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THE CONCURRENCE OF 12a-HYDROXY- AND 12a-O-METHYLROTENOIDS. ISOLATION OF THE FIRST NATURAL 12a-O-METHYLROTENOIDS.

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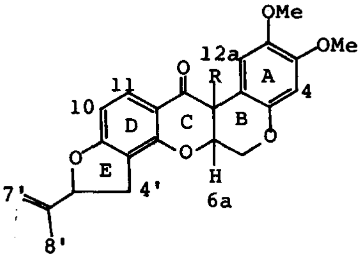
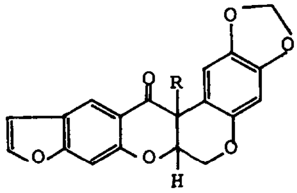
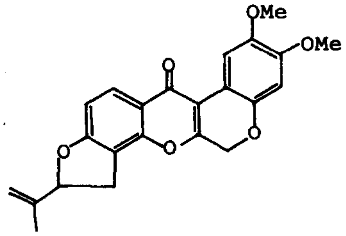
The light petroleum extract of the root of Neorautanenia amboensis Schinz. yielded in addition to rotenone (1), dehydrorotenone (9) and dehydrodolineone (10), four optically active natural compounds (2, 3, 6 and 7). Compounds (2) and (3) were previously obtained only by synthesis[1]. (3) and (7) are the first natural 12a-O-methylrotenoids to be isolated.



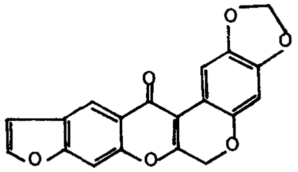
(1): R=H
(2): R=OH
(3): R=OMe
(4): R=OAc



(5): R=H
(6): R=OH
(7): R=OMe
(8): R=OAc



(9)



(10)

N.m.r. comparison[2] (TABLE) of 12a-hydroxyrotenone (2), light yellow oil, (lit.[3] m.p. 88°C), $[\alpha]_D$ -145°, M$^+$ 410, $C_{23}H_{22}O_7$, and 12a-O-methylrotenone (3), light yellow oil, (lit.[4] m.p. 174°C), $[\alpha]_D$ -211°, M$^+$ 424, $C_{24}H_{24}O_7$, with rotenone (1) indicates that these compounds have the same substitution pattern regarding the A, D and E rings, and that structural differences concern

TABLE. Chemical Shifts (τ) of Rotenoid Protons.*

Compound	H-1s	H-4s	H-6	H-6a	H-10d	H-11d	H-12a	H-4'm	H-5'm	H-7'm	Me-8'bs	Meo-2 Meo-3
cis-12a-hydroxy-rotenone (13)	3.33	3.46	5.36m	5.03t	3.47	2.1	5.23 (OH)	6.93	4.67	4.93	8.20	6.17 6.27
rotenone (1)	3.24	3.57	5.41q 5.85bd	5.04m	3.52	2.18	6.21 (H)	6.67	4.76	4.95	8.23	6.22 6.26
cis-12a-O-methyl-rotenone (3)	3.17	3.42	5.37m	5.03m	3.43	2.08	6.43 (OMe)	6.93	4.65	4.93	8.20	6.12 6.20
trans-12a-hydroxy-rotenone (11)	2.18	3.63	5.47m	5.05m	3.40	2.13	6.80 (OH)	6.78	4.62	4.97	8.25	6.20 6.23
cis-12a-acetoxy-rotenone (4)	3.05	3.46	5.53m	5.53m	3.45	2.07	7.83 (OAc)	6.87	4.67	4.95	8.20	6.17 6.20
dehydrorotenone (9)	1.53	3.50	5.03s		3.10	1.90		6.73	4.80	4.89	8.13	6.00 6.13
					H-8s	H-11s	H-12a	H-2'd	H-3'd	OCH_2O		
cis-12a-hydroxy-dolineone (6)†	3.45	3.50	5.49m	5.30t	2.94	1.79	5.17 (OH)	2.27	3.15	4.15q		
cis-12a-acetoxy-dolineone (8)	3.10	2.95	5.47q 5.58q	4.50m	3.48	1.72	7.84 (OAc)	2.40	3.22	4.10q		
cis-12a-O-methyl-dolineone (7)	3.26	3.46	5.46m	5.33t	3.00	1.75	6.45 (OMe)	2.43	3.22	3.94q		
dehydrodolineone (10)††	1.68	3.43	4.91s		2.23	1.79		1.96	2.90	4.04s		

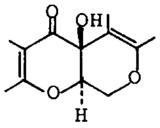
*Abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, b = broad.

