Structure and Synthesis of Isoflavonoid Analogues from *Neorautanenia amboensis* Schinz

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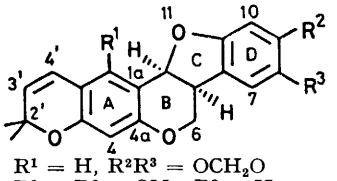
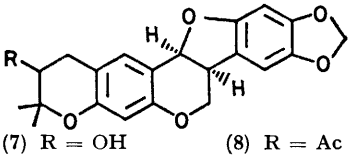
The isolation and structural elucidation of six pterocarpans: neorautenane, neorautanol, edulenane, edulenanol ambonane, and neorautenanol, as well as two new isoflavanones: ambonone and neoraunone, are reported. The structures of neorautenane and neorautanol have also been confirmed by syntheses where the key step involves the reaction between 2*H*-chromen and *o*-chloromercuriphenol in the presence of lithium chloropalladite.

THE use of *Neorautanenia* species in Central and Southern Africa as fish poisons [1] and the characterization of rotenoids and their analogues [2,3] from *N. amboensis* triggered a systematic investigation towards the isolation of possible useful compounds.

The hexane and benzene extracts of the bark of *N. amboensis* proved to be complex and after extensive separations on silica gel six new pterocarpans, neorautenane (1), neorautanol (7), edulenane (2), edulenanol (3), ambonane (9), and neorautenanol (4), as well as two new isoflavanones, ambonone (10) and neoraunone (11), were isolated among other known compounds. Their structures were assigned mainly by spectrometric methods but also confirmed for neorautenane (1) and neorautanol (7) by synthesis.



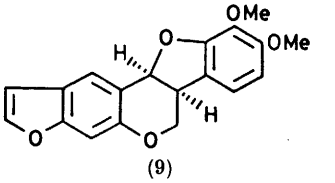
(1) R^1 = H, R^2R^3 = OCH_2O
(2) R^1 = R^2 = OMe, R^3 = H
(3) R^1 = OMe, R^2 = OH, R^3 = H
(4) R^1 = OH, R^2R^3 = OCH_2O
(5) R^1 = OMe, R^2 = OAc, R^3 = H
(6) R^1 = OAc, R^2R^3 = OCH_2O



(7) R = OH (8) R = Ac

The isolated pterocarpans are recognized by the well established ^{1}H n.m.r. spectra [4] of the heterocyclic ring protons, except in edulenane (2), edulenanol (3), and ambonane (9) where the signal from the 6_{ax}.-proton is obscured by the methoxy-resonances, and the characteristic ^{13}C n.m.r. spectra [5] of C-6, C-6a, and C-11a of the B–C ring system in pterocarpans. Neorautenane, $C_{21}H_{18}O_5$ from microanalysis, was assigned structure (1) on the basis of spectral and chemical evidence. It lacks a carbonyl i.r. absorption and gives a yellow-brown colour with perchloric acid–iron(III) chloride. N.m.r. spectra (^{1}H: Table; ^{13}C: Experimental section) are consistent with the proposed structure and show a methylenedioxy-group and a 2,2-dimethylchromen system. Arrangement of the substituents followed from the presence of four *para* coupled protons in the aromatic region and from total synthesis of the compound (see later).

Spectroscopic (^{1}H, ^{13}C n.m.r.; c.d.) similarities between neorautenane (1) and neorautanol (7), $C_{21}H_{20}O_6$,



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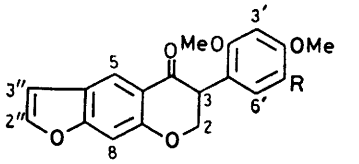
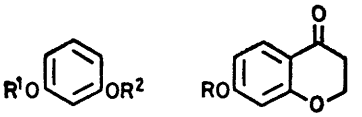


(10) R = OMe (11) R = H

led to the assigned structure of (7). Formation of a monoacetate (8) [δ 2.06 (s, 1 × OAc)] confirmed the presence of a hydroxy-group (δ 2.00; exchangeable with D_2O). The ^{1}H n.m.r. spectrum of (8) showed the typical deshielding of H-3′ on acetylation (Δδ 1.23 Hz) while acid-catalysed dehydration of (7) gave (1) (identical in all respects to the natural compound). Proof of structure (7) was also provided by synthesis.

Our first objective was the synthesis of 7-benzyloxy-2*H*-1-benzopyran (19). All attempts to obtain this through the condensation of resorcinol and prop-2-ynyl

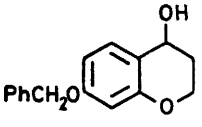


(12) R^1 = H, R^2 = $CH_2C{\equiv}CH$ (16) R = H
(13) R^1 = H, R^2 = CH_2CH_2CN (17) R = CH_2Ph
(14) R^1 = R^2 = CH_2CH_2CN
(15) R^1 = H, R^2 = $CH_2CH_2CO_2H$

bromide and subsequent heating of the intermediate (12) failed.[6] However, when resorcinol was treated with acrylonitrile under strongly basic conditions [7] a mixture of 3-(3-hydroxyphenoxy)propanenitrile (13) (60%) and 1,3-bis-(2-cyanoethoxy)benzene (14) (8.2%) was obtained. Hydrolysis and intramolecular cyclization in an acid medium gave moderate conversion into 2,3-dihydro-7-hydroxy-4*H*-1-benzopyran-4-one (16). Protection of the 7-hydroxy-function through benzylation, followed by sodium borohydride reduction, afforded 7-

benzyloxy-2,3-dihydro-4*H*-1-benzopyran-4-ol (18) in 93% yield. Dehydration, effected by toluene-*p*-sulphonic acid, gave the required ring A unit (19).

