The Synthesis of (±) Mitorubrin

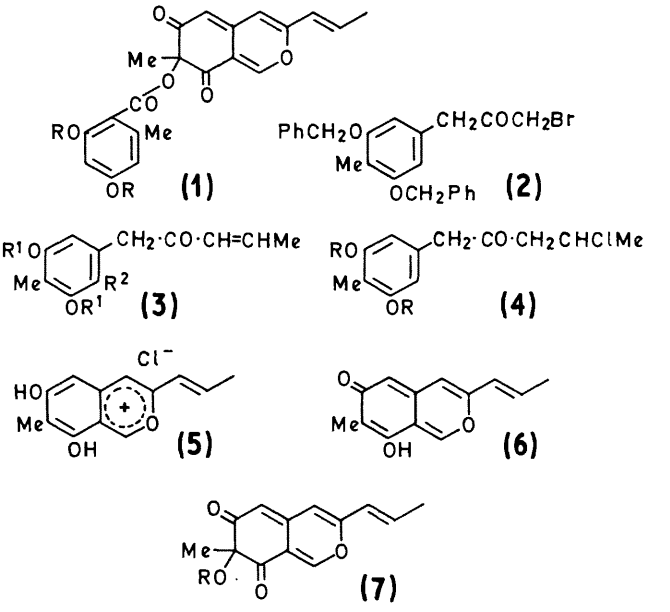
By R. CHONG, R. W. GRAY, R. R. KING, and W. B. WHALLEY*
(*The School of Pharmacy, The University, 29/39 Brunswick Square, London W.C.1*)

Summary The metabolite, mitorubrin, elaborated by the phytotoxic fungus, *Penicillium rubrum*, has been synthesised.

THE phytotoxic fungus, *P. rubrum*, produces a metabolite, mitorubrin[1] (**1**; R=H), a member of the sclerotiorin[2] group of fungal metabolites. In an extension of our recent synthesis[3] of sclerotiorin we now describe the synthesis of (±)mitorubrin, and thus confirm the structure which had previously been based on spectroscopic evidence.[1]

Reaction of the phosphorane of 3,5-dibenzyloxy-4-methylphenyl-ω-bromo-acetone[3] (**2**) [prepared[3] by a process similar to that used for the 3,5-diacetoxy-analogue of (**2**)] with acetaldehyde gave 1-(3,5-dibenzyloxy-4-methylphenyl)pent-*trans*-3-ene-2-one (**3**; $R^1 = PhCH_2$, $R^2 = H$). Addition of hydrogen chloride to (**3**; $R^1 = PhCH_2$, $R^2 = H$) gave the chloro-ketone (**4**; R = $PhCH_2$) which was debenzylated to (**4**; R = H) by BCl_3–CH_2Cl_2 at −70°. Percolation of a solution of (**4**; R = H) through alumina gave 1-(3,5-dihydroxy-4-methylphenyl)pent-*trans*-3-ene-2-one (**3**; $R^1 = R^2 = H$) which was converted by the action of $(EtO)_3CH$–HCl during five seconds followed by precipitation with ether (conditions critical) into the oxonium salt (**5**). This salt rapidly decomposed at room temperature and immediately upon isolation was dissolved in ethanol containing potassium acetate to yield 1-(3,5-dihydroxy-6-formyl-4-methylphenyl)-pent-*trans*-3-ene-2-one (**3**; $R^1 = H$, $R^2 = CHO$), m.p. 167° (decomp.).

This aldehyde was converted into the pyronoquinone (**6**) [too unstable to isolate] by solution in alcohol containing phosphorus pentoxide. Acetoxylation of (**6**) *in situ* by the addition of AcOH–$Pb(OAc)_4$ under N_2 gave (**7**; R = Ac) in yellow prisms, m.p. 180°, which was converted by NaOEt solution at 0° into (**7**; R = H). A solution of (**7**; R = H) in benzene containing 2,4-dibenzyloxy-6-methylbenzoic acid and $(CF_3{\cdot}CO)_2O$ gave (±)-di-*O*-benzylmitorubrin (**1**; R = $PhCH_2$), m.p. 174°. Debenzylation of this at −70° with BCl_3–CH_2Cl_2 gave (±)-mitorubrin (**1**; R = H) indistinguishable on the basis of t.l.c., i.r., u.v., and mass spectra from natural mitorubrin.



The availability of the pyronoquinone (**6**) which is the parent nucleus of monascorubin,[2] rubropunctatin[2] and monascin[2] establishes an approach to the syntheses of these metabolites.

All new compounds had the requisite analytical and spectral characteristics.

We thank Professor L. Merlini, Milan, for a sample of mitorubrin.

(*Received, November 25th*, 1969; *Com.* 1789.)

[1] G. Büchi, J. White, and G. N. Wogan, *J. Amer. Chem. Soc.*, 1965, **87**, 3484.
[2] W. B. Whalley, *Pure Appl. Chem.*, 1963, **7**, 565.
[3] R. Chong, R. R. King, and W. B. Whalley, *Chem. Comm.*, 1969, 1512.