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LETTERS

Diastereoselective Pd/In bimetallic inter–intramolecular (class 2) cascade reactions of allenyl-imines and aryl iodides

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Abstract—A new diastereoselective Pd/In bimetallic inter–intramolecular cascade reaction employing allenyl-sulfinimines and aryl iodides is described. The *tert*-butanesulfinyl chiral auxiliary affords chiral, highly substituted *cis*-pyrrolidines and piperidines. © 2003 Elsevier Science Ltd. All rights reserved.

Recently we reported the development of a new Pd/In bimetallic cascade process involving aryl iodides, allenes and carbonyl compounds.[1–3] The key step in this cascade involves the generation of a nucleophillic allylindium via transmetallation of a π-allyl palladium(II) species with indium powder. Araki et al. also disclosed the generation of allylindium from conventionally generated π-allyl palladium(II) species.[4]

We identified four synthetic variants of this process depending on whether the Pd-catalysed step and the In-mediated allylation are *inter*- or *intra*-molecular (Table 1).

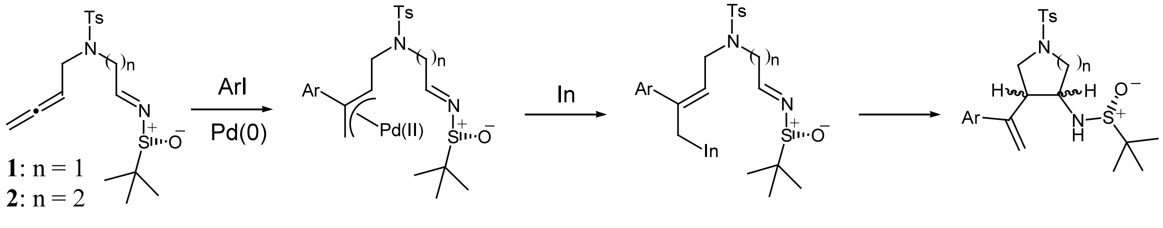
Table 1. Variants of Pd/In cascade

Class	Pd step	In step
1	Intermolecular	Intermolecular
2	Intermolecular	Intramolecular
3	Intramolecular	Intermolecular
4	Intramolecular	Intramolecular

This process has recently been extended to incorporate imines as electrophilic components and the *tert*-butanesulfinyl group was found to be a useful chiral auxiliary exhibiting excellent levels of stereocontrol.[5]

Kang et al. recently described the use of allenyl-aldehydes in a Pd/In cascade involving intermolecular π-allyl formation and subsequent intramolecular allylation (i.e. a class 2 process).[6] In light of this communication we wish to report our preliminary results in this area using the *tert*-butanesulfinyl group as a chiral auxiliary (Scheme 1).

Allenyl sulfinimine **1**, prepared by condensing the appropriate allenyl-aldehyde with Ellman's reagent,[7] was reacted with iodobenzene in the presence of indium powder and a catalytic system comprising 10 mol% $Pd(OAc)_2$ and 20 mol% tris(2-furyl)phosphine at 80°C



Scheme 1.

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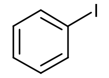
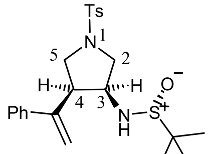
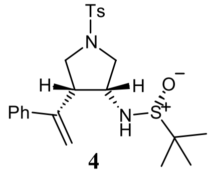
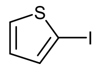
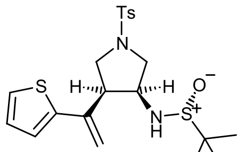
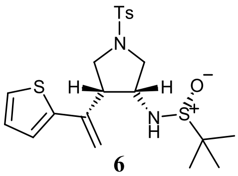
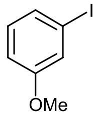
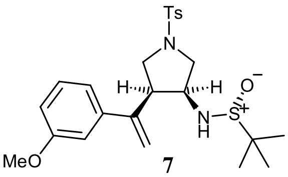
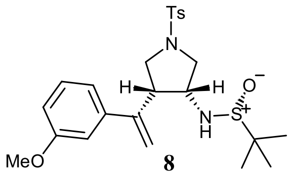
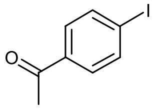
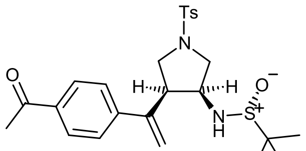
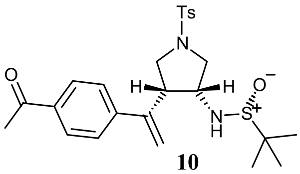
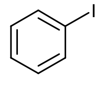
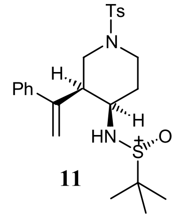
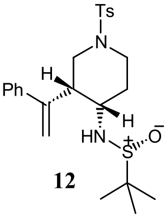
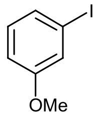
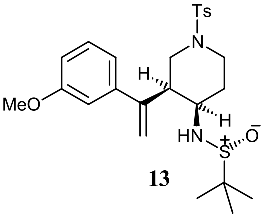
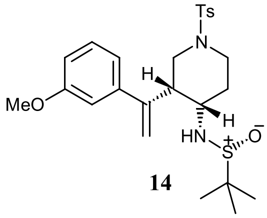
Table 2.

