TERPENOIDS—LXX

STRUCTURE OF DEHYDROCOSTUS LACTONE*

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Abstract—The structure III assigned to dehydrocostus lactone by Sorm *et al.* has been supported by converting it into (i) guaiane, $C_{15}H_{28}$ (I) and (ii) s-guaiazulene and chamazulene in fairly high yield from some of its derivatives. The lactol XII, obtainable from III gives four different products (XIII, XIV, XVIII and XXIV) when subjected to Huang-Minlon reduction at 135° and 170° respectively. The dienic monol (XVIII) the structure of which is supported by UV and NMR spectra, furnished a hydrocarbon $C_{15}H_{16}$ XXVIII, when subjected to metal amine reduction indicating the presence of an allylic hydroxyl in it, which proves that the lactone attachment in III is at C_6–C_7.

Dehydrocostus lactone, $C_{15}H_{18}O_2$, m.p. 60·5°, $(\alpha)_D$ −13·5°, was first isolated by Ukita[1] and later by Crabalona[2] from costus root oil. Its constitution was initially studied by Naves,[3] who on the basis of its quantitative ozonolysis and dehydrogenation of the saturated lactone, concluded that it contains two exocyclic double bonds and possesses a guaiane skeleton (I).

Sorm *et al.*[4] subsequently found that quantitative ozonolysis shows the presence of three exocyclic double bonds and not two, as previously reported. Examination of the IR spectrum[4] of dehydrocostus lactone in chloroform shows the presence of exocyclic methylene groups and absence of any methyl groups. A comparison of the IR spectrum of the saturated lactone with that of dihydrodeoxycarpesia lactone, obtained from carpesia lactone (II), suggests the structure III for dehydrocostus lactone. This is further supported by the NMR spectrum (Fig. 1) of dehydrocostus lactone (III), as well as that of its dihydro derivative (IV).

Selenium dehydrogenation of hexahydrodehydrocostus lactone (V), obtained by complete reduction of III gave a mixture of 4 azulenes in very low yields.

The formation of azulenes in low yields by dehydrogenation, as observed by Naves, Sorm and also by us,[5] does not lend sufficient support to the proposed structure, especially when many non-azulenic terpenoids are known to yield comparable amounts of azulenes on dehydrogenation. An alternative structure (VI) for dehydrocostus lactone also could not be completely ruled out, as most of the deductions, which have led to the structure (III) are based on the IR spectrum of saturated liquid materials

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[1] T. Ukita, *J. Pharm. Soc. Japan* **59**, 231 (1939); *Chem. Abst.* **33**, 4807ᵇ (1939).
[2] L. Crabalona, *Bull. Soc. Chim. Fr.* **15**, 357 (1948).
[3] Y. R. Naves, *Helv. Chim. Acta* **31**, 1172 (1948).
[4] M. Romanuk, V. Herout and F. Sorm, *Coll. Czech. Chem. Commun.* **21**, 894 (1956).
[5] G. H. Kulkarni, A. S. Bawdekar, A. S. Rao, G. R. Kelkar and S. C. Battacharyya, *Perf. and Ess. Oil. Rec.* **54**, 303 (1963).
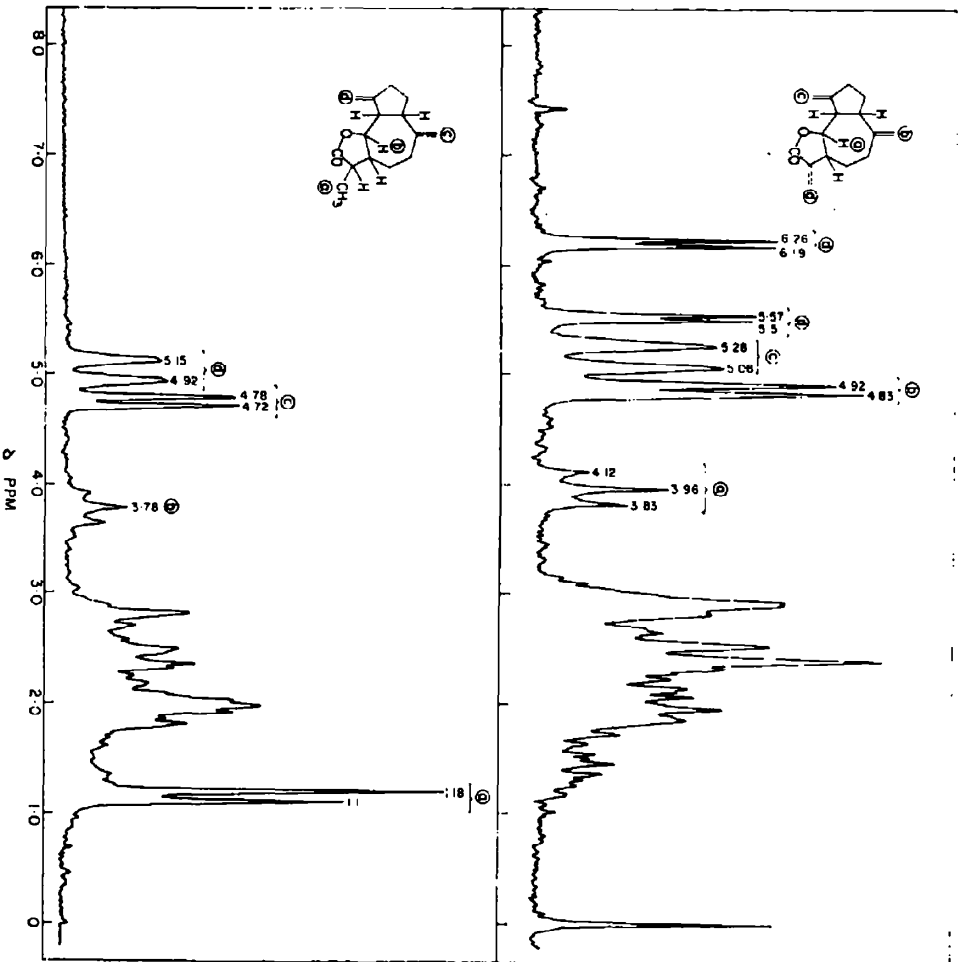
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Chart 1

IV

I

V

II

VI

III

FIG. 1.

δ PPM

5·15

4·92

4·78

4·72

3·78

·18

6·76
6·19

5·37
5·5

5·28

5·06

4·92
4·85

4·12

3·96

3·83
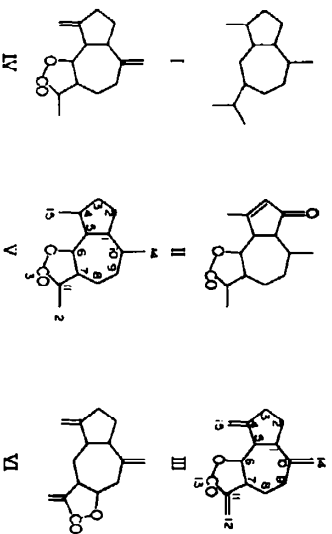
CH₃

(possibly mixture of epimers) of doubtful homogeneity. It was therefore felt desirable to furnish further confirmatory evidences based on reactions involving homogeneous and crystalline materials for the structure (III).

For the sake of convenience, it is being assumed that III represents the correct structure of dehydrocostus lactone.

In our initial experiments III was fully hydrogenated in alcohol medium using platinum catalyst, under pressure to give hexahydrodehydrocostus lactone (V), which from the results of chromatography, GLC analysis, fractionation through spinning band column, etc., was found to be a mixture of epimers, mostly around C_{11}.

