Chromenylation of 2-Naphthol and Alkylhydroquinones: Short Syntheses of (2*RS*,4′*R*,8′*R*)-α-Tocopherol (Vitamin E) and (2*RS*,4′*R*,8′*R*)-β-Tocopherol

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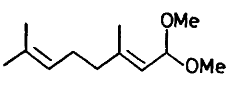
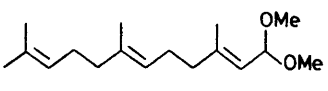
Summary Chromenylation of alkylhydroquinones (and 2-naphthol) can be effected by heating aryloxymagnesium bromides with α-unsaturated acetals in benzene thus providing short and simple syntheses of α- and β-tocopherol and a prenylogue of α-tocotrienol.

In earlier work, many examples of the chromenylation of resorcinol and phloroglucinol systems by heating with pyridine and an α-unsaturated aldehyde or acetal have been described.[1] The reaction is believed to proceed *via* *C*-hydroxy (or alkoxy) alkylation at a position *ortho* to a


(1)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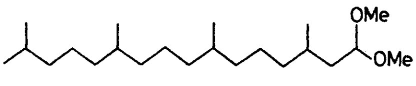
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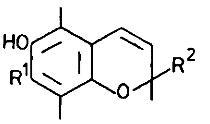

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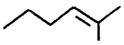
(5) $R^1 =$ Me, $R^2 =$ 
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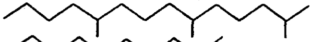
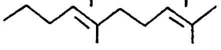
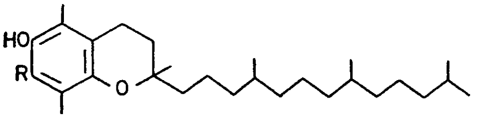
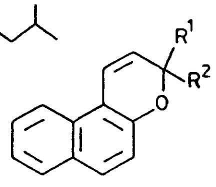
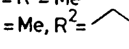
(7) $R^1 =$ H, $R^2 =$ 
(8) $R^1 =$ Me, $R^2 =$ 


(9) R = Me
(10) R = H


(11) $R^1 =$ H, $R^2 =$ Me
(12) $R^1 = R^2 =$ Me
(13) $R^1 =$ Me, $R^2 =$ 

hydroxy group, followed by dienone formation and electrocyclisation.[2] Unfortunately hydroquinones and monohydric phenols are insufficiently nucleophilic to react effectively and this has curbed development in the direction of chromens and chromans of the vitamin E series. Casnati and his colleagues[3] have employed phenoxymagnesium bromides in reactions at a position *ortho* to a phenolic hydroxy group, enhanced reactivity being ascribed to magnesium chelate formation. We report that this modification allows satisfactory chromenylation in the vitamin E series.

Trimethylhydroquinone was treated with ethylmagnesium bromide (1 mol) and heated to reflux in benzene with 3-methylcrotonaldehyde dimethylacetal, citral dimethylacetal (**1**), and phytal dimethylacetal (**3**) (aldehydes were much less satisfactory). Chromens (**4**), (**5**), and (**6**), respectively, were thus isolated in yields of 37, 35, and 26% after purification (yields not optimised). Hydrogenation of dehydro-α-tocopherol (**6**) gave (2*RS*,4′*R*,8′*R*)-α-tocopherol (**9**), identified by spectroscopic and g.l.c. comparison of the compound and its acetate with authentic samples, and by formation of a *p*-phenylazobenzoate, m.p. 66—67 °C. Similarly, 2,5-dimethylhydroquinone gave dehydro-β-tocopherol (**7**), hydrogenated to (2*RS*,4′*R*,8′*R*)-β-tocopherol (**10**). Farnesal dimethylacetal (**2**), on reaction with trimethylhydroquinone, gave the prenylogue (**8**) of α-tocotrienol. These reactions thus offer short and simple pathways to tocopherols and tocotrienols.

Although 2-naphthol can be slowly chromenylated by citral using the pyridine method, yields are very poor.[2] 2-Naphthyloxymagnesium bromide in refluxing benzene, when treated with crotonaldehyde diethylacetal, 3-methylcrotonaldehyde dimethylacetal, and citral dimethylacetal, gave chromens (**11**), (**12**), and (**13**) in unoptimised yields of *ca.* 40%.

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[2] D. G. Clarke, L. Crombie, and D. A. Whiting, *J.C.S. Perkin I*, 1974, 1007.

[3] G. Casiraghi, G. Casnati, G. Puglia, G. Sartori, and G. Terenghi, *J. Chem. Research*, 1977, (*S*) 96; (*M*) 1123; G. Casiraghi, G. Casnati, M. Cornia, G. Sartori, and R. Ungaro, *J.C.S. Perkin I*, 1974, 2077; G. Casiraghi, G. Casnati, and G. Salerno, *J. Chem. Soc.* (*C*), 1971, 2546.