Novel Isoflavan–Pterocarpan Interconversions: Some Structural Requirements for Cyclization

By PIETER J. VAN DER MERWE, GERHARDUS J. H. RALL,* and DAVID G. ROUX
(*Department of Chemistry, University of the Orange Free State, P.O. Box* 339, *Bloemfontein*, 9300 *Republic of South Africa*)

Summary Photolyses of pterocarpans in methanol and in acetic acid solutions provide novel synthetic access to 4-methoxy- and 4-acetoxy-2′-hydroxy-3,4-*trans*-isoflavans, respectively, and hence to 2′,4-dihydroxy-3,4-*trans*- analogues; easy, if not spontaneous, reversion of both 4-methoxy- and 4-hydroxyisoflavans to pterocar-

pans, compared with recalcitrant 2′-hydroxyisoflav-3-enes, indicates the significance of a suitable leaving group in the benzylic 4-position combined with a reduced heterocyclic ring at C-3 in promoting cyclization.

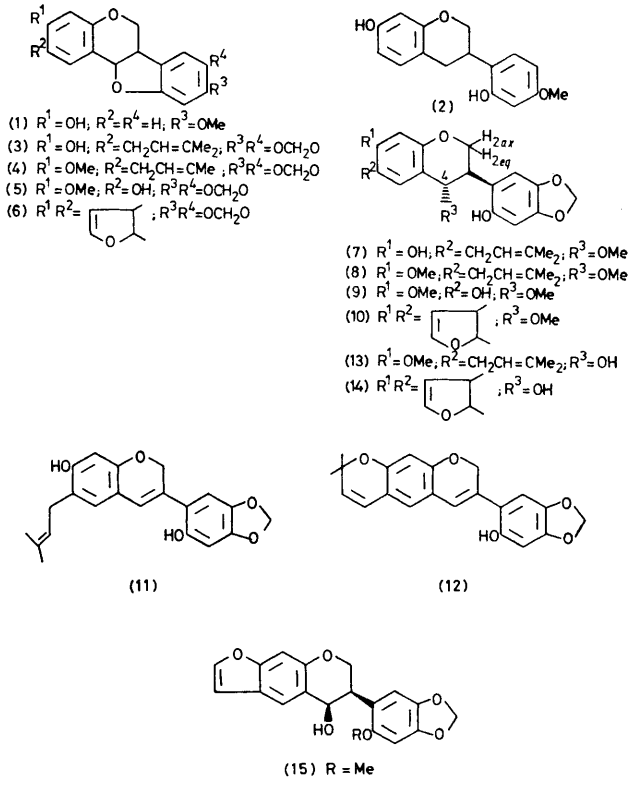
REDUCTIVE processes similar to those postulated[1] for conversion of pterocarpans into 2′-hydroxyisoflavans during isoflavonoid biosynthesis[2] are induced by fungi as part of a phytoalexin detoxification sequence.[3,4] Feeding experiments have also implicated the existence of the reverse process by establishing the mutual interconversion of demethylhomopterocarpin (**1**) and the 2′-hydroxyisoflavan, vestitol (**2**).[5]

The results lend support to the suggestion[5] that a common intermediate exists in the biogenetic pathway linking (**1**) and (**2**). Proposals[5,6] as to the nature of such intermediates include isoflav-3-enes, isoflavonoid quinone methides, and 4-carbonium ions. We now report a novel photochemical ring opening of pterocarpans, chemical evidence favouring a carbonium ion mechanism *via* an isoflavan-4-ol, and similarly based rejection of isoflav-3-enes as likely intermediates in pterocarpan biosynthesis.

Although examples of natural isoflav-3-enes have been reported,[7] our repeated attempts at effecting conversions of the 2′-hydroxyisoflav-3-enes, (**11**) and (**12**) into pterocarpans in acidic media failed, presumably owing to the degree of strain involved in cyclization as is evident from molecular models.

However, the first photochemical fission of the 11–11a C–O bond of the pterocarpans (**3**)—(**6**) (at 300 nm in MeOH) gave the 3,4-*trans*-2′-hydroxy-4-methoxyisoflavans (**7**)—(**10**) *via* zwitterion intermediates (*cf.* ref. 8) as relatively unstable compounds owing to their reversion to pterocarpans.† One of these (**7**) left in MeOH at ambient temperatures slowly reverts to (**3**), while at 50 °C conversion is complete within 1 h. Partial conversions (35—70%) were also obtained when (**8**), (**9**), and (**10**) were heated under the same conditions. As anticipated, these cyclizations to pterocarpans were enhanced dramatically in the presence of acid (3N HCl), running to completion within 30 min in all cases.

