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Four New Naphthoquinone Derivatives from *Diospyros* spp.[1]

Diospyros spp. (Ebenaceae) are rich sources for naphthol and naphthoquinones.[2-4] In the previous communications[5,6] we have reported the structural elucidations on diospyrol (I), mamegakinone (II), isodiospyrin (III), and bisisodiospyrin (IV). In this communication further characterization of four new methyljuglone derivatives (V, IX, XI, and XIV) will be reported.

From methanol extract of fresh roots of *Diospyros kaki* THUNB. (Japanese name: Kaki), a new quinone of mp 209—210° (V), $C_{12}H_{10}O_4$ (M^+ 217.057 *m/e*, Calcd. 218.058), was obtained along with plumbagin (VI), 7-methyljuglone (VIII), II, and III. Spectral data of V, IR ν_{max}^{KBr} cm^{-1}: 1655 (sh), 1638, 1599, UV $\lambda_{max}^{CHCl_3}$ mμ (log ε): 249, 290, 420 (3.83, 4.08, 3.49), showed the characteristics of naphthoquinones. NMR spectra of V and the monomethyl ether (V'), mp 172°, revealed the presence of one each of methoxyl, hydrogen-bonded hydroxyl, aromatic methyl, and quinonoid proton and two *m*-coupled protons in V (Table I). 2-Methoxy-7-methyljuglone (VIII) and 3-methoxy-7-methyljuglone (V) structures suffice the conditions shown by the spectral observations. The final assignment of the structure has been accomplished by the following synthesis. The Thiele acetylation of VII, followed by hydrolysis,[7] afforded two products, mp 196—200° and 197—207°, and they were respectively assigned as 2-hydroxy-7-methyljuglone[8] (VIII'') and 3-hydroxy-7-methyljuglone (V'') by the comparison of NMR spectra (Table I) and UV spectra in alkaline solution with those of the model compounds. Methylation of VIII'' and V'' with diazomethane gave the monomethyl ethers, VIII, mp 212° (decomp.), and V, mp 209°,[9] and the latter was proved to be identical with the natural product.

From chloroform extract of dried roots of *D. kaki* THUNB. a mixture of another new naphthoquinone (IX) and diospyrin[2,10,11] (X) was isolated along with II, III, and VII. Due

1) A part of the work has been presented at the Annual Meeting of Pharmaceutical Society of Japan, Sapporo, July 1970.
2) A. L. Fallas and R. H. Thomson, *J. Chem. Soc.* (*C*), **1968**, 2279.
3) S. H. Harper, A. D. Kemp, and J. Tannock, *J. Chem. Soc.* (*C*), **1970**, 626.
4) G. S. Sidhu and K. K. Prasad, *Tetrahedron Letters*, **1970**, 1739.
5) K. Yoshihira, S. Natori, and P. Kanchanapee, *Tetrahedron Letters*, **1967**, 4857.
6) K. Yoshihira, M. Tezuka, and S. Natori, *Tetrahedron Letters*, **1970**, 7.
7) H. Singh, T. L. Folk, and P. J. Scheuer, *Tetrahedron*, **25**, 5301 (1969).
8) The compound was synthesized by J. E. Davies and J. C. Roberts (*J. Chem. Soc.*, **1956**, 2173) and reported to be mp 200° (decomp.). The direct comparison has not been carried out, because the authentic specimen is now inavailable (Dr. J. C. Roberts, University of Nottingham, private communication).
9) A compound, mp 110—111°, assigned as 3-methoxy-7-methyljuglone, was obtained as the by-product of the oxidation of 1,2,4-trimethoxy-6-methyl-8-hydroxynaphthalene (E. Widmer, J. M. Meyer, A. Walser, and H. Hardegger, *Helv. Chim. Acta*, **48**, 538 (1965)).
10) A. K. Ganguly and T. R. Govindachari, *Tetrahedron Letters*, **1966**, 3373.
11) G. S. Sidhu and M. Pardhasaradhi, *Tetrahedron Letters*, **1967**, 1313, 4263.