Compound (20), 2-chloromercurio-4,5-methylenedioxyphenol, was prepared by the reaction of 3,4-methylenedioxyphenol with mercury(II) acetate in methanol



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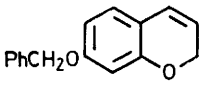

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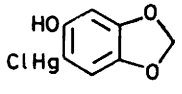
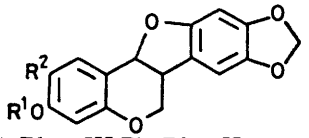
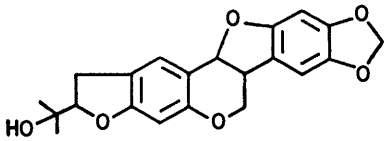


(20)

followed by treatment with lithium chloride. Reaction of (19) and (20) with lithium chloropalladite in dry acetone afforded the protected pterocarpan (21).[8] Reductive removal of the protective group gave (±)-maackiain (22) which, when prenylated,[9] gave (±)-edunol (23). Stirring (23) with *m*-chloroperbenzoic acid in chloroform gave neopranol (24) (δ 4.61, t, H-2′; 3.08, d, *J* 10 Hz, H-3′) while treatment with *m*-chloroperbenzoic acid containing a trace of toluene-*p*-sulphonic acid [10] gave neorautanol (7) in good yield (δ 3.74, t, *J* 5.6, H-3′; 3.06, q, *J* 16 and 5.6, H-4′a; 2.72, q, *J* 16 and 5.6 Hz, H-4′b). Acid-catalysed dehydration of (7) also completes the total synthesis of neorautenane (1).



(21) $R^1 = CH_2Ph$, $R^2 = H$
(22) $R^1 = R^2 = H$
(23) $R^1 = H$, $R^2 = CH_2CH{=}CMe_2$



(24)

High-resolution mass spectrometry established the molecular formula of edulenane (2) as $C_{22}H_{22}O_5$ (M^+ 366.146 7; calc. 366.148 6). The 80-MHz ^{1}H n.m.r. spectrum showed two high-field 3 H-singlets at δ 1.39 and 1.42 assigned to the *gem*-dimethyl group adjacent to an oxygen function while the protons of the aromatic methoxy-groups absorbed at δ 3.72 (3 H) and 3.94 (3 H). The rest of the spectrum (Table) is consistent with the proposed structure.

Edulenanol (3), $C_{21}H_{20}O_5$, gave a brown-purple colour with perchloric acid–iron(III) chloride while mass-spectral data (M^+ 352) were compatible with the assigned structure. The presence of a phenolic hydroxy-group, evident from the strong absorption at 3 380 cm^{-1} and green coloration with iron(III) chloride, was confirmed by the formation of an acetate (5) (M^+ 394; δ 2.16, 3 H) which did not respond to the iron(III) chloride test. An observed long-range coupling [11,12] and the phenomenom that an aromatic hydroxy-group induces a greater downfield shift of *ortho*- than *meta*-protons on acetyl-

^{1}H N.m.r. spectra of pterocarpans (δ values; Me_4Si internal standard; $CDCl_3$ solutions)

Compound	H-1	H-2	H-4	H-7	H-8	H-10	H-11a [a]	H-6$_{eq}$ [b]	H-6$_{ax}$ [b]	H-6a [b]	H-2′	H-3′	H-4′	OCH_2O [c]	OMe	CH_3	OH	OAc
(1)	7.05		6.38	6.64		6.30	5.38	4.15	3.63	3.44		5.50 [d]	6.25 [d]	5.82		1.41		
																1.38		
(2)			6.17	7.07 [o]	6.36 [m]	6.41 [g]	5.56	4.16	3.78	3.63		5.50 [d]	6.47 [d]		3.94	1.42		
															3.72	1.39		
(3)			6.09	6.94 [o]	6.22 [m]	6.25 [g]	5.53	4.20	3.61	3.50		5.47 [d]	6.44 [d]			1.39	5.09	
																1.36		
(4)			6.38	6.63		6.38	5.44	4.06	3.56	3.38		5.72 [d]	6.66 [d]	5.84		1.31	5.44	
																1.28		
(5)			6.08	7.03 [o]	6.47 [m]	6.47 [g]	5.53	4.03	3.59	3.39		5.44 [d]	6.38		3.84	1.36		2.16
																1.33		
(6)			6.50	6.66		6.31	5.47	4.07	3.56	3.38		5.72 [d]	6.68 [d]	5.84		1.40		2.27
																1.39		
(7)	7.13		6.66	6.63		6.66	5.39	4.14	3.75	3.52		3.74 [e]	3.06 [f]	5.83		1.31	2.00	
													2.72 [f]			1.31		
(8)	7.13		6.38	6.65		6.38	5.41	4.13	3.50	3.47		4.97 [e]	3.13 [f]	5.84		1.31		2.06
													2.72 [f]			1.31		
(9)	7.71		7.03	6.84	6.41		5.69	4.22	3.72	3.53	7.50 [g]	6.63 [h]			3.91			
															3.81			
(21) [i]	7.19 [o]	6.41 [m]	6.56 [g]	6.50		6.22	5.31	4.06	3.62	3.41				5.70				
(24)	7.19		6.38	6.66		6.34	5.42	4.14	3.61	3.45	4.61 [k]	3.08 [d]		5.86		1.31	1.64	
																1.19		

[a] Doublet, *J* 6.8 Hz. [b] Multiplet. [c] Quartet, *J* 3.0 and 1.2 Hz. [d] Doublet, *J* 10 Hz. [e] Triplet, *J* 5.6 Hz. [f] Quartet, *J* 16 and 5.6 Hz. [g] Doublet, *J* 2.5 Hz. [h] Quartet, *J* 2.5 and 1.0 Hz. [k] Triplet, *J* 10 Hz. [i] OCH_2: 4.86; Ph: 7.16; [m] Quartet, *J* 8.75 and 2.5 Hz. [o] Doublet, *J* 8.75 Hz.

