$^{-1}$ (–$\overset{|}{\text{C}}$=CH) in the infrared spectrum.

Further evidence for the azulenic nature of the isomerisation products mentioned above arises from the fact that when the unsaturated lactone (XIX) is reduced with lithium aluminium hydride and then dehydrogenated a blue oil, whose spectrum is similar to that of guiazulene or chamazulene, is obtained.

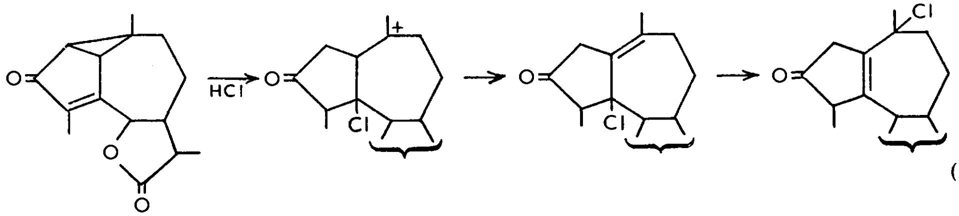
Dehydrochlorination of compound (XIV) gives the conjugated unsaturated ketone, 2-oxoguai-1(9) : 4-dien-8 : 13-olide (XV), which as expected shows maxima at 2375 (log ε 3·8) and 3420 Å (log ε 2·42). The infrared spectrum shows maxima at 1780 (butanolide), 1695 (*cyclo*pentenone), and 1579 cm.$^{-1}$ (conjugated C=C). The unconjugated double bond is placed in the endocyclic position since in the infrared spectrum there is a strong peak at 835 cm.$^{-1}$ characteristic of a trisubstituted double bond. This lactone (XV) differs from that obtained by Barton, de Mayo, and Shafiq[3] by dehydration of (II), which has its isolated double bond in the adjacent exocyclic position. We are grateful to Professor Barton for a sample of his product.

Reduction of 4-chloro-2-oxoguai-9-en-8 : 13-olide (XIV) over platinum rapidly gives its dihydro-compound (XVI). The new compound (XVI) shows infrared maxima (in $CHCl_3$) at 1774 (butanolide) and 1739 cm.$^{-1}$ (*cyclo*pentanone), and on dehydrochlorination gives 2-oxoguai-4(14)-en-8 : 13-olide (XVII) whose structure follows from the following evidence. It shows a single ultraviolet maximum at 2950 Å (log ε 1·69), and infrared maxima at 1775 (butanolide), 1742 (*cyclo*pentanone), and 1630 cm.$^{-1}$ (isolated C=C). The intensity of the methyl peak at 1382 cm.$^{-1}$ (see Table) shows the presence of *two* methyl groups. The exocyclic methylene group is also shown to be present by an infrared band at 908 cm.$^{-1}$. Ozonolysis of this methylene-ketone (XVII) gives the diketo-lactone (XVIII) whose infrared spectrum includes maxima at 1782 (butanolide), 1748 (*cyclo*pentanone), and 1710 cm.$^{-1}$ (*cyclo*heptanone).

Isomerisation of dihydrolumisantonin (VI) with hydrogen chloride in chloroform gives the unsaturated lactone (XIX), which is not identical with (XVII). The new lactone (XIX) shows a single ultraviolet maximum at 2830 Å (log ε 1·67), and infrared maxima at 1778, 1747, and 1640 cm.$^{-1}$; on ozonolysis it gives an aldehyde (positive Schiff's and Tollens's tests) and a methyl ketone (iodoform). The infrared spectrum of the gum confirms the assignment of structure; it has peaks at 2750 (aldehyde), 1780 (butanolide), 1748 cm.$^{-1}$ (*cyclo*pentanone), 1705 (carbonyl), and 1357 (COMe).

The isomerisation involved in the changes (IV) ⟶ (XIV) and (VI) ⟶ (XIX) by hydrogen chloride produces a new " perturbed " methylene group at $C_{(3)}$. This is shown by the following evidence. Peaks at 1402 (ε_0 40·7) and 1409 cm.$^{-1}$ (ε_0 32·3) in the products (XIV) and (XIX) have appreciably higher intensity than the corresponding peaks (ε_0 17·2 and 18·9 respectively) in the deuterated derivatives, these peaks being due to a methylene group next to a keto-group in a five-membered ring.[11] This evidence may be vitiated by hydrogen exchange, but it is a significant fact that all the isomerised products have a strong band in the 1402—1410 cm.$^{-1}$ region which is either absent or is very weak in the unisomerised compounds.

We envisage the isomerisation of lumisantonin as taking place by the annexed route.



(XIV)

Irradiation of 11β(H)-santoninic acid in presence of one equivalent of alkali gives a compound (A), stereoisomeric with lumisantoninic acid (III). We name it lumi-11β(H)-santoninic acid (IIIβ *). On occasion a second compound (B), $C_{15}H_{20}O_4,H_2O$, was also obtained (see below).

The spectra of lumi-11β(H)-santoninic acid (IIIβ) are similar to those of its isomer (III) (see p. 3426). The existence of the αβ-unsaturated ketone system is confirmed, however, by the formation of a 2 : 4-dinitrophenylhydrazone whose long-wavelength maximum is at 3830 Å (log ε 4·54). Ozonolysis gives a gum which rapidly reduces Tollens's reagent and gives a positive iodoform reaction.

Lumi-11β(H)-santoninic acid affords lumi-11β(H)-santonin (IVβ) on treatment with ethereal diazomethane, and on reduction over palladised charcoal or platinum the acid (IIIβ) affords dihydrolumi-11β(H)-santoninic acid (Vβ), which like its isomer (V) is unaffected by ozone. Dihydrolumi-11β(H)-santoninic acid (Vβ) yields its lactone, dihydrolumi-11β(H)-santonin (VIβ), on treatment with diazomethane, and this lactone may be obtained by the reduction of lumi-11β(H)-santonin (IVβ) over palladised charcoal. Dihydrolumi-11β(H)-santonin is inert to ozone.

