Naturally Occurring Quinones. Part 28.[1] Sesquiterpenoid Quinones and Related Compounds from *Hibiscus tiliaceus*

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The heartwood of *H. tiliaceus* is red and fades on exposure to light. Like *H. elatus* heartwood, which behaves similarly, it contains hibiscones A—D and hibiscoquinones A—D; one sample which was devoid of red pigments contained lapachol while roots (from Brazil) contained gossypol, and mansonones D and F.

Hibiscoquinone B can be obtained from hibiscones C and D by autoxidation in alkaline solution, and the formation of other hibiscoquinones can be accounted for by related processes. It is suggested that the hibiscoquinones are derived *in vivo* from the hibiscones.

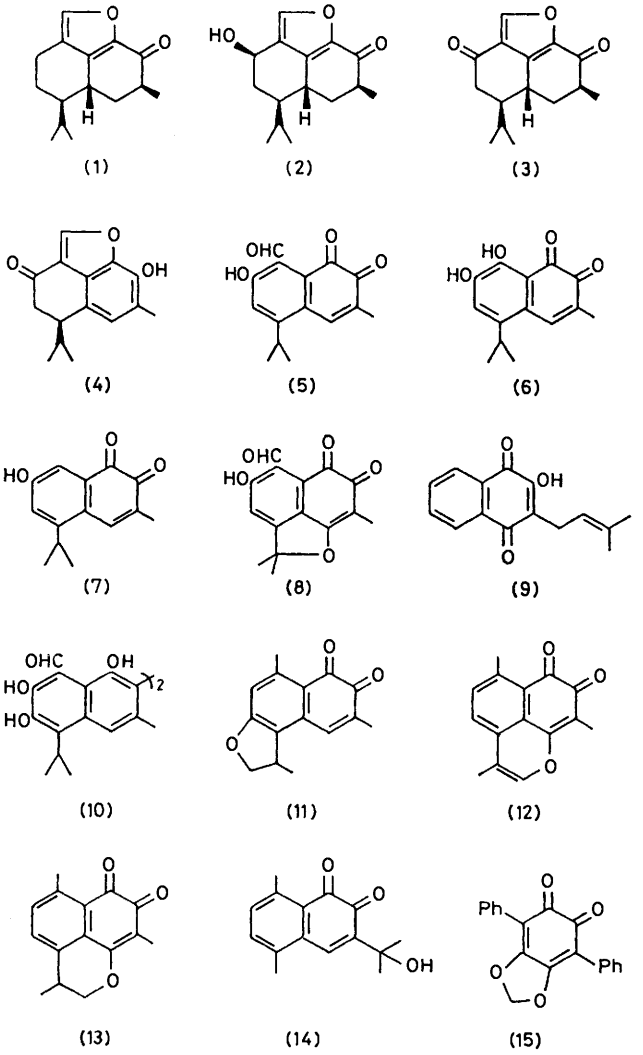
In the preceding paper [1] we reported on the sesquiterpenoid ketones and quinones in the heartwood of *Hibiscus elatus*. As some taxonomists [2] regard *H. elatus* as a subspecies of *H. tiliaceus* it was of interest to compare their extractives. Samples of *H. tiliaceus* wood were obtained from Fiji and from Sri Lanka, and roots were collected in Brazil.

Extraction with chloroform of the Fijian wood yielded the series of hibiscones A—D (1)—(4) previously found [1] in *H. elatus*, and also lapachol (9),[3] hitherto unknown in Malvaceae. The *H. tiliaceus* material from Sri Lanka had reddish heartwood which, like *H. elatus* heartwood, faded on exposure to light (young trees do not have red or pink heartwood). Extraction with chloroform revealed the presence of hibiscones A—D (1)—(4), hibiscoquinones A—D (5)—(8), and hibiscolactone (probably an artefact),[1] all of which we found [1] in *H. elatus*. Thus, apart from the lapachol, the chemical evidence does not distinguish between *H. elatus* and *H. tiliaceus*. Anatomical examination of the *H. tiliaceus* samples confirmed their identity but anatomically they are indistinguishable from *H. elatus*.[4]

The roots of *H. tiliaceus* from Brazil contained none of the foregoing compounds; however four related pigments were isolated. These were gossypol (10) (optically inactive), and mansonones D (11), F(12), and (probably) E (13). Gossypol occurs in *Gossypium* and other Malvaceae genera,[5] so its occurrence in *Hibiscus* is not surprising, but the mansonones have only been reported [6] previously in *Mansonia* (Sterculiaceae) [3] and Ulmaceae.[7]

Biogenesis.—There are several hundred naturally occurring quinones [3] of which about thirty are *ortho*-quinones. Most of the *ortho*-quinones are terpenoid, and *all* the sesquiterpenoid quinones in wood are *ortho*-quinones [mansonones,† hibiscoquinones, and emmotin-H (14) [8]]. There is little doubt that *para*-quinones are formed *in vivo* by the introduction of oxygen into the *para*-position of a phenol, and it is generally assumed that *ortho*-quinones are similarly biosynthesised from precursor phenols although there is little direct evidence. However, the assumption is unwarranted as non-terpenoid *ortho*-quinones are very diverse in structure [3,9,10] and in phlebiarubrone (15), for example, all four oxygen atoms come from phenylpyruvate.[11] We suggest that the hibiscoquinones arise in a different way.

