Stereochemistry and Mechanism of 'Citrylidene' Cyclisation

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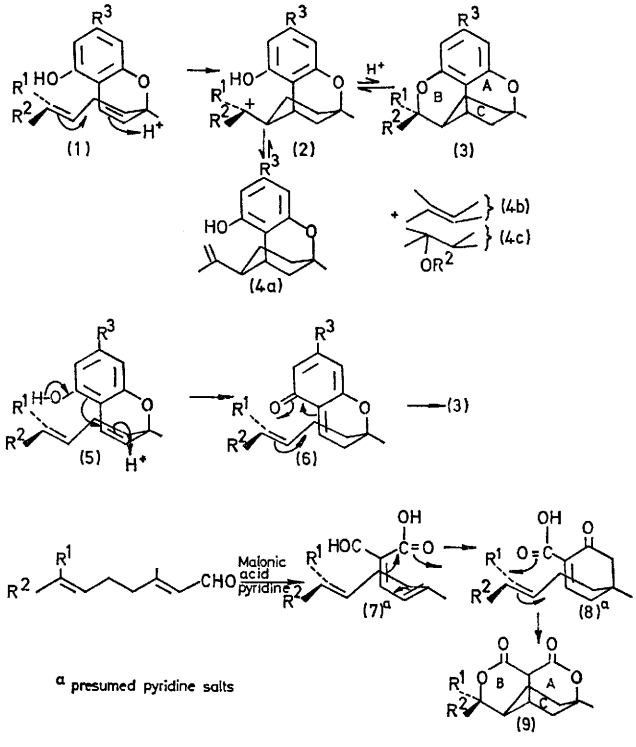
Summary The 'citrylidene' products, obtained when farnesal is condensed with phloroglucinol or malonic acid, by heating in pyridine, are highly stereoselectively dependent on the geometry of the 6-olefin of farnesal; an electrocyclic mechanism is supported.

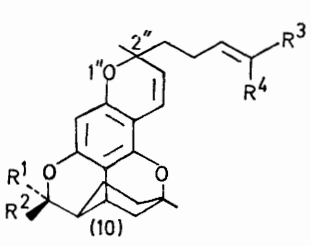
PYRIDINE-catalysed condensations of suitable aldehydes and phenols give chromens which, on further heating in pyridine, cyclise to 'citrylidene' types (**3**).[1] A related reaction is the condensation of citral with malonic acid to give the dilactone (**9**; $R^1 = R^2 = Me$).[2] The 'citrylidene' type of cyclisation has been represented as an ionic process (**1**→**3**); as the geometry is unfavourable to a concerted process, intervention of (**2**), trapped as (**3**) is required. A difficulty is that treatment of (**3**) with acidic reagents gives ring-B-opened (**4a**—**c**), depending on conditions, and the equilibrium is much in favour of these products. Similarly, acid catalysed cyclisations of (**1**) lead to (**4a**—**c**) rather than (**3**).[1] As a result, an electrocyclic mechanism (**5**→**6**→**3**) has been favoured for sometime[3] and we now present evidence that, as required, the formation reaction is highly stereoselective.

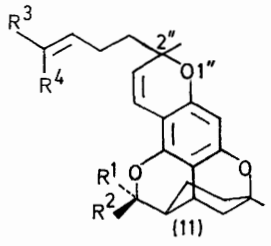
Condensation of phloroglucinol with *trans*-2,*trans*-6-farnesal (1 mol. equiv.) in the presence of pyridine at 110° gave (**3**; $R^1 = Me$, $R^2 = Me_2C{:}CH[CH_2]_2$, $R^3 = OH$), m.p. 105—107° with the R^1–Me resonating at τ 9·04 as expected from data for (**3**; $R^1 = R^2 = Me$, R = OH) where the R^1–Me has τ 8·99 and the R^2–Me 8·50.[1] Similar reaction



with *trans*-2,*cis*-6-farnesal† gave the isomer (**3**; $R^1 = Me_2C:CH[CH_2]_2$, R^2 = Me, R^3 = OH) m.p. 133—136° (solvate from iso-octane) with the R^2–Me at τ 8·53 as expected. If farnesal (2 mol. equiv.) is used in the reaction at 130° *trans*-2,*trans*-6-farnesal gives a pair of non-crystalline chromens, separated by t.l.c., possibly (**10**; $R^1 = R^4$ = Me; $R^2 = R^3 = Me_2C:CH[CH_2]_2$–) and (**11**; $R^1 = R^4$ = Me; $R^2 = R^3 = Me_2C:CH[CH_2]_2$–).‡ The R^1 methyls for this pair resonate at τ 9·04 and 9·05. *trans*-2,*cis*-6-Farnesal similarly gave a different pair, possibly (**10**; $R^2 = R^3$ = Me; $R^1 = R^4 = Me_2C:CH[CH_2]_2$–) and (**11**; $R^2 = R^3$ = Me; $R^1 = R^4 = Me_2C:CH[CH_2]_2$–).‡ The R^2–Me resonated in each compound at τ 8·51.

Pyridine-catalysed condensation of malonic acid with *trans*-2,*trans*-6- and *trans*-2,*cis*-6-farnesal gave similar evidence of high stereoselectivity. The former produced the dilactone (**9**; R^1 = Me, $R^2 = Me_2C:CH[CH_2]_2$–),[2] m.p. 141—142°, with the R^1–Me resonating at τ 8·65 as expected from data for (**9**; $R^1 = R^2$ = Me) where R^1–Me has τ 8·62





and R^2–Me 8·54. Similar reaction with *trans*-2,*cis*-6-farnesal gave (**9**; $R^1 = Me_2C:CH[CH_2]_2$–, R^2 = Me), m.p. 171—172°, R^2–Me τ 8·56. Formation of the dilactone (**9**) may be represented as electrocyclisation (**7**→**8**) followed by a second electrocyclisation (**8**→**9**). This draws together the mechanisms of the two cyclisations, one involving phenols§ and the other malonic acid.

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† Formation of the chromen (**1**) or the lactone (**8**) is independent of the geometry at C-2 in the aldehyde.

‡ Alternatively, they could be isomers of (**10**) or (**11**) differing in geometry at C-2″.

§ A report[4] that cannabigerol and chloranil in boiling benzene gives cannabichromen and 'citrylidene-cannabis' is satisfactorily accommodated.

[1] L. Crombie and R. Ponsford, *J. Chem. Soc.* (*C*), 1971, 788, 794 and references cited.
[2] C. E. Berkoff and L. Crombie, *J. Chem. Soc.*, 1960, 3734.
[3] D. G. Clarke, Ph.D. Thesis, University of Nottingham, 1972.
[4] R. Mechoulam, B. Yagnitinsky, and Y. Gaoni, *J. Amer. Chem. Soc.*, 1968, **90**, 2418.