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Alkylpalladium(II) Species. Reactive Intermediates in a Bis-cyclisation Route to Strained Polyfused Ring Systems.

Ronald Grigg,* Visuvanathar Sridharan and Sukanthini Sukirthalingam.

School of Chemistry, Leeds University, Leeds LS2 9JT.

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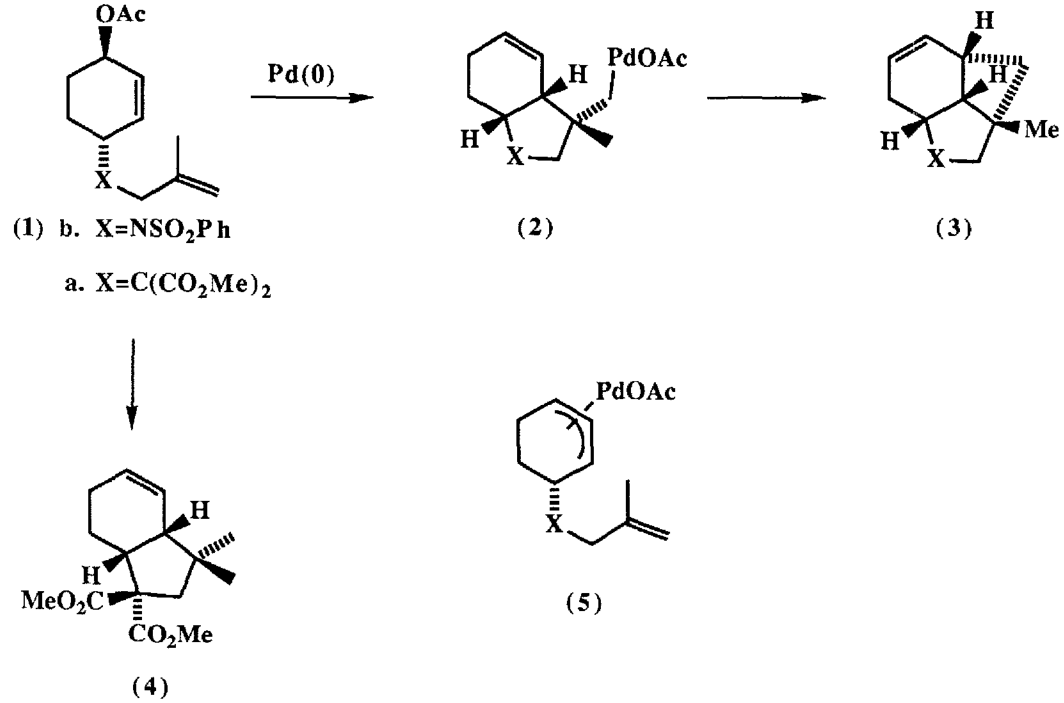
Abstract: *4-Alkenyl-allylic and-vinylic acetates or bromides undergo Pd(0) catalysed bis-cyclisation via an initial 5- or 6-exo-trig ring closure generating an alkylpalladium(II) intermediate which reacts further via a 3-, 4- or 5-exo-trig cyclisation onto a proximate alkene or aryl ring generating strained polyfused ring systems stereospecifically*

Palladium (0) catalysed cyclisation processes are currently attracting much attention consequent on significant progress on extending the intramolecular Heck reaction to the construction of bridged-, fused- and spiro-cyclic systems and tetrasubstituted carbon centres,[1,2] the remarkable stereospecificity of our recently described tandem cyclisation-anion capture process,[3] and developments in metallo-ene cyclisation processes [4] This resurgence of interest has included several isolated examples of the unexpected palladium catalysed formation of strained (3- or 4-membered) ring systems.[3,5,6] We now report results showing that this is a more general process than hitherto realised and that it results from the high reactivity of intermediate alkylpalladium (II) species.

The π-allylpalladium (II) precursor (1a) undergoes a stereospecific bis-cyclisation sequence when treated with a catalytic amount[7] of palladium acetate and triphenylphosphine in anisole containing sodium formate (1 1 mol) giving the 6/5/4/-fused systems (3a) via the intermediate alkylpalladium (II) species (2a). The nitrogen analogue (1a) cyclises (80°, 12h) more rapidly than the carbon-analogue (1b)(110°C, 19h, 62% conversion), but in both cases yields are excellent (80% and 70% respectively) In this latter case complete conversion to product (3b) (61%) occurs when the reaction is carried out in acetonitrile (80°C, 19h) with triethylamine (3 mol) replacing the sodium formate. A trace amount (ca 4%) of an unidentified product is also produced under these conditions. Four new stereocentres and two rings are thus created with complete stereocontrol The stereochemistry of (3a), (3b) and (4) was established by n O.e studies

Interestingly, when formic acid (5 mol) was used in place of sodium formate (1b) underwent Pd(0) catalysed cyclisation-anion capture (H^-)[8] (MeCN, 80°C, 19h) to (4) (64%) The stereochemistry of the alkylpalladium (II) species is that expected based on Oppolzer's reported metallo-ene cyclisation-carbonylation sequence on a closely related substrate [9]

Formation of (3) and (4) proceeds via an initial π-allylpalladium species(5). Examples involving initial formation of a vinyl palladium species are provided by the stereospecific cyclisation of (6a) and (6b)



