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Palladium Catalysed Cyclisation-Cyclopropanation and Cyclisation - Anion Capture Processes of Vinyl Triflates

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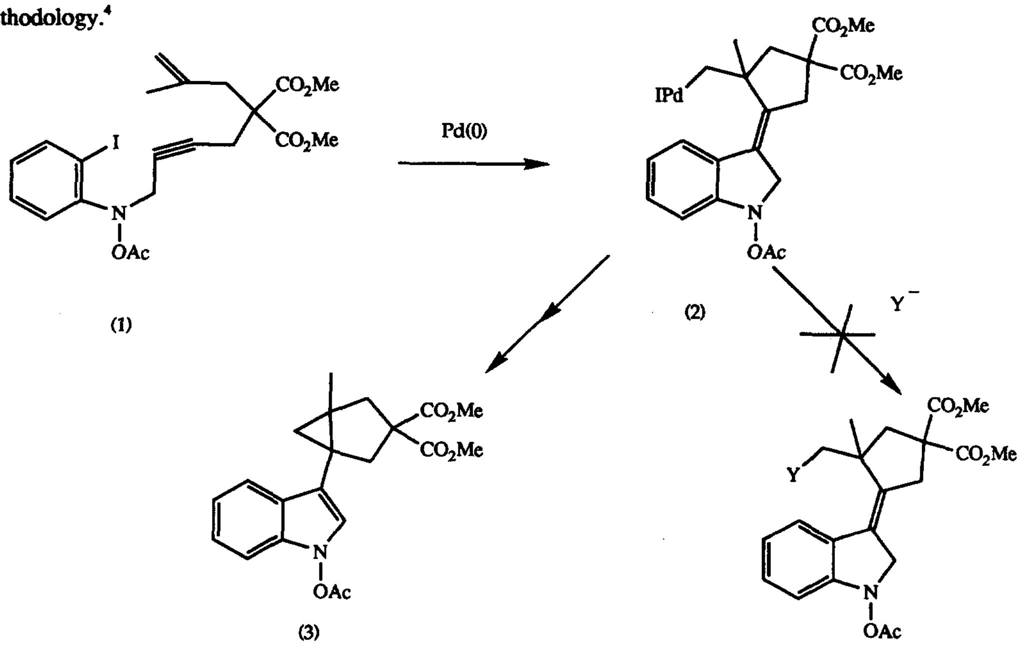
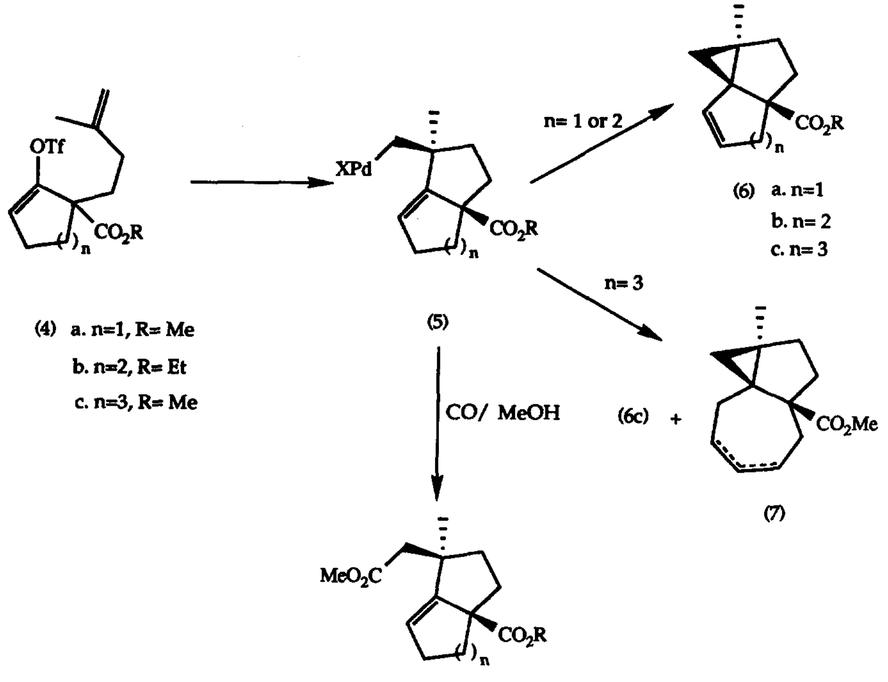
Abstract. *Cyclisation-carbomethoxylation can successfully compete with 3-exo-trig cyclisation of organopallation(II) species. Cyclisation with anion transfer from boron can be achieved in high yield in competition with a 3-exo-trig cyclisation process that lacks a subsequent β-hydride elimination pathway.*

