Tetrahedron, 1967, Vol. 23, pp. 515 to 518. Pergamon Press Ltd. Printed in Northern Ireland

CHEMICAL EXAMINATION OF *CASSIA FISTULA*

V. K. MURTY, T. V. P. RAO and V. VENKATESWARLU
Department of Chemistry, Engineering College, Andhra University, Waltair, India

(*Received* 17 *May* 1966; *accepted for publication* 17 *June* 1966)

Abstract—The bark and hardwood of *Cassia fistula* contain fistucacidin, an optically inactive leucoanthocyanidin, 3,4,7,8,4'-pentahydroxyflavan (I) along with barbaloin (II) and rhein (III).

SEVERAL of the species of Cassia (Leguminosae) occur in India and are used extensively for medicinal purposes.[1,2] Extraction of the stem bark of *C. fistula* first with petroleum ether removed non-crystallizable gums and resins and subsequent extraction with acetone gave one crystalline component (I). The hardwood, on extraction with petrol removed the resins and subsequent extraction with benzene gave a yellow substance (II) and final extraction with alcohol gave three products. (I, II and III).

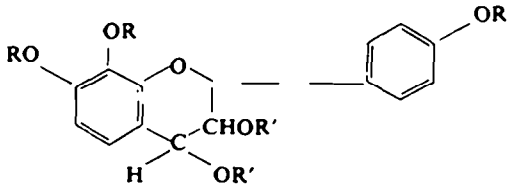
Product I melted at 245–247°d., optically inactive and analysed for $C_{15}H_{14}O_6$. It readily gave a pentaacetate (IV), a trimethyl ether (V) and a trimethyldiacetate (VI) indicative of three phenolic and two alcoholic hydroxyl groups. Oxidation of the trimethyl ether (V) with potassium permanganate gave anisic acid and 2-hydroxy-3,4-dimethoxybenzoic acid identified as their methyl esters. Periodate oxidation of the trimethyl ether (V) was rapid and complete during 40 min which clearly showed the existance and the nature of hydroxyl groups as present on the same side of the C—C link which facilitate rapid oxidation with periodate. It gave the colour reactions of a typical flavandiol which prompted us to assign the structure as 3,4,7,8,4'-pentahydroxyflavan (I).

Compound I shows no detectable optical rotation and must, therefore, be an isomer of (−)-terracacidin isolated by Clark-Lewis.[3] While terracacidin is described as a brown powder, and laevorotatory, product I is optically inactive, and crystalline melting at 245–247°d. This new product I has been designated by us as "fistucacidin", a name derived from *C. fistula*. As no derivative of fistucacidin shows optical activity, it may be a racemate.

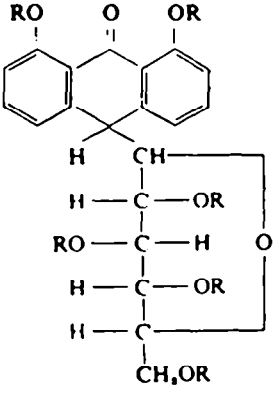
Product II is lemon yellow in colour, m.p. 146–148° and analysed for $C_{21}H_{22}O_9$. It formed a colourless heptaacetate[4] (VII) and a heptamethyl ether (VIII) and by reaction with sodium borate and phenylhydrazine hydrochloride, II was converted to emodinanthrone,[5] identical with an authentical sample.

Product III is yellow in colour, m.p. 310–313°, molecular formula $C_{15}H_8O_6$ and readily soluble with effervescence in sodium bicarbonate indicative of a carboxyl group. It gave a diacetate (IX) and a methyl ester (X) with excess diazomethane. The methyl ester, in turn, gave its diacetate (XI) which indicated the existance of one

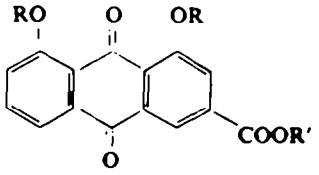
[1] R. N. Chopra, S. L. Nayar and I. C. Chopra, *Glossary of Indian Medicinial Plants*, CSIR Publication (1956).
[2] R. Wasicky, *Anias. Fac. Farn., Odont. Univ. S. Paulo* **2**, 57 (1942).
[3] J. W. Clark-Lewis, G. F. Katekar and P. I. Mortimer, *J. Chem. Soc.* 499 (1961).
[4] A. J. Birch and F. W. Donovan, *Austr. J. Chem.* **8**, 523 (1955).
[5] J. Evelynhay and L. Haynes, *J. Chem. Soc.* 3141 (1956).