With the ultimate object of getting a product related to nepetalinic acid (VII) via the intermediate keto carboxylic acid (VIII), hexahydro dehydrocostus lactone (V), obtained by direct hydrogenation was oxidized with chromic acid in acetic acid, but instead of the desired keto carboxylic acid, the product obtained was a lactone carboxylic acid, possibly represented by IX or X, or a mixture of both. Much of the V was recovered unchanged. Subsequently V was reacted with phenyl magnesium bromide and the product dehydrated to yield, presumably, the diene (XI). But contrary to expectation its oxidation did not lead to any conclusive results.
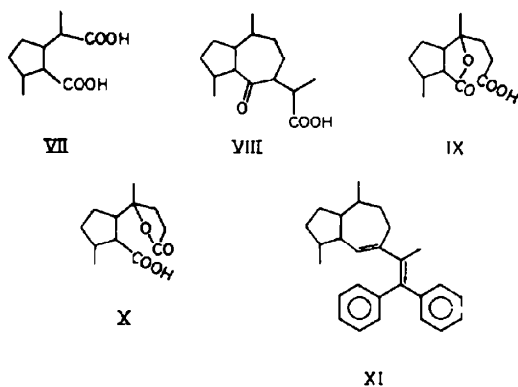

Chart II

We then directed our attention to the preparation of pure dihydrodehydrocostus lactone (IV) by stereospecific reduction of the methylene group in conjugation with the lactone carbonyl to give a single epimer at C_{11}.

Reduction of dehydrocostus lactone to dihydrodehydrocostus lactone using sodium and alcohol has been described earlier by Naves et al.[3]

We, however, did not find it possible to obtain an epimerically pure product by this method, as, apart from a mixture of the epimers at C_{11}, some tetrahydroproducts were also produced unexpectedly. A small amount of the parent lactone also remained unreacted and could be isolated as the solid picrate of the ammonia adduct. Reduction experiments using sodium and aqueous ammonia[6] also failed to give pure IV. Finally the recent method reported by the Japanese workers[7] to get the dihydro lactone via

[6] H. Ueda, Y. Shibahara and S. Shimizu, *Bull. Agrl. Chem. Japan* 23, 375 (1959).

[7] H. Hikino, K. Meguro, G. Kusano and T. Takemoto, *Chem., Pharm. Bull.* Japan 12, 5, 632 (1964).
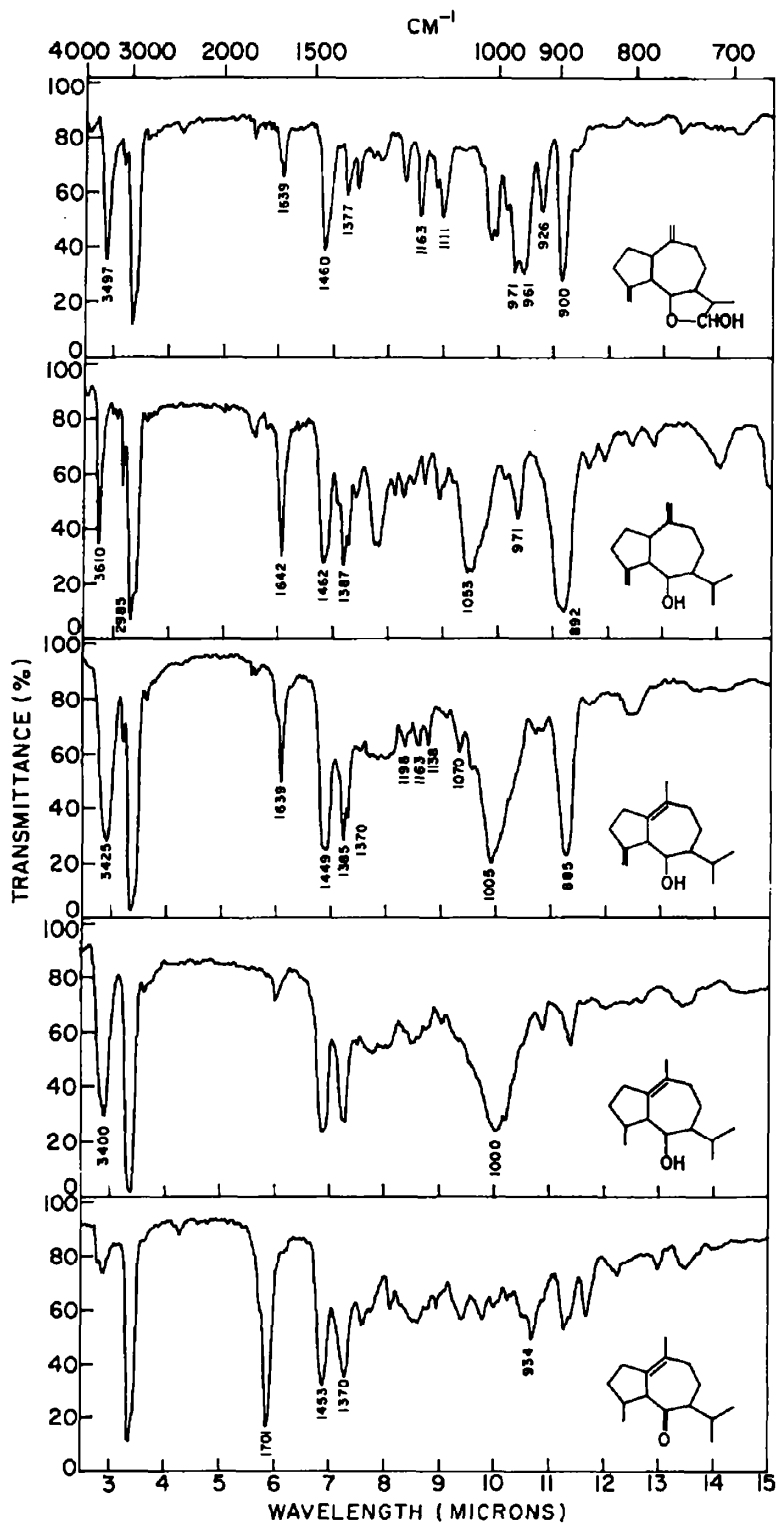
FIG. 2.

oxidation of the pure crystalline lactol (XII), obtained by prolonged reduction of dehydrocostus lactone by sodiumborohydride, was found to give pure dihydro dehydrocostus lactone containing one single epimer (GLC and TLC). Direct reduction of III by sodium borohydride gave 80% pure (GLC) dihydro dehydrocostus lactone. It was further observed by us that the lactol could be obtained more conveniently on a preparative scale by controlled reduction of IV (80% pure) with LAH.

The crystalline lactol (XII), on Huang–Minlon reduction gives different products at different temperatures. When the reduction was carried out at 135°, a mixture of two monols was obtained, which were separated by repeated chromatography over alumina. The monol (XIII), $C_{15}H_{24}O$, (GLC and TLC pure) eluted in the earlier fractions, showed the presence of exo-methylene double bonds in its IR spectrum (Fig. 2). The NMR spectrum showed signals at 0·7, 0·87, 0·96 δ (6H) due to methyls of the isopropyl group at C_7. In the olefinic region it showed signals at 4·66, 4·77, 5·1 δ (4H) due to four protons on exo-methylene double bonds at C_4 and C_{10}. A triplet at 2·89, 3·05, 3·18 δ (1H) was also observed which is due to the proton at C_6. The NMR spectrum is thus in complete agreement with the structure XIII.