Treatment of dihydrolumi-11β(H)-santoninic acid (Vβ) with potassium borohydride, followed by acidification, affords lactone (VIIβ) and dehydrogenation of this with palladised charcoal gives 7-ethyl-1-methylnaphthalene.

Lumi-11β(H)-santonin is isomerised with hydrogen chloride to the α-methylene-ketone (XX) whose spectrum shows bands at 2215 and 3320 Å (log ε 3·93 and 1·8 respectively) and at 1707 (*cyclo*pentenone), 1775 (lactone), and 1600 cm.$^{-1}$ (C=C). The formation of an αβ-unsaturated ketone (cf. XIV) may be the result of extended treatment with hydrogen chloride. The isomerisation product (XX) is smoothly reduced over platinum to the dihydro-compound (XVIβ), showing maxima at 2980 (log ε 1·54; but log ε 2·0 at 2150 Å) and 1740 cm.$^{-1}$, characteristic of a *cyclo*pentanone. Dehydrochlorination gives a diunsaturated compound, probably (XXIβ), which shows maxima at 2200 (log ε 4·05) and

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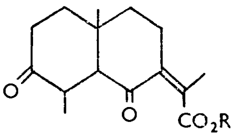
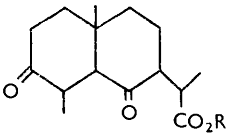
* We use the suffix *β* to indicate that the compound is obtained from 11*β*(H)-santonin.

3250 Å (log ε 1·82), characteristic of an αβ-unsaturated ketone, and at 1785 (lactone), 1720 (*cyclo*pentenone), 1645 (C=C), and 1602 cm.$^{-1}$ (C=C).

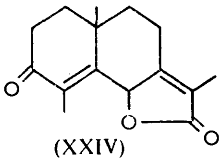
Rearrangement of dihydrolumi-11β(H)-santonin (VIβ) affords an unsaturated compound with a single ultraviolet maximum at 2840 Å (log ε 1·67) and infrared peaks at 1785, 1750 (*cyclo*pentanone), and 1645 cm.$^{-1}$ (C=C). By analogy with the product of isomerisation of the lumi-lactone (VI), the product from its stereoisomer (VIβ) is considered to have structure (XIXβ); its ozonolysis product shows maxima at 2750 (aldehyde), 1780 (lactone), 1748 (*cyclo*pentanone), 1727 (aldehyde), 1704 (ketone), 1356 cm.$^{-1}$ ($CO{\cdot}CH_3$).



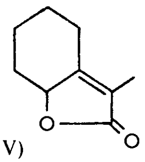
(XXII)



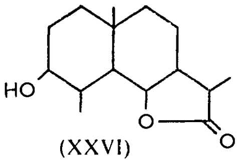
(XXIII)



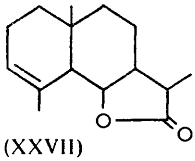
(XXIV)



(XXV)



(XXVI)



(XXVII)

The acid (B) mentioned above has the properties expected of 3 : 6-dioxoeudesm-7(11)en-13-oic acid (XXII; R = H). Although itself hydrated ($C_{15}H_{20}O_4,H_2O$) the acid gives an anhydrous methyl ester (XXII; R = Me) on treatment with diazomethane. The acid exhibits maximum ultraviolet absorption at 2180 Å (log ε 4·0), typical of an αβ-unsaturated acid,[15] and at 2900 Å (log ε 1·64) suggestive of an isolated keto-group, whilst a shoulder at 3200 Å (log ε 1·45) suggests an αβ-unsaturated ketone, the low-wavelength absorption of which is probably merged in the band at 2180 Å. In agreement with these interpretations, the acid exhibits maxima (in CH_2Cl_2) at 1712 (C:O and αβ-unsaturated acid), 1690 (αβ-unsaturated ketone) and 1645 cm.$^{-1}$ (C=C). Similar spectral data are manifested by the methyl ester (XXII; R = Me).

The acid (XXII; R = H) does not decolorise bromine in chloroform, but reacts with permanganate in acetone, and is reduced over platinum to give 3 : 6-dioxoeudesman-13-oic acid (XXIII; R = H) in a hydrated form. Reaction of this acid with diazomethane affords its anhydrous methyl ester (XXIII; R = Me) which may also be obtained by the reduction of methyl 3 : 6-dioxoeudesm-7(11)en-13-oate (XXII; R = Me). The reduced acid (XXIII; R = H) shows a single maximum at 2860 Å (log ε 1·6), whilst its ester shows two maxima at 2750 Å (log ε 1·75) and 2950 Å (log ε 1·58) indicative of isolated keto-groups. The reduced acid shows very strong infrared absorption (in $CHCl_3$) at 1715 (C:O and CO_2H) and weaker absorption at 1745 cm.$^{-1}$ (hindered or hydrogen-bonded C:O); the ester shows a single composite maximum at 1720 cm.$^{-1}$ (C:O and CO_2Me). The ester forms a monoxime which exhibits absorption at 1715 (C:O) and 1728 cm.$^{-1}$ (CO_2Me), but no recognisable C=N absorption; this is probably merged in the strong band at 1715 cm.$^{-1}$.

