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CHEMICAL COMPONENTS OF THE ROOTS OF *CONNARUS MONOCARPUS*

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Abstract—Rapanone, bergenin and (−)-leucopelargonidin have been isolated from the roots of *Connarus monocarpus*. The roots constitute a very good source for rapanone (1·2%) and for bergenin (1·5%).

Connarus monocarpus is an evergreen shrub belonging to the family Connaraceae which is found along the west coast of India and also in Ceylon. The plant has been put to a number of medicinal uses[1] but no chemical work on it has been reported. The roots have been chosen for the present study. They are pale brown to brown in colour, do not appear to deteriorate on keeping, and there is no marked change in the chemical components with season.

The roots were extracted successively with hot petroleum ether, ether, chloroform, benzene, alcohol and finally with cold acetone. Three compounds were isolated: an orange–yellow solid (A), a colourless bitter principle (B) and a leucoanthocyanidin (C). Compounds (A), (B) and (C) were obtained as the major component of the petroleum ether, alcohol and acetone extract respectively. Small amounts of all the three compounds were isolated from the ether and chloroform extracts, whilst the benzene extract gave no crystalline material. In subsequent experiments it was found that better yields of the leucoanthocyanidin could be obtained by acetone extraction prior to alcohol.

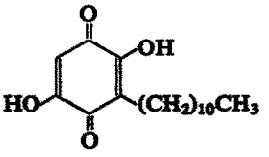
Compound (A): Rapanone

Compound (A) (m.p. 142–143°) showed the properties of a substituted *p*-benzoquinone, and analysis agreed with the molecular formulae $C_{17}H_{26}O_4$ or $C_{19}H_{30}O_4$. Two *p*-benzoquinone derivatives, embelin (I) ($C_{17}H_{26}O_4$) and rapanone (II) ($C_{19}H_{30}O_4$),[2,3] have the same melting point as (A) and mixed melting point with either of these showed no depression. Comparison of the quinol tetraacetates has been reported to be more useful. The quinol tetraacetate of (A) had a melting point of 116° the same as that reported for dihydrorapanone tetraacetate,[3] which suggested that (A) itself may be rapanone. The non-identity of (A) with embelin was established by comparing a number of derivatives of (A) with those of embelin. In this connexion some new derivatives of embelin have been prepared and their properties are recorded. The mixed melting point of embelin derivatives with the corresponding derivatives of (A) were depressed in all cases.

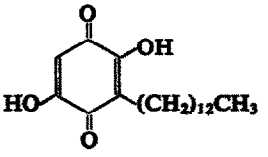
The u.v. and i.r. spectra of (A) are identical with those of rapanone and the identity of the two compounds was confirmed by NMR. The NMR spectra of the dimethyl ether and the quinol tetraacetate of (A) were compared with the spectra of the corresponding derivatives

[1] K. R. KIRTIKAR and B. D. BASU, *Indian medicinal plants* 1, 684 (1935).
[2] M. ASANO and K. YAMAGUTY, *J. Pharm. Soc. Japan* 60, 105, 585 (1940).
[3] L. F. FIESER and E. M. CHAMBERLAIN, *J. Am Chem. Soc.* 70, 71 (1948).

of embelin (a direct comparison with rapanone derivatives could not be made since rapanone was not available in sufficient quantity) and the results indicated that (A) had two more CH_2 groups than embelin in the side chain. Compound (A) thus is rapanone (II).



(I)

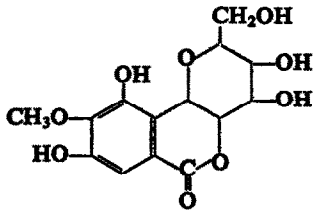


(II)

Compound (B): Bergenin

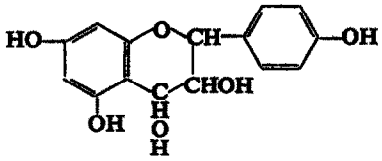
Compound (B) crystallized from absolute alcohol, melted at 237–238° and analysed for $C_{14}H_{18}O_{10}$. It did not give Molisch test and dissolved in cold sodium hydroxide solution from which it could be recovered on acidification. It gave an acetate, m.p. 205°, and a methyl ether, m.p. 199–200°.

The above data suggested that compound (B) may be bergenin (III). This conclusion was confirmed by comparison with authentic bergenin. The mixed melting point was undepressed, and the u.v. and the i.r. spectra of (B), as well as the X-ray diffraction patterns are identical with those of bergenin.[4]



(III)

Compound (C) had the properties of a leucoanthocyanidin since on boiling with alcoholic hydrochloric acid it gave a flavylium salt whose R_f value (phenol–water, lower layer) agreed with that reported for perlargonidin chloride.[5] Oxidation of the leucoanthocyanidin methyl ether gave anisic acid. As compound (C) was laevorotatory it is most probably (−)-leucopelargonidin (IV).



