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REGIOSPECIFIC PALLADIUM CATALYSED TANDEM CYCLISATION-ANION CAPTURE PROCESSES. STEREOSPECIFIC GROUP TRANSFER FROM ORGANOTIN REAGENTS.

Barry Burns, Ronald Grigg*, Piniti Ratananukul, Visuvanathar Sridharan, Paul Stevenson, Sukanthini Sukirthalingam and Tanachat Worakun

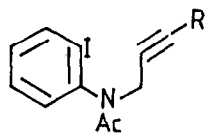
(Department of Chemistry, Queen's University, Belfast BT9 5AG, Northern Ireland)

Abstract. Vinyl-, alkyl- and π-allyl-palladium species arising from regiospecific palladium catalysed 5- or 6-exo-trig cyclisations onto proximate alkynes, alkenes or dienes can be intercepted by organotin reagents with stereospecific transfer of an organic group from tin leading to carbo- and hetero-cyclic compounds in moderate to good yield.

We recently disclosed powerful new synthetic methodology involving palladium catalysed 5- and 6-exo-trig cyclisations onto proximate alkynes, alkenes or dienes generating intermediate vinyl-, alkyl-, or π-allyl-palladium species which could be intercepted by hydride ion sources.[1,2] These tandem processes are both powerful, and synthetically flexible, and we now report an extension of the new tandem cyclisation-anion capture process which involves interception of the organopalladium species by "anion" transfer from organotin compounds.[3] The palladium catalysed intermolecular cross-coupling of vinyl- and aryl- iodides and -triflates with organotin reagents provides a novel approach to the functionalisation of the vinyl and aryl species. A wide range of such processes has been developed[4-6] particularly in extensive and elegant work by Stille.[4]

The o-iodoaniline derivatives (1a-c) react (MeCN, 5-25°C, 2-6h) with (2a), in the presence of 10 mol% palladium acetate and 20 mol% triphenylphosphine[7], via an initial 5-exo-trig cyclisation to give dienes (3a-c) stereospecifically in 40(R=H), 50(R=$SiMe_3$), and 60% (R=Me) yield respectively. These transformations result in the regio- and stereo-specific generation of tetrasubstituted alkenes, a process that is difficult to achieve using conventional methodology. Similarly (1a,b) react (THF, 60°C, 0.5-3h)[8] with (2b) to give (4a) (54%) and (4b) (55%). In these latter cases it was found advantageous to add 1mol. of tetraethylammonium chloride.[9,10] Capture of intermediate vinyl palladium species by (2c) also occurs, eg. (1a) gives (5) in 40% yield.

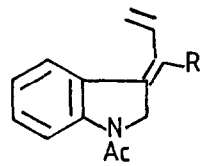
The intermediate vinylpalladium species in the palladium catalysed 6-endo-trig cyclisation[7] of (6) can also be intercepted by either (2a) [MeCN, 60°C, LiCl (3 mol), 2h] to give (20%) a 4:1 mixture of (7a) and (7b), or (2b) [MeCN, 60°C, Et_4NCl (1mol), 1.5h] to give (7c)(50%).



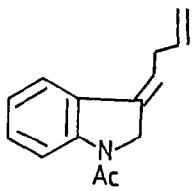
(1) a. R=H
b. R=Me
c. R=$SiMe_3$

$n\text{-}Bu_3SnR$

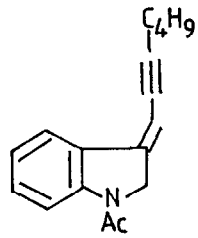
(2) a. R= $CH{=}CH_2$
b. R= $CH_2CH{=}CH_2$
c. R= $C{\equiv}CC_4H_9$
d. R=2-pyridyl
e. R=2-thiazolyl



(3) a. R=H
b. R=Me
c. R=$SiMe_3$



(4) a. R=H
b. R=Me



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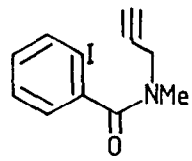

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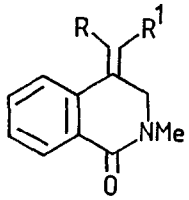
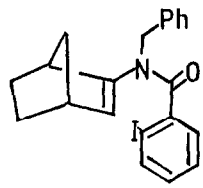
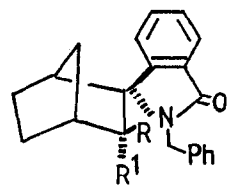


(7) a. R= $CH{=}CH_2$, R^1=H
b. R=H, R^1= $CH{=}CH_2$
c. R= $CH_2CH{=}CH_2$, R^1=H



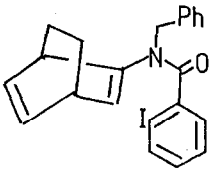
(8)



(9) a. R= $CH{=}CH_2$, R^1=H
b. R=$SnMe_3$, R^1=H
c. R=2-pyridyl, R^1=H
d. R=2-thiazolyl, R^1=H
e. R= CH=CHPh, R^1=H
f. R=H, R^1= CH=CHPh
g. R=H, R^1= CH≡CHPh
h. R= C≡CPh, R^1= H

