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REGIOSPECIFIC PALLADIUM CATALYSED TANDEM CYCLISATION-ANION CAPTURE PROCESSES. STEREOSPECIFIC GROUP TRANSFER FROM ORGANOZINC AND ORGANOBORON REAGENTS.

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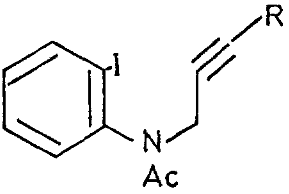
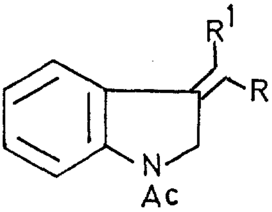
Abstract. Vinyl-, alkyl- and π-allyl-palladium species arising from regiospecific palladium catalysed 5- or 6-exo-dig or -trig cyclisations onto proximate alkynes, alkenes or dienes can be intercepted stereospecifically by organozinc or organo boron reagents leading to carbo-and hetero-cyclic compounds in moderate to good yield.

We recently disclosed powerful and flexible new synthetic methodology involving palladium catalysed 5- and 6-exo-dig or -trig cyclisations onto proximate alkynes, alkenes or dienes generating intermediate vinyl-, alkyl-, and π-allyl-palladium species which could be intercepted by hydride ion sources[1,2] or organotin reagents.[3] The success of these tandem cyclisation-anion capture processes depends on the relative rates of the various desired reactions compared to competing processes.[1-3] We now report the successful extension of this methodology to organozinc and organoboron compounds. The direct palladium catalysed coupling of vinyl- and aryl-halides or -triflates with organozinc[4] and organoboron[5] reagents is well known.

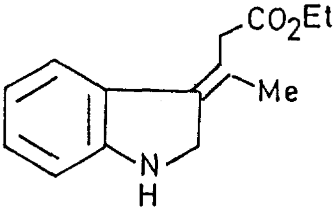
The o-iodoaniline derivatives (1a) and (1b) react (Et_2O-THF, 25°C, 4-5h) stereospecifically with phenylzinc chloride (3 mol.), in the presence of 10 mol % palladium acetate and 20 mol. % triphenylphosphine.[6] The initial 5-exo-dig cyclisation produces a



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



(2) a. R=H, R^1=Ph
b. R=Me, R^1=Ph
c. R=Me, R^1=CH$_2$CO$_2$Et
d. R=Me, R^1=CH=CHC$_4$H$_9$



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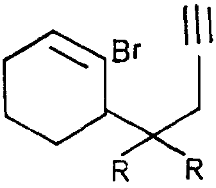
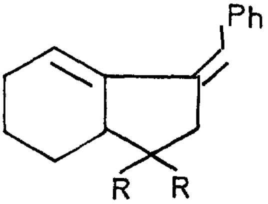
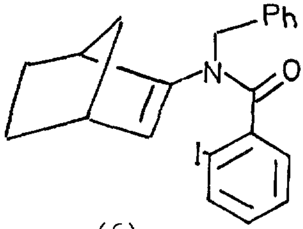


(4) R=CO$_2$Et



(5) R=CO$_2$Et



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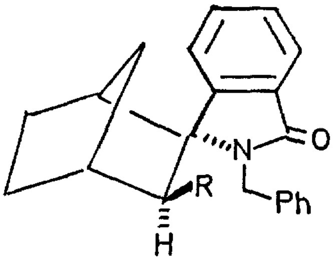
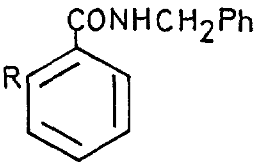
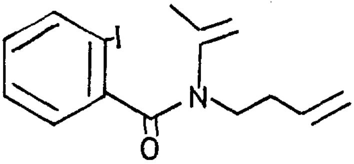
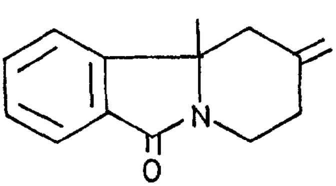


