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CONSTITUTION OF PTEROCARPOL

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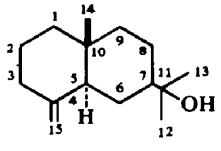
Abstract—Pterocarpol, a sesquiterpene alcohol isolated from *Pterocarpus macrocarpus* and *P. santalinus* has been shown to be 2,11-dihydroxy, $\Delta^{4(15)}$-eudesmene.

THE chemical components of the heartwood of *Pterocarpus macrocarpus* (Burma padauk) have been studied[1–3] but in the course of the present work a sample of wood obtained from Burma in 1961 yielded a new colourless alcohol named pterocarpol $C_{15}H_{26}O_2$, m.p. 104–105°. β-Eudesmol is not found in this or the related *P. dalbergioides*,[5] though it occurs in *P. indicus*.[4] A special variety of *Pterocarpus santalinus*, commonly known as red sandal wood, contains large quantities of pterocarpol together with small amounts of β-eudesmol (I).

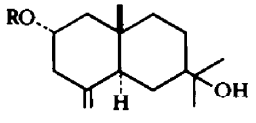
Constitution of pterocarpol. Pterocarpol, $C_{15}H_{26}O_2$, has one double bond and can be hydrogenated over Pd-C to dihydropterocarpol (III), $C_{15}H_{28}O_2$, m.p. 120–121° indicating that it is a bicyclic sesquiterpene. Selenium and also Pd-C dehydrogenation yield eudalene. The cooccurrence of β-eudesmol suggests that pterocarpol has a similar eudesmane skeleton and this is supported by the NMR spectrum.

The double bond stretching and deformation frequencies of pterocarpol at 1650 and 890 cm^{-1} show the presence of an exomethylene group, confirmed by ozonolysis which produces formaldehyde and a ketoalcohol (IV), $C_{14}H_{24}O_3$, m.p. 198–200°, possessing a band at 1710 cm^{-1} (6-membered ring ketone). The latter does not give an iodoform test showing that the original double bond is not in the isopropyl unit and should be at $\Delta^{4(15)}$ of the eudesmene skeleton as in eudesmol.

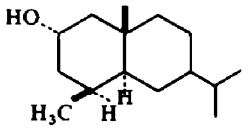
The presence of two active hydrogen atoms in pterocarpol as shown by Zerewitinoff determination suggests that both the O atoms are present as OH groups, one secondary and the other tertiary as revealed by acetylation. Acetic anhydride–pyridine at room temperature yields a mono-acetate (V), m.p. 88–89°, while at reflux temperature a liquid diacetate is produced. The tertiary hydroxyl is in the isopropyl unit since *m/e* 59 is the base peak in the mass spectrum of pterocarpol. Its location at C_{11} is supported by the NMR spectrum which is discussed later.



