983. *The Chemistry of Hardwood Extractives. Part XXXIV.** *Constituents of* Guarea *Species.*

By J. R. HOUSLEY, F. E. KING, T. J. KING, and P. R. TAYLOR.

Investigations in 1954—1956 [1] revealed that considerable quantities of volatile hydrocarbons and a nonvolatile ketone are present in the wood of *Guarea thompsonii*. This ketone has recently been identified as dihydrogedunin [4] and additional evidence in favour of its formulation as (I; R = O, R′ = α-OAc) is now advanced. Minor components of the timber include methyl angolensate [4a] and 7-oxodeacetoxydihydro-α-gedunol (I; R = α-OH, R′ = O).

Guarea thompsonii (Nigerian pearwood) and *G. cedrata* (bossé, African cedar) are the source of two timbers imported into the United Kingdom as substitutes for mahogany. *G. thompsonii* came to our notice from a report that nasal bleeding occurred amongst workers handling the timber but the several specimens of *G. thompsonii* and of *G. cedrata* used during 1954—1956 in a full investigation of its extraneous constituents [1] did not possess this property. Light-petroleum extraction of both woods gives considerable quantities of steam-volatile hydrocarbons. These have not been investigated in detail although one sample yielded impure (+)-cadinene [2] and in another bisabolene [3] was also

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* Part XXXIII, King, King, and Rustidge, *J.*, 1962, 1192.

[1] J. R. Housley, Thesis, Nottingham University, 1956.

[2] "Elsevier's Encyclopaedia of Organic Chemistry," Elsevier Publishing Co. Inc., New York, 1948, **12**, *B*, 180.

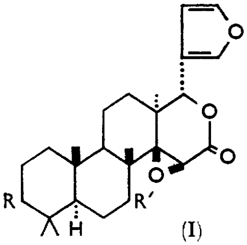
[3] Simonsen and Barton, "The Terpenes," Cambridge University Press, 1962, Vol. III, pp. 9—12.

[4a] Akisanya, Bevan, Hirst, Halsall, and Taylor, *J.*, 1960, 3827.

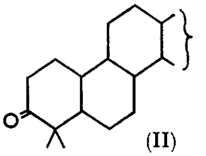
detected. By chloroform extraction of the timber and purification of the extract from methanol–ether a highly crystalline ketone, later shown to be dihydrogedunin, was obtained. Although at least one sample of wood purporting to be *G. cedrata* gave dihydrogedunin more recent failures to obtain the ketone from seven samples of the wood followed by a successful isolation from *G. thompsonii* led us to believe that dihydrogedunin may be restricted to the latter species.

A recent examination of the West African tree *Entandophragma angolense* by Bevan, Halsall, and their co-workers[4a] has disclosed the occurrence of a further ketone, gedunin. The properties of its dihydro-derivative were seen to be indistinguishable from those of our ketone and a direct comparison of the latter with dihydrogedunin has confirmed that they are identical.

Several of the characteristic features of dihydrogedunin were ascertained during the earlier investigations, but the exact nature of its constitution was not apparent until the complexities of the limonin molecule had been fully elucidated by the work of Arigoni, Barton, Corey, *et al.*[5]



(I)



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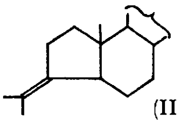
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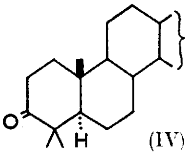

(IV)

Bevan and Halsall have now suggested[4b] complete structures for gedunin and dihydrogedunin (I; R = O, R′ = α-OAc); our experiments are discussed in the light of this formulation for dihydrogedunin, a structure with which they are nearly all compatible.

Preliminary observations on the weakly dextrorotary ketone established its formula as $C_{28}H_{36}O_7$. Methoxyl and hydroxyl groups were absent and the ketone did not dissolve in cold alkali or react with diazomethane. It gave a strong positive Zimmermann test indicating the presence of the grouping $\cdot CO\cdot CH_2\cdot$. The presence of an unhindered carbonyl group was demonstrated by the preparation of a mono-oxime and a mono-2,4-dinitrophenylhydrazone, by the ultraviolet spectrum ($\lambda_{max.}$ 289 mμ, ε 25) and by the infrared absorption at 1701 cm.$^{-1}$. A further band at 1736 cm.$^{-1}$ (in chloroform) suggested the presence of an ester or lactone function. There was no high-intensity absorption above 220 mμ. Peroxy-acid oxidation of dihydrogedunin was slow but two molecular proportions of monoperoxyphthalic acid were consumed in 25 days. Catalytic reduction took place in glacial acetic acid over platinum with the uptake of 3·5 molecular proportions of hydrogen to give a mixture of acidic and neutral gums.

Boiling 2% methanolic potassium hydroxide hydrolysed dihydrogedunin to an alkali-soluble compound which, after acidification, afforded a crystalline monohydric alcohol $C_{26}H_{34}O_6$ (I; R = O, R′ = α-OH), characterised as the oxime, and which was smoothly reconverted into dihydrogedunin by acetylation. This reaction sequence clearly suggests the presence of a lactone moiety and alkalimetry has shown that the deacetyl derivative contains one such group. The hydroxyl group of deacetyldihydrogedunin was secondary, as oxidation with chromic acid gave a crystalline diketone. The deacetyl compound still showed absorption at 1755 cm.$^{-1}$ (in carbon tetrachloride), indicative of the lactone function.

The relationship of the ketone function to the rest of the molecule was next established.

[4b] Akisanya, Bevan, Halsall, Powell, and Taylor, *J.*, 1961, 3705.