(7) a. R=Ph
b. R=CH=CHC$_4$H$_9$



(8) a. R=Ph
b. R=I





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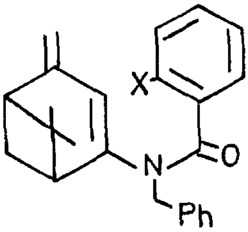
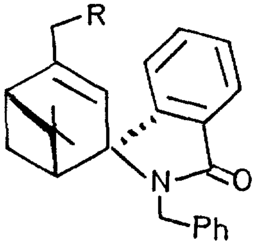


(11) a. X=I
b. X=Ph



(12) a. R=Ph
b. R=CH=CHC$_4$H$_9$.

vinyl palladium species which subsequently gives the corresponding indoline derivatives (2a)(60%) and (2b)(43%) respectively[7], together with a little unchanged (1a) or (1b). Similarly (1b) reacts (4:1 v/v Et_2O-HMPA, 35°C, 18h) with the Reformatsky reagent ($BrZnCH_2CO_2Et$, 2.5 mol) to give a 1.4:1 mixture (62%) of (2c) and the deacylated product (3), whilst (4) and phenylzinc chloride (1:2 v/v Et_2O-THF, 50°C, 2.5h) give (5)(66%).

The intermediate alkyl-palladium species derived from a 5-exo-trig cyclisation of the norbornene enamide (6) can also be intercepted (Et_2O-THF, 25°C, 3h) stereospecifically by phenylzinc chloride giving (7a)(19%) albeit in poor yield. The major product in this case is (8a)(49%) together with (8b)(18%), which presumably arise via traces of water in the solvent. A related process is the tandem palladium catalysed cyclisation of (9) where the initial alkyl palladium species reacts [MeCN, Et_4NCl (1 mol.), K_2CO_3 (2 mol.), 80°C, 3h] further with the proximate alkene to give (10)(92%). Overman has recently reported elegant carbocyclic analogues of this latter process.[8]

An example of the tandem cyclisation-anion capture process involving a π-allylpalladium intermediate is provided by the conversion of (11a)[5 mol % $Pd(OAc)_2$ - 10 mol % PPh_3, THF, 50°C, 7h] to (12a)(21%) (68% conversion) by reaction with phenylzinc chloride (3mol.). However, the major product in this reaction is (11b)(62%).

An analogous series of reactions has been carried out using the alkenyl borane (13) as a transfer reagent. Thus both (1b) and (14) react with (13) [benzene, 60°C, NaOEt (2 mol), 1.5-2h] in the presence of palladium acetate and triphenylphosphine,[6] via intermediate vinyl-palladium species, to give (2d)(30%) and (15)(45%) respectively. Examples of processes involving intermediate alkyl-palladium species are provided by the reaction [benzene, 80°C, NaOEt (2 mol), 6h] of (6) and (13) to give (7b)(46%), and of (16) and (13) under analogous conditions (reaction time 3h), to give (17)(35%). The corresponding process involving a π-allylpalladium intermediate proceeds in poor yield, i.e. (11a) and (13) react [benzene, 80°C, NaOEt (2 mol), 24h] to give (12b) in 17% yield at 60% conversion. The direct coupling of π-allylpalladium species with organoboranes has been reported previously.[9]

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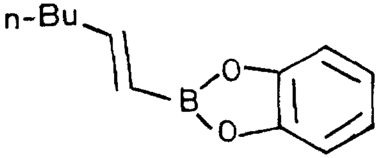

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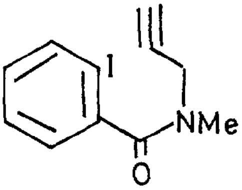

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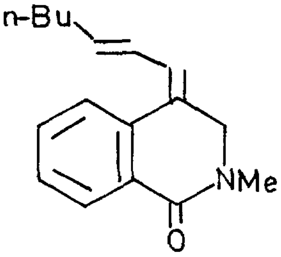

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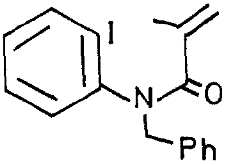

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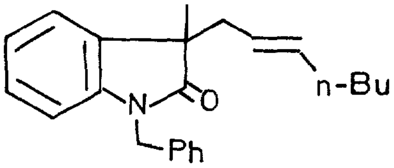

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6. All subsequent reactions reported herein employ 10 mol % palladium acetate and 20 mol % triphenylphosphine unless otherwise noted.
7. Stereochemistry of the products reported herein is based on appropriate n.O.e. experiments.
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