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TERPENOIDS AND RELATED COMPOUNDS- I

CONSTITUENTS OF THE TRUNK BARK OF *MELIA AZADIRACHTA* LINN. AND THE STRUCTURE OF THE KETOPHENOL, NIMBIOL

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Abstract– From the trunk bark of *Melia azadirachta* Linn. have been isolated a branched chain paraffin alcohol, $C_{28}H_{54}O$, nimbosterol, sugiol (I, R = H) and a new ketophenol, nimbiol having the molecular formula, $C_{14}H_{24}O_2$. Nimbosterol has been identified as β-sitosterol and nimbiol has been shown to possess the structure (II, R = H). The biogenetic considerations for the possible formation of sugiol and nimbiol in the same plant have also been discussed.

Melia azadirachta Linn. syn. *Azadirachta indica* Juss (Sanskrit: Nimba) commonly known as "neem" or Indian Lilac is an evergreen tree, usually 40–50 ft in height, belonging to the Meliaceae family. The bark, leaves and fruits have been used in the Ayurvedic system of medicine from very ancient times and are mentioned in most of the ancient Sanskrit medicinal literatures like Susrutasanhita. So much is its popularity as a medicinal plant that almost every house in many parts of rural India has a neem tree in the compound. The bark is regarded as bitter, tonic, astringent and useful in fever, thirst, nausea, vomiting and skin diseases.[1] The earlier chemical work on the different parts of the tree are contradictory and inconclusive.[1] The systematic investigations on the tree were for the first time carried out by Siddiqui *et al.*[2a–g], who isolated besides the amorphous bitter principles, nimbidin and nimbidol, two crystalline bitter principles, nimbin and nimbinin, a nonacosane, a sterol named as nimbosterol, a flavone named as nimbicetin and a glucoside of nimbosterol named as nimbosterin. The flavonoid constituents of neem were identified by Pankajamani and Seshadri[3] and neem gum was investigated by Mukherjee and Srivastava.[4]

From the trunk bark of neem Siddiqui *et al.*[2e,f] isolated besides the amorphous bitter principle, nimbidin, the crystalline compounds, nimbin, nimbinin and nimbosterol. The method of these workers included the percolation of the bark with ethyl alcohol followed by the partition of the extract between petroleum ether and 80 per cent ethyl alcohol. The petroleum ether layer yielded nimbosterol, m.p. 137°. The ethanolic layer yielded nimbidin, nimbinin and nimbin. Because of the medicinal importance of the trunk bark, we undertook a systematic investigation of it and following a different method of extraction were able to isolate[5] three more crystalline

[1] For a review of the chemical and pharmacological studies with different parts of the tree up to the year 1949 see R. N. Chopra, I. C. Chopra, K. L. Handa and L. D. Kapur, *Indigenous Drugs of India* pp. 360 363 U. N. Dhur & Sons Private Ltd., Calcutta, India (1958).

[2a–g] S. Siddiqui, *Curr. Sci.* **11**, 278 (1942); [b] C. Mitra and S. Siddiqui, *Ibid.* **17**, 51 (1948); [c] *J. Sci. & Ind. Res. India* **4**, 5 (1945); [d] C. Mitra, P. N. Rao, S. Bhattacharji and S. Siddiqui, *Ibid.* **6B**, 19 (1947); [e] S. Siddiqui, C. Mitra and S. Bhattacharji, *Ibid.* **8B**, 188 (1949); [f] *Ibid.* **12B**, 154 (1953); [g] C. Mitra, P. N. Rao and S. Siddiqui, *Ibid.* **12B**, 152 (1953).

[3] K. S. Pankajamani and T. R. Seshadri, *Proc. Indian Acad. Sci.* **36A**, 157 (1952).

[4] S. Mukherjee and H. C. Srivastava, *J. Amer. Chem. Soc.* **77**, 422 (1955).

[5] The isolation of these compounds were reported in a short communication, P. Sengupta, S. N. Choudhuri and H. N. Khastgir, *Chem. & Ind.* 861 (1958).

substances besides nimbosterol. The isolation procedure employed consisted in extracting the bark with benzene and separating the benzene extract into (a) a neutral fraction and (b) a sodium hydroxide soluble fraction.

The neutral fraction (a) was partitioned between petroleum ether and aqueous methanol.[6] The oily residue from the petroleum ether extract was saponified with methanolic potassium hydroxide and the unsaponifiable material on chromatography over alumina afforded two crystalline solids. The first solid that was eluted from the column with a mixture of petroleum ether and benzene (7 : 3) melted at 82-83°, $[\alpha]_D$ -- 7·8°. The compound did not show any maxima or any end absorption in the ultra-violet absorption spectra, thus establishing that it was completely saturated. The molecular formula, $C_{26}H_{54}O$, the hydroxyl peak at 2·9 μ in the infra-red spectra and the optical activity indicated that this compound is a branched chain paraffin alcohol having an asymmetric centre.

