

Copper-catalysed 1,6-Addition of a Benzyl Grignard Reagent to a Dienone: a New Synthesis of Ring c Aromatic Diterpenoids

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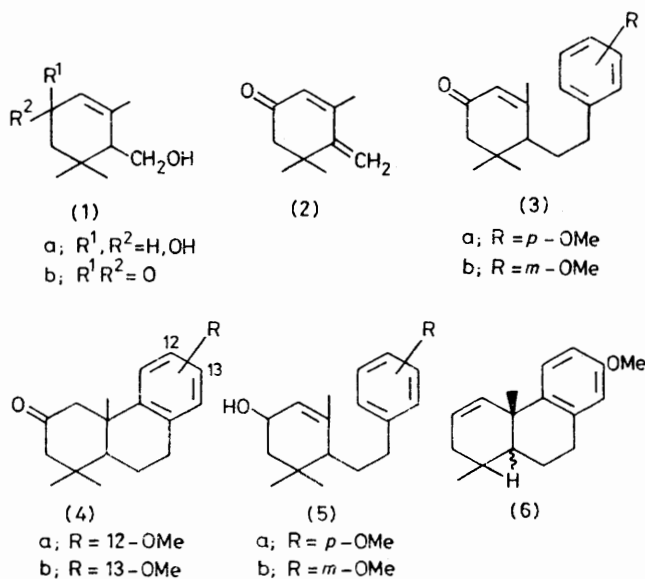
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Summary Copper(I) salts favour the 1,6-addition of *m*- and *p*-methoxybenzyl Grignard reagents to the dienone (**2**); acid-catalysed cyclisation of the products (**3a,b**) gives 2-oxopodocarpa-8,11,13-trienes while cyclisation of the allylic alcohol (**5a**) gives the A/B-*cis* isomer (**6**) in good yield.

DURING the course of work on the stereochemistry of cyclisation reactions leading to podocarpa-8,11,13-trienes¹ we had occasion to require pure samples of the *cis*-A/B (**5β**) isomers. A number of syntheses of this ring system have been reported² but the products have generally been mixtures of the *cis* and *trans* (**5β** and **5α**) isomers.

Electronic factors favour axial attack on a cyclohexenyl cation and Johnson and his co-workers³ have reported examples of nucleophilic attack on this cation to give a *cis*-decalin system. In the podocarpatrienes, attack by the aromatic ring on a cyclohexenyl cation should produce a *cis*-A/B ring junction.

Oxidation of the cyclohexene diol (**1a**)⁴ with manganese dioxide gave the keto-alcohol (**1b**) in 65% yield. Dehydration with sulphuric acid in ether gave the dienone (**2**).⁴



The conjugate addition reaction of benzyl magnesium halides has been observed, although reports in the literature show that the results are variable, particularly with respect to the effect of copper(I) salts.⁵ Reaction of the dienone (2) with *m*- or *p*-methoxybenzylmagnesium bromide gave a slight preponderance of the 1,6-addition product (along with 1,4- and 1,2-products) but the 1,6-product became almost the only isomer when the reaction was carried out in the presence of 10 mol % of copper(I) bromide. The products (3a,b) were cyclised to the crystalline 2-oxo-podocarpa-8,11,13-trienes (4a,b) on treatment with hot phosphoric acid, with the readily separable *cis* and *trans* (5 β and 5 α) isomers being produced in approximately equal amounts.

Lithium aluminium hydride reduction of the cyclohexenones (3a,b) gave the allylic alcohols (5a,b). With

1% trifluoroacetic acid in methylene dichloride for 24 h at 20 °C, the alcohol (5b) gave the 5 β - and 5 α -podocarpa-1,8,11,13-tetraenes (6) in 65 and 15% yield, respectively. The production of both isomers contrasts with literature reports³ but the axial methyl group at pro-C-4 in our system would hinder axial attack on the cation. Hydrogenation of the olefinic bond in the 5 β -isomer (*cis*-6) gave 13-methoxy-5 β -podocarpa-8,11,13-triene, identified, *inter alia*, by its ¹H n.m.r. spectrum.^{2a} The alcohol (5a), where the methoxy group is *meta* to the site of electrophilic attack, underwent elimination on acid treatment and yielded no tricyclic product.

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¹ B. W. Axon and B. R. Davis, unpublished data.

² *E.g.*, (a) M. Fétizon and G. Moreau, *Bull. Soc. chim. France*, 1965, 3479; (b) R. F. Church, R. E. Ireland, and J. A. Marshall, *J. Org. Chem.*, 1966, 31, 2526; J. Delobelle and M. Fétizon, *Bull. Soc. chim. France*, 1961, 1632 and references cited therein.

³ W. S. Johnson and K. E. Harding, *J. Org. Chem.*, 1967, 32, 478; W. S. Johnson, *Angew. Chem. Internat. Edn.*, 1976, 15, 9.

⁴ J. D. Surmatis, A. Walsler, J. Gibas, and R. Thommen, *J. Org. Chem.*, 1970, 35, 1053.

⁵ G. H. Posner, *Org. Reactions*, 1972, 19, 1.