Total Synthesis of (±)-Scabequinone

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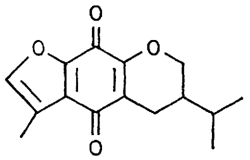
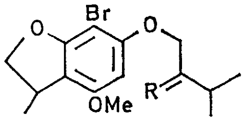
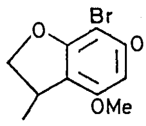
Summary The synthesis of (±)-scabequinone, a novel 5*H*-furo[3,2-*g*] [1]benzopyran-4,9-quinone from *Cyperus scaber*, is reported.

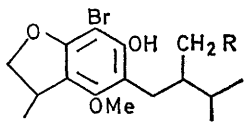

(1)

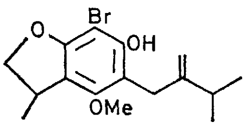
The family *Cyperaceae* is a rich source[1] of quinones, the biogenesis of which has been suggested[2] to involve, in part, the incorporation of a methylene group into a C_{13} aromatic precursor ($C_6 + C_2 + C_5$) to produce compounds containing a β-methylbenzofuran ($C_6 + C_2 + C_1$) or a 3-isopropylchroman ($C_6 + C_5 + C_1$) system. The structure (**1**) suggested for scabequinone[2] a major component of *Cyperus scaber* (R.Br.) Boeck, which possesses both of these ring systems, has now been confirmed by total synthesis.†

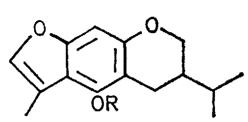

(3) R = O
(4) R = CH_2

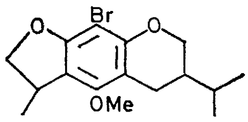

(2)

The substituted dihydrobenzofuran (**2**), whose preparation in eight steps from phloroglucinol has been reported,[3] was condensed with 1-bromo-3-methylbutan-2-one in Me_2CO–K_2CO_3 to produce (**3**), m.p. 79–80°. Treatment of the derived ketone with methyltriphenylphosphorane gave (**4**), b.p. 95°/0·03 mm, in high yield. This substituted allyl ether underwent a Claisen rearrangement in *NN*-dimethylaniline under reflux to afford compound (**5**), having the desired aromatic substitution pattern and six-carbon progenitor of the 3-isopropylchroman ring system. Cyclisation of this side-chain to give (**8**), b.p. 105°/0·03 mm, was effected by hydroboration–peroxide oxidation[4] of the exocyclic double bond to give exclusively the primary alcohol (**6**), followed by bromination [$(C_8H_{17})_3P$–CBr_4],[5] to (**7**), and treatment of the bromide with aqueous base.


(6) R = OH
(7) R = Br


(5)


(9) R = Me
(10) R = H


(8)

The aromatic bromine substituent used as a blocking group was quantitatively removed from compound (**8**), by hydrogenolysis (10% Pd–C), and subsequent aromatisation to the benzofuran system (**9**) carried out using palladised charcoal in diphenyl ether under reflux. Dichlorodicyanoquinone (DDQ) was ineffectual in promoting this dehydrogenation.

Demethylation of the aryl methyl ether (**9**) with the thioethoxide ion in DMF[6] proceeded smoothly to give the unstable phenol (**10**) which was oxidised by Fremy's salt[7]

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† All compounds reported have been fully characterised and their structures are consistent with u.v., i.r., n.m.r., m.s. data and microanalysis.

to the quinone (**1**), m.p. 116–118°. The racemic synthetic compound (**1**) was found to be identical in all respects (m.p. mixed m.p., u.v., i.r., ^{1}H n.m.r., mass spectra) except optical rotation with naturally occurring (+)-scabequinone. Attempts to resolve the phenol (**10**) *via* its (+)-camphor-10-sulphonate have proved unsuccessful.

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