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Base-catalysed Cyclisation of Highly Enolisable Systems: Diversion of Pathway by Magnesium Chelation

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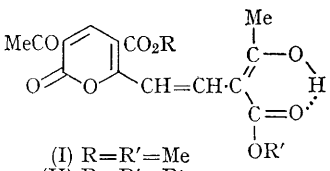
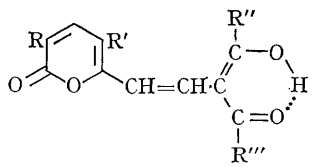
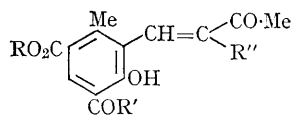
RECENT work in these laboratories[1] has shown a striking contrast between the products of sodium alkoxide and magnesium alkoxide reactions of xanthophanic (I) and glaucophanic (XXI) enols. Dimethyl xanthophanic enol (I) and 2 mol. or less of sodium methoxide in methanol–benzene gives to the acidic and least complexable function in the two possible enolic tautomers (XII and XIII, shown in linear representation undissociated and uncomplexed with metal) formed by opening the pyrone ring in (I) with methoxide ion. Michael–aldol reaction (XIV) gives (VIII, as ester) from



(I) R=R′=Me
(II) R=R′=Et
(III) R=Me, R′=Et
(IV) R=Et, R′=Me



(V) R=R′=CO·Me, R″=R‴=Me
(VI) R=CO_2Et, R′=CO·Me, R″=R‴=Me
(VII) R=CO_2Et, R′=CO·Me, R″=Me, R‴=OEt



(VIII) R=Me, R′=OMe, R″=CO_2H
(IX) R=R′=Me, R″=H

(VIII). With magnesium methoxide in limited amount (1 or 2 mol.) compounds (X) and (XI) were isolated. These three products, which incorporate a 5-substituted 6-hydroxy-4-methylisophthalate unit, derive from the C-6 anion formed adjacent which (VIII), (X), and (XI) are derivable. The xanthyrone (V) gave (IX) on treatment with sodium methoxide whilst (VI) and (VII), in which the aldol condensation is not possible, were recovered largely unchanged.

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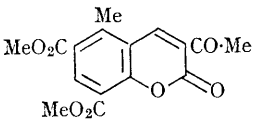
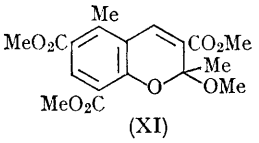
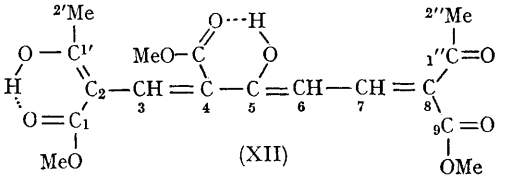
When dimethyl xanthophanic enol is treated with excess of magnesium methoxide (6 mol.) a different structure type (XV), a resacetophenone carboxylic ester derivative, is formed in 78% yield.* The substrate may now be represented as (XVIII), having two stable magnesium-containing conjugate chelate rings: reaction by enol ionisation is blocked and the geometry of the molecule controlled. Excess of base forms the C-2′ anion, geometrically favoured for attack on the C-4 ester the electrophilicity of which is increased by magnesium complexing. Claisen reaction as in (XVIII) ensues, leading to (XIX) and hence (XV). Disposal of the C-2′ anion by Michael–aldol reaction is disfavoured partly perhaps because addition at C-5 disrupts the conjugation. If the amount of magnesium methoxide is limited the species (XII) is important and undergoes enol ionisation at C-5.