3 : 6-Dioxoeudesm-7(11)-en-13-oic acid (XXII; R = H) is lactonised only with difficulty and in small yield. The lactone (XXIV) shows maxima at 2200 (log ε 4·36) and 3250 Å (log ε 1·6), indicating respectively αβ-butenolide and αβ-unsaturated ketone systems, the low-wavelength absorption of the latter appearing as a shoulder at 2350 Å (log ε 4·37). Dauben and Hance [8] found that the αβ-butenolide (XXV) exhibits maximum absorption at 2170 Å (log ε 4·24). The infrared absorption of the lactone (XXIV) supports its structure, having maxima at 1758 (αβ-butenolide), 1700 (C:O), 1686 cm.$^{-1}$ (C=C). Dauben and

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[15] Barton and Seoane, *J.*, 1956, 4150; Cram and Allinger, *J. Amer. Chem. Soc.*, 1956, **78**, 5275.

Hance,[8] and Cocker, Cross, and Hayes,[16] respectively, found that the analogue (XXV) exhibited maxima at 1757 and 1750 cm.$^{-1}$.

3 : 6-Dioxoeudesman-13-oic acid (XXIII; R = H) is reduced by potassium borohydride, *four* hydrogen atoms being taken up, to give 3-hydroxyeudesman-6 : 13-olide (XXVI), which shows no significant ultraviolet absorption, but maxima at 3570 (OH) and 1754 cm.$^{-1}$ (lactone). Dehydrogenation of the lactone affords 7-ethyl-1-methylnaphthalene characterised as its picrate.

Dehydration of 3-hydroxyeudesman-6 : 13-olide (XXVI) with phosphorus oxychloride and pyridine gives the olefin (XXVII) which shows end-absorption at 2200 Å (log ε 2·01), and a maximum at 1760 cm.$^{-1}$ (butanolide). Ozonolysis of the olefin gives a gum which gives a positive Schiff's test, gives iodoform, and has infrared peaks at 2750 (aldehyde), 1770 (lactone), and 1720 cm.$^{-1}$ (C:O).

EXPERIMENTAL

Ultraviolet spectra were measured in ethanol solutions with a Beckman D.U. instrument, and the infrared spectra with a Hilger 800 double-beam instrument. The irradiations were performed with a Hanovia, 500 w ultraviolet lamp (U.V.S. 500 model).

Irradiation of Potassium Santoninate.—A mixture of santonin (125 g.), potassium hydroxide (28 g.), and water (500 c.c.) was heated for 45 min. and allowed to cool. The unchanged santonin was collected, and the filtrate was diluted with water to 750 c.c. (pH 8·0) and irradiated in quartz flasks for 48 hr. After 24 hr. the flasks were turned to allow light to enter, a deposit having formed on the sides of the flasks facing the lamp. The solution was extracted with chloroform to remove santonin (14 g.), acidified, and extracted with chloroform (4 × 75 c.c.). The chloroform solution gradually deposited *lumisantoninic acid* (III) (28 g.) as rhombs (from ethyl acetate), m. p. 142—143° (rapid heating), $[\alpha]_D^{21}$ −78·0° (*c* 2·2 in EtOH) (Found : C, 64·4; H, 7·9%; equiv., 278. $C_{15}H_{22}O_5$ requires C, 63·8; H, 7·8%; equiv., 282). Concentration of the mother-liquor and addition of ether (150 c.c.) to the residue gave an acid (6 g.) as needles, m. p. 154—155°, probably identical with photosantonlactonic acid (Found : C, 67·5; H, 7·8. Calc. for $C_{15}H_{20}O_4$: C, 68·2; H, 7·6%). Further quantities of lumisantoninic acid (11 g.) were obtained by removal of the ether and addition of ethyl acetate (75 c.c.) to the residue. The residual gum was then heated with acetic anhydride (50 c.c.) for 2 hr., the acetic anhydride removed, and the product dissolved in chloroform. Extraction of the chloroform solution with a saturated solution of sodium hydrogen carbonate gave on acidification more photosantonlactonic acid (14 g.).

Lumisantonin (IV).—(*a*) Lumisantoninic acid (1 g.) in methanol (10 c.c.) was treated with excess of diazomethane in ether. Removal of the solvents gave the *lactone* (IV) (0·5 g.) which crystallised from ethyl acetate–light petroleum (b. p. 60—80°) as plates, m. p. 155—156°, $[\alpha]_D$ −180° (*c* 1·5 in $CHCl_3$) (Found : C, 72·7; H, 7·3. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%).

(*b*) Lumisantoninic acid (0·2 g.) was heated with acetic anhydride (5 c.c.) on a water-bath for 15 min. Removal of the acetic anhydride and crystallisation of the residue from ethyl acetate–light petroleum (b. p. 60—80°) gave the lactone (IV) (0·14 g.), m. p. 154—155°.

(*c*) Lumisantoninic acid (1 g.) was heated at 150° for 10 min., to give the lactone (0·75 g.), m. p. 155—156°.

Dihydrolumisantoninic Acid (V).—(*a*) A mixture of lumisantoninic acid (1 g.), platinum oxide (0·2 g.), and ethyl acetate (100 c.c.) was stirred in hydrogen for 18 hr. The *product* (V) (0·5 g.) crystallised from ethyl acetate as needles, m. p. 146—147°, $[\alpha]_D^{17}$ −30·5° (*c* 1·5 in EtOH) (Found : C, 67·5; H, 7·9. $C_{15}H_{22}O_4$ requires C, 67·6; H, 8·3%).

(*b*) Lumisantoninic acid (1·3 g.) was reduced over platinum oxide (0·2 g.) in ethyl acetate (100 c.c.) for 48 hr., and the products were separated by crystallisation from ethanol, giving dihydrolumisantoninic acid (0·7 g.), m. p. 145—146°, and the *acid* (80 mg.), m. p. 174—175°, log ε 2·32 at 2210 Å (no max.) (Found : C, 66·9; H, 8·6. $C_{15}H_{24}O_4$ requires C, 67·1; H, 9·0%), corresponding to the lactone (VII).