[5] Arigoni, Barton, Corey, Jeger, and others, *Experientia*, 1960, **16**, 41.

Rapid Meerwein–Pondorff–Verley reduction of dihydrogedunin gave a monohydric alcohol, $C_{28}H_{38}O_7$, in high yield, which was characterised as the acetate and benzoate and was reoxidised by chromic acid to dihydrogedunin. Dehydrogenation of the alcohol by selenium gave 1,2,7,8-tetramethylphenanthrene identified by comparison with a specimen kindly provided by Professor Ruzicka. This hydrocarbon is not usually obtained by dehydrogenation of pentacyclic triterpenes but many such triterpenes give naphthalenes containing vicinal methyl groups derived by migration in the 3-hydroxy-4,4-dimethyl moiety of ring A. If such a rearrangement takes place during the dehydrogenation of the dihydrogedunin derivative the ketone can be allotted the partial structure (II). Rapid Meerwein–Pondorff reduction of the 3-oxo-group in triterpenes gives[6] a large preponderance of the 3α(axial)-alcohol, and thus the alcohol obtained in this way is termed dihydro-α-gedunol. Prolonged reduction by this method usually gives rise to larger quantities of the more stable equatorial alcohol, and in agreement with this generalisation more prolonged reduction of dihydrogedunin afforded a lower yield of dihydro-α-gedunol together with an isomer (dihydro-β-gedunol) which was less strongly lævorotatory than dihydro-α-gedunol. Dihydro-β-gedunol[4b] was obtained more easily by the borohydride reduction of dihydrogenunin and like the α-isomer was readily reoxidised to the ketone. Both alcohols were characterised as their acetates and by hydrolysis to the corresponding diol. The deacetyl-β-dihydrogedunol so obtained was also made by the borohydride reduction of deacetyldihydrogedunin.

By analogy with the reactions of triterpenes having the partial structure (II) suggested for dihydrogedunin, dehydration by phosphorus oxychloride in pyridine of both dihydrogedunols should give a Δ^2-ene, together with some rearrangement of the β-isomer. Conversely, phosphorus pentachloride dehydration of dihydro-β-gedunol should lead largely to rearrangement to an A-nor-compound of partial structure (III). In agreement with this, the action of phosphorus oxychloride in pyridine on both dihydrogedunols gave a crystalline olefin, $C_{28}H_{36}O_6$, dihydrogedunene, which rapidly absorbed 1 molecular equivalent of hydrogen over palladised charcoal to give dihydrogedunan, characterised as the deacetyl derivative and its derived ketonic oxidation product, and which gave no volatile ketone or aldehyde by ozonolysis. Phosphorus pentachloride acted on dihydro-β-gedunol to form a resin which gave a 26% yield of acetone on ozonolysis. On one occasion the intermediate of type (III) (*iso*dihydrogedunene) was obtained crystalline.

These results confirmed the partial structure (II) and, if one assumes the presence of the usual angular 10-methyl group and takes into account molecular-rotation data, this can be expanded to structure (IV) in which the A/B ring junction is *trans*. This follows from the large decrease in rotation on acetylation of α-dihydrogedunol compared with the small positive change on acetylation of dihydro-β-gedunol.[7] This stereochemical conclusion is confirmed by the large decrease in rotation observed in passing from dihydrogedunene to dihydrogedunan.[8] A similar conclusion was reached by Bevan and Halsall and their co-workers[4b] because of the retropinacolinic rearrangement brought about by the action of phosphorus pentachloride on an impure alcohol derived from the ozonolysis product of dihydrogedunin.

Alkaline treatment of dihydrogedunin, appreciably more vigorous than that needed to hydrolyse the acetoxyl group, led in the main to intractable gummy products, but two observations were made which are now explicable on the basis of structure (I). Thus formic acid is produced and the yellow alkaline solutions obtained showed a characteristic absorption maximum at 272 mμ. These will be a consequence of the further alkaline decomposition of the furan-3-aldehyde now known[4] to be a primary product of the alkaline decomposition of dihydrogedunin. Furthermore it was observed that neither formic acid

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[6] Ruzicka, Rey, Spillman, and Baumgartner, *Helv. Chim. Acta*, 1943, **26**, 1638; Jeger, Montavon, Nowak, and Ruzicka, *ibid.*, 1947, **30**, 1869.

[7] Klyne and Stokes, *J.*, 1954, 1979.

[8] Barton and Klyne, *Chem. and Ind.*, 1948, **67**, 755.

nor the characteristic light absorption was found when the acetoxy- or derived hydroxy-group were absent, *i.e.*, with 7-oxodeacetoxydihydrogedunin or with anhydrodeacetoxydihydrogedunin, produced respectively by oxidation and dehydration of deacetyldihydrogedunin. It has been established [5] that the elimination of furan-3-aldehyde from limonol requires the presence of an axial 7-hydroxyl group, and our failure to obtain evidence for this elimination in the above two cases strongly supports the analogy with limonol on which the suggested structure for gedunin and dehydrogedunin relies heavily. In further accord with the presence of a furan ring in dihydrogedunin, this compound yields rather more than one molecular proportion of formic acid on ozonolysis.

Before the nature of the gedunin molecule was apparent attempts were made to replace the acetoxy-group by hydrogen. The dehydration of deacetyldihydrogedunin or of deacetyldihydrogedunene gave crystalline substances in low yield but the presence of a trisubstituted double bond (infrared spectrum) in the products suggests that a rearrangement takes place during the elimination of water. The bisethylenethioketal derived from the diketone dehydrodeacetyldihydrogedunin was accordingly prepared but we were unable to bring about its desulphurisation. The monoethyleneketal and monoethylenethioketal of dihydrogedunin and the monoethyleneketal of the above diketone (which would not form a bisethyleneketal) were also prepared.

