A Convenient Route to Some Naturally Occurring Hydroxynaphthaquinones

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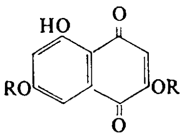
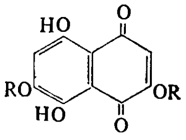
THE biosynthesis of the fungal metabolites, flaviolin[1] (Ia) and mompain[2] (IIa), most probably involves hydroxylation and oxidation of the acetate-malonate derived naphthalene (IIIa). We report a convenient synthesis of these and some related hydroxynaphthaquinones.

Methyl 3,5-dihydroxyphenylacetate, prepared from dimethyl acetonedicarboxylate,[3] reacted smoothly with acetic anhydride in the presence of boron trifluoride etherate to give methyl curvulinate[4] (IV) in 70% yield. Treatment of (IV) with sodium methoxide in refluxing methanol under an atmosphere of nitrogen afforded the unstable tetrahydroxynaphthalene (IIIa), λ_{max} (EtOH) 241, 287, 297, 310, and 325 $m\mu$, which on aerial oxidation in alkaline solution gave the quinone (Ia) in 65% yield, m.p. 250° (decomp.), identical (u.v., i.r., and t.l.c.) with natural flaviolin. A similar oxidation in the tetracycline field has recently been reported.[5] Attempts to prepare mompain by hydroxylation and oxidation of (IIIa) or by hydroxylation of flaviolin have so far been unsuccessful.



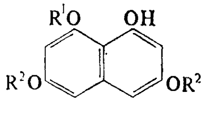
(Ia) R = H

(Ib) R = Me



(IIa) R = H

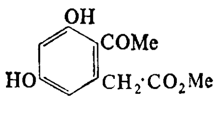
(IIb) R = Me



(IIIa) $R^1 = R^2 = H$

(IIIb) $R^1 = H$, $R^2 = Me$

(IIIc) $R^1 = R^2 = Me$



(IV)

Recently the quinones (Ib) and (IIb) have been isolated[6] from the same *Streptomyces* strain and it is conceivable that either of the naphthalenes

(IIIa) or (IIIb) could be the biosynthetic precursor of these quinones. The dimethoxy-derivative (IIIb) was readily prepared by selective demethylation of the trimethoxynaphthalene[7] (IIIc) with magnesium iodide etherate and characterized as its diacetate, m.p. 160—163°. Oxidation of (IIIb) with Fremys' salt gave the hydroxy-quinone (Ib), 84%, m.p. 264—266°, while oxidation with trifluoroacetic anhydride and hydrogen peroxide in methylene dichloride yielded a mixture of quinonoid material which on chromatography afforded (Ia) as well as the naphthazarin (IIb), m.p. 275—276°. Both quinones were identical (u.v., i.r. and t.l.c.) with the natural products. Acid hydrolysis of (IIb) gave the hydroxy-quinone (IIa) whose physical properties agreed with those reported for mompain.[2] Experiments to test the generality of this synthetic route are in progress.

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[1] B. D. Astill and J. C. Roberts, *J. Chem. Soc.*, 1953, 3302; B. W. Bycroft and J. C. Roberts, *ibid.*, 1962, 2063.
[2] S. Natori, Y. Kumada, and H. Nishikawa, *Chem. and Pharm. Bull.* (*Japan*), 1965, **13**, 633.
[3] W. Theilacker and W. Schmid, *Annalen*, 1950, **570**, 15.
[4] A. Kamal, M. Ali Khan, and A. Ali Qureshi, *Tetrahedron*, 1963, **19**, 111.
[5] C. H. Hassall and T. E. Winters, *Chem. Comm.*, 1967, 77.
[6] N. N. Geber and B. Wieclawek, *J. Org. Chem.*, 1966, **31**, 1496.
[7] B. W. Bycroft and J. C. Roberts, *J. Chem. Soc.*, 1963, 4868.