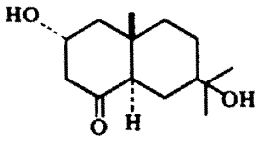
I



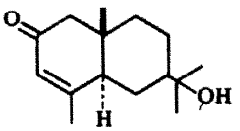
II : R = H
V : R = $COCH_3$



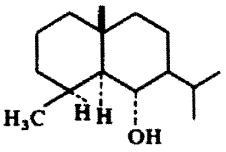
VII



IV



IX

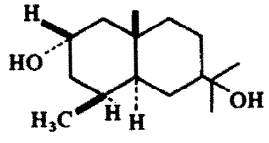


VIII

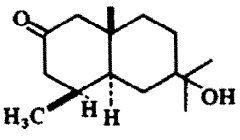
The secondary OH group is not in position 3 since the ketone (IV) obtained by ozonolysis of pterocarpol does not consume periodic acid. When dihydropterocarpol (III) is oxidized with pyridine–chromium trioxide or with dichromate–sulphuric acid in acetone a liquid ketone dihydropterocarpone (VI) is formed, ν_{max} 1710 cm^{-1} (6-membered ring ketone) and 1425 cm^{-1} (ketomethylenes). It also gives a positive Zimmermann colour test and forms a benzylidene derivative, λ_{max} 290, 337 (inflex) and λ_{min} 241 nm. As the keto group cannot therefore be in 6 position this position cannot be assigned to the secondary hydroxyl—a conclusion supported by the following observation. Pterocarpol mono-acetate (V) was dehydrated using pyridine–phosphorus oxychloride in the cold. The product was hydrogenated over Pd-C followed by saponification. The resultant saturated mono-hydric liquid alcohol (VII) differs in IR spectrum and rotation from solid dihydrojunenol[6] (VIII) which could be expected to be formed if pterocarpol like junenol possesses the equatorial hydroxyl at the 6-position. It is explained later that pterocarpol has the same configuration as dihydrojunenol. The same monohydric alcohol is obtained from dihydropterocarpol when subjected to the above transformations.

Of the remaining positions *viz.* 1, 2, 8 and 9, position 2 was indicated by the oxidation of pterocarpol with acid dichromate to an α,β-unsaturated ketone (IX) possessing a UV maximum at 241 nm. This can be explained only if the OH groups is placed in position 2, and the double bond migrated into the ring. The possible alternative of position 3 for the OH has been already ruled out.

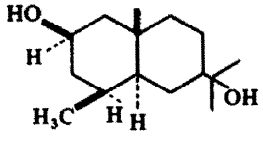
The stereochemistry of the secondary OH group was deduced as follows. Reduction of the ketone (VI) obtained from dihydropterocarpol with sodium borohydride, gives besides minor quantities of dihydropterocarpol, the isomeric diol (X) as the major product which gives a crystalline 3,5-dinitrobenzoate. The reduction of similar 2-keto compounds is known to yield mainly the axial alcohol because of the attack from the less hindered side opposite to the C_{10}-Me group.[7] Hence the secondary OH in dihydropterocarpol is equatorial, and structure II has been assigned to pterocarpol.



III



VI



X

This structure is supported by the NMR spectra of pterocarpol and its mono acetate, taken in $CDCl_3$. The C_{10} Me at τ 9·30 for pterocarpol and at τ 9·21 for the acetate is characteristic of *trans* fused eudesmanes; in the *cis* compounds it occurs at τ 9·03.[8] The methyls of the hydroxyisopropyl group are at τ 8·80 for pterocarpol and τ 8·78 for the acetate (6 protons each), thus supporting the conclusion drawn earlier from the mass spectrum. The exomethylene protons are revealed at τ 5·15 and τ 5·40 (pair of doublets) in pterocarpol and at τ 5·08 and 5·33 (pair of doublets) in the acetate. The proton on C_2 gives its resonance as a multiplet centered at τ 6·12 in pterocarpol. The τ value suggests that the proton is axial and this is further supported by a high band width at half height (17–18 c/s). Similar values are observed for the C_2 proton in dihydropterocarpol (III) and 2-hydroxyeudesmane (VII) as compared to that (10 c/s) in the epimeric diol (X) with equatorial C_2 proton. The C_2-proton signal moves down to τ 4·95 in the acetate (V), partly overlapping with the signals of the exomethylene protons. In the solid monoacetate the acetate signal is at τ 7·95 (3H) while in the liquid diacetate two peaks at τ 8·00 and 8·05, each 3H are present.

EXPERIMENTAL

All m.ps are uncorrected. Petroleum ether used had boiling range of 40–60° unless otherwise stated.

