180. *Photochemical Transformations. Part I. Some Preliminary Investigations.*

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The main photochemical transformation product of santonin in aqueous acetic acid, " *iso*photosantonic lactone," has been shown to be 10-hydroxy-3-oxoguai-4-en-6 : 12-olide (IV).

PREDICTION of the structures of photochemical transformation products is difficult, the types of reaction being frequently without analogy in non-photochemical processes. It is certain, however, that photochemical changes may run against the direction of thermodynamic free-energy change in ordinary chemical reactions and that the absorption of light quanta provides a means for the *specific* activation of individual molecules.

Interest by organic chemists in photochemical transformations has been maintained by, for example, the complex sequence of structural changes induced by light in steroidal 5 : 7-dienes [1] as well as by processes of a less exotic kind.[2] We would cite the elegant papers by Büchi and his collaborators [3] as exemplifying the interesting types of photochemical change still awaiting discovery and exploitation.

It is the purpose of our own papers to investigate, first, specific photochemical transformations and, secondly, the mechanisms of such processes, with the ultimate object of prediction. Our personal interest in this field was first stimulated some years ago by the discovery, by Dr. E. L. Wheeler (now of Harvard University) working in our laboratories, that homoannular *cyclo*hexadienones in general were subject to rapid photochemical change. One of the most accessible of these compounds is santonin. In the present paper we elucidate the course of a rearrangement of this compound induced by light.

Prior knowledge of the photochemical transformation products of santonin (I) has been adequately summarised elsewhere [4] and we content ourselves on this occasion with the citation of only references specific [5, 6, 7, 8] to the chemistry of " *iso*photosantonic acid." This compound is, in our hands, the main product, obtainable in 30% yield or more, of irradiation of santonin with ultraviolet light in aqueous acetic acid. These conditions are as approximate to those of the earlier workers (who used sunlight over a period of weeks) as Glasgow weather permits. No yield was indicated in the earlier work.[8] The so-called " photosantonic acid " is formed at the same time in minor amount.

" *iso*Photosantonic acid " was assigned the composition $C_{15}H_{22}O_5$ and was stated to lose water very easily at 100°, or on treatment with acetyl chloride, to furnish " *iso*photosantonic lactone," $C_{15}H_{20}O_4$. In fact both substances are neutral γ-lactones (infrared bands at 1776 cm.$^{-1}$ in Nujol), and the so-called acid is merely the hydrated form of " *iso*photosantonic lactone." Recrystallisation from aqueous solvent affords the hydrated material; from anhydrous solvents the non-hydrated form results. The earlier work showed that the lactone contained one hydroxyl group (formation of an acetate with sodium acetate–acetic anhydride) and one functionally reactive carbonyl group (formation of an oxime, an acetate oxime, and a phenylhydrazone) which was provisionally regarded as aldehydic. In fact, the lactone is stable to chromic acid in acetic acid at room temperature and gives none of the usual aldehyde colour tests. The hydroxyl group must

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[1] For example, Havinga, Koevoet, and Verloop, *Rec. Trav. chim.*, 1955, **74**, 1230; Fieser and Fieser, " Natural Products related to Phenanthrene," Reinhold Publ. Corp., New York, 1949, pp. 167 *et seq.*

[2] *Inter al.*, Mustafa, *Chem. Rev.*, 1952, **51**, 1; Schönberg *et al.*, *J. Amer. Chem. Soc.*, 1956, **78**, 1224 and previous papers; Schenk and Dunlap, *Angew. Chem.*, 1956, **68**, 248; Schenk *et al.*, *Annalen*, 1953, **584**, 125, 156, 177, 199, 221; Horner and Spietschka, *Chem. Ber.*, 1955, **88**, 934 and earlier papers.

[3] Büchi, Kofron, Koller, and Rosenthal, *J. Amer. Chem. Soc.*, 1956, **78**, 876, and previous papers.

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

[5] Villavecchia, *Atti R. Accad. Lincei*, 1885, **1**, 722; *Ber.*, 1885, **18**, 2859.

[6] Cannizzaro and Fabris, *ibid.*, 1886, **2**, I, 450; *Ber.*, 1886, **19**, 2261.