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Ambonane, $C_{19}H_{16}O_5$ from microanalysis, is assigned structure (9) on the basis of spectral evidence. It gave a brown-green colour with perchloric acid–iron(III) chloride. Elemental analysis and mass-spectral data (M^+ 324) are in good agreement with the formula. In the ^{1}H n.m.r. spectrum of ambonane (9) (Table) the doublet at δ 7.50 (*J* 2.5 Hz; 1 H) and double doublet (due to long-range coupling [14] with H-4) at δ 6.63 (*J* 2.5 and 1 Hz; 1 H) correspond to H-2′ and H-3′ of the benzofuran ring respectively. The high-field singlets (δ 3.91 and 3.81) were attributed to the presence of two methoxy-groups while the heterocyclic protons resonate at the expected position (Table) for a pterocarpan. Signals at

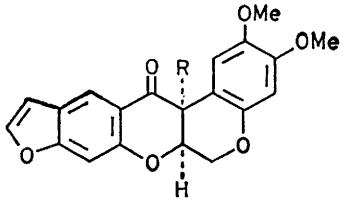
δ 7.71 (1 H) and 7.03 (broadened; 1 H) are in good agreement with H-1 and H-4 of closely related compounds.[15] The remaining doublets at δ 6.84 and 6.41 (*J* 8.75, 1 H for each) are characteristic of two *ortho*-coupled protons.

Neorautenanol (4), $C_{21}H_{18}O_6$ (M^+ 366), is phenolic, as evidenced by positive reaction with ethanolic iron(III) chloride. It gives a yellow-brown colour when sprayed with perchloric acid–iron(III) chloride. Reaction with acetic anhydride–pyridine produced a mono-acetate (6) (δ 2.27, 3 H; M^+ 408) which did not retain phenolic character. ^{1}H N.m.r. (Table) and mass-spectral data were in full agreement with the postulated structure. A phloroglucinol oxygenation for ring A is favoured owing to the observed long-range coupling [11,12] between H-4 and H-4′.

The 6a*S*,11a*S* absolute configuration, indicative of laevorotatory pterocarpans,* has been assigned to compounds (1)—(4), (7), and (9) because of their observed negative optical rotations (*cf.* Experimental section).

The molecular formula of ambonone (10) was determined by high-resolution mass spectrometry as $C_{20}H_{18}O_6$ (M^+ 354.111 1; calc. 354.110 3). The presence of an αβ-unsaturated carbonyl group was shown by characteristic u.v. and i.r. (1 684 cm^{-1}) spectra.[17] The three-proton multiplet (δ 4.44) is in good agreement with the AB_2 system of the heterocyclic protons found in isoflavanones [17] while the furan ring and methoxy-groups are easily discerned in the ^{1}H n.m.r. spectrum (Experimental section). The broad singlet at δ 7.00 is assigned to H-8 as a result of the long-range coupling to H-3″ while the low-field absorption at δ 8.19 is typical of H-5 *peri* to a carbonyl. The mass spectrum of ambonone showed that the fragments at *m/e* 194 (100%), 179 (51), and 160 (14) could only be rationalized if the three *O*-methyl groups are accommodated on ring B.

The co-occurrence of ambonone (10) with the rotenoids neobanone (25) [11,18] and 12a-hydroxyerosone (26) is of



(25) R = OMe
(26) R = H

biosynthetic interest (2′-methoxyisoflavones, derived from flavanone precursors,[19] are readily converted into rotenoids,[20] indicating common intermediates in their biosynthetic pathways).

From spectrometric data it was evident that a close relationship exists between neoraunone (11), $C_{19}H_{16}O_5$, and ambonone (10). The ^{1}H n.m.r. spectra of (10) and (11) (Experimental section) were most informative where an ABX system in the aromatic region represents the only difference except for small chemical shift differences. Mass spectral data fully support the proposed structure where retro-Diels–Alder fragmentation gives rise to fragments at *m/e* 164 (100) and 160 (17) confirming the presence of two methoxy-groups on the phenyl ring.

EXPERIMENTAL

M.p.s were determined with a Reichert Thermopan Microscope. Mass spectra and accurate mass values were measured with a Varian CH-5 double-focusing mass spectrometer, while n.m.r. spectra were recorded on a Bruker WP 80 instrument for solutions in deuteriochloroform unless otherwise stated, using tetramethylsilane as internal standard (80 MHz for ^{1}H and 20.1 MHz for ^{13}C n.m.r.); coupling constants are given in Hz. U.v. spectra were recorded for solutions in spectroscopically pure methanol on a Perkin-Elmer 402 spectrophotometer coupled to a Beckman DB-G recorder. C.d. measurements were done on a Jasco J-20 polarimeter for solutions in methanol while optical rotations were determined for solutions in chloroform on a Bendix NPL polarimeter.

Merck silica gel 60 was used for column chromatography and Merck silica gel PF_{254} for preparative t.l.c. R_F values refer to chromatography on precoated Merck t.l.c. plastic sheets (silica gel 60 F_{254}) and colour reactions to perchloric acid–iron(III) chloride spray reagent.

Isolation of Compounds from the Root Bark of N. amboensis. —Bulbs of *N. amboensis* were collected near Tsokwane, Kruger National Park, Transvaal, South Africa; the bark was removed, dried, and powdered to give 910 g of material which was successively extracted with hexane (3 × 24 h) and benzene (3 × 24 h) producing a brown syrup (67 g) and a brown amorphous solid (93 g) respectively.

