Palladium Catalysed Cascade Bis-Cyclisation-Anion Capture Processes Proceeding Via Allenyl-Palladium(II) Starter Species. 1-Vinyl-3-azabicyclo[3.1.0]hexanes.

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Abstract: An additional starter species [allenylpalladium(II)] has been implemented for palladium catalysed cascade cyclisation-anion capture processes. Good yields of bis-cyclisation-anion products involving anionic ($NaBPh_4$), neutral (CO/MeOH) and organometallic (Bu_3SnR) capture agents are reported. Copyright © 1996 Elsevier Science Ltd

In developing our palladium catalysed cascade cyclisation-anion capture process[1,2] we have implemented a wide range of starter, relay, terminating and Y species (Table 1) and Scheme 1 illustrates a typical cascade[3] which generates a single diastereomer.

Table 1.

Potential Combinations for (Poly)cyclisation Anion-Capture Processes

Starter Species	Relay Species (R)	Terminating Species (T)	Y
alkyl	alkene	alkene	anionic (H, OAcCN, SO_2Ph, $CH(CO_2R)_2$]
aryl	alkyne	alkyne	neutral (amines, MeOH/CO, acrylates)
vinyl	1,2-diene	1,2-diene	organometallics RM[M=Sn(IV),
allyl	1,3-diene	1,3-diene	B(III), Zn(II)]

A missing element from Table 1 is the implementation of an allenic starter species. We now report a range of cascade processes involving initial formation of allenylpalladium(II) species. Tsuji and co-workers have developed extensive chemistry based on the reaction of Pd(0) with propargylic carbonates resulting in the facile irreversible generation of allenylpalladium(II) species (Scheme 2).[4] This procedure offers entry to wide and varied range of allenylpalladium(II) species.

Scheme 1

P=SO$_2$Ph
R=relay moiety
T=terminating moiety
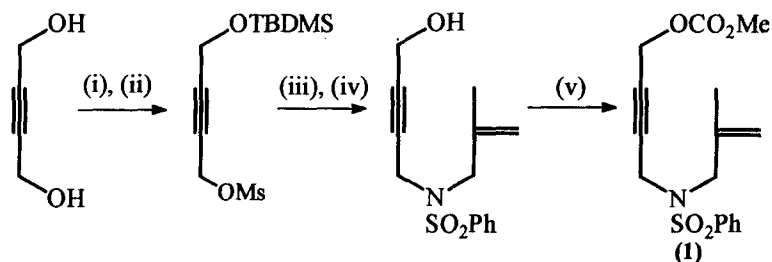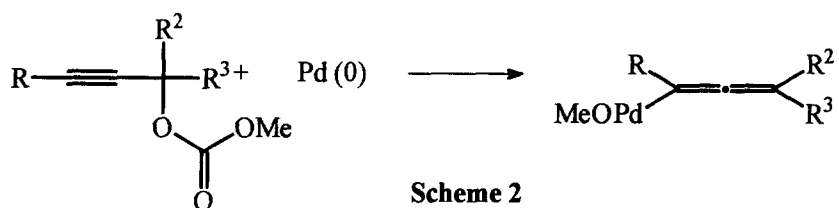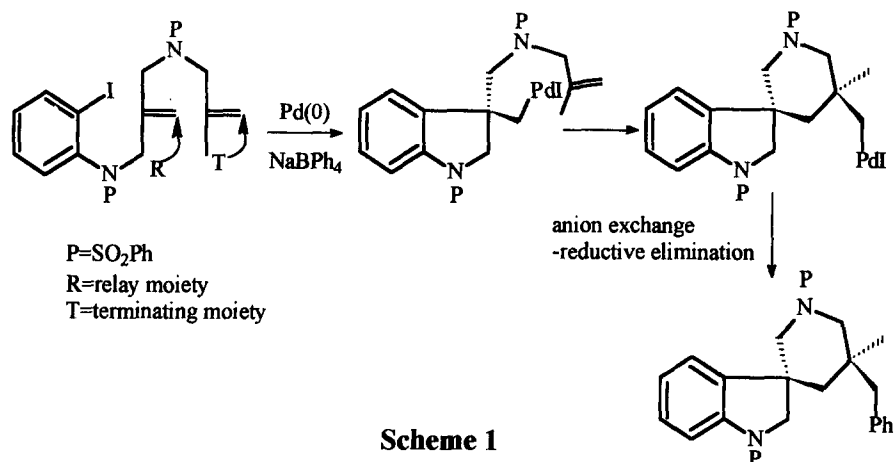
Scheme 2

Scheme 3 (i) Imidazole, TBDMSCl, DMF, 16h, 0-25°C (70%). (ii) MsCl, Et$_3$N, CH$_2$Cl$_2$, 2h, 0-25°C (96%). (iii) NaN(SO$_2$Ph)CH$_2$C(Me)=CH$_2$, DMF 16h, 0-25°C. (iv) TBAF, THF, 2h, 25°C (71%). (v) ^{n}BuLi, ClCO$_2$Me, THF, 3h, -78-25°C (76%).

