

HIGHLY DIASTEREOSELECTIVE REACTIONS OF

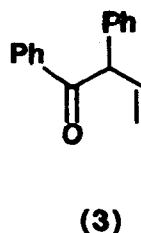
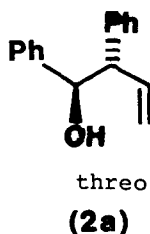
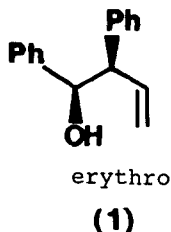
(E)-CINNAMYL CHLORIDE WITH ALDEHYDES MEDIATED BY TIN AND ALUMINIUM

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Abstract: The reactions of (E)-cinnamyl chloride with aldehydes in H₂O:THF:HBr in the presence of tin and aluminium powders proceed with very high stereoselectivity.

There has been much interest in recent years in the control of acyclic stereochemistry by means of the regiospecific reaction between substituted allyl metal compounds and aldehydes.¹ The stereochemistry (erythro or threo) of the homoallylic alcohols produced is highly dependent on the metal (Mg, B, Si, Ti, Cr, Sn, Cd, Zr, Mn, Zn etc) used.^{1,2} We have recently reported³ the preparation of the erythro alcohol (1) obtained by fractional crystallisation

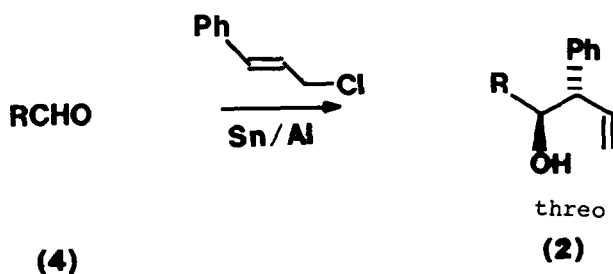


of the mixture of alcohols obtained from the reaction between benzaldehyde and cinnamylmagnesium chloride. Attempts to purify the threo isomer (2a) were unsuccessful. We now report a stereoselective synthesis of (2a) and of a number of analogues.

Reduction of the ketone (3)³ with lithium aluminium hydride or sodium borohydride/cerium chloride⁴ produced the erythro⁵ isomer (1) as the major product (80% and 65% respectively). Since crotyl chromium and zinc reagents

have been reported⁶ to react with aldehydes with threo selectivity we examined the corresponding reactions of the cinnamyl reagents. Thus the chromium (II) mediated procedure reported by Hiyama⁷ and the zinc metal catalysed method recently reported by Luche⁸ both produced the threo isomer with moderate stereoselectivity (85% and 80% respectively). The reaction of benzaldehyde with crotyl bromide in the presence of tin and aluminium powders has been reported⁹ by Nokami to occur with modest erythro stereoselectivity. We find for reaction of cinnamyl chloride with benzaldehyde this method proceeded with complete threo selectivity. This is consistent with the report¹⁰ that crotyl-triphenyltin reacts with aldehydes with opposite stereochemistry to that of cinnamyl-triphenyltin.

In view of this remarkably high selectivity we examined the corresponding reactions of a variety of other aldehydes (Scheme 1). For all the aromatic



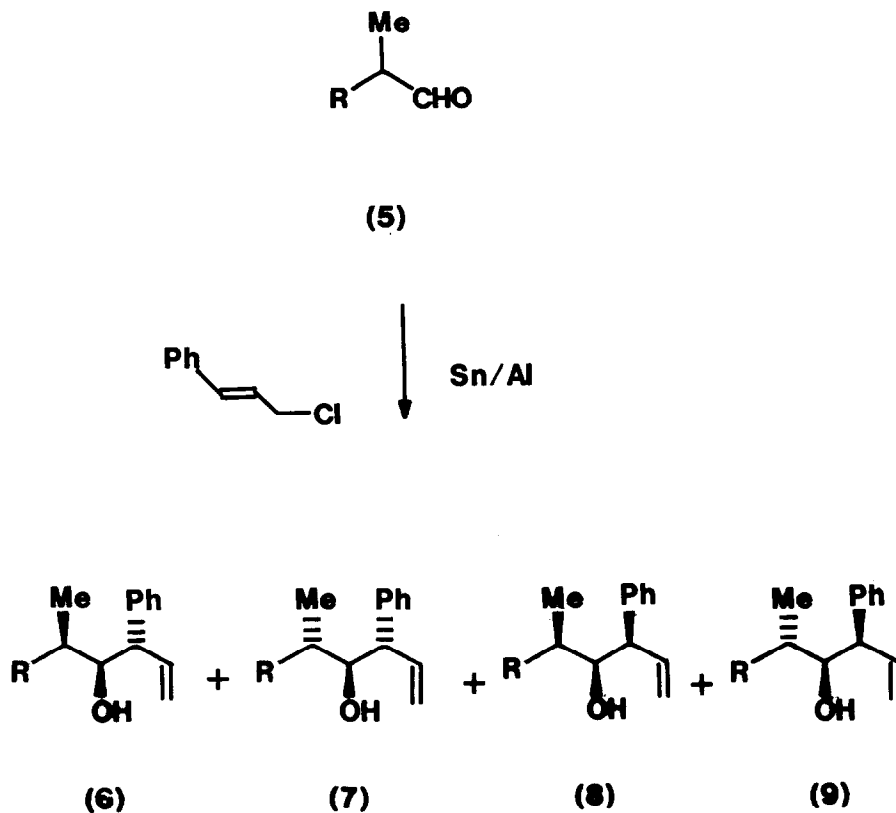
- | | | |
|-----------------|---|---|
| a R = Ph | e CH ₃ | i (CH ₃) ₂ CH |
| b 4-MeO-Ph | f CH ₃ CH ₂ | j CH ₃ (CH ₂) ₅ |
| c 4-CN-Ph | g CH ₃ CH ₂ CH ₂ | k CH ₃ CH=CH |
| d 9-anthracenyl | h PhCH ₂ | l PhCH=CH |

Scheme 1

(4a-d) and aliphatic (4e-j) aldehydes examined the reaction proceeded with complete threo stereoselectivity. α,β -Unsaturated aldehydes (4k,l) react exclusively by 1,2-addition in reactions which occur stereoselectively and with double regioselectivity.

The reactions of three aldehydes possessing an asymmetric centre adjacent to the carbonyl group (5a-c) were examined (Scheme 2). In each case complete

threo selectivity was observed (6+7/8+9). In addition the reactions occurred with high Cram selectivity (6/7). The reaction of (5c) is noteworthy in that the three adjacent chiral centres in the product are assembled with complete



(a) R = CH ₃ CH ₂	75%	25%	0%	0%
(b) R = Ph	80%	20%	0%	0%
(c) R = Me ₃ CCH ₂	100%	0%	0%	0%

Scheme 2

stereochemical control. In contrast the reaction of aldehyde (5b) with cinnamylmagnesium chloride gave a mixture of all four diastereoisomers (6b-9b). We are currently exploring further the scope of this reaction procedure in stereoselective synthesis.

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