(1) b. $X=NSO_2Ph$

a. $X=C(CO_2Me)_2$

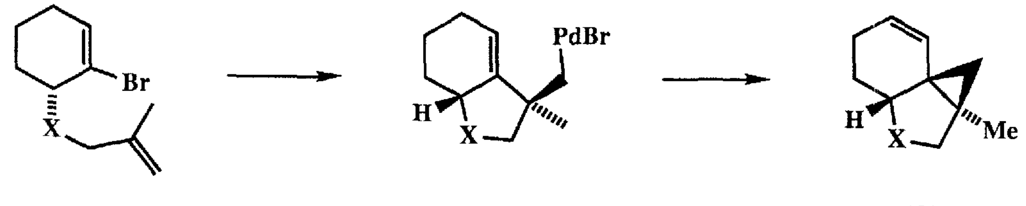
(2)

(3)

(4)

(5)

Thus (6a) cyclises [anisole, KOAc(2 mol), 80°C, 12h] to (8a) (78%) via the alkylpalladium (II) species (7a) The carbon analogue (6b) cyclises [MeCN, K_2CO_3(2 mol), Et_4NCl(1 mol), 80°C, 9h] to (8b) (67%) The stereochemistry of (8a) and (8b) was established by n.O.e. studies No products arising from 6-endo-trig cyclisation were detected.



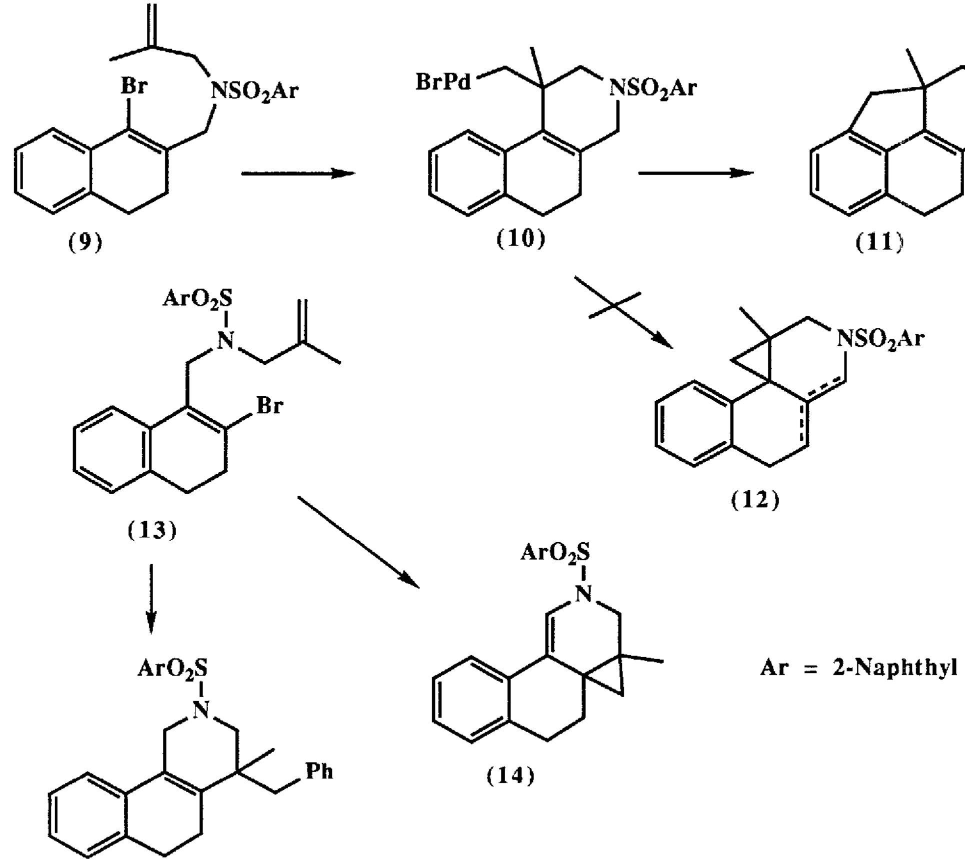
(6) a. $X = NSO_2Ph$

b. $X = C(CO_2Me)_2$

(7)

(8)

An interesting example involving a final cyclisation onto an aromatic ring is provided by the conversion [anisole, KOAc(2 mol), 140-150°C, 18h] of (9)h to (11) (50%). In this example the intermediate alkylpalladium species (10) could cyclise to give a 5- or 3-membered ring product (11) or (12) respectively No 3-exo-trig cyclisation product (12) is observed Related cyclisation of alkylpalladium (11) species onto aromatic rings have been reported.[10]



The possible influence of peri-steric effects arising from the ortho aryl-H on the conversion (9) → (11) was probed by studying the cyclisation of (13) The bis-cyclisation (13) → (14) failed to occur at 90° [anisole, KOAc (1.1 mol), 24h] although the initial 6-exo-trig cyclisation occurred readily (anisole, 80°, 12h) and in the presence of sodium tetraphenylborate afforded the cyclisation-anion capture product (15) (75%). However, cyclisation of (13) at elevated temperature [anisole, KOAc (1.1 mol), 140°C] gave rise to a mixture of products one of which was the cyclopropane (14).

Further exploration of these processes are in hand.

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