Similar results were observed with the 3,4-*trans*-2′,4-dihydroxyisoflavans (**13**) and (**14**), obtained by photolysis of their pterocarpan analogues in AcOH–Me_2CO (9 : 1 v/v) and mild hydrolysis of the resultant 3,4-*trans*-4-acetoxy-2′-hydroxyisoflavans.‡ Easy conversion of isoflavans into



pterocarpans, therefore, appears to be primarily dependent on a reduced heterocyclic ring (at C-3) and an effective leaving group (hydroxy, alkoxy), or on the oxidative generation of a (hypothetical) quinone methide intermediate.

In view of the ease of cyclization to pterocarpans, as demonstrated above, it seems unlikely that 2′-hydroxyisoflavan-4-ols will be encountered as natural products. The reason for the existence of the hitherto only member of this group, (+)-ambanol (**15**),[9] with the C-2′ functional group blocked by methylation, is self-evident.[10]

We thank the South African Council of Scientific and Industrial Research, Pretoria, and the Sentrale Navorsingsfonds of this University for financial support.

(*Received, 6th October* 1977; *Com.* 1050.)

† Satisfactory ^{1}H n.m.r. spectra of these compounds and their *O*-acetates were obtained.

‡ The 3,4-*trans*-2′-*O*-methyl and/or their 2′-*O*-acetates gave satisfactory elemental analyses. Their 3,4-*trans* relative configuration follows from ^{1}H n.m.r. (Bruker WP-80 instrument) spectrometry [*e.g.*, 4-*O*-acetate of (**14**) gave τ($CDCl_3$) 3·76 (4-H, d, $J_{3,4}$ 5·0 Hz), 6·39 (3-H, m), and 5·55 (CH_2, d)] in comparison with the 3,4-*cis* stereochemistry of (+)-ambanol acetate [τ($CDCl_3$) 3·75 (4-H, m, $J_{3,4}$ 4, $J_{2eq,4}$ 1·5 Hz), 6·19 (3-H, sextet, $J_{2ax,3}$ 12·5, $J_{3,4}$ 4·0, $J_{2eq,3}$ 4·0 Hz), 5·70 (2_{eq}-H, octet, $|J_{2eq,2ax}|$ 10·5, $J_{2eq,3}$ 3·5, $J_{2eq,4}$ 1·5 Hz), and 5·38 (2_{ax}-H, q, $|J_{2eq,2eq}|$ 10·5, $J_{2ax,3}$ 12·5 Hz)]. The assignments are in accordance with published data on isoflavan-4-ols (S. Yamaguchi, S. Ito, A. Nakamura, and N. Inoue, *Bull. Chem. Soc. Japan*, 1965, **38**, 2187; S. Yamaguchi, K. Kabuto, Y. Ninomiya, and N. Inoue, *ibid.*, 1970, **43**, 3952).

[1] E. Wong, in 'The Flavonoids,' eds. J. B. Harborne, T. J. Mabry, and H. Mabry, Chapman and Hall, London, 1975, p. 772, and references therein.
[2] E. Wong, *Fortschr. Chem. org. Naturstoffe*, 1970, **28**, 1.
[3] P. W. Steiner and R. L. Millar, *Phytopathology*, 1974, **64**, 586.
[4] V. J. Higgins, *Physiol. Plant Pathol.*, 1975, **6**, 5.
[5] M. Cornia and L. Merlini, *J.C.S. Chem. Comm.*, 1975, 428.
[6] P. M. Dewick and M. Martin, *J.C.S. Chem. Comm.*, 1975, 637.
[7] A. J. Brink, G. J. H. Rall, and J. P. Engelbrecht, *Tetrahedron*, 1974, **30**, 311; T. Kinoshita, T. Saitoh, and S. Shibata, *Chem. Pharm. Bull.*, 1976, **24**, 991; L. Jurd, *Tetrahedron Letters*, 1976, 1741.
[8] L. Salem, *Israel J. Chem.*, 1975, **14**, 89; *Science*, 1976, **191**, 822; T. G. Fourie, D. Ferreira, and D. G. Roux, *J.C.S. Perkin I*, 1977, 125; J. H. van der Westhuizen, D. Ferreira, and D. G. Roux, *ibid.*, p. 1517.
[9] M. E. Oberholzer, G. J. H. Rall, and D. G. Roux, *Tetrahedron Letters*, 1977, 1165.
[10] L. Crombie, P. M. Dewick, and D. A. Whiting, *J.C.S. Perkin I*, 1973, 1285.