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SYNTHESIS OF GREVILLINS AND THEIR BIOGENETIC INTERRELATIONSHIP WITH TERPHENYLQUINONES, XYLERYTHRINS AND PULVINIC ACIDS

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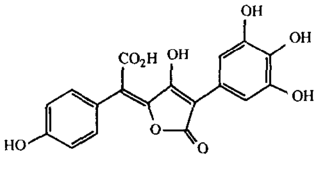
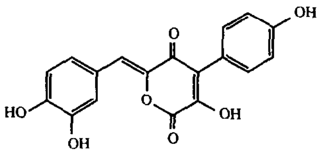
Summary: A synthesis of the grevillin group [e.g.(2),(16)], of pigments present in fungi, using benzylacyloins, *viz* (9), as key intermediates is described, and the biogenetic interrelationships between them and the terphenylquinone, xylerythrin and pulvinic acid families of natural colouring matter, are exemplified with the *in vitro* conversions (16)→(17), (17)→(20) and (17)→(22).

A very wide range of oxygen ring compounds occur in Nature as colouring matters. Some of the most striking examples are produced by fungi (Macromycetes)[1], and include yellow and red pulvinic acid pigments(1), orange grevillins(2), the magenta terphenylquinones(3), the red xylerythrins(4), together with the orange-coloured furanones(5) and yellow-green fluorescent pulvinones(6)[2-4]. As part of an investigation into the origins and biogenetic interrelationships between the fungal pigment types (1)→(6), we have developed a synthesis of the grevillins(8) using benzylacyloins, *viz* (9), as key intermediates [Nature is thought to use corresponding substituted 1,2-dione dimers(7) of arylpyruvic acids (Scheme 1)[1]] and illustrate their *in vitro* conversions into terphenylquinones(17), and thence the



(1)



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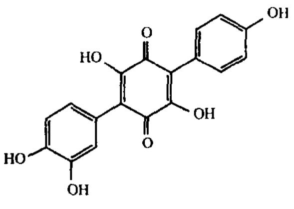

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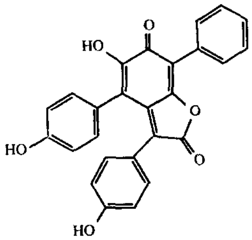

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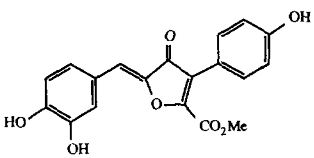

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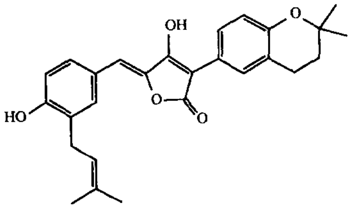
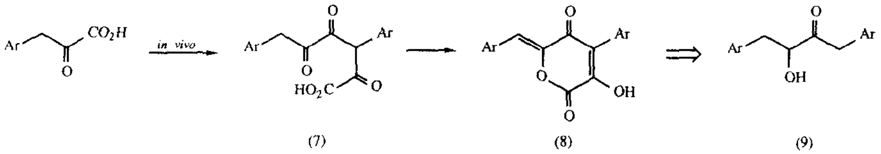


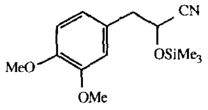
(6)

xylerythrins(20) and pulvinic acids(22).

Using established methodology[5], addition of the Grignard reagent derived from 4-methoxybenzyl chloride to the O-trimethylsilylcyanohydrin(10) first led to the unsymmetrically substituted benzylacyloin(11, 71%). Addition of ethyl oxalyl chloride to (11) in the presence of triethylamine (THF, 25°C, 10min) next led to the oxalate(12, 58%), which with 1,8-diazabicyclo[5.4.0]undec-7-ene(DBU) (2 equivs., DMF, -15°C)[6] was smoothly converted into the dihydrogrevillin(13a, 72%). Methylation of (13a), using diazomethane, followed by treatment of the resulting methyl ether(13b) with bromine in acetic acid then led (77%) to the bromo-derivative(14)[7]. Elimination of the elements of hydrobromic acid from (14) (DBU, C_6H_6), followed by demethylation in the presence of boron tribromide (reflux CH_2Cl_2, 3h) finally produced grevillin B(2, 38%) as red crystals, m.p. 258°C (decomp.) which showed identical spectroscopic data to those of natural material produced by the fruiting bodies of *Suillus grevillei*[4,8].



Scheme 1



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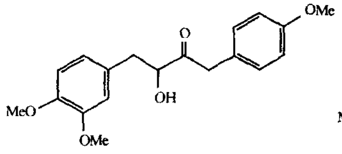

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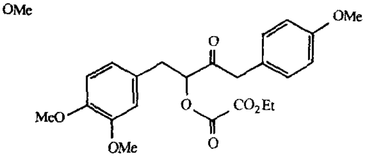

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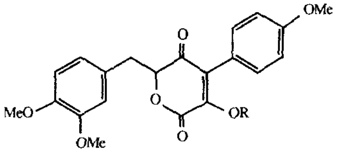
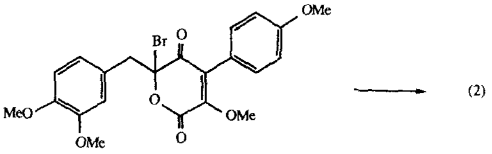


(13)

a, R = H; *b*, R = Me

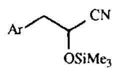


(14)

In a similar sequence of reactions, the cyanohydrins(15a) and (15b) were elaborated to the corresponding grevillins (16a) and (16b) respectively.

