New Members of the Xanthyrone Class: Reactions with the Chelating Base, Magnesium Methoxide

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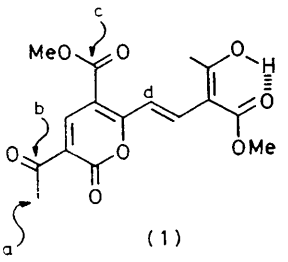
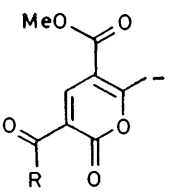
Summary Novel types of xanthyrones are reported: their reactions with magnesium methoxide add support to ideas on the role of this chelating base.

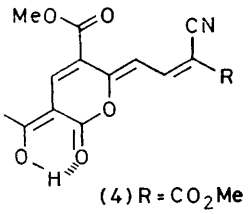
HITHERTO reported xanthyrones, a class of synthetic compounds having (**1**) as a typical member, have in all cases possessed enolised propenyl side-chain end groups which appear to exert a stabilising effect on the structures.[1] By Michael reaction between the pyrone anion (**2**) and methyl methoxymethylenecyanoacetate or methoxymethylenemalononitrile we have now obtained the red ester (**4**), m.p. 185 °C (89%), and the purple-black dinitrile (**5**), m.p 197 °C (83%). N.m.r. data (chelated OH, τ −3·85, ABq 1·55 and 2·83, J 12 Hz) show that in $CDCl_3$ the former has a structure (**4**) in which the pyrone acetyl is enolised. Similarly the dinitrile has the pyrone acetyl enolised (**5**). In $CHCl_3$, (**5**) has λ_{max} 431 (ϵ 45,700) nm but in ethanol it is virtually completely ionised as the spectrum [λ_{max} 236 (4400), 247 (5200), 295 (6400), 326 (9200), 358 (10,900), 493 infl. (52,700), and 521 (90,000) nm] is unchanged in 0·01 M ethanolic KOH. The cyanoester (**4**) is also largely ionised in ethanol.



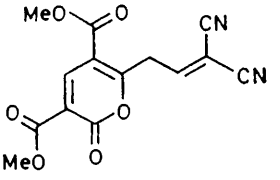
(1)



(2) R = Me
(3) R = OMe



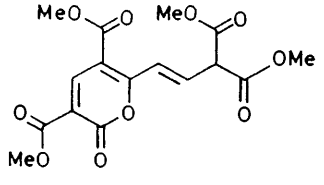
(4) R = CO_2Me
(5) R = CN



(6)

In order to block this second type of enolisation, the pyrone (**2**) was replaced by (**3**) in the Michael reaction with methoxymethylenemalononitrile. This gave a red compound, m.p. 300 °C (decomp.), which was examined by n.m.r. spectroscopy in $CDCl_3$–CF_3CO_2H (9 : 1) because of low solubility in $CDCl_3$. Apart from the pyrone resonance (τ 1·18,s) there was a signal at τ 2·50 (t, J 8 Hz) assigned to the 2′-proton, and a doublet (2H) at τ 5·48 (J 8 Hz) assigned to the 1′-methylene indicating that in this solvent the compound exists in the 1′-H form (**6**). In $(CD_3)_2SO$ the n.m.r. spectrum is best interpreted as that of the delocalised anion from (**6**) having an AB quartet at (τ 2·36 and 3·24, J 13 Hz). In $CHCl_3$–CF_3CO_2H (**6**) has λ_{max} 317 (7900) and 460 (1600) nm but in ethanol or 0·01 M-ethanolic KOH or HCl it has the same spectrum [λ_{max} 229 (10,700), 247 (12,400), 317 (7000), 352 (10,200), and 507 (79,000) nm], in all three solvents and is thus strongly acidic.

From a 'melt' reaction between (**3**), dry sodium methoxide, and dimethyl methoxymethylenemalonate, we have isolated in low yield a new gold-coloured tetra-ester xanthyrone, m.p. 138—139 °C, the major product being a glaucyrone.[2,3] In $CDCl_3$ solution n.m.r. data indicate the structure of this to be the 3′-H form (**7**) as, apart from the four ester and one pyrone hydrogen resonances (τ 1·24) it has a doublet at τ 5·63 (J 9 Hz) coupled to the high-field component of an AB quartet at τ 2·30 and 2·70 (J 16 Hz). Using the pyrone (**2**), a yellow monoacetyl triester xanthyrone was similarly isolated and this appears to be a mixture (*ca.* 1 : 4) of two forms in $CDCl_3$ with the ring acetyl partly enolised, but mainly unenolised.



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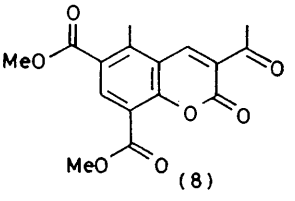

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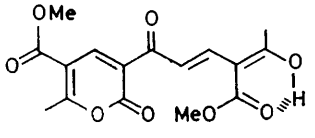

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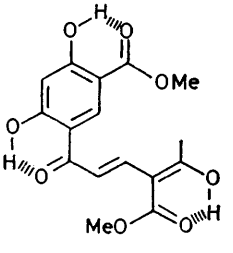

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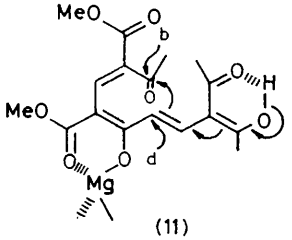