to the scarcity of the amount of the mixture and the closely similar properties of IX and **X**, the separation of the two was achieved after methylation with methyl iodide and silver oxide in chloroform and the one was proved to be identical with diospyrin dimethyl ether (X′).[12] The other (IX′), mp 245—247°, $C_{24}H_{18}O_6$ (M^+ 402.107 *m/e*, Calcd. 402.100), was suggested to be another unsymmetrical dimer of 7-methyljuglone methyl ether from IR (ν_{max}^{KBr} cm^{-1}: 1660, 1621, 1602), UV (λ_{max}^{EtOH} mμ (log ε): 253, 404 (4.36, 3.89)), and NMR (Table I). The NMR data suggested that the linkage of the two 7-methyljuglone moieties must be located at the peri-position of the one and the quinonoid ring of the other, *i.e.* 8- and 2′- or 3′-positions. Thus the new quinone was expressed by the formula (IX) and designated as neodiospyrin.

From chloroform extract of dried roots of *D. maritima* Blume (Japanese name: Kurobo), a quinone (XI), mp 195°, $C_{22}H_{14}O_6$ (M^+ 374.076, Calcd. 374.079), IR ν_{max}^{KBr} cm^{-1}: 1656(sh), 1647,

Table I. NMR Spectra of the Naphthoquinones[a]

Compound	2- and 2′-CH_3 or H	3- and 3′-H or CH_3O	5- and 5′-OH or CH_3O	6- and 6′-H	7- and 7′-H or CH_3	8- and 8′-H, OH or OCH_3
Plumbagin (VI)	2.13(3H) d, J=1.5	6.66(1H) q, J=1.5	11.73(1H) s	7.07(1H)[b] dd	7.39(1H)[b] dd	7.47(1H) dd
7-Methyljuglone (VII)	6.98(1H) s	6.98(1H) s	11.91(1H) s	7.14(1H) d, J=1.5	2.36(3H) s	7.50(1H) d, J=1.5
3-Methoxy-7-methyl-juglone (V)	6.16(1H) s	3.93(3H) s	11.80(1H) s	7.11(1H) d, J=1.5	2.44(3H) s	7.52(1H) d, J=1.5
3,5-Dimethoxy-7-methyl-naphthoquinone (V′)	6.00(1H) s	3.84(3H)[b] s	3.96(3H)[b] s	7.00(1H) d, J=1.5	2.45(3H) s	7.50(1H) d, J=1.5
3,5-Dihydroxy-7-methyl-naphthoquinone (V″)	6.25(1H) s	not observed[c]	10.90(1H) s	6.98(1H) d, J=1.5	2.44(3H) s	7.44(1H) d, J=1.5
2,5-Dihydroxy-7-methyl-naphthoquinone (VIII″)	not observed[c]	6.20(1H) s	12.15(1H) s	7.08(1H) d, J=1.5	2.41(3H) s	7.46(1H) d, J=1.5
Neodiospyrin dimethyl ether (IX′)	6.57(1H)[b] d, J=10	6.71(1H)[b] d, J=10	3.99(3H)[b] s	7.18(1H) s	2.30(3H)[b] s	—
	6.45(1H)[b] s	—[b]	3.91(3H)[b] s	7.06(1H) d, J=1.5	2.49(3H)[b] s	7.56(1H) d, J=1.5
Diospyrin dimethyl ether (X′)	6.69(1H)[b] s	—[b]	3.98(3H)[b] s	7.05(1H) d, J=1.5	2.47(3H)[b] s	7.52(1H) d, J=1.5
	6.81(1H) s	6.81(1H) s	3.65(3H)[b] s	—	2.26(3H)[b] s	7.74(1H) s
Maritinone (XI)	1.99(6H) d, J=1.5	6.76(2H) q, J=1.5	12.36(2H) s	7.10(2H)[b] d, J=9	7.19(2H)[b] d, J=9	—
Maritinone dimethyl ether (XI′)	1.91(6H) d, J=1.5	6.65(2H) q, J=1.5	3.99(6H) s	7.14(2H)[b] d, J=9	7.23(2H)[b] d, J=9	—
Isodiospyrin (III)	6.77(1H)[b] d, J=10	6.94(1H)[b] d, J=10	12.12(1H) s	7.35(1H) s	2.05(3H) s	—
	6.98(1H) s	6.98(1H) s	12.50(1H) s	—	2.02(3H) s	7.67(1H) s
Hydroxyisodiospyrin (XIV)	6.71(1H)[b] d, J=10	6.90(1H)[b] d, J=10	12.35(1H)[b] s	[d]	2.18(3H) s	—
	1.85(3H) s	—	12.22(1H)[b] s	[d]	[d]	12.18(1H)[b] s
Hydroxyisodiospyrin trimethyl ether (XIV′)	6.55(1H)[b] d, J=10	6.70(1H)[b] d, J=10	3.99(3H)[b] s	[e]	2.21(3H) s	—
	1.72(3H) s	—	3.94(3H)[b] s	[e]	[e]	3.85(3H)[b] s

