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STRUCTURES OF NINE QUINONES ISOLATED FROM TWO CONOSPERMUM SPECIES

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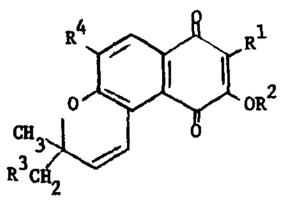
Fractionation of an extract of the roots of Conospermum teretifolium R. Br. with alkalis, followed by extensive chromatography, led to the isolation of ten quinones. Two of these were identified as lapachol and 3-geranyllawsone; the remainder were assigned the novel structures (1) to (8) inclusive. The roots of a related species, C.brownii Meissn., gave a high yield of a single naphthaquinone, m.p. 203-4°, which was assigned structure (9). The structures (1) to (9) inclusive, have been confirmed by unambiguous syntheses.

The relatively simple n.m.r. spectrum of (1), m.p. 176-7°, revealed that one proton of the pyran moiety was deshielded by a neighbouring quinone carbonyl and was also involved in a long range coupling (J=0.8 Hz) with the β-proton of the naphthaquinone residue. This, and other spectroscopic evidence, together with the assumption (which may not be warranted in this case) that the quinone was derived via the acetate pathway[1] led to structure (1) for this substance.

Essentially the same arguments were used to deduce the structures of (+)-(2) [m.p. 100.5-101.5°, $[\alpha]_D$ + 39° (c, 1.2 in $CHCl_3$)], (+)-(3) [double m.p., 88-90° then 100-101°, $[\alpha]_D$ + 40° (c, 1.5 in $CHCl_3$)], and (±)-(4) [m.p. 61.5-62.5°, $[\alpha]_D$ + 0.6° (c, 4.2 in $CHCl_3$)]. These assignments were supported by C-methylation[2] of (+)-(2) which afforded (+)-(3) and O-methylation of (+)-(3) which gave (+)-(4) [m.p. 50-2°, $[\alpha]_D$ + 50° (c, 1.5 in $CHCl_3$)]. Although (+)-(4) had the same spectroscopic properties as (±)-(4), the mixed m.p. of the optically-active substance and racemate was 47-61°.

Attention was then turned to the naphthaquinones. C-methylation[2] of (9) yielded (7). Demethylation of (7) with sodium thioethoxide[3] gave (6), m.p. 220-1°, which did not depress the m.p. (215-6°) of the very small amount of (6) obtained from C.teretifolium; the spectra of the two samples were identical. When (7) was heated with HBr in acetic acid demethylation was followed by cyclization and the product, m.p. 184-5°, proved to be identical with the dihydro derivative of (1). The remaining naphthaquinone (8) m.p. 158.5-160.5° was assigned its



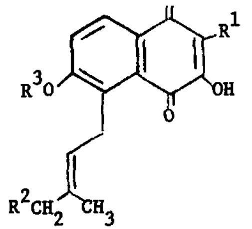
(1) $R^1=CH_3$, $R^2=R^3=R^4=H$

(2) $R^1=R^2=R^4=H$, $R^3=(CH_3)_2C=CHCH_2$

(3) $R^1=CH_3, R^2=R^4=H$, $R^3=(CH_3)_2C=CHCH_2$

(4) $R^1=R^2=CH_3, R^3=(CH_3)_2C=CHCH_2, R^4=H$

(5) $R^1=CH_3, R^2=R^3=H$, $R^4=OH$



(6) $R^1=CH_3$, $R^2=R^3=H$

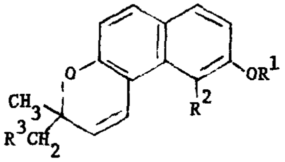
(7) $R^1=R^3=CH_3, R^2=H$

(8) $R^1=CH_3$, $R^2=(CH_3)_2C=CHCH_2, R^3=H$

(9) $R^1=R^2=H$, $R^3=CH_3$

(10) $R^1=H$, $R^2=(CH_3)_2C=CHCH_2$, $R^3=CH_3$

(11) $R^1=R^3=CH_3$, $R^2=(CH_3)_2C=CHCH_2$



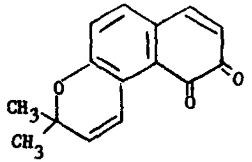
(12) $R^1=R^2=R^3=H$

(13) $R^1=R^3=H$, $R^2=C_6H_5N=N$

(14) $R^1=R^2=H$, $R^3=(CH_3)_2C=CHCH_2$

(15) $R^1=CH_3OCH_2, R^2=R^3=H$

(16) $R^1=CH_3OCH_2$, $R^2=H$, $R^3=(CH_3)_2C=CHCH_2$



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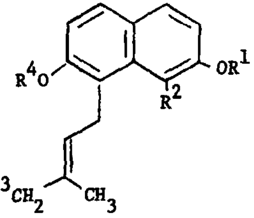


(19) $R^1=CH_3OCH_2$, $R^2=R^3=R^4=H$

(20) $R^1=CH_3OCH_2$, $R^2=R^3=H$, $R^4=CH_3$

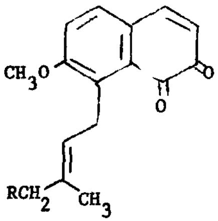
(21) $R^1=R^2=R^3=H$, $R^4=CH_3$

(22) $R^1=R^3=H$, $R^2=C_6H_5N=N$, $R^4=CH_3$

(23) $R^1=CH_3OCH_2$, $R^2=R^4=H$, $R^3=(CH_3)_2C=CHCH_2$

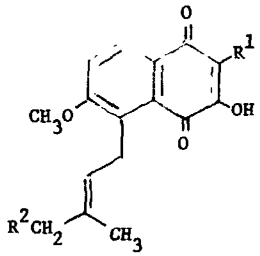
(24) $R^1=CH_3OCH_2, R^2=H$, $R^3=(CH_3)_2C=CHCH_2, R^4=CH_3$