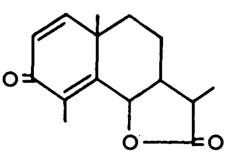
[7] Francesconi and Villavecchia, *Gazzetta*, 1902, **32**, I, 315.

[8] Francesconi and Venditti, *ibid.*, 1902, **32**, I, 318.

therefore be tertiary and the reactive carbonyl group a ketonic function. The lactone showed infrared bands at 3470 (OH), 1776 (mentioned above), 1693 (CO of *cyclo*pentenone) and 1660 cm.$^{-1}$ (conjugated ethylenic linkage of *cyclo*pentenone). The presence of the *cyclo*pentenone grouping was supported by the ultraviolet absorption which included a strong band at 239 mμ (ε 13,000), corresponding[9] to a fully substituted *cyclo*pentenone as in deacetyl*neo*tenulin (II) which shows[10] $\lambda_{max.}$ 240 mμ (ε 16,000).

Treatment of "*iso*photosantonic lactone" with pyridine–thionyl chloride gave an anhydro-compound containing the system $>C=CH_2$, demonstrated by the infrared spectrum [bands at 1770 (γ-lactone), 1690 and 1643 (*cyclo*pentenone), and 906 cm.$^{-1}$ ($>C=CH_2$) in $CHCl_3$] and by *C*-Me determinations (three *C*-Me in the parent compound, only two in the anhydro-derivative). The original lactone, therefore, contains the grouping $>CMe\cdot OH$. Since the ultraviolet absorption spectrum of the anhydro-derivative is essentially the same as that of the parent lactone the methylene grouping is not conjugated with the same system. In contrast, dehydration of the parent lactone under acidic conditions gave an oily conjugated dienone ($\lambda_{max.}$ 305 mμ) characterised as its 2 : 4-dinitrophenylhydrazone.

Ozonolysis of the lactone followed by steam-distillation gave acetic acid and a neutral compound, $C_{13}H_{16}O_5$, $[\alpha]_D$ $-31°$ (in pyridine). This did not show a hydroxyl band in the infrared spectrum and clearly had two γ-lactone bands (1777 and 1760 cm.$^{-1}$). The presence of a ketone grouping was indicated by oxime formation, by the ultraviolet absorption maximum at 294 mμ (ε 50), and by an infrared band at 1720 cm.$^{-1}$. The formation of acetic acid on ozonolysis of an $\alpha\beta$-unsaturated ketone, as in the case of deacetyl*neo*tenulin,[10] implies the presence of the system $\cdot CO\cdot CMe{:}C<$. It is clear, in addition, that the original hydroxyl group must be involved in lactonisation with the carboxyl group generated by fission of the enone system in order to explain the disappearance of the hydroxyl band and the appearance of *two* γ-lactone bands in the compound $C_{13}H_{16}O_5$.



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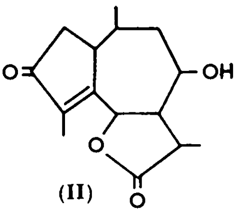

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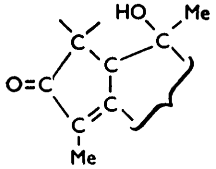

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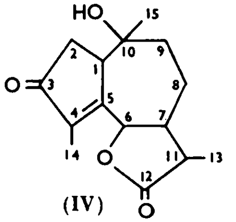

(IV)

One can therefore write the partial expression (III) for "*iso*photosantonic lactone" and, if one has regard to the constitution of its precursor santonin (I), the interesting structure (IV) for the photo-lactone. The ozonolysis product $C_{13}H_{16}O_5$ can then be formulated satisfactorily as (V). The structure (IV), 10-hydroxy-3-oxoguai-4-en-6 : 12-olide,* was confirmed in a simple manner. Whilst hydrogenation under neutral conditions gave a crystalline dihydro-compound (VI), acid-catalysed hydrogenation afforded a mixture of alcohols (no *cyclo*pentenone band in the infrared region), dehydrogenated over palladised charcoal to chamazulene[12] (VII). The anhydro-compounds mentioned above can then, of course, be formulated as (VIII) for the non-conjugated isomer and (IX) for the conjugated dienone.