The isomeric relationship between the grevillin(16) and terphenylquinone(17) structures is formally analogous to the relationship between the ylidenebutenolide and cyclopentenedione structures, *viz* (18) and (19), which we have examined in detail much earlier[9]. This analogy could be fully demonstrated when the grevillin(16a) was treated with sodium ethoxide in ethanol[10]. A dense purple precipitate formed almost immediately;

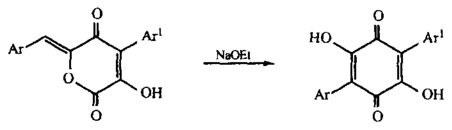
acidification and work-up then gave the known terphenylquinone(17a, 90%)[11]. In a similar manner the synthetic grevillins (16c)[12] and (16d) could be isomerised in the presence of sodium ethoxide to the terphenylquinones (17c) and (17d) respectively.



(15)

a Ar = C_6H_5

b Ar = 4 - $OMe{\cdot}C_6H_4$



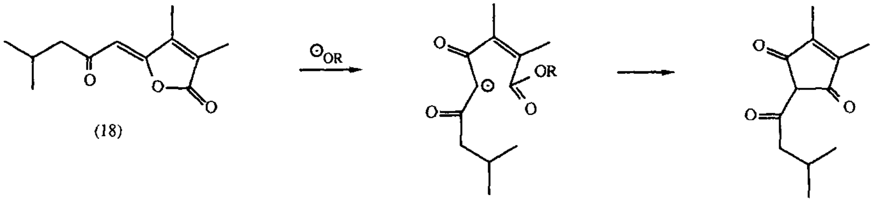
(16) (17)

a Ar = Ar^1 = C_6H_5

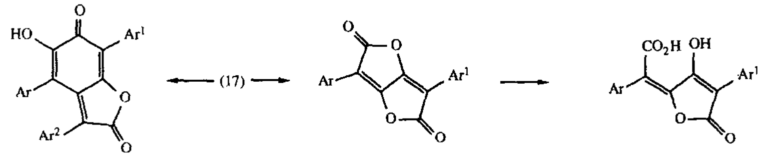
b Ar = 4 - $OH{\cdot}C_6H_4$; Ar^1 = C_6H_5

c Ar = 4 - $OMe{\cdot}C_6H_4$; Ar^1 = C_6H_5

d Ar = $PhCH_2OC_6H_4$; Ar^1 = C_6H_5



(18) (19)



(20) (21) (22)

a Ar = Ar^1 = Ar^2 = C_6H_5

b Ar = Ar^1 = C_6H_5; Ar^2 = 4 - $OH{\cdot}C_6H_4$

c Ar = Ar^1 = C_6H_5; Ar^2 = 4 - $NH_2{\cdot}C_6H_4$

d Ar = C_6H_5; Ar^1 = Ar^2 = 4 - $OH{\cdot}C_6H_4$

a Ar = Ar^1 = C_6H_5

b Ar = 4 - $OMe{\cdot}C_6H_4$; Ar^1 = C_6H_5

a Ar = Ar^1 = C_6H_5

b Ar = 4 - $OH{\cdot}C_6H_4$; Ar^1 = C_6H_5

c Ar = C_6H_5; Ar^1 = 4 - $OH{\cdot}C_6H_4$

Terphenylquinones have previously been linked biogenetically to the xylerythrin(4) and the pulvinic acid(1) families of natural pigments[1-4]. In this work we have added further support for this biogenetic link with the conversion of the terphenylquinones (17a) and (17d) to the corresponding xylerythrins(20)[including peniophorin(4)] (using $Ar^2CH_2CO_2H$, Ac_2O, NaOAc; then HBr-HOAc)[2], together with the conversions of (17a) and (17c) to the pulvinic acids (22a) and (22b)/(22c) respectively *via* the corresponding dilactone intermediates (21a) and (21b) (i, DMSO, Ac_2O, 100°C[13]; ii, NaOMe-MeOH; iii, c.HCl; iv, CH_2N_2[14]; v, Me_3SiI[15])[16].

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6. cf. H-J. Lohrisch, L. Kopanski, R. Herrmann, H. Schmidt and W. Steglich, Liebigs Ann.Chem., 1986, 177.
7. Attempted direct bromination of (13a), using a range of methods (e.g. Br_2-HOAc; NBS-$h\nu$), resulted in the formation of intractable gums.
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12. The grevillin (17c) was obtained from the corresponding bis-methyl ether, following selective deprotection of the pyrandione OMe ether group using BBr_3 (CH_2Cl_2, Δ, 0.5h), whereas grevillin (17d) was produced by the procedure described by W. Steglich et.al.[6]
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16. Satisfactory spectroscopic data together with microanalytical and/or mass spectroscopic data were obtained for all new compounds. Known natural and non-natural pigments synthesized in this study showed physical and spectroscopic data consistent with those in the literature.

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