Extraction of pterocarpol

(1) *From* Pterocarpus macrocarpus. The heartwood shavings (1 kg) were extracted with pet. ether in the cold (2 × 4 l.); the pale yellow extract was concentrated and kept in the refrigerator. A solid separated and was recrystallized from alcohol to yield homopterocarpin (2 g), m.p. 88–89°, undepressed by an authentic sample. The alcoholic mother liquor was evaporated and the residue taken up in a small quantity of pet. ether. On standing, a colourless crystalline solid (100 mg) separated, m.p. 134–136°. It gave a pink Liebermann–Burchard test. The pet. ether concentrate, after removal of homopterocarpin was freed from the solvent and chromatographed over neutral alumina and the column was eluted successively with pet. ether, benzene, EtOAc and finally alcohol. The first 3 fractions did not yield any solid. The alcohol eluate on concentration left a colourless residue which readily crystallized from EtOH. It gave a positive Liebermann–Burchard test (pink colour), m.p. 258–260° (100 mg). In the IR spectrum (Nujol) it had the following peaks (cm^{-1}): 3850, 3225, 1725 (s), 1680 (m), 1250 (s), 1175, 1160, 1030 (m), 1010 (m), suggesting that it might be a derivative of a triterpene carboxylic acid.

The wood shavings were next extracted with hot alcohol (3 × 4 l.), the extract concentrated and the concentrate poured into excess ether with shaking. when a dark brown viscous mass was thrown down. The soln was extracted in succession with $NaHCO_3$aq, Na_2CO_3aq and NaOHaq; but no crystalline material was obtained on acidification. The remaining ether soln was washed with water, dried ($MgSO_4$) and evaporated yielding pterocarpol as a pale coloured solid which crystallized from benzene as colourless needles, m.p. 104–105°; $[\alpha]_D$ +39° (*c*, 1·05, $CHCl_3$; 8 g); no absorption maximum in the UV ν_{max} 3000 cm^{-1} (OH), 890 cm^{-1} and 1650 cm^{-1} ($\rangle C{=}CH_2$). (Found: C, 75·4; H, 10·7. $C_{15}H_{26}O_2$ requires: C, 75·6; H, 10·9); *m/e* 220 (10·6), 202 (22·4), 187 (12·8), 162 (20·4), 159 (30·8), 147 (25·6), 133 (12·8), 121 (19·6), 119 (14·9), 107 (16·0), 105 (19·2), 95 (13·9), 91 (18·1), 79 (17·4), 59 (100), 55 (18·1), 43 (27·6), 41 (24·2).

(2) *From* P. santalinus. The heartwood shavings (1 kg) were successively extracted with pet. ether (60–80°) and ether. The pet. ether extract on concentration gave a pale yellow oil. The oil was taken up in benzene and kept at room temp for a few hr when a pale yellow solid (400 mg) was deposited; it crystallized from benzene as colourless needles, m.p. 104–105°, mixed m.p. with pterocarpol from *P. macrocarpus* was undepressed. The ether extract on concentration deposited a dark red resinous mass which was extracted with hot benzene. The yellow benzene soln was washed with aqueous alkali to remove the colouring matter; the pale yellow benzene soln on concentration deposited colourless needles (6 g), m.p., and m.m.p. with pterocarpol 104°. The mother liquor after removal of pterocarpol was steam distilled when some colourless needles, which agreed on TLC (silica gel) with authentic sample of β-eudesmol in three solvents (C_6H_6, C_6H_6:$CHCl_3$ (1:1), and $CHCl_3$) were obtained.

Dehydrogenation of pterocarpol to eudalene

(a) *Using selenium.* An intimate mixture of pterocarpol (500 mg) and selenium (1·5 g) was heated in a sealed tube between 300–350° for 30 hr. The tube was then broken and the contents extracted with ether and the ether soln clarified by passing through charcoal. It was washed with 5% NaOHaq to remove any phenolic matter and dried (Na_2SO_4). The solvent was then distilled off and the residue dissolved in a small volume of pet. ether and chromatographed on neutral alumina and the column eluted with light petroleum. The eluate on distillation left a pale coloured liquid; λ_{max} 320·5, 313, 305, 290, 280, 227·5 (strongest) and a shoulder at 222·5 nm, ν_{max} (thin film) 750, 828, 1373, 1459, 1508, 1607, 1633 cm^{-1} which agreed with the spectra of eudalene.[9] The picrate was prepared in benzene soln and recrystallized from benzene–pet. ether, m.p. 90–92°, undepressed by an authentic sample.