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* We adopt here the proposal by Šorm and his co-workers[11] that such lactones should be named in terms of guaianolide. The numbering we employ is convenient in that it shows the relation of the guaiane skeleton to the santanic acid or eudesmane skeleton. It also corresponds to steroid and polyterpenoid numbering and may have implications in terms of absolute configuration.

[9] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 76; Gillam and West, *J.*, 1942, 486.

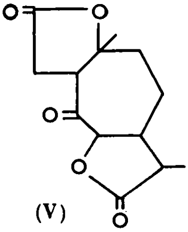
[10] Barton and de Mayo, *J.*, 1956, 142.

[11] Cekan, Herout, and Šorm, *Chem. and Ind.*, 1954, 604.

[12] Meisels and Weizmann, *J. Amer. Chem. Soc.*, 1953, **75**, 3865; Šorm, Herout, and Takeda, *Chem. Listy*, 1954, **48**, 281; Novak, Šorm, and Sicher, *ibid.*, p. 1648.

The novel constitution (IV) for the photo-product was supported by the following experiments. A more detailed study of its ozonolysis showed that, if the ozonide was decomposed hydrolytically but without steam-distillation, an isomeric neutral $C_{13}H_{16}O_5$ compound, $[\alpha]_D$ +70° (in pyridine), resulted. The infrared spectrum of this (in Nujol) showed no hydroxyl band, two γ-lactone bands (at 1777 and 1750 cm.$^{-1}$) and a ketone band (at 1720 cm.$^{-1}$). The pyridine solution mutarotated to −31° in 18 hr. and the first-mentioned $C_{13}H_{16}O_5$ compound was formed in quantitative yield. It is obvious that the two compounds are stereoisomers at one or both of the asymmetric centres α to the ketone group and that steam-distillation is a sufficiently vigorous process to provoke the isomerisation. When the ozonide was decomposed by hydrogenation, the triketone (X), $C_{15}H_{20}O_6$, resulted. This is not unexpected on mechanistic grounds.[13] Treatment of this triketone (X) with alkaline hydrogen peroxide afforded, in accordance with the α-diketone formulation, one mol. of acetic acid.

Reduction of the photo-product (IV) with sodium borohydride gave the unsaturated alcohol (XI; R = H) and the corresponding saturated alcohol (XII). Ozonolysis of the former alcohol afforded the corresponding diketo-alcohol (XIII; R = H), and acetylation gave an oily monoacetate (XI; R = Ac) characterised by ozonolysis to the crystalline acetoxy-diketone (XIII; R = Ac). Treatment of the unsaturated acetate (XI; R = Ac) with osmium tetroxide gave a crystalline α-glycol (XIV) which consumed periodic acid only slowly. In a corresponding experiment, the photo-product (IV) itself was treated with osmium tetroxide and thus converted into a glycol (XV). In contrast to the previous glycol (XIV), this trihydroxy-ketone (XV) consumed one mol. of periodic acid or lead tetra-acetate very rapidly, to give a neutral dilactone $C_{15}H_{20}O_6$. This substance was shown to be identical with the so-called "bishydroxy*iso*photosantonic acid" obtained earlier [8] by oxidation of the photo-product (IV) with potassium permanganate. In the



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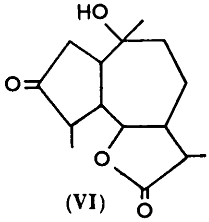

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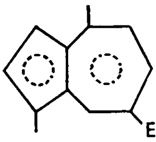

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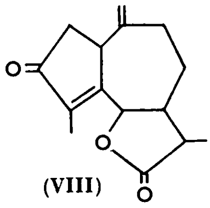

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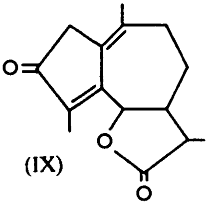

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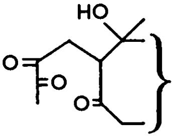

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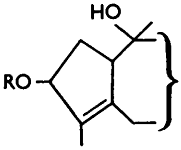

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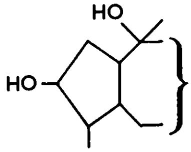