(25) $R^1=R^2=H$, $R^3=(CH_3)_2C=CHCH_2$, $R^4=CH_3$



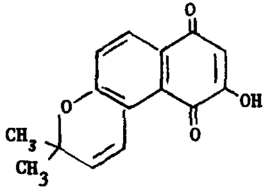
(26) R=H

(27) $R=(CH_3)_2C=CHCH_2$



(28) $R^1=H$, $R^2=(CH_3)_2C=CHCH_2$

(29) $R^1=CH_3, R^2=(CH_3)_2C=CHCH_2$



(18)

structure on the basis of its spectroscopic properties, which were analogous to those of (6).

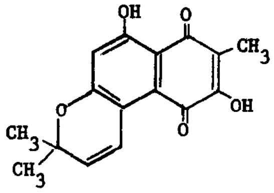
Syntheses of (1) to (9), with the exception of (5), were then undertaken. Reaction of naphthalene-2,7-diol with 1,1-dimethoxy-3-methylbutan-3-ol and pyridine[4] gave (12),m.p.146-8° which was converted into the azo dye (13), m.p. 141.5-2.5°. Reduction of (13) with $Na_2S_2O_4$ followed by oxidation of the product with $FeCl_3$ then yielded the o-quinone (17), m.p.108-10°. After the method of Baillie and Thomson[5] (17) was converted into (18), m.p.178-9°; C-methylation[2] of (18) then gave (1), m.p. and mixed m.p. 176-7°.

The same series of reactions was used to convert (14)[6] into (±)-(2), m.p.96-8°; the mixed m.p. with (+)-(2) was 92-100° but the spectra of the two samples were identical. C-methylation[2] of (±)-(2) gave (±)-(3), m.p. 98.5-100.5°; the mixed m.p. with (+)-(3) was 91-98° but again the spectra of the two samples were identical. O-methylation of (±)-(3) yielded (±)-(4) which was identical with the substance isolated from C. teretifolium.

Next, (12) was converted into (15) which was reduced[7] with 2.5 moles of Li in liquid NH_3 for 3 minutes to give (19) which was methylated immediately, whereupon the oily (20) was obtained. Mild acid hydrolysis of (20) gave (21), m.p. 88-9°, which furnished the azo dye (22), m.p. 102-3°. As before, (22) was converted into the o-quinone (26), m.p. 119-20°, and thence[5] into (9), m.p. and mixed m.p. 202-3°. As (9) had already been converted into (7) and (6) this sequence also provides syntheses of these compounds.

In similar fashion (14) yielded (16), reduction[7] of which afforded (23) which was immediately converted into the oily (24). Mild acid hydrolysis of (24) then gave (25). In this case, treatment of (25) with Fremy's salt gave a good yield of the o-quinone (27) which was immediately converted[5] into (28), m.p. 128-9°. C-methylation[2] of (28) afforded (29), m.p. 112.5-3.5°. When (29) was demethylated by heating with sodium thioethoxide[3], (8), m.p. and mixed m.p. 157.5-159.5°, was obtained.

Following these successful syntheses we considered the structure (30) for the remaining tricyclic pigment (5), m.p. 243-4°, from C.teretifolium. Such a structure (30) would be favoured on the basis of biogenesis via an acetate pathway. However, other synthetic studies made this conclusion untenable and it also seemed that the n.m.r. spectrum of the substance was in better agreement with (5). In particular, there was no evidence of any long range coupling between the single aromatic proton and the proton of the pyran moiety which was deshielded by the quinone carbonyl. The structure (5) has now been confirmed by synthesis.



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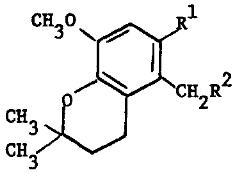
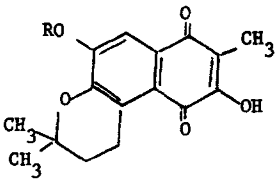


(31) $R^1=H,R^2=OH$

(32) $R^1=H,R^2=CO_2CH_3$

(33) $R^1=COCH_2CH_3,R^2=CO_2CH_3$



(34) $R=CH_3$

(35) $R=H$

Isovanillin was converted, after the method of Hlubucek, Ritchie, and Taylor[8], into 2,2-dimethyl-5-formyl-8-methoxychromene, m.p.73-4°, catalytic reduction of an alkaline solution of which afforded (31), m.p.92-3°. This substance was converted via the corresponding bromide (m.p.79-80°), nitrile (m.p. 90.5-91.5°), and acid (m.p. 126.5-8.5°), into the ester (32), m.p.51.5-52.0°. Treatment of (32) with propionyl chloride and $SnCl_4$ gave (33), m.p.116.5-117°, which, after the method of Bycroft and Roberts[9] yielded (34), m.p. 218-218.5°. This substance (34) proved to be identical with the dihydro mono-O-methyl ether which had been prepared from the natural product by standard methods. Demethylation[3] of (34) afforded (35), m.p. 254-5°; the leucotetracetate, m.p. 188-9°, of (35) was dehydrogenated[10] with DDQ. Hydrolysis of the dehydrogenation product followed by aerial oxidation then afforded (5), m.p. and mixed m.p. 242-4°

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