On some occasions only it was possible to isolate a pure neutral compound, by the catalytic reduction of dihydrogedunene, which corresponds in its composition with a hexahydrogedunan, and thus presumably has both furan double bonds reduced. This compound was not resinified by potassium hydroxide but was converted into a crystalline salt, which with acid gave deacetylhexahydrogedunan, obtainable from hexahydrogedunan by mild alkaline hydrolysis, and which was characterised as the derived ketone.

The environment and stereochemistry of the acetoxy-group as delineated in (I; $R = O$, $R' = \alpha\text{-OAc}$) rests on analogy with limonol and on molecular rotation evidence.[4b] We can provide no direct evidence for the position of this group but it must be adjacent to methylene because the ketone derived from deacetyldihydrogedunan (I; $R = H_2$, $R' = O$), in solution in t-butyl alcohol containing potassium t-butoxide, rapidly absorbed one molecular proportion of oxygen to give a compound with the properties of a diosphenol—a reaction well established in the chemistry of limonin.[5] However, the overall triterpenoid nature of dihydrogedunin being assumed, it is clear that positions 6 and 11 can be excluded for the acetoxyl group because of the comparative reactivity towards ketone reagents of those compounds which we have made in which a ketone replaces an acetoxy-group.

Further analogy for the assigned stereochemistry can be drawn from limonin chemistry in that reduction of the ketone (I; $R = H_2$, $R' = O$) by the Pondorff method regenerated deacetyldihydrogedunan whereas borohydride reduction of the dione (I; $R = R' = O$) gave a diol different from deacetyl-β-dihydrogedunol, in which the difference must be in the stereochemistry at position 7. Significantly, this compound, on appropriate alkali treatment, did not afford a solution with an absorption maximum at *ca.* 272 mμ which we have attributed (above) to the formation of degradation products of furan-3-aldehyde. These two methods of reduction of the 7-oxo-group of limonin give, respectively, the α- and β-alcohols.

Amongst other derivatives of dihydrogedunin that we have made are the chloro- and iodo-acetate of dihydro-β-gedunol prepared to facilitate the determination of their structure by *X*-ray methods.*

Accompanying dihydrogedunin we have found small amounts of other crystalline compounds. One of these has been identified as methyl angolensate,[4] the other has the molecular formula $C_{26}H_{34}O_6$ and contains a keto-group and a secondary hydroxy-group. It can be oxidised to 7-oxodeacetoxydihydrogedunin (I; $R = R' = O$) and because

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*[*Added in Proof.*] The *X*-ray analysis of dihydrogedun-β-yl iodoacetate, by Sutherland, Sim, and Robertson (*Proc. Chem. Soc.*, 1962, 222), confirms the suggestions made here and by Bevan, Halsall *et al.* in all respects.

inter al. it fails to give the Zimmermann test it must therefore be one of the two possible 7-oxodeacetoxydihydrogedunols. Consideration of its molecular rotation strongly suggests a 3α-hydroxy-group. Unfortunately the acetate is not crystalline so the diagnostic change in rotation on acetylation cannot be measured. However, the molecular-rotation changes consequent on the introduction of, respectively, the 3α- and the 3β-hydroxyl group into dihydrogedunane are −68° and −9°, and the difference in molecular rotation between the compound under discussion (I; R = OH, R′ = O) and 7-oxodeacetoxydihydrogedunane (I; $R = H_2$, R′ = O) is −101°. Furthermore, the change in molecular rotation on oxidation of the alcohol is +161° which is in better agreement with the change on oxidation of dihydro-α-gedunol (+150°) than of dihydro-β-gedunol (+89°).

EXPERIMENTAL

Ultraviolet spectra were determined in ethanol by using a Unicam S.P. 500 spectrophotometer. Optical rotations were measured in chloroform for the D line at room temperature. Light petroleum was the fraction, b. p. 60—80°, and alumina was Peter Spence's Grade H.

Extraction of Guarea *Species.*—(*a*) Ground heartwood (10 kg.) was percolated by refluxing light petroleum for 18 hr. The cold extract contained a resinous deposit which crystallised from methanol to give dihydrogedunin (4·1 g.), and similar treatment of the waxy solid left after evaporation of the light petroleum afforded a further 3·1 g. of the ketone. Steam distillation of the combined mother liquors gave a pale yellow oil (50·2 g.). Subsequent extraction of the wood by ether gave further amounts of dihydrogedunin (1·6 g.) but no homogeneous product was obtained from the phenolic resins extracted from the wood by acetone and ethanol. (*b*) The wood (3 kg.) was percolated during 12 hr. with boiling chloroform and the residue (90—230 g.), after evaporation of the solvent, was dissolved in the minimum amount of boiling methanol (50—150 c.c.), the solution was cooled to 20°, and enough ether was added to produce a clear solution. After 5—6 days at 0° crude dihydrogedunin (12—35 g.) was deposited and was purified by trituration with ether and passage, in chloroform, down a short column of alumina. The eluate crystallised from chloroform–methanol giving an average yield of pure ketone of 0·39%. Steam distillation of the original mother liquors gave a yellow oil (0·78%).