Dihydrolumisantonin.—Lumisantonin (IV) (0·8 g.), platinum oxide (0·1 g.), and ethyl acetate (50 c.c.) were stirred in hydrogen for 18 hr. Crystallisation of the product from ethyl acetate gave *dihydrolumisantonin* (VI) (0·65 g.), as needles, m. p. 161—162°, $[\alpha]_D$ −52·6° (*c*

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[16] Cocker, Cross, and Hayes, *Chem. and Ind.*, 1952, 314.

1·6 in $CHCl_3$) (Found : C, 72·3; H, 7·8. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%) [*semicarbazone*, m. p. 265° (Found : C, 62·8; H, 7·4. $C_{16}H_{23}O_3N_3$ requires C, 62·9; H, 7·5%)].

Reduction of Dihydrolumisantonin.—A solution of dihydrolumisantonin (VI) (1 g.) and potassium borohydride (0·3 g.) in methanol (30 c.c.) and water (5 c.c.) was set aside for 24 hr., then acidified. The product, crystallised from ethanol, gave the *olefinic lactone* (VIII) (0·3 g.) as plates, m. p. 144—145°, $[\alpha]_D^{23}$ $-81·9°$; (*c* 1·3 in $CHCl_3$) (Found : C, 77·1; H ,8·6. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·7%).

This compound (0·12 g.) in methyl acetate (20 c.c.) was treated with excess of ozone at $-20°$, and the ozonide was reduced with hydrogen over 10% palladised charcoal (0·1 g.). The product was a gum, which gave positive reactions with Tollens's and Schiff's reagents, and also iodoform with sodium hypoiodite.

Dehydrogenation Experiments.—Lumisantoninic acid (7 g.) in methanol (100 c.c.) was reduced over Raney nickel (1 g.) at 100—120°/80 atm. of hydrogen. The oily product was heated with selenium (10 g.) at 280—300° for 30 hr. The mixture was extracted with ether, and the extract was distilled in steam, to give an oil (1·8 g.), b. p. 140°/20 mm. Redistillation gave an oil whose infrared spectrum was essentially identical with that of 1-ethyl-7-methylnaphthalene. The oil was further characterised by formation of a picrate, m. p. 96—97°, and styphnate, m. p. 126°, both undepressed on admixture with the respective derivatives of 1-ethyl-7-methylnaphthalene.

Oxidation of Lumisantonin with Osmium Tetroxide.—A solution of lumisantonin (IV) (0·11 g.) and osmium tetroxide (0·22 g.) in dioxan (9 c.c.) was set aside for 48 hr. The osmic ester was decomposed by hydrogen sulphide, and the product crystallised from ethyl acetate, to give *dihydrolumisantonindiol* (60 mg.) as rhombs, m. p. 185° (decomp.) (Found : C, 63·6; H, 7·1. $C_{15}H_{20}O_5$ requires C, 64·2; H, 7·2%).

4-*Chloro*-2-*oxoguai*-9-*en*-8 : 13-*olide* (XIV).—Lumisantonin (IV) (1 g.) in chloroform (20 c.c.) was treated with a stream of hydrogen chloride for 4 hr. The solution was washed with sodium hydrogen carbonate, then dried, and the chloroform was removed. Recrystallisation of the product from ethyl acetate–light petroleum (b. p. 60—80°) gave 4-*chloro*-2-*oxoguai*-9-*en*-8 : 13-*olide* (XIV) (0·52 g.) as needles, m. p. 151—152°, $[\alpha]_D^{20}$ $-186°$ (*c* 1·18 in $CHCl_3$) (Found : C, 63·6; H, 6·4. $C_{15}H_{19}O_3Cl$ requires C, 63·7; H, 6·7%).

2-*Oxoguai*-1(9) : 4-*dien*-8 : 13-*olide* (XV).—The previous compound (XIV) (0·2 g.), anhydrous sodium acetate (0·25 g.), and ethanol (15 c.c.) were refluxed for 1 hr. The product was recrystallised from aqueous ethanol, to give 2-*oxoguai*-1(9) : 4-*dien*-8 : 13-*olide* (XV) (60 mg.) as plates, m. p. 150—151°, $[\alpha]_D^{20}$ $-136·5°$ (*c* 0·26 in $CHCl_3$) (Found : C, 72·9; H, 7·1. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%).

4-*Chloro*-2-*oxoguaian*-8 : 13-*olide* (XVI).—4-Chloro-2-oxoguai-9-en-8 : 13-olide (XIV) (0·8 g.), platinum oxide (0·1 g.), and ethyl acetate (30 c.c.) were stirred in hydrogen for 4 hr. The product, recrystallised from ethanol, was 4-*chloro*-2-*oxoguaian*-8 : 13-*olide* (XVI) (0·6 g.), needles, m. p. 198—199°, $[\alpha]_D^{20}$ $-155·7°$ (*c* 0·53 in $CHCl_3$) (Found : C, 63·0; H, 7·4. $C_{15}H_{21}O_3Cl$ requires C, 63·3; H, 7·4%).

2-*Oxoguai*-4(14)-*en*-8 : 13-*olide* (XVII).—The above compound (XVI) (0·24 g.), anhydrous sodium acetate (0·3 g.), and ethanol (30 c.c.) were refluxed for 4 hr. The product was recrystallised from aqueous ethanol, to give 2-*oxoguai*-4(14)-*en*-8 : 13-*olide* (XVII) (0·1 g.) as rods, m. p. 105—106°, $[\alpha]_D^{23}$ $-0·5°$ (*c* 0·43 in $CHCl_3$) (Found : C, 72·5; H, 7·9. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%).