The second solid from the chromatogram which was eluted with benzene melted at 136- 137°, $[\alpha]_D$ −37·6°. On acetylation it formed an acetate, m.p. 129 130°. The melting points of the alcohol and the acetate were not depressed when mixed with authentic specimens of β-sitosterol and its acetate respectively. Siddiqui *et al.*[2e,f] isolated nimbosterol from the same unsaponifiable fraction and assigned[2d] the molecular formula, $C_{20}H_{34}O$ to it. Nevertheless the melting point of nimbosterol (137°) and its acetate (128°) suggested that nimbosterol was the β-sitosterol isolated by us.[5] Almost simultaneously, Brochere-Ferreol *et al.*[7] arrived at the same conclusion.

The sodium hydroxide soluble fraction (b) reported above was freed from any acidic material by washing with sodium carbonate solution and the phenolic fraction of the bark thus obtained was chromatographed over acid washed alumina. The first crystalline solid eluted from the column was found to be identical with sugiol or 7-ketoferruginol (I, R H).[8,9] It may be pointed out however that it is for the first time that sugiol has been isolated from a member of the Meliaceae family. So far the occurrence of sugiol has been reported only in several Coniferous species.

The second solid that immediately followed sugiol in the above chromatogram has been assigned the name Nimbiol by us. It melted at 250–251°, $[\alpha]_D$ -- 32·3° and the elementary analysis corresponded[10] to the molecular formula $C_{18}H_{24}O_2$. The infra-red spectra of nimbiol exhibited peaks at 3·05 μ and 6·03 μ indicating the presence of a phenolic hydroxyl group and a conjugated ketonic carbonyl group respectively. The phenolic nature of nimbiol was exhibited by its solubility in 10 per cent cold sodium hydroxide solution although it failed to give colour with alcoholic ferric chloride solution. Further nimbiol formed a monomethyl ether, $C_{19}H_{28}O_2$, m.p. 142- 143° and a monoacetate, $C_{20}H_{26}O_3$, m.p. 111–112°. The infra-red spectra of nimbiol acetate showed the absence of the hydroxyl peak of nimbiol but showed peaks at 5·69 μ and 8·4 μ (phenolic acetate) and 5·97 μ (conjugated ketone). The presence of a carbonyl function in nimbiol was further demonstrated by the formation of a semicarbazone, m.p. 208–210° of nimbiol methyl ether. The presence of an aromatic

[6] Nimbin was isolated from the methanolic layer of the partition, the details of which will be published in a separate communication. See also P. Sengupta, S. K. Sengupta and H. N. Khastgir, *Chem. & Ind.* 1402 (1958); 397 and 1194 (1959).

[7] G. Brochere-Ferreol, J. Polonsky and C. Mitra, *C.R. Acad. Sci., Paris* **246**, 3082 (1958).

[8] J. Simonsen, *The Terpenes* Vol. III, p. 359. University Press, Cambridge (1952).

[9a] C. W. Brandt and B. R. Thomas, *J. Chem. Soc.* 2442 (1952); [b] *New Zealand J. Sci. Technol.* **33B**, No. 1, 30 (1951).

[10] S. N. Choudhuri, H. N. Khastgir and P. Sengupta, *Chem. & Ind.* 634 (1959).

nucleus in nimbiol was indicated by the peaks at 6·25, 6·35 and 6·7 μ in the infra-red spectra of nimbiol.

The presence of *p*-hydroxyphenylketone moiety in nimbiol, as is present in sugiol was indicated by the ultra-violet absorption spectra of nimbiol, which in neutral alcoholic solution exhibited maxima at 231 mμ and 286 mμ. The spectra in 0·1 N NaOH in alcohol exhibited maxima at 251 mμ and 344 mμ. We have observed that

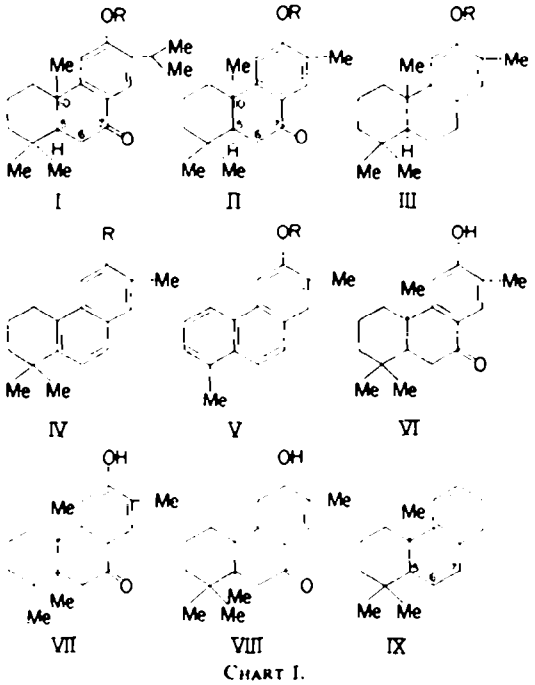

CHART I.

