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DEHYDRATON REACTION OF GUAIOL AND DIHYDROGUAIOLS AND TRANSFORMATION OF 1α,5α-DIHYDROGUAIOL TO 1α,5α-HEXAHYDRODEHYDROCOSTUS LACTONE[*]

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Abstract—Dehydration of guaiol and the epimeric dihydroguaiols in the presence of many acidic dehydrating agents has been studied and the products characterized by GLC, spectroscopic analysis and by chemical transformations. The most interesting dehydration products are Bates' guaioxide (VIIIa, VIIIb) obtained by perchloric acid–acetic acid dehydration of guaiol (I); a methyl ketone (XIII) having a novel skeleton, obtained by the isomerization of the epoxide prepared from 1β,5β-dihydro-β-guaiene (XIb); and the secondary alcohol (XVI) formed by hydroboration–oxidation of 1α,5α-dihydro-ε-guaiene (XIIa).

1α,5α-Dihydro-α-guaiene (XVIIa) on hydroboration–oxidation is converted to the primary alcohol 1α,5α-guaian-12-ol (XXI) which on oxidation with chromic acid affords the corresponding aldehyde and the acid. On treatment with lead tetraacetate in benzene solution, XXI is converted to the 1α,5α-guaian-12-6 oxide (XXII), chromic acid oxidation of which affords 1α,5α-hexahydrodehydrocostus lactone (XXIII).

RECENTLY many bi- and tricycle sesquiterpenic hydrocarbons and oxygenated compounds, having guaiane or modified guaine skeletons, such as patchoulenone,[1] isopatchoulenone,[2,3] and cyperene,[4] have been isolated from natural sources. It was therefore felt that the study of dehydration and cyclization reactions of guaiol and its dihydro derivatives and also their behaviour towards oxidizing agents might lead to the synthesis of some of these natural products or their closely related derivatives.

The structure and stereochemistry of guaiol has been the subject of intensive investigation by several groups of workers.[5-8] It is now represented by the stereoformula I and the crystalline (−)-dihydroguaiol and liquid (+)-dihydroguaiol by IIa and IIb respectively.

Initially we studied the action of various dehydrating agents on guaiol and both the isomers of dihydroguaiol. The products obtained were characterized by a combination of spectroscopic and GLC analyses[9] and also by chemical transformations.

[*] Communication No. 933, from the National Chemical Laboratory, Poona-8, India.

[1] B. Trivedi, O. Motl, V. Herout and F. Šorm, *Coll. Czech. Chem. Comm.* 29, 1675 (1964).

[2] H. Hikino, K. Aota and T. Takemoto, *Chem. Pharm. Bull.*, 13, (5), 631 (1965).

[3] S. B. Nerali, P. S. Kalsi, K. K. Chakravarti and S. C. Bhattacharyya, *Tetrahedron Letters* No. 45, 4053 (1965).

[4] B. Trivedi, O. Motl, J. Smolikora and F. Šorm, *Tetrahedron Letters* No. 19, 1197 (1964).

[5] E. J. Eisenbraun, T. George, B. Riniker and C. Djerassi, *J. Amer. Chem. Soc.* 82, 3648 (1960).

[6] K. Takeda and H. Minato, *Chem. Pharm. Bull.* 9, 619 (1961).

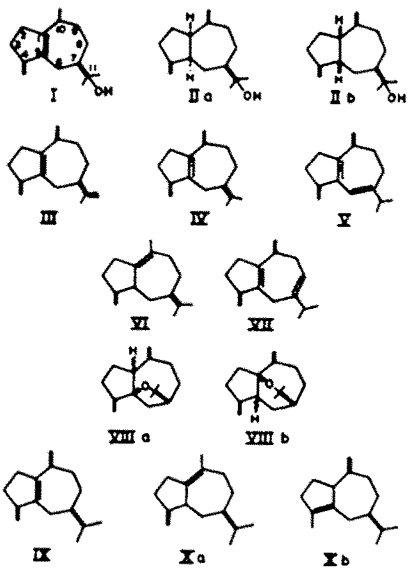
[7] H. Minato, *Tetrahedron* 18, 365 (1962).

[8] K. Takeda, H. Minato, T. Terasava and C. Yanaihara, *Chem. Pharm. Bull.* 13(8), 942 (1965).

The GLC analyses* of the sulphuric acid dehydration[9] product of guaiol (I) shows three peaks corresponding to α-guaiene (III; 80%, Rt 4·70′), β-guaiene (IV; 12%, Rt 5·55′) and δ-guaiene (VI; 8%, Rt 6·50′). The UV spectrum of the mixture shows a strong end absorption $\varepsilon_{211}^{11000}$ and no absorption due to double bond conjugation. The IR spectrum shows maxima at 1640 and 890 cm^{-1}, indicated the presence of a methylenic double bond. The NMR spectrum confirms the presence of α-guaiene (a sharp signal at 5·4 τ) and does not show the presence of γ-guaiene (V). Further, the integrated intensities of the olefinic and secondary methyl signals also indicate the presence of δ-guaiene (VI) in small proportion.

Guaiol on treatment with formic acid[10a] affords a mixture of hydrocarbons rich in the conjugated diene, γ-guaiene (40%; Rt 4·23′). It also contains ε-guaiene (VII; 26%; Rt 3·31′) and another hydrocarbon (34%; Rt 3·78′). The UV spectrum shows an absorption maximum at 256 mμ (ε 3740; pure γ-guaiene ε 8990) and an end absorption $\varepsilon_{212}^{11270}$.