From the middle fractions of chromatography, another pure (GLC, TLC) monol (XIV), $C_{15}H_{24}O$, whose IR spectrum (Fig. 2) clearly indicated the presence of exo-methylene group was obtained. Its NMR spectrum (Fig. 3) however, indicated the presence of only one exo-methylene group (signals at 4·55, 4·65 δ, 2H) and a methyl group on a double bond (signal at 1·65 δ, 3H) but did not show a signal due to a proton on a trialkylated double bond. It is, therefore, obvious that one of the two original exomethylene double bonds has migrated inside the ring. The spectral data would suggest that the alcohol could be represented by either of the structures XIV or XIVa. Preferential hydrogenation of the exo-methylene group with 5% Pd on charcoal in alcohol medium, followed by chromic acid oxidation of the resulting dihydro alcohol, XV or XVI afforded a number of products, from which a fraction rich in ketone was obtained by chromatography. The IR and UV spectra of this fraction indicated the presence of a nonconjugated ketone in it, necessarily represented as XVII. It therefore appears that the alcohol should be represented as XIV and its dihydro derivative as XV. The other products of oxidation include an oxidoketone $C_{15}H_{24}O_2$ mp. 95°, with the keto group located in a seven membered ring (IR spectrum, 1705 cm^{-1}).

This keto oxide is possibly formed from an intermediate keto alcohol containing OH group at C_7, formed by further oxidation of the ketone (XVII). The oxidoketone may be represented as XVIIb or XVIIc, although the possibility of other structures is not excluded. The NMR spectrum of the oxidoketone showed signals at 0·84, 0·88, 0·92, 0·99, 1·03 δ (9H) due to 3-methyls at C_4 and C_7. It also showed a signal at 1·32 δ (3H) due to the methyl group at C_{10} which is carrying the oxygen bridge (XVIIc). The NMR spectrum thus suggests structure XVIIc for the oxidoketone. The formation of a ketolactone possibly represented as XVIIa, during oxidation of XV, was also indicated from the IR spectrum of certain fractions of chromatography of the oxidation product.

When the Huang–Minlon reduction of the lactol was carried out at a higher temperature (170°), along with other products, the pure (TLC) hetero-annular dienic alcohol (XVIII) was obtained as the main component, in which both the original methylenic double bonds have migrated inside the ring. Its IR spectrum
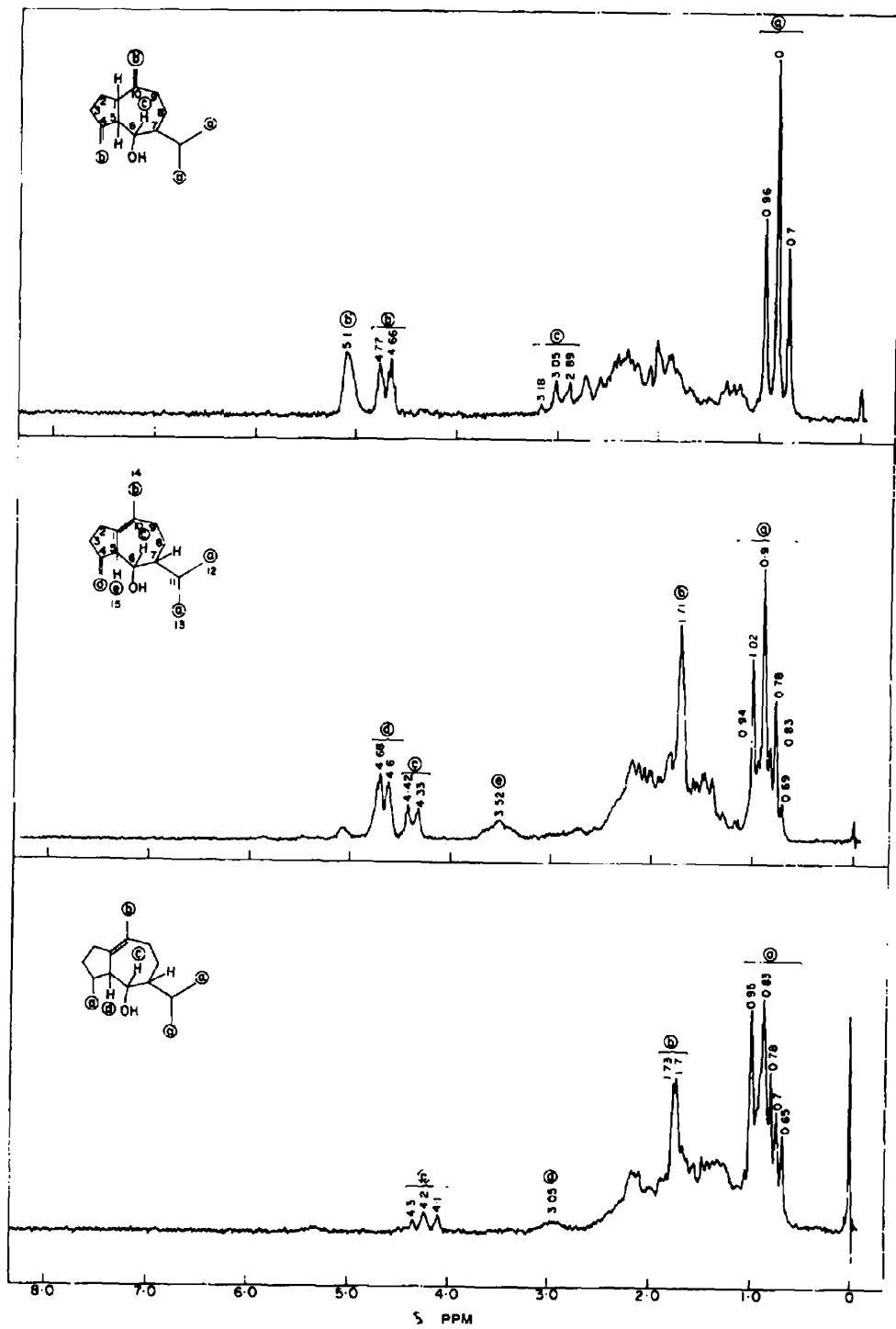
FIG. 3.

XII   XIII

XIV   XIV a   XV
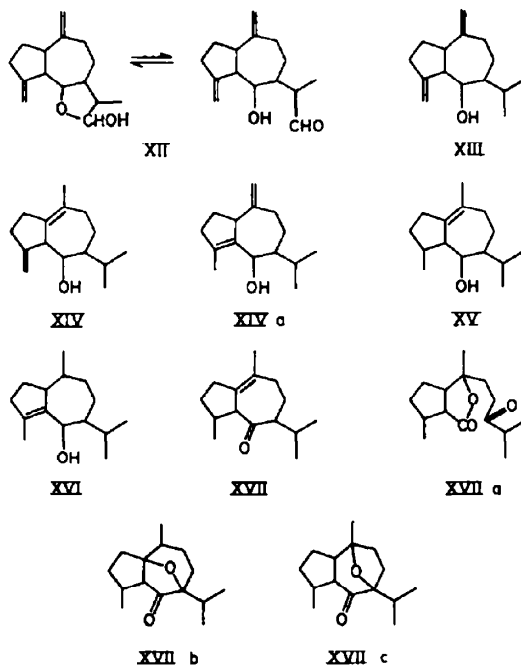
XVI   XVII   XVII a

XVII b   XVII c

Chart III

(Fig. 4) did not show the presence of any exo-methylene group. The NMR spectrum (Fig. 5) indicated the presence of two methyl groups on double bonds, signals at 1·59 δ (3H) and 1·82 δ (3H) and did not show any signals due to trialkylated protons. In conformity with this, it showed the characteristic UV absorption at 252 mμ (ε_{max} 9000). Oxidation of the compound with Jones' reagent, as well as other oxidizing agents like CrO_3–pyridine; and MnO_2, however, failed to give the expected conjugated dienone (XIX) in pure condition, although indication as to its formation, as one of the products, was observed in the UV spectrum of the oxidized product (λ_{max} 290, ε_{max} 3000). Much of the monol remained unaffected, even when the reaction is carried out for a longer time, suggesting that the alcoholic OH group is in a hindered position. During the formation of XVIII from XII, S-guaiazulene (XXIV; characterized through its TNB derivative), was also obtained as a by-product in 1·5% yield. It was also observed that the proportion of S-guaiazulene is raised to 3% when the same reaction is carried out at 220°.