Characterisation of the Volatile Extracts.—(*a*) Fractionation of the volatile component from extraction (*a*) finally gave (+)-cadinene (9 g.) as an oil, b. p. 131—132°/14 mm., n_D 1·5100, d^{18} 0·918, [α] +31·4° (*c* 2·44) (Found: C, 87·4; H, 11·7. Calc. for $C_{15}H_{24}$: C, 88·2; H, 11·8%). In acetic acid over Adams catalyst at room temperature and pressure the hydrocarbon absorbed 1·9 mol. equiv. of hydrogen, and after 48 hr. at 0° it had reacted with 1·88 mol. of monoperoxyphthalic acid in ether. With hydrogen chloride in ether at 0° it formed (−)-cadinene dihydrochloride, m. p. and mixed m. p. 115—116° (Found: C, 64·6; H, 9·2; Cl, 25·3. Calc. for $C_{15}H_{26}Cl_2$: C, 65·0; H, 9·4; Cl, 25·6%). Dehydrogenation of the hydrocarbon with selenium at 300—315° for 30 hr. gave a mixture, separated by distillation into a more volatile fraction corresponding to 1,6-dimethylnaphthalene [1,3,5-trinitrobenzene adduct, m. p. 129—131° (lit., 132—133°); picrate, m. p. 112—113° (lit., 114°)] and a less volatile fraction corresponding to cadalene [1,3,5-trinitrobenzene adduct, m. p. 110—111° (lit., 112—113°)].

(*b*) Fractionation of the volatile components of the chloroform extract of a different sample of the timber gave two main fractions, the more volatile (b. p. 134—138°/18 mm.) giving (−)-cadinene dihydrochloride with hydrogen chloride, and the less volatile giving an optically inactive trihydrochloride, m. p. 79—80°, probably bisabolene trihydrochloride (Found: C, 57·3; H, 8·7. Calc. for $C_{15}H_{27}Cl_3$: C, 57·4; H, 8·7%).

Dihydrogedunin.—After several crystallisations from acetone or chloroform–methanol, dihydrogedunin formed glistening orthorhombic prisms, m. p. 237—238°, [α] +3·7° [Found: C, 69·4; H, 7·6%; *M* (Rast), 464, (*X*-ray), 484 ± 2. Calc. for $C_{28}H_{36}O_7$: C, 69·4; H, 7·5%; *M*, 484·6], $\lambda_{max.}$ 207 (ε 6600) and 289 mμ (ε 25). Dihydrogedunin is reported as having m. p. 240°, [α] +8°, $\lambda_{max.}$ 205 (log ε 3·8) and 285 mμ (log ε 1·4). The ketone was very soluble in chloroform and pyridine, quite soluble in acetone and ethyl acetate, and only sparingly soluble in ether. It gave a strong positive Zimmermann test, and was unaffected by diazomethane, boiling acetic anhydride, or cold aqueous sodium hydroxide. It formed an *oxime*, prisms,

m. p. 239—240°, from aqueous ethanol (Found: C, 67·2; H, 7·1; N, 2·8. $C_{28}H_{37}NO_7$ requires C, 67·3; H, 7·5; N, 2·8%), and a 2,4-*dinitrophenylhydrazone*, yellow needles, m. p. 189—191°, from methanol (Found: C, 61·0; H, 6·2; N, 8·4. $C_{34}H_{40}N_4O_{11}$ requires C, 61·4; H, 6·1; N, 8·4%), $\lambda_{max.}$ 367 mμ (ε 23,800). In 80% chloroform–ether dihydrogedunin absorbed one double-bond equivalent of monoperoxyphthalic acid after 6 days and 1·8 equivalents after 27 days. No crystalline material was obtainable from this reaction either after complete oxidation or when the reaction was interrupted after 6 days. Catalytic hydrogenation of dihydrogedunin gave variable results: with palladium catalysts there was a slow uptake of hydrogen but even after 1·5 double-bond equivalents of hydrogen had been absorbed dihydrogedunin (70%) was the only pure compound isolated from the reaction. Adams catalyst in acetic acid caused the uptake of 2·5 mol. of hydrogen in 8 hr. and the product was a mixture of intractable neutral and acidic gums.

Deacetyldihydrogedunin.—Dihydrogedunin (1 g.) was heated under reflux for 30 min. with methanolic potassium hydroxide (2%; 50 c.c.) and the cooled solution was poured into excess of dilute hydrochloric acid. The precipitate crystallised from methanol to give *deacetyldihydrogedunin* (0·8 g.) as prisms, m. p. 264°, [α] +43° (Found: C, 70·9; H, 7·6. $C_{26}H_{34}O_6$ requires C, 70·6; H, 7·7%), $\lambda_{max.}$ 287 mμ (ε 27). The *oxime* separated from aqueous methanol as elongated prisms, m. p. 252—254° (Found: C, 67·9; H, 7·6; N, 3·1. $C_{26}H_{35}NO_6$ requires C, 68·2; H, 7·7; N, 3·1%). Acetic anhydride in pyridine at 100° regenerated dihydrogedunin.

Titration of the Lactone Ring.—Deacetyldihydrogedunin (0·591 g.) was treated with 2% "AnalaR" methanolic sodium hydroxide solution (10 ml.), and the mixture was refluxed for 10 min. The solution was then cooled, diluted, and titrated potentiometrically with hydrochloric acid (0·1185N). A blank determination was immediately carried out and the difference between the acid titres was 11·7 ml., giving an equivalent weight for deacetyldihydrogedunin of 427 (Calc. for one lactone ring, 442).

7-*Oxodeacetoxydihydrogedunin* (I; R = R′ = O).—A solution of deacetyldihydrogedunin (0·528 g.) in acetone was titrated with a solution of chromic oxide (8N in aqueous sulphuric acid) until an orange colour persisted (0·32 c.c.; theory, 0·30 c.c.). After 10 min. the mixture was diluted with water to give the *diketone* (0·4 g.) which crystallised from methanol in plates, m. p. 236—238°, [α] −90° (Found: C, 70·8; H, 6·8. $C_{26}H_{32}O_6$ requires C, 70·9; H, 7·3%), $\lambda_{max.}$ 291 mμ (ε 75). The oxime and dinitrophenylhydrazone were amorphous.

