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NEORAUTANENIA PTEROCARPANS

THE ISOLATION, STRUCTURE AND ABSOLUTE CONFIGURATION OF (−)-2-HYDROXYPTEROCARPIN, A NEW PTEROCARPAN FROM *NEORAUTANENIA EDULIS*

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Abstract—A new pterocarpan obtained from *Neorautanenia edulis* has been identified as (−)-2-hydroxypterocarpin on the basis of several chemical and physical observations.

DURING a study on constituents of the sub-family Papilionatae, family Leguminosae, a few pterocarpans[1,2] were isolated from the root of *N. edulis*. We now wish to report the isolation of (−)-2-hydroxypterocarpin, a new pterocarpan from the root bark of *N. edulis*. The structure 2-hydroxy-3-methoxy-8, 9-methylenedioxypterocarpan (II) is ascribed to the compound on the basis of chemical and spectroscopical evidence.

(−)-2-Hydroxypterocarpin (II) m.p. 238–239°C; ν_{max}^{KBr} 3405 cm^{-1} (OH); $[\alpha]_D^{23} = -227{\cdot}7°$ (*c* 0·8 in $CHCl_3$) analysed for the empirical formula $C_{17}H_{14}O_6$ in agreement with the mass spectrum. Presence of the functional group was evidenced by methylation and acetylation.

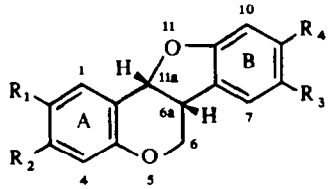
The mass spectrum was compatible with the structure suggested for 2-hydroxy-3-methoxy-8,9-methylenedioxypterocarpan and it agreed well with the established pattern for pterocarpans.[2] Scheme A shows the main fragmentations of the isoflavan (Xa). According to the well known fragmentation of isoflavans[2] it is possible to assign the various groups to ring A and B since the fragments *m/e* 166 (38) and *m/e* 178 (100), 167 (7) can only be formulated as arising from ring A and B respectively.

Determination of the positions of the substituents in the pterocarpan skeleton (I) was achieved by a combination of degradation reactions, NMR and mass spectra. The aromatic region in the spectrum of II consisted of two pairs of para related protons. The methylenedioxy group could therefore be either in the 2,3- or 8,9-position. Choice between these two possibilities can be made in two ways. Firstly, the mass spectrum (Scheme A) of Xa made it clear that the fragments *m/e* 167 and *m/e* 178 could only be rationalized if the methylenedioxy group was assigned to ring B and consequently to the 8,9-position. Secondly, examination of the degradation products (Scheme B) of II afforded 6-methoxypiperonylic acid, and thus confirmed the result of the mass spectrum. The OH group ($\tau = 4{\cdot}72$; disappears after D_2O addition) was assigned to position 2 due to the chemical shift, of the ortho proton in IIb (Table 1), to lower field. The assignments of the methoxy, methylenedioxy and the heterocyclic proton resonances (Table 1) was straightforward by comparison with other reported

data.[3–5] From the above data it was concluded that compound II has structure (−)-2-hydroxy-3-methoxy-8,9-methylenedioxypterocarpan.

The degradation (Scheme B) of II was effected by hydrogenolysis to X, methylation to the isoflavan Xa and subsequent oxidation to XI. Dehydrogenation of the isoflavanone (XII) followed by alkaline peroxide oxidation yielded 6-methoxy-piperonylic acid (XIII) and 2-hydroxy-4,5-dimethoxy-benzoic acid (XIV).

Absolute configuration. Recent work by Pachler,[3] who analysed the contributions of the 6-, 6a-, and 11a-protons to the NMR spectra of some pterocarpans, confirms the generally accepted *cis*-fusion of the two heterocyclic rings in the pterocarpans, and has established the conformation of the hetero-rings.[3] The absolute configuration[6] at C-11a in (−)-trifolirhizin (V) has recently been established as (*R*),[7] and if the *cis* relationship at C-6a and C-11a is accepted, the absolute configuration of (−)-pterocarpin (IV)[8] ($[\alpha]_D^{24}$ −224·1°), and (−)-2-hydroxy-3-methoxy-8,9-methylenedioxypterocarpan (II) ($[\alpha]_D^{23}$ −227·7°) may be taken as (6a*R*, 11a*R*).



