HIGH PRESSURE ALLYLSTANNANE ADDITION TO α -AMINO ALDEHYDES: **SYN DIASTEREOSELECTIVITY** **IN THE ABSENCE OF CHELATION CONTROL.**

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Abstract: Contrary to expectations, the high pressure (9 kbar, 30 °C) mediated addition of allyltrimethylstannane (**2**) to α -amino aldehydes (**1**) proceeds via an anti - Felkin - Anh mode to provide predominantly (60 - 88%) *syn* homoallylic alcohols. The diastereoselectivity of this reaction is dependent on the amino aldehyde side chain.

The allylation of α -amino aldehydes has received considerable attention as a key step in the stereoselective synthesis of statine, ketomethylene and hydroxyethylene dipeptide isosteres¹. Stereocontrol is most commonly achieved by chelation of the substrate to a Lewis acid with "Cram-chelation" addition of an allylic metal species to yield the *syn* diastereomer preferentially^{1,2}. Non-chelation controlled additions favour *anti* products in agreement with the Felkin-Anh model and consideration of ground - state aldehyde structure², although predominant *syn* addition has also been reported in allylation reactions for which chelation would not be expected^{1a,b}.

High pressure is an alternative method of promoting the addition of allylic stannanes to aldehydes and can proceed with opposite stereochemistry to that achieved with Lewis acids³. While the latter most probably promote addition via an acyclic transition state (in the absence of a prior transmetallation), high pressure mediated reactions proceed via a metallo-ene process and can be associated with high levels of diastereoselectivity^{3,4}. We decided, therefore, to examine the allylation of α -amino aldehydes with allylic stannanes at elevated pressures. In addition to offering an alternative to chelation control of this reaction, high pressure is a relatively mild technique and so particularly suited to these relatively unstable substrates.

The amino aldehydes (**1**) was placed in a Teflon capsule with 2 equivalents of allyltrimethylstannane (**2**) and compressed to ca 9 kbar at 30 °C. Pressure was maintained for 14 days, but reaction may be complete in substantially less time^{3,4}. Hydrolysis with aqueous KF and nmr spectroscopic analysis revealed that the homoallyl alcohols **3** and **4** were formed quantitatively (Scheme).

Scheme

Diastereomeric assignments and ratios (Table) were determined from ¹H and ¹³C nmr spectra by comparison with spectroscopic data for the corresponding Cbz derivatives^{1c,5}.

Table. The High Pressure (9 kbar) reaction of α -Amino Aldehydes (1) with Allyltrimethylstannane (2).

Entry	R	Ratio of <i>syn</i> (3) : <i>anti</i> (4) ^a	de (%)
1	Me	62 : 38	24
2	CH ₂ OPh	60 : 40	20
3	i-Pr	76 : 24	52
4	CH ₂ Ph	88 : 12	76

^adetermined by ¹H and ¹³C nmr spectroscopy.

Despite the absence of chelation control, all reactions proceeded with *syn* diastereoselectivity which was dependent on the amino aldehyde side chain (R). This "anti-Felkin-Anh" mode of reaction is consistent with *si* metallo-ene addition to a hydrogen bonded conformer of the α -amino aldehyde (Figure). The same argument has been invoked to explain the comparable *syn* diastereoselectivity of the corresponding high pressure Diels - Alder reaction⁶.

Figure: Possible transition state for allyltin addition

These preliminary findings suggest the possibility of improved diastereoselectivity with manipulation of R, the amine protecting group and / or the alkyl groups on tin and we are presently investigating this hypothesis.

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