In another series of experiments, V as obtained by direct catalytic hydrogenation of III or hydrogenation of epimerically pure IV, was reduced by LAH under controlled conditions, and the resulting hydroxyaldehyde (lactol), subjected to Huang–Minlon reduction to furnish in good yield the pure (TLC, GLC) crystalline monol, $C_{15}H_{28}O$ (XX). Dehydration of the monol by potassium hydrogen sulphate gave a mixture (GLC) of two unsaturated hydrocarbons, $C_{15}H_{26}$, both containing trialkylated double bonds (IR and NMR). Hydrogenation of this mixture (XXI) gave a saturated hydrocarbon, $C_{15}H_{28}$ (GLC, two isomers 80:20), identified as guaiane (I), by IR spectrum (Fig. 6) and physical properties. Formation of guaiane from III would

therefore support that the latter possesses a guaiane skeleton. Sulphur dehydrogenation of the monol (XX) gave s-guaiazulene (XXIV) in 8% yield, identified by IR spectrum, GLC and characterized through its TNB adduct. When IV was heated with alkali in diethylene glycol in an atmosphere of nitrogen at 180–200° for 5 hr, along with other products, chamazulene (XXV) could be isolated in 8% yield, identified by IR spectrum,[8] GLC and characterized through its TNB adduct.
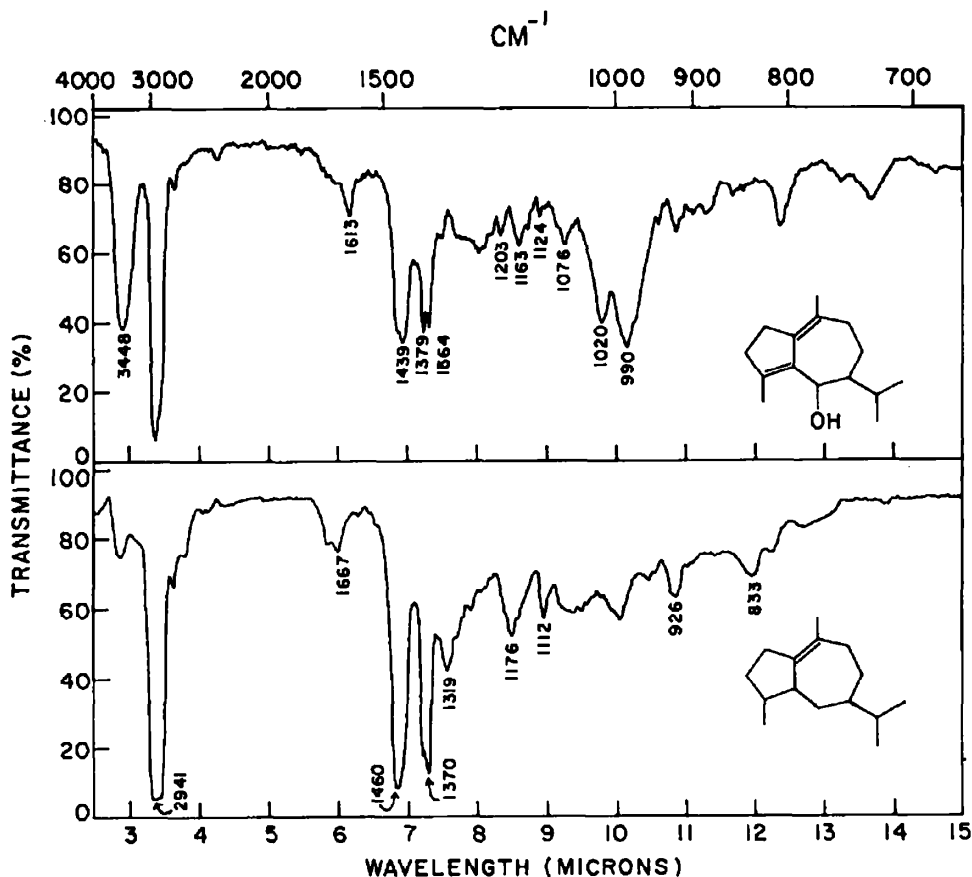

FIG. 4.

In our further examination of the monol (XX), it was oxidized with chromic acid to yield the pure (GLC, TLC), crystalline ketone, $C_{15}H_{26}O$ (XXII), along with a ketocarboxylic acid, $C_{15}H_{26}O_3$, characterized through its methyl ester, $C_{16}H_{28}O_3$ (XXIII, R = CH₃), the spectral properties of which would suggest structure XXIII for it. It is a suitable material for degradation to nepetalinic acid. Since it has been obtained via oxidation of the crystalline ketone (XXII) under mild conditions, its steric purity could be safely assumed.

Although the above experiments would strongly support the guainolide nature of the lactone, the point of attachment of the lactone ring had to be unequivocally

