A New Method for the Synthesis of Flav-2-enes

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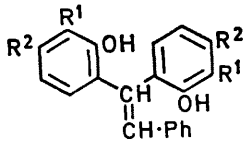
Summary 2,5-Dialkylphenoxymagnesium bromides react with cinnamaldehyde to give the corresponding flavenes, and flav-3-enes isomerize to flav-2-enes when heated under reflux in benzene in the presence of the corresponding phenoxymagnesium bromide.

IN contrast to a previous report,[1] phenoxymagnesium halides have been shown recently[2] to react as ambifunctional anions, mainly *via* the *ortho*-carbon of the aromatic system.

We have now studied the reaction between phenol Grignards and cinnamaldehyde. Phenoxy-, 2-methylphenoxy-, and phenylene-1,3-dioxy-magnesium bromides react with cinnamaldehyde in benzene to give diphenylmethane derivatives†: (Ia) (m.p. 99—100°; yield 40%); (Ib) (m.p. 111–112°; yield 52%), (Ic) (m.p. 165°; yield 65%)



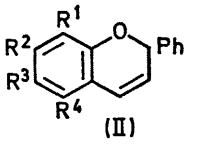
(I) a; $R^1 = R^2 = H$
b; $R^1 = Me, R^2 = H$
c; $R^1 = H, R^2 = OH$

respectively, are obtained‡. In the case of phenol the flav-2-ene (IIa) has been also isolated in small yield (2%). In contrast, (IIa) is the only product if the reaction is carried out in tetrahydrofuran (yield 5% after 12 hr).

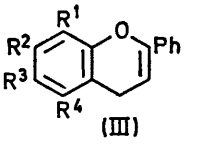
The reaction with 2,5-dialkylphenoxymagnesium bromides is even more interesting. In this case, flav-2-enes and flav-3-enes are the only products formed.

The ratio of flav-2-enes to flav-3-enes increases as the reaction proceeds. In practice, flav-2-enes are the sole products of prolonged reaction; after 15 hr, the yields are, respectively, (IIIb) 65%; (IIIc) 25%); (111d) 60%.

We have also proved that flav-3-enes (IIb) and (IIc) isomerize to flav-2-enes (IIIb) 98·5%, and (IIIc) 98%, on reflux (8 hr) in benzene with the corresponding phenoxymagnesium bromide.



(II)



(III)

	R^1	R^2	R^3	R^4
a	H	H	H	H
b	Pr^i	H	H	Me
c	Me	H	H	Pr^i
d	Me	Me	OH	Me

Furthermore, this method can be used for the preparation of chromenes: 2-isopropyl-5-methylphenoxymagnesium bromide reacts with crotonaldehyde in benzene to give as the sole product 8-isopropyl-2,5-dimethylchrom-3-ene in very good yield.

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TABLE

Phenol	Solvent (reflux)	Flavenes (m.p.)	(III)/(II)
2-Isopropyl-5-methyl-	C_6H_6	(IIb) (oil); (IIIb) (65°)	1·5[a]
5-Isopropyl-2-methyl-	C_6H_6	(IIc) (oil); (IIIc) (oil)	1·4[a]
4-Hydroxy-2,3,5-trimethyl-	THF	(IId) (101°); (IIId) (155°)	1·6[b]

[a] After 3 hr; [b] after 12 hr.

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† The reaction is carried out under reflux in benzene in the case of phenol and 2-methylphenol; at room temperature in the case of 1,3-dihydroxybenzene.

‡ All structures are based on analytical, mass spectral, n.m.r., i.r., and u.v. data. The quantitative data concerning yields were obtained by g.l.c.

[1] H. Gilman and F. Schultz, *Rec. Trav. chim.*, 1928, **47**, 752.
[2] B. Cardillo, G. Casnati, and A. Pochini, *Chimica e Industria*, 1967, **49**, 630.