Synthesis of Retrochinensin; a New Naturally Occurring 4-Aryl-2,3-naphthalide Lignan

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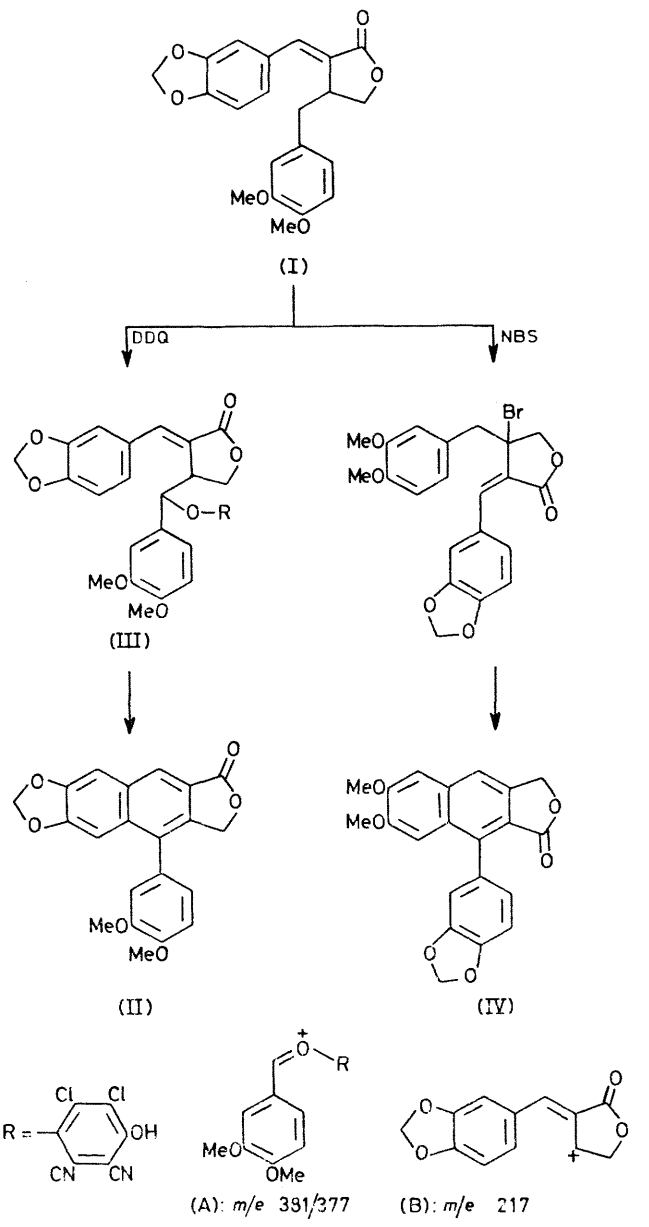
Summary 2,3-Dichloro-5,6-dicyanobenzoquinone-induced oxidative cyclization of suchilactone (I) afforded retrochinensin (II), a new naturally occurring 4-aryl-2,3-naphthalide lignan, in high yield; treatment of (I) with *N*-bromosuccimide on the other hand, afforded justicidin B (IV) in high yield.

THE ontogenic and seasonal variations of the lignan constituents of *Polygala chinensis*[1,2] prompted us to examine the role, if any, of its major monoarylidenebutyrolactone lignan, suchilactone (I), in the formation of the congener 1- and 4-aryl-2,3-naphthalide lignans. Previous reports[3–5] suggested diarylidenebutyrolactone lignans as likely intermediates (*via* cyclic peroxides or β-apolignans) to arylnaphthalide lignans.

In the present study, two routes, (i) allylic bromination by *N*-bromosuccinimide (NBS) followed by dehydrobromination, and (ii) dehydrogenation by 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), were envisaged for the synthesis of the diarylidene from (I). A three-step synthesis of (I) has been reported before.[6]

Refluxing (I) with NBS, in CCl_4, directly afforded justicidin B (IV) in high yield (72%). Dehydrogenation of (I) (1 mmol) with DDQ (1 mmol), in dioxan, on the other hand, gave a 4-aryl-2,3-naphthalide lignan (II), (34%), an unstable lignan–DDQ adduct (III), (15%), and unchanged (I) (43%). The lignan–DDQ adduct was assigned structure (III) on the basis of the following evidence. It showed u.v. maxima similar to those of (I); when the mass spectrum was recorded, it fragmented in the direct inlet system before exhibiting any molecular ion peak but characteristic fragment-ion peaks appeared at *m/e* 381 (rel. int., 1·2%), 377 (2·8) (species A) 366 (68, diarylidene), 232 (3·8), 231 (6), 228 (12·5), 227 (18) (DDQ–H_2), 217 (100, species B), 187 (5·5), 165 (3), 150 (2), 149 (5), and 121 (2). On treatment with HCl it afforded the corresponding diarylidene and DDQ–H_2. The synthesis of the diarylidene has been reported before.[3] When kept in acetone solution, (III) was converted into diphyllin, presumably *via* the diarylidene, while refluxing in benzene with a further quantity (1 : 1) of DDQ afforded (II).

Compound (II)† crystallized from alcohol as colourless needles, m.p. 234 °C; R_f 0·38 (C_6H_6–HOAc, 98 : 2), blue fluorescence under short-wave u.v. lamp; λ_{max} (log ε) 250 (4·61), 315 (3·95), and 350 infl. (3·57) nm; ν_{max} (Nujol) 1766, 1635, and 938 cm^{-1}; δ ($CDCl_3$) 8·3 (1H, s, 1-H), 7·36—6·95 (5H, m, aromatic), 6·14 (2H, s, $-OCH_2O-$), 5·24 (2H, q, lactone $-CH_2-$), 4·02 (3H, OMe), and 3·91 (3H, OMe); *m/e* 364 (M^+, 100%, $C_{21}H_{16}O_6$), 349 (4), 335 (7), 307 (3), and 306 (2). The yield of (II) was much improved (255 mg, 85%) when (I) (298 mg, 0·8 mmol) was refluxed (18 h) with DDQ (365 mg, 1·6 mmol) in anhydrous benzene. The product was obtained as a homogeneous entity by a single crystallization from alcohol.



† Munakata *et al.* (K. Munakata, S. Marumo, K. Ohta, and Y.-L. Chen, *Tetrahedron Letters*, 1967, 3821) also synthesized (II) by a multistep procedure and reported its m.p. (280 °C), u.v., and i.r. data; the spectral data are comparable to those given here. Rao *et al.* (B. V. G. Rao, L. R. Row, and P. Satyanarayana, *Indian J. Chem.* (*B*), 1978, **16**, 68) recently obtained (II) in traces, while synthesizing chinensin[2] and reported only its m.p. (240 °C).

The method exemplifies one of the simplest synthetic processes for 4-aryl-2,3-naphthalide lignans. Incidentally, it provides the first laboratory analogy for the biogenesis of 'retro-disposed' lignans from monoarylidenebutyrolactone intermediates. Compound (II), which we named retrochinensin, has been recently found in *Justicia prostata* (Acanthaceae) along with a number of 4-aryl-2,3-naphthalide lignans.[7]

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