The substrate (1) utilised in this series of cascades was prepared as outlined in Scheme 3. When (1) was reacted (anisole, 85°C, 16h) with sodium tetraphenylborate (1mol eq) and a catalyst system comprising 10mol% Pd(OAc)$_2$ and 20mol% PPh$_3$ it afforded the 3-azabicyclo[3.1.0] hexane (5) (Scheme 4) in 73% yield.[5] The mechanism of the process is outlined in Scheme 4. Formation of the allenylpalladium(II) species is followed by 5-exo-trig cyclisation generating (3). The normal preference for attack of an organopalladium(II) species at the central carbon atom of an allene[1,6] is circumscribed by the geometrical constraints imposed by the ring in (3). We have previously observed that 3-exo-trig cyclisations generating bicyclo [3.2.1] hexane systems are facile processes[7] and in this case cyclisation (3) → (4) is not impeded by geometrical constraints. The vinylpalladium(II) species (4) then undergoes anion capture generating (5).

a. R= 2-thienyl
b. R=C≡CPh
c. R= 2-furyl
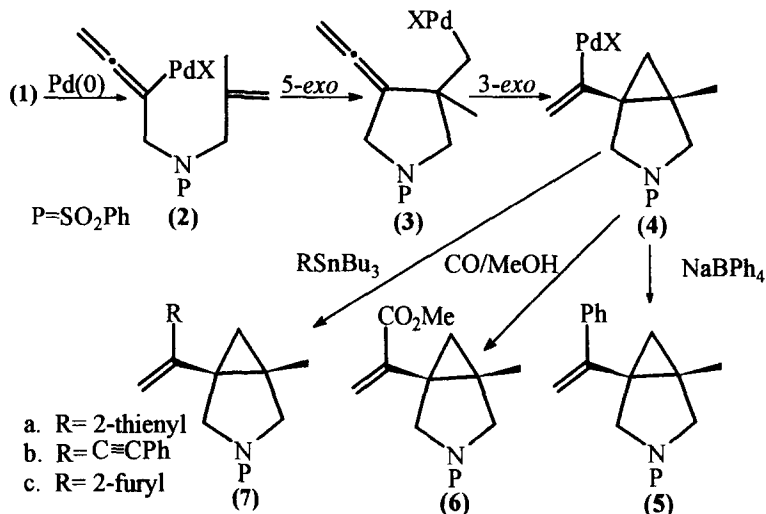
Scheme 4

A similar anion capture process was then carried out using CO/MeOH as the capture agent. The same catalyst as before was employed and the reaction was carried out in boiling methanol under 1atm of carbon monoxide. The product (6) was isolated in 80% yield. No products such as (8) or (9) arising from premature insertion of carbon monoxide were detected.
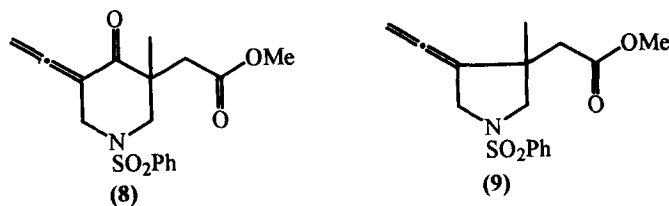
Attempts to implement the same catalyst system with anion capture from organotin(IV) reagents gave only moderate yields (30-46%) of azabicyclo [3.1.0] hexanes (7). Substantially improved yields were obtained in boiling THF with a catalyst system comprising 10mol% Pd(OAc)$_2$ and 40mol% Ph$_3$As[8]. Thus Bu$_3$ (2-thienyl) Sn(IV) (1.1eq) afforded (7a)(64%), Bu$_3$SnC≡CPh afforded (7b)(62%) and Bu$_3$(2-furyl)Sn(IV) afforded (7c)(54%).

The successful implementation of allenylpalladium(II) starter species for cascade cyclisation-anion capture has been achieved. The process outlined in Scheme 4 procedes via an alkene relay species and a 1,2-diene terminating species and examples of all three types of anion capture agents (Table 1) have been provided.

Further developments of these versatile starter species are in hand.

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