(b) *Using palladium charcoal.* Pterocarpol (200 mg) mixed with Pd-C (5%, 200 mg) was heated in a sealed tube at 200° for 15 hr and worked up as under (a). The liquid product was directly converted into the picrate in alcohol and crystallized from EtOH, m.p. 94°, undepressed by eudalene picrate and the IR spectra were superimposable.

Dihydropterocarpol. Pterocarpol (400 mg) in MeOH soln was hydrogenated in presence of Pd-C (200 mg, 5%); 30 cc (about 1 mole) of H_2 was absorbed in 2 hr. After filtering off the catalyst, the solvent was distilled off. The residue crystallized from EtOAc–pet. ether as colourless hygroscopic needles, m.p. 120–121°, $[\alpha]_D$ +22° (*c*, 1·2, $CHCl_3$). (Found: C, 75·4; H, 11·9. $C_{15}H_{28}O_2$ requires: C, 75·0; H, 11·7%). In the IR spectrum of the dihydro compound bands at 1650 and 890 cm^{-1} were absent indicating the absence of unsaturation. It was converted into its 3,5-dinitrobenzoate by treating with 3,5-dinitrobenzoyl chloride and pyridine. After keeping for 24 hr it was poured over ice and extracted with ether. The ether soln was washed successively with dil HCl, NaHCOaq, water and then dried (Na_2SO_4) and the ether evaporated; the 3,5-dinitrobenzoate crystallized from EtOAc as colourless plates, m.p. 185–186°. (Found: C, 54·7; H, 5·1. $C_{29}H_{32}N_4O_{12}$ requires: C, 55·4; H, 5·1%).

Acetylation to pterocarpol monoacetate. Pterocarpol (500 mg) was kept with pyridine–Ac_2O at room temp for 24 hr. The mixture was poured over crushed ice. The ppt was filtered off and crystallized from ether–light petroleum, m.p. 88–89°, $[\alpha]_D$ +47° (*c*, 0·86, $CHCl_3$), (400 mg). (Found: C, 73·0; H, 10·9; acetyl 15·5. $C_{17}H_{28}O_3$ requires: C, 72·9; H, 10·6; acetyl 15·4%); ν_{max} 3350 cm^{-1} (hydroxyl), 1750 cm^{-1}, 1245 cm^{-1} (acetoxyl), 890 cm^{-1}, 1660 cm^{-1} (exomethylene group).

Pterocarpol diacetate. Pterocarpol (200 mg) was refluxed with Ac_2O and pyridine for 3 hr. The mixture was poured over crushed ice and extracted with ether. The ether soln was successively washed with dil HCl, $NaHCO_3$aq, water and then dried ($MgSO_4$). The ether was evaporated and the diacetate obtained as a colourless oil; it was purified by chromatography over silica gel. It did not show an OH band in the IR.

NMR (τ values): C_{10}—CH_3 9·25 (s); C_{11}—$(CH_3)_2$ 8·55 (s); $>C=CH_2$ 5·09 (d), 5·46 (d); C_2—H 5·00 (m); —$OCOCH_3$ at C_2 and C_{11}, 8·00, 8·05 (s).

Ozonolysis of pterocarpol to norketone. Excess 3% ozonized O_2 was passed into a pterocarpol (500 mg) soln in EtOAc. The ozonide soln was directly hydrogenated over freshly reduced Pd-C (5%, 500 mg). The mixture was filtered, the filtrate distilled and the distillate collected in an aqueous sulphuric acid soln of 2,4-dinitrophenylhydrazine. The EtOAc layer was separated and evaporated and the residue macerated with conc HCl to remove excess reagent. The insoluble portion crystallized from benzene–light petroleum to yield formaldehyde -2,4-dinitrophenylhydrazone, m.p. 159–160° alone or admixed with an authentic sample.