The hexane extract was absorbed on silica gel and chromatographed on a column using n-hexane–benzene–acetone (3 : 1 : 1) as eluant to give seven main fractions. Fraction III (12.5 g) was re-chromatographed [column chromatography: i, n-C_6H_{14}–C_6H_6–EtOAc (4 : 4 : 1); ii, 1,2-$C_2H_4Cl_2$–n-C_6H_{14} (4 : 1); iii, EtOAc–Et_2O (19 : 1)] to give besides the known pterocarpans (−)-edulenol [21] (160 mg) and (−)-neoraucarpanol [21] (22 mg), neorautenane (1) (45 mg). Fraction V (7.1 g) yielded on column chromatography [i, n-C_6H_{14}–C_6H_6–Me_2CO (1 : 8 : 1); ii, CH_2Cl_2–n-C_6H_{14} (9 : 1)] and t.l.c. (n-C_6H_{14}–C_6H_6–EtOAc, 5 : 4 : 1) the known compounds (−)-medicarpin [22] (27 mg) and (−)-neodunol [15] (165 mg) as well as neorautanol (7) (34 mg) and ambonone (10) (10 mg). Fraction VII (2.0 g) contained the recently reported [23] rotenoid 12a-hydroxyerosone (26) (58 mg) and neorautenanol (4) (5.5 mg) which required separation by column chromatography (1,2-$C_2H_4Cl_2$–n-C_6H_{14}, 9 : 1) and t.l.c. [i, C_6H_6–EtOAc (24 : 1); 88, C_6H_6–n-C_6H_{14}–Me_2CO (5 : 4 : 1)].

The benzene extract was separated (column chromatography: C_6H_6–n-C_6H_{14}–MeOH, 18 : 1 : 1) into eight fractions, A—G. Fraction A (7.23 g) delivered on column chromatography (C_6H_6–n-C_6H_{14}, 24 : 1) and t.l.c. (n-C_6H_{14}–$CHCl_3$, 4 : 1) colourless cubes of edulenane (2) (28.6 mg). Fraction B (14.35 g) was re-chromatographed [column chromatography: i, CH_2Cl_2–n-C_6H_{14} (4 : 1); ii, C_6H_6–

* *cf.* C. DeMartinis, M. F. Mackay, D. R. Perrin, and B. J. Poppleton, *Tetrahedron Letters*, 1977, **2981**, and D. R. Perrin, *ibid.*, **1964**, **29**; the dextrorotatory allocation in ref. **16** is erroneous and must be reversed. These results are in direct conflict with those derived by S. Ito, Y. Fujise, and A. Mori, *Chem. Comm.*, **1965**, 595, and J. W. Clark-Lewis, I. Dainis, and G. C. Ramsay, *Austral. J. Chem.*, **1965**, **18**, 1035.

n-C_6H_{14} (24 : 1); t.l.c.: C_6H_6–n-C_6H_{14} (4 : 1)] to give another crop of neorautenane (1) (81 mg) as well as ambonane (9) (10.2 mg). Fraction C (21.30 g) consisted of several isoflavonoids and was separated [column chromatography: i, C_6H_6–n-C_6H_{14} (9 : 1); ii, n-C_6H_{14}–Me_2CO (9 : 1); iii, $CHCl_3$–n-C_6H_{14} (4 : 1); t.l.c.: i, C_6H_6–EtOAc (49 : 1); ii, C_6H_6–n-C_6H_{14}–EtOAc (5 : 4 : 1); iii, $CHCl_3$–n-C_6H_{14} (7 : 3)] to give the new isoflavanone, neoraunone (11) (26.1 mg). Edulenanol (3) (41.4 mg) was obtained after repeated column chromatography [i, n-C_6H_{14}–CH_2Cl_2–MeOH (5 : 4 : 0.5); ii, n-C_6H_{14}–C_6H_6–EtOAc (5 : 4 : 1); iii, light petroleum–n-C_6H_{14}–Me_2CO (5 : 4 : 1)] and t.l.c. (C_6H_6–EtOAc, 9 : 1) of fraction G (6.71 g).

Constituents of N. amboensis *Bark and their Derivatives.*—*Neorautenane* (1) (*7a,13a-dihydro*-3,3-*dimethyl*-3H,7H-[1,3]-*dioxolo*[5,6]*benzofuran*[3,2-c]*pyrano*[3,2-g][1]*benzopyran*). Neorautenane (1) crystallized as colourless *needles* (from EtOH), m.p. 165—166 °C, yellow-brown with the spray reagent, R_F 0.13 (n-C_6H_{14}–Me_2CO, 19 : 1) (Found: C, 71.9; H, 5.2; M^+, 350.114 1. $C_{21}H_{18}O_5$ requires C, 72.0; H, 5.1%; M^+, 350.115 4); $[\alpha]_D$ −200° (*c* 0.1 in $CHCl_3$); c.d. (*c* 0.13 in MeOH): $[\theta]_{224}$ 0; $[\theta]_{230}$ −291; $[\theta]_{244}$ −11 157; $[\theta]_{255}$ 0; $[\theta]_{272}$ +6 582; $[\theta]_{288}$ 0; $[\theta]_{295}$ +671; $[\theta]_{300}$ 0; $[\theta]_{310}$ +3 212; $[\theta]_{324}$ +5 522; $[\theta]_{322}$ 0; *m/e* 350 (M^+; 61.5%), 336 (48.4), 335 (100), 198 (32.5), 185 (37.9), 175 (30.1), and 162 (20.9); δ_C [$(CD_3)_2SO$]: 128.4 (q, *J* 155 and 5, C-1), 113.0 (q, *J* 6 and 2.5, C-1a), 115.6 (d, *J* 7.5, C-2), 154.7 (q, *J* 10 and 2.5, C-3), 103.7 (d, *J* 155, C-4), 153.7 (d, *J* 5, C-4a), 68.5 (d, *J* 147.5, C-6), 39.6 (d, *J* 140, C-6a), 118.1 (d, *J* 165, C-7), 105.0 (d, *J* 5, C-7a), 141.1 (d, *J* 2.5, C-8), 147.5 (d, *J* 2.5, C-9), 93.0 (d, *J* 165, C-10), 153.7 (d, *J* 5, C-10a), 77.7 (d, *J* 155, C-11a), 76.2 (m, C-2′), 121.0 (q, C-3′), 129.0 (q, C-4′), 27.6 (qm, 2 × Me), and 101.0 (d, *J* 172.5, OCH_2O).