sugiol in 0·1 N NaOH in alcohol exhibited maxima at 251 mμ and 346 mμ in the ultra-violet region. The ultra-violet absorption spectra of nimbiol acetate showed maxima at 257 mμ and 294 mμ in neutral alcoholic solution. Further that the carbonyl group of nimbiol is present in conjugation with the aromatic nucleus was demonstrated by the fact that on hydrogenation in presence of palladium charcoal catalyst and perchloric acid[11] nimbiol acetate smoothly took up two mole equivalents of hydrogen and afforded deoxonimbiol acetate, $C_{20}H_{28}O_2$, m.p. 102-103°. The latter showed absorption maxima in the ultra-violet at 268 mμ and 277 mμ showing the presence of a substituted phenyl acetate type of chromophore. The infra-red spectra showed the acetate peak at 5·71 and 8·3 μ and the absence of the conjugated carbonyl peak. When nimbiol or its acetate was shaken in an atmosphere of hydrogen in presence of palladium charcoal catalyst without the addition of perchloric acid, there was no appreciable uptake of hydrogen. Evidently nimbiol is devoid of any isolated ethylenic linkage. On the basis of the foregoing experiment coupled with the observations made so far, it may be deduced that nimbiol is tricyclic.

Hydrolysis of deoxonimbiol acetate with methanolic potassium hydroxide furnished deoxonimbiol as a resinous mass, which resisted all attempts at crystallization. The ultra-violet absorption spectra of deoxonimbiol exhibited maxima at 283 mμ

[11] K. W. Rosenmund, F. Karg and F. K. Marcus, *Ber. Dtsch. Chem. Ges.* **75B**, 1850 (1942).

indicating that a phenol has been generated. Deoxonimbiol on reacetylation yielded deoxonimbiol acetate, m.p. 102-103°. Nimbiol on Clemmensen reduction also gave deoxonimbiol, identified as its acetate. It is interesting to point out here that deoxonimbiol was very slightly soluble in aqueous alkali like the diterpene phenols, ferruginol and totarol and in contrast to its parent compound, nimbiol which was fairly readily soluble in dilute alkali.

Finally the interesting compounds obtained by the selenium dehydrogenation of deoxonimbiol under varying conditions gave a clear insight into the structure of nimbiol. On mild dehydrogenation deoxonimbiol gave a phenolic compound, $C_{17}H_{20}O$, m.p. 147-148° (monomethyl ether, m.p. 145-146°) whose ultra-violet absorption spectra strongly indicated that it was a tetrahydrophenanthrol derivative. On more drastic dehydrogenation, in addition to the above tetrahydrophenanthrol, a tetrahydrophenanthrene, $C_{17}H_{20}$, m.p.82- 83° and a new phenanthrol, $C_{16}H_{14}O$, m.p. 189-190° (monomethyl ether, m.p. 119-120°) were isolated. The ultra-violet absorption spectra of this phenanthrol was identical with those of 1-methyl-6-hydroxyphenanthrene, prepared from podocarpic acid.[12] Thus it seemed to us that this phenanthrol, m.p. 189-190° was a dimethylphenanthrol. Our assumption was found to be quite correct, since on still more drastic dehydrogenation, deoxonimbiol gave pimanthrene (1,7-dimethylphenanthrene), m.p. 83 84° along with the phenanthrol, m.p. 189-190°. The melting point of the former was not depressed when mixed with an authentic specimen of pimanthrene. Further the picrate, m.p. 130-131° did not depress the melting point of an authentic specimen.

The foregoing results of selenium dehydrogenation experiments led us to envisage for nimbiol a hydrophenanthrene structure related to tricyclic diterpenes. The isolation of pimanthrene suggested that the phenanthrol, m.p. 189-190° was 1,7-dimethyl-6-hydroxyphenanthrene (V, R = H), the formation of which is conceivable if nimbiol possessed any of the three structures VI, VII or VIII. But the structure VII cannot explain the formation of the C_{17}-tetrahydrophenanthrol, which evidently has the structure IV (R = OH) or of the C_{17}-tetrahydrophenanthrene, which has the structure IV (R = H). Finally, of the alternative structures, VI and VIII, we prefer structure VI for nimbiol, because of its occurrence with sugiol (I, R = H) in the same plant. The rotatory dispersion curves of nimbiol methyl ether and sugiol methyl ether (I, R = Me) are so strikingly similar that we consider this also as a strong evidence in support of structure VI for nimbiol. Further the rotatory dispersion data established the identity of the steric configuration of nimbiol with that of sugiol. The absolute configuration of nimbiol could now be expressed by the structure II (R = H)[13,14] and of deoxonimbiol by the structure III (R = H). This conclusion was further corroborated by chemical evidences.

Recently Wenkert *et al.*[15] discovered that chromic acid oxidation could be employed as a diagnostic tool in elucidating the nature of the A/B ring juncture of a monobenzenoid tricarbocyclic diterpene system. They observed that all *trans* A/B

[12] See Ref. 8, p. 473.
[13] S. N. Choudhuri, H. N. Khastgir and P. Sengupta, *Chem. & Ind.* 1284 (1959).
[14] After the announcement of our structure of nimbiol in a preliminary communication (Ref. 13) Dr. Roy H Bible, Jr. of G. D. Searle & Co., Chicago, Illinois, U.S.A. has kindly informed us that he has synthesized the phenol II (R = H) from podocarpic acid. The synthetic phenol and its methyl ether were found to be identical with our nimbiol and its methyl ether respectively. We are highly indebted to Dr. Bible for this information.
[15] E. Wenkert and B. G. Jackson, *J. Amer. Chem. Soc.* **80**, 211 (1958).