[8] J. Pliva, M. Horak, V. Herout and F. Sorm, *Sammlung der Spektren Und Physikalischen Konstanten* S, 123 and 127 (1960).
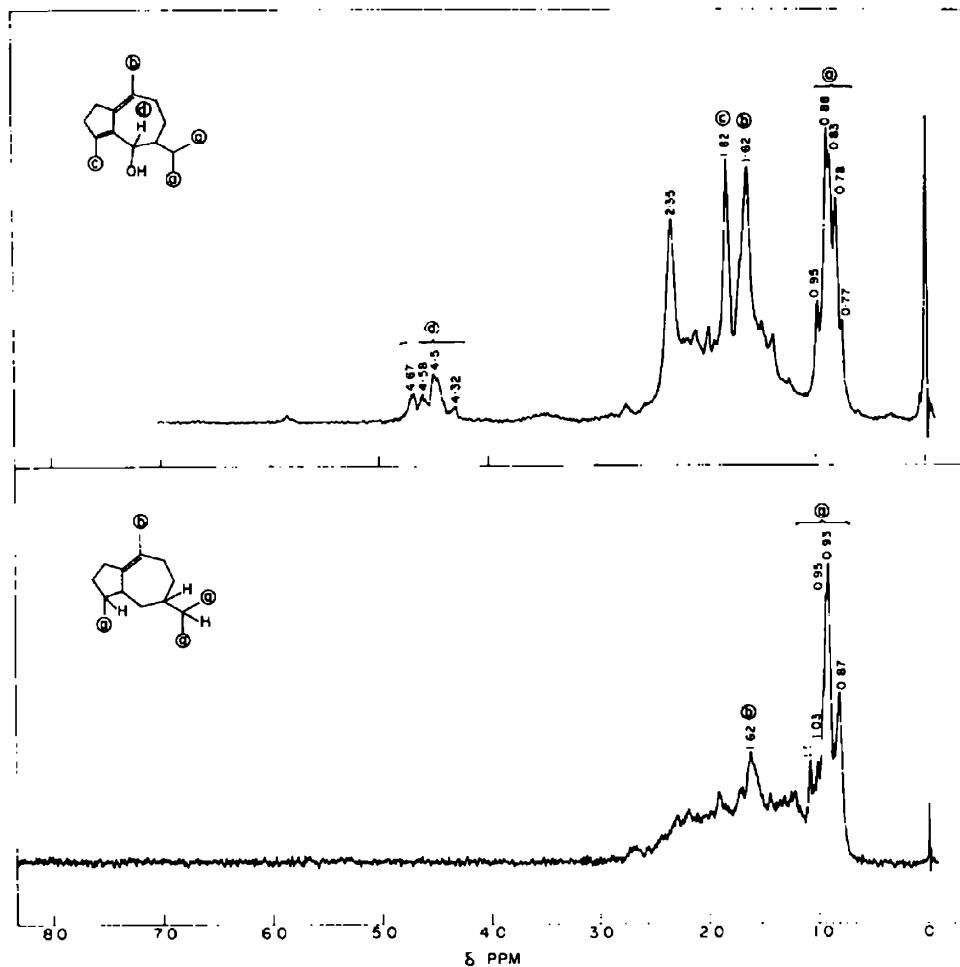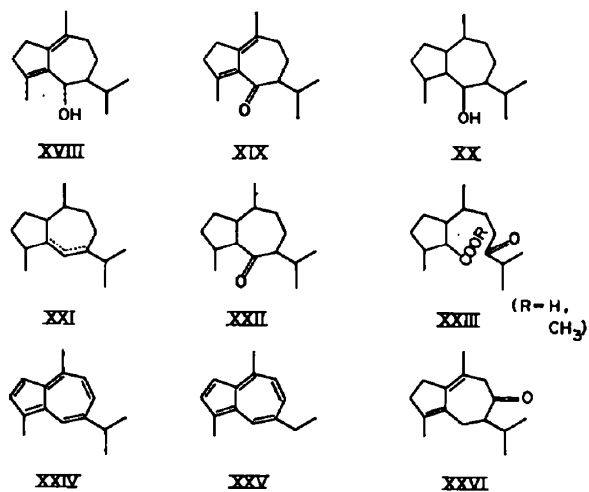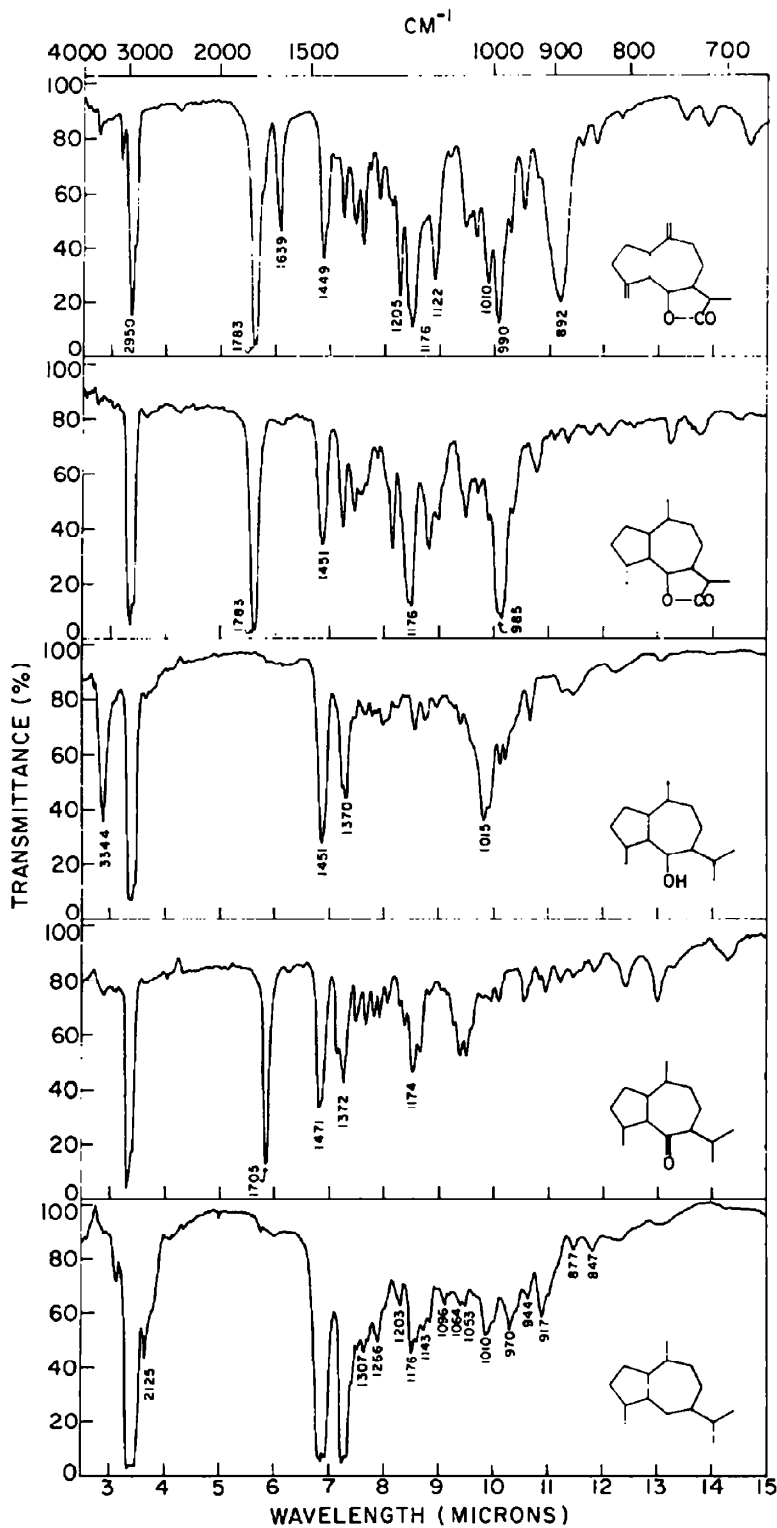
FIG. 5.

