Synthesis of the Pulvinic Acid Pigments of Lichen and Fungi

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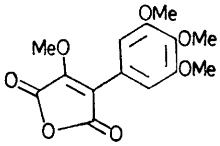
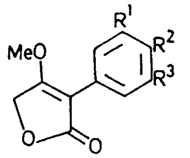
Summary The total syntheses of permethylated derivatives of gomphidic acid (**4a**) and pinastric acid (**5a**), the pulvinic acid pigments found in *Gomphidius glutinosus* and *Lepraria flava*, respectively, are described.

PULVINIC acids have long been recognised as the pigments responsible for the striking yellow and orange colours of lichens.[1] In more recent years they have also been isolated from certain higher fungi belonging to the Boletaceae and Gomphidiaceae.[2] Structural elucidation amongst members of this class of compound has been hampered by the absence of an unambiguous synthetic route to the basic pulvinic acid skeleton.[3] We have recently described an approach towards the synthesis of the related pulvinones,[4] and now report the development of this procedure leading to the first unambiguous synthesis of unsymmetrical pulvinic acids as exemplified by gomphidic acid (**4a**) from *Gomphidius glutinosus*[5] and pinastric acid (**5a**) from *Lepraria flava*[6] and other lichens.

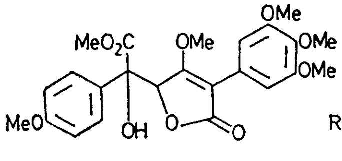
The maleic anhydride derivative, (**1**), yellow needles, m.p. 151—152 °C, ν_{max} 1819, 1758, and 1648 cm^{-1}, was first prepared from 3,4,5-trimethoxyphenylacetonitrile by the methods outlined previously.[4] The reduction of (**1**) with $LiAlH_4$ then produced the 3-methoxybutenolide (**2a**), colourless prisms, m.p. 136—137 °C, ν_{max} 1732 and 1636 cm^{-1}, τ 2·76 (2H), 5·19 (CH_2), 6·01 (OMe), and 6·09 (2 × OMe), and the corresponding 4-OH derivative was also formed. The metallation of (**2a**) with lithium *N*-cyclohexyl-*N*-isopropylamide at −78 °C followed by reaction with methyl 4-methoxybenzoylformate was largely regioselective producing the tertiary alcohol (**3**). The dehydration of (**3**), accomplished only with extreme difficulty in a hot suspension of P_2O_5 and dry benzene, followed by chromatography and crystallisation then produced permethylated gomphidic acid (**4b**) as orange crystals, m.p. 66—70 °C, λ_{max} 352 and 279 nm, ν_{max} 1765, 1730, 1665, 1632, and 1605 cm^{-1}, τ 2·85 (2H), 3·1—3·4 m (4H), and 6·1—6·3 (6 × OMe); a comparison of these ^1H n.m.r. shift data with those reported for gomphidic acid from *G.glutinosus*[7] establishes the structure (**4a**) for the natural metabolite.



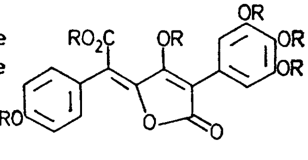
(1)



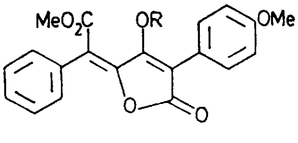
(2) a; $R^1=R^2=R^3=$ OMe
b; $R^1=R^3=$ H; $R^2=$OMe
c; $R^1=R^2=R^3=$H



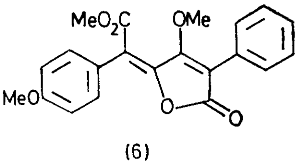
(3)



(4) a; R = H
b; R = Me



(5) a; R = H
b; R = Me



(6)

In a similar sequence the butenolide (**2b**) and methyl benzylformate gave the *O*-methyl pinastric acid (**5b**), pale yellow needles, m.p. 139—140 °C, λ_{max} 340 nm, ν_{max} 1772, 1722, 1630, and 1601 cm^{-1}, which was identical (mixed m.p. and spectral data) with the *O*-methyl isomer of a synthetic pinastric acid correlated previously with the natural metabolite from *L.flava*.[3] The isomeric *O*-methyl pinastric acid (**6**) obtained in a similar manner from the butenolide (**2c**) and methyl 4-methoxybenzoylformate showed a m.p. of 175—176 °C, λ_{max} 358 nm, ν_{max} 1760, 1724, 1635, and 1602 cm^{-1}.

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[1] See F. M. Dean, 'Naturally Occurring Oxygen Ring Compounds,' Butterworths, London, 1963.

[2] *Cf.* (a) R. L. Edwards and M. Gill, *J.C.S. Perkin I*, 1973, 1529, 1538, and refs. therein; (b) A. Bresinsky, H. Besl, and W. Steglich, *Phytochemistry*, 1974, **13**, 271, and refs. therein; (c) M. C. Gaylord, R. G. Benedict, G. M. Hatfield, and L. R. Brady, *J. Pharm. Sci.*, 1970, **59**, 1419.

[3] See extensive investigations of the structure of pinastric acid by Seshadri *et. al.* 1955—1963; S. C. Agarwal and T. R. Seshadri, *Tetrahedron*, 1963, **19**, 1965 and refs. therein; *cf.* ref. 2a.

[4] D. W. Knight and G. Pattenden, *J.C.S. Chem. Comm.*, 1975, 876.

[5] W. Steglich, W. Furtner, and A. Prox, *Z. Naturforsch*, 1969, **24b**, 941.

[6] *Cf.* ref. 1; O. P. Mittal and T. R. Seshadri, *J. Chem. Soc.*, 1956, 1734.

[7] W. Steglich, H. Besl, and K. Zipfel, *Z. Naturforsch*, 1974, **29b**, 96.