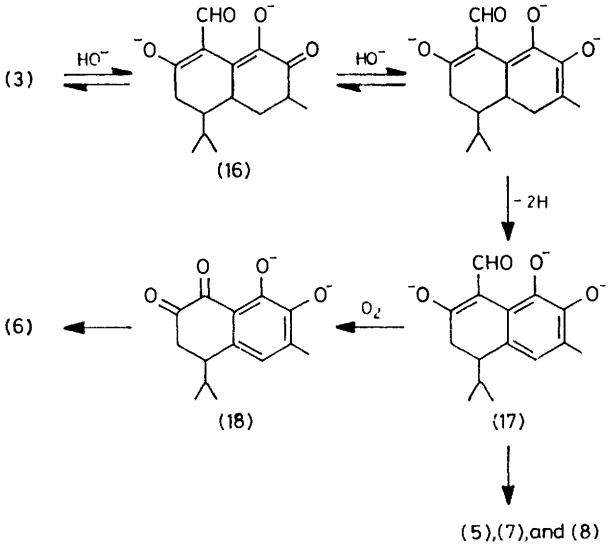
The hibiscones A—D form an oxidation sequence



below the level of the hibiscoquinones. Oxidation of the ketones to the quinones can be shown as follows. Hibiscone C (gmelofuran) (3) is a colourless compound but when left on a silica gel t.l.c. plate exposed to light

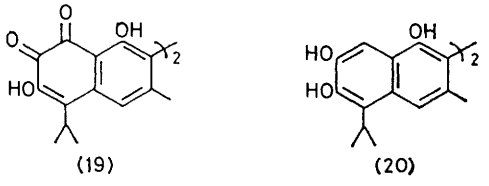
† Mansonone B is a 2-hydroxy-1,4-quinone which is tautomeric with a 4-hydroxy-1,2-quinone.

and air for a day, it becomes green. This green colour is due to the anion of hibiscoquinone B (6) (the quinone is acidic and the silica gel slightly basic). Similarly, if a solution of hibiscone C is stirred in alkaline methanol the yellow solution [1] slowly becomes green, and if the solution is shaken in air until two molar equivalents of oxygen have been taken up, hibiscoquinone B is formed



SCHEME

along with colourless products. Autoxidation of hibiscone D (4) proceeds under the same conditions to give hibiscoquinone B (6), exclusively. A likely course of events is outline in the Scheme although other sequences can be written. The formation of the yellow anion (16) from hibiscone C (3) has been discussed.[1] Aromatisation to give (17) should be an easy oxidative process, and further reaction of (17) with oxygen to give (18) [and thus hibiscoquinone B (6)] follows the normal α-fission of aliphatic aldehydes by autoxidation in alkaline solution.[12,13] An analogous reaction is the



conversion of gossypol (10) into the di-*o*-quinone (19) by autoxidation in alkaline solution.[14]

Although no other quinones were detected in the autoxidation experiments it can be seen that (17) is also a plausible precursor of hibiscoquinone A (5), hibiscoquinone D (8) by aromatisation and oxygenation at C-4,[15] and hibiscoquinone C (7) by β-cleavage of the formyl group. A parallel for that is seen in the formation of (20) from gossypol (10) under alkaline conditions.[16,17] Thus all the hibiscoquinones can be derived from hibiscones C and D by reasonable oxidative processes which leads us to suggest that the quinones are formed *in vivo* from the ketones, the two oxygen atoms which eventually appear in the quinone carbonyl groups being introduced at an early stage after (or before) the formation of the carbon skeleton from farnesyl pyrophosphate.

In principle, the mansonones in *H. tiliaceus* roots could be derived by a similar pathway although no other sesquiterpenes were found. However, in Ulmaceae the mansonones frequently co-occur with 7-hydroxycadalene and other naphthols which could obviously be the quinone precursors, as has been suggested.[7c]

EXPERIMENTAL

Known compounds were identified by direct comparison (i.r., n.m.r., and mass spectra, and t.l.c.) with authentic samples. All operations involving hibiscoquinones were conducted as far as possible in the absence of light.

