Some Novel Cyclisations through Benzophenone Carbanions

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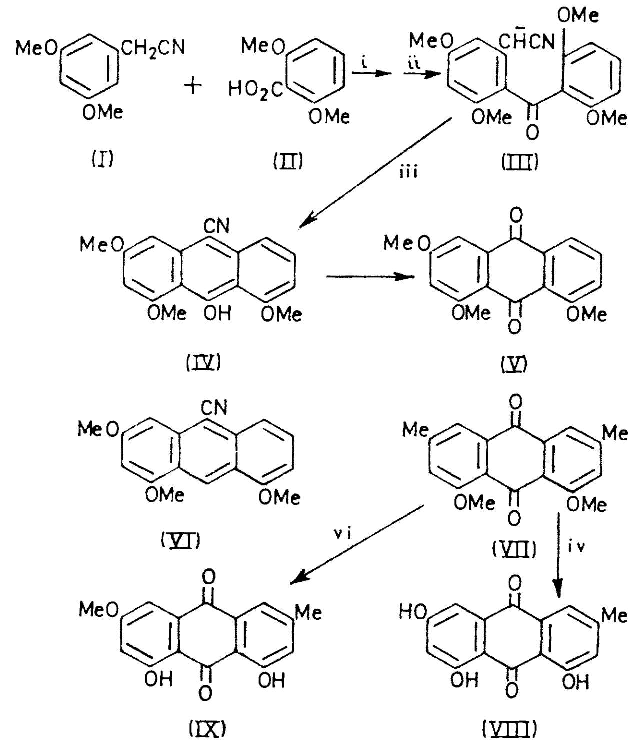
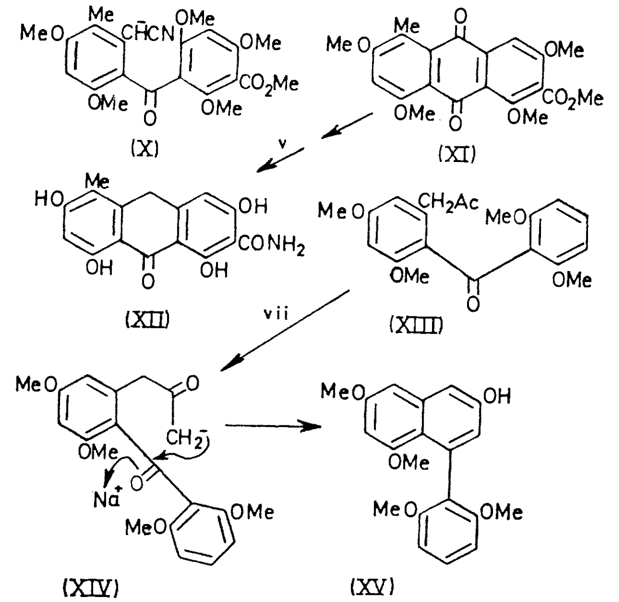
Summary Anthraquinones, including emodin and physcion, and an amide related to the tetracyclines, have been synthesised in high yield through appropriately substituted 2-cyanomethyl-2′-methoxybenzophenones.

As an extension of an earlier investigation,[1] we have established that the anthraquinones (V), emodin (VIII), physcion (IX), and the amide (XII), which is an analogue of the pretetramids, biosynthetic precursors of tetracyclines,[2] may be synthesised in high yield through the related benzophenones. These benzophenones were prepared very readily by the action of a suitably substituted 2-methoxybenzoic acid such as (II) on 1-cyanomethyl-3,5-dimethoxybenzene (I) in the presence of trifluoroacetic anhydride. In a typical case, intramolecular elimination of the 2′-methoxy-group from the carbanion (III) gave an excellent yield of the nitrile (IV), which was converted into the corresponding anthraquinone, quantitatively, by oxidation.



A similar reaction sequence gave tri-*O*-methylemodin (VII) which was converted into physcion (IX) and into emodin (VIII) by demethylation processes. The amide (XII) was prepared through the appropriate carbanion (X) by a sequence involving conversion of the anthraquinone (XI) into the corresponding amide which was demethylated with hydriodic acid in phenol. In one experiment using sodium hydride–dimethylformamide at 100° to generate the carbanion (III), rather than the sodium methoxide–dimethylformamide (or dimethyl sulphoxide) which was used for the other syntheses, the reduction product (VI) was obtained.



(i) $(CF_3CO)_2O$. (ii) NaOMe-$HCONMe_2$. (iii) NaH-$HCONMe_2$ at 100°. (iv) C_5H_5N,HCl. (v) HI-PhOH. (vi) HBr-HOAc. (vii) NaOMe-MeOH.

When the benzophenone (XIII) was used as an alternative to the nitrilo-derivative (III), the base-catalysed ring closure took a different course. There was an excellent yield (95%) of the naphthalene derivative (XV) [^{1}H n.m.r. signals: τ 2·82 (tr), 3·24 (d), 3·44 (d), 3·53 (d), 3·82 (d), 3·41 (obscured) all integrating for 7H; 6·22 (s, 3H), 6·42 (s, 6H), 6·65 (s, 3H); 5·0 (br band, O*H*)]. Evidently, in this case, the alternative carbanion (XIV) was an intermediate.

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[1] J. S. Davies, V. H. Davies, and C. H. Hassall, *J. Chem. Soc.* (*C*), 1969, 1873.

[2] J. R. D. McCormick in "Biogenesis of Antibiotic Substances," Czechoslovak Academy of Sciences, Prague, 1965, p. 73.