I : $R_1 = R_2 = R_3 = R_4 = H$
II : $R_1 = OH$; $R_2 = OCH_3$; $R_3 + R_4 = O—CH_2—O$
IIa : $R_1 = R_2 = OCH_3$; $R_3 + R_4 = O—CH_2—O$
IIb : $R_1 = OCOCH_3$; $R_2 = OCH_3$; $R_3 + R_4 = O—CH_2—O$
III : $R_1 = R_3 = H$; $R_2 = R_4 = OCH_3$
IV : $R_1 = H$; $R_2 = OCH_3$; $R_3 + R_4 = O—CH_2—O$
V : $R_1 = H$; $R_2 = O$-glucose; $R_3 + R_4 = O—CH_2—O$

EXPERIMENTAL

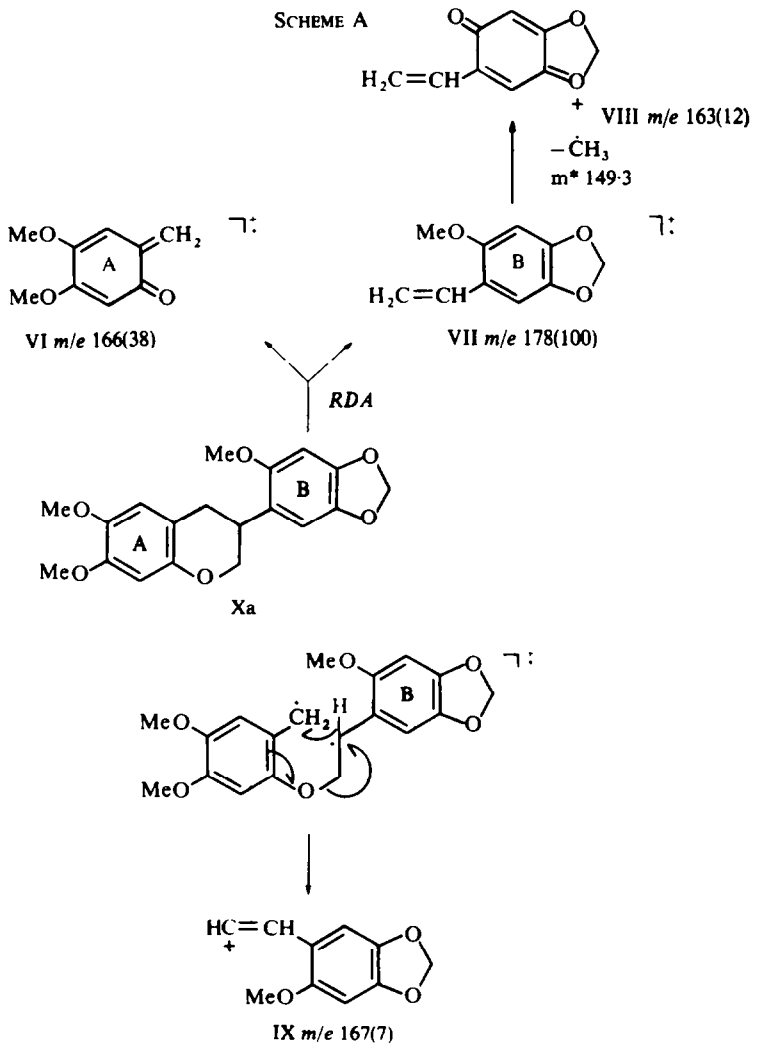
M.ps were determined on a Gallenkamp instrument and are uncorrected. IR spectra were determined on a Unicam SP-200 spectrophotometer, as specified for each case. Mass spectra were measured with an AEI MS-9 spectrometer, with direct insertion technique. NMR spectra were recorded on a Varian HA-100 or T-60 instrument with TMS as internal standard (τ = 10·00) in $CDCl_3$. Elementary analysis were done by Dr. Pascher, Mikroanalytisches Laboratorium, Bonn. Optical rotations were measured in chloroform with a Hilger–Watts M142 polarimeter.

