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PREPARATION OF CIS-3-METHYLFLAVANONES

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We wish to report a new and useful method for the preparation of 2,3-cis-3-methylflavanones.

Cyclisation of α-methylchalcones with alkali gives in good yield the corresponding 2,3-trans-3-methylflavanones. It has now been found that oximation of these latter compounds (1) and subsequent treatment with sodium bisulphite followed by dilute hydrochloric acid at 0° (2) causes epimerisation at the 3-position and results in the formation of the 2,3-cis-3-methylflavanones (average yields 50-60%).

An indication that the epimerisation occurred during oximation was obtained from an experiment in which 2,3-trans-3-methylflavanone was treated with hydroxylamine in pyridine/D_2O. The resulting oxime was the 3-deutero compound and on hydrolysis, as described above, retained the deuterium to give 3-deutero-3-methylflavanone.

When hydrolysis of the oximes was carried out under more vigorous conditions a mixture of 2,3-cis- and 2,3-trans- flavanones resulted. For example, treatment of the oxime formed from 2,3-trans-3-methyl-3',4'-methylenedioxyflavanone regenerated the starting compound (56%), together with 2,3-cis-3-methyl-3',4'-methlenedioxyflavanone (26%). The technique described above was not successful (3) for the preparation of cis-3-hydroxyflavanone, the less stable of the two isomers.

Pertinent nmr data ($CDCl_3$) for some 2,3-cis- and 2,3-trans- 3-methylflavanones are tabulated below.

TABLE 1

Compound	C_3-H (τ)		C_2-H (τ)		$J_{2,3}$(c./sec.)	
	trans	cis	trans	cis	trans	cis
3-methylflavanone (4)	6.98	7.2	4.95	4.49	12.5	2.65
3-methyl-3',4'-methylenedioxyflavanone	6.9	7.2	5.0	4.49	12.2	2.52
3-deutero-3-methyl-3',4'-methylenedioxyflavanone	-	-	5.0	4.51	-	-
4'-methoxyl-3,5,7-trimethylflavanone	6.95	7.15	4.97	4.49	12.0	2.6

Japanese workers (5) have reported that controlled treatment of α-alkylchalcones with acid or condensation of resorcinol with α-methylcinnamic acid in the presence of PPA results in the formation of both cis- and trans-3-alkylflavanones. Both isomers of 3-bromo- (6) and 3-methoxyflavanones (7) are known.

Satisfactory spectroscopic and analytical data were obtained for the new compounds now described. The work has been extended to include a variety of 2,3-substituted chromanones.

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