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STRUCTURES OF SOME MINOR PTEROCARPANS OF *NEORAUTANENIA EDULIS*

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Key Word Index—*Neorautanenia edulis*, Leguminosae, pterocarpans, 6a, 11a-dehydropterocarpans

Abstract—The constitution of five new compounds, (−)-neorautenol, (−)-neodunol, (−)-homoedudiol, neorauteen and neoduleen, has been established in the root bark of *Neorautanenia edulis*

INTRODUCTION

THE POSITION of the genus *Neorautanenia* in the family Leguminosae suggests that these plants could be sources of isoflavonoids and rotenoids and this apparently correlates with claims that some *Neorautanenia* species have been used extensively throughout Central and Southern Africa as fish poisons.[1] *N edulis* in particular has been the subject of several investigations[2–5] concerned with the isolation of the active principles responsible for these properties. The present communication discusses the isolation, structural elucidation and biogenetic significance of the concurrence of pterocarpanoids and 6a,11a-dehydropterocarpans in this plant.

RESULTS AND DISCUSSION

Neorautenol (1)

The compound, $[\alpha]_D^{22} -273°$ (c = 0·3, $CHCl_3$), was shown by analysis, and MS to have a formula $C_{20}H_{18}O_4$. The presence of a single OH group was shown by the formation of a mono-methyl ether and mono-acetate. NMR comparison (Table 1) of neorautenol with other pterocarpans indicates that these compounds have the same A/B/C/D ring system and that structural differences concern the accompanying substitution pattern. The protons in the *para*-position on ring A resonate as singlets and the three ring-D aromatic protons are readily analysed in terms of an ABX system. The characteristic ABCD pattern of pterocarpans[6] (arising from the 6a-, 11a-, 6_{eq}- and 6_{ax}-protons) is easily discerned, although the signal from the 6_{ax}-proton is partly obscured by the methoxy-resonances.

The MS of the resulting methoxylated isoflavan (7) agrees well with the established pattern for isoflavans[7,8] on the assumption that ring A has a γ,γ-dimethylchromon group and

[1] WATT, J M and BREYER-BRANDWIJK, M G (1962) *Medical and Poisonous Plants of Southern and Eastern Africa*, 2nd Edit, pp 636, E and S Livingstone, London
[2] RALL, G J H, ENGELBRECHT, J P and BRINK, A J (1972) *J S. African Chem. Inst.* **25**, 131
[3] VAN DUUREN, B L (1961) *J Org Chem* **26**, 5013
[4] VAN DUUREN, B L and GROENEWOUD, P W G (1950) *J S. African Chem. Inst.* **3**, 29
[5] VAN DUUREN, B L and GROENEWOUD, P W G (1950) *J S. African Chem. Inst.* **3**, 35
[6] PACHLER, K G R and UNDERWOOD, W G E (1967) *Tetrahedron* **23**, 1817
[7] PELTER, A, STAINTON, P and BARBER, M (1965) *J Heterocyclic Chem* **2**, 262
[8] PELTER, A and AMENECHI, P I (1969) *J Chem Soc* (*C*) 887

