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CHEMICAL EXAMINATION OF *ARDISIA MACROCARPA* WALL

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Abstract—The bark and hardwood of *Ardisia macrocarpa* Wall contain rapanone (I), along with a leucoanthocyanidin, (−)3,4,5,7,3′,4′,5′-heptahydroxyflavan (II).

Ardisia is a large genus of the Myrsinaceae family several species of which are indigenous to India. The bark of *Ardisia colorato* Roxb is used as a febrifuge and in diarrhoea and also applied externally to ulcers. The *A. humilis* occurs throughout India and its ripe berries yield an unknown yellow dye. In this paper, the chemical examination of the bark and hardwood of *A. macrocarpa* and the isolation of rapanone (I) and (−)3,4,5,7,3′,4′,5′-heptahydroxyflavan (II) as the only constituents is reported.

Compound I has a molecular formula, $C_{19}H_{30}O_4$ and due to its acidic properties forms several metallic salts. It is orange yellow in colour, m.p. 140–141° and exhibits properties of a dihydroxybenzoquinone in the formation of a yellow diacetate (III), a dibenzoate (IV) and a violet dianilino derivative (V). On reductive acetylation, it forms a dihydrotetraacetate (X), indicative thereby of not only two phenolic hydroxyl groups but also the existence of a *p*-benzoquinone system which is further supported by the ready formation of a di-2,4-dinitrophenylhydrazone (VI), a dioxime (VII), a diphenylhydrazone (VIII) and a disemicarbazone (IX). Hydrolysis of I using aqueous alkali in an hydrogen atmosphere gives α-ketopalmitic acid (XI), further characterized by the formation of its oxime. Further oxidation of this acid (XI) with alkaline hydrogen peroxide gives pentadeconic acid, identified as its amide. These results support the structure as being 2,5-dihydroxy-6-tridecyl-1,4-benzoquinone (I). A comparison of the properties of I with rapanone isolated earlier[2–5] establishes its identity, further confirmed by mixed m.p. determinations with authentic samples of rapanone and its dihydrotetraacetate.

Compound II is colourless and melts at 300°. Its molecular formula agrees with $C_{15}H_{14}O_8$, H_2O confirmed by a Rast's molecular weight determination of 332. It is leavorotatory and the hydrated product dehydrates quite readily at 150° *in vacuo*. It forms a colourless heptaacetate (XII), a pentamethyl ether (XIII), $[\alpha]_D^{30} = -50{\cdot}5°$ and a pentamethyldiacetate (XIV) indicative of five phenolic and two alcoholic hydroxyl groups. The colour reactions, viz. a blue ferric colour, appearance of a red colour or precipitate with alcoholic HCl on warming and a cherry red colour with vanillin and HCl in the cold suggest that II is a leucoanthocyanidin. Oxidation of XIII with neutral potassium permanganate yields trimethyl gallic acid while oxidation

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[1] *Dictionary of economic products of India* **1**, 290 (1889).

[2] Z. Kawamura, *Rep. Jap. Sci. Ass.* **12**, 377 (1937).

[3] M. Asano and K. Yamaguti, *J. Pharm. Soc. Japan* **60**, 105 (1940).

[4] O. Fernandz and A. Pizarroso, *Farm. Nueva. Madrid* **11**, 1 (1946).

[5] S. N. Aiyar, M. K. Jain, M. Krishnamurty and T. R. Seshadri, *Phytochem.* **3**, 335 (1964).

with sodium metaperiodate indicates the existence of a 3,4-diol system. These results suggest that II is (−)3,4,5,7,3′,4′,5′-heptahydroxyflavan possibly identical with a similar product isolated from Karada bark.[6] This structure II is further supported by its conversion to delphinidin chloride having an absorption maxima at 552 mμ in ethanolic HCl.

EXPERIMENTAL

Isolation of rapanone (I). Powdered bark and wood shavings (1 kg) of *A. macrocarpa* were extracted continuously in a Soxhlet with petrol or benzene until the extract was no longer coloured yellow. Concentration of the extract gave lustrous orange plates and prisms (yield: bark, 1% and hardwood, 2·6%), m.p. 140–141°, showing a purple ferric reaction. (Found: C, 70·83; H, 9·41; $C_{19}H_{30}O_4$ requires: C, 70·79; H, 9·32%). It dissolved readily in KOH aq, NaOH aq and NH_4OH forming violet solutions which regenerated the original compound on acidification. With boric acid in conc. H_2SO_4, it exhibited a green fluorescence under the UV light.

Reactions of I. Di-O-acetylrapanone (III) was obtained by the acetylation of I using boiling acetic anhydride for 3½ hr and crystallized as yellow prisms and plates, m.p. 64–66° from pet. ether, giving a negative ferric reaction. (Found: C, 68·12; H, 8·56; $—COCH_3$, 21·42. $C_{23}H_{34}O_6$ requires: C, 67·98; H, 8·38; $—COCH_3$, 21·18%).

Its *dibenzoate*[8] (IV), crystallized as light yellow needles, m.p. 88–90° from pet. ether. (Found: C, 75·04; H, 7·34. Calc. for $C_{33}H_{38}O_6$: C, 74·71; H, 7·17%).

