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Palladium Catalysed Tetramolecular Cascade Processes Incorporating Allene and Carbon Monoxide

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Abstract. Chemo- and regio-specific palladium catalysed four component cascade processes, involving formation of 4 new bonds, initiated by oxidative addition of Pd(0) with aryl/heteroaryl iodides followed by sequential incorporation of CO(1atm), allene (1atm) and an S- or N-nucleophile[$PhSO_2$- or $(RNTs)^-$] occur in good to excellent yield at 50°C.

The scope of our palladium catalysed cyclisation-anion capture methodology has been considerably extended by the introduction of the relay switch concept[1]. We have recently provided examples of tri-, tetra- and penta- molecular queuing cascades[2,3,4] using these new relay switches.

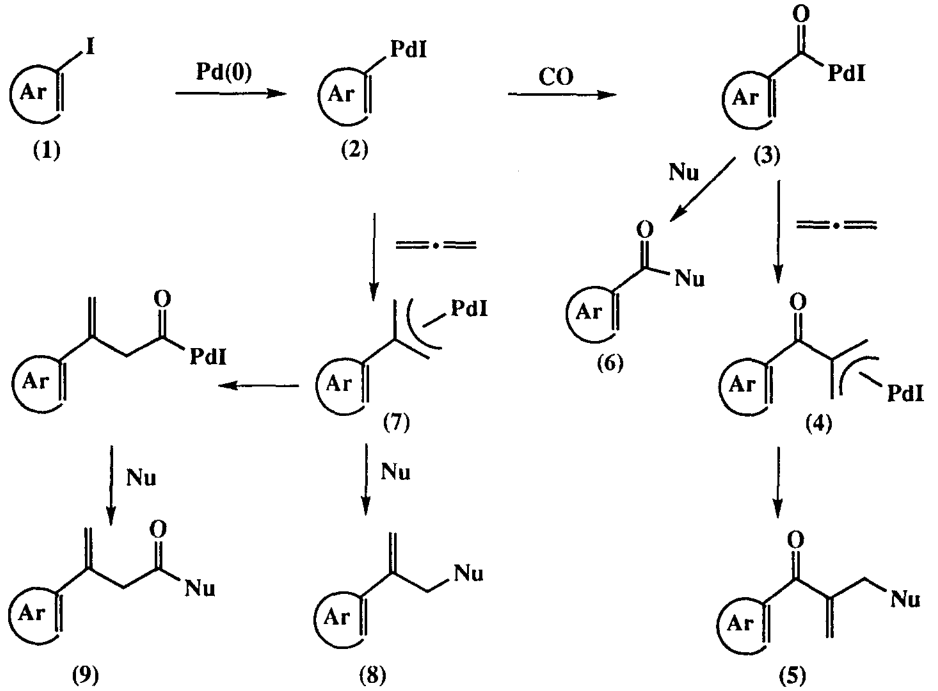
In this communication we report examples of intermolecular cascade processes employing both CO and allene as the relay phase, aryl or heteroaryl iodides as the starter species and either sodium benzene sulphinate or sulphonamides as the terminating species. (Scheme 1).

It is well known that both CO and allene insert into aryl palladium halides generating acylpalladium(II) (3) or π-allylpalladium(II) intermediates (7) respectively. Both of these intermediates have been intercepted by nucleophiles in either inter- or intra-molecular processes.[5,6]

Recently we have shown that the rate of insertion of CO is faster than the rate of insertion of allene into alkylpalladium(II) species and have utilised this rate difference to devise a series of pentamolecular queuing cascades.[4] Thus when both allene (1atm) and CO (1atm) are used in combination with aryl/heteroaryl halides we would expect the cascade to precede via (2), (3) and (4) to furnish (5) (Scheme 1). The realisation of this cascade is now reported. Thus a series of reactions were carried out with aryl/heteroaryl iodides, carbon monoxide (1atm) and sodium benzene sulphinate or sulphonamides (Table 1).

The outline mechanism is shown in Scheme 1 and proceeds via the acylpalladium(II) complex (3) which attacks the allene at the centre carbon atom to give the π-allylpalladium(II) complex (4) which is, in turn, intercepted by the S- or N-nucleophile to give (5) in good to excellent yields.[7]

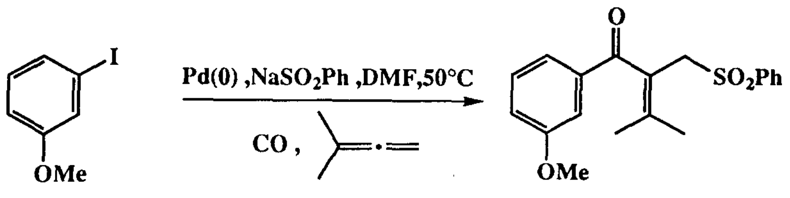
These cascades are 4-component processes and result in the formation of four new bonds. The potential products (6), (8) and (9) were not observed. Recently Alper et al[8] have reported some related processes.