ArI	Substrate	Product		Yield (%)	D.r.
		Major isomer	Minor isomer		
	**1**	 **3**	 **4**	60	87:13
	**1**	 **5**	 **6**	37	77:23
	**1**	 **7**	 **8**	58	89:11
	**1**	 **9**	 **10**	56	85:15
	**2**	 **11**	 **12**	61	91:9
	**2**	 **13**	 **14**	55	91:9

for 16 h in DMA affording an 87:13 mixture of pyrrolidine diastereoisomers in 60% combined yield (Table 2). In contrast to allenyl-aldehydes[6] no *trans* isomer was observed. The absolute stereochemistry of both the major and minor isomers has been determined by X-ray crystallography (Figs. 1 and 2).[8] We propose a chelation control model[5,9] involving coordination of the imine and sulfinyl groups to indium to explain the observed stereochemistry of the major isomer (Fig. 3). The *R* sulfinyl chiral auxilliary induces *S* configurations at the newly formed proximal and distal stereocentres. The stereochemistry of the minor isomer (Fig. 2) is thus *R*,*R*,*R* and appears to arise from a cyclic transition state without the sulfinyl-oxygen atom binding to indium.

A variety of aryl iodides have been successfully incorporated into the cascade and their structures had little effect on the ratio of diastereoisomers. A slightly reduced diastereoselectivity was observed when 2-iodothiophene was employed. This could be due to the thiophene-sulfur atom binding competitively with the

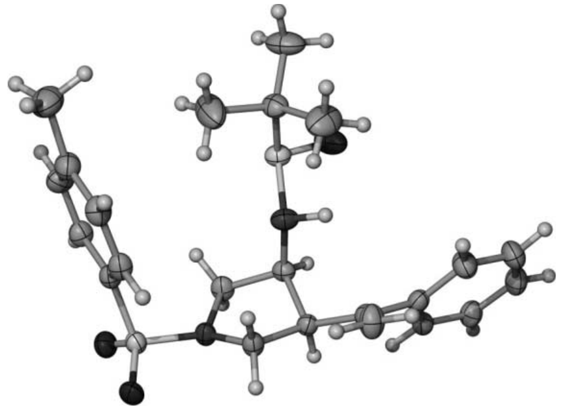


Figure 1. X-Ray crystal structure of **3**.

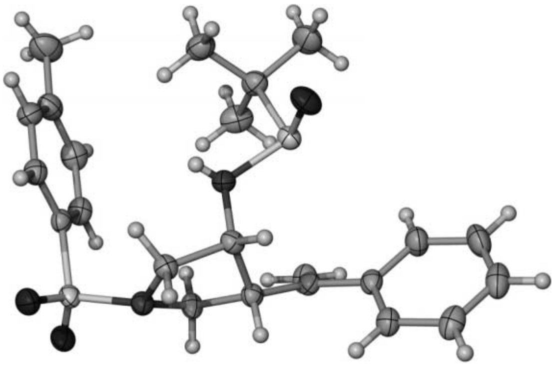


Figure 2. X-Ray crystal structure of **4**.

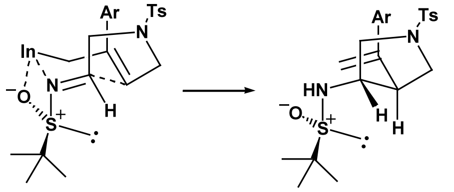
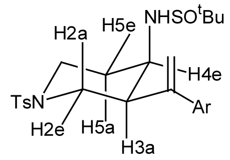


Figure 3.

sulfinyl-oxygen atom to indium in the cyclisation transition state. Variation of the substrate to allow six-membered ring formation resulted in increased diastereoselectivity. This could be because the chelated transition state becomes less strained and therefore more favourable.

The structures of products **5**–**14** are assigned on the basis of the X-ray crystal structures of **3** and **4** together with the very close similarities of the ^{1}H NMR spectra of the major and minor isomers of the five- and six-membered products. Thus for **3**–**10** the 3-H signals appear as triple–triplets or multiplets at δ 3.83–4.00, whilst the 4-H signals appear as multiplets at δ 3.40–3.45. The six-membered products **11**–**14** give rise to a similar tight grouping of signals for the 3-H and 4-H signals which appear as multiplets at δ 3.13–3.40. In the six-membered series the NHSO^{t}Bu is axial since H-5a in **15** shows only one axial–axial coupling ($J\sim 13$ Hz) as does H-2a indicating H-4e is equatorial and H-3a axial.



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This process provides diastereoselective access to a range of chiral functionalised pyrrolidines and piperidines. Further studies using these and related substrates are in hand.

Acknowledgements

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8. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 194644 (major isomer **2**) and CCDC 194645 (minor isomer **3**: obtained as a co-crystal with trace amounts of the major isomer resulting in the presence of both isomers in the unit cell). Copies of the data can be obtained, free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).
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