Dihydro-α-gedunol.—A solution of dihydrogedunin (5 g.) and aluminium isopropoxide (6 g.) in isopropyl alcohol (100 c.c.) was heated under partial reflux with a distillation rate of 1—2 drops/min. After 2 hr. evolution of acetone ceased and the solvent was evaporated. The residue was shaken with aqueous hydrochloric acid and ether, and the ethereal extract, after having been washed with water and dried (Na_2SO_4), was evaporated. The residue crystallised from methanol to give *dihydro-α-gedunol* (4·5 g.) as flat prisms, m. p. 200—202°, [α] −27° (Found: C, 69·3; H, 7·7. $C_{28}H_{36}O_7$ requires C, 69·1; H, 7·9%). The *acetate* formed prisms (from chloroform–methanol), m. p. 251—252°, [α] −60° (Found: C, 68·4; H, 7·6. $C_{30}H_{40}O_8$ requires C, 68·2; H, 7·6%), and the *benzoate* formed prisms (from methanol), m. p. 255—257°, [α] −91° (Found: C, 71·4; H, 7·1. $C_{35}H_{42}O_8$ requires C, 71·2; H, 7·2%). Oxidation of dihydro-α-gedunol with acetone–chromic acid–sulphuric acid regenerated dihydrogedunin in 82% yield.

Dehydrogenation of Dihydro-α-gedunol.—A mixture of dihydro-α-gedunol (4 g.) and selenium (8 g.) was heated at 300—320° for 36 hr. and then for 30 min. at 340—350°. The cooled mass was pulverised and extracted with warm benzene, and the resulting solution was percolated through alumina, evaporated, and distilled. The fraction, b. p. 130—160° (bath)/0·1 mm., was treated with an alcoholic solution of an excess of 1,3,5-trinitrobenzene, and the crude precipitate was decomposed by passage in benzene through alumina. The hydrocarbon so obtained crystallised in plates, m. p. 158°; the m. p. of a mixture with authentic 1,2,7,8-tetramethylphenanthrene of m. p. 168—170° was 167—170°. The ultraviolet absorption spectra of the two samples were virtually identical. The trinitrobenzene adduct had m. p. 200—202° (Found: C, 64·2; H, 5·1; N, 9·3. Calc. for $C_{18}H_{18},C_6H_3N_3O_6$: C, 64·4; H, 4·7; N, 9·4%) and the mixed m. p. with an authentic specimen (m. p. 208°) was 206—208°.

Dihydro-β-gedunol.—Dihydrogedunin (3 g.) in pyridine (30 c.c.) was treated with concentrated aqueous sodium borohydride (0·5 g.). After 3 hr. the solution was poured into excess of dilute hydrochloric acid, and the precipitate of dihydro-β-gedunol was crystallised from aqueous methanol, forming needles (2·4 g.), m. p. 209—211°, [α] −15° (Found: C, 69·2; H, 7·8.

Calc. for $C_{28}H_{38}O_7$: C, 69·1; H, 7·9%). Dihydrogedunol [4b] is reported as having m. p. 209—211°, [α] −15° ± 3°. The *acetate* crystallised from methanol as flat prisms, m. p. 132—134°, [α] −13° (Found: C, 67·9; H, 7·55. $C_{30}H_{40}O_8$ requires C, 68·2; H, 7·6%). Prolonged Pondorff reduction of dihydrogedunin (6 hr.) gave not only dihydro-α-gedunol (70%) but from the mother liquors *ca.* 15% of dihydro-β-gedunol.

Deacetyldihydro-α-gedunol.—Dihydro-α-gedunol was hydrolysed by heating for 1 hr. in boiling 2% methanolic potassium hydroxide. Working up in the usual way gave *deacetyldihydro-α gedunol* as needles (from methanol), m. p. 306—308°, [α] −6° (Found: C, 70·5; H, 8·1. $C_{26}H_{36}O_6$ requires C, 70·3; H, 8·2%). Acetylation of this product gave dihydro-α-gedunyl acetate, m. p. and mixed m. p. 248—250°.

Deacetyldihydro-β-gedunol.—Dihydro-β-gedunol, hydrolysed in the same way as dihydro-α-gedunol, gave the *deacetyl derivative* as needles (from aqueous methanol), m. p. 137—139°, [α] *ca.* +0·1° (Found: C, 70·3; H, 7·9%).

Dihydrogedun-2-ene.—A solution of dihydro-α-gedunol (3 g.) in pyridine (30 c.c.) was treated with phosphorus oxychloride (7·5 c.c.) and heated at 100° for 75 min. The solution was then poured on ice and hydrochloric acid, and the product was collected with chloroform. The extract was washed and evaporated and the residue crystallised from methanol to give *dihydrogedun-2-ene* (70—75%) as prisms, m. p. 184°, [α] +33° (Found: C, 71·8; H, 7·8. $C_{28}H_{36}O_6$ requires C, 71·8; H, 7·75%). Ozonolysis of the olefin in chloroform at −10° failed to give any volatile carbonylic products. Hydrolysis with boiling 5% methanolic potassium hydroxide for 30 min. gave *deacetyldihydrogedun-2-ene* as laths from methanol, m. p. 206°, [α] +53° (Found: C, 73·3; H, 7·95. $C_{26}H_{34}O_5$ requires C, 73·2; H, 8·0%).