TABLE 1 ASSIGNMENTS OF CHEMICAL SHIFTS (τ IN ppm) IN THE NMR SPECTRA OF SOME PTEROCARPANS AND RELATED COMPOUNDS

	H6a*	H6a*	H6a*	H11a†	H2	H3	H4	H1	H4	H6	H7‡	H8§	H9	H10
Neorautenol														
1	6.48	6.38	5.78	4.51	8.57 s, 3H 8.59 s, 3H	4.44 *d* *J* 10.0	3.67 *d* *J* 10.0	2.84 s	3.58 s		2.91 *J* 9.0	3.64 *J*, 9.0 *J*, 2.5		3.60 *J* 2.5
1a	6.55	6.42	5.85	4.59	8.60 *br* s 6H	4.44 *d* *J* 10.0	3.68 *d* *J* 10.0	2.89 s	3.58 s		2.92 *J* 9.0	3.58 *J*, 9.0, *J*, 2.5	6.30 s OCH_3	3.58 *J* 2.5
1b	6.50	6.33	5.77	4.53	8.58 *br* s 6H	4.46 *d* *J* 10.0	3.68 *d* *J* 10.0	2.88 s	3.60 s		2.80 *J* 9.0	3.38 *J*, 9.0 *J* 2.5	7.74 s $OCOCH_3$	3.39 *J* 2.5
Neodunol														
2	6.37	6.27	5.68	4.30	2.42 *d* *J* 2.2	3.25 *d* *J* 2.2		2.23 s	2.87 s		2.89 *J* 8.5	3.61 *J*, 8.5 *J*, 2.5		3.60 *J* 2.5
2a	6.37	6.18	5.70	4.30	2.44 *d* *J* 2.2	3.26 *d* *J* 2.2		2.27 s	2.88 s		2.83 *J* 9.0	3.53 *J*, 9.0 *J*, 2.5	6.23 s OCH_3	3.52 *J* 2.5
2b	6.35	6.25	5.68	4.29	2.44 *d* *J* 2.2	3.28 *d* *J* 2.2		2.27 s	2.89 s		2.77 *J* 9.0	3.36 *J* 9.0 *J* 2.5	7.75 s $OCOCH_3$	3.38 *J* 2.5
Homoedudiol														
3	6.48	6.33	5.72	4.51	8.22 *br* s 6H[9,10]	6.71 *d* *J* 7.0 2H	4.74 *t* *J* 7.0 1H		3.59 s		2.59 *J* 8.5	3.43 *J*, 8.5 *J*, 2.5		3.55 *J* 2.5
3a	6.52	6.38	5.74	4.53	8.27 *br* s 6H	6.71 *d* *J* 7.0 2H	4.74 *t* *J* 7.0 1H	2.73 s	3.56 s		2.68 *J* 8.5	3.56 *J*, 8.5 *J*, 2.5	6.26 s 3H 6.22 s 3H	3.53 *J* 2.5
Neorauteen Methylether														
4a					2.48 *d* *J* 2.2	3.29 *d* *J* 2.2		2.36 s	2.93 s	4.45 s 2H	2.76 *J* 8.5	3.14 *J*, 8.5 *J*, 2.5	6.13 s OCH_3	2.92 *J* 2.5
4b					2.49 *d* *J* 2.2	3.31 *d* *J* 2.2		2.35 s	2.95 s	4.47 s 2H	2.68 *J* 8.5	3.03 *J*, 8.5 *J* 2.5	7.73 s $OCOCH_3$	2.71 *J* 2.5
Neoduleen														
5					2.49 *d* *J* 2.2	3.31 *d* *J* 2.2		2.37 s	2.94 s	4.49 s 2H	2.76 s	OCH_2O 4.02 s		3.25 s

* A multiplet centred at the τ value given
† A doublet at the τ value given, showing signs of further splitting
‡ The A proton in an ABX system appearing as a doublet
§ The B proton in an ABX system appearing as a quartet centred at the τ value given
‖ The X proton in an ABX system appearing as a doublet

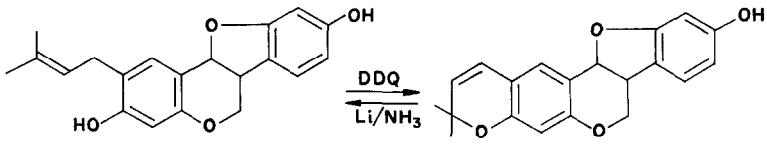
ring B two methoxy substituents [VII $\xrightarrow{RDA}$ *m/e* 190 (14), *m/e* 164 (100)] This evidence suggests that neorautenol is the phenolic pterocarpan (**1**) This was confirmed by the conversion of **1** to homoedudiol (**3**)

Homoedudiol (**3**)

This compound, $C_{20}H_{20}O_4$, had ν_{max} ($CHCl_3$) 3370 cm^{-1}. M^+ 324. The presence of two phenolic OH groups as indicated by the formation of a dimethyl ether. M^+ 352 Reduction of neorautenol (**1**) with lithium and ammonia afforded a major product identical to the substance (**3**) This was confirmed by the conversion of homoedudiol (**3**) to (**1**) with DDQ

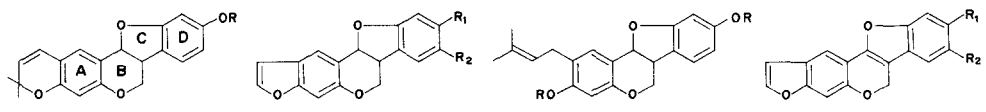
[9] OLLIS, W D, RAMSAY, M V J, SUTHERLAND, I O and MONGKOLSUK S (1965) *Tetrahedron* **21**, 1453
[10] BATES R B and GALE D M (1960) *J Am Chem Soc* **82**, 5749