(IV)

EXPERIMENTAL

Extraction of the Roots

The roots (2 kg), cut into small pieces, were extracted (soxhlet) with petroleum ether until the extract was colourless. On concentration of the extract the quinone (A) separated as an

[4] M. K. Jain and R. Gupta, *J. Indian Chem. Soc.* **39**, 559 (1962).
[5] L. Ponniah and T. R. Seshadri, *J. Sci. Ind. Research* (India) **12B**, 605 (1953).

orange–yellow solid (20 g). The residual roots were extracted with ether and this extract, on cooling, deposited a buff-coloured solid, which was extracted with cold ethyl acetate (5 ml × 3). The ethyl acetate solution was dried ($MgSO_4$), concentrated to small volume under reduced pressure and petroleum ether was added. A buff-coloured substance which gave the tests for leucoanthocyanidin was precipitated (0·3 g). The residue insoluble in ethyl acetate was crystallized from alcohol (animal charcoal) when colourless crystals of (B) were obtained (0·4 g). From the ethereal mother liquor further quantities of the quinone (A) (2 g) were isolated.

The roots were subsequently extracted with chloroform and the extract deposited the leucoanthocyanidin (1·5 g) on cooling. This was filtered off, and the solution kept at 10–15° for 24 hr when colourless crystals of (B) (0·5 g) separated out. Concentration of the filtrate and cooling (0°) yielded further amounts of (A) (2 g).

The roots were then extracted with benzene followed by alcohol. The alcohol extract on concentration deposited colourless crystals of (B), and the mother liquor was diluted with alcohol, and ethyl acetate was added to give a clear solution. On keeping in the refrigerator overnight more (B) was deposited (30 g).

The roots were finally extracted with cold acetone. Acetone was removed under reduced pressure and the leucoanthocyanidin in the residue was taken up in ethyl acetate and purified by fractional precipitation with petroleum ether (10 g).

Modified Method for Improving the Yield of the Leucoanthocyanidin

The root (2 kg) was first exhaustively extracted with hot petroleum ether followed by hot chloroform till the extract was colourless. It was then extracted with acetone at room temperature and the acetone extract worked up as described above. From the ethyl acetate insoluble portion the bitter principle was isolated. Yields: leucoanthocyanidin 25 g; bitter principle 10 g.

Examination of Compound (A): Rapanone

Compound (A) crystallized from alcohol as lustrous orange–yellow plates or prismatic needles, m.p. 142–143°. It formed salts with caustic alkalis, ammonium hydroxide and magnesium acetate solutions. These salts which are violet in colour, are sparingly soluble in the cold but dissolve on warming, and the quinone is recovered on acidification. u.v.: λ_{max}^{EtOH} 290 mμ (log ε 4·24); i.r. ($CHCl_3$): 6·12 μ.

The quinol tetraacetate prepared by the reductive acetylation of the quinone (A) with zinc, acetic anhydride and a little pyridine crystallized from alcohol as flat needles, m.p. 116°.[3] The dibenzoate (benzoyl chloride–pyridine) crystallized from alcohol as shining rectangular plates, m.p. 86–87° (88–90°).[2]

Methylation of the Compound (A)

(*a*) Powdered (A) (1 g) was refluxed with dimethyl sulphate (2 ml) and anhydrous potassium carbonate (5 g) in dry acetone (150 ml) for 30 hr. The product crystallized from alcohol as deep yellow rectangular tablets of rapanone dimethyl ether, m.p. 64–65°. (Found: C, 72·0; H, 9·8. $C_{21}H_{34}O_4$ required: C, 72·0; H, 9·7%.) (*b*) The quinone (in methanol) was methylated with diazomethane (2·5 moles) and yielded the same product as in (*a*).

Oxidation of quinone (A). The quinone (5 g) in acetone (500 ml) was oxidized with a saturated solution of potassium permanganate (145 ml) at room temperature. The product

worked up in the usual manner gave myristic acid, m.p. 53–54° (amide, m.p. and mixed m.p. with an authentic sample, 102°; anilide, m.p. 81°) and oxalic acid. Oxidation with alkaline permanganate, chromic acid or nitric acid gave the same results.

3 (or 6)-Monoanilino quinone (A). The quinone (1 g) and distilled aniline (10 ml) were heated till a clear violet solution resulted. After cooling hydrochloric acid (250 ml; 1:1) was added and the monoanilino derivative filtered off. It crystallized from alcohol as small violet needles, m.p. 180–181°. (Found: N, 3·6. $C_{25}H_{35}O_3N$ required: N, 3·5%.)

Dianilino quinone (A). When the reactants in the above experiment were refluxed for half an hour the dianilino derivative was formed which crystallized from alcohol as bottle-green flakes, m.p. 168–169°. (Found: N, 5·5. $C_{31}H_{40}O_2N_2$ required: N, 5·9%.)

3 (or 6)-Mono-o-toluidino quinone (A). The quinone (1 g) and *o*-toluidine (10 ml) were heated till a clear violet solution was obtained. Hydrochloric acid (200 ml; 1:4) was added and the pinkish violet solid that separated was crystallized from alcohol when it separated in the form of deep violet tiny prisms, m.p. 124–125°. (Found: N, 3·6. $C_{26}H_{37}O_3N$ required: N, 3·4%.)