Isodihydrogedunene.—A mixture of dihydro-β-gedunol (0·5 g.) and phosphorus pentachloride (0·5 g.) in dry benzene (30 c.c.) was kept at 20° for 2 hr. The solution was then washed with water, dried, and evaporated to give a resin (0·35 g.) which was absorbed on alumina (50 g.) from benzene. Elution with benzene gave an oil (A) which crystallised from methanol as elongated prisms of *isodihydrogedunene*, m. p. 252—256°, [α] +20° (Found: C, 71·7; H, 7·9%). In another experiment the crude oil (A) (0·2 g.) was ozonised in carbon tetrachloride at 0°. The solution was then treated with aqueous ferrous sulphate (2%, 50 c.c.) and distilled into saturated aqueous 2,4-dinitrophenylhydrazine hydrochloride. The organic layer was separated and the residue, after removal of solvent, was purified by chromatography over alumina, eventually giving acetone 2,4-dinitrophenylhydrazone (26 mg., 26%), m. p. and mixed m. p. 124—125° (Found: N, 23·1. Calc. for $C_9H_{10}N_4O_4$: N, 23·5%).

Dihydrogedunan.—Dihydrogedun-2-ene (7 g.) in ethyl acetate (200 c.c.) was shaken at room temperature and pressure in hydrogen with 30% palladium–charcoal (0·7 g.). After 22 hr. absorption of hydrogen stopped, 1·1 mol. of hydrogen having been absorbed. Evaporation of the filtered solution gave a residue of *dihydrogedunan* (6·7 g.) which crystallised from methanol in long prisms, m. p. 191—192°, [α] −13·5° (Found: C, 71·1; H, 8·4. $C_{28}H_{38}O_6$ requires C, 71·5; H, 8·1%). Hydrolysis of dihydrogedunan with 5% methanolic potassium hydroxide at the b. p. for 1 hr. gave *deacetyldihydrogedunan* as needles (from methanol), m. p. 262—264°, [α] +9° (Found: C, 72·6; H, 8·7. $C_{26}H_{36}O_5$ requires C, 72·9; H, 8·5%). Acetone–chromic acid–sulphuric acid oxidised this alcohol to the derived *ketone* which separated from methanol as plates, m. p. 209—211°, [α] −107° (Found: C, 73·2; H, 8·0. $C_{26}H_{34}O_5$ requires C, 73·2; H, 8·0%), which gave a negative Zimmermann test. The derived 2,4-*dinitrophenylhydrazone* separated from chloroform–methanol as yellow needles, m. p. 269—270° (decomp.) (Found: N, 9·2. $C_{32}H_{40}N_4O_8$ requires N, 9·0%), $\lambda_{max.}$ 362 mμ (ε 24,600). Meerwein–Pondorff reduction of this ketone gave a good yield of deacetyldihydrogedunan.

Alkaline Degradation of Deacetyldihydrogedunin.—(*a*) Deacetyldihydrogedunin (2 g.) was heated at the b. p. in 6% ethanolic potassium hydroxide for 30 min., and the solution was then distilled in steam. The alkaline residue was acidified with dilute sulphuric acid and distilled with addition of water when necessary until the distillate was neutral. The total distillate consumed alkali equivalent to the formation of 80% of one mol. of formic acid. An aqueous solution of the acid decolorised potassium permanganate and reduced ammoniacal silver nitrate. The acid was isolated as its sodium salt and its identity was proved by conversion into *NN'*-di-*p*-tolylformamidine hydrochloride,[9] m. p. and mixed m. p. 266—269° (decomp.).

(*b*) Deacetyldihydrogedunin (5—10 mg.) was heated under reflux for 30 min. with 5% ethanolic potassium hydroxide and the solution was then diluted to 250 c.c. with ethanol.

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[9] Whalley, *J.*, 1948, 1014.

The pale yellow solution had $\lambda_{max.}$ 272 mμ (E_1^1, 270) displaced to 250 mμ by acidification to pH 3·5. Similar behaviour was shown by all derivatives of dihydrogedunin having the original acetoxy- or derived hydroxy-group but not by those derivatives in which this group was absent, or was replaced by oxo, or was in the epimeric configuration.

Ozonolysis of Dihydrogedunin.—Dihydrogedunin (2 g.) in ethyl acetate (40 c.c.) at −70° was treated with an excess of ozone. The solvent was evaporated at room temperature and the residue was decomposed by warming it with water and zinc dust, finally at 100° for 1 hr. The aqueous phase was decanted and the residue was washed with water. Distillation of the combined washings gave an acid solution containing 1·1 equivalents of acid per mol. of dihydrogedunin. The acid was identified as formic acid by its reducing properties and by the formation of *NN'*-di-*p*-tolylformamidine. Under these conditions we were unable to obtain a homogeneous product from the water-insoluble fraction of the product.

Anhydrodeacetyldihydrogedunin.—Deacetyldihydrogedunin (0·5 g.) in pyridine (15 c.c.) was treated with phosphorus oxychloride (1 c.c.), and the mixture was boiled for 2 min. The solution was then poured on ice and hydrochloric acid, and the product was collected with chloroform. The washed and dried extract was concentrated and percolated through a short column of alumina. The solid from the eluate crystallised from chloroform–methanol to give the *anhydro-derivative* as rods, m. p. 248°, [α] +100° (Found: C, 73·3; H, 7·3. $C_{26}H_{32}O_5$ requires C, 73·6; H, 7·6%), $\lambda_{max.}$ 293 mμ (ε 80), $\nu_{max.}$ *inter al.* 3023, 1675, 833 cm.$^{-1}$ (in carbon disulphide). The yield was very variable, never greater than 33%, and was considerably reduced when the dehydration was on a larger scale.