14-*Demethyl*-2 : 4-*dioxoguaian*-8 : 13-*olide* (XVIII).—2-Oxoguai-4(14)-en-8 : 13-olide (100 mg.) in methyl acetate (15 c.c.) was treated with excess of ozone at $-20°$. The ozonide was reduced with hydrogen over palladised charcoal, to give 14-*demethyl*-2 : 4-*dioxoguaian*-8 : 13-*olide* (70 mg.) as rhombs, m. p. 180—181° (Found : C, 67·1; H, 7·2. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%).

Ozonolysis of 4-*Chloro*-2-*oxoguai*-9-*en*-8 : 13-*olide* (XIV).—The chloro-ketone (0·1 g.) in methyl acetate (15 c.c.) was treated with excess of ozone at $-20°$. The ozonide, reduced with hydrogen over palladised charcoal, gave a gum, which gave a negative Schiff's test but positive reactions with ferric chloride and Tollens's reagent and iodoform with sodium hypoiodite.

2-*Oxoguai*-4-*en*-8 : 13-*olide* (XIX).—Dihydrolumisantonin (VI) (0·5 g.) in chloroform (15 c.c.) was saturated with hydrogen chloride for 4 hr. After addition of sodium hydrogen carbonate and filtration, the chloroform was removed, and the product recrystallised from ethanol, to give 2-*oxoguai*-4-*en*-8 : 13-*olide* (XIX) (0·2 g.), plates, m. p. 210—211°, $[\alpha]_D^{20}$ $+47·9°$ (*c* 1·03 in $CHCl_3$)

(Found : C, 72·2; H, 7·8. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%). The *semicarbazone* had m. p. 246° (Found : C, 62·2; H, 7·6. $C_{16}H_{23}O_3N_3$ requires C, 62·9; H, 7·5%).

Ozonolysis of 2-*Oxoguai*-4-*en*-8 : 13-*olide* (XIX).—Excess of ozone was passed into a solution of this lactone (0·1 g.) in methyl acetate (15 c.c.), and the ozonide reduced with hydrogen over palladised charcoal. The product was a gum, which gave positive reactions with Schiff's and Tollens's reagents, and also iodoform with sodium hypoiodite.

Dehydrogenation Experiment.—2- Oxoguai-4-en-8 : 13-olide (XIX) (0·4 g.), lithium aluminium hydride (1 g.), and dry ether (200 c.c.) were refluxed for 5 hr. The product, a glass (0·4 g.), was isolated in the usual way and heated (0·2 g.) with 10% palladised charcoal (0·13 g.) under nitrogen at 300° rising to 360° during 6 min., and kept at 360° for 6 min. The product was extracted with light petroleum, and the extract washed with 90% phosphoric acid (5 × 3 c.c.). The acid was diluted with water to 150 c.c. and extracted with light petroleum from which a dark blue oil (3·9 mg.), $\lambda_{max.}$ 3730, 3560, 3420, 2910, 2480, and 2320 Å (log ε 2·94, 3·16, 3·2, 4·0, 3·94, and 3·96), was obtained.[17]

Rearrangements with Deuterium Chloride.—(*a*) Deuterium chloride, prepared by dropping deuterium oxide into a mixture of phosphorus pentachloride and sand, was passed into a solution of lumisantonin (0·5 g.) in chloroform, and the whole was kept for 14 hr. The product was deuterated 4-chloro-2-oxoguai-9-en-8 : 13-olide (XIV), m. p. 151—152°, infrared max. at 1778 (butanolide), 1756 cm.$^{-1}$ (*cyclo*pentanone). (*b*) Similar treatment of dihydrolumisantonin gave deuterated 2-oxoguai-4-en-8 : 13-olide (XIX), m. p. 202—207°, infrared max. at 1775 and 1745 cm.$^{-1}$.

Isomerisation of Lumisantonin with Boron Trifluoride.—A mixture of lumisantonin (0·85 g.), acetic acid (10 c.c.), and boron trifluoride–ether complex (2 c.c.) was set aside for 20 hr. The mixture was poured into water and neutralised with sodium hydrogen carbonate. The resulting solid crystallised from ethanol, giving 4-acetoxy-2-oxoguai-1(9)-en-8 : 13-olide as needles (0·2 g.), m. p. and mixed m. p. 181—182°, $[\alpha]_D^{18}$ +56·1° (*c* 1·07 in $CHCl_3$)[2, 3] (Found : C, 67·1; H, 6·9. Calc. for $C_{17}H_{22}O_5$: C, 66·7; H, 7·2%) and 2-*oxoguai*-1(15) : 4-*dien*-8 : 13-*olide*, needles, m. p. 129—130°, $[\alpha]_D^{19}$ −171° (*c* 0·4 in $CHCl_3$) (Found : C, 73·4; H, 7·6. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%).

Reduction of Santonic Acid.—A solution of santonic acid (0·5 g.) in 0·1N-sodium hydroxide (30 c.c.) was treated with potassium borohydride (0·5 g.) and set aside for 36 hr. Careful acidification gave a gum which was extracted with chloroform, and the extract was washed with dilute aqueous ammonia. Removal of solvent gave the *lactone* (XIII) (0·3 g.), m. p. 153—157°, which after crystallisation from ethyl acetate–light petroleum was obtained as needles, m. p. 158°, $[\alpha]_D^{19}$ +40° (*c* 1·4 in $CHCl_3$) (Found: C, 71·8; H, 8·9. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·8%). It showed no ultraviolet absorption maximum.

