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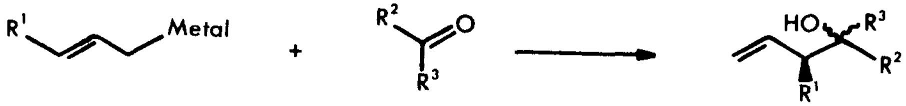
THE STEREOCHEMISTRY OF THE PRODUCT HOMOALLYLIC ALCOHOLS FROM A MODIFIED GRIGNARD REACTION OF 3-PHENYLPROPEN-1-YL CHLORIDE AND BENZALDEHYDE.

James M. Coxon*, Gregory W. Simpson, Peter J. Steel and V. Craige Trenerry.

Chemistry Department, University of Canterbury, Christchurch, New Zealand.

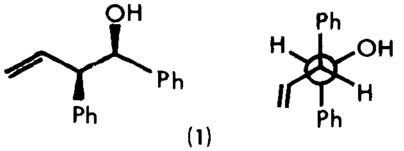
Abstract: The reaction of 3-phenylpropen-1-yl magnesium chloride with benzaldehyde gave a mixture (7:3) of homoallylic alcohols (1) and (2) the relative configuration of which was determined from an X-ray analysis of the major epoxide formed by m-chloroperbenzoic oxidation of alcohol (1).

The stereochemistry inherent in the reaction of 3-substituted propen-1-yl metallic compounds with aldehydes and unsymmetrical ketones[1,2] marks the usefulness of such reactions in the synthesis of compounds containing multiple centres but necessitates effective delineation of the relative chirality of the asymmetric carbons in the product homoallylic alcohols (Scheme 1).

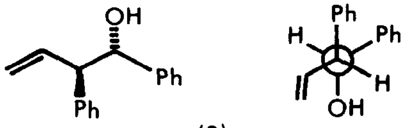


Scheme 1

We have had occasion to examine the reaction of 3-phenylpropen-1-yl magnesium chloride with benzaldehyde, a reaction surprisingly not reported in the literature, and have found that coupling of the organomagnesium halide with unreacted 3-phenyl-propen-1-yl chloride, the predominant process under normal Grignard conditions, can be supressed by adding an ethereal solution of an equimolar mixture of the allylic chloride and benzaldehyde to a reaction initiated by the addition of a trace of the allylic chloride to magnesium in ether[3]. Under these conditions a mixture (7:3) of two homoallylic alcohols (1) and (2) is obtained. The major stereoisomer can be separated by crystallisation of the mixture from dichloromethane-pentane, m.p. 76^{o} ^{13}C n.m.r. δ_C 58.4, C2; 77.5, C1; 117.2, C4; 137.7, C3; 127.8, 128.1, 128.3, 128.7, 140.3, 141.9, Ph's but determining the



(1)



(2)

relative stereochemistry of the homoallylic alcohols is not trivial [4,5] since the more favoured staggered conformations of each isomer would be expected to exhibit a large vicinal proton coupling in the ^1H n.m.r. spectra.

We attempted unsuccessfully several chemical approaches to distinguish the isomers which included chemistry on the epoxidation products of the major homoallylic alcohol. To establish the stereochemistry of the homoallylic alcohols (1) and (2) we now report the X-ray analysis (figure 1) of the major epoxide formed from reaction of the major homoallylic alcohol with m-chloroperbenzoic acid and recrystallisation of the product mixture from methanol, m.p. 162-164°, ^{13}C n.m.r. δ_C 46.6, C4; 53.2, C3; 56.4, C2; 75,4, C1; 126.5, 127.3, 127.6, 128.0, 128.3, 129.2, Ph's. The identity of this epoxide (3) establishes the relative configuration of the major homoallylic alcohol (1) and by exclusion the minor isomer (2).

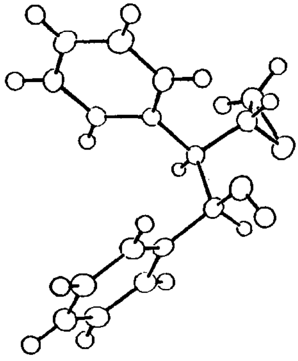


Figure 1

The stereoselectivity of the Grignard reaction parallels, but is more marked than that observed for reaction of 3-methylpropen-1-yl chloride with benzaldehyde[6] where the stereochemistry of the products has been rigorously established by chemical methods. The mechanism of allylic Grignard reactions is in much debate and the stereoselectivity observed for the reaction of 3-phenylpropen-1-yl magnesium chloride with benzaldehyde mitigates against the importance of a cyclic mechanism and for an open chain mechanism[7].

The unambiguous assignment of the stereochemistry of (1) and (2) and the facility to effect this particular reaction will allow the use of these alcohols for the synthesis of compounds containing multiple chiral centres.

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