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PALLADIUM CATALYSED TANDEM CYCLISATION-ANION CAPTURE PROCESSES. HYDRIDE ION CAPTURE BY ALKYL- AND π-ALLYL-PALLADIUM SPECIES

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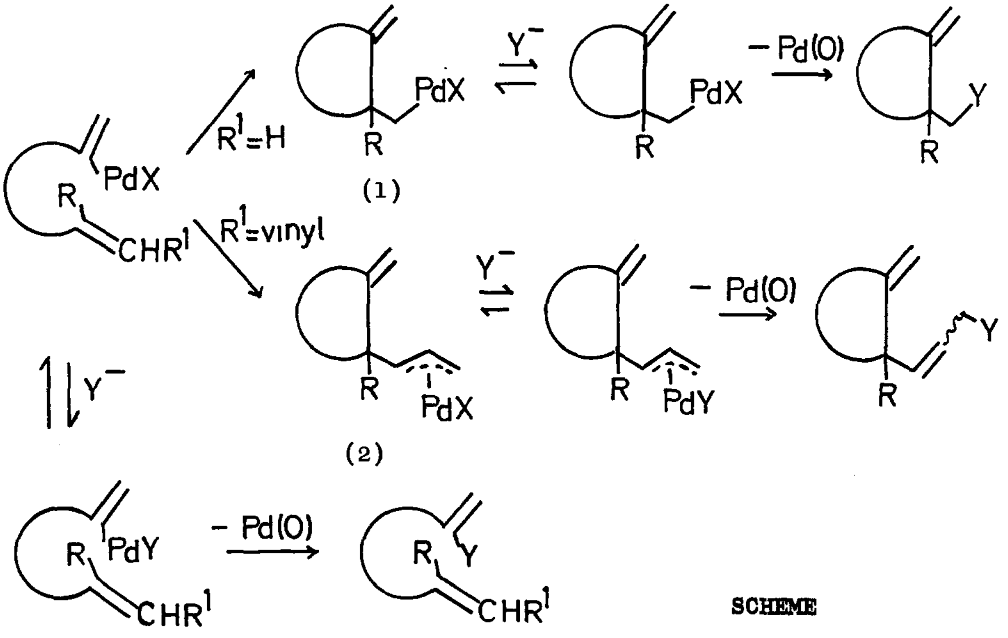
Abstract. Alkyl- and π-allyl-palladium species arising from 5-exo-trig cyclisations onto proximate alkenes or dienes can be intercepted by hydride ion sources leading to carbo- and hetero-cyclic compounds usually in good yield.

In the preceeding paper[1] we provided examples of a new tandem cyclisation-anion capture process which involved interception of an intermediate vinyl-palladium species by hydride ion transfer from formate. Analogous processes can be envisaged (Scheme) involving interception of intermediate alkyl- and π-allyl-palladium species (1)[2] and (2) respectively. The successful synthetic realisation of these processes will depend on the relative rates of the intermediate steps (Scheme) including, in addition, the relative rates of β-hydride elimination where possible.

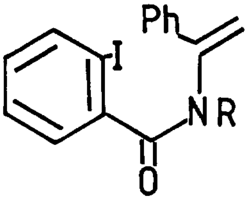


(1)

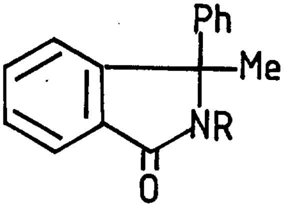
(2)

(3)

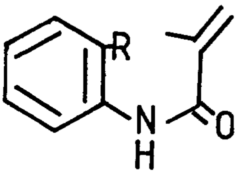
SCHEME



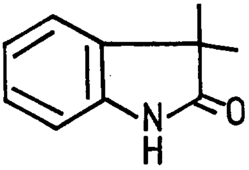
(4) R=CH$_2$Ph



(5) R=CH$_2$Ph



(6) a. R=I
b. R=H



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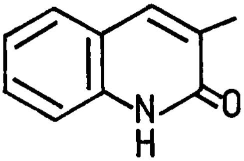

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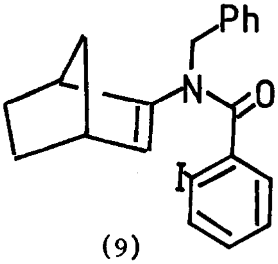

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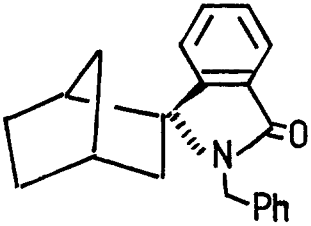

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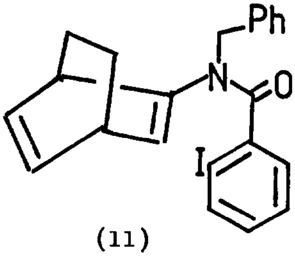

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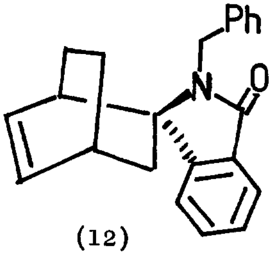

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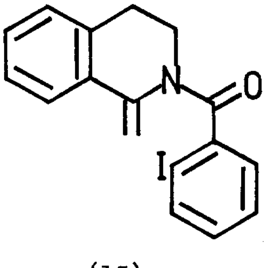

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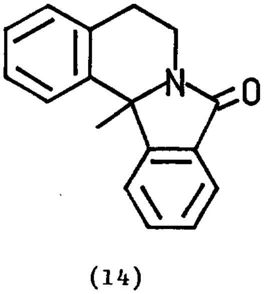