Photosantoninic Acid.—(*a*) Santonin (8·2 g.) was dissolved in a solution of potassium hydroxide (5·6 g.) in water (100 c.c.) and irradiated for 48 hr. The product obtained on acidification was recrystallised from ethanol three times, to give photosantoninic acid, m. p. 272—273°, $[\alpha]_D^{14}$ −33·0° (*c* 3·3 in $CHCl_3$) (Found : C, 65·8; H, 7·6%; equiv., 270. Calc. for $C_{30}H_{42}O_9$: C, 65·9; H, 7·7%; equiv., 273). (*b*) Lumisantoninic acid (III) (0·2 g.), potassium hydroxide (0·75 g.), methanol (20 c.c.), and water (10 c.c.) were set aside for 24 hr. Acidification of the solution gave photosantoninic acid, m. p. and mixed m. p. 272°.

Action of Acetic Anhydride on Photosantoninic Acid.—The acid (0·3 g.) was heated on the water-bath for 2 hr. with acetic anhydride (15 c.c.), and the excess of anhydride then removed in a vacuum. The product was recrystallised from ethyl acetate, giving the mixed anhydride as needles (0·15 g.), m. p. 199° (Francesconi and Maggi [1] record m. p. 199°) (Found : C, 69·5; H, 7·2; Ac, 7·9. Calc. for $C_{32}H_{40}O_8$: C, 69·5; H, 7·3; 1Ac, 7·8%).

Dihydrophotosantoninic Acid.—Photosantoninic acid (0·5 g.) and platinum oxide (0·1 g.) in ethyl acetate (30 c.c.) were stirred in hydrogen for 48 hr. The product was recrystallised from ethanol, to give *dihydrophotosantoninic acid,* m. p. 275—280°, $[\alpha]_D^{15}$ −42° (*c* 0·6 in $CHCl_3$) (Found : C, 68·1; H, 7·9. $C_{30}H_{42}O_8$ requires C, 67·9; H, 8·0%).

Irradiation of 11β(H)-*Santonin.*—Dilute aqueous solutions of potassium 11β(H)-santoninate at pH 8 were irradiated and processed as described for potassium santoninate. The chloroform extract of the irradiation products deposited overnight a white powder, m. p. 90—120°. Crystallisation of this from ethyl acetate–light petroleum (b. p. 40—60°) gave two types of

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[17] Cf. Čekan, Herout, and Šorm, *Coll. Czech. Chem. Comm.*, 1954, **19**, 798; Treibs and Barchet, *Annalen*, 1950, **566**, 89.

crystals and by hand-picking large hexagonal plates of (B) 3 : 6-*dioxoeudesm*-7(11)-*en*-13-*oic acid* (XXII; R = H) were obtained almost pure. Further crystallisation from ethanol gave pure acid (B), m. p. 174—175°, $[\alpha]_D^{21}$ $-49°$ (*c* 1·9 in EtOH) (Found : C, 63·6; H, 7·9. $C_{15}H_{22}O_5$ requires C, 63·8; H, 7·8%).

The mother-liquors from which acid (B) had separated were allowed to evaporate slowly; acid (A) was deposited in a *hydrated form*, m. p. 110—140°, $[\alpha]_D$ $-105°$ (Found : C, 62·6; H, 7·8. $C_{15}H_{20}O_4,1{\cdot}5H_2O$ requires C, 61·8; H, 7·8%). Refluxing for 2 hr. with benzene in a Dean and Stark apparatus gave a white powder, m. p. 160°. Crystallisation from ethyl acetate gave *lumi*-11β(H)-*santoninic acid* (IIIβ), $\lambda_{max.}$ 2440, 3350 (log ε 3·75 and 2·38), $\nu_{max.}$ 3550, 1698, 1658, and 1580 cm.$^{-1}$ (in Nujol) (Found : C, 68·2; H, 7·6%; equiv., 289. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%; equiv., 264). Its 2 : 4-*dinitrophenylhydrazone* consisted of deep orange needles (from ethanol), m. p. 259—260°, $\lambda_{max.}$ 2220, 2580, (2850), 3830 Å (log ε 4·12, 4·15, 3·94, 4·54) (Found : C, 56·8; H, 5·4. $C_{21}H_{24}O_7N_4$ requires C, 56·8; H, 5·4%).

Lumi-11β(H)-*santonin*.—(*a*) The acid A (0·5 g.) in ethanol (10 c.c.), treated with diazomethane, gave the *lactone* (IVβ) (0·4 g.) which crystallised from ethyl acetate–light petroleum (b. p. 40—60°) as needles, m. p. 125°, $[\alpha]_D$ $-112°$ (*c* 1·46 in MeOH), $\lambda_{max.}$ 2380 and 3400 Å (log ε 3·66 and 2·41), $\nu_{max.}$ 1780, 1689, and 1585 cm.$^{-1}$ (in Nujol) (Found : C, 73·2; H, 7·4. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). (*b*) The lactone (0·3 g.) was obtained when the acid (0·5 g.) was heated on the water-bath with acetic anhydride (5 c.c.).

Reduction of Lumi-11β(H)-*santoninic Acid* (IIIβ).—The acid (0·5 g.) in ethyl acetate (100 c.c.) was reduced over Adams catalyst (0·2 g.) at 1 atm. of hydrogen. *Dihydrolumi*-11β(H)-*santoninic acid* (Vβ) (0·45 g.) was obtained and crystallised from ethyl acetate as prisms, m. p. 150°, $[\alpha]_D$ $-88°$ (*c* 1·4 in MeOH), $\lambda_{max.}$ 2830 Å (log ε 1·95), log ε 3·73 at 2200 Å (not a max.), $\nu_{max.}$ 1713 cm.$^{-1}$ (Found : C, 63·7; H, 8·2. $C_{15}H_{22}O_4,H_2O$ requires C, 63·4; H, 8·5%). This gave a 2 : 4-*dinitrophenylhydrazone*, scarlet needles (from ethanol), m. p. 226° (Found : C, 57·8; H, 5·4. $C_{21}H_{26}O_7N_4$ requires C, 56·5; H, 5·8%).

