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ASYMMETRIC INDUCTION IN THE CREATION OF TRI- AND TETRA-SUBSTITUTED CARBON STEREOCENTRES BY THE INTRAMOLECULAR HECK REACTION

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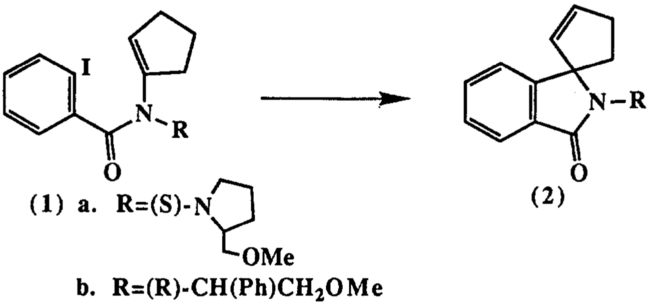
Abstract A preliminary survey of the use of aminoethers as chiral auxiliaries, in combination with both chiral and achiral phosphines, for palladium catalysed cyclisations is reported. A 55% d.e. was observed for a process creating a tetrasubstituted carbon centre and >95% d.e. for a process creating a trisubstituted carbon centre.

We have recently been concerned with developing palladium and rhodium catalysed cyclisation processes for the construction of fused, spiro- and bridged-ring systems and extending these processes to palladium catalysed cyclisation-and polycyclisation-anion capture processes.[1] In the foregoing processes the requirement for control of chirality at newly created tri- and tetra-substituted carbon centres has become increasingly obvious and recently two preliminary reports of the creation of tri-[2] and tetra-substituted[3] carbon stereocentres by the cyclisation of vinyl-palladium species have appeared. In both these cases chiral phosphines were employed and the maximum enantiomeric (or diasteromeric) excess observed was 45-46%. We have been studying analogous reactions and now report that portion of our studies in which chiral auxiliaries are employed and which result in >95% d.e. in certain cases.

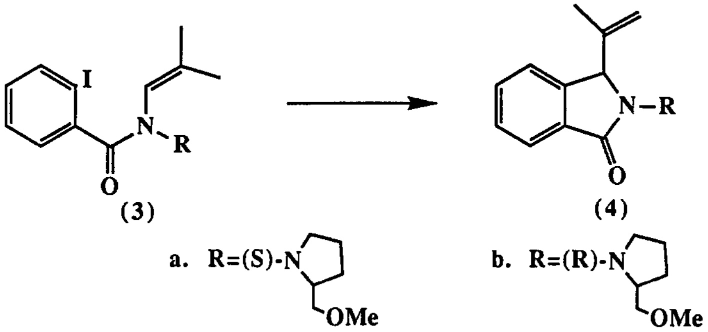
The cyclisation of two enamides (1) → (2) and (3) → (4) were selected as model processes and the effect of varying the chiral auxiliary was studied. The enamides (1) and (3) were prepared according to our general procedure[1] and cyclised in boiling acetonitrile using our standard catalyst system[1] of 10 mol% palladium acetate, 20 mol% phosphine, and anhydrous potassium carbonate (2 mol). In addition tetraethylammonium chloride (1 mol)[4] was added in the cyclisation of (1) → (2), and silver nitrate (1 mol)[5] in the cyclisation of (3) → (4).

Very little stereoselection was observed in the cyclisation of (1a,b) to (2a,b) when non-chiral phosphines were employed. When homochiral phosphines were employed some improvement in stereoselection occurred with BINAP proving the most effective. Thus (1a) cyclised to (2a) in the presence of (S)-BINAP in 48% d.e. whilst (1b) similarly gave (2b) in 55% d.e.



(1) a. R=(S)-N
b. R=(R)-CH(Ph)CH$_2$OMe

(2)

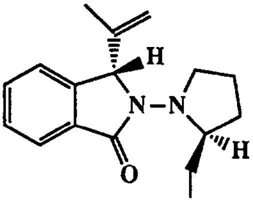


(3)

(4)

a. R=(S)-N

b. R=(R)-N



(5)

Studies of the cyclisation of (3) to (4) showed RAMP and SAMP to be the most effective chiral auxiliaries. Both (3a) and (3b) cyclised, in the presence of triphenyl phosphine, to a single diastereomer as far as could be seen by ^{13}C and ^{1}H n.m.r. studies of the product. An X-ray structure determination of the product derived from (3a) showed it to be the (S,S)-diastereomer (5).

Further studies of these and related processes are underway.

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5. The use of silver salts for suppressing olefin isomerisation in Heck reactions was introduced by Hallberg, see e.g. Karabelas, K.; Hallberg, A., *J. Org. Chem.,* 1986, 51, 5286-5290.

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