



Palladium Catalysed Pentamolecular Queuing Cascades.

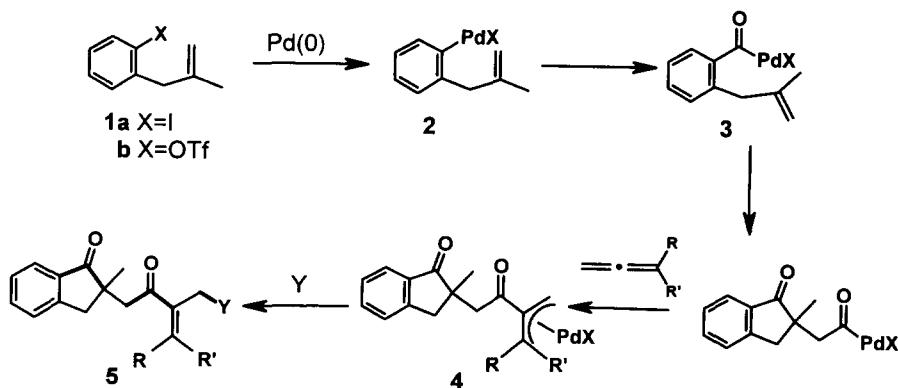
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Abstract: Regiospecific pentamolecular queuing cascades involving formation of 5 new bonds and cycloacylpalladation have been achieved. The processes employ vinyl and aryl halide or triflate starter species together with allenes and carbon monoxide (1atm) and both preformed and in situ generated Pd(0) catalysts. © 1997 Elsevier Science Ltd.

The scope of our palladium catalysed cyclisation-anion capture methodology¹ has been considerably extended by the introduction of substrates that expand the relay phase of the cascade and which, in appropriate cases, permit switching between inter- and intra-molecular processes in the relay phase leading to polymolecular queuing cascades. We have provided examples of tri- and tetra-molecular queuing cascades^{2,3} and in this communication we report examples of pentamolecular queuing cascades employing both carbon monoxide and allene in the relay phase and aryl and vinyl halides or triflates as the starter species.¹

2-Methallyliodobenzene (1a) and the analogous triflate (1b) were selected as representative aryl starter species.



Scheme 1

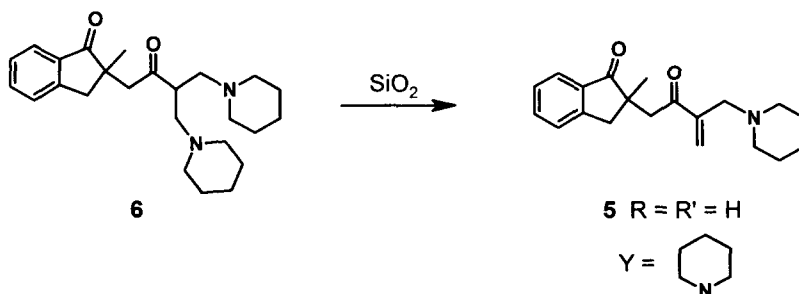
A series of reactions were carried out with (1a) and (1b) varying the allene and the "anion-transfer" agents Y (Scheme 1) (Table 1). These cascades incorporated 2 molecules of carbon monoxide, result in the formation of 5 new bonds and constitute pentamolecular queuing processes.

Table 1. Pentamolecular queuing cascades.^a

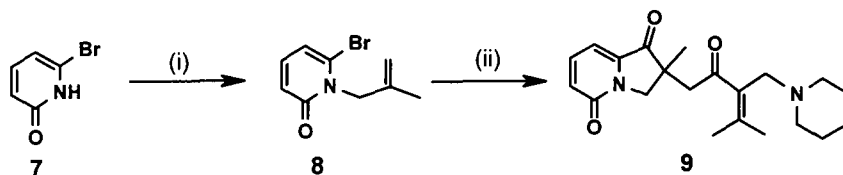
Starter Species	Allene ^b	Y	Time(h)	Yield(%) ^c
1a	2,R=R ¹ =H	piperidine	17	55
1a	2,R=R ¹ =H	pyrrolidine	16	57
1a	2,R=R ¹ =H	morpholine	18	67 ^b
1a	2,R=R ¹ =H	Ph (NaBPh ₄)	0.5	50
1a	2,R=R ¹ =Me	piperidine	2.5	80 ^d
1a	2,R=R ¹ =Me	morpholine	18	78 ^d
1a	2,R=H,R ¹ =Ph	piperidine	0.5	30 ^d
1b	2,R=R ¹ =Me	morpholine	20	30 ^e