Dihydrolumi-11β(H)-*santonin* (VIβ).—(*a*) Lumi-11β(H)-santonin (IVβ) (0·2 g.) in ethyl acetate (25 c.c.) was reduced over Adams catalyst (20 mg.), giving a solid (0·15 g.), m. p. 171·5—172·5°. Crystallisation from ethyl acetate–light petroleum (b. p. 40—60°) gave the desired *lactone* as prisms, m. p. 173° (Found : C, 72·8; H, 8·1. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%). (*b*) Dihydrolumi-11β(H)-santoninic acid (Vβ) (1 g.) was treated in methanol with ethereal diazomethane, giving the lactone (VIβ) (0·9 g.), m. p. 172° (from ethyl acetate–light petroleum), $\lambda_{max.}$ 2850 (log ε 1·89), log ε 3·7 at 2200 Å (not a max), $\nu_{max.}$ 1780, 1720 cm.$^{-1}$ (Found : C, 72·6; H, 7·7%).

Reduction of Dihydrolumi-11β(H)-*santoninic Acid* (Vβ) *with Potassium Borohydride*.—A solution of the acid (0·2 g.) in 0·05N-sodium hydroxide (20 c.c.) containing potassium borohydride (0·2 g.) was set aside for 36 hr. It was acidified and extracted with chloroform, from which a gum was obtained. Trituration with light petroleum gave a solid (0·15 g.), m. p. 108—110°, which on crystallisation from light petroleum gave the required *lactone* (VIIβ) as needles, m. p. 114° (Found : C, 72·0; H, 8·7. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·9%).

Isomerisation of Lumi-11β(H)-*santonin* (IVβ).—A stream of hydrogen chloride was passed for 4 hr. into a solution of the lactone (1·8 g.) in chloroform (100 c.c.), and the solution was set aside for 12 hr., then washed with water and dried. The gum produced when the solution was evaporated was dissolved in ethyl acetate–light petroleum (b. p. 40—60°) and set aside. The *chloro-lactone* (XX) (1·3 g.) was deposited as prisms, m. p. 130—135°. After chromatography on neutral alumina with light petroleum–benzene it had m. p. 139—140°. Crystallisation from ethyl acetate–ligroin gave prisms, m. p. 139—140°, $[\alpha]_D$ $-182°$ (*c* 1·44 in MeOH), $\lambda_{max.}$ 2215 (log ε 3·93) and 3320 Å (log ε 1·8), $\nu_{max.}$ 1775, 1707 (*cyclo*pentenone), 1600 cm.$^{-1}$ (in $CHCl_3$) (Found : C, 64·1; H, 6·7. $C_{15}H_{19}O_3Cl$ requires C, 63·7; H, 6·7%).

Reduction of the Lactone (XX). 4-*Chloro*-2-*oxoguaian*-8 : 13-*olide* (XVIβ).—The preceding compound (XX) (0·15 g.) in ethyl acetate (50 c.c.) was hydrogenated over Adams catalyst (50 mg.). The *product* (0·15 g.), isolated in the usual way, had m. p. 167—168°. Two crystallisations from ethyl acetate–light petroleum gave needles, m. p. 191—192°, $\lambda_{max.}$ 2980 (log ε 1·54), $\nu_{max.}$ 1770, 1740 cm.$^{-1}$ (in $CHCl_3$) (Found : C, 63·6; H, 7·5. $C_{15}H_{21}O_3Cl$ requires C, 63·3; H, 7·4%).

Dehydrochlorination of the Lactone (XX). 2-*Oxoguai*-1(15) : 4-*dien*-8 : 13-*olide* (XXIβ).—The chloro-compound (XX) (0·3 g.) was refluxed with fused sodium acetate (0·35 g.) in dry ethanol (15 c.c.) for 7 hr., then set aside overnight. The ethanol was removed, the residue was extracted with ethyl acetate, and the extract washed with water, dried, partly evaporated, and diluted with light petroleum. The *diene* was then obtained as rods (70 mg.), m. p. 114—116°. Crystallisation from ethyl acetate–light petroleum raised the m. p. to 117—118° (Found: C, 73·1; H, 7·4. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%).

Isomerisation of Dihydrolumi-11β(H)-*santonin* (VIβ).—The lactone (0·9 g.) in chloroform (100 c.c.) was treated as described previously, affording a gum, which dissolved in ethyl acetate–light petroleum. The *guiaenolide* (XIXβ) (0·36 g.), m. p. 142—170°, was gradually deposited. Crystallisation from ethyl acetate–light petroleum gave needles, m. p. 181°, $\lambda_{\max.}$ 2840 Å (log ε 1·67), log ε 2·9 at 2140 Å (no max.) (Found: C, 72·8; H, 8·1. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%). Ozonolysis of this product (XIXβ) gave a gum whose infrared spectrum showed maxima at 2750 (aldehyde), 1780 (lactone), 1748 (*cyclo*pentanone), 1727 (aldehyde), 1704 (ketone), and 1356 cm.$^{-1}$ ($CO{\cdot}CH_3$).

Dehydrogenation of the Acid (Vβ).—The acid was reduced with potassium borohydride as described above. The lactone (VII) (0·25 g.) was heated with 10% palladised charcoal (0·25 g.) for 14 min. at 300—320°. The product was extracted several times with light petroleum, and the combined extracts from three experiments were reduced to 4 c.c. This residue was then chromatographed on a 6 cm. column of neutral alumina. 7-Ethyl-1-methylnaphthalene (100 mg.) was obtained and characterised as its picrate and by means of its ultraviolet and infrared spectra.

