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Tandem asymmetric allylboration–alkene metathesis: a novel strategy for the synthesis of *trans*-disubstituted homoallylic alcohols

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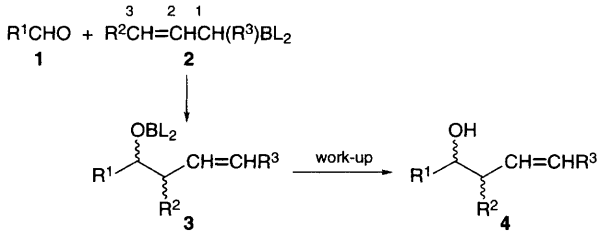
Tandem use of Brown's asymmetric allylboration technology and crossed-alkene metathesis provides exclusively *trans*-disubstituted homoallylic alcohols in good yields.

The condensation reaction of allylborane reagents with aldehydes represents a strategy of considerable merit in asymmetric synthesis (Scheme 1). The reaction of an aldehyde **1** with an allylborane **2** proceeds *via* a 6-centre chair transition state to provide the adduct **3** and subsequently the homoallylic alcohol **4** on work-up. There is considerable versatility in this process. Variation of the substituent R^2 affords polyfunctional homoallylic alcohols [R^2 = H, Me, OMe, OCH_2OMe, NPh_2, $N{=}CPh_2$, $SiMe_2(NPr^i_2)$, *etc.*].[1,2] The absolute stereochemistry of the reaction can be controlled by the choice of boron ligands, L, and the relative stereochemistry by the geometry of the allylborane **2**: *Z*-allylboranes provide *syn*-β-substituted homoallylic alcohols, and *E*-allylboranes give rise to the *anti*-isomers. There is currently a serious limitation to this methodology. For a given chiral α-substituted allylborane **2** (R^3 ≠ H), control of the alkene geometry in the product **4** requires that the absolute stereochemistry at C1 in reagent **2** be fixed.[3] Whilst this is possible, preparation of chiral α-substituted allylboranes is by no means experimentally easy and the applications are not general; the existing methods are more appropriate for preparing *Z*-homoallylic alcohols.

The molybdenum alkene metathesis catalyst $Mo(OR_{F6})_2(NAr)(CHCMe_2)Ph$ [R_{F6} = $C(CF_3)_2Me$, Ar = 2,6-$Pr^i_2C_6H_3$] **5** (Fig. 1) has found widespread use in ring opening metathesis polymerisation and ring closing metathesis of functionalised terminal alkenes.[4,5] Until recently, this catalyst had not been applied to the cross-metathesis of unlike alkenes as the selectivity of the cross-coupling reaction had yet to be ascertained. Crowe has demonstrated that very high cross-metathesis selectivities can be achieved during the cross-couplings of both functionalised aryl alkenes and aryl/alkyl-substituted alkenes using 1 mol% catalyst.[6] Furthermore, these reactions are mild, operationally facile, and, most strikingly, proceed with >95% *trans* selectivity making crossed-alkene metathesis an enormously useful synthetic tool. Indeed, crossed-metathetic exchange could become quite powerful if used in tandem with other synthetic transformations. We now report that tandem asymmetric allylboration–alkene metathesis provides a convenient method for the preparation of *E*-homoallylic alcohols **4** from simple allylboranes **2** (R^3 = H).



Scheme 1

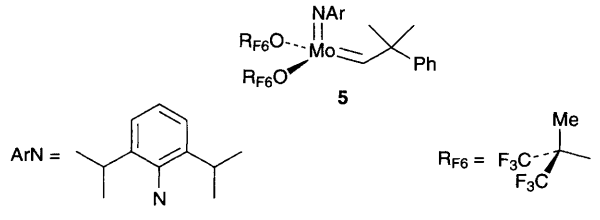
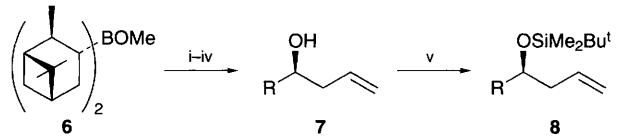


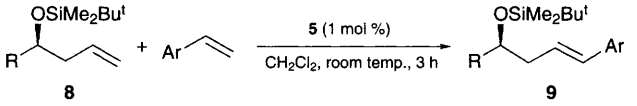
Fig. 1

Asymmetric allylboration reactions were conducted on a variety of achiral aldehydes at −100 °C using (−)-*B*-methoxydiisopinocampheylborane **6** under Brown's 'salt-free' conditions[7] to furnish secondary homoallylic alcohols **7** in excellent ees.† To eliminate the Brønsted acidity, and thus permit tolerance by molybdenum catalyst **5**, homoallylic alcohols **7** were quantitatively converted to their *tert*-butyldimethylsilyl ethers (Scheme 2). Cross-metathesis of homoallylic silyl ethers **8** with a variety of *para*-substituted styrenes at room temperature using 1 mol% of catalyst **5** provided exclusively *trans*- disubstituted homoallylic alcohols in good yields (Scheme 3).‡ The results are summarised in Table 1.§ It is again evident that the chemical yields are correlated with the degree of styrene activation.[6]

In conclusion, tandem asymmetric allylboration–alkene metathesis is an excellent procedure for the exclusive preparation of *trans*-disubstituted homoallylic alcohols. Investigations into the



Scheme 2 *Reagents and conditions*: i, $CH_2{=}CHCH_2MgBr$, Et_2O, room temp., 1 h; ii, anhydrous filtration; iii, RCHO, Et_2O, −100 °C, 1 h; iv, NaOH, H_2O_2; v, $Bu^tMe_2SiOSO_2CF_3$, 2,6-lutidine, CH_2Cl_2, 0 °C, 15 min



Scheme 3

Table 1 Cross-metathesis reactions of homoallylic silyl ethers with *p*-substituted styrenes

Entry	R	Ar	Yield (%)
1	Phenyl	Phenyl	72
2	Phenyl	*p*-ClC_6H_4	54
3	Phenyl	*p*-$MeOC_6H_4$	52
4	Cyclohexyl	Phenyl	65
5	Cyclohexyl	*p*-ClC_6H_4	60
6	Cyclohexyl	*p*-$MeOC_6H_4$	50
7	Propyl	Phenyl	54
8	Propyl	*p*-ClC_6H_4	65
9	Propyl	*p*-$MeOC_6H_4$	43

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versatility of this novel methodology are currently underway. Further applications will be reported in due course.

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Footnotes

† The purification procedure and spectral data for homoallylic alcohols derived from benzaldehyde and butyraldehyde are available from ref.7.

‡ A typical experimental procedure is as follows: to a solution of styrene (2 equiv.) and **5** (1 mol%) in CH_2Cl_2 (0.1 ml) was added a CH_2Cl_2 solution of **8** (0.5 M). The solution was allowed to stand for 3 h then adsorbed onto Na_2SO_4. Purification was accomplished by either flash or radial chromatography providing **9** as a clear, colourless oil.

§ All new compounds were fully characterised by spectroscopic data and combustion analysis or HRMS.

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