Tautomerically Symmetrical and Unsymmetrical Glaucyrones: Reactions with Magnesium Methoxide as a Chelating Base

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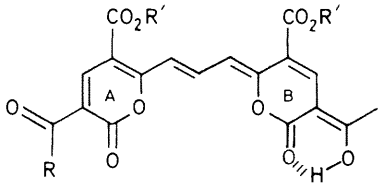
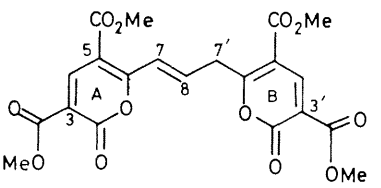
Summary The first tautomerically unsymmetrical glaucyrone has been made, along with a second symmetrical type; their reactions with magnesium methoxide are informative of the part played by magnesium chelates in the chemistry of multi-1,3-dicarbonyls.

LACK of understanding of the way in which glaucyrones[1] are formed has hitherto confined their availability to esters of type (**1**). This has circumscribed study of the directing influences which magnesium methoxide, when employed as a chelating base, exerts on reactions of multi-β-ketonic arrays. Using information from the preceding Communication[2] we have now synthesised the symmetrical tetra-ester glaucyrone (**3**), black plates having a green sheen from benzene, m.p. 104—106 °C, by heating 3,5-dimethoxycarbonyl-6-methyl-2-pyrone (2 mol. equiv.) with dimethyl methoxymethylenemalonate (1 mol. equiv.) and dry sodium methoxide. Though tautomerically symmetrical it exists mainly in the 7′-H form in $CDCl_3$, having an AB quartet τ 2·46 and *ca.* 2·94, J 15 Hz, with the high field component coupled to a methylene at τ 5·84, J 6·5 Hz. Using a mixture of 3,5-dimethoxycarbonyl-6-methyl-2-pyrone and 3-acetyl-5-methoxycarbonyl-6-methyl-2-pyrone in a similar procedure we have isolated, together with (**3**), the black unsymmetrical glaucyrone (**2**), m.p. 178—180 °C.

In earlier work it was shown that (**1**, R′ = Me or Et) gives (**5**, R′ = Me) on treatment with methanolic magnesium methoxide (12 mol. equiv.);[1] by modifying conditions we can now control ester exchange in the case of (**1**, R′ = Et), giving (**5**, R′ = Et). The reaction is envisaged as proceeding by opening of the pyrones by alkoxide ion attack to give a bismagnesio-chelated species, one terminus cyclising by aldol, and the other by Claisen, attack, as pictorially summarised in (**4**). Because of the tautomeric symmetry



(1) R = Me
(2) R = OMe



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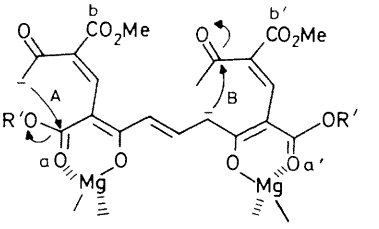
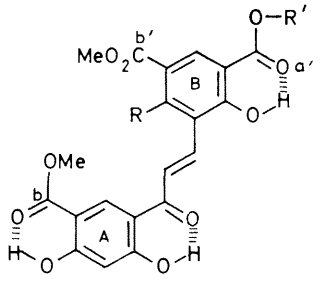
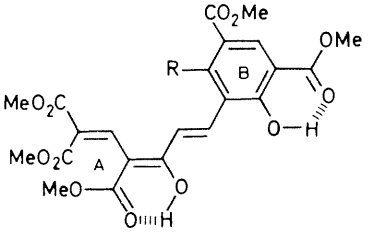


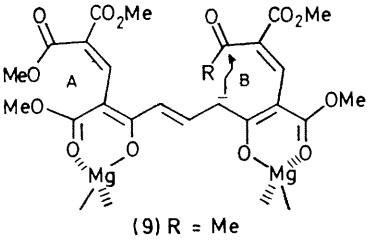
(4)