I, R = R′ = H
IV, R = R′ = —COMe
V, R = —Me; R′ = H
VI, R = —Me; R′ = —COMe



II, R = H
VII, R = —COMe
VIII, R = —Me



III, R = R′ = H
IX, R = —COMe; R′ = H
X, R = H; R′ = —Me
XI, R = —COMe; R′ = —Me

carboxyl and two hydroxyl groups which resist methylation. From these considerations and a comparison of its properties with rhein,[6] product III is assigned the structure, 1,8-dihydroxy-3-carboxyanthraquinone (III).

EXPERIMENTAL

Extraction of the stem bark

Isolation of fistucacidin (I). The powdered stem bark (1 kg) was continuously extracted in a Soxhlet first with pet. ether (b.p. 40–60°) and subsequently with acetone until the extracts were no longer coloured. The petrol extract gave only noncrystallizable waxy impurities. The acetone extract on concentration, gave a dry residue which was eluted with cold AcOEt. The AcOEt was carefully treated with pet. ether till the coloured impurities were completely precipitated. Subsequent addition of more pet. ether gave a crystalline product which was recrystallized from AcOEt–pet. ether in the cold as a colourless crystalline powder, m.p. 245–247°d and optically inactive. It turned brown on storage and dissolved readily in MeOH, EtOH and acetone and sparingly in pet. ether, benzene and chf. (Found: C, 62·36; H, 5·04. $C_{18}H_{14}O_6$ requires; C, 62·07; H, 4·83%.) It gave the following colour reactions: (i) with alcoholic HCl it developed a red colour which deepened on warming, (ii) with alcoholic $FeCl_3$, it gave a greenish-blue colour (iii) with vanillin and HCl, it gave a cherry red colour and (iv) in conc H_2SO_4 it formed an orange red soln.

Extraction of the hardwood

Isolation of products I, II, *and* III. Chippings of the hardwood (1 kg) were freed from waxy impurities using pet. ether and subsequently extracted with benzene and AcOEt. The benzene concentrate gave a small quantity (1 g) of a yellow substance (II), which crystallized as lemon yellow

[6] H. Hauptmann and L. Lacerda Nazario, *J. Amer. Chem. Soc.* 72, 1492 (1950).

needles, m.p. 146–148°, from MeOH. (Found: C, 60·42; H, 5·34. $C_{21}H_{20}O_9$ requires: C, 6·29; H, 5·26%.) Concentration of the alcoholic extract gave a dry residue which was eluted with ether to give some more II (1 g), leaving a brown residue (III) which crystallized as lemon yellow needles, m.p. 310–313°, from excess AcOEt, giving a brown-red $FeCl_3$ reaction. (Found: C, 63·52; H, 3·12. $C_{15}H_8O_8$ requires: C, 63·36; H, 2·84%.)

The AcOEt extract on careful treatment with pet. ether eliminated first the coloured impurities and subsequent addition of petrol gave colourless crystals of I, m.p. 245–247° d., identical with the product isolated from the stem bark.

Reactions of fistucacidin (I)

3,4,7,8,4′-*Penta-O-acetylfistucacidin* (IV). Fistucacidin was acetylated using Ac_2O and pyridine (boiling ½ hr; or in the cold 24 hrs). It crystallized as colourless short prisms, m.p. 172–173°, from MeOH, giving a negative $FeCl_3$ reaction. (Found: C, 60·04; H, 5·24; —$COCH_3$, 43·27. $C_{28}H_{24}O_{11}$ requires; C, 59·99; H, 4·80; —$COCH_3$ 42·99%). Hydrolysis with aqueous alkali in the cold regenerated fistucacidin.

7,8,4′-*Tri-O-methylfistucacidin* (V). A sol of I (1 g) in EtOH was treated with excess diazomethane. The methyl ether crystallized as colourless long tapering rectangular prisms, m.p. 158–159°, from EtOH, giving a negative $FeCl_3$ reaction. (Found: C, 65·18; H, 6·14; —OCH_3 28·17; $C_{18}H_{20}O_6$ requires: C, 65·07; H, 6·02; —OCH_3, 28·02%.) Its diacetate, (VI) obtained by the acetylation of V using Ac_2O and pyridine, crystallized as colourless short prisms, m.p. 132–133° from benzene, giving no $FeCl_3$ reaction. (Found: C, 63·54; H, 6·04. $C_{22}H_{24}O_8$ requires: C, 63·46; H, 5·77%.)