Chart IV

FIG. 6.

established. The absolute stereochemistry of dehydrocostus lactone at the ring juncture as well as that of the lactonic moiety had also to be decided. As such, the NMR spectrum of III would suggest that the point of attachment of the hydroxyl oxygen atom of the lactone moiety is at C_6 and not at C_8 as the spectrum shows a
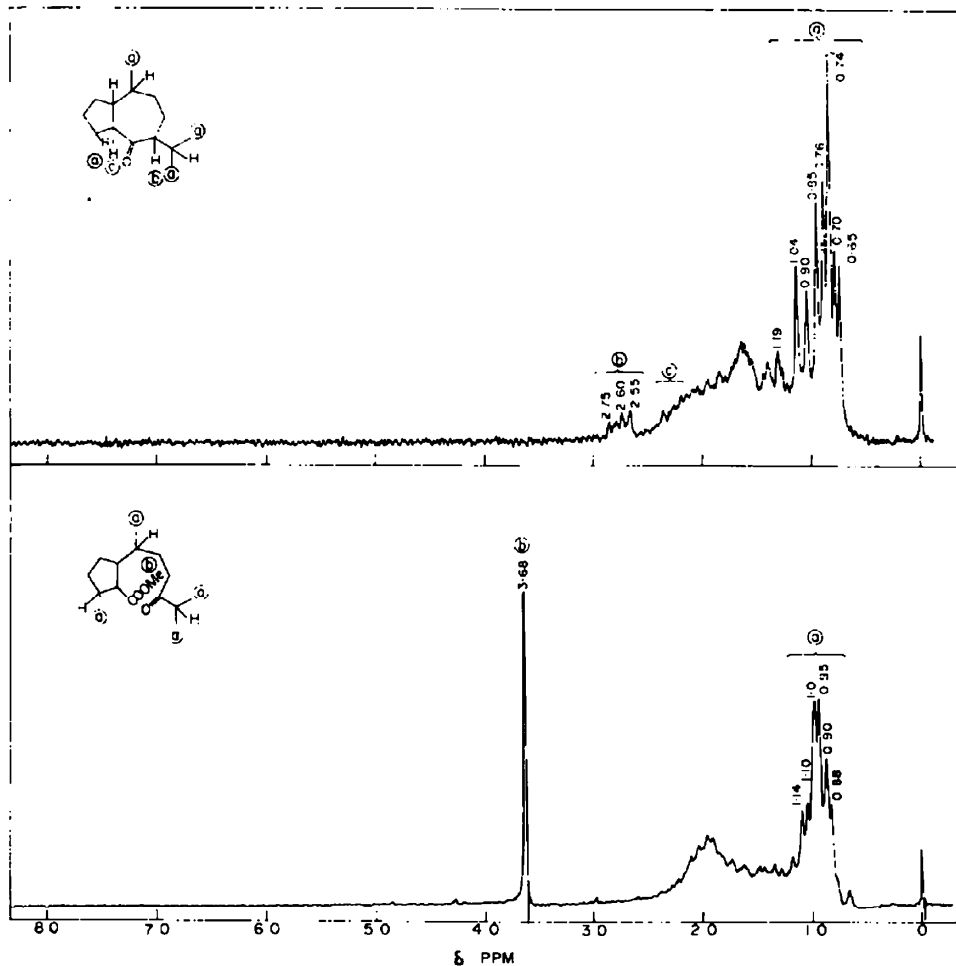
FIG. 7.

triplet at 3·83, 3·96 and 4·12 δ (1H) and not a quadruplet as would have been expected if the attachment were at C_8. Similar triplets were also observed in the NMR spectra of IV, XIII, XIV and XV (Figs 1, 3). This is also chemically supported by the formation of the conjugated dienone (XIX) as one of the products of oxidation of XVIII. The alternative structure (VI) would have resulted in the formation of a product (XXVI) with an isolated keto function.

When the dienic monol (XVIII) was subjected to metal amine reduction using either sodium or lithium in liquid ammonia, a hydrocarbon, $C_{15}H_{24}$ (XXVIII) was formed as the main product, along with traces of conjugated hydrocarbon (UV). The

structure of XXVIII is supported by its NMR spectrum, which showed the presence of 3-saturated methyl groups (signals at 0·87, 0·93, 1·03, 1·1 δ (9H) and one methyl group on a double bond [signal at 1·62 δ (3H)]. In the olefinic region, no signals were observed indicating that the double bond must be tetra alkylated. The hydrocarbon (XXVIII) must have been obtained by the further reduction of the conjugated hydrocarbon (XXVII) obtained as the primary product of hydrogenolysis. The possibility of any allylic migration of the double bond leading to the formation of XXIX, during metal amine reduction is not likely, as a heteroannular dienic system is expected to be more stable. The formation of the hydrocarbon (XXVIII) via the intermediate (XXVII) clearly establishes the position of the hydroxyl group at C_6.

For further elucidation of this, dihydrodehydrocostus lactone (IV) was hydrobrominated to yield a bromo compound (XXX) which as such on dehydrobromination was expected to give the dienic lactone (XXXI) showing characteristic UV absorption round about 250 mμ. Although some indication as to its formation has been obtained by UV spectrum of the crude lactone, its characterization is still in progress. Its conversion to guaiol (XXXIV) and related products is receiving our attention.
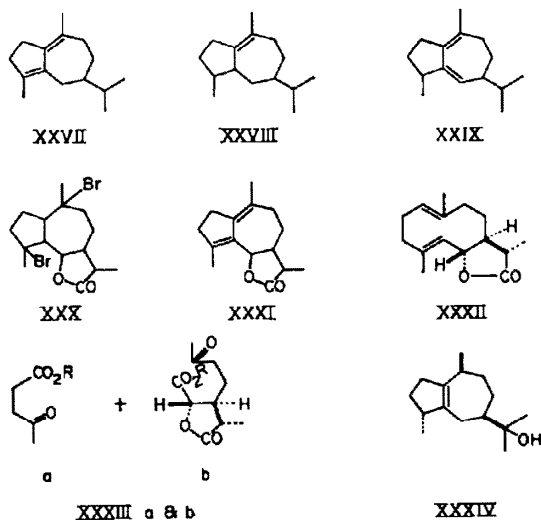

Chart $\underline{V}$

On ozonization XXXI is expected to give, along with laevulinic acid, the keto lactone carboxylic acid (XXXIII b) expected to be identical with the keto lactone carboxylic acid of known absolute configuration obtained under similar conditions from solid dihydrocostunolide (XXXII). This aspect of the investigation also is in progress.

The ORD curve of the ketone (XXII) showed a +ve Cotton effect (a, +64 units) which did not alter much on addition of hydrochloric acid, indicating thereby that the ketone group is in a hindered position.[9] Due to the paucity of reference compounds of this series, it was, however, not possible to draw any conclusions as regards the stereochemistry of ring juncture. From these evidences it is clear that the lactone attachment is at C_6–C_7.

[9] C. Djerassi, L. A. Mitscher and B. J. Mitscher, *J. Amer. Chem. Soc.* **81**, 947 (1959).

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Rotations were determined in $CHCl_3$ solution. The IR spectra (solids in nujol and liquids as liquid films, unless otherwise stated) were recorded on an Infracord spectrophotometer Model 137-B using NaCl optics by Mr. K. G. Deshpande. The NMR spectra were taken in CCl_4 solution using TMS as internal reference by Dr. P. M. Nair and colleagues. Microanalyses were carried out by Mr. Pansare and colleagues. GLC analyses were carried out by Mr. Bapat and Mr. Sankpal, on a Griffin & George apparatus (MK IIA model) on a polyester column using hydrogen as carrier gas.

Hexahydrodehydrocostus lactone (V). Dehydrocostus lactone, m.p.60–61°, $(\alpha)_D$ −13° (50 g) dissolved in alcohol (250 ml) was hydrogenated under press (1000 lbs/sq.in) using Pt catalyst initially at room temp (6 hr) and then at 50° (6 hr). Alcohol was removed under suction, the residue diluted with water and extracted with ether. Removal of ether furnished a liquid (48 g) purified by distillation, b.p. 130–135°/0·5 mm, n_D^{29} 1·4980, $(\alpha)_D$ +36° (c, 4·2). (Found: C, 76·68; H, 9·89. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%.)