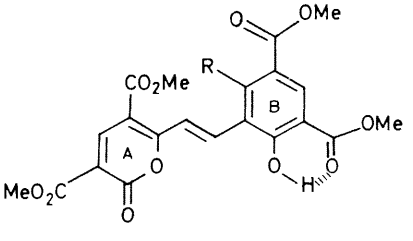
(5) R = Me
(6) R = OH



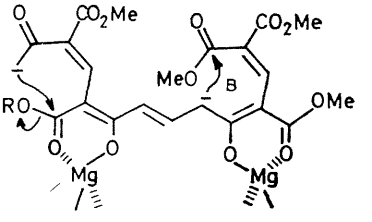
(7) R = Me
(8) R = OMe



(9) R = Me
(10) R = OMe



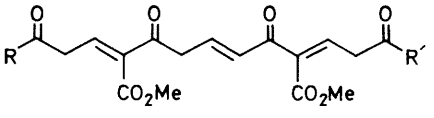
(11) R = Me
(12) R = OMe



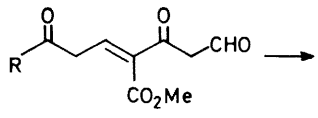
(13)

of the chain only two species having fully conjugated bischelates are possible and they may equilibrate in solution. Since accumulated evidence suggests that magnesiochelated carbonyls form poor aldol acceptors,[3] we prefer the aldol representation shown in (**4**) to that of the alternative view.[1] The timing of events is considered below.

Treatment of the unsymmetrical glaucyrone (**2**) with an excess of methanolic magnesium methoxide gave the yellow crystalline monocyclic (**7**) containing five ester methyls (τ 6·08—6·35), two chelated hydroxy-groups (−1·40 and −2·80), an AB system 2·90 and 2·31, J 16 Hz, proton singlets at 1·73 and 2·29, and an aromatic methyl at 7·56.



(14)



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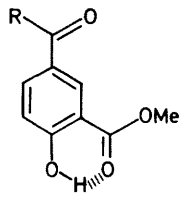

(16)

(1) ⟶ R = R′ = Me — R = Me — R = Me

(2) ⟶ R = Me, R′ = OMe ⇌ R = OMe, R′ = Me — R = Me+OMe — R = Me+OMe

(3) ⟶ R = R′ = OMe — R = OMe — R = OMe

The origins of the B ring are shown in (**9**): once aldol condensation has taken place the A section is incapable of further carbocyclisation by Claisen or aldol reactions. In a similar fashion the tautomerically symmetrical glaucyrone (**3**) gave yellow crystalline (**8**), this time necessarily using a Claisen condensation for ring B formation (**10**). Freed from the protection of magnesium chelation, (**7**) and (**8**) were comparatively reactive compounds and heating in an inert solvent gave the orange pyrones (**11**) and (**12**). These are of the xanthyrone class having as a side-chain terminus a substituted aromatic system.

Comparison of the aromatic cyclisation pattern of (**2**) with that of (**1**) and (**3**) is instructive, as (**2**) has a choice of routes. Were ring B cyclisation to proceed by the Claisen mechanism as indicated in (**13**), the route used by (**3**) [compare with (**10**)], then a second Claisen cyclisation to form an A ring [see (**13**)] could also proceed, leading to (**6**) as its magnesium chelate. Apparently the aldol reaction of (**9**) proceeds considerably faster than either of the two available Claisen reactions and is product-determining. This makes it likely that in (**4**) the aldol condensation proceeds to give the B ring before Claisen cyclisation gives the A ring to form (**5**). It is of course also possible that one pyrone ring, *e.g.* in (**1**), opens and cyclises by the aldol mechanism before the other pyrone has opened: (**4**) would then represent a summary of events.

Refluxing glaucyrones with water causes pyrone decarboxylation, as happens in the xanthyrone series.[4,5] Release of a reactive chain (**14**) which undergoes retroaldol cleavage and hence, by reaction of the newly produced aldehyde, aromatic formation, may be envisaged. In the case of the unsymmetrical glaucyrone (**2**), two aldehydes are possible and two aromatics are formed. As in the case of xanthyrones, the timing of pyrone decarboxylation and retroaldol cleavage is uncertain and retroaldol reaction might alternatively be written as an earlier event.

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[1] L. Crombie, D. E. Games, and M. H. Knight, *J. Chem. Soc.*, (*C*), 1967, 773.
[2] S. R. Baker and L. Crombie, *J.C.S. Chem. Comm.*, preceding communication.
[3] L. Crombie, D. E. Games, and A. W. G. James, *J.C.S. Perkin I*, 1979, 464.
[4] L. Crombie, M. Eskins, D. E. Games, and C. Loader, *J.C.S. Perkin I*, 1979, 478.
[5] S. R. Baker, L. Crombie, and R. V. Dove, *J.C.S. Chem. Comm.*, 1979, 666.