Origins of Glaucophanic Enol in Certain 'Melt' Reactions

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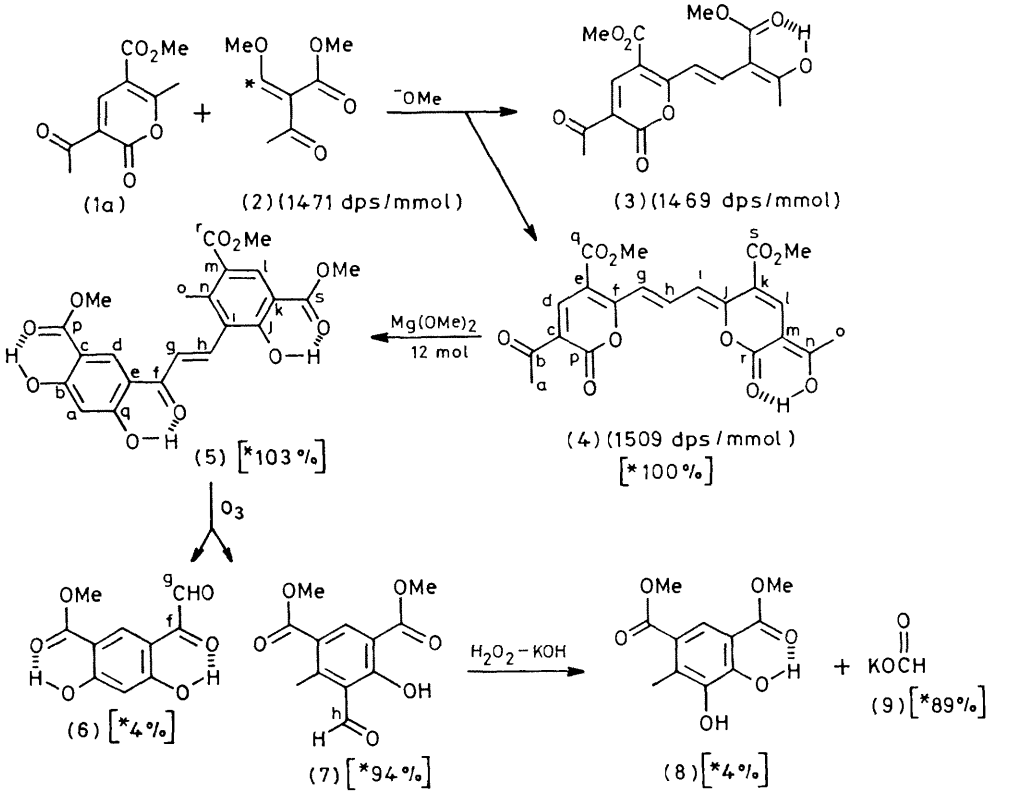
Summary Chemical and [^{14}C]-labelling studies lead to interdependent mechanisms for the formation of glaucophanic and xanthophanic enols, the scheme is supported by consideration of the effects of different alkoxymethylene compounds on the relative yields of glaucyrones and xanthyrones

ALTHOUGH the origin of dimethyl xanthophanic enol (**3**) in the 'melt' reaction at 100 °C between dry methyl sodioacetoacetate and methyl methoxymethyleneacetoacetate (**2**) has been clarified,[1] the origin of the black crystalline dimethyl glaucophanic enol (a glaucyrone) (**4**)[2] has remained obscure Since the glaucyrones possess unusual and potentially useful crystal and solution properties, we have