Methyl 3 : 6-*Dioxoeudesm*-7(11)-*en*-13-*oate* (XXII; R = Me).—The acid (XXII; R = H) (100 mg.) in methanol (10 c.c.) was treated with excess of diazomethane in ether. After 30 min. the solvents were removed, giving the *ester* (100 mg.), which crystallised from ethyl acetate–light petroleum as needles, m. p. 121—121·5°, $\lambda_{\max.}$ 2150 (2900), and 3300 (log ε 4·12, 1·68, and 1·42), $\nu_{\max.}$ 1727 (αβ-unsaturated ester), 1710 (C:O), 1680 (αβ-unsaturated ketone), 1646 cm.$^{-1}$ (C=C) (Found: C, 68·8; H, 7·8. $C_{16}H_{22}O_4$ requires C, 69·1; H, 7·9%).

3-*Oxoeudesma*-4 : 7(11)-*dien*-6 : 13-*olide* (XXIV).—The acid (XXII; R = H) (0·48 g.) was heated with acetic anhydride (5 c.c.) for 7 hr. and the mixture was then evaporated to dryness in a vacuum. The residual oil was chromatographed in ethyl acetate–light petroleum on neutral alumina. Elution with benzene–light petroleum (3 : 2) gave a colourless gum which rapidly solidified. Crystallisation from ethyl acetate–light petroleum gave the *lactone* (7 mg.) as needles, m. p. 135° (Found: C, 73·3; H, 7·4. $C_{15}H_{18}O_3$ requires C, 73·1; H, 7·4%).

3 : 6-*Dioxoeudesman*-13-*oic Acid* (XXIII; R = H).—The acid (XXII; R = H) (0·63 g.) in ethyl acetate (30 c.c.) was stirred overnight with Adams catalyst (70 mg.) in hydrogen. After filtration and removal of solvent 3 : 6-*dioxoeudesman*-13-*oic acid* (0·3 g.), m. p. 171—172·5°, was obtained, which crystallised from methanol as needles (0·23 g.), m. p. 176—177°, $[\alpha]_D^{18}$ −25° (*c* 1·3 in MeOH) (Found: C, 63·7; H, 8·2. $C_{15}H_{22}O_4,H_2O$ requires C, 63·4; H, 8·5%). Its *methyl ester* (XXIII; R = Me) crystallised from ethyl acetate–light petroleum as rods, m. p. 124°, $[\alpha]_D^{17}$ −37° (*c* 1·59 in MeOH) (Found: C, 69·1; H, 8·7; OMe, 10·9. $C_{16}H_{24}O_4$ requires C, 68·6; H, 8·6; OMe, 11·1%). The ester affords the acid when kept with 5% methanolic potassium hydroxide. The *monoxime* of the ester crystallised from methanol as needles, m. p. 162—163° (Found: N, 4·8; OMe, 10·5. $C_{16}H_{25}O_4N$ requires N, 4·7; OMe, 10·5%).

3-*Hydroxyeudesman*-6 : 13-*olide* (XXVI).—A solution of 3 : 6-dioxoeudesman-13-oic acid (0·4 g.) in methanol (20 c.c.) and water (20 c.c.) containing a slight excess of potassium hydroxide and potassium borohydride (0·5 g.) was set aside for 3 days, then acidified and extracted with ethyl acetate. The extract was washed with sodium carbonate solution and dried. The required *lactone* (0·17 g.) was obtained having m. p. 147—149° and crystallised from ethyl acetate–light petroleum as needles, m. p. 149—151°, $[\alpha]_D^{19}$ +52° (*c* 1·4 in $CHCl_3$) (Found: C, 71·5; H, 9·7%; equiv., 240. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·6%; equiv., 252).

Eudesm-3-*en*-6 : 13-*olide* (XXVII).—The preceding compound (100 mg.), dissolved in phosphorus oxychloride (0·5 c.c.) and pyridine (5 c.c.), was set aside for 24 hr. The *product* (50 mg.) crystallised from aqueous ethanol as needles, m. p. 93—94° (Found: C, 77·1; H, 9·4. $C_{15}H_{22}O_2$ requires C, 76·9; H, 9·5%). Ozonolysis of this product followed by reduction of the ozonide over palladised charcoal gave a gum which with sodium hypoiodite gave iodoform and gave positive Tollens's and Schiff's tests.

Dehydrogenation of 3-*Hydroxyeudesman*-6 : 13-*olide* (XXVI).—The lactone (2·5 g.), as a gum obtained from the potassium borohydride reduction, was heated at 295° for 19 hr. with 10% palladised charcoal in a stream of nitrogen. The product was extracted with light petroleum, and the extract filtered, reduced to 20 c.c., and passed through a 4″ column of neutral alumina.

The eluate, on removal of solvent, gave a colourless oil (0·4 g.) indistinguishable in spectrum from 7-ethyl-1-methylnaphthalene, $\lambda_{max.}$ 2285, 2820 (3200 Å) (log ε 4·84, 3·68, and 2·45). Its picrate, m. p. 87°, did not depress the m. p. of authentic 7-ethyl-1-methylnaphthalene picrate. The alumina in the column was washed with 90% phosphoric acid (40 c.c.), and the acid was diluted with water to 150 c.c. and extracted with light petroleum, giving a blue extract having absorption maxima at 2850 (3250) Å (log ε 4·65 and 4·22). A second dehydrogenation of the pure lactone (XXVI) (390 mg.) afforded 7-ethyl-1-methylnaphthalene (170 mg.) whose picrate had m. p. and mixed m. p. 90—91°. No azulene-like compound was observed in this experiment.

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