4,4-disubstituted hydrophenanthrenes of the type IX on oxidation with chromic acid invariably yielded 7-keto derivatives, whereas those possessing A/B *cis* ring juncture gave the 6,7-diketo compounds. By using the above method Ghatak[16] assigned the correct stereochemistry to his synthetic desoxypodocarpic acids. In the present study, we exposed deoxonimbiol acetate (III, R = CO·Me) to the action of chromic acid and from the reaction product could isolate only nimbiol. This fact was in conformity with the structure II (R = H) for nimbiol.

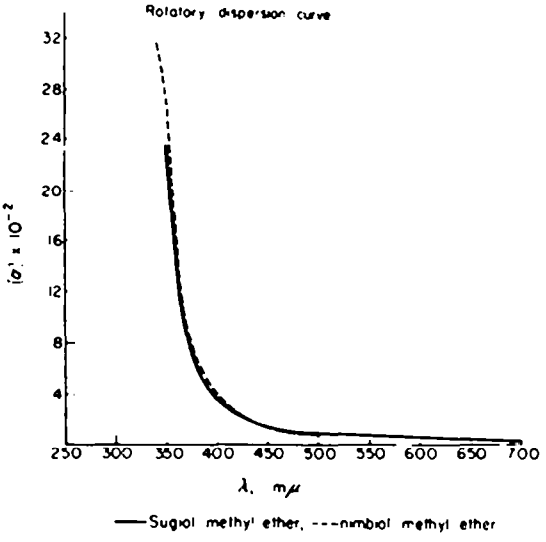

CHART II.

We observed further that neither sugiol methyl ether nor nimbiol methyl ether (II, R = Me) could be condensed with ethyl formate or furfural in presence of base, which could be explained by the fact that the equatorial methyl group at C_4 strongly hindered positon 6, since the A/B ring juncture was *trans* in both these compounds.

The occurrence of sugiol and nimbiol in the same plant is very interesting from the biogenetic point of view.[17] It seems to us that both sugiol and nimbiol could have been formed from a hypothetical pimaric acid type intermediate X. Nimbiol and sugiol might have been formed along Route A and Route B respectively as shown in Chart III on page 50.

EXPERIMENTAL

The petroleum ether used throughout the investigation had b.p. 60–80°.

Examination of the Neutral Fraction of the Trunk Bark of Melia azadirachta *Linn.*

Isolation of the paraffin alcohol, $C_{26}H_{54}O$ *and β-Sitosterol*

1 Kg dried and powdered trunk bark of *M. azadirachta* Linn. was extracted in a Soxhlet with benzene for 30 hr. The resinous mass (25 g) on removal of benzene, was taken up in ether and washed with cold 5% NaOH (4 × 100 cc), then with water and dried (Na_2SO_4). The neutral material (8 g) after removal of ether was dissolved in pet. ether (200 cc) and extracted several times with 80% aqueous methanol (total 200 cc). The dark residue (5·5 g) after evaporation of pet. ether layer was saponified by refluxing for 6 hr with KOH (5 g), methanol (90 cc) and water (10 cc). The ether extract yielded a gummy material (2·5 g). This was chromatographed (alumina, 60 g) and pet. ether

[16] U. R. Ghatak, *Tetrahedron Letters* No. 1, 19 (1959).
[17] For a general scheme for the biogenesis of diterpenes see E. Wenkert and J. W. Chamberlin, *J. Amer. Chem. Soc.* **81**, 688 (1959).

and benzene (7 : 3) eluted a crystalline solid (0·8 g), m.p. 70–74°, while benzene eluted a second crystalline solid (0·45 g), m.p. 125–130°.

The paraffin alcohol, $C_{28}H_{44}O$. The crystalline solids (0·8 g), m.p. 70–74° in the above chromatogram after crystallization from cyclohexane gave the paraffin alcohol (0·09 g), m.p. 82–83°, $[\alpha]_D$ −7·8° ($CHCl_3$). (Found: C, 81·60; H, 14·13. $C_{28}H_{44}O$ requires: C, 81·59; H, 14·22%). Mol. wt., Found (Rast), 375. Calc., 382.

U.V. No maxima and no end absorption.

I.R. ($CHCl_3$) Peak at 2·9 μ.