Nu = SO_2Ph, or NRTs

Scheme 1

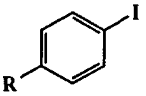
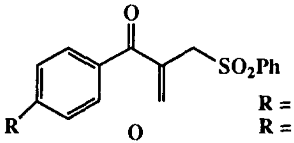
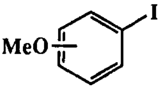
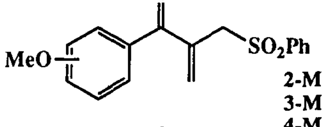
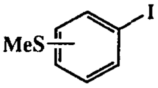
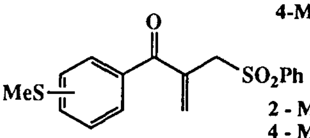
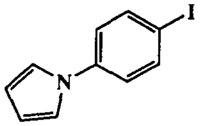
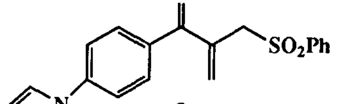
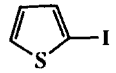
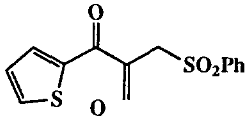
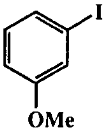
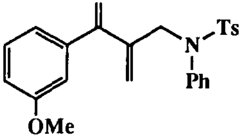
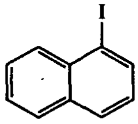
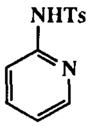
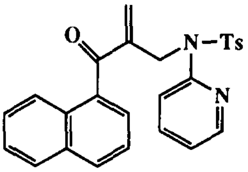
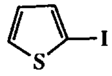
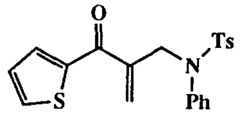
We have briefly studied one example involving a 1,1-disubstituted allene. The reaction of 3-methoxyiodobenzene with carbon monoxide (1atm), 1,1-dimethyl allene and sodium benzene sulphinate (2mol equiv.) using 10mol% $Pd(OAc)_2$ and 20mol% PPh_3 as the catalyst precursor afforded (10) in 40% yield.



(10)

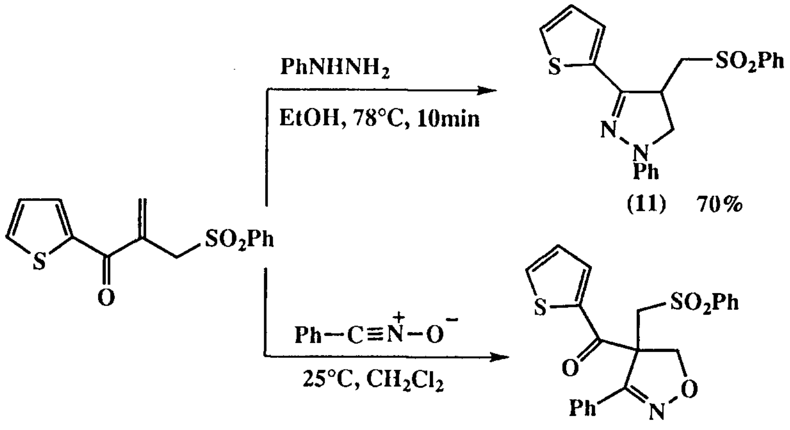
The products of these 4-component cascades are themselves capable of transformation into a wide range of compounds incorporating additional heterocyclic rings. Two examples generating (11) and (12) are shown in Scheme 2.

Table 1. Four component cascades furnishing(5)[a]

Aryl Iodide	Nucleophile[b]	Time (h)	Product (%)
	$NaSO_2Ph$	6	 R = H (58) R = Me (61)
	$NaSO_2Ph$	6(2-MeO) 3(3-MeO) 24(4-MeO)	 2-MeO (53) 3-MeO (91) 4-MeO (60)
	$NaSO_2Ph$	5	 2 - MeS (65) 4 - MeS (55)
	$NaSO_2Ph$	17	 (48)
	$NaSO_2Ph$	6	 (95)
	PhNHTs	6	 (98)
		6	 (50)
	PhNHTs	6	 (95)

a. All reactions carried out at 50°C in a Schlenk tube and employed 1atm CO and 1atm. allene.

b. Cascades involving $NaSO_2Ph$ utlised a catalyst system comprising 5mol% $Pd(PPh_3)_4$, Et_4NCl (1mol equiv) and $NaSO_2Ph$ (2mol equiv) in DMF. Cascades employing sulphonamides employed a catalyst system comprising 10mol% $Pd(OAc)_2$, 20mol% PPh_3, Et_4NCl (1mol equiv), K_2CO_3(2mol equiv) and sulphonamide(2mol equiv) in toluene



Scheme 2

In summary tetramolecular queuing cascades employing aryl/heteroaryl iodides as starter species have been achieved with regiospecific incorporation of allene and CO. The products of the catalytic cascades are versatile substrates for the construction of additional heterocyclic rings.

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