

## 4 $\alpha$ -Aryloxyflavans

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**Summary** 4 $\alpha$ -Aryloxyflavans have been synthesised by reaction of phenols with flavan-4-ols catalysed by boron trifluoride in ether or dioxan.

THOUGH 4-alkyloxyflavans are known,<sup>1</sup> 4-aryloxyflavans (I) have not hitherto been prepared. Nevertheless, results<sup>2</sup> from ozonolysis<sup>3</sup> led us to postulate such structures as the basic flavanoid units in the tannin from common heather (*Calluna vulgaris*).

Haslam has suggested<sup>4</sup> that 4-aryloxyflavans (I) might result, along with the 4-arylflavans (II) which we had isolated, from reaction of flavan-4-ols with phenols in alcoholic hydrogen chloride.<sup>5</sup> A re-examination of this reaction has shown that 4-aryloxyflavans are not present among the products and we have subsequently shown that 4-aryloxyflavans (I) react more rapidly with phenols than does flavan-4 $\beta$ -ol under these conditions to yield 4-arylflavans (II).

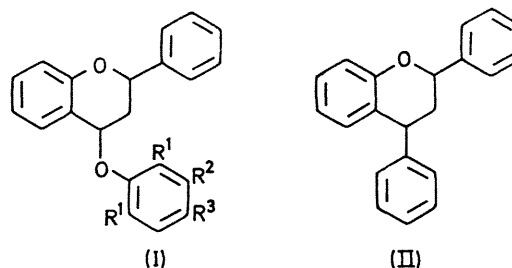
Attempts to prepare 4-aryloxyflavans by reaction of alkaline salts of phenols with 4-halogenoflavans were not encouraging: elimination of hydrogen halide is thought to occur giving initially flav-3-enes.

*Synthesis of 4 $\alpha$ -aryloxyflavans from flavan-4 $\beta$ -ol and phenols with BF<sub>3</sub> as catalyst at room temperature.*

Product (I)			Solvent	Yield %	M.p.
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>			
H	H	H	Ether	25	164—165°
H	H	Me	Dioxan	40	87—92°
Me	H	Me	Ether	70	84.5—85.5°
H	NO <sub>2</sub>	H	Ether	30	106.5—108°

The fact that phenols and alcohols are known to react in the presence of boron trifluoride to yield ethers<sup>6</sup> led us, in

view of the failures mentioned above, to investigate this method. The table shows our results. Along with the compounds (I; R<sup>1</sup> = R<sup>2</sup> = R<sup>3</sup> = H and R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = Me) the main by-product is the corresponding 4-arylflavan; with the compounds (I; R<sup>1</sup> = R<sup>3</sup> = Me, R<sup>2</sup> = H and R<sup>1</sup> = R<sup>3</sup> = H, R<sup>2</sup> = NO<sub>2</sub>) the major initial by-product



is flav-3-ene. Detailed examination of the reaction between *p*-cresol and flavan-4 $\beta$ -ol has shown that use of dioxan as solvent for short reaction times (*e.g.* 12 min.) is a procedure which favours maximum yield of this 4-aryloxyflavan (I; R<sup>1</sup> = R<sup>2</sup> = H, R<sup>3</sup> = Me).

The structures of the compounds are based upon elemental analysis, i.r., n.m.r., and mass spectra, and from the n.m.r. spectra it can be concluded that the compounds are 4 $\alpha$ -aryloxyflavans. Treatment of the compound (I; R<sup>1</sup> = R<sup>3</sup> = Me, R<sup>2</sup> = H) with mercaptoacetic acid yielded the known 4-mercaptoacetic acid derivative of the flavan.<sup>7</sup>

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<sup>1</sup> J. W. Clark-Lewis and L. R. Williams, *Austral. J. Chem.*, 1967, **20**, 2151.

<sup>2</sup> M. J. Betts, B. R. Brown, P. E. Brown, and W. T. Pike, *Chem. Comm.*, 1967, 1110.

<sup>3</sup> Not from reaction with mercaptoacetic acid as misquoted by K. D. Sears and R. L. Casebier, *Chem. Comm.*, 1968, 1437; *Phytochemistry*, 1970, **9**, 1589.

<sup>4</sup> E. Haslam, "Chemistry of Vegetable Tannins," Academic Press, London, 1966, pp. 79 and 80.

<sup>5</sup> B. R. Brown, W. Cummings, and J. Newbould, *J. Chem. Soc.*, 1961, 3677.

<sup>6</sup> *e.g.* F. J. Sowa, G. F. Hennion, and J. A. Nieuwland, *J. Amer. Chem. Soc.*, 1935, **57**, 709.

<sup>7</sup> M. J. Betts, B. R. Brown, and M. R. Shaw, *J. Chem. Soc. (C)*, 1969, 1178.