We recently reported a series of facile palladium catalysed bis-cyclisation processes of both aryl halides and allylic acetates which result in the stereospecific formation of tricyclic systems containing 3- and 4-membered rings in excellent yield.[1,2] Subsequently we showed that cyclopropanation could be achieved intermolecularly.[3] In our initial work,[1] we observed that the substrate (1) gave (3) despite attempts to intercept intermediate (2) by hydride (from HCO_2Na) or Ph^-(from $NaBPh_4$) using our cyclisation-anion capture methodology.[4]



The synthetic application of our novel cyclisation-anion capture methodology requires a knowledge of the relative rates of cyclisation versus anion capture. It was of interest to extend the cyclopropanation methodology to vinyl triflates and explore the ability of carbon monoxide insertion to compete with a 3-exo-trig cyclisation. The vinyl triflates (4a-c) were prepared by standard methods using Comin's triflating reagent.[5] Cyclisation-cyclopropanation to (6a,b) and a mixture of (6c) (major isomer) plus (7, mixed double bond isomers) occurred smoothly in 70-73% yield in acetonitrile at 80°C using a catalyst system comprising 10mol% $Pd(OAc)_2$, 20mol% PPh_3, anhydrous sodium carbonate (2mol) and tetraethylammonium chloride (1mol).



(4) a. n=1, R= Me
b. n=2, R= Et
c. n=3, R= Me

(5)

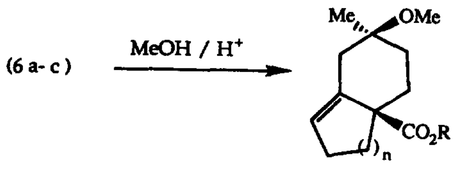
(6) a. n=1
b. n= 2
c. n= 3

(7)

(8)

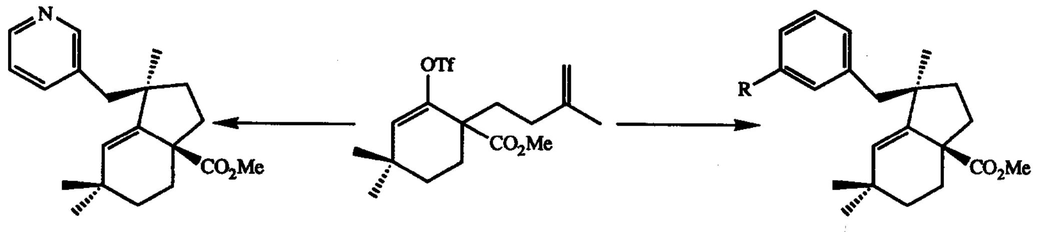
When the vinyl triflates were cyclised in boiling methanol under an atmosphere of carbon monoxide it proved possible to intercept (5) and the carbomethoxylated products (8a-c) were obtained stereospecifically in 56-69% yield.[6] Thus carbon monoxide insertion can successfully compete with 3-exo trig cyclisation in (5).

The vinyl cyclopropane derivatives [6a-c,(6c) was separated chromatographically in 50% yield from the mixture with (7)] underwent stereospecific methanolysis to (9a-c) in 70, 60 and 40% yield respectively on boiling in methanol containing a few drops of concentrated hydrochloric acid.



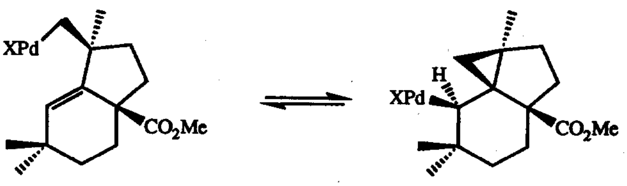
(9) a. n=1, R= Me
b. n=2, R=Et
c. n=3, R= Me

Lack of a β-hydride elimination pathway also allows cyclisation-anion capture processes to proceed in good yield as illustrated by the chemistry of enol triflate (10). Thus (10) reacts with 3-nitrophenylboronic acid in boiling toluene in the presence of Pd(0)[6] to afford (11a) (94%). Using the same catalyst system and solvent but reacting (10) with diethyl(3-pyridyl)borane afforded (12) (92%), whilst reaction of (10) with sodium tetraphenylborate in DMF (100°C, 8h) in the presence of a catalytic amount of Pd(0) afforded (11b) (90%).