Neorautanol (7) (1,2,*7a,13a-tetrahydro*-3,3-*dimethyl*-3H,7H-[1,3]*dioxolo*[5,6]*benzofuro*[3,2-c]*pyrano*[3,2-g][1]*benzopyran*-3-*ol*). Neorautanol (7) was obtained as a colourless *glass*, m.p. 93—95 °C; yellow-brown with the spray reagent, R_F 0.13 (n-C_6H_{14}–C_6H_6–EtOAc, 5 : 4 : 1) (Found: M^+ 368.127 8. $C_{21}H_{20}O_6$ requires M^+ 368.125 9); $[\alpha]_D$ −291° (*c* 0.08 in $CHCl_3$); $\nu_{max.}$: 720, 1 135, 1 355, 1 510, and 1 645 cm^{-1}; c.d. (*c* 0.16 in MeOH): $[\theta]_{220}$ 0; $[\theta]_{237}$ −23 459; $[\theta]_{260}$ −2 291; $[\theta]_{278}$ −3 678; $[\theta]_{290}$ 0; $[\theta]_{300}$ +4 830; $[\theta]_{325}$ 0; *m/e*: 368 (M^+; 100%), 350 (2.1), 335 (8.6), 298 (21.3), 297 (96.6), 296 (23.2), 175 (7.8), 162 (17.4), and 147 (6.2); δ_C: 131.9 (q, *J* 155 and 5, C-1), 112.0 (q, *J* 6 and 2.5, C-1a), 114.5 (d, *J* 7.5, C-2), 155.5 (q, *J* 10 and 2.5, C-3), 103.5 (d, *J* 155, C-4), 153.9 (d, *J* 5, C-4a), 65.9 (t, *J* 147.5, C-6), 39.4 (d, *J* 140, C-6a), 105.3 (d, *J* 165, C-7), 118.4 (d, *J* 5, C-7a), 141.2 (d, *J* 2.5, C-8), 147.5 (d, *J* 2.5, C-9), 93.1 (d, *J* 165, C-10), 153.7 (d, *J* 7.5, C-10a), 77.8 (d, *J* 155, C-11a), 101.0 (t, *J* 172.5, OCH_2O), 77.4 (m, C-2′), 89.9 (m, C-3′), 30.2 (m, C-4′), 25.5 (m, *J* 250, Me), and 25.8 (m, *J* 250, Me).

3′-O-*Acetylneorautanol* (8). Acetylation of neorautanol (7) (10 mg) with acetic anhydride–pyridine gave a colourless *oil*, R_F 0.32 (n-C_6H_{14}–C_6H_6–Me_2CO, 5 : 4 : 1), yellow-brown with the spray reagent (Found: M^+ 410.138 1. $C_{23}H_{22}O_7$ requires M^+ 410.136 5) *m/e*: 410 (M^+; 99.4%), 368 (17.7), 352 (31.6), 351 (38.7), 350 (67.6), 335 (100), 307 (10.3), 297 (74.1), 296 (56.7), 279 (27.7), 267 (29.1), 225 (16.1), 198 (20.4), 185 (17.6), 175 (57.7), 167 (74.3), and 162 (51.5).

Ambonone (10) {6,7-*dihydro*-6-(2,4,5-*trimethoxyphenyl*)-5H-*furo*[3,2-g][1]*benzopyran*-5-*one*}. Ambonone (10), bright-yellow with the spray reagent, crystallized as light yellow *rosettes* (C_6H_6), m.p. 153—155 °C; R_F 0.47 (C_6H_6–Me_2CO, 4 : 1) (Found: M^+, 354.111 0. $C_{20}H_{18}O_6$ requires M^+, 354.110 3); $[\alpha]_D$ 0; $\nu_{max.}$: 910, 1 450, 1 574, 1 633, and 1 684 cm^{-1}; $\lambda_{max.}$ (log ε): 234 (4.62), 275 (4.11), and 333 (3.81) nm; c.d. (*c* 0.14): 0; *m/e* 354 (M^+; 52.5%), 323 (3.3), 297 (15.7), 194 (100), 181 (38.4), 179 (51.2), 164 (13.9), 160 (16.2), 151 (37.3), 148 (18.2), 136 (19.4), and 132 (11.4); δ_H: 8.19 (s, H-5), 7.00br (s, H-8), 7.50 (d, *J* 2.5, H-2″), 6.70 (q, *J* 2.5 and 1, H-3″), 5.63 (s, H-3′), 6.53 (s, H-6′), 4.44 (m, H-2 and H-3), and 3.84, 3.75, and 3.72 (3 × s, 3 × OMe).