Chromic acid oxidation of V. To a solution of V (67 g) in acetic acid (250 ml), was added a solution of CrO_3 (28·2 g) in water (267 ml) containing acetic acid (83 ml) and H_2SO_4 (67 ml). The mixture was stirred at 45° for 30 hr. Excess of CrO_3 was destroyed by MeOH (15 ml) followed by dilution with water (2 l.) and extracted with ether. The ether layer, after washing with water was extracted with Na_2CO_3 aq and the combined Na_2CO_3-extracts (from 2 batches) were acidified with dil. H_2SO_4 and the crude acid (17 g), extracted with ether, was esterified azeotropically in benzene solution (150 ml) containing EtOH (30 ml) and H_2SO_4 (2 ml). The ethyl ester (11 g) processed in the usual way was fractionated using a short vigreux column (15 cm) and collected into 4 fractions:

F. No.	n_D^{25}	$(\alpha)_D$	Eq. wt.	Elemental analysis		
				C	H	% OC_2H_5
1	1·4688	−9°	146·4	67·3	9·6	20·15
2	1·4815	−8·7°	151·7	66·4	8·85	18·6
3	1·4853	−12·4°	137·4	66·5	8·8	18·2
4	1·4835	−16·6°	132·0	65·2	8·7	18·4

$C_{14}H_{22}O_4$ requires: C, 66·11; H, 8·72; OC_2H_5 17·7%.

Eq. wt. 127·16. IR bands at: 1764 and 1721 (ester) cm^{-1}.

$NaBH_4$ *reduction of* III. Dehydrocostus lactone (23·0 g), dissolved in MeOH (70 ml) was treated with $NaBH_4$ (1 g) in instalments during 1 hr and the reaction mixture kept at room temp for 24 hr. After dilution with water containing HCl it was extracted with ether. The ether layer was washed with water and dried. Removal of ether gave a liquid product (22·3 g) which was chromatographed on alumina (gr. III, 440 g) and eluted with pet. ether and ether. The pet. ether eluted fraction (13 g) contained mostly the lactone (IV), $(\alpha)_D$ +10°. The ether eluted portion (4 g) on cooling in pet. ether solution gave the solid lactol (XII; 1 g), crystallized from pet. ether, m.p. 110–111°, $(\alpha)_D$ −36° (c, 2·5).

Controlled LAH *reduction of* IV. The lactone IV (22 g) was reduced by gradual addition of an ethereal solution of LAH (1·6 g of 75% purity in 200 ml) under cooling (−10°). The reaction mixture was stirred for 3 hr at −10° and for another 3 hr at room temp. It was then worked up to give a solid (21 g) m.p. 90–95°, which was crystallized from pet. ether to give the pure lactol (16 g), m.p. 110–111°, $(\alpha)_D$ −32° (c, 3·5). (Found: C, 77·45; H, 9·77. $C_{15}H_{22}O_2$ requires: C, 76·88; H, 9·46%.) IR spectrum is shown in Fig. 2.

Chromic acid oxidation of the lactol. The lactol (XII, 1·14 g) was dissolved in acetone (30 ml) and Jones' reagent was added dropwise till a brown colour persisted. It was kept at room temp for 1 hr and worked up to give a liquid, purified by chromatography and distillation to give pure IV (GLC), b.p. 155–160° (bath)/0·25 mm, n_D^{25} 1·5211, $(\alpha)_D$ +19° (c, 2·28). (Found: C, 77·30; H, 8·58. $C_{15}H_{20}O_2$ requires: C, 77·55; H, 8·68%.) IR spectrum is shown in Fig. 6.

Huang-Minlon reduction of the lactol (XII) *at* 135°. The lactol (20 g) dissolved in freshly distilled diethylene glycol (200 ml) was taken in a 3-necked flask, fitted with a condenser, a thermometer and a gas inlet. N_2 was allowed to bubble through and KOH (20 g) and hydrazine hydrate (25 ml) were introduced. The contents were heated to 135° and maintained for 4 hr. After cooling, it was diluted

with water and extracted with ether to furnish a liquid (14 g) which was chromatographed on alumina (gr. II, 420 g).

Fr. No.	Solvent	Vol. in ml	Wt. in g
1	Pet. ether	500	2·5
2	Pet. ether + benzene (1:1)	1000	4·2
3	Benzene	500	3·0
4	Ether	500	0·7

Fraction 1 was purified by rechromatography and distillation to give the monol (XIII), b.p. 120° (bath)/0·5 mm, n_D^{24} 1·5090; $(\alpha)_D$ +28·3° (c, 4·4). (Found: C, 81·53; H, 10·86. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98%.) The IR and NMR spectra are shown in Figs. 2 and 3.

Fractions 2 and 3 which contain essentially the monol (XIV) were mixed and purified by distillation to give the pure monol (GLC, TLC) b.p. 120–125° (bath)/0·3 mm, $n_D^{28·5}$ 1·5126; $(\alpha)_D$ +32° (c, 2·18). (Found: C, 81·08; H, 10·98. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98%.) IR spectrum is shown in Fig. 2.

Partial hydrogenation of the monol (XIV). The pure monol (1·53 g) absorbed 158 ml H_2 at NTP on hydrogenation in alcohol medium using 5% Pd–charcoal catalyst, corresponding to one double bond. The product was worked up in the usual manner and purified by distillation, to yield (XV), b.p. 140–150° (bath)/0·5 mm, n_D^{24} 1·5000, $(\alpha)_D$ +39·3°. (Found: C, 81·02; H, 11·70. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%.)

Chromic acid oxidation of the monol (XV). The monol (5 g) was dissolved in acetone (50 ml) and Jones' reagent was added drop by drop till a brown colour persisted. It was kept at room temp for 2·5 hr and worked up to give a liquid (4·8 g) which was separated into acidic and neutral parts by $NaHCO_3$ aq. The neutral part (4 g) was chromatographed on alumina (gr. II, 200 g) and eluted with pet. ether, pet. ether–benzene, benzene and ether. The pet. ether–benzene fraction (0·6 g) was rechromatographed to give the impure ketone (0·13 g) eluted with pet. ether, purified further by distillation (70% by GLC), b.p. 120° (bath)/0·6 mm. The ketone did not show any absorption in the region, 220–340 mμ, indicating it to be a non-conjugated ketone. The IR spectrum of the ketone showed a band at 1705 cm^{-1} characteristic of a non-conjugated seven membered ring ketone. From the later fractions of the rechromatography, a crystalline oxido ketone $C_{15}H_{24}O_2$, m.p. 95°; was isolated, whose IR spectrum indicated it to be a seven-membered ring ketone (1705 cm^{-1}). (Found: C, 76·49; H, 10·44. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%.) It may be represented by either of the structures (XVII b or c) as tetranitromethane test indicated it to be a saturated compound. The NMR spectrum favours structure XVIIc. From the tail fractions of rechromatography a keto lactone, possibly represented by (XVIIa) was isolated, b.p. 140–145° (bath)/0·8 mm, $(\alpha)_D$ +8·7° (c, 2·3). The IR spectrum showed bands at 1776 cm^{-1} (γ-lactone) and 1710 cm^{-1} (carbonyl group).