(Scheme 1). Structure (**3**) was hence indicated, the *ortho*-(3,3-dimethylallyl)-phenol explaining the facile loss of isobutene (M^+-55) in the MS.[17]



Neodunol (**2**)

The third compound, formulated as the new pterocarpan (**2**), was isolated as the acetate and the free phenol was regenerated by hydrolysis with ammonium hydroxide. The presence of a benzofuran ring system[11] was indicated by characteristic UV and NMR spectra [λ_{max} 246 nm (log ϵ 4·34); τ 2·42, *d*, *J* 2·2 Hz, H2′ and τ 3·25, *d*, *J* 2·2 Hz, H3′], while the aromatic region in the NMR spectrum (Table 1) of neodunol suggests a similar oxygenation pattern as in neorautenol (**1**) and homoedudiol (**3**). The new compound is hence identified as the phenolic pterocarpan (**2**) and its MS fully supports this structure with prominent ions at *m/e* 147 (M^+ −133), 263 (M^+ −17, metastable at 246·8) and 171 (M^+ −1−108).



(**1**) R = H
(**1a**) R = Me
(**1b**) R = Ac

(**2**) R_1 = OH; R_2 = H
(**2a**) R_1 = OMe, R_2 = H
(**2b**) R_1 = OAc, R_2 = H
(**6**) $R_1 + R_2 = OCH_2O$

(**3**) R = H
(**3a**) R = Me

(**4**) R_1 = OH, R_2 = H
(**4a**) R_1 = OMe, R_2 = H
(**4b**) R_1 = OAc, R_2 = H
(**5**) $R_1 + R_2 = OCH_2O$

The pterocarpenes, neorauteen (**4**) *and neoduleen* (**5**)

The UV spectra of neorauteen (**4**), $C_{17}H_{10}O_4$ and neoduleen (**5**), $C_{18}H_{10}O_5$, were very similar to that of dehydrohomopterocarpin (**8**)[12] and flemichapparin-B (**9**)[13] (Table 2).

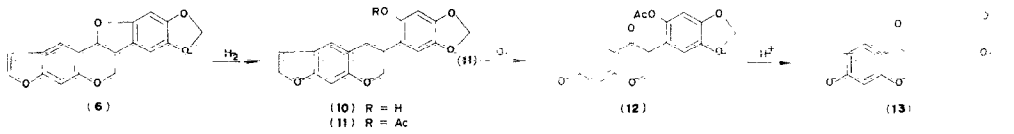
TABLE 2 UV ABSORPTION SPECTRA OF NEODULEEN, NEORAUTEEN AND RELATED PTEROCARPENES

	λ_{max} nm (log ϵ) in EtOH				
Neoduleen (**5**)	224 (4·30),	252 (4·16),	294 (3·84),	346 (4·28),	364 (4·18)
Neorauteen (**4**)	222 (4·35);	250 (4·17),	294 (3·82),	344 (4·36),	360 (4·21)
Dehydrohomopterocarpin (**8**)[12]		244 (4·23),	303 (3·81),	342 (4·61)	
Flemichaparrin-B (**9**)[13]	215 (4·40),	244 (4·20),	291 (3·80);	339 (4·58),	358 (4·16)

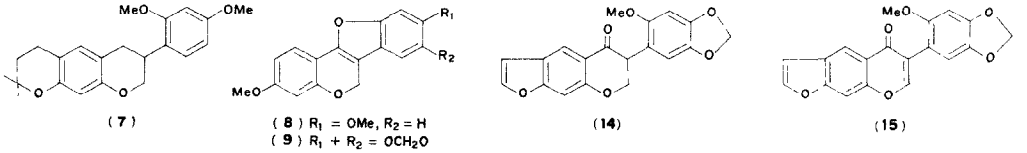
Compound (**5**) gave a positive Labat test for a methylenedioxy group. The IR showed no OH or carbonyl absorption, but a band at 1660 cm^{-1} indicated olefinic unsaturation. This was reflected in the UV spectrum which showed high intensity absorption with maxima up to 364 nm (log ϵ 4·18). The NMR spectrum contained a peak at τ 4·02 expected for a methylenedioxy group. The aromatic region of the spectrum consisted of 4 singlets (τ 2·37, H1; 2·94, H4; 3·25, H10; 2·97, H7) and 2 doublets [τ 2·42, 3·36; *J* 2·2 Hz (H2′ and H3′)] indicative of a furan ring, while the remainder of the spectrum consisted of a singlet representing two protons at τ 4·49 (CH_2 at C-6). From this evidence compound (**5**) was