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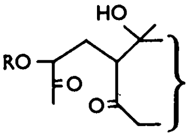

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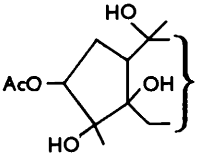

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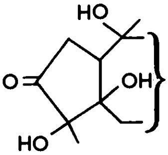

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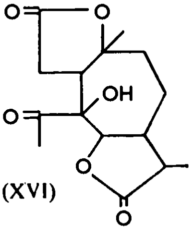

(XVI)

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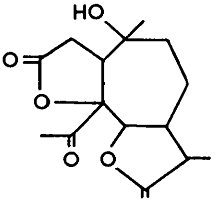
[13] Barton and Seoane, *J.*, 1956, 4150.

infrared spectrum the oxidation product showed bands at 3430 (OH), 1760 (strength indicative of two γ-lactones), and 1710 cm.$^{-1}$ (aliphatic CO or equivalent), the last assignment being confirmed by the ultraviolet absorption spectrum ($\lambda_{max.}$ at 295 mμ; ϵ 40). The compound was stable to chromic acid, showing that the hydroxyl group was tertiary, and gave a positive iodoform test. It can, therefore, be formulated as (XVI) or (XVII). In so far as there is analogy in (V) for the lactone system of (XVI), and in so far as the oxidation product could not be dehydrated with thionyl chloride and pyridine under conditions which dehydrate (IV) readily, we favour structure (XVI). The resistance of this compound to further oxidation by periodic acid or lead tetra-acetate is, perhaps, evidence in favour of structure (XVII), except that steroidal 17α-hydroxy-20-ketones of the partial structure (XVIII) are notoriously resistant [14] to these reagents.

The mechanism of the rearrangement of santonin to 10-hydroxy-3-oxoguai-4-en-6 : 12-olide (IV) can possibly be visualised as follows. Photoactivation of santonin provides sufficiently energised molecules for occurrence of the acid-catalysed rearrangement shown in (XIX) or equivalent. The anion X^- which is added at $C_{(10)}$ can either be hydroxyl from water, as in the present case and in that of the investigations by Francesconi and Venditti,[8] or acetate, from the glacial acetic acid employed in some experiments by the Italian workers.



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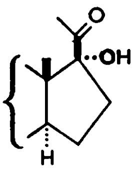

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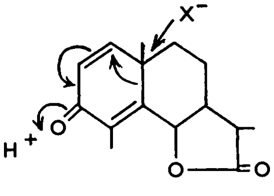

(XIX)

We are studying other aspects of the photochemistry of santonin, as well as the generality of the rearrangement reported in the present paper. We are particularly concerned to effect such rearrangements with the physiologically active 1-dehydrosteroids.[15]

EXPERIMENTAL

M. p.s were taken on the Kōfler block unless specified to the contrary. Ultraviolet absorption spectra were determined in EtOH solution with the Unicam S.P. 500 Spectrophotometer. Infrared spectra were kindly determined by Dr. G. Eglinton and his colleagues for Nujol suspensions except as otherwise qualified. [α]$_D$ are in CHCl$_3$ unless stated otherwise. Light petroleum refers to the fraction of b. p. 40—60°. Microanalyses were carried out by Mr. J. M. L. Cameron, Miss M. W. Christie, and their associates.

iso*Photosantonic Lactone* (10-*Hydroxy*-3-*oxoguai*-4-*en*-6 : 12-*olide* (IV).—Santonin (4·0 g.) in 4 : 5 acetic acid–water (110 ml.) was irradiated in a quartz flask under reflux with a bare mercury-arc (125 w) lamp until the rotation fell to approx. 2° ($\sim$7 hr.). Removal of the solvent under reduced pressure afforded a gum which was separated by means of sodium hydrogen carbonate into acidic and neutral fractions. The neutral fraction (3·2 g.) was chromatographed over silica gel (110 g.), 20 fractions being collected. Elution with ether–acetone (1 : 2) (four fractions) afforded "*iso*photosantonic lactone" (1·2 g.), m. p. (from ethyl acetate–light petroleum) 165—167°, [α]$_D$ +129° (*c* 1·34), $\lambda_{max.}$ 239 mμ (ϵ 13,000) (Found : C, 68·2; H, 7·35; *C*-Me, 17·5. Calc. for $C_{15}H_{20}O_4$: C, 68·15; H, 7·65; 3*C*-Me, 17·0%). Crystallisation from aqueous ethanol afforded material of the same m. p. (Found : C, 64·05; H, 7·6. Calc. for $C_{15}H_{20}O_4,H_2O$: C, 63·8; H, 7·85%). The compound gave negative Schiff, Angeli–Rimini, and Fehling tests.