Extraction of Hibiscus tiliaceus *Wood from Fiji.*—The ground wood (1.2 kg) was extracted (Soxhlet) in portions (200 g) with chloroform for 24 h. Evaporation left a brown gum (21 g) which was chromatographed on acid-washed silica gel in chloroform containing increasing amounts of methanol (0—20%); 28 fractions (*ca.* 250 ml each) were collected. Fractions 10—15 yielded two major compounds which were separated by preparative t.l.c. on silica gel in chloroform (× 2) followed by chloroform–methanol (9 : 1) to give lapachol (9) as yellow plates, m.p. 140° (from chloroform–light petroleum) (42 mg), and hibiscone A (1) as needles, m.p. 94—95° (from chloroform–light petroleum) (20 mg). Fractions 16—21 also contained two major components which were separated by repeated preparative t.l.c. in the above systems yielding hibiscone C (gmelofuran) (3) as needles, m.p. 124—125° (from chloroform–methanol) (560 mg), and hibiscone D (4) as needles, m.p. 139° (from chloroform) (20 mg). The residue from fractions 22—26 was rechromatographed on silica gel in chloroform–methanol (successively 5 : 1, 2 : 1, and 1 : 1). The 1 : 1 eluate was evaporated leaving a residue which crystallised from chloroform–methanol to give hibiscone B (2) as needles, m.p. 122—123° (260 mg).

Extraction of Hibiscus tiliaceus *Wood from Sri Lanka.*—The ground heartwood (500 g) was extracted (Soxhlet) with chloroform for 36 h. Evaporation left a dark brown sticky mass which was chromatographed on silica gel in chloroform. Two fractions, green and red, were collected. The first (green) fraction was shaken with 2M-hydrochloric acid. The solution became pink, and after drying, evaporation, and repeated preparative t.l.c. on silica gel (made up in 0.5M-hydrochloric acid) in chloroform afforded hibiscoquinone B [6] as purple-brown crystals, m.p. 169° (from benzene) (28 mg). The second (red) fraction was separated by preparative t.l.c. on silica gel in chloroform–methanol to give, in order of decreasing R_F values, hibiscoquinone A (5) as purple-brown needles, m.p. 145° (from methanol) (75 mg), hibiscones A (1) (5 mg), C (3) (1.7 g), and D (4) (180 mg), hibiscoquinone C (7) as red-brown needles, decomp. > 220° (from methanol) (52 mg), hibiscone B (2) as needles, m.p. 121° (from methanol) (196 mg), and hibiscolactone as needles, m.p. 225—226° (from acetone) (7 mg). Finally the bluish-green zone at the top of the column was stripped off with 10% acetic acid in methanol. The pink eluate was evaporated and purified by preparative t.l.c., as above, to give more hibiscoquinone B (28 mg).

Extraction of the heartwood (150 g) with cold chloroform, gave, in addition to the above compounds, hibiscoquinone

D (8) and a trace of an unidentified blue quinone. Hibiscoquinone D was isolated by preparative t.l.c. on silica gel in chloroform–methanol (50 : 1) to give dark brown needles, decomp. >350° (from chloroform) (15 mg).

Extraction of Hibiscus tiliaceus *Roots from Brazil.*—The ground root (300 g) was extracted (Soxhlet) with light petroleum (b.p. 60—80°) and chloroform, successively. On concentration of the petroleum extract gossypol (10) separated; it crystallised from chloroform–light petroleum as small yellow prisms, m.p. 192—194° (decomp.) (425 mg), $[\alpha]_D^{20}$ 0.0 (*c* 2.10 in $CHCl_3$). The hexamethyl ether formed needles, m.p. 214° (from chloroform) (lit.,[13] 216—218°) (Found: M^+, 602.287 9. Calc. for $C_{36}H_{42}O_8$: *M*, 602.287 8). The chloroform extract contained two major coloured components and a trace of gossypol. Evaporation left a viscous mass which was chromatographed on silica gel in chloroform (twice), and further purified by repeated preparative t.l.c. in the same solvent to give mansonone D (11) as dark orange prisms, m.p. 174° (from chloroform–light petroleum) (145 mg), and mansonone F (12) as violet-brown needles, m.p. 213° (from chloroform) (40 mg). A fourth pigment (5 mg) was almost certainly mansonone E (n.m.r. and mass spectra) but was not obtained pure.

Autoxidations.—(*a*) Hibiscone C (gmelofuran) (100 mg) in methanol (25 ml) and 2M-sodium hydroxide (2.5 ml) was shaken in air until 2 mol. equiv. (19.5 ml) of oxygen had been absorbed (7.5 h). The green solution was acidified with 2M-hydrochloric acid, becoming pink, extracted with chloroform, washed, dried, and evaporated. The residue crystallised from benzene to give hibiscoquinone B, m.p. 168° (18.4 mg), spectroscopically identical with authentic material.

(*b*) Similarly, hibiscone D (24.4 mg) in methanol (10 ml) and 2M-sodium hydroxide (1 ml) was shaken in air with uptake of 4 ml (*ca.* 1.5 mol. equiv.) of oxygen. Work-up of the green solution as in (*a*) gave hibiscoquinone B (20 mg).

(*c*) Experiment (*a*) was repeated using ethanol (10 ml) and water (10 ml) in place of methanol. The pink solution was diluted and distilled. The distillate was made alkaline (NaOH), evaporated to small bulk, and acidified with acetic acid. It gave a positive test for formic acid with mercuric chloride.[18]

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