3 (or 6)-Monomethylamino quinone (A). This was prepared by reacting the quinone with methylamine in the cold. It crystallized from alcohol as chocolate brown shining plates, m.p. 160–161°. (Found: N, 3·7. $C_{20}H_{33}O_3N$ required: N, 4·2%.)

Mono-2:4-dinitrophenylhydrazone of (A). The *2:4-dinitrophenylhydrazone* crystallized from alcohol as tiny prisms having a deep chocolate colour, m.p. 169° (d). (Found: N, 11·8. $C_{25}H_{34}O_7N_4$ required: N, 11·2%.)

Disemicarbazone of (A)

The disemicarbazone was prepared by refluxing the quinone in alcohol with semicarbazide hydrochloride and sodium acetate for 2 hr. It crystallized from alcohol as pale yellow prismatic needles, m.p. 250° (d). (Found: N, 19·0. $C_{21}H_{36}O_4N_6$ required: N, 19·3%.)

Embelin dimethyl ether. The *dimethyl ether* crystallized from alcohol as deep yellow rectangular tablets, m.p. 58–59°. (Found: C, 70·3; H, 9·6. $C_{19}H_{30}O_4$ required: C, 70·8; H, 9·3%.)

3 (or 6)-Monoanilino embelin. The monoanilino derivative crystallized from alcohol as violet-coloured small needles, m.p. 184–185°. (Found: N, 3·7. $C_{23}H_{31}O_3N$ required: N, 3·8%.)

3 (or 6)-Mono-o-toluidino embelin. The *o*-toluidino derivative separated from alcohol as deep violet tiny needles, m.p. 135–136°. (Found: N, 3·8. $C_{24}H_{33}O_3N$ required: N, 3·7%.)

Mono-2:4-dinitrophenylhydrazone of embelin. The dinitrophenyl hydrazone crystallized from alcohol as chocolate tiny prisms, m.p. 167° (d). (Found: N, 11·8. $C_{23}H_{30}O_7N_4$ required: N, 11·8%.)

Identification of the compound (B): bergenin. On crystallization from water or rectified spirit, the compound melted at 148–150° with effervescence (dehydration). But on repeated crystallization from absolute alcohol the product obtained melted at 237°. (Found: C, 49·0; H, 5·0; OCH_3, 8·2. Calc. for $C_{14}H_{18}O_{10}$: C, 48·6; H, 5·2; OCH_3, 9·0%.) It did not give Molisch test and the compound was recovered unchanged after boiling with 7% sulphuric acid for 2 hr. It dissolved in cold solutions of sodium carbonate and hydroxide from which it could be recovered unchanged on acidification. The sodium carbonate solution is pale yellow changing to light violet, while the colour of the sodium hydroxide solution is light yellow. It had the following spectral absorptions: λ_{max} 275 mμ ($\log\epsilon$ 3·8) (ethanol) showing a bathochromic shift to 310 mμ on being made alkaline with aqueous sodium hydroxide;

i.r. (nujol): 2·92, 5·90, 6·24 and 6·59 μ. It gave the following derivatives: dimethyl ether, m.p. 195–196°; pentaacetate, m.p. 205°.

Characterization of the leucoanthocyanidin (C). The leucoanthocyanidin was purified by dissolving in ethyl acetate and fractional precipitation with petroleum ether finally being obtained as a colourless solid (laevorotatory), m.p. 245–250°. (Found: C, 61·4; H, 5·5. Calc. for $C_{15}H_{14}O_6$: C, 62·1; H, 4·8%.)

Compound (C) dissolved in sodium hydroxide solution forming a pinkish red solution which turned brownish red with excess of the reagent. It gave no marked colour with alcoholic ferric chloride. With warm alcoholic hydrochloric acid the compound developed a red colour which could be extracted by amyl alcohol. It gave a crimson colour with vanillin and hydrochloric acid.

The acetate (acetic anhydride–pyridine) separated as clusters of small prisms from alcohol, m.p. 185–187° (d). (Found: C, 59·6; H, 5·1. Calc. for $C_{25}H_{24}O_{11}$: C, 60·0; H, 4·8%.) Methyl ether (diazomethane) crystallized from alcohol as colourless tiny needles, m.p. 168–170°. (Found: C, 65·4; H, 6·4; Calc. for $C_{18}H_{20}O_6$: C, 65·1; H, 6·0%.) Acetate of the methyl ether crystallized from alcohol as elongated flat needles, m.p. 203–205°. (Found: C, 63·2; H, 6·1. Calc. for $C_{22}H_{24}O_8$: C, 63·5; H, 5·8%.)

Potassium permanganate oxidation of the methyl ether. The methyl ether of (C) (2 g) in acetone solution (100 ml) was oxidized with permanganate (3 g) by refluxing for 4 hr. The product was worked up in the usual manner and gave anisic acid, m.p. and mixed m.p. with an authentic sample, 181°.

Conversion of the Compound (C) into Pelargonidin Chloride

The leucoanthocyanidin (1 g) was refluxed with alcoholic hydrochloric acid (200 ml; 8%) for 2 hr and the solution worked up as usual. The colour reactions and the chromatographic behaviour of the flavylium salt obtained corresponded with pelargonidin chloride.[5]

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