The acidic fraction (760 mg.) was chromatographed over silica gel (27 g.) (20 fractions).

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[14] For example, Brooks and Norymberski, *Biochem. J.*, 1953, **55**, 371.

[15] Herzog, Payne, Jevnik, Gould, Shapiro, Oliveto, and Hershberg, *J. Amer. Chem. Soc.*, 1955, **77**, 4781; Nobile, Charney, Perlman, Herzog, Payne, Tully, Jevnik, and Hershberg, *ibid.*, p. 4184.

Elution with benzene–ether (5 : 1) (4 fractions) gave photosantonic acid (160 mg.), m. p. (from chloroform–light petroleum) 154—155°, $\lambda_{max.}$ 210 mμ (ε 6700), $[\alpha]_D$ −129° (*c* 1·3) (Found: C, 68·4; H, 7·6. Calc. for $C_{15}H_{20}O_4$: C, 68·15; H, 7·65%). Further elution with ether–acetone (2 : 1) (3 fractions) afforded some " *iso*photosantonic lactone " (144 mg.).

Photosantonic acid, on crystallisation from aqueous ethanol, formed a hydrate, sintering below 100° and melting at 154—155° (Found: C, 64·2; H, 7·1. Calc. for $C_{15}H_{20}O_4,H_2O$: C, 63·8; H, 7·85%). Both the hydrated and the anhydrous form of photosantonic acid showed γ-lactone bands in the infrared spectrum, and the relation between the forms is the same as that between the hydrated and the anhydrous form of " *iso*photosantonic lactone " (see above). We hope to discuss this matter in more detail in a further communication.

The acetate of " *iso*photosantonic acid lactone " was prepared by Cannizzaro and Fabris's [6] method. Recrystallised from ethyl acetate–light petroleum it had m. p. 175—177° (capillary), $[\alpha]_D$ +58° (*c* 0·53 in EtOH), $\lambda_{max.}$ 239 mμ (ε 13,000). Cannizzaro and Fabris recorded m. p. 183°, $[\alpha]_D$ +59° (in EtOH). The acetate showed infrared bands at 1770 (γ-lactone), 1730 and 1260 (acetate), 1703 and 1635 cm.$^{-1}$ (*cyclo*pentenone).

3-Oxoguai-4 : 10(15)-dien-6 : 12-olide (VIII).—10-Hydroxy-3-oxoguai-4-en-6 : 12-olide (IV) (56 mg.) in pyridine (3 ml.) was treated with thionyl chloride (240 mg.) at 0° for 10 min. Isolation of the product and chromatography over silica gel (2 g.) (six fractions) gave, on elution with benzene (two fractions), *3-oxoguai-4 : 10(15)-dien-6 : 12-olide* (VIII) (20 mg.), m. p. (from ethyl acetate–ether–light petroleum) 113—115°, $\lambda_{max.}$ 236 mμ (ε 12,600), $[\alpha]_D$ +378° (*c* 1·21) (Found: C, 73·15; H, 7·1; *C*-Me, 14·9. $C_{15}H_{18}O_3$ requires C, 73·15; H, 7·35; 2*C*-Me, 12·2%). Ozonolysis of the anhydro-compound (73 mg.) in methylene dichloride (50 ml.) at −30° for 30 min. (disappearance of ultraviolet max. at 236 mμ), followed by steam-distillation into aqueous dimedone after removal of methylene dichloride *in vacuo*, gave the formaldehyde-dimedone compound (17·8 mg., 20%), identified by m. p. and mixed m. p. Similar ozonolysis of the anhydro-compound (65 mg.), followed by conversion of the acidic portion of the steam-distillate into the *p*-bromophenacyl ester, gave, after chromatography over alumina (2 g.; Brockmann grade 5), *p*-bromophenacyl acetate (29 mg., 50%), identified by m. p. and mixed m. p.