[11] WESSELY, F and KOTLAN, J (1955) *Monatsh* **86**, 431
[12] HARPER, S H, KEMP, A D, UNDERWOOD, W G E and CAMPBELL, R V M (1969) *J Chem Soc* (*C*), 1109
[13] CHANDHURY, N A and GUPTA, P K (1970) *Chem Ind*, 745

considered to be 2,3,4,5-furo-8,9-methylen[illegible] carpen. Confi[illegible] tion of (1) was determined by the direct synthetic [illegible] of neodulin (6) [illegible] and neodo[illegible] (Scheme 2). Hydrogenolysis of (6) gave the [illegible] (10). Oxidation of the corresponding acetate (11) afforded the isoflavanone (12) [illegible] of which underwent cyclization on acid treatment to (13). Treatment of (13) with DDQ gave a compound identical with the natural product



Neorauteen (**4**) was isolated as the acetate and methyl ether. From the spectrometric information it was evident that a very close relationship exists between neorauteen and neoduleen (**5**). The NMR spectra of (**4a**) and (**4b**) were most informative where an ABX system (τ 2·76, *d*, *J* 8·5 Hz, H7; τ 3·14, *q*, J_1 8·5 Hz, J_2 2·5 Hz, H8; τ 2·92, *d*, *J* 8·5 Hz, H10) in the aromatic region was discernable as the only difference. Neorauteen was thus the phenolic pterocarpen with constitution (**4**).



The co-occurrence of dehydroneotenone (**15**),[14] neotenone (**14**),[14] neodulin (**6**)[13] and neoduleen (**5**) in the same plant provides circumstantial evidence for the hypothesis[15,16] that pterocarpenes, via direct oxidative cyclization of 2′-hydroxyisoflavanones, are intermediates in the biosynthesis of pterocarpans. This was also shown by the chemical conversion of the isoflavanone (**12**) to the pterocarpan (**13**) (Scheme 2).

EXPERIMENTAL

M ps are uncorrected. IR spectra were recorded in KBr discs and UV spectra in EtOH. NMR were determined using a Varian T-60 spectrometer and MS were recorded on an AEI MS-9 instrument. Chemical shifts are expressed in ppm downfield from TMS. Abbreviations: *s* = singlet, *d* = doublet, *m* = multiplet and *br* = broad. Preparative TLC was carried out on silica gel GF_{254} plates (1 mm thick).

Isolation of compounds. Dried, milled bark (5 kg) was extracted in 120 g portions with refluxing hexane for 24 hr. The combined hexane soln was concentrated to give an extract (47 g) which was carefully chromatographed on silica gel (170–230 mesh) with C_6H_6–$CHCl_3$ (with increasing concentrations of $CHCl_3$ from 5 to 60%) as solvent. Combined fractions were submitted to preparative TLC to purify the compounds. (a) Neorautenol (**1**) gave colourless needles (70 mg) from MeOH, m.p. 168·5–170°, after TLC in hexane–Me_2CO (13:7). R_f 0·61, M^+ 322, $[\alpha]_D^{22}$ −188·2 (*c* 1·5; $CHCl_3$). (b) Neodunol (**2**), TLC R_f 0·54 in hexane–Me_2CO (13:7) was crystallized from C_6H_6–hexane (9:1) to give colourless needles (43 mg), m.p. 170·5–171·5°, M^+ 280, $[\alpha]_D^{22}$ −284·9 (*c* 0·8, $CHCl_3$). (c) Homoedudiol (**3**) was obtained as a colourless oil (57 mg) after purification by TLC in $CHCl_3$–EtOAc (13:7). R_f 0·53, M^+ 324, $[\alpha]_D^{22}$ −246·1 (*c* 0·8, $CHCl_3$). (d) After TLC in $CHCl_3$–MeOH (96:4), R_f 0·53, neorauteen (**4**) (73 mg), was crystallized from MeOH to give white plates, m.p. 202·5–204·0°, M^+ 278. (e) Neoduleen (**5**) was obtained by TLC in C_6H_6–hexane (3:1), R_f 0·72. Crystallization from MeOH afforded white needles (80 mg), m.p. 221·5–223·0°, M^+ 306.