Extraction and isolation of (−)-2-*hydroxypterocarpin* (II)

The following procedure, as applied to Neorautanenia material, exemplifies the method used for large-scale extractions. Dried, milled bark (5 kg) was extracted in 30 batches of hexane and the extract was concentrated to a brown syrup (47g). The syrup was dissolved in hot EtOH. Some white, insoluble material, which separated, was filtered off and recrystallization from acetone afforded II as long colourless needles (12·3 g), m.p. 238·0–239·0°C; IR(KBr) 3405 (OH), 1260 (OCH_3), 932, 1028 and 1196 cm^{-1} (O—CH_2—O); (Found: M^+, 314·0761. $C_{17}H_{14}O_6$ requires: 314·0790), *m/e* 314(100), 313(9·5), 299(28·0), 297(3·8), 271(5·5), 177(5·8), 175(5·1), 164(5·8), 162(23·3), 149(7·9); $[\alpha]_D^{33}$-227·7° (*c* 0·8 in $CHCl_3$); R_f 0·65; MeOH:$CHCl_3$-(2:98); (Found: C, 65·05; H, 4·3, OCH_3, 9·9; $C_{17}H_{14}O_6$ requires: C, 65·2; H, 4·2; OCH_3, 10·1%).

2,3-*Dimethoxy*-8,9-*methylenedioxypterocarpan* (IIa)

Compound II (400 mg) was dissolved in dry acetone (50 ml), and anhyd K_2CO_3 (2·0 g) added. Me_2SO_4 (1·5 ml) was added dropwise to the mixture over a period of 60 min at a temp of 50° with stirring. Evaporation of the acetone filtrate afforded an oily residue to which a soln of 5% KOH (50 ml) was added.

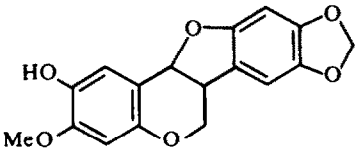


After the addition of water (50 ml) the mixture was extracted with benzene (3 × 50 ml). The extract was washed with water, dried ($MgSO_4$) and filtered. The solvent was evaporated and the solid that separated (405 mg) was recrystallized from benzene to give IIa as colourless prisms, m.p. 155·0–156·0°. (Found: C, 66·15; H, 4·9; OCH_3, 19·1; $C_{18}H_{16}O_6$ requires: C, 66·3; H, 4·9; OCH_3, 19·4%); *m/e* 328 (100), 327 (7·0), 314 (8·0), 313 (40·0), 312 (22·0), 311 (30·0), 298 (24·0), 178 (13·6), 176 (13·8), 175 (18·6), 164 (20·6), 163 (20·0), 162 (70·0), 155 (15·8), 149 (10·0), 126 (13·6), 85 (28·4), 83 (41·7), 78 (46·6), 77 (18·8).

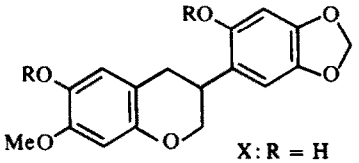
2-*Acetoxypterocarpin* (IIb)

Compound II (400 mg) was taken up in dry pyridine (3·0 ml) and Ac_2O (4·0 ml) was added. The mixture was refluxed for 30 min on a waterbath. The soln was then poured into ice water (50 ml) and kept at 0° for 30 min. The light-brown ppt was extracted with benzene (3 × 50 ml), N HCl (4 × 25 ml) and distilled water. The extract was dried ($MgSO_4$), and after evaporation of the solvent IIb crystallized from benzene as fine white needles (410 mg), m.p. 147·5–148·5°; IR(KBr) 1756 cm^{-1} (acetyl C=O). (Found: C, 63·91; H, 4·42; $C_{19}H_{16}O_7$ requires: C, 64·04; H, 4·49%); *m/e* 356 (44·2), 315 (17·3), 314 (100·0), 299 (26·9), 229 (9·1), 175 (7·3), 164 (10·0), 162 (61·5), 83 (16·7).

