

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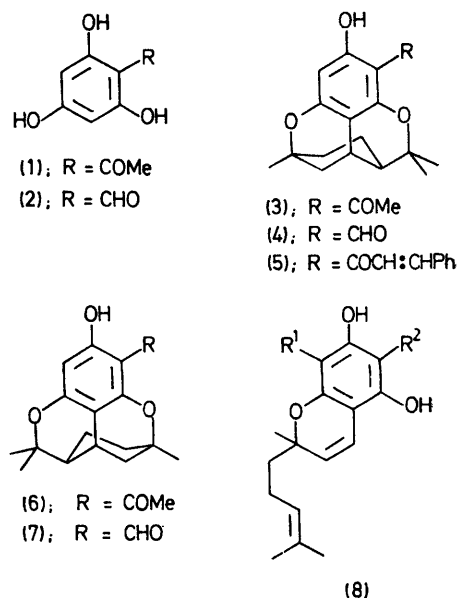
Summary Phloracetophenone and phloroglucinaldehyde each give two isomeric citrans [(3) and (6) (8:1), and (4) and (7) (6:1)] respectively on heating (110 °C) with citral in pyridine; the structures of the major isomers (3) and (4) have been established by X-ray methods.

THE tetracyclic monoterpene-resorcinol 'citrans' unit occurs in natural meroterpenoids,¹ and in earlier work² 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 described³ 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-pinocebrin condensation and apparently proceeds through an intermediate chromen (8, R¹ = H, R² = COCH=CHPh). However, structure (5) for rubranine follows only if bicyclisation^{2b} of (8) goes forward without rearrangement, either of R¹, R², 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 structural⁶ 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.

Acetylcitrans (3), m.p. 138–140 °C crystallised (monoclinic) from ether-n-hexane in space group $P2_1/c$, with $a = 9.94$, $b = 11.57$, $c = 14.14$ Å, $\beta = 105.09^\circ$, $Z = 4$. 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 formylcitrans (4) was solved using 1798 reflections. It crystallised (monoclinic) from ethanol, m.p. 127–128 °C in space group $P2_1/c$, with $a = 15.87$, $b = 7.56$, $c = 12.15$ Å, $\beta = 98.04^\circ$, $Z = 4$ (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.



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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¹ e.g. A. M. Duffield, P. R. Jeffries, F. N. Maslen, and A. I. M. Rae, *Tetrahedron*, 1963, **19**, 593; C. A. L. Bercht, J. J. C. Lousberg, F. J. E. M. Kuppens, and C. A. Salemink, *Phytochemistry*, 1974, **13**, 619.

² (a) L. Crombie and R. J. Ponsford, *J. Chem. Soc. (C)*, 1971, 788, 796; (b) D. G. Clarke, L. Crombie, and D. A. Whiting, *J.C.S. Perkin I*, 1974, 1007.

³ V. V. Kane and T. L. Grayeck, *Tetrahedron Letters*, 1971, **43**, 3991; G. Combes, J. L. Montero, and F. Winternitz, *Compt. rend.*, 1972, 1313; J. L. Montero and F. Winternitz, *Tetrahedron*, 1973, **29**, 1243.

⁴ G. Combes, F. Vassort, and F. Winternitz, *Tetrahedron*, 1970, **26**, 5981.

⁵ W. M. Bandaranayake, L. Crombie, and D. A. Whiting, *J. Chem. Soc. (C)*, 1971, 804.

⁶ M. J. Begley, L. Crombie, D. A. Slack, and D. A. Whiting, following communications.

⁷ G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.