- All reactions carried out in toluene at 110°C using a catalyst system comprising 10mol% Pd(OAc)₂, 20mol%PPh₃, K₂CO₃ (4mol.eq.), Et₄NCl (1mol.eq.) and Y(2mol.eq).
- Allene gas (1atm) and CO (1atm) employed in a Schlenk tube. Appropriate reactions employed dimethylallene (5-10 mol.eq.) and phenylallene (1.1 mol.eq.).
- Isolated yields.
- 5 mol% Pd(PPh₃)₄ used as catalyst.
- 10mol% PdCl₂ (dppf) used as catalyst.

The inherently slow rate of 4-exo-trig cyclopalladation of the initial oxidative addition product (2) (Scheme 1) allows carbonylation to occur generating (3) which has a considerably enhanced cyclisation rate (5-exo-trig cycloacylpalladation). A second carbonylation is followed by acylpalladation of the allene at the centre carbon atom⁴ and anion capture at the least substituted terminus of the π -allyl species to give (5). In this cascade five new bonds are formed [shown in bold in (5)]. The isolated yields underestimate the actual yields due to the instability of the products to chromatography on silica. This is illustrated by the reaction of (1a) with allene, CO and piperidine. When piperidine (2mol.eq.) was added to the cooled reaction mixture prior to workup the Michael adduct (6) was formed. Chromatography then resulted in a retro-Michael reaction but gave (5, R=R¹=H, Y=N-piperidinyl) in 75% overall yield from (1a).



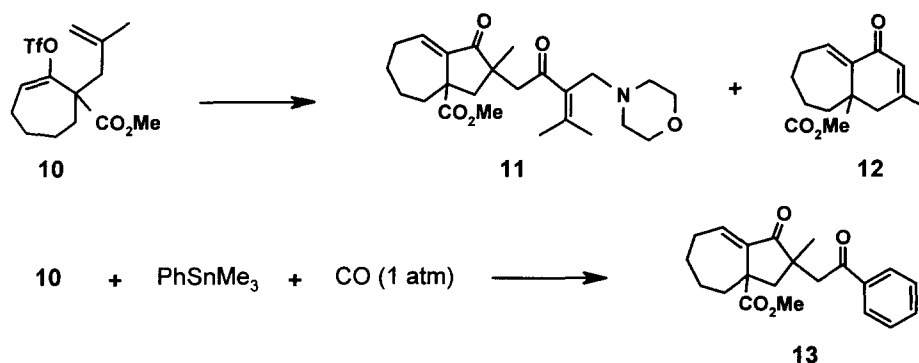
Vinyl bromide (7)⁵ was alkylated with methallyl chloride to provide the cascade substrate (8) (52%). Reaction of (8) with carbon monoxide 1,1-dimethylallene and piperidine using Pd(PPh₃)₄ as catalyst afforded (9) (54%) (Scheme 2).



- (i) NaH, LiBr, methallyl chloride⁵
 (ii) 1,1-dimethylallene (10 mol.eq.), CO (1 atm), piperidine (2 mol.eq.)
 Bu₄NBr (1 mol.eq.), 5 mol% Pd(PPh₃)₄, toluene, 100°C, 3.5 h

Scheme 2

A vinyl triflate example has been examined using (10) as substrate. Reaction (DMF, 110°C, 3h) of (10) with 1,1-dimethylallene (5mol.eq.), CO (1atm) and morpholine (3mol.eq.) in the presence of 10mol% of PdCl₂(dppf) afforded a mixture of (11) (32%) (6:1 mixture of diastereomers) and (12) (10%). A related tetramolecular process was carried out by reacting (10) with CO(1atm) and PhSnMe₃ (1.1mol.eq.) using the same catalyst and conditions but with the addition of LiCl (3mol.eq.). This reaction afforded (13)(51%) as a 3:1 mixture of diastereomers.



In summary, pentamolecular queuing cascades employing vinyl and aryl halides and triflates as starter species have been achieved with regioselective incorporation of allene and a mono- and di-substituted allenes in addition to carbon monoxide.

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References.

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