CHART 1



Treatment of guaiol with perchloric acid in acetic acid[10b] yields only a very small amount of the expected conjugated diene V, the major component being an oxide which is identical with the guaioxide obtained previously by Bates *et al.*[9] by treating guaiol with sulphuric acid–acetic acid mixture. The GLC analysis shows the mixture to consist of guaioxide (VIIIa or VIIIb, 85%; Rt 5·55′) and γ-guaiene (15%, Rt 4·23′). The UV spectrum is in complete agreement with this, showing an absorption

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* The authors are grateful to Mr. B. V. Bapat and Mr. T. K. Sankpal for carrying out the GLC analysis.

[9] R. B. Bates and R. C. Slagel, *Chem. & Ind.* (*Lond*) 1715 (1962). We have made convenient use of these data and express our gratitude to the authors.

[10a] J. Plíva and F. Šorm, *Coll. Czech. Chem. Comm.* **14**, 274 (1949).

[10b] S. K. Paknikar and S. C. Bhattacharyya, *Tetrahedron* **18**, 1509 (1962).

band at 256 mμ (ε 1632; ε^{211} 1016). The NMR spectrum of the guaioxide obtained in a pure form from this mixture by column chromatography is superimposable on that of Bates' guaioxide.

Guaiol on heating with polyphosphoric[11] acid gives a complex mixture of hydrocarbons. At elevated temperatures (160°) larger amount of guaiazulene is obtained. The reaction product contains α,β- γ- and ε-guaienes, and s-guaiazulene. A saturated hydrocarbon, not yet identified, has also been isolated from the mixture. The product, on chromatography of the less polar fractions (30% of the total), shows the presence of two saturated hydrocarbons (A, 5%; Rt 1·8′ and B, 46%; Rt 2·6′), ε-guaiene (35%; Rt 3·31′) and α-guaiene (12%, 4·70′). The more polar fractions of the chromatography indicate the presence of β- and γ-guaienes and s-guaiazulene. UV spectrum of the total mixture shows bands at 350, 280 and 256 mμ, indicating the presence of aromatic and conjugated double bonds.

The major saturated hydrocarbon B, isolated via column chromatography of the less polar fraction analyses for $C_{15}H_{26}$ and does not show any characteristic features in the IR and UV spectra. This is found to be not identical with guaianes and other saturated hydrocarbons available, having the guaiane and related tricyclic skeletons. Our expectation to obtain a product like cyperene[4] by cyclodehydration of guaiol was not realized.

Guaiol benzoate on pyrolysis gives pure α-guaiene (purity 97%; Rt 4·70′) along with traces of β-guaiene (3%; Rt 5·55′). α-Guaiene on hydrogenation[12] gives a product consisting of α-dihydroguaiene (IX, 67%; Rt 3·7′), unreacted α-guaiene (10%; Rt 4·7′), β-guaiene which was an impurity in the starting α-guaiene (3%; Rt 5·55′), and, probably, products of double bond isomerization (Xa and Xb, 18%, Rts 6·7′ and 7·0′ respectively).

For our subsequent series of experiments, guaiol was hydrogenated[5,8,13] under pressure at 100° with Raney nickel. 1α,5α-Dihydroguaiol (IIa) separates out on cooling an acetone solution of the alcohol mixture. The mother liquor affords on fractional distillation through an efficient column 1β,5β-dihydroguaiol (IIB; $[\alpha]^{25}_{D}$ +42°). This does not resolve on GLC on a polyester column of high efficiency, nor does it separate on TLC plates with the different solvent systems employed. However, from the GLC analysis of its dehydration products, its purity would appear to be about 82%; "pure" IIb ($[\alpha]_D$ +46°), obtained by the Japanese workers[8] by the repeated fractionation of the mother liquor, would thus appear to be only 85% pure, as the calculated rotation of this isomer is +73°. This is in good agreement with their finding that their dextrorotatory alcohol on chromic acid oxidation yielded a C_{12}-ketone mixture containing an appreciable amount of the di-α-isomer.[8]

Dehydration of liquid IIb, $[\alpha]_D$ +42°, with perchloric acid–acetic acid mixture, gives 1β,5β-dihydro-β-guaiene (XIb, 36%; Rt 3·25′), 1β,5β-dihydro-ε-guaiene (XIIb, 45%; Rt 4·52′), along with their di-α-isomers XIa (8%, Rt 4·1′) and XIIa (11%, Rt 5·9′). The mixture on epoxidation followed by BF_3-ethereate isomerization[14] affords in the mixture XIII formed by the methyl migration from C_{11} to C_7. This ketone isolated and purified through its semicarbazone (m.p. 173°) shows in its NMR

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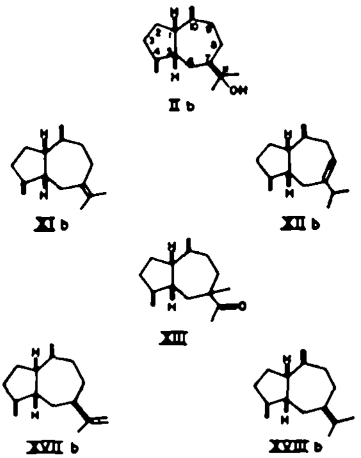
[11] Sukh Dev, *J. Ind. Chem. Soc.* 32, 262 (1955); 34, 265 (1957).