Oxidation of trimethylfistucacidin (V)

(a) *Using neutral potassium permanganate.* Oxidation of V (1 g) in acetone (25 ml) using $KMnO_4$ (1·2 g) during 6 hr resulted in the isolation of a solid residue. This residue was methylated using excess diazomethane and separated into (i) an alkali soluble fraction and (ii) and alkali insoluble fraction, m.p. 48–49° identified as methyl anisate by comparison with an authentic sample. The alkali soluble fraction gave methyl-2-hydroxy-3,4-dimethoxybenzoate, identified by mixed m.p. with a synthetic sample. (Found: C, 56·82; H, 5·72; $C_{10}H_{12}O_5$ requires: C, 56·61; H, 5·66%.)

(b) *Oxidation using sodium metaperiodate.* Oxidation of V using sodium metaperiodate gave two products which were identified as (i)2-hydroxy-3,4-dimethoxybenzaldehyde as its semicarbazone, m.p. 211–212° and anisaldehyde as its 2,4-dinitrophenylhydrazone, m.p. 249–251°.

Reactions of product II

The *heptaacetate* (VII). This was obtained via Ac_2O and pyridine by boiling for ½ hr. It crystallized as colourless needles, m.p. 129–130° from EtOH, possibly identical with barbaloin heptaacetate reported earlier by Birch *et al.*[6] (Found: C, 59·12; H, 5·24; $C_{34}H_{36}O_{16}$ requires: C, 58·98; H, 5·06%.)

The methyl ether (VIII). This was obtained via MeI and Ag_2O as a syrupy liquid and after short column chromatography in benzene soln, the heptamethyl ether crystallized as colourless prisms, m.p. 180–182°, $(\alpha)_D^{28}$ −12·4° (*c*, 1·46 in chf) possibly identical with that reported earlier m.p. 177–179° by Simonsen[7] and m.p. 180–182° by Evelynhey.[8] (Found: C, 65·28; H, 7·14; —OCH_3, 42·44; $C_{21}H_{16}O_9(OCH_3)_7$ requires: C, 65·11; H, 6·98; —OCH_3, 42·07%.)

Preparation of aloe-emodinanthrone[4] *from* II

A soln of II in water (2·5 g in 50 ml) was treated with sodium borate (5 g) and phenylhydrazine hydrochloride (1 g) and subsequently boiled for 2 hr in an inert atmosphere. The dark red sol was acidified using dil HCl giving a yellow residue which on extraction with ether and subsequent crystallization from AcOH gave yellow needles (0·25 g) of aloe-emodinanthrone, m.p. 199°. (Found: C, 70·42; H, 4·54; $C_{15}H_{10}O_4$ requires: C, 70·33; H, 4·69%.) A comparison of the properties of II and its derivatives with barbaloin[9] established its identity.

[7] R. S. Cahn and J. L. Simonsen, *J. Chem. Soc.* 2573 (1932).
[8] F. Hauser, *Pharm. Acta Helv.* 6, 79 (1931).

Reaction of product III

The diacetate (IX) of III obtained via Ac_2O and H_2SO_4, crystallized as yellow plates flattened at the edges, m.p. 217–218° from AcOH and is possibly identical with the diacetate of rhein reported by Hauptmann *et al.*[6] (Found: C, 62·04; H, 3·42; —$COCH_3$, 23·62. $C_{18}H_{12}O_8$ requires: C, 61·95; H, 3·26; —$COCH_3$, 23·37%.)

The methyl ester (X) *of* III obtained using excess diazomethane in ether soln (24 hr) crystallized as pale orange yellow prisms, m.p. 174–175° from benzene and is possibly identical with that reported earlier by Hauptmann *et al.*[6] (Found: C, 64·72; H, 3·52; $C_{16}H_{10}O_8$ requires: C, 64·43; H, 3·36%.)

The diacetate of XI obtained by (i) acetylation of X using Ac_2O and pyridine or by (ii) methylation of IX using excess diazomethane, crystallized as colourless prisms, m.p. 194–195° from benzene, identical with that reported by Hauptmann *et al.*[6] (Found: C, 63·14: H, 3·72; $C_{20}H_{14}O_8$ requires: C, 62·82; H, 3·66%.)

Acknowledgement—Two of the authors (V.K.M. and T.V.P.R.) convey their thanks to the University Grants Commission and the Council of Scientific and Industrial Research, New Delhi, respectively for the award of maintenance grants.