δ in ppm from the internal standard TMS in $CDCl_3$. Coupling constant in ppm.

a) The detailed discussion of the assignment of NMR spectra will be made in full papers (K. Yoshihira, M. Kuroyanagi, M. Tezuka, C. Takahashi, and S. Natori, *Chem. Pharm. Bull.* (Tokyo), to be published).

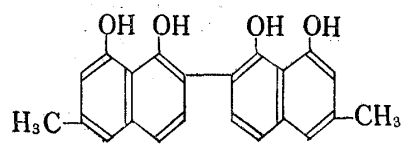
b) The assignment is tentative.

c) *cf.* R. E. Moore and P. J. Scheuer, *J. Org. Chem.*, **31**, 3272 (1966).

d) 7.3 (3H, m)

e) 7.2 (3H, m)

12) The authors thank Professor R. H. Thomson, University of Aberdeen, for his kind donation of the authentic sample.



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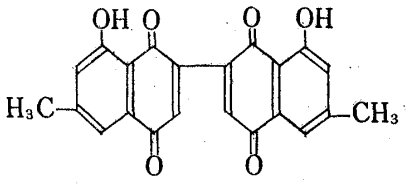

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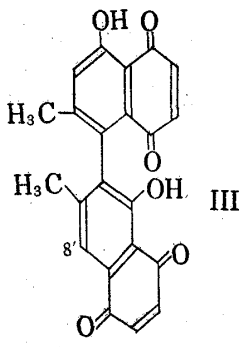

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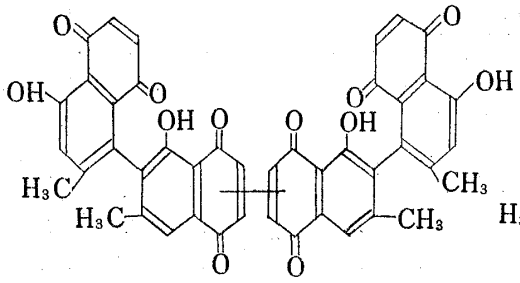

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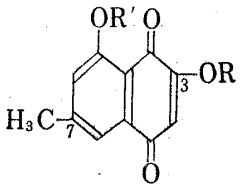
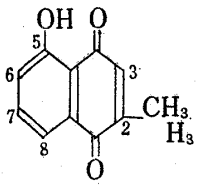


V : R=CH_3, R′=H
V′ : R=CH_3, R′=CH_3
V″ : R=H, R′=H



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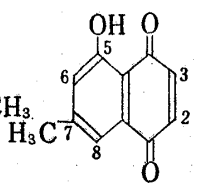

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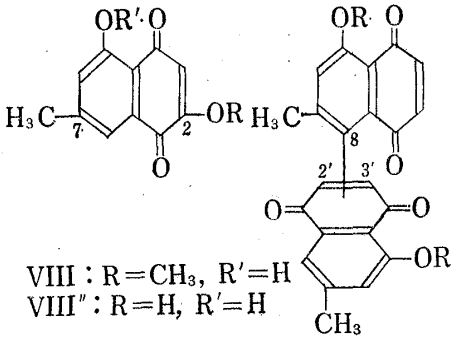
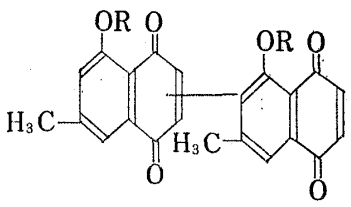
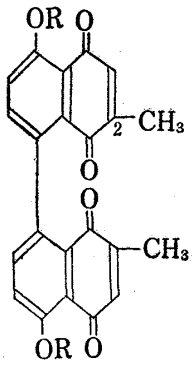