Anhydrodeacetyldihydrogedun-2-ene.—Deacetyldihydrogedun-2-ene (1 g.) in pyridine (10 c.c.) and phosphorus oxychloride (2·5 c.c.) was heated at 100° for 75 min. and then worked up as above. The *anhydro-derivative* (0·24 g.) crystallised, with difficulty, from methanol as rods, m. p. 178°, [α] +115° (Found: C, 76·2; H, 7·5. $C_{26}H_{32}O_4$ requires C, 76·4; H, 7·8%).

3-*Ethylenedioxydihydrogedunan.*—Finely ground dihydrogedunin (2 g.) was dissolved at 120° in ethylene glycol (25 c.c.) and 3 drops of concentrated hydrochloric acid were added. The solution was cooled and diluted with aqueous sodium hydrogen carbonate, and the precipitate crystallised from chloroform–methanol, giving the *ketal* (1·7 g.) as plates, m. p. 255°, [α] +46° (Found: C, 68·2; H, 7·7. $C_{30}H_{40}O_8$ requires C, 68·2; H, 7·6%). The ketal in methanolic hydrogen chloride at the b. p. for 1½ hr. was reconverted into dihydrogedunin.

3-*Ethylenedioxy*-7-*oxodeacetoxydihydrogedunan.*—7-Oxodeacetoxydihydrogedunin was treated as in the previous experiment. The *ketal* crystallised from chloroform–methanol as laths, m. p. 262°, [α] −12° (Found: C, 69·2; H, 7·2. $C_{28}H_{36}O_7$ requires C, 69·4; H, 7·5%), $\nu_{max.}$ 1700 cm.$^{-1}$.

3-*Ethylenedithiodihydrogedunan.*—Dihydrogedunin (211 mg.) was dissolved in glacial acetic acid (7·4 c.c.) and treated with a mixture of ethanedithiol (0·5 c.c.) and boron trifluoride etherate (0·5 c.c.). After 20 min. the solution was diluted with water, and the precipitated *thioketal* was crystallised from chloroform–methanol, forming prisms (202 mg.), m. p. 318—320° (decomp.), [α] −20°, which sublimed to a solid, m. p. 352° (Found: C, 63·8; H, 7·15; S, 11·4. $C_{30}H_{40}O_6S_2$ requires C, 64·3; H, 7·2; S, 11·4%).

3,7-*Bisethylenedithiodeacetoxydihydrogedunan.*—7-Oxodeacetoxydihydrogedunin (246 mg.) was suspended in ethanedithiol (0·3 c.c.) and treated with boron trifluoride etherate (0·4 c.c.). After 20 min. methanol was added and the precipitated *bisthioketal* was purified from chloroform–methanol as an amorphous solid (Found: C, 60·4; H, 6·9; S, 21·4. $C_{30}H_{40}O_4S_4$ requires C, 60·8; H, 6·8; S, 21·6%). The products formed by treating this compound with Raney nickel in refluxing tetrahydrofuran or ethanol for up to 40 hr. were amorphous and still contained considerable amounts of sulphur.

Hexahydrogedunan.—Dihydrogedunene (5 g.) in acetic acid (100 c.c.) was hydrogenated over Adams catalyst and absorbed 3·5 molar proportions of hydrogen after 30 hr. at room temperature and pressure. The filtered solution was poured into water, and the product was collected into chloroform. The neutral fraction of the extract which remained after alkali-washing, partially crystallised from methanol to give prisms (1·5 g.) of *hexahydrogedunan*, m. p. 192—193°, raised by wasteful recrystallisation to 224—226°, [α] −58° (Found: C, 70·5; H, 9·0. $C_{28}H_{42}O_6$ requires C, 70·9; H, 8·9%). Hydrolysis of this compound with 2% methanolic potassium hydroxide gave the *deacetyl derivative* as prisms (from methanol), m. p. 280—282° (Found: 72·1; H, 9·2. $C_{26}H_{40}O_5$ requires C, 72·2; H, 9·3%). This was readily oxidised to the *ketone*, plates (from methanol), m. p. 232—234° (Found: C, 72·8; H, 8·7.

$C_{26}H_{38}O_5$ requires C, 72·5; H, 8·9%), which gave a yellow 2,4-*dinitrophenylhydrazone* as needles (from ethyl acetate), m. p. 242—243° (Found: N, 9·0. $C_{32}H_{44}N_4O_8$ requires N, 8·9%).

When hexahydrogedunan (1 g.) was hydrolysed with 20% methanolic potassium hydroxide (40 c.c.) under reflux a salt separated after 15 min. This was readily soluble in water. Attempts to prepare the corresponding ester by reaction with methyl iodide or methyl sulphate led to the formation of deacetylhexahydrogedunan, as did attempts to isolate the free acid from the salt.

Oxidation of 7-*Oxodeacetoxydihydrogedunan to a Diosphenol.*—A suspension of powdered 7-oxodeacetoxydihydrogedunan (0·4 g.) in dry t-butyl alcohol (35 c.c.) containing potassium t-butoxide (4 g., *ca.* 1N) was shaken in an atmosphere of oxygen. The ketone dissolved rapidly and the uptake of oxygen ceased after 10 min., 20·2 c.c. having been absorbed (theory 20·4 c.c.). The solution was diluted and acidified and the product was collected with chloroform from which aqueous alkali extracted the *diosphenol* (280 mg.), which crystallised from ethanol as prisms, m. p. 202°, [α] −184° (Found: C, 70·5; H, 7·1. $C_{26}H_{32}O_6$ requires C, 70·9; H, 7·3%), $\lambda_{max.}$ 284 mμ (ε 9500), and in 0·1N-ethanolic sodium hydroxide 355 mμ (ε 5400).