[12] K. Takeda, H. Minato and S. Mosaka, *Tetrahedron* 13, 308 (1961).

[13] P. A. Plattner and L. Lemay, *Helv. Chim. Acta* 23, 897 (1940).

[14] H. B. Henbest and T. I. Wrigley, *J. Chem. Soc.* 4596 (1957).

CHART 2



spectrum the absence of the isopropyl side chain and the presence of a methyl ketone (7·98 τ, 3H), a tertiary methyl (8·97 τ, 3H) and two secondary methyls (around 9·1 τ, 6H). The product also gives iodoform test characteristic of a methyl ketone.

The mother liquor after the separation of this semicarbazone on oxalic acid treatment affords a ketonic product showing an absorption at 1418 cm^{-1}, indicating the presence of a keto group having a methylene adjacent to it. This ketone could not be isolated in a pure form due to the paucity of material.

Dehydration of crystalline IIa, with perchloric acid–acetic acid mixture, furnishes 1α,5α-dihydro-β-guaiene (XIa, 40%; Rt 4·1′) and 1α,5α-dihydro-ε-guaiene (XIIa, 55%; Rt 5·9′) and traces of another hydrocarbon, probably 1α,5α-dihydro-γ-guaiene (XIV, 5%). Pure dihydro-β- and ε-guaienes could be separated from this mixture by column chromatography over silver nitrate-impregnated silica gel.[15] The UV spectrum of XIa shows a strong end absorption ε_{211}^{6000} and the NMR spectrum shows the presence of two methyl groups on double bond (8·33 τ and 8·38 τ; 6H) and the absence of olefinic protons. On ozonization it furnishes acetone and the known C_{13}-ketone[8] (XV); the latter is characterized through its semicarbazone m.p. 200°. Compound XIIa shows IR absorption bands at 840 and 812 cm^{-1}, characteristic of a trisubstituted double bond, Its NMR spectrum shows a triplet centred at 4·5 τ due to an olefinic proton coupling with the adjacent methylene group, fixing the double bond to be between C_7 and C_8. On hydroboration–oxidation,[16] this hydrocarbon furnishes the expected secondary alcohol XVI, confirming structure XIIa.

1α,5α-Dihydroguaiol benzoate gives on pyrolysis 1α,5α-Dihydro-α-guaiene (XVIIa; Rt 4·3′) in 97% purity, containing only traces of XIa (Rt 5·9′). Hydrogenation of XVIIa affords pure 1α,5α-guaiane (XVIIIa, 98% pure; Rt 3·65′).

1β,5β-Dihydro-α-guaiene, obtained by the pyrolysis of the benzoate of the somewhat impure dextrorotatory dihydroguaiol, on purification by preparative TLC

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[15] A. S. Gupta and S. Dev, *J. Chromatog.* 12, 190 (1963).

[16] [a] H. C. Brown and P. A. Tierney, *J. Amer. Chem. Soc.* 80, 1552 (1958); [b] H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.* 81, 247 (1959); [c] A. D. Wagh, S. K. Paknikar and S. C. Bhattacharyya, *Tetrahedron* 20, 2647 (1964).

CHART 3

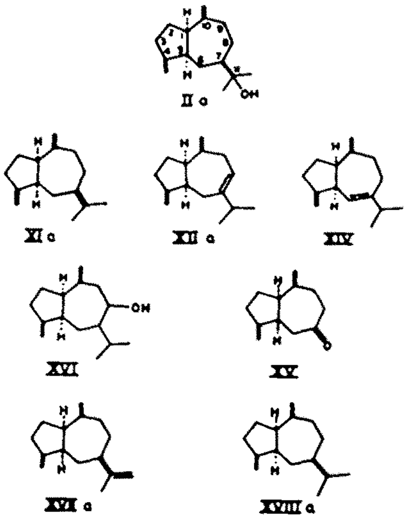
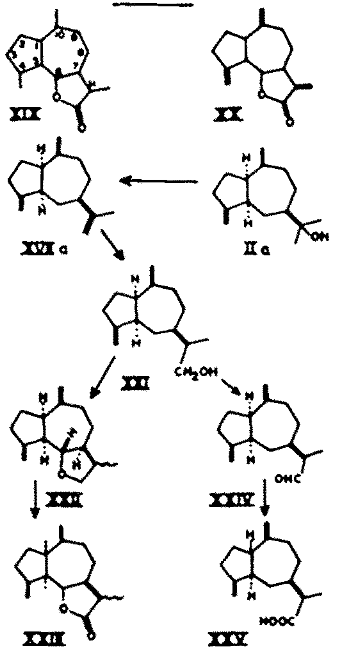


CHART 4



affords nearly pure 1β,5β-dihydro-α-guaiene (XVIIb; Rt 4·63′). This on hydrogenation gives 1β,5β-guaiane (XVIIIb; Rt 2·8′).

The stereochemistry of hexahydrodehydrocostus lactone (XIX) is yet unsolved[17–19] and it was felt that guaiol, the structure and stereochemistry of which has been unambiguously established, may prove useful via synthetic routes to throw some light on the stereochemistry of hexahydrodehydrocostus lactone or its isomers, and consequently on that of dehydrocostus[19] lactone (XX) itself.