Acid-catalysed Dehydration of 10-Hydroxy-3-oxoguai-4-en-6 : 12-olide (IV).—The hydroxy-lactone (300 mg.) in acetic acid (10 ml.) was treated on the steam-bath for 45 min. with a 7% solution (30 ml.) of perchloric acid in acetic acid. Chromatography of the product over silica (9 g.) gave, on elution with benzene and with benzene–ether (2 : 1), a gum showing $\lambda_{max.}$ 305 mμ (ε 11·300). This was converted into the 2 : 4-dinitrophenylhydrazone in the usual way. Chromatography over bentonite–Celite and elution with chloroform gave *3-oxoguai-4 : 1(10)-dien-6 : 12-olide* (IX) *2 : 4-dinitrophenylhydrazone*, m. p. (from chloroform–ethanol) 232—238° (decomp.), $\lambda_{max.}$ 405 mμ (ε 26,600 in $CHCl_3$) (Found: N, 13·4. $C_{21}H_{22}O_6N_4$ requires N, 13·15%), infrared band at 1765 cm.$^{-1}$ (γ-lactone).

Ozonolysis of 10-Hydroxy-3-oxoguai-4-en-6 : 12-olide (IV).—(*a*) The keto-lactone (100 mg.) in chloroform (40 ml.) was ozonised at −10° for 25 min. (disappearance of band at 239 mμ). Steam-distillation and conversion of the volatile acidic portion into the *p*-bromophenacyl ester (removal of $CHCl_3$ *in vacuo*) gave, on chromatography over alumina (2·5 g.; Brockmann grade 5) and elution with benzene–light petroleum (b. p. 60—80°) (1 : 20), *p*-bromophenacyl acetate (20 mg., 20%), identified by m. p. and mixed m. p. The residue from the steam-distillation afforded the stable *2 : 5-dihydroxy-5-methyl-3-oxo*cyclo*heptane-4-acetic-1-α-propionic dilactone* (V), m. p. (from ethyl acetate) 198—212° (decomp.), $[\alpha]_D$ −31° (*c* 0·80 in pyridine), $\lambda_{max.}$ 294 mμ (ε, 50) (Found: C, 61·8; H, 6·65; *C*-Me, 12·25%; equiv., 126·1, 126·4. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·4; 2*C*-Me, 11·9%; equiv., 126·1). This compound gave a positive Fehling's test, but was stable to chromic acid in acetic acid at room temperature during 1½ hr. Its *oxime*, prepared with pyridine–hydroxylamine hydrochloride in the usual way, had m. p. (from methanol–ether–light petroleum) 214—224° (decomp.), $[\alpha]_D$ +90° (*c* 0·66) (Found: C, 58·25; H, 6·1; N, 5·75. $C_{13}H_{17}O_5N$ requires C, 58·4; H, 6·4; N, 5·25%).

(*b*) A similar ozonolysis, but with decomposition of the ozonide with cold water, furnished the labile *dilactone* (V), m. p. (from ethyl acetate) 198—212° (decomp.), $[\alpha]_D$ +70° (*c* 0·69 in pyridine) (Found: C, 61·7; H, 6·65%). After 18 hr. in pyridine the rotation had changed to −31°, characteristic of the stable dilactone (see above). Isolation gave the stable dilactone itself, identified by m. p., rotation, and infrared spectrum.