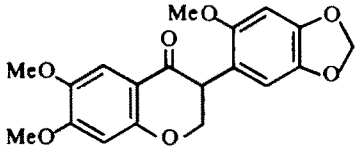
SCHEME B



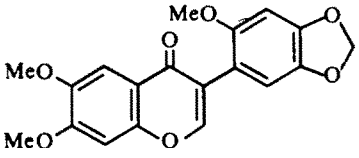
II



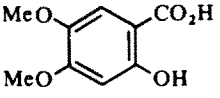
X: R = H
Xa: R = CH_3



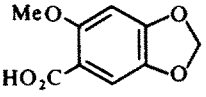
XI



XII



XIV



XIII

2',7-Dihydroxy-6-methoxy-4',5'-methylenedioxyisoflavan (X)

Compound II (1·0 g) was hydrogenated in EtOAc:AcOH (1:1) (80 ml) containing 10% Pd-C (1·0 g) at 60° for 20 hr at 6 atm. Absorption was complete in 3 hr. The catalyst and solvent were removed to give X. Due to the instability of the compound it was converted directly to Xa.

2',6,7-Trimethoxy-4,5'-methylenedioxyisoflavan (Xa)

The product from the preceding hydrogenolysis (1·0 g) was taken up in dry acetone (50 ml) and methylated with Me_2SO_4 in a manner similar to that described for 2,3-dimethoxy-8,9-methylenedioxypterocarpan. The solvents were removed and the product was purified by preparative TLC [silica gel GF_{254}, chloroform] to give Xa (917 mg), m.p. 142·0–143·0° (from MeOH) as colourless needles. (Found: C, 66·19; H, 5·78; OCH_3, 26·17. $C_{19}H_{20}O_6$ requires: C 66·28; H, 5·81; OCH_3, 27·03%); *m/e* 344 (37·0), 179 (31·0), 178 (100·0), 166 (38·0), 165 (49·0), 163 (12·0), 151 (9·0), 135 (9·0), 133 (19·0), 77 (10·0); τ 3·33 (s, 5-H), 3·40 (s, 8-H), 3·53 (s, 3'-H), 3·38 (s, 6'-H), 4·07 (s, O—CH_2—O), 6·15 and 6·20 (3 aromatic OMe).

2',6,7-Trimethoxy-4',5'-methylenedioxyisoflavanone (XI)

Compound Xa (200 mg) in acetone (30 ml) was treated at room temp with $KMnO_4$ (1·0 g) in acetone (30 ml). After being stirred for 24 hr water (50 ml) was added. The MnO_2 was decomposed by SO_2, and the mixture then concentrated under reduced press to give an oily product. Extraction with benzene and

TABLE 1. ASSIGNMENTS OF CHEMICAL SHIFTS (τ in ppm) IN THE NMR SPECTRA OF SOME PTEROCARPANS (*J* in c/s)

Groups and positions		Compounds		
		II	IIa	IIb
Aromatic protons	1	2·99	3·03	2·82
	4	3·56	3·50	3·46
	7	3·30	3·28	3·28
	10	3·58	3·55	3·57
Heterocyclic protons	6a	6·55[c]	6·54[c]	6·50[c]
	11a	4·57[b]	4·56[b]	4·55[b]
	6*ax*	6·35[c]	6·37[c]	6·33[c]
	6*eq*	5·78[c]	5·80[c]	5·80[c]
Hydroxyl	2	4·72	—	—
Methoxy	2	—	6·12	—
	3	6·13	6·16	6·21
Methylenedioxy	8,9	4·10[a]	4·10[a]	4·10[a]

[a] An AB quartet (when recorded at 100 Mc/s) centred at the τ value given, due to different environments of the two protons in the methylenedioxy group (J_{OCH_2O} = 1·3).

[b] A doublet centred at the τ value given, showing signs of further long-range splitting.

[c] A multiplet centred at the τ value given. The coupling constants are only an approximation, being the observed splitting.