We therefore subjected pure XVIIa, prepared by the pyrolysis of the benzoate of the crystalline *cis*-dihydroguaiol (IIa) to hydroboration–oxidation to obtain 1α,5α-guaian-12-ol (XXI). Oxidation of this alcohol with Jones chromic acid reagent[20] furnishes the 1α,5α-guaian-12-al (XXIV) and 1α,5α-guaian-12-oic acid (XXV), the former is characterized as its semicarbazone and the latter as its methyl ester.

1α,5α-Guaian-12-ol (XXI), on lead tetraacetate oxidation[16c,21] in benzene medium, furnishes the tetrahydrofuran derivative (XXII). The oxide ring in this compound is between C_{12} and C_8; its NMR spectrum, shows triplet around 6·08 τ, whereas the C_{12}–C_6 oxide should have shown a typical 8-line pattern.[22] The coupling of the C_8 proton with protons at C_9 (J = 10 c/s) and C_7 (J = 10 c/s), shows the oxide ring to be *trans*-oriented. Chromic acid oxidation of this oxide affords the dextrorotatory 1α,5α-isomer of hexahydro-dehydrocostus lactone (XXIII). The NMR spectrum of

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[17] Y. R. Naves, *Helv. Chim. Acta* 31, 1172 (1948).

[18] M. Romaňuk, V. Herout and F. Šorm, *Coll. Czech. Chem. Comm.* 21, 894 (1956).

[19] S. B. Mathur, S. V. Hiremath, G. H. Kulkarni, G. R. Kelkar and S. C. Bhattacharyya and in part by D. Simonovic and A. S. Rao, *Tetrahedron* 21, 3575 (1965).

[20] A. Bowers, T. G. Halsall, E. R. H. Jones and (in part) A. J. Lemin. *J. Chem. Soc.* 2548 (1953).

[21] V. M. Mićović, R. Mamuzić, D. Jeremić and M. Lj. Mihailović, *Tetrahedron* 20, 2279 (1964).

[22] R. B. Bates, V. Procházka and Z. Čekan, *Tetrahedron Letters* No. 14, 877 (1963).

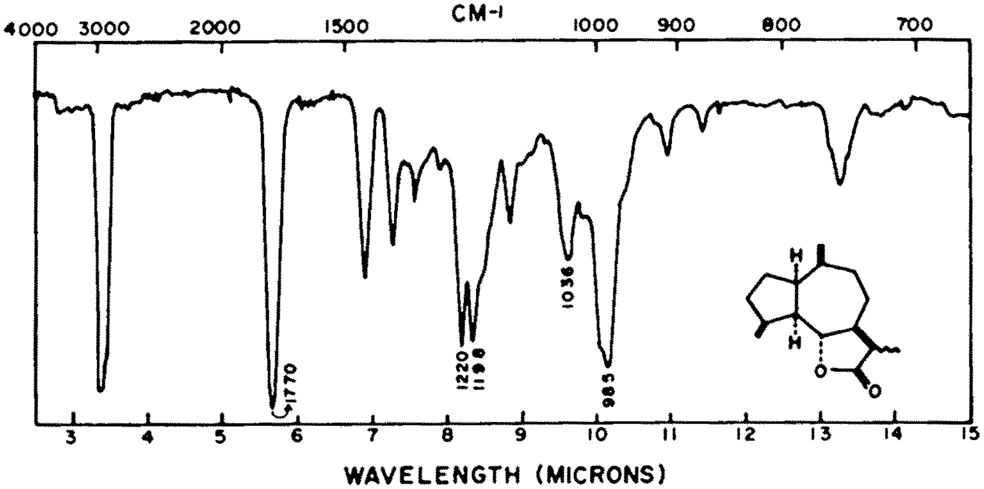

FIG. 1. 1α,5α-Hexahydrodehydrocostus lactone (XXIII).

this lactone also is in agreement with the stereoformula assigned to it. It is however different from hexahydrodehydrocostus lactone obtained by the hydrogenation of dehydrocostus lactone.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. B.Ps refer to bath temp unless otherwise stated. Rotations (in chf solns. IR (solids in nujol and liquids as liquid films); Perkin–Elmer Infracord spectrophotometer, Model 137B). UV (Beckman DK-2 ratio-recording spectrophotometer in the spectroscopy section of our laboratory). GLC analyses (Griffin and George apparatus MK II-A Model, operating under pressure on 6-ft polyester and carbowax columns using H_2 at a flow rate of 75 ml/min). NMR (in CCl_4 solns using TMS as the internal ref.). Microanalyses (in our Microanalytical section). Anhydrous Na_2SO_4 was used for drying.

Purification of guaiol (I). Guacum wood oil (supplied by Industrial Perfumes-RBF, Bombay; and Fritzsche Bros. Inc.,* New York) was fractionally distilled and the fractions, b.p. 90–100° (actual)/0·1 mm were mixed and crystallized from pet. ether or preferably from acetone at −15° m.p. 89–90°, $[\alpha]_D$ −41° (*c*, 3·5). GLC single peak, TLC single spot; ν_{max} 3400, 1155, 1140, 885 and 825; UV ε^{210}_{EtOH} 6840. (Found: C, 80·63; H, 11·73. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%.)