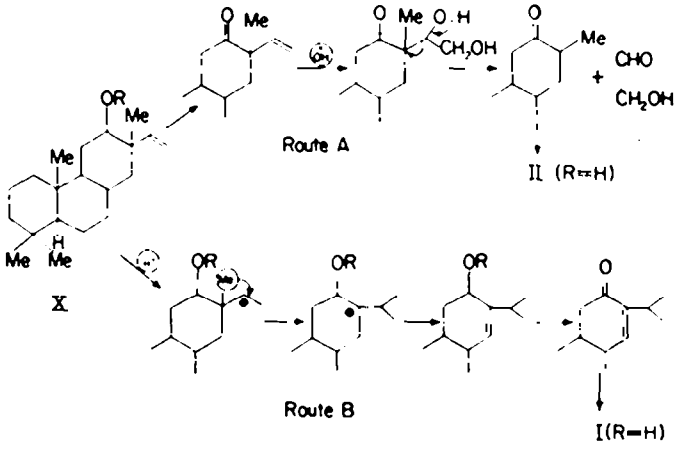

CHART III.

β-Sitosterol. The crystalline solids (0·45 g), m.p. 125–130° eluted with benzene in the above chromatogram were crystallized from methanol, yielding β-sitosterol (0·04 g), m.p. 136–137°, $[\alpha]_D$ −37·6° ($CHCl_3$), identical with an authentic sample of β-sitosterol.

β-Sitosterol acetate. β-Sitosterol (0·16 g) was acetylated with pyridine (2 cc) and acetic anhydride (2 cc) and the *acetate* (0·16 g), m.p. 124–125° crystallized from methanol (0·06 g), m.p. 129–130°, $[\alpha]_D$ 38° ($CHCl_3$), was identical with an authentic sample of β-sitosterol acetate. (Found: C, 82·06; H, 11·24. Calc. for $C_{31}H_{52}O_2$: C, 81·52; H, 11·48%).

Examination of the Phenolic Fraction of the Trunk Bark of Melia azadirachta *Linn.*

Isolation of sugiol (I, R = H) *and nimbiol* (II, R = H)

3·6 Kg dried and powdered trunk bark of *M. azadirachta* was extracted with benzene. The residue was dissolved in ether and extracted with 5% NaOH (4 × 200 cc). This solution after acidification with cold and dil HCl was extracted with ether, washed with cold 5% Na_2CO_3, then with water, and dried (Na_2SO_4). The gummy phenolic residue (12·5 g) was chromatographed over alumina (400 g, deactivated with 12 cc of 10% aqueous acetic acid). Elution with benzene gave crystalline solids (0·52 g), m.p. 260–280°, while elution with a mixture of benzene and ether (9:1) gave a second crystalline solid (0·82 g), m.p. 230–238°.

Sugiol (I, R = H). The crystalline solids (0·52 g), m.p. 260–280° in the above chromatogram were crystallized from methanol, yielding sugiol (0·25 g, 0·007% yield on dried trunk bark), m.p. 292–294° (reported[14] m.p. 295–297°), $[\alpha]_D$ +26° (EtOH). (Found: C, 80·44; H, 9·36. Calc. for $C_{20}H_{28}O_2$: C, 79·95; H, 9·39%). Mol. wt., Found (Rast), 312. Calc., 300.

U.V. (95% EtOH) λ_{max} 232 mμ (log E 4·19) and 284 mμ (log E 4·12) (0·1 N NaOH in EtOH) λ_{max} 251 mμ (log E 3·53) and 346 mμ (log E 4·41)

I.R. (KBr disk) Peaks at 3·2 μ and 6·05 μ.

Sugiol methyl ether (I, R = Me)

(a) To a warm solution of sugiol (0·09 g) in methanol (0·15 cc) and 10% NaOH (0·16 cc) was added dimethyl sulphate (0·04 cc) and the reaction mixture shaken vigorously, cooled and poured

into water. The methyl ether (0·05 g) crystallized from methanol, m.p. 137–138° (Lit.[56] m.p. 138–139°) $[\alpha]_D$ +37·4° ($CHCl_3$). (Found: C, 80·00; H, 9·60. Calc. for $C_{31}H_{50}O_2$: C, 80·21; H, 9·62%).
U.V. (95% EtOH) λ_{max} 231 mμ (log E 4·29) and 280 mμ (log E 4·18).

(b) A mixture of sugiol (0·32 g), dry acetone (25 cc), anhydrous potassium carbonate (2 g) and dimethyl sulphate (1·5 cc) was refluxed for 5 hr, cooled and poured into cold water. Crystallization from methanol gave *methyl ether* (0·25 g), m.p. 137–138°.

Sugiol acetate (I, R = CO·Me). Sugiol (0·11 g) was acetylated with pyridine (2 cc) and acetic anhydride (2 cc) and the *acetate* crystallized from methanol (0·05 g), m.p. 164–165° (Lit.[56] m.p. 165–167°).

Sugiol benzoate (I, R = CO·C_6H_5). Sugiol (0·24 g), pyridine (3 cc) and benzoyl chloride (0·24 cc) gave *sugiol benzoate* (0·08 g), m.p. 184° (Lit.[56] m.p. 185–186°).