(II : $J_{1,4}$0; $J_{7,10}$0; $J_{6a,11a}$7·0; $J_{6a,6ax}$10·1; $J_{6a,6eq}$5·2).
(IIa : $J_{1,4}$0; $J_{7,10}$0; $J_{6a,11a}$7·1; $J_{6a,6ax}$10·3; $J_{6a,6eq}$5·0).
(IIb : $J_{1,4}$0; $J_{7,10}$0; $J_{6a,11a}$7·2; $J_{6a,6ax}$10·1; $J_{6a,6eq}$5·1).

subsequent evaporation of the solvent yielded a colourless oil which on crystallization from benzene : hexane (10 : 1) gave XI as white needles (117 mg), m.p. 179–180°; IR(KBr) 1671 cm^{-1} (isoflavanone C=O); τ 2·58 (s, 5-H), 3·42 (s, 8-H), 3·53 (s, 3′-H), 3·39 (s, 6′-H), 4·08 (s, O—CH_2—O), 6·08, 6·10 and 6·25 (3 aromatic OMe).

2′,6,7-Trimethoxy-4′,5′-methylenedioxyisoflavone (XII)

(a) *With DDQ.* XI (200 mg), DDQ (500 mg), and pure, Na-dried benzene (20 ml) was refluxed for 24 hr. The mixture was filtered, and the filtrate chromatographed on a short column unactivated alumina with benzene as solvent to remove the excess DDQ. Evaporation of the benzene afforded an oil which rapidly solidified. Recrystallization from MeOH gave XII (51 mg) as long colourless needles, m.p. 218–219°C, IR(KBr) 1635 cm^{-1} (α, β-unsaturated C=O). The mass spectrum exhibited a peak at *m/e* 356 (M^+, $C_{19}H_{16}O_7$).

(b) *With active* MnO_2.[9] XI (200 mg), dissolved in pure dry acetone (40 ml), was dehydrogenated with active MnO_2 (1·5 g) according to the method of Crombie *et al.*,[10] to yield XII (170 mg), m.p. 218–219°; identical with the product from DDQ dehydrogenation.

6-Methoxypiperonylic acid (XIII) *and 2-hydroxy-4,5-dimethoxybenzoic acid* (XIV)

A soln of KOH (300 mg) in EtOH (10 ml), water (1·5 ml) and 30% H_2O_2 (1·0 ml) was added slowly (1 hr) with stirring to XII (60 mg). The temp was raised to 40° and kept there for 70 min with intermittent additions of H_2O_2 according to the procedure used by Crombie.[10] The mixture was acidified with conc HCl, and after removal of the alcohol, extracted with ether (4 × 30 ml). The products of two such sequences were purified by preparative TLC [silica gel GF_{254} in $CHCl_3$–MeOH (9 : 1)], running each plate once. Three bands could be discerned (one being the starting material); these were removed and extracted with $CHCl_3$. The extracts were evaporated to give (a) XIII (R_f 0·55) as white needles (26 mg), m.p. 146–147° (from MeOH), lit.[11] m.p. 148–149°; τ 2·39 (s, 5-H), 3·37 (s, 2-H), 3·94 (s, O—CH_2—O), 5·98 (s) (aromatic OMe), *m/e* 196 (100·0), 181 (11·4), 179 (28·2), 165 (9·6), 164 (9·1), 151 (9·0), 149 (14·6), 140 (11·8), 137 (11·4), 126 (14·1),

123 (10·5), 121 (9·6), 120 (6·8), 107 (32·3), 93 (17·4), 85 (11·8), 84 (15·9), 83 (18·2). (Found: M^+, 196·0375. $C_9H_8O_5$ requires: 196·0371), and (b) XIV (11 mg), m.p. 198–199° (from aqueous MeOH) Lit.[12] m.p. 202° (dec), (R_f 0·41), *m/e* 198 (41·0), 181 (13·1), 180 (100·0), 165 (30·4), 152 (5·9), 149 (7·7), 137 (25·6), 124 (7·7), 111 (7·6), 109 (18·7), 97 (12·8), 95 (11·2), 91 (11·7), 85 (11·7), 83 (16·5), 81 (16·5), 73 (13·3), 71 (24·0). (Found: M^+, 198·0536. $C_9H_{10}O_5$ requires: 198·0528).

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