Dehydration of guaiol with H_2SO_4. Guaiol (2 g) was heated with H_2SO_4 (25%; 3 ml) at 100° for 9 hr. The product was cooled, diluted with water and extracted with pet. ether. The extract was washed successively with water, satd $NaHCO_3$aq and water till neutral and dried. The solvents was removed and the residue freed from more polar components by filtration over neutral alumina (gr. I, 50 g). The pet. ether eluate furnished a hydrocarbon mixture (1·4 g), b.p. 110–140°/1·5 mm, ε^{210}_{EtOH} 11,270. IR spectrum (ν_{max} 1640 and 890) showed the presence of α-guaiene which was confirmed by the NMR spectrum (sharp signal at 5·4 τ, $>C=CH_2$). GLC showed the mixture to consist of α-guaiene (III; Rt 4·70′; 80%), β-guaiene (IV, Rt 5·55′; 12%) and δ-guaiene (VI, Rt 6·50′; 8%).

Dehydration of guaiol with formic acid. A mixture of guaiol (4 g) and formic acid (98%; 18 ml) was heated at 90° for 3 hr, and the product was poured into water (500 ml) and extracted with ether. The extract was washed free of acid, dried, solvent removed and the residue filtered through a column of alumina (gr. I, 100 g) to afford in the pet. ether eluate a hydrocarbon mixture (1·5 g), b.p. 100–140°/0·7 mm, n_D^{30} 1·5015. UV: an absorption maximum at 256 mμ (ε 3740) and end absorption ε^{215}_{EtOH} 11270. GLC: 3 peaks corresponding to ε-guaiene (VII) Rt, 3·31′; 26%), another hydrocarbon (Rt 3·78′; 34%) and γ-guaiene (V: Rt 4·23′ ; 40%); traces of azulene were also obtained. The total mixture showed bands at 1620, 1600 and 813 cm^{-1}.

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* We are very grateful to these two firms for the generous gift of guacum wood oil.

Action of perchloric acid on guaiol. Guaiol (5 g) was dissolved in AcOH (50 ml) and perchloric acid (20%; 6 ml) was added dropwise to the clear soln. The colour changed to dark brown on addition of the reagent. The mixture was (kept at room temp for 72 hr with stirring. The dark soln was diluted with water, extracted with ether, the ether layer washed free from acid and dried. On removal of the solvent and filtration of the residue through alumina (gr. I, 250 g), a mixture of guaioxide and the conjugated diene-γ-guaiene was obtained. GLC: 2 peaks corresponding to γ-guaiene (V; Rt 4·23′) and guaioxide (VIIIa or VIIIb; Rt 5·55′) respectively. UV: 256 mμ (ε 1632); $\epsilon^{211}_{\mathrm{EtOH}}$ 1016. The guaioxide was further purified by rechromatography over neutral alumina (gr. I, 100 g), b.p. 120–125°/1·5 mm, n_D^{26} 1·4810; $[\alpha]_D^{26}$ −38·2° (*c*, 3·46); ν_{max} 1039, 1015, 1000, 980, 940, 917, 892, 850 and 806. UV: no end absorptoon. NMR: 9·0, 9·05, 9·09, 9·14 τ (Me on C_4 and C_{10}); 8·69 and 8·84 τ (Me on C_{11}). (Found: C, 81·34; H, 11·89. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%.)

Polyphosphoric acid dehydration of guaiol. P_2O_5 (7 g) was added to orthophosphoric acid, freshly prepared by heating phosphoric acid (6 g) at 160° for 2·5 hr and the mixture was heated at 160° for 3 hr to get a clear viscous liquid. Guaiol (1·2 g) was added at 100° and the temp was maintained at 100° with vigorous stirring. Addition of water and extraction with ether followed by the removal of ether and filtration through neutral alumina (gr. I, 20 g) furnished a mixture of hydrocarbons (0·6 g) which was rechromatographed over alumina (gr. I, 25 g). Two fractions were collected. The early pet. ether fraction (0·18 g) on GLC analysis showed peaks corresponding to two unidentified saturated hydrocarbons (A, Rt 1·8′; 5% B, Rt 2·6′; 46%), ε-guaiene (Rt 3·31′; 35%) and α-guaiene (Rt 4·70′; 12%). The mixture showed IR absorption bands at 1640, 897 and 813 cm⁻¹. The later pet. ether fractions showed the presence of s-guaiazulene, β- and γ-guaienes. UV spectrum of the total mixture showed bands at 350, 280 and 256 mμ.

The saturated hydrocarbon (Rt 2·6′) could be separated in a pure form by rechromatography of the mixture. This did not show any UV absorption even in the end region and no characteristic feature in the IR region; b.p. 100–120°/2 mm, n_D^{30} 1·4840; $[\alpha]_D^{30}$ −4·49° (*c*, 3·34). (Found: C, 87·64; H, 12·64. $C_{15}H_{26}$ requires: C, 87·30; H, 12·70%.)

Preparation of α-guaiene. Guaiol (5 g) and BzCl (10 ml) were taken in pyridine (25 ml) and the mixture was left at room temp for 36 hr. It was then warmed on a water bath for 4 hr. The benzoate was separated by extraction with ether and filtration through alumina (gr. II, 100 g). Elution with pet. ether–benzene (60:40) furnished the pure benzoate (6 g), b.p. 180–85°/0·1 mm, n_D^{30} 1·5232; ν_{max} 3077, 1712, 1282, 1112, 1067, 1026, 800 and 714. (Found: C, 80·65; H, 9·35. $C_{22}H_{30}O_2$ requires: C, 80·93; H, 9·26%.)

