The Control of Pyrone and Aromatic Cyclisation in Polyketonic–Polyenolic Systems by Magnesium Alkoxide Concentration

By L. CROMBIE and A. W. G. JAMES

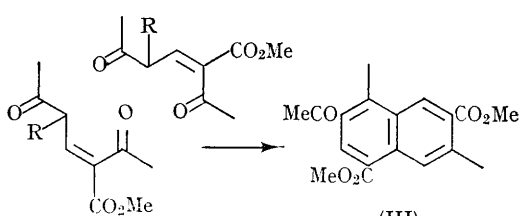
[*Department of Chemistry, University College, (University of Wales), Cathays Park, Cardiff*]

ILLUSTRATION of the way the direction of base-catalysed cyclisation leading to benzenoid systems can be altered by magnesium chelation in polyketonic–polyenolic systems has been given.[1] We now report diversions of pathway in the cyclisation of dimethyl 2,5-diacetylglutaconate. Sodium hydroxide (1 mol.) in benzene containing a little methanol yields dimethyl 3-acetyl-4,7-dimethynaphthalene-1,6-dicarboxylate (III) (46%), formed by hydrolysis and decarboxylation with bimolecular condensation of the glutaconic acid (I) or ketone (II). With sodium methoxide, lithium methoxide, and calcium methoxide in methanol–benzene the pyrone (V) is formed from the diacetylglutaconate anion (IV, *trans*-enol) (See Table 1).

In the presence of sodium methoxide the anion (VI) can be trapped from the pyrone as dimethyl (VII) (46%) or methyl ethylxanthophanic enol (VIII).

When the base used is magnesium methoxide three products, the pyrone (V), dimethyl 4-methyl-6-hydroxyisophthalate (IX) and methyl resacetophenonecarboxylate (X) can result from dimethyl 2,5-diacetylglutaconate depending on the amount of magnesium methoxide employed (see Table 2).

It appears that the acetylpyrone can bind 1 mol. of magnesium* as the chelate from (VIb), but with sufficient magnesium methoxide present the glutaconic ester held in equilibrium as the magnesium chelate is attacked by excess of base and cyclises as shown. According to the geometry, which is assumed to be fairly labile in a system of this type, the anion can cyclise irreversibly *via*



(III)

(I) R=CO_2H
(II) R=H

TABLE 1

% *Yields of isolated pyrone*

Mol. ratio base/ester	½/1	1/1	2/1	4/1
NaOMe	44	76	81	66
LiOMe	30	80	79	75
$Ca(OMe)_2$	67	79	81	81

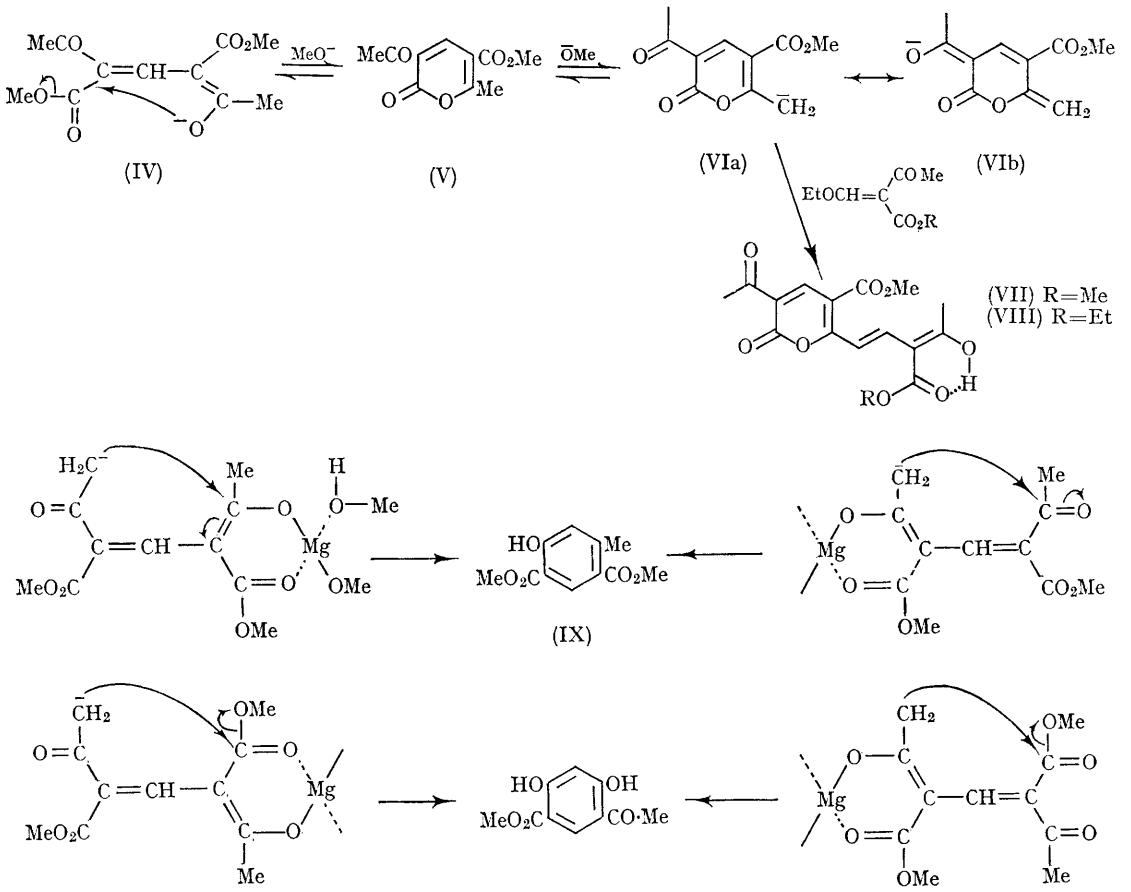
* On adding 1 mol. of magnesium methoxide to the pyrone it is recovered unchanged after acidification: on adding 2 mol. the isophthalate and resacetophenone are formed.

