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Three Component Palladium Catalysed Cyclisation-Carbonylation-Anion Capture Processes

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Abstract. *A series of palladium catalysed three component cyclisation-carbonylation-anion capture processes involving aryl iodides, carbon monoxide (1 atm) and Sn(IV)R or B(III)R reagents are reported. The stereo- and regio-specific cascade processes furnish tetrasubstituted carbon centres and fused- and spirocyclic-rings in excellent yield.*

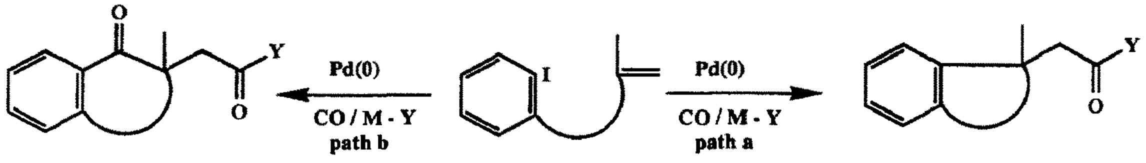
We have recently developed a wide ranging regio- and stereo-specific palladium catalysed cascade cyclisation-anion capture process.[1] The current scope of the process is summarised in Table 1.

Table 1. Reactant Combinations for Cascade (Poly) Cyclisation-Anion Capture Processes.

Starter Species	Relay Species (R)	Terminating Species (T)	Y
alkyl	alkene	alkene	**anionic** [H,OAc, CN, SO_2Ph, $CH(CO_2Me)_2$] **neutral** (amines,
aryl	alkyne	alkyne	
vinyl	1,2-diene	1,2-diene	MeOH/CO,CO, acrylates) **organometallics**
allyl	1,3-diene	1,3-diene	RM[M=Sn(IV), B(III), Zn(II)]

The process involves oxidative addition of Pd(0) to the starter species (halide, OTf) followed by cyclisation onto the terminating species (for monocyclisations) and transfer of the atom or group Y. In polycyclisations the initial cyclisation occurs onto a relay species and further cyclisations can occur in the relay phase before the terminating species is engaged. The methodology has been realised for all the "anion" transfer reagents (anionic[1,2], neutral[3], organometallic[4]) shown in Table 1. However, the scope of the anion transfer segment of the cascade appears capable of significant further extension, both by the introduction of new Y reagents and by making use of combinations of the existing Y reagents. This communication is concerned with the latter.

We recently reported palladium catalysed cascade cyclisation-anion processes involving insertion of carbon monoxide and subsequent methanolysis leading to incorporation of a CO_2Me moiety. The rate enhancing effects of Tl(I) salts on these processes were notable and enabled the carbonylations to be achieved at atmospheric pressure.[5] Subsequently we showed that such cyclisation-carbonylation processes could be terminated intramolecularly by a proximate carbon-, nitrogen- or oxygen-centred nucleophile leading to spirocycles.[6] Thus carbon monoxide, a neutral Y species, has been combined with an anionic Y species (malonate)[6] and with neutral Y species (amines, alcohols)[5,6] giving neutral-anionic and neutral-neutral combinations of two different Y species. We now report examples of the neutral (CO)-organometallic combination (Scheme 1, path a) utilising aryl halide starter species (Table 2).



Scheme 1

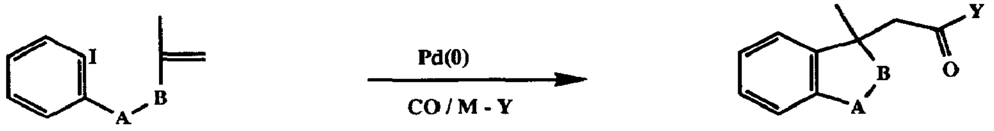
Table 2. Products from the reaction of (1a-c), carbon monoxide, and (3), (4) or $NaBPh_4$.[a]

Aryl Iodide	M-Y	Product	Yield(%)
1a	3a	2a	88
1b	3a	2b	87
1a	3b	2c	83
1c	3b	2d	71
1a	3c	2e	61
1b	3c	2f	78
1a	4	5a	52
1b	4	5b	61
1a	$NaBPh_4$[b]	2g	80
1c	$NaBPh_4$[b]	2h	82
6	$NaBPh_4$[b]	7	60

a. Reactions carried out in toluene at 110°C for 15h, unless otherwise noted, and employed a catalyst system comprising 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3 and Et_4NC(1 mol).

b. Reaction carried out in anisole at 110°C [120°C for (6) → (7)] for 15h and employed a catalyst system comprising 10 mol% $Pd(OAc)_2$ and 20 mol% tri(2-furyl)phosphine.

