Isomerization of Phenolic Chromens

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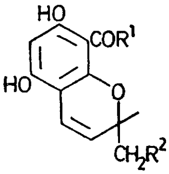
Summary Direct evidence of thermal, acid, and base catalysed isomerization of phenolic 2,2-dialkylchromens has been obtained with the monochromens formed from 2,4-dihydroxyacetophenone.

CROMBIE *et al.*[1] recently reported that the reaction of phloracetophenone with citral at 40 °C in pyridine yields the chromen (**1**) (R^1 = Me, R^2 = prenyl). At 110 °C in pyridine, (**1**) forms two isomeric citrans, suggesting that at higher temperatures in pyridine an unexpected rearrangement of (**1**) occurs to form the intermediate, isomeric chromen (**2**). This intermediate chromen was not detected directly, however, in the reaction.

We have reported[2] a similar unusual rearrangement in connection with the synthesis of tetrahydroguayacanin, where the acid-catalysed condensation of (**3**) with the isomeric chromens (**4**) or (**5**) yields the common product (**6**). The recent observations prompt this report on additional studies which provide direct evidence for phenolic chromen rearrangements of the type proposed.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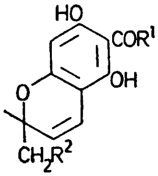
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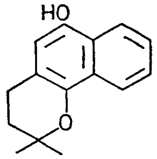
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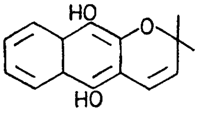
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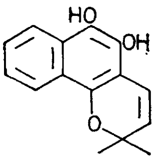
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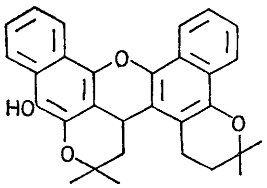
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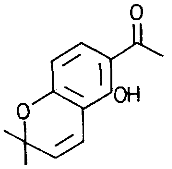
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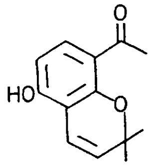
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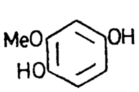
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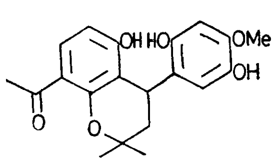
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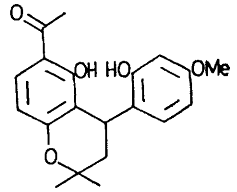
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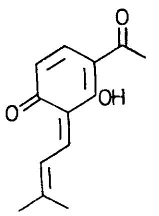
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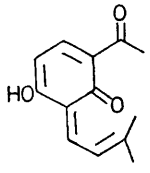
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Chromenylation of 2,4-dihydroxyacetophenone gives, as previously reported[3] the chromen (**7**) (m.p. 101 °C). When treated with 50% aqueous NaOH (90 min, N_2), (**7**) yields the crystalline, isomeric chromen (**8**) (53%, m.p. 149—150 °C). Attempted acid-catalysed condensation of (**8**) with methoxyquinol (**9**) to form (**10**), a reaction similar to that employed in the synthesis of tetrahydroguayacanin, gave only (**11**), suggesting the rearrangement of (**7**) to (**8**) is reversible under acidic conditions.[4] The isomerization of (**8**) to (**7**) is also effected in boiling benzene, with about 50% conversion in 48 h. Thermal rearrangement to (**8**) occurs most rapidly upon heating to 30 °C above its m.p. with about 70% conversion of (**8**) into (**7**) occurring in 5 min. The interconversion of the chromens (**7**) and (**8**) probably involves formation of the isomeric intermediate *ortho*-quinone methides, (**12**) and (**13**).

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[1] L. Crombie, D. A. Slack, and D. A. Whiting, *J.C.S. Chem. Comm.*, 1976, 139.

[2] G. D. Manners, L. Jurd, R. Wong, and K. Palmer, *Tetrahedron*, 1975, **31**, 3019.

[3] W. M. Bandaranayake, L. Crombie, and D. A. Whiting, *J. Chem. Soc.* (*C*), 1971, 811.

[4] M. Nakayama, S. Nishimura, T. Matsui, S. Hayashi, and K. Fukui, *Nippon Kagaku Zasshi*, 1970, **91**, 1092 (*Chem. Abs.*, 1971, **75**, 20110n).