THE ISOLATION, STRUCTURE, AND SYNTHESIS OF HALKENDIN

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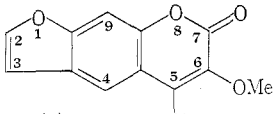
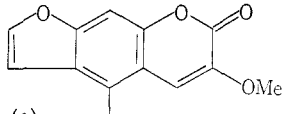
Co-occurring with halfordin[1] in the bark of *Halfordia kendack*, but separable from the major constituents by column chromatography, was a small quantity of a crystalline compound, m.p. 173–173·5°, which we have named halkendin (1).



(1)



(2)

Microanalyses and mass spectrometry established the composition of halkendin as $C_{13}H_{10}O_5$. Its u.v. spectrum was comparable to that of the unsubstituted linear furocoumarin, psoralene, whilst its i.r. spectrum above 1200 cm^{-1} bore a similarity to that of halfordin.[1] The p.m.r. spectrum of halkendin in deuterochloroform solution showed two methoxyl signals at δ values of 4·35 and 3·98 and the 2- and 3-furan ring protons at δ 7·73 and 6·87 respectively (J 2·5 Hz), the latter being long range coupled[2] (J *c.* 1 Hz) to the 9-proton (δ 7·44) on the aromatic ring. The remaining singlet at δ 8·04 could be assigned to a proton at either the 4- or 5-position suggesting (1) or (2) as the most probable structure of halkendin.

The synthesis of (1) was carried out following essentially the same route described previously for the preparation of isohalfordin.[3] Hoesch condensation[4] of 6-hydroxy-2,3-dihydrobenzo[*b*]furan (3) with methoxyacetonitrile gave the 5-methoxyacetyl derivative (4) which cyclized to 5-hydroxy-6-methoxy-7-oxo-2,3-dihydro-7*H*-furo[3,2-*g*][1]benzopyran (5) on treatment with ethyl carbonate and sodium.[5] Compound (5) was further characterized by forming an acetate derivative (6). (See Scheme 1.)

Methylation of (5) with diazomethane furnished 5,6-dimethoxy-7-oxo-2,3-dihydro-7*H*-furo[3,2-*g*][1]benzopyran (7) which on dehydrogenation with either 10%

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[1] Lahey, F. N., and MacLeod, J. K., *Tetrahedron Lett.*, 1968, **4**, 447; Hegarty, M. P., and Lahey, F. N., *Aust. J. Chem.*, 1956, **9**, 120.

[2] Jarvis, M. W., and Moritz, A. G., *Aust. J. Chem.*, 1968, **21**, 2445.

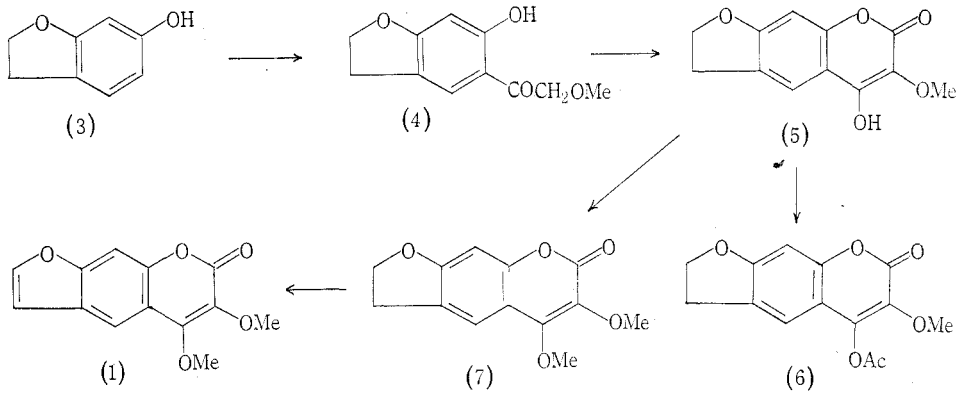
[3] Fukui, K., Nakayama, M., Fujimoto, S., and Fukuda, O., *Experientia*, 1969, **25**, 354.

[4] Pavanaram, S. K., and Row, R., L., *Chem. Abstr.*, 1956, **50**, 12040*a*.

[5] Boyd, J., and Robertson, A., *J. chem. Soc.* 1948. 174.

Pd–C in diphenyl ether or DDQ in benzene gave 5,6-dimethoxypsoralene (1), identical in all respects (m.p., mixed m.p., u.v., p.m.r. spectra) with naturally occurring halkendin.

Halkendin thus joins halfordin,[1] isohalfordin,[1] and halfordinin[6] as the fourth 3,4-dioxygenated linear furocoumarin to be derived from natural sources.



