Pyrone Studies: Conversion of 2-Pyrones into Aromatic Compounds

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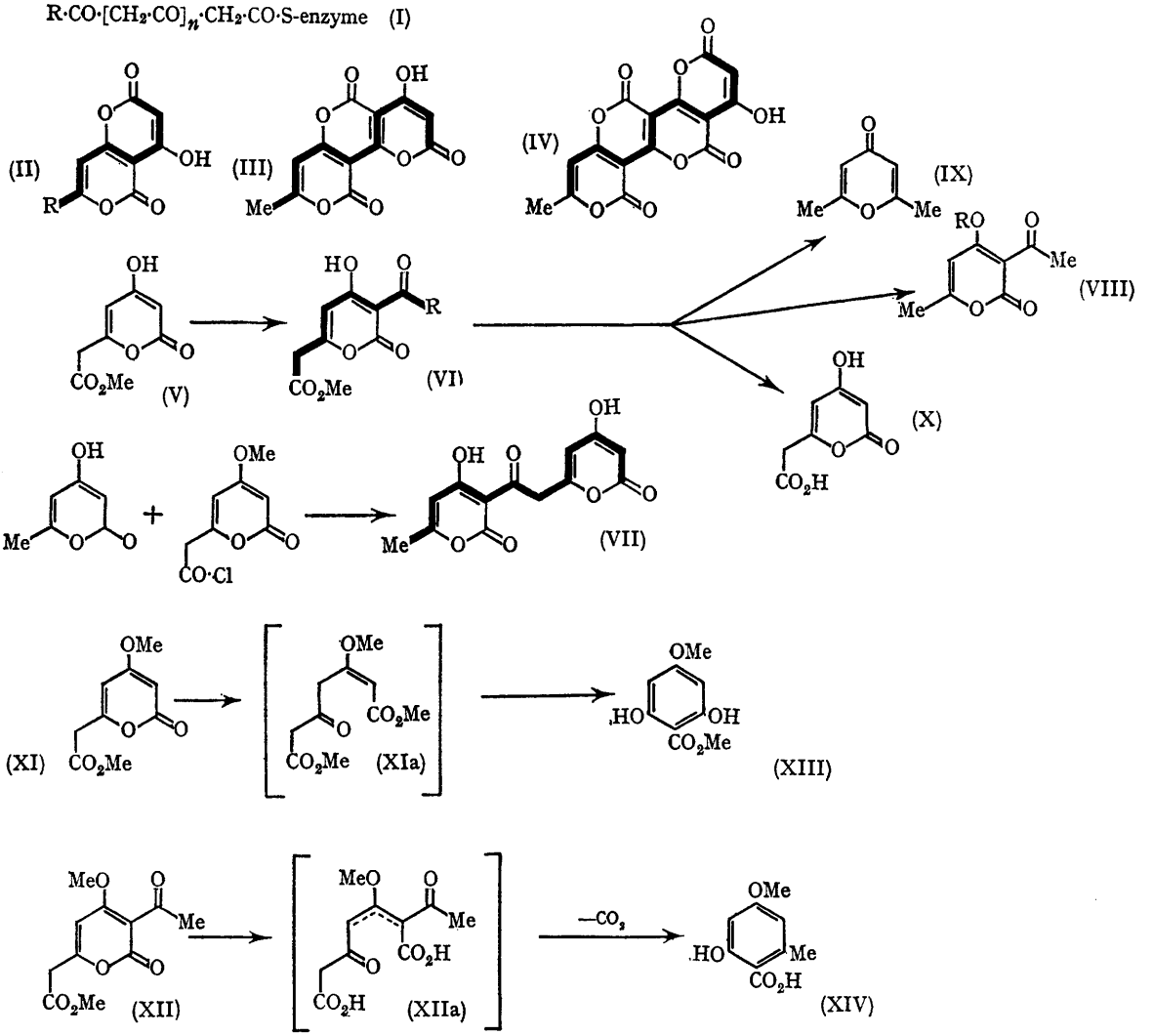
THE acyl-polymalonate route[1] to naturally occurring phenolic compounds is believed to involve enzyme-bound β-polyketo-thiolesters (I; n = 2—8) as intermediates. Our previous reports[2] have indicated that the dipyrones (II; R = Me, Ph, PhCH=CH–, or $PhCH_2{\cdot}CH_2$–) can be regarded as the protected form of the β-triketo-esters (I; n = 2; R = Me, Ph, PhCH=CH–, or $PhCH_2{\cdot}CH_2$–). Additional studies[3] also demonstrated that the tripyrone (III) could serve as the protected form of the β-tetraketo-ester (I; n = 3; R = Me). The logical extension of this scheme was the synthesis of a tetrapyrone (IV) (potentially equivalent to a C_{12}-β-pentaketo-ester) and its subsequent conversion into aromatic compounds of natural type. As such a synthesis of (IV) was difficult, parallel studies into the synthesis of higher members of the β-polyketo-ester series (I; n = 4—8) were started.[4]