The *acetate*[8] (X) of the reduction product of I prepared using acetic anhydride and Zn dust in presence of triethylamine by boiling for 2 hr, crystallized as colourless silky lustrous plates and prisms, m.p. 117° from petrol, giving a negative ferric reaction. (Found: C, 66·12; H, 8·24; $—COCH_3$, 35·27. Calc. for $C_{27}H_{40}O_8$: C, 65·85; H, 8·13; $—COCH_3$, 34·95%).

The *di-2,4-dinitrophenylhydrazone* (VI) of I crystallized as dark red prisms, m.p. 174–175° from EtOH. (Found: N, 16·62. $C_{31}H_{38}O_{10}N_8$ requires: N, 16·43%).

The *dioxime* of I crystallized as pale brown short prisms, m.p. 129–130° from acetone showing an intense brown ferric reaction. (Found: N, 8·27. $C_{19}H_{32}O_4N_2$ requires: N, 7·96%).

The *diphenylhydrazone* (VIII) of I prepared by following the general procedure crystallized as red brown prisms, m.p. 204–206°d. from acetone. (Found: N, 11·24. $C_{31}H_{42}O_2N_4$: requires: N, 11·15%).

The *disemicarbazone* (IX) of I crystallized as brown prisms, m.p. 228–230°d. from acetone. (Found: N, 19·43. $C_{21}H_{36}O_4N_6$ requires: N, 19·27%).

Oxidation of I using $KMnO_4$ in acetone solution gave myristic acid, m.p. 50–51°. (Found: C, 73·84; H, 12·42. $C_{14}H_{28}O_2$ requires: C, 73·69; H, 12·28%).

Hydrolysis of I (1 g) using aqueous alkali (10% NaOH; 100 ml) by heating under reflux for 12 hr yielded α-ketopalmitic acid (XI). (Found: C, 71·42; H, 11·40. $C_{16}H_{30}O_3$ requires: C, 71·11; H, 11·11%). Further oxidation of α-ketopalmitic acid with alkaline H_2O_2 gave pentadeconic acid, m.p. 51–52°, further identified as its amide, m.p. 100–102°.

Isolation of leucoanthocyanidin (II). The bark and the woody portions after extraction with benzene were subsequently extracted with acetone for 36 hr. The product crystallized from acetone as colourless small prisms, m.p. 300°d. giving a blue ferric reaction. (Found: C, 56·21; H, 4·52. $C_{15}H_{14}O_8$ requires: C, 55·90; H, 4·35%). It is leavorotatory but no definite value could be obtained as its solution rapidly developed colour. With alcoholic HCl, it developed a red colour which deepened on warming while a precipitate settled down and with vanillin and HCl in the cold, it gave a cherry red colour.

3,4,5,7,3′,4′,5′-*Heptaacetyloxyflavan* (XII). Acetylation of II (1 g) with acetic anhydride and pyridine in the cold for 48 hr yielded a heptaacetate which crystallized as colourless plates and prisms, m.p. 228–230°d. giving a negative ferric reaction. (Found: C, 56·62; H, 4·74. $C_{29}H_{28}O_{15}$ requires: C, 56·49; H, 4·55%).

5,7,3′,4′,5′-*Pentamethoxyflavan*-3,4-*diol* (XIII). A solution of II (1 g) in MeOH (40 ml) was treated with excess diazomethane in ether in the cold for 24 hr. The methyl ether crystallized as colourless prisms, m.p. 182–185° from benzene, $[\alpha]_D^{30°}$ $-50·5°$ (*c*, 0·218 g, MeOH) giving a negative ferric reaction. (Found: C, 61·42: H, 6·24. $C_{20}H_{24}O_8$ requires: C, 61·21; H, 6·12%).

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[6] A. K. Ganguly, T. R. Seshadri and P. Subramanian, *Tetrahedron* 3, 225 (1958).

Its *diacetate* (XIV) crystallized as colourless prisms, m.p. 208–210° from benzene. (Found: C, 60·72; H, 6·12. $C_{24}H_{28}O_{10}$ requires: C, 60·50; H, 5·88%).

Oxidation of the pentamethyl ether (XIII) *using* $KMnO_4$. Compound XIII (1 g) in acetone (100 ml) was treated under reflux with $KMnO_4$ (5 g) added in small quantities during 6 hr. The acetone was removed by evaporation while water was added and the solution decolourized using SO_2. The sticky mass thus obtained was crystallized from benzene when a colourless product, m.p. 166–167° was obtained, identified as trimethylgallic acid.

Conversion of 3,4,5,7,3′,4′,5′-*heptahydroxyflavan to delphinidin chloride*. Compound II (1 g) was boiled under reflux for 2 hr in ethanolic HCl (200 ml, 8%) and the clear solution after filtration was extracted with isoamyl alcohol. The colouring matter was transferred to HCl solution (1%) by the addition pet. ether. The acid solution was washed thoroughly with benzene and concentrated at ordinary temp over KOH in a vacuum desiccator. The delphinidin chloride (100 mg) gave a positive ferric reaction and no extraction was observed with cyanidin reagent while its ethanolic HCl solution showed an absorption maxima at 552 mμ.

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