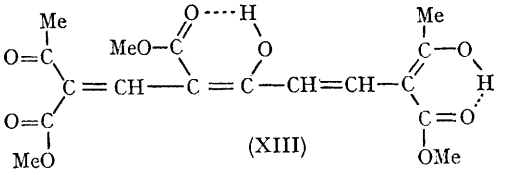
(X)



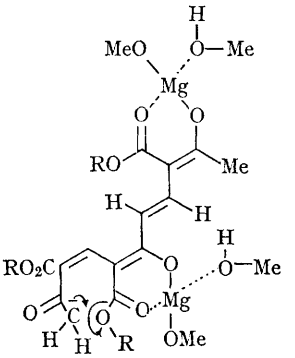
(XI)



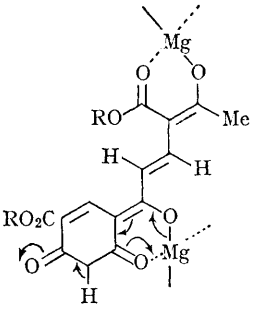
(XII)



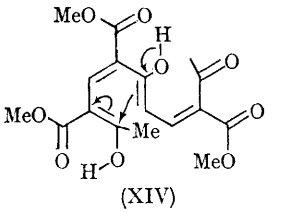
(XIII)



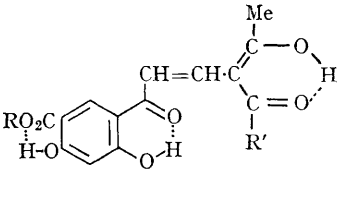
(XVIII)



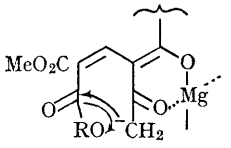
(XIX)



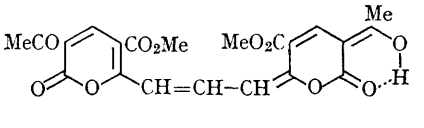
(XIV)



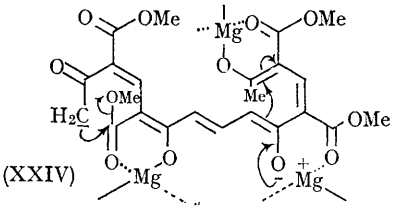
(XV) R=Me, R′=OMe
(XVI) R=Me; R′=OEt
(XVII) R=R′=Me



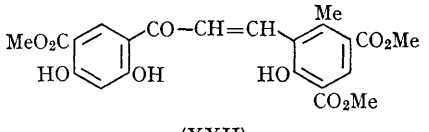
(XX)



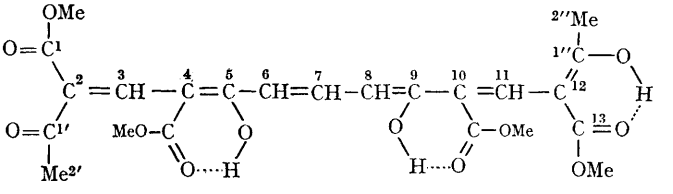
(XXI)



(XXIV)



(XXII)



(XXIII)

* The xanthyrones (II) and (III) give the product (XVI) whilst (IV) gives (XV) as required by the mechanism.

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Michael–aldol condensation supervenes to give the isophthalates (X) and (XI). The xanthyrone enol (VI), when treated with an excess of magnesium methoxide, gives (XVII) by a similar Claisen process except that in this case the carbanion (XX) is stabilised by electron withdrawal by the metal chelate ring.

On treatment with an excess of magnesium methoxide in methanol–benzene, dimethyl glaucophanic enol (XXI) gives the bis-aromatic (XXII) in 83% yield. This is predictable from the above. Opening of the two pyrone rings by methoxide ion can give only one enol-tautomer (XXIII) and when magnesium complexed this contains two conjugate chelate rings and a third more dissociable at the 9-enol to give a C-8 carbanion (see XXIV). Michael–aldol reaction proceeds at this end and Claisen reaction using a more basic C-2′ anion at the other. Exercise of control on the pattern of aromatic cyclisation by metal ions in polyketo-ester and related compounds containing complexable systems, is a principle of interest in biogenetic-type problems and would appear to have some general applicability.

(*Received, March 28th*, 1966; *Com.* 198.)

[1] L. Crombie, D. E. Games, and M. H. Knight, *Tetrahedron Letters*, 1964, 2313.