[14] BRINK, C. v. D. M. DEKKER, I. L. HANEKOM, E. C., MEIRING, D. H. and BALL, G. J. H. (1965) *J. S. African. Chem. Inst* **18**, 21.
[15] ADITYACHANDHURY, N. and GUPTA, P. K. (1970) *Chem. Ind.* 1113.
[16] WONG, E. (1976) In: *Progress in Chemistry of Organic Natural Products* (HERZ, W. GRISEBACH, H. and SCOTT, A. I., eds) pp. 28, 57, Springer, New York.
[17] BALLANTINE, J. A., FRANCIS, D. I. HASSALL, C. H. and WRIGHT, L. L. C. (1970) *J. Chem. Soc.* (*C*), 1175.

Acetylation and methylation methods A soln of the compound (20–40 mg) in dry pyridine (2 ml) and Ac_2O (3 ml) was heated for 1 hr at 100° and the soln was poured into ice (20 g) The ppt was extracted with Et_2O (3 × 50 ml), washed with cold M HCl (2 × 20 ml) and H_2O (3 × 20 ml) Evaporation of the solvent from the dried ($MgSO_4$) extract afforded the acetates Me_2SO_4 (1 ml) was added slowly over a period of 1 hr to a refluxing mixture of the compound (20–40 mg) in dry Me_2CO (50 ml) and anhyd K_2CO_3 (1 5 g) The mixture was stirred for 1 hr while heating continued After cooling 5% NaOH (20 ml) was added The soln was allowed to stand overnight, and the resulting ppt extracted with Et_2O (3 × 50 ml) Evaporation of the solvent from the dried ($MgSO_4$) extract gave the methyl ethers

Neorautenol monomethylether (**1a**) Methylation of (**1**) (30 mg) afforded **1a** (24 mg) as a colourless oil, M^+ 336

Neorautenol acetate (**1b**) Acetylation of (**1**) (25 mg) gave (**1b**) (20 mg) as colourless needles, m p 102 5–104°, M^+ 380

2″,2″-Dimethyl-6,7,5″,6″-chroman-2′,4′-dimethoxyisoflavan (**7**) Hydrogenolysis of neorautenol (**1**) (50 mg) in EtOAc (50 ml) over 10% Pd catalyst (on carbon support), according to standard procedure gave the corresponding phenol Due to the instability of this compound it was methylated to give (**7**) as a colourless oil, M^+ 354, τ (100 MHz) 5 67, *q*, J_1 10 Hz, J_2 3 5 Hz, 2-H, 6 00, *t*, *J* 10 Hz, 2-H, 6 20–6 56, *m*, 3-H, 7 06, *br s*, 4-H, 7 23, *br s*, 4-H, 6 25, *s*, OMe, 6 26, *s*, OMe, 3 53, *d*, *J* 2 5 Hz, 3′-H, 3 49, *q*, J_1 9 Hz, J_2 2 5 Hz, 5′-H, 2 91, *d*, *J* 9 Hz, 6′-H, 8 58, *br s*, 2″-C ($C\underline{H}_3$)$_2$, 8 24, *t*, *J* 6 5 Hz, 3″-$C\underline{H}_2$, 7 24, *t*, *J* 6 5 Hz, 4″-$C\underline{H}_2$, 3 73, *s*, 5-H, 3 78, *s*, 8-H

Birch reduction of neorautenol (**1**) Li (50 mg) was added to a soln of (**1**) (50 mg) in ethyleneglycoldimethylether (20 ml) and liquid NH_3 (30 ml) After 3 min, H_2O (30 ml) was added The organic phase was evaporated under red. pres after acidification (6 N HCl) The mixture was extracted with Et_2O (3 × 50 ml) and evaporation of the solvent gave a mixture of compounds which was separated on TLC in hexane–Me_2CO (13 7) to give (**3**) (15 mg) as an oil, M^+ 324, identical to an authentic sample

Homoedudiolmethylether (**3a**), (**3**) (30 mg) was treated with an excess of CH_2N_2 in ether at 0° for 24 hrs Evaporation of the solvent yielded (**3a**) as a colourless oil M^+ 352, identical to an authentic specimen

Reaction of homoedudiol (**3**) *with DDQ* A mixture of (**3**) (30 mg) and DDQ (25 mg) in Na dried C_6H_6 (20 ml) was refluxed for 30 min The reaction mixture was filtered and chromatographed on a short alumina column After evaporation of the solvent the residue was submitted to preparative TLC in hexane–Me_2CO (13 7), R_f 0 61, to give neorautenol (**1**) (12 mg) as colourless needles m p 168 5–170° from MeOH, identical to an authentic sample