(*c*) 10-Hydroxy-3-oxoguai-4-en-6 : 12-olide (70 mg.) in ethyl acetate (5 ml.) was ozonised at −60° for about 30 min. (disappearance of ultraviolet max. at 239 mμ). Palladised charcoal was added and the solution hydrogenated as it warmed to room temperature. Crystallisation from ethanol–light petroleum gave the *triketone* {*α-[4-(2 : 3-dioxobutyl)-2 : 5-dihydroxy-5-methyl-3-oxo*cyclo*heptyl]propionic 2-lactone*} (X), m. p. 154—156°, $[\alpha]_D$ +20° (*c*, 0·66 in ethanol), $\lambda_{max.}$ 290 mμ (ε, 71) (Found: C, 61·05; H, 6·5. $C_{15}H_{20}O_6$ requires C, 60·8; H, 6·8%). The compound gave a positive Fehling's test but was not cleaved by lead tetra-acetate in acetic acid at room temperature. Treatment of the triketone (54 mg.) in ethanol (5 ml.) containing aqueous 4N-sodium hydroxide (1 ml.) with 30% hydrogen peroxide (3 ml.) for 15 min. (excess of peroxide destroyed with platinum black) gave, on acidification with diluted sulphuric acid and steam-distillation, acetic acid (0·9 mol. by titration), characterised as the *p*-bromophenacyl ester (m. p. and mixed m. p.), as sole volatile product.

10-*Hydroxy*-3-*oxoguaian*-6 : 12-*olide*.—10-Hydroxy-3-oxoguai-4-en-6 : 12-olide (1·0 g.) in ethanol (100 ml.) was hydrogenated over 5% palladised charcoal (500 mg.) for 3 hr. (uptake of 1 mol. of hydrogen). Chromatography of the product over silica gel (35 g.) (17 fractions) afforded, on elution with ether (6 fractions), 10-*hydroxy*-3-*oxoguaian*-6 : 12-*olide* (VI), m. p. (from ethyl acetate–benzene–light petroleum) 135—138°, $[\alpha]_D$ −46° (*c* 1·16) (Found: C, 67·45; H, 8·1. $C_{15}H_{22}O_4$ requires C, 67·65; H, 8·35%).

Oxidation of 10-*Hydroxy*-3-*oxoguai*-4-*en*-6 : 12-*olide with Potassium Permanganate*.—The hydroxy-lactone was oxidised with potassium permanganate as described by Francesconi and Venditti [8] to furnish the dilactone (XVI). Recrystallised from ethyl acetate this had m. p. 286—288°, $[\alpha]_D$ +34° (*c* 1·0), $[\alpha]_D$ +112° (*c* 0·67 in pyridine), $\lambda_{max.}$ 295 mμ (ε 40) (Found: *C*-Me, 16·1. $C_{15}H_{20}O_6$ requires 3*C*-Me, 15·2%). The compound gave a positive iodoform test and was stable to chromic acid for 2 hr. at 60° in acetic acid. It was not dehydrated by thionyl chloride–pyridine at 0° or at room temperature (recovered unchanged).

This dilactone was also obtained in the following way. 10-Hydroxy-3-oxoguai-4-en-6 : 12-olide (50 mg.) in dry dioxan (0·5 ml.) was treated with osmium tetroxide (63 mg.) for 4 days at room temperature. Cleavage of the osmate with hydrogen sulphide and crystallisation of the product from methanol–ethyl acetate–light petroleum afforded 4 : 5 : 10-*trihydroxy*-3-*oxoguaian*-6 : 12-*olide* (XV), m. p. 193—198° (decomp.), $[\alpha]_D$ −17° (*c* 1·02), infrared bands at 3400 (OH), 1760 (γ-lactone) and 1740 cm.$^{-1}$ (*cyclo*pentanone) (Found: C, 59·95; H, 7·65. $C_{15}H_{22}O_6$ requires C, 60·4; H, 7·45%). This triol consumed 0·96 mol. of periodic acid in 15 min. after which there was no further uptake of oxidant. Consumption of lead tetra-acetate in acetic acid was the same. The triol (90 mg.) in water (45 ml.) was treated with 0·05N-periodic acid (27 ml.) until one mol. of oxidant had been consumed (15 min.). Crystallisation of the product from ethyl acetate gave the dilactone (XVI) (see above), identified by m. p., mixed m. p., rotation {$[\alpha]_D$ +113° (*c* 0·62 in pyridine)}, and infrared spectrum (Found: C, 60·55; H, 6·85. Calc. for $C_{15}H_{20}O_6$: C, 60·8; H, 6·8%).