Neorautenanol (4) (*7a,13a-dihydro*-3,3-*dimethyl*-3H,7H-[1,3]*dioxolo*[5,6]*benzofuro*[3,2-c]*pyrano*[3,2-g][1]*benzopyran*-5-*ol*). Neorautenanol (4) was obtained as a colourless *glass*; R_F 0.49 (C_6H_6–n-C_6H_{14}–Me_2CO, 5 : 4 : 1), yellow-brown with the spray reagent (Found: M^+ 366.111 5. $C_{21}H_{18}O_6$ requires 366.110 3); *m/e*: 366 (M^+; 100%), 251 (89.7), 333 (36.2), 323 (60.8), 310 (56.6), 293 (44.9), 265 (41.7), 228 (56.5), 213 (54.0), 201 (57.8), 189 (54.7), 175 (70.0), and 165 (51.4).

1-O-*Acetylneorautenanol* (6). Compound (6) was obtained as a light yellow *glass* by acetylation of neorautenanol (4), R_F 0.72 ($CHCl_3$–n-C_6H_{14}, 9 : 1), yellow-brown with the spray reagent; *m/e*: 408 (M^+; 32.8%), 366 (30.5), 351 (40.9), 279 (10.3), 254 (19.4), 212 (79.7), 195 (39.3), 183 (22.4), 170 (98.0), 167 (25.5), and 153 (100).

Edulenane (2) (*7a,12a-dihydro*-10,13-*dimethoxy*-3,3-*dimethyl*-3H,7H-*benzofuro*[3,2-c]*pyrano*[3,2-g]*benzopyran*). Edulenane (2) formed colourless *cubes* (EtOH or Me_2CO) or colourless *needles* (Et_2O), m.p. 185—186 °C; R_F 0.37 (C_6H_6), brown with the spray reagent (Found: M^+, 366.148 8. $C_{22}H_{22}O_5$ requires 366.146 7); $[\alpha]_D$ −205° (*c* 0.001); $\nu_{max.}$: 700—810, 950, 1 085, 1 145, 1 350, 1 505, 1 590, 1 630, and 3 040 cm^{-1}; *m/e*: 366 (M^+; 72.8%), 351 (100), 336 (50.4), 321 (43.0), 297 (20.2), 215 (50.8), 200 (38.9), 175 (51.1), 168 (46.9), and 161 (31.7).

Ambonane (9) *6a,11a-dihydro*-9,10-*dimethoxy*-6*H*-*benzofuro*[3,2-c]*furo*[3,2-g][1]*benzopyran*). Ambonane (9) developed a brown-green colour with the spray reagent, R_F 0.45 ($CHCl_3$–n-C_6H_{14}, 2 : 1); light yellow *needles* (n-C_6H_{14}–Me_2CO), m.p. 125—127 °C (Found: C, 70.5; H, 4.9; M^+, 324.097 7; $C_{19}H_{16}O_5$ requires C, 70.5; H, 5.0%; M^+ 324.099 7); $[\alpha]_D$ −214° (*c* 0.01); $\nu_{max.}$: 940, 1 330, and 1 560 cm^{-1}; $\lambda_{max.}$ (log ε): 365 (3.19), 350 (3.23), 295 (3.57), and 250 (3.72) nm; c.d. (*c* 0.15): $[\theta]_{225}$ 0; $[\theta]_{248}$ +10 848; $[\theta]_{263}$ +2 240; $[\theta]_{287}$ +16 757; $[\theta]_{314}$ 0; *m/e*: 324 (M^+, 100%), 323 (14.0), 309 (50.6), 178 (22.5), 171 (13.3), 167 (15.8), and 162 (14.0).

Neoraunone (11) {6,7-*dihydro*-6-(2,4-*dimethoxyphenyl*)-5H-*furo*[3,2-g][1]*benzopyran*-5-*one*). Neoraunone (11) crystallized as light yellow *needles* (EtOH), m.p. 154—155 °C; R_F 0.46 (C_6H_6–Me_2CO, 19 : 1); purple colour with the spray reagent (Found: M^+, 324.103 0. $C_{19}H_{16}O_5$ requires M^+, 324.099 7); $[\alpha]_D$ 0; $\nu_{max.}$: 830, 1 040—1 150, 1 275, 1 375, 1 360, 1 490, 1 525, 1 600, 1 630, 1 700, and 3 000 cm^{-1}; *m/e*: 324 (M^+; 10.6%), 164 (100), 160 (21.7), 151 (25.2), 149 (66.7), 132 (22.6), and 121 (69.2); δ_H: 8.22 (s, H-5), 7.50 (d, *J* 2.2, H-2″), 7.03 (s, H-8), 6.97 (d, *J* 8.75, H-6′), 6.72 (q, *J* 2.2 and 1, H-3″), 6.47 (d, *J* 2.5, H-3′), 6.41 (q, *J* 8.75 and 2.5, H-5′), 4.66—4.16 (m, H-2 and H-3), 3.77 (s, OMe), and 3.74 (s, OMe).

Edulenanol (3) (*7a,12a-dihydro*-10-*hydroxy*-13-*methoxy*-3H,7H-*benzofuro*[3,2-c]*pyrano*[3,2-g][1]*benzopyran*). Edulenanol (3) was obtained as a yellow *glass*, R_F 0.24 ($CHCl_3$); brown-purple with the spray reagent (Found: M^+, 352.133 3. $C_{21}H_{20}O_5$ requires M^+, 352.131 1); $[\alpha]_D$ −224°

(*c* 0.8); $\nu_{max.}$: 830, 970, 1 010—1 270, 1 360, 1 480, 1 645, 1 735, 3 000, 3 380, and 3 610 cm^{-1}; c.d. (*c* 0.12): $[\theta]_{220}$ 0; $[\theta]_{230}$ −4 393; $[\theta]_{241}$ −6 575; $[\theta]_{248}$ 0; $[\theta]_{284}$ +7 182; $[\theta]_{325}$ 0; *m/e*: 352 (M^+; 74.6%), 337 (100), 322 (68.4), 305 (17.3), 293 (14.7), 215 (69.7), 200 (35.9), 168 (67.0), and 161 (66.6).