7-epi-*Deacetyldihydro*-β-*gedunol.*—7-Oxodeacetoxydihydrogedunin (0·5 g.) was shaken at room temperature in aqueous dioxan containing potassium borohydride (200 mg.) for 2 hr. The *diol* was isolated by dilution and acidification of the solution and crystallised from ethyl acetate–carbon tetrachloride as octahedral prisms (160 mg.), m. p. 206—210° (decomp.), [α] +53° (Found: C, 61·5; H, 7·2. $C_{26}H_{36}O_6,\frac{1}{2}CCl_4$ requires C, 61·1; H, 6·9%).

Dihydro-β-*gedunyl Chloroacetate.*—Dihydro-β-gedunol (1·2 g.) in pyridine (15 c.c.) was added to a solution of chloroacetic acid (0·3 g.) and toluene-*p*-sulphonyl chloride in pyridine (15 c.c.) at 0°. After 1 hr. at 0° the mixture was poured on ice and hydrochloric acid, and the product was isolated with ether. The washed and dried ethereal solution was concentrated and passed through acid-washed alumina (Brockmann Grade 2) from which ether eluted the *chloroacetate* (665 mg.), which crystallised as plates (from chloroform–methanol), m. p. 208—210°, [α] −80° (Found: Cl, 6·8. $C_{30}H_{39}ClO_8$ requires Cl, 6·3%).

Dihydro-β-*gedunyl Iodoacetate.*—A solution of the above chloroacetate (0·4 g.) and sodium iodide (1·2 g.) in acetone (20 c.c.) was boiled for 3 hr. The suspension was diluted and the product was collected with chloroform. It was purified by chromatography on acid-washed alumina (Grade 2) from which chloroform eluted the *iodoacetate* (386 mg.), which crystallised from ethanol as prisms, m. p. 173° (decomp.), [α] −1° (Found: C, 55·7; H, 5·7; I, 19·1. $C_{30}H_{39}IO_8$ requires C, 55·1; H, 6·0; I, 19·4%).

Minor Constituents of Guarea *Species.*—The combined steam-involatile residues from the original mother liquors of 8 extractions by method (*b*) were dissolved in methanol (300 c.c.) and ether (200 c.c.) and after six months the brown solid (87 g.) which had separated was collected, triturated with ether, dissolved in chloroform, and percolated through alumina (200 g.). Evaporation of the eluate gave a colourless solid (53 g.) which was continuously extracted with light petroleum.

The light-petroleum extract was separated by chromatography on alumina in benzene into dihydrogedunin (3·5 g.) and a solid, m. p. 77—83° (0·6 g.), further purification of which from acetone and from ethyl acetate gave needles, m. p. 82—83°, [α] −6°, raised to 84—87° on admixture with β-sitosteryl palmitate,[10] m. p. 87—88° (Found: C, 83·2; H, 12·2. Calc. for $C_{45}H_{80}O_2$: C, 82·75; H, 12·35%). Hydrolysis of the ester gave a neutral fraction, m. p. 135—135·5° undepressed by β-sitosterol (Found: C, 84·0; H, 12·1. Calc. for $C_{29}H_{50}O$: C, 84·1; H, 12·2%).

Further elution of the column with acetone gave 7-*oxodeacetoxydihydro*-α-*gedunol* (10·83 g.), hexagonal plates (from acetone), m. p. 300—301°, [α] −126° [Found: C, 70·5; H, 8·2; OMe, 0%; *M* (Rast), 412. $C_{26}H_{34}O_6$ requires C, 70·6; H, 7·7%; *M*, 442·5], $\lambda_{max.}$ 207 (ε 6600) and 291 mμ (ε 48). The ketone gave a negative Zimmermann test but gave an *oxime*, m. p. 244—246° (Found: C, 68·2; H, 7·9; N, 3·2. $C_{26}H_{35}NO_6$ requires C, 68·2; H, 7·7; N, 3·1%), and a 2,4-*dinitrophenylhydrazone*, m. p. 296—298° (decomp.) (Found: C, 61·0; H, 6·1; N, 8·75. $C_{32}H_{38}N_4O_9$ requires C, 61·7; H, 6·1; N, 9·0%). Acetone–chromic acid–sulphuric acid oxidised this compound in good yield to 7-oxodeacetoxydihydrogedunin. The light-petroleum insoluble portion of the extract crystallised from chloroform–methanol to give more dihydrogedunin and methyl angolensate[4a] (4·2 g.) which separated from methanol as prisms, m. p. 199—201°, [α] −48° (lit., m. p. 197°, [α] −43°) [Found: C, 69·2; H, 6·9; OMe, 6·5%; *M* (Rast),

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[10] King and Jurd, *J.*, 1953, 1192.

447. Calc. for $C_{27}H_{34}O_7$: C, 68·9; H, 7·3; 1OMe, 7·7%; *M*, 470·5], $\lambda_{max.}$ 206 (ε 3100) and 287 mμ (ε 26). The *oxime* crystallised from aqueous ethanol as needles, m. p. 228—229° (Found: C, 66·6; H, 7·1; N, 2·9. $C_{27}H_{35}NO_7$ requires C, 66·8; H, 7·3; N, 2·9%), and the 2,4-*dinitrophenylhydrazone* as golden-yellow prisms (from methanol), m. p. 258° (decomp.) (Found: C, 60·8; H, 6·2; N, 8·7. $C_{33}H_{38}N_4O_{10}$ requires C, 60·9; H, 5·9; N, 8·6%).

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