Regioselective Citran Formation from Phloracetophenone and Phloroglucinaldehyde using a Pyridine-catalysed Citral Condensation: Elucidation of Product Structures by *X*-Ray Analysis

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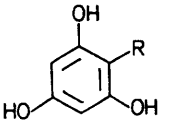
Summary Phloracetophenone and phloroglucinaldehyde each give two isomeric citrans [(**3**) and (**6**) (8:1), and (**4**) and (**7**) (6:1)] respectively on heating (110 °C) with citral in pyridine; the structures of the major isomers (**3**) and (**4**) have been established by *X*-ray methods.

THE tetracyclic monoterpene–resorcinol 'citran' unit occurs in natural meroterpenoids,[1] and in earlier work[2] we have demonstrated its synthesis through citral–resorcinol condensations catalysed by pyridine. We now report such reactions involving acetylphloroglucinol (**1**) and formylphloroglucinol (**2**). The first reaction has been described[3] as leading to a single citran, formulated as (**3**) on the basis of its status as a degradation product of the natural chalcone rubranine (**5**).[4] The constitution of rubranine rests in turn on its synthesis,[5] which involves a citral–pinocembrin condensation and apparently proceeds through an intermediate chromen (**8**, $R^1 = H$, $R^2 = COCH{=}CHPh$). However, structure (**5**) for rubranine follows only if bicyclisation[2b] of (**8**) goes forward without rearrangement, either of R^1, R^2, or as a consequence of rupture of the heterocyclic ring. Our current work has shown the latter assumption to be unjustified in certain cases.[6] Since important mechanistic and structural[6] consequences flow from knowledge of the course of the citral-pyridine reactions with (**1**) and (**2**), we have now examined these reactions.

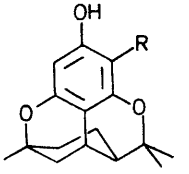
Condensation of (**1**) with citral (1:1) in pyridine at 110 °C for 6 h gave a mixture (76%) of citrans (**3**) and (**6**) (8:1), and the similar reaction with (**2**) gave (69%) citrans (**4**) and (**7**) (6:1). The major isomer in each case was isolated by repeated crystallisation. In addition the isomers (**4**) and (**7**) could be separated and isolated with difficulty, by t.l.c. using multiple elution. Structural assignments were then made for (**3**) and (**4**), the major isomers, by *X*-ray analysis.

Acetylcitran (**3**), m.p. 138—140 °C crystallised (monoclinic) from ether–n-hexane in space group $P2_1/c$, with $a = 9{\cdot}94$, $b = 11{\cdot}57$, $c = 14{\cdot}14$ Å, $\beta = 105{\cdot}09°$, $Z = 4$. Data were collected with an automatic four circle diffractometer using Mo–K_α radiation and 2037 reflections were considered observed. The structure was solved using Multan programmes,[7] and refined to a current *R* index of 4·2%.

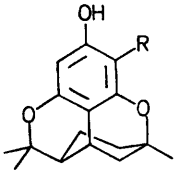
Similarly, the structure of formylcitran (**4**) was solved using 1798 reflections. It crystallised (monoclinic) from ethanol, m.p. 127—128 °C in space group $P2_1/c$, with $a = 15{\cdot}87$, $b = 7{\cdot}56$, $c = 12{\cdot}15$ Å, $\beta = 98{\cdot}04°$, $Z = 4$ (*R* index 9·7%). In order to be sure that the crystal selected was truly representative, it was removed from the diffractometer and its FT ^1H n.m.r. spectrum checked with that of the original bulk sample.



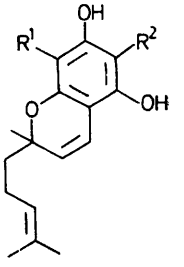
(1); R = COMe
(2); R = CHO



(3); R = COMe
(4); R = CHO
(5); R = COCH:CHPh



(6); R = COMe
(7); R = CHO



(8)

The consequences of these assignments emerge in the accompanying communications,[6] and it is apparent that although highly regioselective, neither condensation shows total regiospecificity. Prolonged heating of (**4**) in pyridine did not lead to any detectable isomerisation to (**7**) and thus the final step in citran formation appears essentially irreversible.

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