TABLE 2

% Yields of isolated products: reagent magnesium methoxide.

Mol. ratio base/ester	½/1	1/1	2/1	4/1
Pyrone (V)	84	78	nil	nil
Isophthalate (IX)	nil	trace*	55	59
Resacetophenone (X)	nil	trace*	26	19

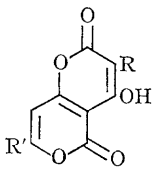
* Detected by thin-layer chromatography



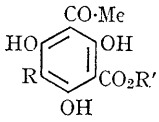
Michael–aldol pathway to give (IX) or irreversibly *via* Claisen condensation to give (X), as magnesio-derivatives. Addition of 1 mol. of magnesium methoxide to the 2,5-diacetylglutaconate followed by 1 mol. of sodium or calcium methoxide causes, as expected, substantial formation of (IX) and (X).

The Ziegler bispyrone (XI)[2] gives the phloroglucinol (XV) when treated with 10 mol. of magnesium ethoxide: similarly, 10 mol. of magnesium methoxide reacts with the bispyrone (XII) to give the phloroglucinol (XVI). The latter reaction (amount of magnesium methoxide unstated) has very recently[3] been reported† and these authors find that aqueous potassium hydroxide reacts with (XII) to give the degraded resorcinol (XVII), explicable as a product of aldol-type reaction with hydrolysis and decarboxylation. We suggest that an excess of magnesium methoxide causes chelate formation, and products (XV) and (XVI) being formed *via* the bischelates (XVIII) and (XIX).

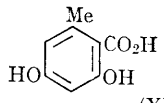
† It is presumed that there is an error in formula (XI) of that communication as the cypher possesses a ring methyl more than our (XVI).



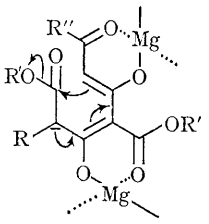
(XI) R=PhCH$_2$, R′=Me
(XII) R=H, R′=Me
(XIII) R=H, R′=Ph·[CH$_2$]$_2$
(XIV) R=H, R′=Ph·CH=CH



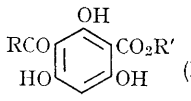
(XV) R=PhCH$_2$, R′=Et
(XVI) R=H, R′=Me



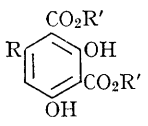
(XVII)



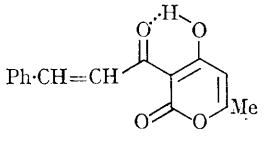
(XVIII) R=PhCH$_2$, R′=Et, R″=Me
(XIX) R=H, R′=R″=Me
(XX) R=H, R′=Me, R″=Ph·[CH$_2$]$_2$
(XXI) R=H, R′=Me, R″=Ph·CH=CH



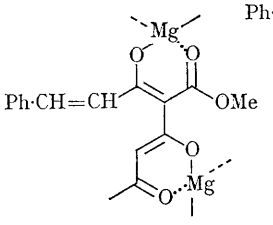
(XXII) R=Ph·[CH$_2$]$_2$, R′=Me
(XXIII) R=Ph·CH=CH, R′=Me



(XXIV) R=Ph·[CH$_2$]$_2$, R′=Me
(XXV) R=Ph·CH=CH, R′=Me



(XXVI)



Ph·CH=CH·[CO·CH$_2$]$_2$·CO·Me

(XXVIII)

(XXVII)

Chelate formation and geometry prevents aldol-type cyclisation, and Claisen cyclisation ensues as shown to give the phloroglucinol system.

The bispyrones (XIII) and (XIV) yield resorcinols (XXIV) and (XXV) (and relatives) by 2,7-aldol-type condensation when methanolic potassium hydroxide is used, but magnesium methoxide gives types (XXII) and (XXIII).[3] This is understandable if chelate involvement (XX)—(XXI) applies: in the case of the styryl derivative (XXIII) further cyclisation to a 4-pyrone[3] ensues. Significantly we find that the pyrone (XXVI) and the triketone (XXVIII) resistant even on refluxing with 10 mol. of magnesium methoxide. The β-ketonic centres can be considered immobilised as in (XXVII) for the pyrone, and possibly as a bis-magnesio-complex in the case of the triketone. These are geometrically unsuitable substrates for aromatic cyclisation despite the expectancy that a terminal carbanion would be formed.

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[1] L. Crombie, D. E. Games and M. H. Knight, *Chem. Comm.*, 1966, 355; *Tetrahedron Letters*, 1964, 2313.
[2] E. Ziegler and H. Junek, *Monatsh.*, 1958, **89**, 323.
[3] T. Money, J. L. Douglas and A. I. Scott, *J. Amer. Chem. Soc.*, 1966, **88**, 624.