Huang–Minlon reduction of the lactol at 170–175°. The lactol (XII, 18 g) dissolved in diethylene glycol (130 ml) was taken in a 3-necked flask fitted with a condenser, a thermometer, and an inlet for N_2. N_2 was allowed to bubble through and KOH (18 g) and hydrazine hydrate (25 ml) were introduced. The contents were heated to 170–175° and maintained at that for 4 hr. After cooling the reaction product was diluted with water and extracted with ether. Removal of ether furnished a dark liquid (15·8 g) which was chromatographed on alumina (gr. II, 600 g) and eluted as follows:

F. No.	Solvent	Vol. in ml	Wt. in g
1	Pet. ether	1500	4·2
2	Pet. ether + benzene (1:1)	1800	0·65
3	Benzene	1000	0·375
4	Ether	1500	4·2
5	Methanol	1000	5·5

Fraction 4 was rechromatographed on alumina (gr. III, 84 g) and eluted with pet. ether and ether. The fraction eluted with pet. ether (1·1 g) (TLC, pure) showed λ_{max} 252 mμ, (ε_{max} 9000), $(\alpha)_D$ +45°. (Found: C, 81·28; H, 10·77. $C_{15}H_{24}O$ requires: C, 81·76; 10·98%.)

From fraction 1 s-guaiazulene was isolated and characterized through its TNB adduct, m.p. and mixed m.p. 149°.

Controlled LAH *reduction of* V. The lactone (V, 27 g) was reduced by gradual addition of an ethereal solution of LAH (2·6 g; 75% in 200 ml) under cooling at −10°. The reaction mixture was stirred for 3 hr at −10° and for another 3 hr at room temp. It was decomposed by alcohol and water and worked up to give crude hydroxy-aldehyde (26 g) containing some unreacted lactone (IR spectrum).

Huang–Minlon reduction of the above hydroxy aldehyde. A mixture of the hydroxy aldehyde (26 g), diethylene-glycol (150 ml), KOH (27 g) and hydrazine hydrate (26 ml), was heated at 200–220° for 5 hr in an atmosphere of N_2 and the product worked up as described earlier to give a liquid (21 g), which was chromatographed on alumina (gr. II, 1100 g) and eluted as follows:

F. No.	Solvent	Vol. in ml	Wt. in g
1	Pet. ether	600	6·155
2	Pet. ether + benzene (2:1)	4500	10·8
3	Pet. ether + benzene (1:1)	2000	0·8
4	Ether	500	1·5

Fraction 2 which solidified was crystallized from dilute alcohol to a const m.p. to give XX (GLC, TLC pure), m.p. 53–54°, $(\alpha)_D$ +6·3° (Found: C, 80·37; H, 12·58. $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%). IR spectrum is shown in Fig. 6.

Chromic acid oxidation of the monol (XX). The monol (1 g) was dissolved in acetone (20 ml) and Jones' reagent (5 ml) was added drop by drop till a brown colour persisted. The product was diluted with water and extracted with ether. The ether layer was washed with water, and extracted with Na_2CO_3 aq to remove the acid. The neutral portion (0·5 g) obtained after removal of ether was chromatographed on alumina (gr. III, 15 g) and eluted with pet. ether to give the ketone (XXII), purified by distillation and crystallization from pet. ether to give the pure (GLC, TLC) solid ketone (XXII), m.p. 54–55°; $(\alpha)_D$ −50°. (Found: C, 80·81; H, 11·7. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%.) IR spectrum is shown in Fig. 6. The ORD curve of the ketone, showed a +ve Cotton effect (amplitude +64 units), but the amplitude did not alter appreciably on addition of HCl, indicating it to be a hindered ketone. The NMR spectrum is shown in Fig. 7.

The Na_2CO_3-extract was acidified with dil. H_2SO_4 and extracted with ether. The acid obtained after removal of ether was esterified with diazomethane to give XXIII (GLC pure), b.p. 150–155 (bath)/ 0·6 mm, n_D^{25} 1·5200, $(\alpha)_D$ +20°. (Found: C, 71·60; H, 10·93. $C_{16}H_{28}O_2$ requires: C, 71·60; H, 10·52%.) The NMR spectrum (Fig. 7) indicated the presence of four saturated methyl groups.

Potassium hydrogensulphate dehydration of monol (XX). The monol (2·38 g) and $KHSO_4$ (3·5 g) were taken in a flask fitted with a reflux condenser and heated in an atmosphere of N_2 at 180–190° for 3 hr. After cooling, the product was dissolved in pet. ether and chromatographed on alumina (gr. I, 100 g), and eluted with pet. ether to give a mixture (GLC) of two hydrocarbons (XXI, 2·12 g) purified by distillation, b.p. 110–115° (bath)/9·5 mm, n_D^{25} 1·4860, $(\alpha)_D$ −3·7° (c, 6·4). (Found: C, 87·00; H, 12·70. $C_{15}H_{26}$ requires: C, 87·30; H, 12·70%.)

Hydrogenation of XXI *to* I. The mixture of hydrocarbons (0·7177 g) absorbed (90·5 ml of H_2 at NTP) on hydrogenation in acetic acid medium using Pt catalyst, corresponding to one double bond. The hydrogenated product, worked up in the usual manner was purified by distillation, b.p. 125–130° (bath)/1·5 mm, n_D^{25} 1·4734, $(\alpha)_D$ −19° (c, 5·4). (Found: C, 86·80; H, 13·5. $C_{15}H_{28}$ requires: C, 86·46; H, 13·54%.) The IR spectrum is shown in Fig. 6.

Sulphur dehydrogenation of the monol (XX). The monol (0·5 g) was heated with S (1 g) for 5 hr at 200–220° in an atmosphere of N_2. The product dissolved in pet. ether was chromatographed on alumina (gr. I, 20 g) and eluted with pet. ether. The blue coloured fraction was separated into azulenic and non-azulenic parts by 80% phosphoric acid. The azulenic part (40 mg) gave a TNB adduct m.p. 149–150°. (Found: C, 61·67; H, 4·80; N, 10·23. $C_{21}H_{21}N_3O_6$ requires: C, 61·36; H, 5·15; N, 10·21%.)

Chamazulene from dihydrodehydrocostus lactone (IV). The lactone IV (3 g), dissolved in diethylene glycol (50 ml) was heated with KOH (3 g), in an atmosphere of N_2 at 180–200° for 5 hr. It was then diluted with water, and extracted with ether. The product obtained after removal of ether (1·5 g) was chromatographed on alumina (50 g; gr. I) and the violet coloured fraction eluted with pet. ether was separated into azulenic and non-azulenic portions by 80% phosphoric acid. The azulene obtained was further purified by chromatography and identified as chamazulene by its IR spectrum and TNB adduct, m.p. 131–132°. (Found: C, 61·53; H, 5·02; N, 10·2. $C_{20}H_{19}N_3O_6$ requires: C, 60·45; H, 4·82; N, 10·58%.)

Metal amine reduction of the dienic monol (XVIII). In a 500 ml 3-necked flask equipped with a Hg seal stirrer liquid ammonia (150 ml) was drawn. Li (1·5 g) was carefully added during 15–20 min. A solution of the monol (0·73 g) in ether (60 ml) was added gradually and the mixture stirred for 3 hr. Ammonia was allowed to evaporate and the residue decomposed by the dropwise addition of alcohol followed by water. After further dilution with water it was extracted with ether, washed repeatedly with water and dried (Na_2SO_4). After removal of ether, the product was chromatographed on neutral alumina (gr. I, 21 g) and the fraction eluted with pet. ether was distilled to give the hydrocarbon (0·23 g) (XXVIII) b.p. 120–125°/4·5 mm, n_D^{23} 1·4930; $(\alpha)_D$ +15° (c, 1·36). UV end absorption ε 210, 4,350. (Found: C, 87·10; H, 12·37. $C_{16}H_{26}$ requires: C, 87·30; H, 12·70%.) The NMR spectrum is shown in Fig. 5.