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3-Component palladium–indium mediated diastereoselective cascade allylation of imines with allenes and aryl iodides†

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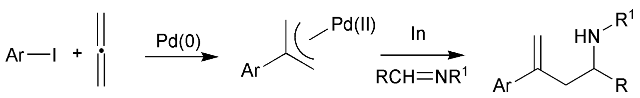
A new palladium–indium diastereoselective cascade allylation of imines using allenes and aryl iodides is described; *N*-tosyl and *N*-aryl homoallyl amines were obtained in moderate to good yields and excellent diastereoselectivity was observed when enantiomerically pure *N*-*tert*-butanesulfinyl imines were employed in the cascade.

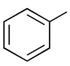
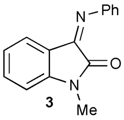
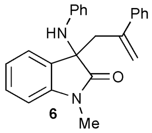
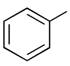
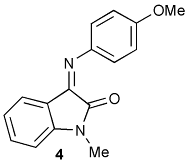
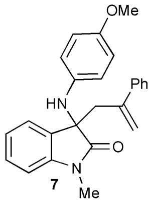
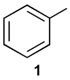
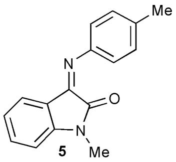
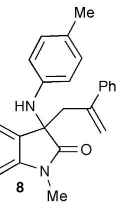
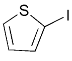
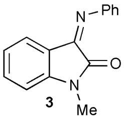
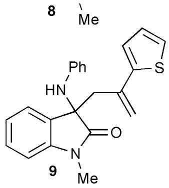
Allylation of carbonyl compounds and imines giving the corresponding homoallylic alcohols or amines is an important synthetic transformation and a number of reagents have been developed for this purpose.[1] Indium has emerged as the metal of choice to mediate the reaction because of its environmentally benign properties allied with a high degree of chemo-, regio- and diastereo-selectivity especially in aqueous media.[2–5] This process requires no activation of the electrophiles and produces fewer side products than other main group allyl derivatives. Recently we reported the multi-component palladium–indium mediated allylation of aldehydes with allenes[6,7] and identified four synthetic variants of this process depending on whether the Pd and In steps are inter- or intra-molecular.

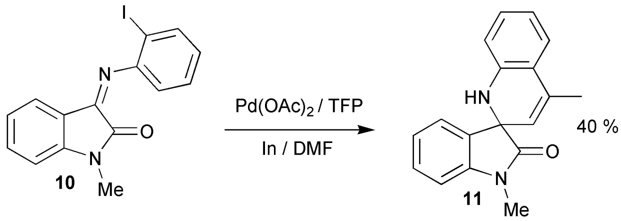
We now describe reactions of allyl indium species, generated by transmetallation[8–10] of π-allyl palladium(II) complexes arising from aryl iodides and allenes, with imines to afford



Scheme 1

Table 1 Cascade allylation of isatin imines

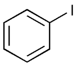
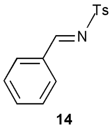
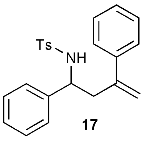
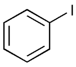
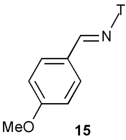
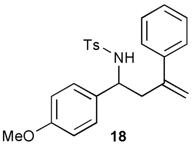
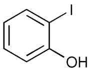
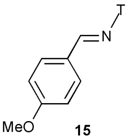
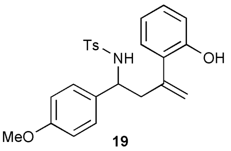
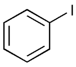
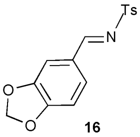
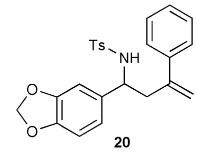
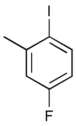
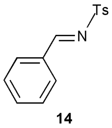
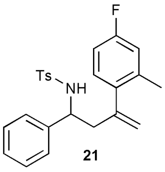
ArI	Imine	Product	Yield (%)
 **1**	 **3**	 **6**	61
 **1**	 **4**	 **7**	51
 **1**	 **5**	 **8**	50
 **2**	 **3**	 **9**	53



10 **11**

Scheme 2

Table 2 Cascade allylation of aryl aldimines

ArI	Imine	Product	Yield (%)
 **1**	 **14**	 **17**	61
 **1**	 **15**	 **18**	51
 **12**	 **15**	 **19**	50
 **1**	 **16**	 **20**	53
 **13**	 **14**	 **21**	53