A variety of hydrocarbon (styryl) and heterocyclic (furyl, pyridyl) moieties are transferred from Sn(IV) in excellent yield in a three component cyclisation-anion transfer process (1a-c) → (2a-f) involving concomitant carbonylation (Table 2). The SEM protected indole (4) reacts in an analogous manner with (1a) and (1b) to give (5a)(52%) and (5b)(71%) respectively. Sodium tetraphenylborate proved an effective phenyl transfer agent in this three component process. Thus (1a) and (1c) give (2g) and (2h) respectively in excellent yield, whilst (6) gives (7) (Table 2).

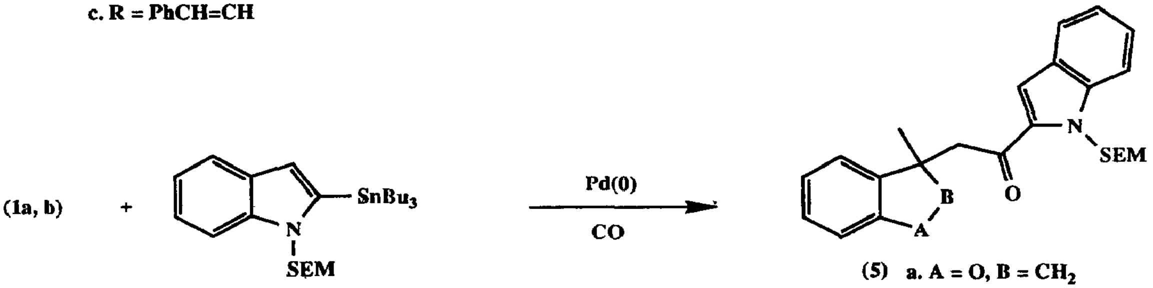


(1) a. $A = O, B = CH_2$
b. $A = NCH_2Ph, B = CO$
c. $A = NSO_2Ph, B = CH_2$

(2) a. $A = O, B = CH_2, Y = 2$ - furyl
b. $A = NCH_2Ph, B = CO, Y = 2$ - furyl
c. $A = O, B = CH_2, Y = 2$ - pyridyl
d. $A = NSO_2Ph, B = CH_2, Y = 2$ - pyridyl
e. $A = O, B = CH_2, Y = CH{=}CHPh$
f. $A = NCH_2Ph, B = CO, Y = CH{=}CHPh$
g. $A = O, B = CH_2, Y = Ph$
h. $A = NSO_2Ph, B = CH_2, Y = Ph$

$n\text{-}Bu_3SnR$

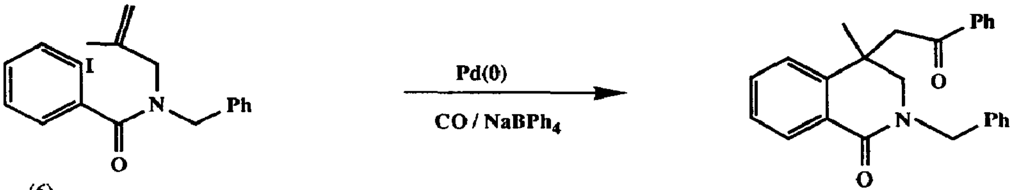
(3) a. R = 2 - furyl
b. R = 2 - pyridyl
c. $R = PhCH{=}CH$



(4) $SEM = CH_2OCH_2CH_2SiMe_3$

(5) a. $A = O, B = CH_2$
b. $A = NCH_2Ph, B = CO$

The potential of the three component process for creating fused rings stereospecifically with concomitant ring junction functionalisation is illustrated by the conversion (anisole, 120°C, CO, $NaBPh_4$) of (8) into (9)(84%).[8]



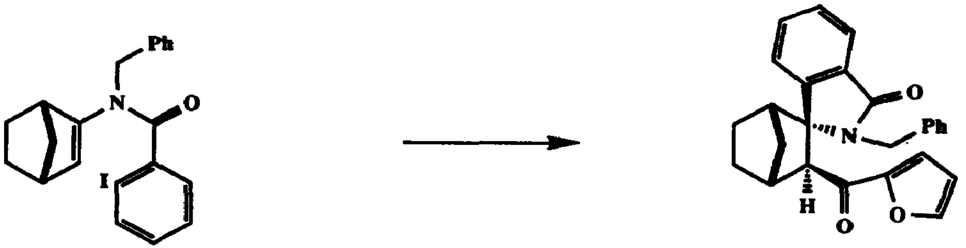
(6)

(7)

(8)

(9)

Spirocycle formation is illustrated by the stereospecific conversion [toluene, 110°C, CO, Bu_3Sn(2-fury)] of (10) to (11)(82%).[8]



(10) (11)

Further studies on three component processes including Scheme 1, path b, and related reactions are underway.

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7. Solutions were saturated with CO prior to attachment of a CO filled balloon to the condenser.
8. Stereochemistry assigned from n.O.e. data.

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