Reduction of 10-*Hydroxy*-3-*oxoguai*-4-*en*-6 : 12-*olide with Sodium Borohydride*.—The hydroxy-lactone (300 mg.) in ethanol (2 ml.) was treated with sodium borohydride (400 mg.) in the same solvent (3 ml.) for 90 min. Crystallisation of the product from ethyl acetate–light petroleum furnished 3 : 10-*dihydroxyguai*-4-*en*-6 : 12-*olide* (XI; R = H), m. p. 205—208°, $[\alpha]_D$ +87° (*c* 0·86), no high-intensity ultraviolet absorption (Found: C, 67·6; H, 8·45. $C_{15}H_{22}O_4$ requires C, 67·65; H, 8·35%). Acetylation (pyridine–acetic anhydride at room temperature overnight) gave an oily monoacetate to which further reference is made below.

Fractional crystallisation of the mother-liquors from the sodium borohydride reduction from methanol–ethyl acetate–light petroleum gave the saturated 3 : 10-*dihydroxyguaian*-6 : 12-*olide* (XII), m. p. 95—97°, $[\alpha]_D$ +16° (*c* 0·82) (Found: C, 63·0; H, 9·0. $C_{15}H_{24}O_4,H_2O$ requires C, 62·9; H, 9·15%).

Ozonolysis of 3 : 10-dihydroxyguai-4-en-6 : 12-olide (100 mg.) in chloroform (100 ml.) at −25° for 30 min., decomposition of the ozonide with water, and crystallisation of the product from ethyl acetate–light petroleum afforded the *dihydroxy-diketone* {*α-[2 : 5-dihydroxy-4-(2-hydroxy-3-oxobutyl)-5-methyl-3-oxo*cyclo*heptyl]propionic 2-lactone*} (XIII; R = H), m. p. 196—208° (decomp.), $[\alpha]_D$ −8° (*c* 0·58 in pyridine) (Found: C, 60·75; H, 7·45. $C_{15}H_{22}O_6$ requires C, 60·4; H, 7·45%). Similar ozonolysis of the oily acetate gave the *acetate* (XIII; R = Ac), m. p. (from ethyl acetate–light petroleum) 178—181°, $[\alpha]_D$ +104° (*c* 1·04) (Found: C, 57·15; H, 7·45. $C_{17}H_{24}O_7,H_2O$ requires C, 56·95; H, 7·3%). The compound gave a positive Fehling's test.

Treatment of the oily acetate (47 mg.) in dioxan (6 ml.) with osmium tetroxide (56 mg.) for

14 days at room temperature and cleavage of the derived osmate with hydrogen sulphide gave 3-*acetoxy*-4 : 5 : 10-*trihydroxyguaian*-6 : 12-*olide* (XIV), m. p. (from methanol–ethyl acetate–light petroleum) 192—194°, $[\alpha]_D$ +19° (*c* 0·95) (Found: C, 58·25; H, 7·45. $C_{17}H_{26}O_7,\frac{1}{2}H_2O$ requires C, 58·15; H, 7·75%). This compound consumed 1·1 mol. of periodic acid during 18 hr at room temperature after which there was no further uptake.

Dehydrogenation.—10-Hydroxy-3-oxoguai-4-en-6 : 12-olide (1·0 g.) in "AnalaR" acetic acid (80 ml.) containing 72% perchloric acid (5 drops) was hydrogenated at a platinum catalyst. The gummy product (no ketonic band group in the infrared spectrum) was dehydrogenated in portions (200 mg.) by heating it with 10% palladised charcoal (200 mg.) for 15 min. under nitrogen at 320° (Wood's-metal bath). The combined product was extracted with light petroleum (b. p. 60—80°), and the blue solution filtered through alumina (5 g.; Brockmann grade 5), the column being further developed with benzene–light petroleum (b. p. 60—80°) (1 : 2). The combined eluates were extracted with 80% phosphoric acid to concentrate the azulenic material. Isolation from the phosphoric acid solution in the usual way gave, on treatment with trinitrobenzene, the chamazulene–trinitrobenzene adduct (equiv. to 6·2 mg. of chamazulene), identified by m. p., mixed m. p. and ultraviolet and visible absorption spectra.

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