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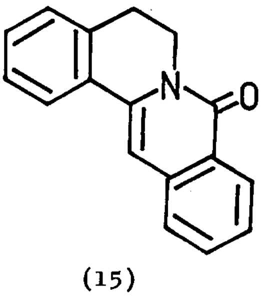
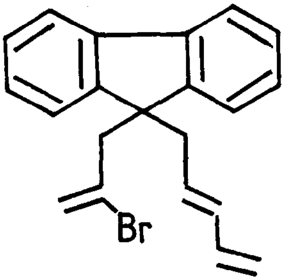


(15)

Preliminary studies with a range of potential precursors (1) and (2) (Scheme) show the tandem cyclisation-hydride capture process to be viable in both hetero- and carbo-cyclic systems. Several variations of the catalyst system have been employed: 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3, and HCO_2Na (1.1 mol) in DMF (catalyst system A), or acetonitrile (catalyst system B); 10 mol% $Pd(OAc)_2$, 20 mol% PPh_3, and piperidine (4mol) and HCO_2H (3 mol) in acetonitrile (catalyst system C); 5 mol% $Pd(OAc)_2$, 10 mol% PPh_3, and HCO_2Na (1 mol) in DMF (catalyst system D).

The enamide (4) is cyclised (80°C, 16h) to (5) (55%) using catalyst system A with the addition of tetraethylammonium chloride (1 mol).[3] Enamide (6a) is less efficiently cyclised (60°C, 1.25h) by catalyst system B giving a mixture of (7b) (22%), (6b) (38%), and (8) (45%). The substantial amount of (6b) formed in this reaction shows that anion exchange of the initial vinylpalladium species leading to (3) (Scheme) competes favourably with cyclisation in this case. Heck has previously reported the cyclisation of (6a) with rearrangement in the absence of a hydride source.[4] The bridged ring enamides (9) and (11) are cyclised (80°C, 1-2h) regio- and stereo-specifically to (10) (65%) and (12) (68%) respectively[5,6] by catalyst system C. The stereochemistry of these palladium catalysed cyclisations thus accords with that usually observed for electrophilic attack on these bicyclic systems. Enamide (13) on treatment (80°C, 24h) with catalyst system D displays competition between 5-exo- and 6-endo-trig cyclisations giving a 2:1 mixture of (14) and (15) in 74% combined yield. Under non-reductive conditions (13) slowly cyclises to (15) in moderate yield.[7]



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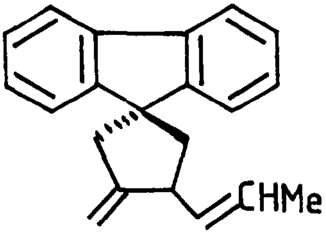

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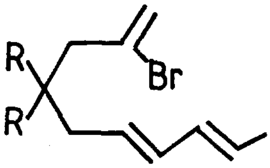
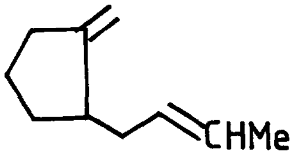
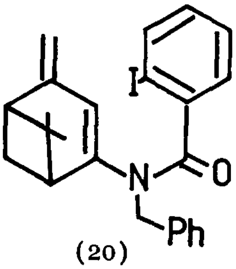


(18) R=CO_2Et



(19) R=CO_2Et



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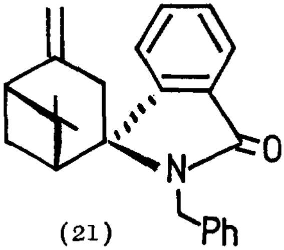

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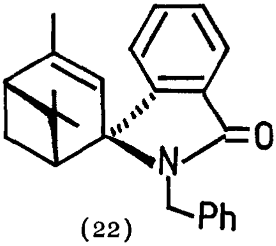

(22)

Examples of the regiospecific interception of intermediate π-allylpalladium species are provided by the cyclisation of (16)→(17) (90%) (1.3:1 E/Z mixture) and (18)→(19) (77%) (1:1 E/Z mixture) using catalyst system C but with pyrrolidine (1 mol) and formic acid (1 mol) as the hydride source.[8] Enamide (20) is cyclised (80°C, 24h) by catalyst system D to a 4:1 mixture of (21) and (22) in 80% combined yield.

The palladium catalysed tandem cyclisation-anion capture process in which hydride ion is transferred is remarkably powerful and flexible. Further examples involving transfer of other anions are under study.

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References

1. B. Burns, R. Grigg, V. Sridharan & T. Worakun, Tetrahedron Letters, preceeding paper.
2. For a related case involving a palladium catalysed reductive cyclisation of 1,6- and 1,7-enynes using polymethylhydrosiloxane as a hydride source see B.M. Trost & F. Rise, J. Am. Chem. Soc., 1987, 109, 3161.
3. T. Jeffrey, Synthesis, 1987, 70 and earlier references; R. Grigg, P. Stevenson & T. Worakun, Tetrahedron, 1988, 44, 2033.
4. R.F. Heck & M.O. Terpko, J. Am. Chem. Soc., 1979, 101, 5281.
5. Stereochemistry assigned on the basis of n.O.e. studies.
6. For related intermolecular cases see M. Catellani, G.P. Chinsoli & A. Mari, J. Organomet. Chem., 1984, 275, 129; R.C. Larock, S.S. Hershberger, K. Takagi & M.A. Mitchell, J. Org. Chem., 1986, 51, 2450; R.C. Larock, D.R. Leach & S.M. Bjorge, ibid, 1986, 51, 5221.
7. R. Grigg, V. Sridharan, P. Stevenson & T. Worakun, J. Chem. Soc., Chem. Commun., 1986, 1697.
8. The cyclisation of (17) (18) employed 5 mol% $Pd(OAc)_2$ and 10 mol% PPh_3.

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