Nimbiol (II, R = H). The second crystalline solids (0·82 g), m.p. 230–238° eluted with benzene–ether (9 : 1) in the above chromatogram on crystallization from benzene and then from methanol yielded nimbiol (0·42 g, 0·011% yield on dried bark), m.p. 245–247°. Purification gave the analytical sample, m.p. 250–251°, $[\alpha]_D$ −32·3° ($CHCl_3$). (Found: C, 79·14; H, 8·88. $C_{18}H_{24}O_2$ requires: C, 79·37; H, 8·88%). Mol. wt., Found (Rast), 280. Calc., 272.
U.V. (95% EtOH) λ_{max} 231 mμ (log E 4·07) and 286 mμ (log E 4·06) (0·1 N NaOH in EtOH) λ_{max} 251 mμ (log E 3·89) and 344 mμ (log E 4·33)
I.R. ($CHCl_3$) Peaks at 3·05 μ (phenolic hydroxyl), 6·03 μ (conjugated ketone) and 6·25, 6·35 and 6·7 μ (aromatic nucleus).

Nimbiol acetate (II, R = CO·Me). A solution of nimbiol (1·46 g) in pyridine (15 cc) and acetic anhydride (15 cc) was heated on the steam bath for 4 hr. The crude *acetate* m.p. 100–103° was crystallized from aqueous methanol (0·75 g), m.p. 111–112°, $[\alpha]_D$ +22·6° ($CHCl_3$). (Found: C, 76·50; H, 8·70. $C_{20}H_{26}O_3$ requires: C, 76·40; H, 8·34%).
U.V. (95% EtOH) λ_{max} 257 mμ (log E 4·09) and 294 mμ (log E 3·41)
I.R. ($CHCl_3$) Peaks at 5·97 μ (conjugated carbonyl) and 5·69 and 8·4 μ (phenolic acetate).

Hydrolysis of nimbiol acetate: regeneration of nimbiol. Nimbiol acetate (0·1 g) was refluxed with 5% methanolic KOH (2 cc) for 3 hr and extracted with ether. The aqueous alkaline solution on acidification with dil. HCl gave nimbiol, m.p. 244–245°.

Nimbiol methyl ether (II, R = Me)

(a) To a warm solution of nimbiol (0·5 g) in 10% NaOH (1 cc) dimethyl sulphate (0·5 cc) was added with shaking. The ether extract was washed with 10% NaOH, and water and dried (Na_2SO_4). The *methyl ether* crystallized from methanol (0·26 g), m.p. 142–143°, $[\alpha]_D$ −43·7° ($CHCl_3$). (Found: C, 79·14; H, 8·87. $C_{19}H_{26}O_2$ requires: C, 79·68; H, 9·15%).

(b) A mixture of nimbiol (0·38 g), dry acetone (25 cc), anhydrous potassium carbonate (2 g) and dimethyl sulphate (1·6 cc) was refluxed for 5 hr. Crystallization of the product from methanol gave *nimbiol methyl ether* (0·24 g), m.p. 142–143°.

Semicarbazone of nimbiol methyl ether. A mixture of nimbiol methyl ether (0·07 g), semicarbazide hydrochloride (0·07 g), ethanol (5 cc) and pyridine (0·1 cc) was refluxed for 5 hr. The *semicarbazone* (0·04 g), m.p. 208–210° crystallized from methanol. (Found: C, 69·58; H, 8·37. $C_{20}H_{29}O_2N_3$ requires: C, 69·94; H, 8·51%).

Deoxonimbiol acetate (III, R = CO·Me)

(a) A mixture of nimbiol acetate (1·1 g), glacial acetic acid (20 cc), 10% palladium charcoal catalyst (0·5 g) and perchloric acid (0·2 cc) was stirred at room temp in an atmosphere of hydrogen until two molar equivalents were absorbed. The reaction mixture was filtered, diluted with water, and extracted with ether. The ether layer was washed with dil. Na_2CO_3 aq and water, and dried (Na_2SO_4). The oily residue (1·1 g) crystallized from methanol yielding *deoxonimbiol acetate* (0·7 g), m.p. 102–103°, $[\alpha]_D$ +56·4° ($CHCl_3$). (Found: C, 80·35; H, 9·26. $C_{20}H_{28}O_3$ requires: C, 79·95; H, 9·39%).
U.V. (95% EtOH) λ_{max} 268 mμ (log E 2·97) and 277 mμ (log E 2·96).
I.R. ($CHCl_3$) Peaks at 5·71 μ and 8·3 μ (phenyl acetate).

(b) To zinc amalgam, prepared from 1·8 g of zinc, were added conc. HCl (2 cc), water (2 cc) and nimbiol (0·3 g) dissolved in toluene (4 cc) and ethanol (1 cc) and the mixture refluxed for 24 hr. Conc. HCl (0·1 cc) was added to the reaction mixture every hour during the reflux period. The

ether extract was washed with water, dried (Na_2SO_4) and yielded a resinous residue (0·23 g, λ_{max} 283 mμ, log E 3·58) of *deoxonimbiol*. It was acetylated with pyridine (2 cc) and acetic anhydride (2 cc) and the *acetate* (0·2 g) was chromatographed over alumina (10 g, deactivated with 0·3 cc of 10% aqueous acetic acid). On elution with pet. ether, *deoxonimbiol acetate* (0·08 g), m.p. 102–103° was obtained.

