Total Synthesis of Bikaverin Involving the Novel Rearrangement of an *ortho*-Quinone to a *para*-Quinone

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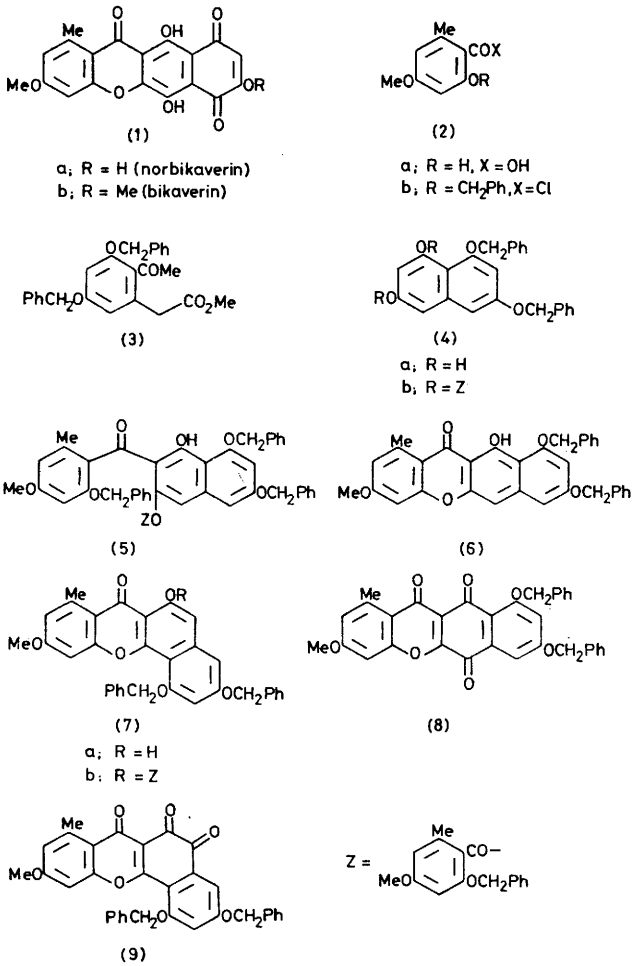
Summary Bikaverin (**1b**) has been synthesised from curvulinic acid and everninic acid.

BIKAVERIN is a red pigment having antiprotozoal activity; ts structure has been determined to be that shown as (**1b**),[1–3] and recently Barton and his co-workers have accomplished its total synthesis.[4] The ready availability of everninic acid (**2a**) in our laboratory[5] prompted us to investigate the synthesis of bikaverin. We now report its total synthesis from curvulinic acid and everninic acid.

Protected methyl curvulinate (**3**) synthesised by the procedure of Roberts *et al.*[6] was cyclized in the presence of NaH in tetrahydrofuran to give the naphthalene derivative (**4**) as an unstable intermediate, which was subsequently treated with 2 equiv. of protected everninic acid chloride (**2b**) to afford the *O*-diacylated naphthalene derivative (**4b**) (45%), m.p. 118 °C. Photo-induced Fries rearrangement (low-pressure mercury lamp, 3000 Å) of (**4b**) gave (**5**) (26·7%), m.p. 68 °C. Treatment of (**5**) with KOH in EtOH gave two isomeric cyclized products, the linear benzoxanthone (**6**) (9·3%), m.p. 234 °C, and the angular isomer (**7a**) (31·4%), m.p. 208 °C.

Cyclization of (**5**) with Me_4NOH instead of KOH afforded (**7a**) (59%), and its *O*-acylated product (**7b**) (17%), m.p. 212 °C. Compound (**7b**) was hydrolysed with ethanolic KOH to give (**7a**) in quantitative yield. Compounds (**6**) and (**7a**) were each oxidized with potassium dichromate in glacial acetic and dioxan to give the *para*-quinone (**8**) (65%), m.p. 250 °C, and the *ortho*-quinone (**9**) (52%), m.p. 250 °C, respectively. By a novel type of rearrangement, (**9**) was transformed into (**8**) in almost quantitative yield by treatment with silica gel.

Treatment of (**8**) with MnO_2 in conc. H_2SO_4 at 60 °C for 20 min gave norbikaverin (**1a**) (28%), m.p. 310 °C (de-



comp.). Treatment of (**1a**) with MeI–Ag_2O[2] gave bikaverin (**1b**), which was identical with an authentic sample provided by Cornforth and Ryback.

All new compounds were characterized satisfactorily by elemental and spectral analyses.

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