In particular we have studied the effect of acid or base on the acetyl derivative (VI; R = Me)[4] with a view to obtaining aromatic compounds of natural type; in general mainly degradation products [(VIII; R = H), (X), and/or (X)], formed by deacylation or hydrolysis–decarboxylation reactions, were obtained. To overcome this difficulty, two methods were found: one involves a photochemical reaction of 2-pyrones[5] and the other involves the preliminary formation of the methyl ether (XII) and its subsequent treatment with base. Observations on the methanol–base ultraviolet spectrum† of dehydroacetic acid methyl ether (XIII; R = Me) prompted us to conclude that prior protection of the 4-hydroxy-group in (VI) was essential. Thus treatment of 4-methoxy-6-methoxycarbonylmethyl-2-pyrone (XI)† with N-NaOMe–MeOH resulted in smooth conversion (~ 50% yield), into the benzoic ester (XIII), λ_{max} (MeOH) 222, 268, 307 mμ (ε 26500, 19100, 3500). The formation of (XIII) is easily rationalised by postulating Claisen condensation of the acyclic intermediate (XIa). The success of this reaction prompted us to study the effect of base on the methyl ether (XII)‡ [synthesised from the corresponding hydroxy-pyrone (VI; R = Me) by treatment with diazomethane]. It was realized, however, that if (XII) was treated in a similar

† The u.v. spectrum [λ_{max} (MeOH) 310 mμ] of dehydroacetic acid (VIII; R = H) changes to λ_{max} 286 mμ on treatment with base and corresponds to conversion of the 4-hydroxy-group into the corresponding anion. By contrast the spectrum [λ_{max} (MeOH) 313 mμ] of dehydroacetic acid methyl ether (VII; R = Me) changes to λ_{max} 384 mμ on treatment with base and indicates that ready ring opening has occurred.

‡ Satisfactory analytical and spectroscopic data have been obtained for the new compounds described.



fashion Claisen condensation could take place involving the branched ester group in the intermediate (XIIa). To reduce this possibility aqueous methanolic potassium hydroxide was used. Treatment of (XII) with N-KOH–MeOH,–H_2O (1 : 1) resulted in the formation of 2-hydroxy-4-methoxy-6-methylbenzoic acid (sparassol; everninic acid) (XIV), λ_{max} (MeOH) 260 and 302 mμ (ϵ 7400 and 2600) in ~ 20% yield. The formation of (XIV) *via* aldol condensation of the expected intermediate (XIIa) demonstrates the validity of this route to protected β-polyketo-esters. The application of these techniques to more complex pyrones [*e.g.* (VII)][4] is presently being investigated.

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[1] A. J. Birch and F. W. Donovan, *Austral. J. Chem.*, 1953, **36**, 360; A. J. Birch, *Proc. Chem. Soc.*, 1962, 3; *cf.* J. H. Richards and J. B. Hendrickson, "The Biosynthesis of Steroids, Terpenes and Acetogenins", W. A. Benjamin, New York, 1964; F. Lynen and M. Tada, *Angew. Chem.*, 1961, **73**, 513.

[2] T. Money, F. W. Comer, G. R. B. Webster, I. G. Wright, and A. I. Scott, *Tetrahedron*, 1967, **23**, 3435; J. L. Douglas and T. Money, *Tetrahedron*, 1967, **23**, 3545; J. L. Douglas and T. Money, *Canad. J. Chem.*, 1967, **45**, 1990.

[3] F. W. Comer, T. Money, and A. I. Scott, *Chem. Comm.*, 1967, 231.

[4] J. L. Douglas and T. Money, *Canad. J. Chem.*, 1968, **46**, 695.

[5] C. T. Bedford, J. M. Forrester, and T. Money, unpublished observations.