The benzoate (5 g) was pyrolysed at 230°/110 mm and the product purified by chromatography over neutral alumina (gr. I, 150 g) to afford pure α-guaiene (Rt 4·70′; 97%), b.p. 110–115°/3 mm, n_D^{26} 1·4955; $[\alpha]_D^{30}$ −64·3° (*c*, 3·1); GLC single peak; TLC single spot; ν_{max} 3106, 1770, 1639 and 887. (Found: C, 88·2; H, 12·0. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%.)

Hydrogenation of α-guaiene.[13] To α-guaiene (1·8 g), dioxane (20 ml), MeOH (5 ml) containing 0·2 ml of aq NaOH and Raney Ni (3·5 g) were added. The mixture was reduced by catalytic hydrogenation at room temp. Catalyst and the solvent were removed and the residue was extracted with ether. The extract was washed with water, dried and, after removal of ether was distilled, b.p. 110–102/3 mm, n_D^{33} 1·4880; $[\alpha]_D^{30}$ 11·08° (*c*, 4·33); ν_{max} (0·05 mm cell), 870, 790 and 710. GLC: 3 peaks corresponding to α-dihydroguaiene (IX: Rt 3·7′; 67%), unreacted α-guaiene (4·7′; 10%), β-guaiene (Rt 5·55′; 3%) and products of double bond isomerization (Xa and Xb; Rt 6·7′ and 7·0′; 15%).

Hydrogenation of guaiol. Guaiol (16 g) was dissolved in EtOH (150 ml) and hydrogenated with Raney Ni (8 g) at 100°/100 atm. for 72 hr. The product after filtration of the catalyst and removal of EtOH was distilled to furnish dihydroguaiols (IIa and IIb, 12 g), b.p. (actual) 119–125°/0·2 mm, $[\alpha]_D$ −11·41° (*c*, 7·3). The mixture was dissolved in acetone (15 ml) and left overnight at −15°, filtered, and the solid thus obtained recrystallized from acetone to yield 1α,5α-dihydroguaiol (IIa, 6 g), m.p. 75–76°; $[\alpha]_D$ −54·63° (*c*, 3·62); GLC single peak, TLC single spot; ν_{max} 3448, 1130, 885 and 840. (Found: C, 80·60; H, 12·65. $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%.) The mother liquor on fractional distillation gave 1β,5β-dihydroguaiol, b.p. 120–25° (actual)/0·2 mm, $[\alpha]_D$ +42° (*c*, 4·9).

Dehydration of 1β,5β-dihydroguaiol (IIb) *with perchloric acid.* To a soln of IIb (3 g) in glacial AcOH (30 ml), perchloric acid (60%, 1·8 ml) was added dropwise and the mixture left at room temp for 72 hr with stirring and then processed as described earlier. The product was chromatographed over neutral alumina (gr. I, 50 g) and eluted with pet. ether to furnish a mixture of four hydrocarbons

(2·3 g), b.p. 115–120°/2 mm, n_D^{25} 1·4840; $[\alpha]_D^{30}$ +50·13° (*c*, 3·75). GLC: 4 components with Rt 3·25′ (36%), 4·52′ (45%); 4·1′ (8%) and 5·9′ (11%) corresponding to XIb, XIIb, XIa and XIIa respectively; ν_{max} 1658, 840, 830, 794 and 770. (Found: C, 88·0; H, 12·7. $C_{15}H_{26}$ requires: C, 87·30; H, (12·70%.) This hydrocarbon mixture (1·7 g) was treated with perbenzoic acid (1·08N, 15 ml) at 0° for 16 hr to obtain the epoxides (1·6 g). The mixture of epoxides was treated with BF_3-etherate (25 ml) at 0° for 16 hr. Treatment of the ketones with semicarbazide hydrochloride and AcOH and recrystallization of the semicarbazones from EtOH gave the pure semicarbazone of XIII (0·1 g), m.p. 173°. (Found: N. 15·47. $C_{16}H_{29}ON_3$ requires: N, 15·04%.)

The semicarbazone (0·055 g) on treatment with oxalic acid (0·3 g) in aq EtOH (80%; 20 ml) and pet. ether (100 ml) gave XIII. TLC did not resolve the product but on GLC it showed two overlapping peaks of equal intensity, presumably epimers at C_7, b.p. 135–40°/0·1 mm, ν_{max} 1700 (CO). NMR: 7·98 τ (3H, $COCH_3$), 8·97 τ (3H, Me of C_7); 9·02, 9·05, 9·13 τ (6H, Me on C_4 and C_{10}). (Found: C, 81·08; H, 12·05. $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%.) This ketone on treatment with I_2 in KI and strong alkali gave a yellowish sediment of CHI_3.

The non semicarbazone-forming portion was equilibrated at 100° in alcoholic KOH (0·5N, 20 ml), but the resultant mixture could not be separated by chromatography. The IR spectrum indicated the presence of $-CH_2-\overset{|}{C}=O$ grouping (ν_{max} 1418).