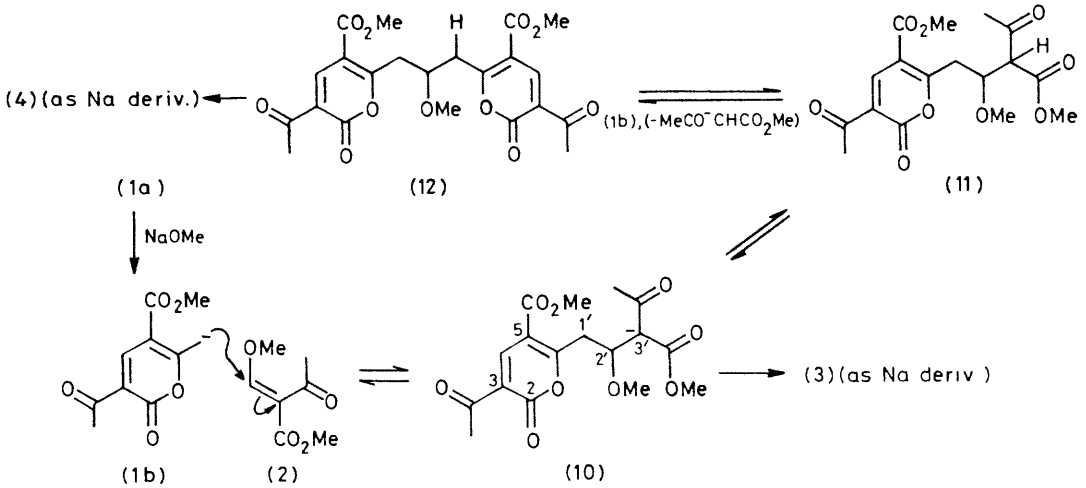


SCHEME 1 Incorporation of methyl methoxy[^{14}C]methyleneacetoacetate

investigated further the way in which they are formed. The xanthyrone (**3**) arises by reaction of the pyrone anion (**1b**), which is formed in the melt, with (**2**), but attempts to couple two residues of (**1b**) through various one-carbon suppliers such as ethyl orthoformate, to give glaucyrone (**4**), were not successful. Nor could (**4**) be obtained, apart from traces, from melts containing the xanthyrone (**3**), the pyrone (**1a**), and sodium methoxide under various conditions. However, 'melt' reaction between the pyrone (**1a**) (2 mol. equiv.), methyl methoxymethyleneacetoacetate (**2**) (1 mol. equiv.) and dry sodium methoxide (2 mol. equiv.) gave the glaucyrone (**4**) in 49% yield as compared with 25% from the earlier melt system. Radiochemical labelling as follows makes clear that the central linking carbon of dimethyl glaucophanic enol is provided by the methoxymethylene carbon of (**2**).

protonation to give (**11**) or its tautomer. The latter might then be attacked by pyrone anion (**1b**) displacing acetoacetate anion. Alternatively, (**11**) → (**12**) may be viewed as involving β-elimination of acetoacetate anion followed by Michael addition of (**1b**) to the alkoxymethylenepyrone so produced. Glaucyrone (**4**) is formed as its sodium salt after loss of methanol and enolisation. Since reaction of (**10**) to give the sodium salt (**3**) is essentially irreversible, xanthyrone (**3**) does not form a suitable starting source for (**4**).

So far as glaucophanic enol formation is concerned, the protonation step (**10**) → (**11**) appears critical. To examine the situation further, the pyrone (**1a**) was allowed to react with various alkoxymethylenes in the presence of sodium methoxide under melt conditions with the results shown in the Table. Only in the case of methyl methoxymethylene



SCHEME 2. Formation of xanthophanic and glaucophanic enols: unified scheme.

Trimethyl [^{14}C]orthoformate was converted into methyl methoxy[^{14}C]methyleneacetoacetate with methyl acetoacetate and acetic anhydride, and transformed into glaucyrone (**4**) and xanthyrone (**3**) using the pyrone melt procedure (Scheme 1): the specific activities of both (**3**) and (**4**) were virtually the same. The labelled glaucyrone was treated with an excess of magnesium methoxide in methanol, forming the crystalline chalcone (**5**)[2] which was ozonised to the keto-aldehyde (**6**), carrying 4% of the original activity, and the formyl hydroxyisophthalate (**7**) carrying 94% of the label. Its specific labelling position was located by Dakin oxidation, giving the catechol isophthalate (**8**) (4% of label) and potassium formate, characterised and counted as the crystalline *p*-bromophenacyl ester, carrying 89% of the label. Thus the primary source of the central carbon of (**4**) is as shown in Scheme 1: the small escape of label into each pyrone ring, indicated by residual labelling in (**6**) and (**8**) can be reasonably accounted for by various equilibria involved in the reaction system.

A unified mechanism for the formation of xanthyrone (**3**) and glaucyrone (**4**) can now be put forward (Scheme 2), involving Michael reaction to give (**10**). One of two fates may await this: elimination to give (**3**), as its sodium salt, along with methanol which is removed by distillation, or

acetoacetate and dimethyl methoxymethylenemalonate is the glaucyrone obtained in good yield: broadly, the yield of glaucyrone decreases as the stability of the leaving anion increases whilst xanthyrone yields show the reverse trend.

TABLE. Methoxymethylenes as sources of xanthyrones and glaucyrones

Methoxymethylene	Glaucyrone/%	Xanthyrone/%
MeO·CH=C(CN)$_2$	nil	86
MeO·CH=C(CN)CO$_2$Me	trace	88
MeO·CH=C(COMe)$_2$	2	85
MeO·CH=C(COMe)CO$_2$Me	49	44
MeO·CH=C(CO$_2$Me)$_2$	56	4

Increasing acidity at 3′ [*cf.* the analogues of (**10**)] diminishes the availability of the analogues of (**11**) so, despite better leaving groups, elimination (**10**) → (**3**) takes preference over displacement (**10**) ⇌ (**11**) ⇌ (**12**) → (**4**). Apparently glaucyrone formation requires a compromise in the form of an adequate leaving group, but one which does not make (**11**) too acidic.

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[1] L. Crombie, D. E. Games, and A. W. G. James, *J.C.S. Perkin I*, 1979, 464.
[2] L. Crombie, D. E. Games, and M. H. Knight, *J. Chem. Soc.* (*C*), 1967, 773.