Neodunol methylether (**2a**) Methylation of (**2**) (20 mg) gave (**2a**) (14 mg) as colourless needles (C_6H_6), m p 158–159°, M^+ 294

Neodunol acetate (**2b**) Acetylation of **2** (20 mg) with Ac_2O and dry pyridine according to standard procedure afforded (**2b**)(16 mg) as plates, m p 136–137°, M^+ 338 Hydrolysis with 5% NH_4OH of (**2b**) (25 mg) gave neodunol (**2**) (16 mg) as colourless needles C_6H_6–hexane (9 1), m p 170 5–171 5°, M^+ 280

2″,3″-Dihydro-6,7,4″,5″-furo-2′-acetoxy-4′,5′-methylenedioxyisoflavan (**11**) Hydrogenolysis of neodulin (**6**) (900 mg) in EtOAc–HOAc (1 1) (50 ml) with 10% Pd/C (500 mg) at 60° for 24 hrs afforded a mixture of the phenolic isoflavan (**10**) and starting material After filtration and evaporation of the solvent under red pres the crude mixture was acetylated After work-up the mixture was separated by TLC in $CHCl_3$ to give (**11**) (320 mg) as colourless needles, m p 144–145 5°, M^+ 354, τ (100 MHz) 7 73, *s*, $OCOC\underline{H}_3$, 7 23, *s*, 4-H, 7 12, *s*, 4-H, 6 93, *t*, *J* 8 2 Hz, 3″-H, 6 08, *t*, *J* 10 Hz, 2-H, 5·77, *q*, J_1 10 Hz, J_2 3 5 Hz, 2-H; 5 48, *t*, *J* 8 2 Hz, 2″-H, 4 05, *s*, $OC\underline{H}_2O$, 3 65, *s*, 3′-H, 3 40, *s*, 8-H, 3 33, *s*, 6′-H, 2 75, *s*, 5-H

2″,3″-Dihydro-6,7,4″,5″-furo-2′-acetoxy-4′,5′-methylenedioxyisoflavanone (**12**) A soln of the isoflavan (**11**) (350 mg) in Me_2CO (50 ml) was oxidized by the dropwise addition of 5% aq $KMnO_4$ (40 ml) over a period of 4 hr H_2O (50 ml) was added before SO_2 was passed through the soln The H_2O layer was extracted with Et_2O (4 × 50 ml) after evaporation of the Me_2CO The residue from the Et_2O extract was separated by TLC in $CHCl_3$ to give (**12**) (100 mg) as colourless needles (MeOH), m p 180 5–182°, M^+ 368, τ (60 MHz) 7 78, *s*, $OCOC\underline{H}_3$, 6 87, *t*, *J* 8 2 Hz, 3″-H, 5 98, *d*, *J* 8 Hz, 3-H, 5 56, *d*, *J* 8 Hz, 2-H, 5 35, *d*, *J* 8 2 Hz, 2″-H, 4 05, *s*, $OC\underline{H}_2O$, 3 65, *s*, 3′-H, 3 33, *s*, 6′-H, 3 33, *s*, 8-H, 2 22, *s*, 5-H

2′,3′-Dihydroneoduleen (**13**) A soln of (**12**) (100 mg) in HOAc (8 ml) and conc HCl (4 ml) was heated for 30 min at 100° The resulting white ppt was filtered and crystallized from MeOH to give colourless needles, m p 194–195 5°, of (**13**) (67 mg)

Neoduleen (**5**) (**13**) (60 mg) and DDQ (40 mg) in dry C_6H_6 (30 ml) was stirred under reflux for 2 hrs After filtration the mixture was separated by TLC in C_6H_6–hexane (3 2), R_f 0 72, to give (**5**) (15 mg) as colourless needles, m p 222–223°, M^+ 306, identical with an authentic sample

Neorauteen methylether (**4a**) Methylation of (**4**) (20 mg) afforded (**4a**) (13 mg) as a white powder, m p 200–201 5°, M^+ 292

Neorauteen acetate (**4b**) Acetylation of (**4**) (20 mg) gave (**4b**) (16 mg) as colourless needles, m p 197 5–199°, M^+ 336

Acknowledgement—One of us (A J B) thanks the C S I R for financial support