Dehydration of 1α,5α-*dihydroguaiol* (IIa) *with perchloric acid*. Compound IIa (2 g) in AcOH (20 ml) was mixed with perchloric acid (3 ml) and stirred for 72 hr at room temp. After working up as usual the hydrocarbon obtained was distilled, b.p. 140–45°/5 mm. TLC on $AgNO_3$-impregnated silica gel (15%) showed the presence of 3 components which was confirmed by GLC analysis. Chromatography of the mixture (1·4 g) over $AgNO_3$ impregnated silica gel (15%; 45 g) afforded pure 1α,5α-dihydro-β-guaiene (XIa, 0·4 g) and 1α,5α-dihydro-ε-guaiene (XIIa, 0·3 g). Compound XIa had the following properties, Rt 4·1′, b.p. 120–25°/3 mm, n_D^{30} 1·4948; $[\alpha]_D^{27}$ −58·88° (*c*, 3·6). GLC single peak, UV ϵ_{EtOH}^{211} 6600. NMR: 8·97, 9·08, 9·11, 9·2 τ (6H, secondary Me's); 8·33, 8·38 τ (6H, Me's on double bond). (Found: C, 87·36; H, 12·7. $C_{15}H_{26}$ requires: C, 87·30; H, 12·70%.) On ozonolysis it gave acetone and XV, identified through its semicarbazone, m.p. 200°. Compound XIIa had the following properties, Rt 5·9′, b.p. 120–130°/3 mm, n_D^{30} 1·4830; $[\alpha]_D^{27}$ −2·9° (*c*, 3·34). GLC single peak ν_{max} at 840 and 812. NMR: 8·92, 9·12, 9·2 τ (12H, 4 secondary Me's), 4·5 τ (triplet 1H, C_6 proton). (Found: C, 87·55; H, 12·55. $C_{15}H_{26}$ requires: C, 87·30; H, 12·70%.)

Hydroboration of 1α,5α-*dihydro-ε-guaiene* (XIIa). To a THF soln of XIIa (0·25 g), diborane gas (B_2H_6) was passed for 1 hr at 0° and for further 1 hr at room temp. The reaction was carried out in N_2. After working up in the usual manner, the resultant alcohol was purified by chromatography and distilled, b.p. 140°/0·10 mm, n_D^{30} 1·4880; $[\alpha]_D^{30}$ −10·78° (*c*, 3·6); GLC single peak, TLC single spot; ν_{max} 3365, 1053, and 1012. NMR: 6·6 τ (multiplet, 1H; proton at C_6), 7·65 τ (1H, broad singlet disappearing on D_2O exchange O*H*) and 9·0, 9·06, 9·12, 9·2 τ (superimposed secondary Me's, 12H). (Found: C, 79·89; H, 12·38. $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%.)

1α,5α-*Dihydroguaiol benzoate*. Compound IIa, (5 g) in pyridine (15 ml) was mixed with BzCl (10 ml) and the mixture left at room temp for 48 hr and then warmed on a water bath for 4 hr. The reaction mixture was poured into cold water, extracted with ether and the ether layer successively washed with 10% HCl, 5% Na_2CO_3 and water till neutral. The extract on removal of the solvent and filtration through a column of neutral alumina (gr. II, 100 g) in the pet. ether–benzene eluate gave the benzoate (6 g), b.p. 180–200/0·5 mm; ν_{max} 3701, 1704, 1598, 1580, 1272, 1111, 1064, 1022, 798 and 708. (Found: C, 80·35; H, 9·63. $C_{22}H_{32}O_2$ requires: C, 80·44; H, 9·83%.)

1α,5α-*Dihydro-α-guaiene* (XVIIa). 1α,5α-Dihydroguaiol benzoate (5 g) was pyrolysed at 230° (bath)/100 mm during 1 hr. The distillate was filtered through neutral alumina (gr. I, 100 g) and eluted with pet. ether. The eluate on removal of the solvent was refluxed and distilled over Na to afford XVIIa (Rt 4·3′; 4 g), b.p. 100–120°/2 mm, n_D^{22} 1·4910; $[\alpha]_D^{27}$ −53·39° (*c*, 4·6). GLC single peak, TLC single spot; ν_{max} 3125, 1786; 1647 and 892 ($>C=CH_2$). (Found: C, 87·34; H, 11·82. $C_{15}H_{26}$ requires: C, 87·30; H, 12·70%.)

Hydrogenation of (XVIIa). Compound XVIIa (0·2 g) was hydrogenated in presence of Adams catalyst (0·020 g) in EtOH (10 ml) at atm. press. and room temp. The residue after filtration of the catalyst and evaporation of the solvent, was passed over neutral alumina (gr. I, 10 g). The pet. ether eluate afforded (XVIIIa Rt 3·65′), b.p. 100–110°/2 mm, n_D^{30} 1·4751; $[\alpha]_D^{27}$ −38° (*c*, 2·3) (Found: C, 86·34; H, 13·54. $C_{15}G_{28}$ requires: C, 86·46; H, 13·54%.)

Preparation of 1β,5β-dihydro-α-guaiene (XVIIb). Compound IIb (1 g) on benzolyation and pyrolysis at 230°/110 mm furnished XVIIb in 60% yield, which was further separated by preparative TLC to furnish pure XVIIb (Rt 4·63′), b.p. 100–110°/1 mm, n_D^{28} 1·4902; $[\alpha]_D^{28}$ +63·69° (*c*, 3·2). GLC single peak, TLC single spot. (Found: C, 87·43; H, 12·54. $C_{15}H_{26}$ requires: C, 87·30; H, 12·70%.)

Hydrogenation of XVIIb. It was hydrogenated as described earlier in presence of Adams catalyst in alcohol to furnish XVIIIb (Rt 2·8′), b.p. 105–110°/2 mm, n_D^{31} 1·4731; $[\alpha]_D^{30}$ +37° (*c*, 2·15). Because of paucity of material compds XVIIb and XVIIIb could not be critically examined.