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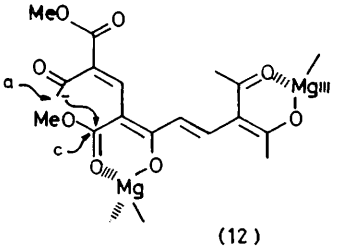

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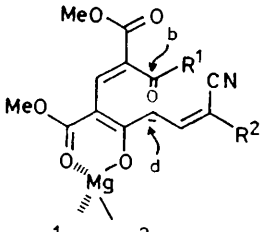
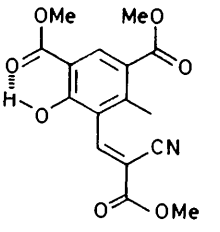


(13) R^1 = Me, R^2 = CO_2Me
(14) R^1 = OMe, R^2 = CN



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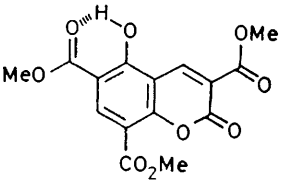
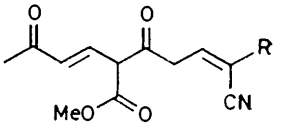
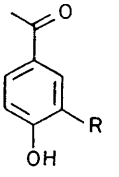


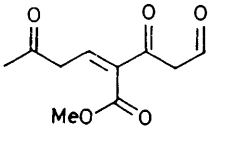
(16)



(17) R = CO_2Me
(18) R = CN



(20) R = CO_2Me
(21) R = H



(19)

In earlier work we have shown that the xanthyrone (**1**), on addition of slightly more than 1 mol. equiv. of reagent gives the aldol product (**8**), whilst the pyrone (**9**) is the major product when *ca.* 2 mol. equiv. is used; with an initial excess of the chelating base (6 mol. equiv.), however, the Claisen product (**10**) is formed almost completely.[4,5] These facts have been explained on the following basis.[4,5] The first mol. of magnesium methoxide forms a chelate with the terminus of (**1**), and thereafter sufficient methoxide ion is available to open the pyrone ring. Chelate equilibration then leads to (**11**) which cyclises using sites d and b for the aldol process. When a larger initial molarity of magnesium methoxide is used however, the

second available site also forms a metal chelate, adequate charge now not being declocalised to position d in (**11**). Effectively, the aldol-initiating centre is capped as a magnesium chelate and on work up stabilisation of the product is achieved as the pyrone (**9**).[5] If, however, excess of magnesium methoxide is employed an anion can form at 'a' in (**12**). Conjugated magnesio-chelates, whilst protected towards aldol attack when in the role of an acceptor, are prone to Claisen attack,[2] and ring closure a–c occurs to give (**10**). Formation of the products in suitably magnesio-chelated form favours cyclisation reactions, particularly if the product chelates are rather insoluble.

Apart from the nitrile replacing the acetyl at the 3'-position, (**1**) and (**4**) have similar structural features. The cyano-ester (**4**), however, does not have a chelating terminus as (**1**) does. Consequently the second chelate capping cannot take place as in (**12**) which leads to the pyrone (**9**) or, in the presence of 6 mol. equiv. of magnesium methoxide, to the Claisen product (**10**). The xanthyrone (**4**) would thus be expected to give products of an aldol reaction [d–b in (**13**)] even when an excess of magnesium methoxide is used. Treatment of (**4**) with 6 mol. equiv. of magnesium methoxide in methanol–benzene at 20 °C gave the isophthalate (**15**) in 73% yield, ν_{max} (KBr) 2220(CN), 1725 (esters), and 1680 (chelated esters) cm^{-1}, τ ($CDCl_3$) 7·40 (Ar Me), 6·01, 6·05, and 6·11 (3 methyl esters), 1·60 and 1·42 (olefinic and aromatic H), and −1·74 (chelated OH). The predicted aldol pathway is thus confirmed. In a similar way, the xanthyrone (**6**) gave the coumarin (**16**) (34%) [*cf.* (**14**)]. Here again the d–b condensation route is taken, but as the normally more rapid aldol condensation pathway is now not available, a Claisen condensation necessarily occurs. The xanthyrones (**5**) and (**7**) also gave products from the d–b condensation pathway when treated with excess of magnesium methoxide, again as would be expected, though yields were poor.

Refluxing the xanthyrone (**4**) with water gave, *via* (**17**) and (**19**), the phenols (**20**) and (**21**) along with methyl cyanoacetate. Similarly the xanthyrone (**5**) gave the same two phenols and malononitrile *via* (**18**). This is in agreement with the decarboxylative reactions of other xanthyrones under similar circumstances.[1]

(*Received, 2nd April* 1979; *Com.* 348.)

[1] L. Crombie, M. Eskins, D. E. Games, and C. Loader, *J.C.S. Perkin I*, 1979, 478.
[2] L. Crombie, D. E. Games, and A. W. G. James, *J.C.S. Perkin I*, 1979, 464.
[3] L. Crombie, D. E. Games, and M. H. Knight, *J. Chem. Soc.* (*C*), 1967, 773.
[4] L. Crombie, D. E. Games, and M. H. Knight, *J. Chem. Soc.* (*C*), 1967, 763.
[5] L. Crombie, M. Eskins, D. E. Games, and C. Loader, *J.C.S. Perkin I*, 1979, 472; L. Crombie, M. Eskins, and D. E. Games, *Chem. Comm.*, 1968, 1015.