VIII : R=CH_3, R′=H
VIII″ : R=H, R′=H

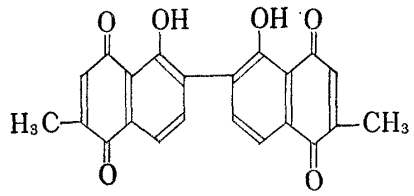
IX : R=H
IX′ : R=CH_3



X : R=H
X′ : R=CH_3



XI : R=H
XI′ : R=CH_3



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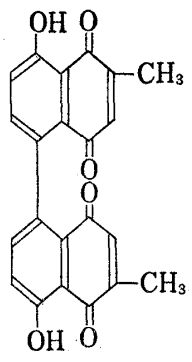
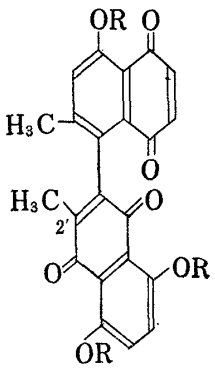


XIII



XIV : R=H
XIV′ : R=CH_3

1614, UV λ_{max}^{EtOH} (log ε): 264, 436 (4.42, 3.87), was obtained along with VI and elliptinone[2,5] (XII). The compound (XI) formed dimethyl ether (XI′), mp 272—274°, IR ν_{max}^{KBr} cm^{-1}; 1660, 1635(sh), by methyl iodide-silver oxide treatment, and the NMR spectra (Table I) of XI

and XI′ suggested that the quinone is a symmetrical dimer, each unit of which bears one each of hydroxyl, quinonoid methyl (showing allylic coupling with a quinonoid proton) and the quinonoid proton, and two *o*-coupled protons. Since the hydroxyl group is hydrogen-bonding with the carbonyl group (IR and NMR) and the chemical shifts of the *o*-coupled protons indicate that they are in 6- and 7-positions of naphthoquinone ring, the new quinone must be 8-8′ dimer of plumbagin (XI) and designated as maritinone. The alternative 3-methyljuglone structure (XIII) was excluded from biogenetical grounds. Sodium dithionite reduction[13] of XI gave VI in a low yield.

Chloroform extract of dried roots of *Maba buxifolia* Pers. (Japanese name: Ryukyu-kokutan) gave III, VII, and a red quinone (XIV) of mp 275—277°, $[\alpha]_D^{23}$ −720° (dioxane), UV $\lambda_{max}^{CHCl_3}$ mμ (log ε): 253, 300, 434, 460, 484, 514, 554 (4.24, 3.93, 3.84, 3.92, 3.91, 3.90, 3.66), IR ν_{max}^{KBr} cm^{-1}: 1670(sh), 1640, 1600. The compound (XIV) formed trimethyl ether (XIV′), mp 122—123°, IR ν_{max}^{KBr} cm^{-1}: 1650, 1580, $C_{25}H_{20}O_7$ (M^+ 432.115 *m/e*, Calcd. 432.120), by methyl iodide-silver oxide treatment. The UV spectrum of XIV coincides well with the summation of those of 7-methyljuglone and naphthazarin. NMR spectra of XIV and XIV′ (Table I) revealed the presence of one quinonoid methyl (no allylic coupling), one aromatic methyl, two *o*-coupled quinonoid protons, three aromatic protons (not in peri-positions), and three hydrogen-bonded hydroxyl groups in XIV. The comparison of the NMR data with those of III and the related compounds suggested that the quinone (XIV) is 8′-hydroxy derivative of III (one unit in the tautomeric 2-methylnaphthazarin form). This was confirmed by hydrogen peroxide oxidation of III in acetic acid to form (XIV) and the compound was designated as 8′-hydroxyisodiospyrin.

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