Attempted hydrogenation of nimbiol (without perchloric acid). A mixture of nimbiol (0·3 g), ethyl acetate (45 cc) and 10% palladium charcoal catalyst (0·15 g) was stirred in an atmosphere of hydrogen. No absorption of hydrogen took place even after 8 hr, and unchanged nimbiol (0·29 g), m.p. 244–246° was recovered.

Hydrolysis of deoxonimbiol acetate. A solution of deoxonimbiol acetate (1·7 g) in 10% methanolic KOH (10 cc) was refluxed for 4 hr, cooled, acidified with dil. HCl and extracted with ether, yielding a resinous mass (1·1 g) which was insoluble in aqueous alkali and could not be crystallized.
U.V. (95% EtOH) λ_{max} 283 mμ (log E 3·56).

The resinous material on reacetylation in the usual manner gave deoxonimbiol acetate, m.p. 101–103°.

Selenium dehydrogenation experiments

Isolation of 1,1,7-*trimethyl*-6-*hydroxy*-1,2,3,4-*tetrahydrophenanthrene* (IV, R = OH). An intimate mixture of deoxonimbiol (0·8 g) and selenium powder (2 g) was heated at 300–320° for 11 hr. The reaction product was thoroughly extracted with ether and the evaporation product chromatographed over alumina (20 g, deactivated with 2 cc of 10% aqueous acetic acid). The petroleum ether–benzene (1 : 1) eluate (0·33 g), after 3 crystallizations from pet. ether gave 1,1,7-trimethyl-6-hydroxy-1,2,3,4-tetrahydrophenanthrene (0·08 g), m.p. 147–148°. (Found: C, 84·85; H, 8·38. $C_{13}H_{20}O$ requires: C, 84·95; H, 8·39%).
U.V. (95% EtOH) λ_{max} 235 mμ (log E 4·8), 283 mμ (log E 3·7), 316 mμ (log E 3·27) and 330 mμ (log E 3·39).

Methyl ether (IV, R = OMe). A mixture of the above tetrahydrophenanthrol (0·05 g), dry acetone (10 cc), anhydrous potassium carbonate (0·5 g) and dimethyl sulphate (0·4 cc) was refluxed for 5 hr. Crystallization of the product from methanol gave the *monomethyl ether* of the tetrahydrophenanthrol, m.p. 145–146°, not identical with the starting tetrahydrophenanthrol.

Isolation of 1,1,7-*trimethyl*-1,2,3,4-*tetrahydrophenanthrene* (IV, R = H), 1,1,7-*trimethyl*-6-*hydroxy*-1,2,3,4-*tetrahydrophenanthrene* (IV, R = OH) *and* 1,7-*dimethyl*-6-*hydroxyphenanthrene* (V, R = H).

A mixture of deoxonimbiol (1·1 g) and selenium powder (4 g) was heated at 320–340° for 50 hr. The reaction mixture, gave a gummy residue (1 g), which afforded a crystalline solid (0·25 g), m.p. 155–156° from pet. ether. The pet. ether mother liquor was evaporated leaving a gummy residue (0·7 g), which was chromatographed over alumina (40 g), and the gummy residue (0·26 g) eluted with pet. ether was rechromatographed over alumina (26 g). Pet. ether eluted a crystalline solid (0·18 g), m.p. 77–78°, which on crystallization from absolute alcohol gave the tetrahydrophenanthrene (IV, R = H), m.p. 78–79°. On sublimation at 95°/0·2 mm it melted at 82–83°. (Found: C, 90·98; H, 8·99. $C_{17}H_{18}$ requires: C, 91·01; H, 8·99%).
U.V. (95% EtOH) λ_{max} 230 mμ (log E 4·86), 279 mμ (log E 3·73), 310 mμ (log E 3·0) and 324 mμ (log E 3·11).

The pet. ether insoluble solid, m.p. 155–156° reported above was chromatographed over alumina (30 g, deactivated with 1·5 cc of 10% aqueous acetic acid). A mixture of pet. ether and benzene (7 : 3) eluted a solid (0·1 g), m.p. 132–140°, while benzene eluted a second solid (0·1 g), m.p. 179–182°.

The crystalline solids (0·1 g), m.p. 132–140° on recrystallization from pet. ether gave the tetrahydrophenanthrol (IV, R = OH), m.p. 146–148° identical with the tetrahydrophenanthrol reported before.

The crystalline solids (0·1 g), m.p. 179–182° eluted with benzene was rechromatographed over alumina (10 g, deactivated with 0·7 cc of 10% aqueous acetic acid). The benzene eluate gave crystalline solids (0·06 g), m.p. 184–186°, which after crystallization from a mixture of benzene and pet. ether afforded 1,7-dimethyl-6-hydroxyphenanthrene (V, R = H), m.p. 189–190°. On sublimation at 170°/0·2 mm the analytical sample, m.p. 189–190° was obtained. (Found: C, 86·24; H, 6·42. $C_{16}H_{14}O$ requires: C, 86·45; H, 6·35%).