Hydroboration of XVIIa *to* 1α,5α-*guaian*-12-*ol* XXI. Through a soln of 1α,5α-dihydro-α-guaiene (5 g) in dry THF (30 ml), diborane gas, prepared from $NaBH_4$ (1·5 g) in diglyme (30 ml) and BF_3-etherate (15 ml) in diglyme (15 ml), was passed at 0° for 1 hr and then at room temp for further 1 hr. The reaction was carried out in an inert atm. The reaction flask was left overnight. Excess diborane was decomposed by careful addition of ice. The mixture was cooled in ice bath, made alkaline with 10% KOHaq (30 ml) and H_2O_2 (30 ml) was added dropwise during 1 hr. The mixture was left at room temp for 4 hr. The upper layer was separated, the aqueous layer extracted with ether and the combined extracts, washed repeatedly with water and dried. On removal of the solvent, purification through chromatography and distillation gave XXI (3 g), b.p. 140–145°/0·5 mm, n_D^{26} 1·4910; $[\alpha]_D^{26}$ −42·04° (*c*, 4·4); GLC single peak, TLC single spot; ν_{max} 3448 and 1031 (hydroxy group). (Found: C, 80·87; H, 12·81. $C_{15}H_{28}O$ requires: C, 80·29; H, 12·58%.)

Action of Jones reagent on XXI. To XXI (0·7 g) in acetone (25 ml), Jones reagent (1 ml) was added during 5 min. Excess reagent was destroyed by MeOH and the mixture poured into water and extracted with ether. The extract was washed with water, $NaHCO_3$aq and finally with water till neutral and dried. The solvent was removed and the semicarbazone of XXIV was prepared without further purification by adding semicarbazone HCl (0·5 g) and AcONa (0·8 g) in water (5 ml). The semicarbazone was crystallized from MeOH, m.p. 162–162·5°. (Found: N, 14·9. $C_{16}H_{29}N_3O$ requires: N, 15·04%.) The semicarbazone was decomposed with levulenic acid (5 ml) and HCl (1 ml) in EtOH (2 ml) and pet. ether (50 ml), keeping at reflux for 6 hr to yield XXIV, b.p. 120–135°/0·1 mm, n_D^{30} 1·4830; $[\alpha]_D$ −35·39° (*c*, 3·48); ν_{max} 2700 and 1750 (saturated aldehyde $C{=}O$).

The bicarbonate layer was acidified and extracted with ether. The extract was washed free of acid with water, dried and the ether removed. The residue was distilled to obtain 1α,5α-guaian-12-oic acid (XXV), b.p. 140–145°/0·005 mm n_D^{30} 1·4880; $[\alpha]_D$ −52° (*c*, 2·73;) ν_{max} 1695 (carboxyl). (Found: C, 75·58; H, 11·00. $C_{15}H_{26}O_2$ requires: C, 75·48; H, 10·45%.) The acid was esterified with ethereal soln of diazomethane to yield the methyl ester, b.p. 140–145°/0·1 mm. GLC single peak, TLC single spot; ν_{max} 1724, 1149 and 1053 (ester $>C{=}O$).

Lead tetra-acetate oxidation of XXI. Compound XXI (2·4 g) in dry benzene (75 ml) was taken in a RB flask fitted with a reflux condenser and Hg sealed stirrer and $(AcO)_4Pb$ (3·5 g) was added. The mixture was refluxed with stirring on a water bath for 2 hr in N_2 atm. The cooled reaction mixture was filtered, the ppt washed thoroughly with benzene and the combined filtrate washed with water, $NaCO_3$aq and finally with water till neutral. After drying the filtrate, the solvent was removed and the residue passed through neutral alumina (gr. II, 50 g) and eluted with pet. ether. Removal of the solvent gave the oxide with some acetate as impurity. Saponification, followed by filtration through alumina (gr. I, 30 g) afforded the pure oxide (XXII; 1 g), b.p. 120–125°/2 mm, n_D^{28} 1·4885; $[\alpha]_D^{26}$ +20° (*c*, 2·8); GLC single peak; TLC single spot. ν_{max} 1055 and 1031. NMR: 6·08 τ (1H, triplet; proton at C_6); 6·7 τ (2H, multiplet; CH_2—O); 8·96; 9·03; 9·11 τ (9H, 3 secondary Me's). (Found: C, 81·34; H, 11·6 $C_{15}H_{26}O$ requires: C, 81·02; H, 11·79%.)

Chromic acid oxidation of XXII *to* 1α,5α-*hexahydrocostus lactone* (XXIII). To a soln of XXII (1 g) in AcOH (30 ml) at 0°, CrO_3 soln (1·5 g) in water (5 ml) was added dropwise in 10 min. The reaction mixture was kept at room temp for 48 hr. The product was poured into excess water, extracted with ether, washed with $NaHCO_3$ (5%) and water. After removal of ether, from the dried extract, the residue was filtered through neutral alumina (gr. II, 10 g). The pet. ether eluate gave the unreacted oxide. The benzene eluate furnished XXIII (0·050 g), b.p. 180–185°/0·05 mm, n_D^{28} 1·4985; $[\alpha]_D^{27}$ +76·19° (*c*, 2·1); ν_{max} 1770 (γ-lactone); 1220, 1198, 1036, 985 and 755. NMR: 5·9 τ (1H, triplet, proton at C_6), 8·9, 9·0, 9·1 τ (9H, 3 secondary Me's). (Found: C, 76·45; H, 10·33. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%.)