(12) (10) (11) a. R= NO$_2$

b. R= H



(13) (14)

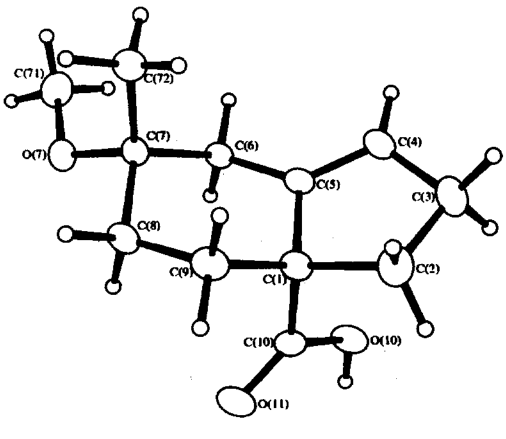


Figure 1

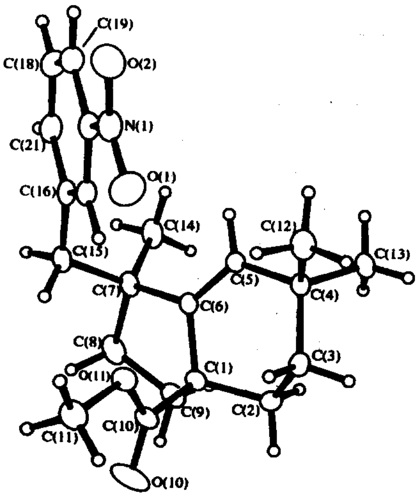


Figure 2

It seems probable that in these latter three cases the alkylpalladium(II) intermediates (13) and (14) are interconverting and that lack of a β-hydride elimination pathway in (14) allows (13) to intercept the boron reagents, with anion transfer to (14) being sterically retarded. Negishi has reported evidence for interconversions analogous to (13) ⇌ (14)[7] and Overman has reported an example of a cyclisation-cyclopropanation involving a vinyl triflate.[8]

The stereochemistry of all the products in this paper is assigned based on n.O.e and ROESY data together with single crystal X-ray structures of (9a; free acid) (figure 1) and (11a) (figure 2).[9]

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2. For other reports of palladium catalysed cyclisation-cyclopropanation see: Meyer, F.E.; Parsons, P.J.; de Meijere, A.; *J. Org. Chem.*, 1991, **56**, 6487-6488; Negishi, E.-I.; *Pure Appl. Chem.*, 1992, **64**, 323-334; Torii, S.; Okumoto, H.; Ozaki, H.; Nakayasu, S.; Todokoro, T.; Kotani, T.; *Tetrahedron Lett.*, 1992, **33**, 3499-3502.
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4. Burns, B.; Grigg, R.; Santhakumar, V.; Sridharan, V.; Stevenson, P.; Worakun, T.; *Tetrahedron* 1992, **48**, 7297-7320.
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6. The catalyst system employed for (4a,b) consisted of 10mol% $Pd(OAc)_2$, 20mol% PPh_3 and Et_3N(1mol). For (4c) the Et_3N was replaced by Ag_2CO_3(1mol). The catalyst system employed for (11a) and (12) comprised 10mol% $Pd(OAc)_2$, 20mol% PPh_3, Et_4NCl(1mol) and Na_2CO_3(2mol).
7. Dwczarczyk, Z.; Lamaty, F.; Vawter, E.J.; Negishi, E.I; *J. Am. Chem. Soc.*, 1992, **114**, 10091-10092.
8. Overman, L.E.; Abelman, M.M.; Kucera, D.J.; Tran, V.D.; Ricca, D.J.; *Pure Appl. Chem.*, 1992, **64**, 1813-1819.
9. *Crystal data for* **9a** (free acid): $C_{12}H_{18}O_3$,M_r = 210.26, monoclinic, a = 9.080(6), b = 10.0060(6), c = 12.2690(7)Å,β = 103.520(5)°, U-1146.83(12)Å^3, space group Cc,Z = 4,Dx = 1.218gcm^{-3}, μ = 0.698mm^{-1}, F000) = 456,wR_2 [$=(\Sigma\{w(F_o^2-F_c^2)^2\}/\Sigma[w(F_o^2)^2]^{1/2}]$ = 0.1286,[conventional R_{obs} = 0.0423 using 1813 data with $F_{obs} > 2.0\sigma(F_{obs})$].

   Crystal data for **11a**: $C_{21}H_{27}NO_4$,M_r = 357.44, monoclinic, a = 13.1282(6),b = 9.5891(6),c = 15.2037(7)Å,β = 90.695(4)°, U = 1913.83(14)Å^3, space group P2$_1$/a,Z = 4,D_x = 1.241gcm^{-3}, μ = 0.689mm^{-1}, F(000) = 768,wR_2 = 1030, [conventional R_{obs} = 0.0438 using 2754 data with $F_{obs} > 2.0\sigma(F_{obs})$].

   All crystallographic measurements for both structures were made at 200K on a Stoe STAD14 operating in the ω-θ scan mode using Cu-K_α radiation to a 2θ limit of 130°. Both data-sets were corrected for Lorentz-Polarization and absorption (azimuthal ψ-scans) effects. Both structures were solved by direct methods using SHELXS-86 and were refined by full-matrix least squares (based on F^2) using SHELXL-93. Full supplementary data for the X-ray work is available from the Cambridge Crystallographic Data Centre, Lensfield Road, Cambridge, CB2 1EH, England.

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