Scheme I

Experimental

Isolation of Halkendin

The tarry non-basic fraction of a methanolic extract of the bark of *Halfordia kendack* was extracted with light petroleum (60–80°) for 18 hr and the solvent removed under vacuum. The resulting white solid residue was chromatographed on neutral alumina following the procedure of Hegarty and Lahey.[1] The first fraction, eluted with light petroleum–benzene (1 : 1), contained halkendin (1), m.p. 168–170°. *Halkendin* recrystallized from methanol as colourless needles, m.p. 173–173·5° (Found: C, 63·5; H, 4·25; OCH_3, 24·0. $C_{13}H_{10}O_5$ requires C, 63·4; H, 4·1; OCH_3, 25·2% ($2\times OCH_3$)). λ_{max} (EtOH) 320 (4·06), 293 (4·05), 246 (4·32), 238 nm (4·33), ν_{max} 1707, 1620, 1590, 1540, 1340, 1270, 1230, 1195, 1160, 1115, 1070, 1025, 1000, 955, 910, 870, 860, 840, 815, 760, 735, 705, 665 cm^{-1}. Mass spectrum: *m/e* 246 (80% rel. abund., M^+), 251 (19%), 203 (100%), 160 (62%).

6-Hydroxy-5-(ω-methoxyacetyl)-2,3-dihydrobenzo[b]*furan* (*4*)

The above compound was prepared by condensing 6-hydroxy-2,3-dihydrobenzo[*b*]furan (3) with methoxyacetonitrile in the presence of $ZnCl_2$ according to the method of Pavanaram and Row.[4] It crystallized from methanol as colourless needles, m.p. 124–125°. λ_{max} (EtOH) 330 (3·94), 283 (4·04), 240 nm (4·01); ν_{max} 1631 cm^{-1}.

*5-Hydroxy-6-methoxy-7-oxo-2,3-dihydro-7*H-*furo*[*3,2-g*][*1*]*benzopyran* (*5*)

A mixture of (4) (3·2 g), ethyl carbonate (100 ml), and pulverized sodium (3·0 g) was warmed on a steam-bath for 20 min. After the vigorous reaction had ceased, sufficient methanol was added to the cooled mixture to destroy the excess of sodium, and then the residue was added to ether. The extraction of the sodium salt of the product with water and acidification of it with 2N hydrochloric acid gave *compound* (*5*), which formed colourless needles from methanol, m.p. 257–258°; yield, 2·1 g (58%) (Found: C, 61·3; H, 4·4. $C_{12}H_{10}O_5$ requires C, 61·5; H, 4·3%); λ_{max} 321 (4·31), 290 (3·85), 259 infl. (3·54), 246 infl. nm (3·74); ν_{max} 3160, 1685 cm^{-1}.

[6] MacLeod, J. K., *Tetrahedron Lett.*, 1970, 1319, 3611.

With acetic anhydride and sodium acetate (5) formed an *acetate* (6), m.p. 213–215° (colourless plates from ethanol) (Found: C, 60·6; H, 4·3. $C_{14}H_{12}O_6$ requires C, 60·9; H, 4·4%); λ_{max} (EtOH) 333 (4·27), 300 infl. (3·80), 257 infl. nm (3·56); ν_{max} 1777, 1707 cm^{-1}. N.m.r. ($CDCl_3$ solution, δ values) 2·45 s (3H); 3·25 t (*J* 9 Hz) (2H); 3·94 s (3H); 4·71 t (*J* 9 Hz) (2H); 6·74 s; 7·28 br s.

*5,6-Dimethoxy-7-oxo-2,3-dihydro-7*H*-furo[3,2-g][1]benzopyran* (*7*)

Methylation of (5) in methanol solution using ethereal diazomethane afforded the *dimethoxy compound* (7), m.p. 147–148° (colourless needles from ethanol) (Found: C, 62·9; H, 4·85. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·9%). λ_{max} (EtOH) 321·5 (4·21), 290 (3·73), 230 nm (4·09); ν_{max} 1700 cm^{-1}. N.m.r. ($CDCl_3$ solution, δ values) 3·9 s (3H); 4·32 s (3H); 3·27 t (*J* 9 Hz) (2H); 4·72 t (*J* 9 Hz) (2H); 6·72 s (1H); 7·63 s (1H).

*5,6-Dimethoxy-7-oxo-7*H*-furo[3,2-g][1]benzopyran* (*1*)

(i) *With DDQ.*—A mixture of (7) (1·0 g), DDQ (1·0 g), and absolute benzene (50 ml) was refluxed for 8 hr. After the solution had then been cooled, the precipitated hydroquinone derivative was filtered off and the solvent was removed under vacuum. The residual solid was recrystallized from ethanol to give compound (1), m.p. 173–173·5°; yield, 0·7 g (71%).

(ii) *With 10% palladium–charcoal.*—A mixture of (7) (1·0 g), 10% Pd–C (0·7 g), and diphenyl ether (15 ml) was refluxed for 8 hr. The catalyst was then filtered off, and the solvent removed by steam distillation. The resulting solid was recrystallized from ethanol to give compound (1), m.p. 173–173·5°; 0·5 g (51%) (Found: C, 63·3; H, 4·3. Calc. for $C_{13}H_{10}O_5$: C, 63·4; H, 4·1%).

Compound (1) showed no depression of m.p. on admixture with a sample of natural halkendin. Likewise, the u.v., i.r., and p.m.r. spectra of the two compounds were identical.