U.V. (95% EtOH) λ_{max} 257 mμ (log E 4·43), 279 mμ (log E 3·97),
298 mμ (log E 3·66), 308 mμ (log E 3·78),
339 mμ (log E 3·13) and 356 mμ (log E 3·15).

Methyl ether (V, R = Me). A mixture of the phenanthrol (0·09 g), m.p. 189–190°, acetone (10 cc), anhydrous potassium carbonate (0·5 g) and dimethyl sulphate (0·4 cc) was refluxed for 10 hr. The product, m.p. 113–115° on crystallization from methanol gave the methyl ether of 1,7-dimethyl-6-hydroxyphenanthrene (0·06 g), m.p. 119–120°. (Found: C, 86·23; H, 6·90. $C_{17}H_{16}O$ requires: C, 86·40; H, 6·83%).

Isolation of pimanthrene and 1,7-dimethyl-6-hydroxyphenanthrene (V, R = H)

A mixture of deoxonimbiol (0·62 g) and selenium powder (3 g) was heated at 340–360° for 42 hr. The product of dehydrogenation (0·6 g) on crystallization from pet. ether and a mixture of benzene and pet. ether gave 1,7-dimethyl-6-hydroxyphenanthrene, identical with the compound reported above.

The residue (0·4 g) obtained on the evaporation of the pet. ether mother liquor above was chromatographed over alumina (30 g). Pet. ether eluted a crystalline solid (0·2 g), m.p. 70–74°, which was rechromatographed over alumina (25 g). After a forerun of an oil (0·06 g), pet. ether eluted a crystalline solid (0·12 g), m.p. 74–78°, which on crystallization from methanol gave *pimanthrene* (0·05 g), m.p. 81°. On sublimation at 100–115°/0·1 mm the analytical sample melted at 83–84° identical with an authentic sample of pimanthrene. (Found: C, 93·04; H, 6·64. Calc. for $C_{18}H_{14}$: C, 93·16; H, 6·84%)
U.V. (95% EtOH) λ_{max} 258 mμ (log E 4·75), 279 mμ (log E 4·11),
288 mμ (log E 4·02), 300 mμ (log E 4·12),
318 mμ (log E 2·47), 327 mμ (log E 2·35),
333 mμ (log E 2·5), 339 mμ (log E 2·29) and
350 mμ (log E 2·24).

Pimanthrene picrate. The picrate, prepared in the usual manner m.p. 130–131° was not depressed when mixed with an authentic specimen of pimanthrene picrate.

1-*Methyl-6-hydroxyphenanthrene.*[12] Podocarpic acid was dehydrogenated with palladium charcoal catalyst and 1-methyl-6-hydroxyphenanthrene, m.p. 160° was isolated in the usual manner.
U.V. (95% EtOH) λ_{max} 257 mμ (log E 4·6), 279 mμ (log E 4·0),
297 mμ (log E 3·94), 306 mμ (log E 4·02),
340 mμ (log E 3·27) and 357 mμ (log E 3·32).

Attempted preparation of the furfurylidine derivative of (a) sugiol methyl ether and (b) nimbiol methyl ether

(a) A mixture of sugiol methyl ether (0·18 g), 95% ethanol (10 cc), 15% NaOH (0·36 cc), freshly distilled furfural (0·1 cc) and water (1 cc) was kept at room temp. for 4 hr. On working up unchanged sugiol methyl ether (0·15 g), m.p. 137–138° was recovered.

(b) From a similar reaction mixture of nimbiol methyl ether (0·2 g), 95% ethanol (10 cc), 15% NaOH (0·4 cc), furfural (0·11 cc) and water (1 cc) was recovered unchanged nimbiol methyl ether (0·17 g), m.p. 138–140°.

Attempted condensation of ethyl formate with (a) sugiol methyl ether and (b) nimbiol methyl ether

(a) A solution of sugiol methyl ether (0·15 g) in benzene (10 cc) was added with swirling to a cooled mixture of ethyl formate (0·2 g), sodium hydride (0·05 g) and benzene (5 cc). The mixture was allowed to stand overnight. On working up unchanged sugiol methyl ether (0·12 g), m.p. and mixed m.p. 136–137° was recovered.

(b) A similar reaction of nimbiol methyl ether (0·15 g) in benzene (20 cc) with ethyl formate (0·2 g), sodium hydride (0·05 g) and benzene (5 cc) gave unchanged nimbiol methyl ether (0·11 g), m.p. and mixed m.p. 138–140°.

Chromic acid oxidation of deoxonimbiol acetate. Deoxonimbiol acetate (0·1 g) was oxidized in glacial acetic acid (1 cc) and chromic acid (0·13 g) in 80% acetic acid (0·6 cc). The gummy product (0·08 g) isolated by means of chloroform was hydrolysed by refluxing for 5 hr with 5% methanolic KOH (2 cc), and extracted with ether. The aqueous alkaline solution was acidified and extracted with ether yielding a residue (0·05 g), m.p. 240–244°, which on crystallization from benzene afforded *nimbiol*, m.p. and mixed m.p. 246–248°.

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