The intermediate alkylpalladium species arising from the cyclisation (MeCN, 80°C,1h)[7] of (8) is intercepted stereospecifically by (2a) to give (9a)(63%). Under the same conditions (8) reacts with hexamethylditin to give (9b)(80%). Replacing acetonitrile by THF as solvent for the reaction, and lowering the reaction temperature to 60°C, allows (8) to react in a tandem fashion with (2d) and (2e) to give (9c)(38%) and (9d)(40%) respectively. Similarly reaction (THF, 60°C,4h) of (8) with (2, R=CH=CHPh) gives (46%), an 8:1 mixture of (9e) and (9f), whilst (8) and (2, R=C≡CPh) (THF,60°,15h) give (38%) a 1:1 mixture of (9g) and (9h). The bridged ring enamide (10) undergoes analogous reactions to (8), although these have only been briefly investigated so far. Thus (10) reacts [MeCN,80°C,Et_4NCl (1mol), 4.5h][7] stereoselectively with (2a) to give (55%) a 1:6 mixture of (11a) & (11b), and with (2b) to give (35%) a 1:2 mixture of (11c) and (11d).

Tandem cyclisation-anion capture processes have also been exemplified for systems involving intermediate π-allylpalladium species. Thus (12)[11] and (14) react [MeCN,80°C,LiCl (1mol)] with (2a) slowly (24 and 48h



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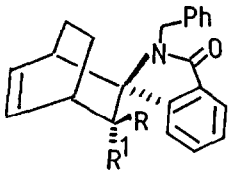
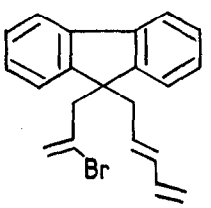


(11) a. R = $CH{=}CH_2$, R^1= H
b. R = H, R^1= $CH{=}CH_2$
c. R = $CH_2CH{=}CH_2$, R^1= H
d. R=H, R^1= $CH_2CH{=}CH_2$



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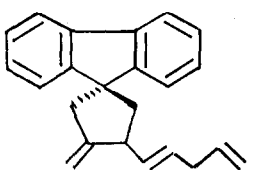

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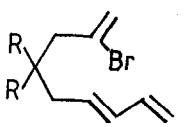
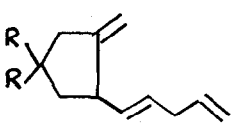
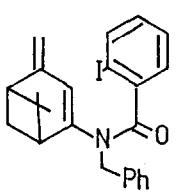


(14) R = CO_2Et



(15) R = CO_2Et



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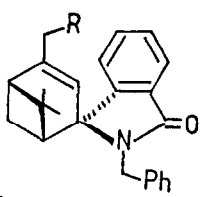
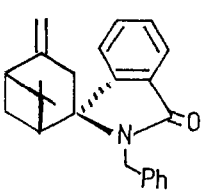


(17) a. R= $CH{=}CH_2$
b. R= 2-thiazolyl
c. R= $SnMe_3$



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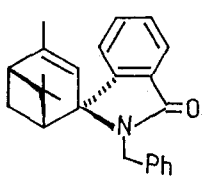

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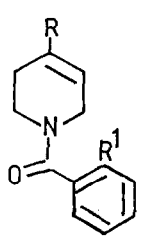

(20) a. R=H, R^1= I
b. R=Ph, R^1= I
c. R=H, R^1= $CH{=}CH_2$
d. R=Ph, R^1= $CH{=}CH_2$

respectively) to give (13)(60%) and (15)(60%) respectively, whilst (16) and (2a) [MeCN,80°C,Et_4NCl (1mol)][11] give (17a)(60%). The reaction of (16) with (2e) or hexamethylditin occurs in poor yield giving (17b)(10%) and (17c)(10%) together with varying amounts of (18) and (19).

Not all such palladium catalysed tandem processes are successful since, as pointed out previously[2], the success or otherwise of the tandem process depends on the relative rates of the various reactions. Thus (20a & b)[10] react with (2a) to give (20c)and (20d) respectively in $\geq$90% yield.

The wide range of palladium mediated reactions of organotin compounds offers considerable scope for further development of the methodology described in this paper. In addition further extensions of the palladium catalysed tandem cyclisation-anion capture process are under investigation.

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7. All reactions reported herein employ 10 mol% palladium acetate and 20 mol% triphenylphosphine unless otherwise noted.
8. The effects of choice of solvent on % conversion in palladium catalysed cross-coupling reactions with vinyl halides have been previously noted. J.K. Stille & B.L. Groh, J.Am.Chem.Soc., 1987, 109, 813.
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10. R. Grigg, V. Sridharan, P. Stevenson & T. Worakun, J. Chem. Soc., Chem. Commun., 1986, 1697.
11. 5 Mol% palladium acetate and 10 mol% triphenylphosphine used as catalyst

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