The residue left in the distilling flask was crystallized from EtOAc yielding the ketone as colourless plates, m.p. 198–200°. (Found: C, 65·4; H, 9·6. $C_{14}H_{24}O_3H_2O$ requires: C, 65·1; H, 10·1%), ν_{max} 890, 1650 cm^{-1} due to exomethylene group were absent; 1719 cm^{-1} (cyclohexanone carbonyl) present.

Oxidation

(a) Dihydropterocarpol (300 mg; obtained by catalytic hydrogenation of pterocarpol) dissolved in acetone (20 cc) was treated with 10% $K_2Cr_2O_7$ in 5N H_2SO_4aq (4 cc), kept for ½ hr at room temp, diluted with an equal volume of water and left overnight. The excess dichromate was destroyed with Na_2SO_3, the mixture extracted with ether, the ether extract dried (Na_2SO_4) and the solvent removed. The ketone dihydropterocarpone was obtained as a liquid; ν_{max} at 1709 cm^{-1}, DNP melted at 180–182°.

(b) Dihydropterocarpol (400 mg) was added to Py–CrO_3 reagent in pyridine, left overnight diluted with water and extracted with ether. The ether extract was washed with dil HCl and dried ($MgSO_4$). On removal of the solvent, the ketone was obtained as a thick oil, giving a positive Zimmerman reaction. The ketone formed a benzylidene derivative, λ_{max} 290, 337 (inflex) nm.

(c) Pterocarpol (200 mg) was oxidized according to the procedure (a). The product was a liquid λ_{max} 241 nm (ε, 15,000) and ν_{max} 1660 cm^{-1} (α,β-unsaturated ketone).

2-Hydroxyeudesmane. To pterocarpol acetate (1 g) in pyridine (30 ml), $POCl_3$ (4 cc) was added, left overnight, the mixture poured into ice cold HCl aq and extracted with ether. The extract was washed with water, dried and the ether distilled off. The thick oily product was dissolved in EtOAc and hydrogenated over Pd-C (200 mg). Approximately two moles of H_2 were absorbed. The catalyst was filtered off, the filtrate evaporated and the residue boiled for 3 hr with 5 g NaOH in 50 cc of 50% aqueous alcohol. The alcohol was distilled off and the residue extracted with ether. The product was purified by chromatography on silica gel and was obtained as an oil, $[\alpha]_D$ +23° (EtOH), n 1·518, ν_{max} (thin film) 1471, 1391, 1374, 1163, 1050, 1030, 975, 917, 885 and 862 cm^{-1} (differed considerably from the spectrum of dihydrojunenol); 3,5-dinitrobenzoate, m.p. 144–146°. (Found: C, 63·2; H, 7·4. $C_{22}H_{30}N_2O_6$ requires: C, 63·2; H, 7·2%).

Sodium borohydride reduction of dihydropterocarpone. Dihydropterocarpone (200 mg) was dissolved in MeOH (25 ml), $NaBH_4$ (200 mg) added in small lots, the mixture kept 1 hr at room temp and refluxed for ½ hr. It was then acidified (HCl), extracted with ether and the ether evaporated. The product was a mixture on TLC (using silica gel and $CHCl_3$–benzene, 1:1) of two components, dihydropterocarpol being minor and *epi*dihydropterocarpol being major. It was converted into its 3,5-dinitrobenzoate as in an earlier case; it crystallized from EtOAc as colourless plates, m.p. 164–165°. (Found: C, 55·9; H, 5·8. $C_{29}H_{32}N_4O_{12}$ requires: C, 55·4; H, 5·1%). This is the derivative of *epi*dihydropterocarpol and mixed m.p. was depressed by that of dihydropterocarpol.

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