

The Cleavage and Aromatic Recyclization of 4-Hydroxy-6-phenacyl-2-pyrone. A Novel Metallic Cation Effect

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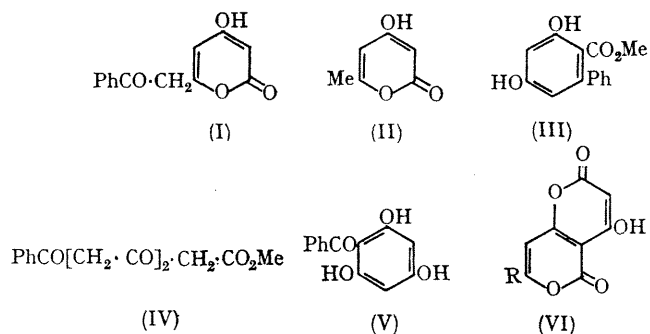
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NUMEROUS reports have described conversions of complex pyrones into phenolic compounds.¹⁻³ The reactions are of significance in relation to the biosynthesis of phenolic natural products because pyrones in the presence of bases presumably undergo ring-opening to form polyketide-type intermediates, although oligo- β -ketonic derivatives have not been detected. We describe (a) metal ion-controlled conversions of the pyrone (I) into aromatic systems, and (b) isolation of a triketo-ester from the reaction of (I) with base. These reactions provide new insight into the role of metallic cations.

The pyrone (I) was synthesized (44%) by acylation of 4-hydroxy-6-methyl-2-pyrone (II) with methyl benzoate in the presence of sodium amide (2 equiv.) in liquid ammonia. Treatment of (I) (a) with methanolic potassium hydroxide (1 mole; 17 hr.; 25°) gave benzoate (III) (56%) as the only phenolic product; whereas (b) with magnesium methoxide (3.5 equiv.) in refluxing methanol (47 hr.) phloroglucinol (V) was the predominant phenolic product (40%). A smaller quantity (< 10%) of benzoate (III) was detected in the latter reaction mixture. The reactions of (I) are to be contrasted with those of triketo-ester (IV), which under conditions (a) and (b) gave only benzoate (III).

A magnesium complex of triketo-ester (IV) was shown to be the initial product of reaction of (I) with an excess of magnesium methoxide in methanol. Periodic examination by n.m.r. of portions of reaction mixtures (after neutralization and separation from the magnesium salts) showed accumulation of (IV). The effect was more pronounced with calcium methoxide; 29% of (IV) was isolated from a mixture of (I) and calcium methoxide (30 equiv.) in methanol after 2.5 hr. under reflux. Accumulation of (IV) was not observed when methanolic potassium hydroxide was used. Although triketo-ester (IV) can be synthesized by another

route,⁴ many other oligoketo-compounds remain inaccessible. Conceivably, some of these can now be obtained by cleavage of suitable pyrones with calcium or magnesium bases.



The reaction of (I) with an excess of magnesium methoxide afforded a Claisen product, whereas the reaction of (IV) afforded an aldol product, in spite of the fact that (IV) is an intermediate in the reaction of (I). We conclude that the magnesium complexes of (IV) produced by the two methods are structurally different. Furthermore, they show different reaction preferences and do not equilibrate with one other.

Other workers studying cleavage and subsequent aromatization reactions of related pyranopyrones (VI) have observed aldol-type cyclizations effected by alcoholic potassium hydroxide and Claisen-type cyclizations effected by methanolic magnesium methoxide.¹⁻³ A rationale for the latter involving magnesium bis-chelates of the polyketide intermediates has been suggested by Crombie and his co-workers.² Although it is a reasonable and adequate

explanation for the reactions of (VI), it fails to account for the present results with (I) and (IV), where bis-chelates cannot be involved in the cyclization processes.

We thank Professor A. I. Scott for informing us of related studies with pyrone (I) prior to publication.⁵ We also thank

the U.S.P.H.S. for financial support and for a Research Career Development Award (T.M.H.), the A.P. Sloan Foundation for a fellowship (T.M.H.), and the N.S.F. for a traineeship (M.P.W.).

(Received, September 30th, 1968; Com. 1332.)

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