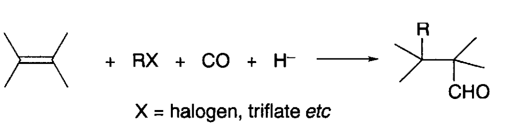
Palladium-catalysed Cyclisation–Carboformylation. Molecular Queuing Cascades

Stephen Brown,[a] Steven Clarkson,[b] Ronald Grigg*[b] and Visuvanathar Sridharan[b]

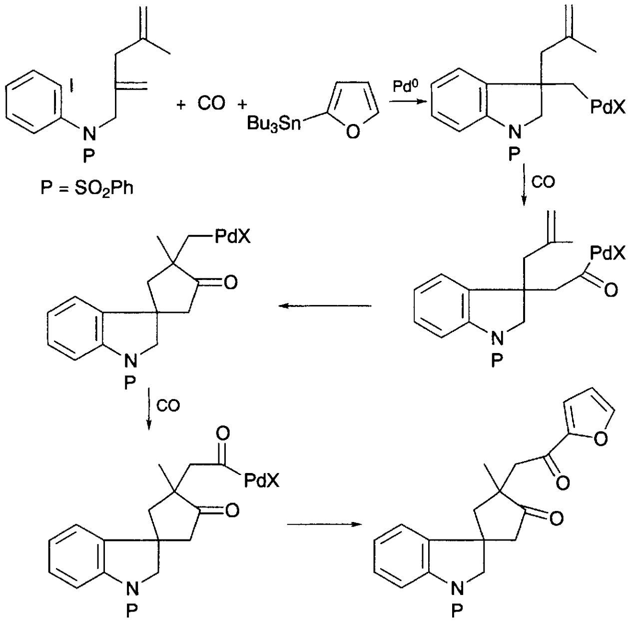
[a] *Zeneca Fine Chemicals Manufacturing Organisation, Leeds Road, Huddersfield, UK HD2 1FF*
[b] *School of Chemistry, Leeds University, Leeds, UK LS2 9JT*

Palladium(0)-catalysed tri- and tetra-molecular queuing cascades are described involving five- and six-membered ring formation accompanied by carboformylation of a proximate alkene and employing carbon monoxide (1 atm) and diphenylmethylsilane as the source of the formyl group.

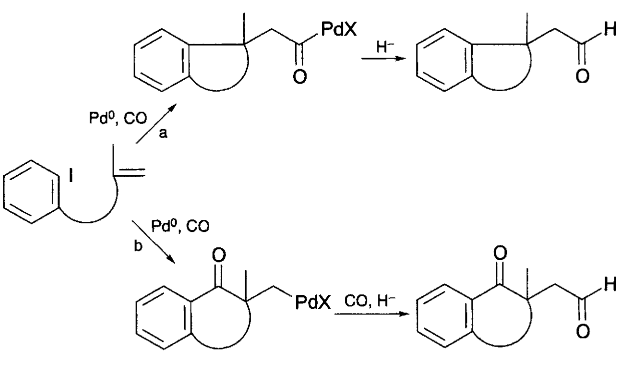
The catalytic hydroformylation of alkenes is a major industrial process[1] which has also attracted substantial applications in fine chemical synthesis.[2] It is nevertheless a process in which control of regioselectivity is a perennial problem. A related process of similar wide potential would be catalytic carboformylation (Scheme 1). Our novel palladium catalysed cyclisation–anion capture method[3] has very recently been significantly expanded in scope and synthetic utility by our demonstration of tri- and tetra-molecular queuing processes employing carbon monoxide[4,5] of which Scheme 2 is an example.



Scheme 1



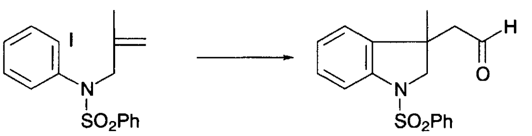
Scheme 2



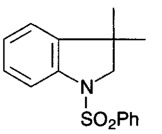
Scheme 3

Molecular queuing processes such as that depicted in Scheme 2 require the relative rates of the various desired and other potentially possible processes to be in the correct order for the desired process. Examples of related processes involving trapping of acylpalladium intermediates by alcohols and amines have also been reported.[6,7] In this communication we report further extensions of our cascade cyclisation–anion capture process involving tri- and tetra-molecular queuing processes which result in the first examples of palladium catalysed cyclisation–carboformylation (Scheme 3).

For the operation of the trimolecular queuing process (Scheme 3, path a) the relative rate of hydride capture is required to be slower than both cyclisation and carbonylation. Such a situation is obtained when **1** is treated (toluene, 110 °C, 7 h) with carbon monoxide (1 atm) and diphenylmethylsilane (2 mol) as hydride source using a catalyst system comprising 10 mol% palladium acetate, 20 mol% triphenylphosphine and tetraethylammonium chloride (1 mol).[8] The desired product **2** is obtained in 61% yield.



1 **2**



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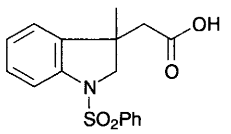

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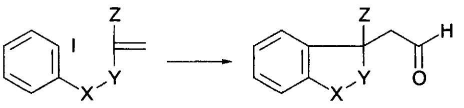
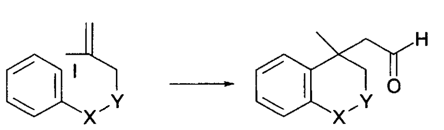


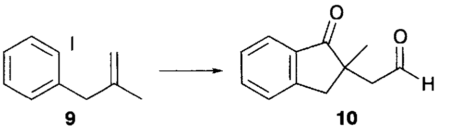
5 **6**

a X = O, Y = CH$_2$, Z = Me
b X = NCH$_2$Ph, Y = CO, Z = Me
c X = NSO$_2$Ph, Y = CH$_2$, Z = CO$_2$Me



7 **8**

a X = O, Y = CH$_2$
b X = CO, Y = NCH$_2$Ph



9 **10**

When sodium formate is used as the hydride source in place of diphenylmethylsilane the carbonylation fails to occur and **3** (70%) is the sole product. Use of diphenylmethylsilane (1 mol) results in a slower reaction and formation of up to 10% of acid **4**.

When substrates **5a–c** were subjected to analogous conditions to those used for **1** → **2** they also underwent 5-*exo-trig* cyclisation–carboformylation to **6a–c** in 45–60% yield.

Two representative examples of cyclisation–carboformylation involving an initial 6-*exo-trig* cyclisation have been studied. Thus **7a** and **7b** give **8a** (61%) and **8b** (54%), respectively, using the same conditions as those employed for **1** → **2**.

One example of a tetramolecular queuing process (Scheme 3, path b) has been studied. Thus **9** reacted (toluene, 110 °C, 7 h) with carbon monoxide (1 atm) and diphenylmethylsilane (2 mol), using the same catalyst system as before, to give **10** (45%).

Further developments of the cyclisation–carboformylation and carboformylation of alkenes are under study.

We thank Leeds University, Zeneca Fine Chemicals Manufacturing Organisation, and the EPSRC for support.

Received, 31st January 1995; Com. 5/00582E

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