

BIOGENETIC-LIKE SYNTHESIS OF FLAV-3-ENES FROM *o*-CINNAMYLPHENOLS

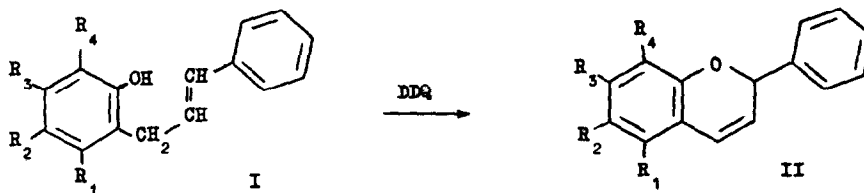
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Recent interest has arisen on cinnamylphenols and flav-3-enes. The co-occurrence of the former with neoflavonoids in nature (1) has led to the proposal of attractive biogenetical schemes (2,3), where the role of cinnamylphenols in the biogenesis of neoflavonoids and their congeners has been emphasized. An elegant paper by Jurd (2) has also indicated the facility of cinnamylation of phenols under mildly acidic conditions. In the same paper, Jurd suggested that oxidation of the allylic methylene group of *o*-cinnamylphenols could lead to flav-3-enes. The possibility of natural conversion of flav-3-enes into flavans and flavylum salts has been suggested by Clark-Lewis (4), who has also found a new facile synthesis of flav-3-enes by NaBH₄ reduction of 2'-hydroxychalcones (4,5,6).

All this prompts us to report the easy conversion of *o*-cinnamylphenols (I) into flav-3-enes (II) by dehydrogenation with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ):



| | R ₁ | R ₂ | R ₃ | R ₄ |
|---------|------------------|------------------|------------------|----------------|
| I, II a | H | H | H | H |
| b | H | OCH ₃ | H | H |
| c | H | OCH ₃ | H | Cin |
| d | OCH ₃ | H (or Cin) | H | Cin (or H) |
| e | OCH ₃ | H (or Cin) | OCH ₃ | Cin (or H) |
| f | OH | H | H | H |

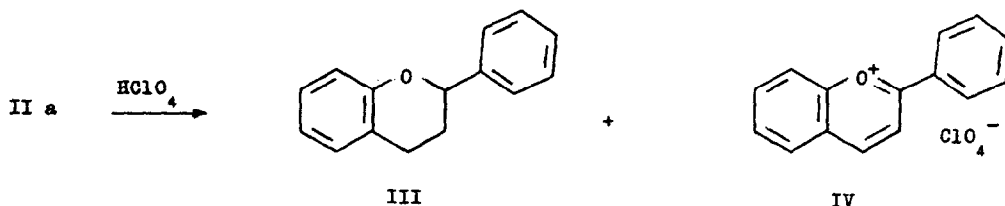


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The cinnamylphenols (I b-f) were prepared with Jurd's method (2), by reaction of cinnamyl alcohol with the phenol in aqueous acetic acid, and separated by chromatography through silica gel. The cyclodehydrogenation with DDQ was accomplished with 1 mol/mol DDQ in boiling benzene (150 ml/g DDQ) for 12-20 hrs. Flav-3-ene (IIa) was obtained in 40% yield after chromatography through silica gel with hexane. For IIb-e, where smaller amounts of starting material (50-300 mg) were used, yields were around 15-20% after preparative TLC on silica gel with hexane/benzene 1/1. IIf was obtained only in traces, probably due to the facility of oxidation to flavylum salt (4). The structures of the flav-3-enes were established from their NMR (4) and mass spectra. The main fragmentation shown was the loss of 77 mass units to give the stable oxonium ion (5), accompanied by the loss of 31 (OCH_3) and 117 ($\text{PhCH}=\text{CHCH}_2$) in the case of II c-e.

The cyclodehydrogenation with DDQ, already employed by us (7) and others (8,9) in the synthesis of natural chromenes, may be a good chemical equivalent of a biological dehydrogenation through pyridine nucleotide or quinonoid coenzymes (10).

Treatment of flav-3-ene (II a) with 35% HClO_4 at 60-70° for 2 hrs. (11) gave flavan (III), identified from UV and mass spectra, and flavylum perchlorate (IV) (NMR: 9 arom. H (7.8-8.5 δ), $\text{H}_3 + \text{H}_4$: AB system at 8.67 and 9.42 δ ($J = 9$ Hz) in CF_3COOH):



REFERENCES

- (1) M.Gregson, K.Kurosawa, W.D.Ollis, B.T.Redman, R.J.Roberts, I.O.Sutherland, A. Braga de Oliveira, W.B. Eyton, O.R. Gottlieb and H.H. Dietrichs, *Chem. Comm.* **1968**, 1390
- (2) L. Jurd, *Experientia* **24**, 838 (1968)
- (3) W.D. Ollis and O.R. Gottlieb, *Chem. Comm.* **1968**, 1396
- (4) J.W. Clark-Lewis and R.W. Jemison, *Austral. J. Chem.* **21**, 2247 (1968)
- (5) A. Pelter and P. Stainton, *J. Chem. Soc.* **1967 C**, 1933
- (6) G. Cardillo, R. Cricchio, L. Merlini and G. Nasini, *Gazz. Chim. Ital.* in the press
- (7) G. Cardillo, R. Cricchio and L. Merlini, *Tetrahedron* **24**, 4825 (1968). See this paper, references quoted therein, and present ref. 9 and 10 for the mechanism of the reaction. It must be noted that flavan was not dehydrogenated by DDQ in boiling benzene.
- (8) I.M. Campbell, C.H. Calzadilla and N.J. McCorkindale, *Tetrahedron Letters* **1966**, 5107
- (9) R. Mechoulam, B. Yagnitinsky and Y. Gaoni, *J. Am. Chem. Soc.* **90**, 2418 (1968)
- (10) A.B. Turner, *Quarterly Reviews* **18**, 347 (1964)
- (11) B.D. Tilak and Z. Muljani, *Tetrahedron* **24**, 949 (1968)