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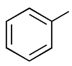
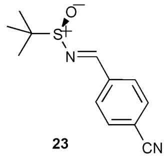
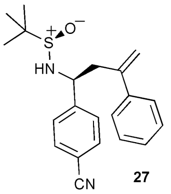
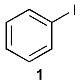
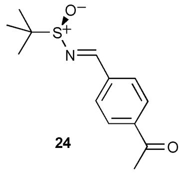
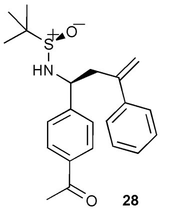
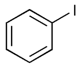
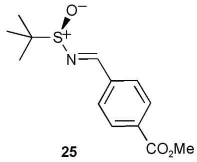
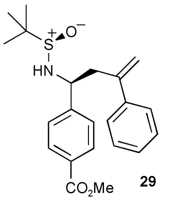
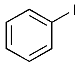
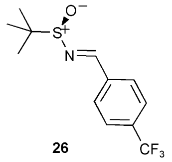
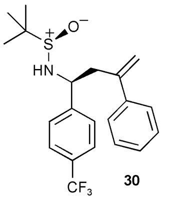
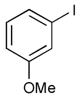
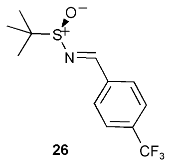
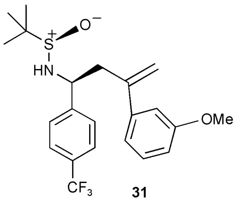
† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b2/b202940e/

DOI: 10.1039/b202940e

Table 3 Enantioselective cascade allylation of (*R*)-*N*-*tert*-butanesulfinyl imines

ArI	Imine[a]	Product	Yield (%)
 **1**	 **23**	 **27**	52
 **1**	 **24**	 **28**	45
 **1**	 **25**	 **29**	56[b]
 **1**	 **26**	 **30**	56
 **22**	 **26**	 **31**	54[c]

[a] All imines are derived from (*R*)-(+)-*N*-*tert*-butanesulfinamide. [b] Based on 83% conversion of imine. [c] Based on 81% conversion of imine.

homoallylic amines (Scheme 1). Initially we explored the class 1 process (intermolecular π-allyl formation, intermolecular allylation) using isatin imines. Thus aryl/heteroaryl iodides **1** and **2** (1.5 mmol) react (DMF, 80 °C, 24 h, Schlenk tube) with allene (1 bar) and isatin imines **3**–**5** (1 mmol) in the presence of indium (1.5 mmol), Pd(OAc)$_2$ (0.1 mmol) and tris(2-furyl)phosphine (0.2 mmol) affording 3,3-disubstituted oxindoles **6**–**9** in 50–61% yield (Table 1). The class 2 process (intermolecular π-allyl formation, intramolecular allylation)(Scheme 2) proceeds *via* a π-allyl Pd(II) complex, transmetallation by indium and subsequent 6-*endo-trig* cyclisation followed by isomerisation of the double bond affording the spiro-oxindole **11**.

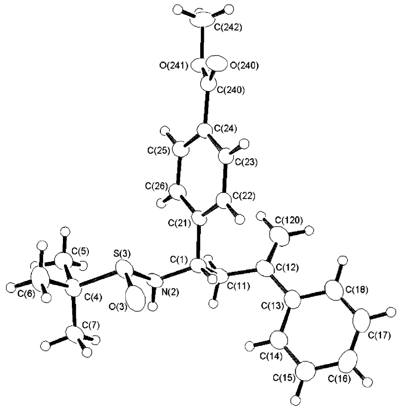


Fig. 1 X-Ray crystal structure of **29**.

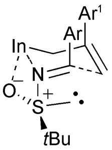


Fig. 2

Sulfonimines **14**–**16** and aryl iodides **1**, **12** and **13** were also successfully incorporated into the cascade yielding substituted homoallylic sulfonamides **17**–**21** in 60–72% yield (Table 2).

Excellent levels of diastereoselectivity are observed when enantiopure (*R*)-*N*-*tert*-butanesulfinyl imines[11] are employed in the cascade (Table 3). Aryl iodides (1.5 mmol), imines (1 mmol) and allene (1 bar) react in the presence of Pd(OAc)$_2$ (10 mol%), tris(2-furyl)phosphine (20 mol%) and In (1.5 mmol) in DMA at 100 °C for 48–60 h to afford a single diastereoisomer **27**–**31**, according to ^{1}H and ^{13}C NMR studies, in each of the cases explored so far (Table 3). The absolute stereochemistry of one of the products, **29**, has been determined by X-ray crystallography (Fig. 1) to be S at the new chiral centre.[12] To rationalise the observed stereochemistry we propose a chelation control model (Fig. 2). Similar transition states have been proposed by others.[13] Yanada *et al* have recently reported a related process using optically active aldimines, palladium(0) and indium(I) iodide.[14]

In conclusion, we have demonstrated a powerful three-component cascade reaction allowing much greater levels of molecular diversity and complexity than classical Barbier-type allylations. Further work is in hand incorporating substituted allenes and other electrophiles into these processes.

We thank the University of Leeds and GlaxoSmithKline for support.

Notes and references

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