9-O-*Acetyledulenanol* (5). Acetylation of edulenanol (3) (10 mg) with acetic anhydride–pyridine produced compound (5) as a yellow-brown with the spray reagent; R_F 0.52 ($CHCl_3$); *m/e* 394 (M^+; 50.6%) 337 (29.2), 321 (25.6), 215 (48.0), and 149 (10.4).

Synthesis of Neorautanol (7) *and Neorautenane* (1).—3-(3-*Hydroxyphenoxy*)*propanenitrile* (13). Compound (13) was prepared from resorcinol (11 g, 0.1 mmol) according to the procedure of Bachman and Levine.[7] Crystallization of the ether solution gave 1,3-bis-(2-cyanoethoxy)-benzene (14) (1.65 g, 8.16%) as white needles (C_6H_6), m.p. 113—114 °C (lit.,[24] 112 °C, EtOH) while column chromatography ($CHCl_3$–Me_2CO, 9 : 1) of the residue delivered unchanged resorcinol (2.5 g, 22.7%) and compound (13) (9.85 g, 60.4%) as white needles (C_6H_6), m.p. 87—88 °C, R_F 0.55 ($CHCl_3$–Me_2CO, 9 : 1); *m/e* 163 (M^+; 100%), 123 (22.1), 110 (88.7), and 93 (28.0); δ_H 7.09 (m, H-2′), 6.44 (m, H-4′, H-5′, and H-6′), 5.38br (s, OH), 4.11 (t, *J* 6.75, OCH_2), and 2.75 (t, *J* 6.75, CH_2CN) (primed numbers refer to the phenyl ring).

2,3-*Dihydro*-7-*hydroxy*-4H-1-*benzopyran*-4-*one* (16). The nitrile (13) (3.0 g) was heated for 5 h on a boiling water-bath in concentrated sulphuric acid–glacial acetic acid–water (1 : 1 : 1; 15 cm^3). The deep red mixture was taken up in ether, washed (5 × 100 cm^3 of satd. $NaHCO_3$ and 3 × 100 cm^3 of H_2O), dried (Na_2SO_4), and evaporated. Column chromatography ($CHCl_3$–MeOH, 9 : 1) yielded 3-(3-hydroxyphenoxy)propanoic acid (15) (310 mg, 9.25%) as white needles (light petroleum), m.p. 111—113 °C, and the product (16) (1.35 g, 44.7%) as white plates (C_6H_6), m.p. 174—175 °C (lit.,[25] 147—148 °C; H_2O); *m/e*: 164 (M^+; 95.8%), 136 (100), and 108 (56.0); δ_H [$(CD_3)_2CO$]: 7.69 (d, *J* 8.75, H-5), 6.53 (q, *J* 8.75 and 2.5, H-6), 6.38 (d, *J* 2.5, H-8), 4.50 (t, *J* 6.75, H-2), and 2.69 (t, *J* 6.75, H-3).

7-*Benzyloxy*-2,3-*dihydro*-4H-1-*benzopyran*-4-*one* (17). Compound (17) was prepared from the benzopyran-4-one (16) according to the method of Fitton *et al.*[26] It crystallized as white cubes (EtOH, Me_2CO, or C_6H_6), m.p. 120—121 °C (lit.,[26] 103—104 °C, MeOH), slight yellow colour with the spray reagent: R_F 0.47 (C_6H_6–n-C_6H_{14}–Me_2CO, 5 : 4 : 1); *m/e*: 254 (M^+; 42.5%), 226 (4.2), and 91 (100); δ_H: 7.78 (d, *J* 8.75, H-5), 7.34 (s, C_6H_5), 6.59 (q, *J* 8.75 and 2.5, H-6), 6.47 (d, *J* 2.5, H-8), 5.03 (s, OCH_2), 4.47 (t, *J* 6.75, H-2), and 2.66 (t, *J* 6.75, H-3).

7-*Benzyloxy*-3,4-*dihydro*-2H-1-*benzopyran*-4-*ol* (18). Compound (18) was obtained in quantitative yield by reduction ($NaBH_4$) of (17) following the method of Heyns *et al.*[27] It produced a brick-red colour with the spray reagent and crystallized as white needles (EtOH); m.p. 112—114 °C: R_F 0.33 ($CHCl_3$); *m/e* 256 (M^+; 41.4%), 238 (38.0), 165 (12.8), and 91 (100); δ_H: 7.31 (s, C_6H_5), 7.13 (d, *J* 8.75, H-5), 6.50 (q, *J* 8.75 and 2.5, H-6), 6.41 (d, *J* 2.5, H-8), 4.97 (s, OCH_2), 4.69 (t, *J* 5.0, H-4), 4.20 (q, *J* 7.5 and 5.0, H-2), 2.00 (*m*, H-3), and 1.81br (s, OH).

7-*Benzyloxy*-2H-1-*benzopyran* (19). Toluene-*p*-sulphonic acid (5 mg) was added to the benzopyran-4-ol (18) (640 mg, 2.5 mmol) in benzene (15 cm^3) and the mixture was heated at 45 °C for 30 min, after which it was washed (3 × 10 cm^3 of satd. $NaHCO_3$ and 2 × 10 cm^3 of H_2O), dried ($CaCl_2$), and evaporated. T.l.c. (n-C_6H_{14}–Me_2CO, 17 : 3) delivered the product (19) as a yellow oil (454 mg, 76.3%); R_F 0.39 (n-C_6H_{14}–Me_2CO, 9 : 1), yellow-brown with the spray reagent; *m/e* 238 (M^+; 46.6%), 147 (10.9), 118 (14.5), and 91 (100); δ_H: 7.25 (s, C_6H_5), 6.73 (d, *J* 8.75, H-5), 6.38 (q, *J* 8.75 and 2.5, H-6), 6.31 (d, *J* 2.5, H-8), 6.25 (sextet, *J* 10.0 and 2.5, H-4), 5.53 (sextet, *J* 10.0 and 3.75, H-3), 4.92 (s, OCH_2), and 4.69 (q, *J* 3.75 and 2.5, H-2).