† CD_3CN used as solvent; †† Deuterated DMSO used as solvent.

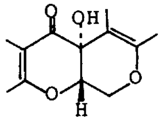
deviations from the characteristic ABCD pattern (arising from the 6-, 6a-, and 12a-protons) of rotenoids[5].

The presence of a hydroxy group in (2) was shown by the i.r. (3355 cm^{-1}) and n.m.r. spectra [τ 5.23, broad s, (exchangeable)]; the compound gave no colour with ferric chloride. A mono-acetate (4), colourless oil, M^+ 452, was formed on acetylation while methylation with Me_2SO_4 gave a product identical (t.l.c., n.m.r. and c.d.) with (3). Acid-catalyzed dehydration of (2) afforded 6a,12a-dehydrorotenone (9), suggesting that the hydroxy group was accommodated on the B/C-ring junction. The presence of an ABC system (TABLE) in the n.m.r. spectrum and the mass spectrum, typical of 12a-hydroxyrotenoids[6], suggests that (2) is the 12a-hydroxy derivative of rotenone.

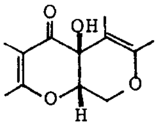
This structure was confirmed by the aerial oxidation of rotenone in basic medium to give a mixture of four compounds[7]. Separation of these by fractional crystallization (MeOH) and preparative t.l.c. [Merck silica gel PF_{254}; 6:4:1 (v/v) benzene:hexane:ethylacetate] gave two trans-enantiomers, m.p. 249-251°C (11 and 12) and two cis-enantiomers (13 and 14) as colourless oils.



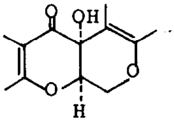
(11): (-)-(6aR,12aS)



(12): (+)-(6aS,12aR)



(13): (-)-(6aS,12aS)



(14): (+)-(6aR,12aR)

Comparison of the n.m.r. and c.d. data proved that the natural product (2) has a cis B/C-ring junction with absolute configuration (6aS,12aS) as in (13).

The constitution and absolute stereochemistry of compound (3) was established by n.m.r. (TABLE) and c.d. comparison as well as by chemical conversion of (2) into (3).

Compounds (6), m.p. 194-5°C, $[\alpha]_D$ +42°, M^+ 352, $C_{19}H_{12}O_7$, and (7), colourless oil, $[\alpha]_D$ +58°, M^+ 366, $C_{20}H_{14}O_7$ revealed the same ABC system in the n.m.r. spectra suggesting a similar oxygenation pattern on the B/C-ring junction as observed in the spectra of (2) and (3). The presence of a hydroxyl group in (6) was supported by the formation of a mono-acetate (8), colourless oil, M^+ 394, and O-methylether (7) as before.

The τ-value of the 1-proton (TABLE) in (6) and (7) demonstrates that the

B/C-ring junctions are cis[2].

Dehydrodolineone (10), $C_{19}H_{10}O_6$; M^+ 334; $\nu_{C=O}$ (1650 cm^{-1}) was isolated as yellow needles, m.p. 290-292°C. The n.m.r. spectrum was in full agreement with the proposed structure while dehydration of 12a-hydroxydolineone (6) gave a product identical to dehydrodolineone (10).

Although (10) could represent an artefact due to the established ease of dehydration of 12a-hydroxyrotenoids, the isolation of (2), (3), (6) and (7) as optically pure compounds suggest that they exist as natural products. Comparative chromatographic examination of extracts by mild procedure (light petroleum) from fresh plant material support their presence in the natural state.

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References:

1. F.B. LaForge and L.E. Smith, J. Amer. Chem. Soc., **52**, 3603 (1930).
2. L. Crombie and J.W. Lown, Proc. Chem. Soc., 299 (1961); J. Chem. Soc., 775 (1962).
3. L. Crombie and P.J. Godin, J. Chem. Soc., 2861 (1961).
4. F.B. LaForge and H.L. Haller, J. Amer. Chem. Soc., **56**, 1620 (1934).
5. D.J. Adam, L. Crombie and D.A. Whiting, J. Chem. Soc. (C), 542 (1966).
6. W.D. Ollis, C.A. Rhodes and I.O. Sutherland, Tetrahedron, **23**, 4741 (1967).
7. T. Unai, I. Yamamoto, Cheng Hong-Ming and J.E. Casida, Agr. Biol. Chem., **37**(2), 387 (1973).