2-*Chloromercurio*-4,5-*methylenedioxyphenol* (20).[28] 3,4-Methylenedioxyphenol (6.9 g, 0.05 mol) and mercury(II) acetate (15.9 g, 0.05 mol) dissolved in methanol were stirred at room temperature for 2 h. A slurry of lithium chloride in acetone was added and the mixture was stirred for 15 min. Water was added until precipitation was complete. The precipitate was filtered off, washed (H_2O), dried, and recrystallized (ether) to give (20) (16.5 g, 88.7%) as colourless needles, m.p. 200 °C (decomp.); R_F 0.41 (C_6H_6–Me_2CO, 9 : 1); *m/e* 374 (M^+; 66.8%), 373 (37.9), 372 (50.3), 371 (30.0), 339 (6.5), 338 (30.8), 336 (26.9), 274 (19.2), 273 (15.0), 202 (19.0), 200 (19.1), 138 (36.6), 137 (50.9), 136 (100), and 107 (28.1); δ_H [$(CD_3)_2CO$]: 7.00 and 6.60 (2 × s; H-3 and H-6), 5.93 (s, OCH_2O), and 2.99br. (s, OH).

(±)-3-*Benzyloxymaackiain* (21). Compound (21) was prepared according to the following modified procedure:[8] palladium dichloride (335 mg, 1.89 mmol) and lithium chloride (159 mg, 3.78 mmol) were mixed with dry acetone (15 cm^3) and 7-benzyloxy-2*H*-1-benzopyran (19) (450 mg, 1.89 mmol) in dry acetone (5 cm^3) was added. The mixture was stirred for 15 min, when compound (20) (707 mg, 1.89 mmol) in dry acetone (15 cm^3) was added. The mixture was stirred for 5 h at room temperature. Twice its volume of saturated brine was added, and the mixture was shaken, extracted with benzene, dried (Na_2SO_4), and evaporated. T.l.c. (n-C_6H_{14}–Me_2CO, 4 : 1) gave the pterocarpan (21) (468 mg, 66.2%) as colourless needles (Me_2CO); m.p. 173—174 °C; R_F 0.33 (n-C_6H_{14}–Me_2CO, 4 : 1), yellow-brown with the spray reagent; *m/e*: 374 (M^+; 71.8%), 283 (100), 255 (13.1), 253 (15.6), 137 (29.6), and 91 (89.8).

(±)-*Maackiain* (22). Hydrogenation of (21) (200 mg) in acetone with 10% palladium–charcoal as catalyst gave (±)-maackiain (22) (130 mg, 85.6%) as plates (EtOH), m.p. 104—105 °C (lit.,[22] 100—105 °C).

(±)-*Edunol* (23). Prenylation of (±)-maackiain (22) (100 mg, 0.35 mmol) in dry methanol containing sodium methoxide according to the procedure of Jain *et al.*,[9] gave (±)-edunol (23) (71 mg, 57.6%) as colourless needles (EtOH), m.p. 185—187 °C (lit., [29] 147 °C).

(±)-*Neorautanol* (7) *and* (±)-*neopranol* (24). Starting with edunol (23) (100 mg) and following the method of Crombie *et al.*,[10] (±)-neorautanol (7) (74.8 mg, 71.5%) was obtained as a colourless glass identical to the natural product except for optical properties. The same starting material (100 mg) and the procedure of Crombie *et al.*[20] gave (±)-*neopranol* (24) (56.8 mg, 54.3%) as a light-yellow glass; R_F 0.51 (C_6H_6–n-C_6H_{14}–Me_2CO, 5 : 4 : 1); yellow with the spray reagent (Found: M^+, 368.123 8. $C_{21}H_{20}O_6$ requires M^+, 368.125 9); *m/e* 368 (M^+; 100%), 353 (1.6), 335 (14.1), 310 (16.4), 297 (24.6), 175 (19.2), 162 (28.7), 160 (10.2), 151 (11.6), and 148 (14.5); δ_C: 126.7 (q, *J* 160 and 5, C-1), 112.0 (q, *J* 6 and 2.5, C-1a), 121.4 (d, *J* 7.5, C-2), 161.0 (q, *J* 10 and 2.5, C-3), 97.2 (d, *J* 160, C-4), 153.9 (d, *J* 5, C-4a), 66.0 (t, *J* 147.5, C-6), 39.6 (d, *J* 140, C-6a), 105.4 (d, *J* 165, C-7), 118.5 (d, *J* 5, C-7a), 141.2 (d, *J* 2.5, C-8),

147.6 (d, *J* 2.5, C-9), 93.2 (d, *J* 165, C-10), 155.6 (d, *J* 5, C-10a), 78.4 (d, J 155, C-11a), 101.0 (t, *J* 172.5, OCH_2O), 70.1 (m, C-2′), 29.1 (t, *J* 135, C-3′), 90.0 (m, C–OH), 25.9 (qm, *J* 250, Me), and 24.6 (qm, *J* 250, Me).

(±)-*Neorautenane* (1). Treatment of (±)-neorautanol (7) (50 mg) with toluene-*p*-sulphonic acid gave (±)-neorautenane (1) (39 mg), indistinguishable from the natural product by n.m.r. and mass spectrometry.

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