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SUPPRESSION OF ALKENE ISOMERISATION IN PRODUCTS FROM INTRAMOLECULAR HECK REACTIONS BY ADDITION OF Tl(1) SALTS.

**Ronald Grigg,* Vani Loganathan, Vijayaratnam Santhakumar,
Visuvanathar Sridharan and Andrew Teasdale.**

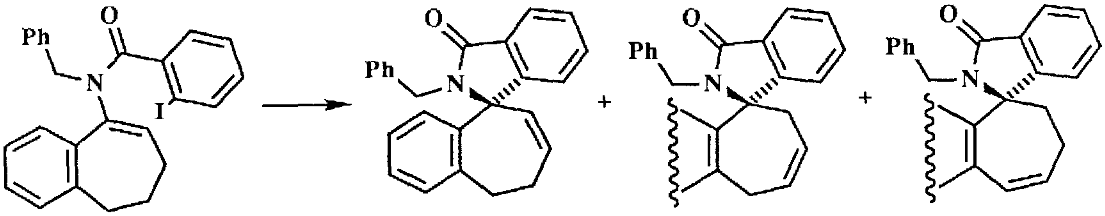
Chemistry Department, Leeds University, Leeds LS2 9JT.

Abstract Palladium catalysed cyclisations creating products possessing spiro-, fused- and bridged-rings, and tetrasubstituted carbon centres as mixtures of double bond isomers are modified to give single products in the presence of Tl(1) salts

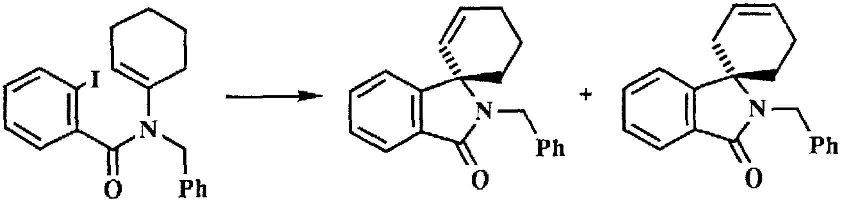
We recently reported[1] the effect of NEt_4Cl, and Ag(I) and Tl(I) salts on selectively suppressing unwanted direct capture processes which sometimes compete with our newly developed palladium catalysed tandem cyclisation-anion capture processes.[2] Tl(1) salts were shown to be especially valuable in these circumstances. In both inter- and intra-molecular Heck reactions a lack of regioselectivety in the β-hydride elimination step or subsequent double bond isomerisation in the product sometimes severely limits the synthetic utility of the reaction Silver (I) salts have been shown to be efficacious in controlling both these processes.[3,4] We now report that Tl(I) salts in many instances are more effective than Ag(I) salts.

We have previously reported the palladium catalysed spirocyclisation of (1) to a 1:1.95:4.86 mixture of (2)-(4) [5,6] Catalytic cyclisation (MeCN, 80°C, 4 h) of (1) in the presence of Tl_2CO_3 (1.2 mol) gave a 5 75:1 mixture of (2) and (3) [selective suppression of (4)] whilst TlOAc (1 2 mol) in a slower reaction (46 h)[7] afforded only (2) (65%). AgOAc(1 2 mol) and Ag_2CO_3(1.2 mol) are also specific for (2) but the reactions are much slower

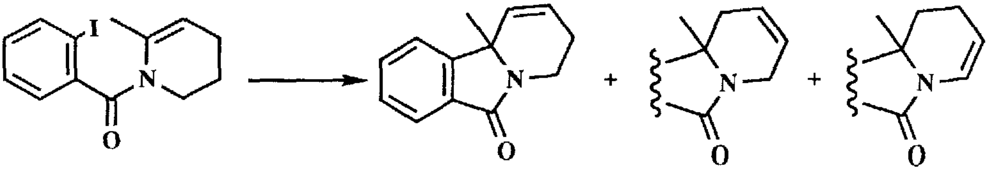
The catalytic cyclisation of (5) in the absence of additives gives a *ca.* 4:1 mixture of (6) and (7).[5] When the reaction is repeated (MeCN, 80°C, 18h) in the presence of TlOAc(1.2 mol) or AgOAc(1 2 mol) the ratios of (6) to (7) are respectively TlOAc(17.5·1), and AgOAc[(6) only, but incomplete reaction (43% conversion)].



(1) (2) (3) (4)

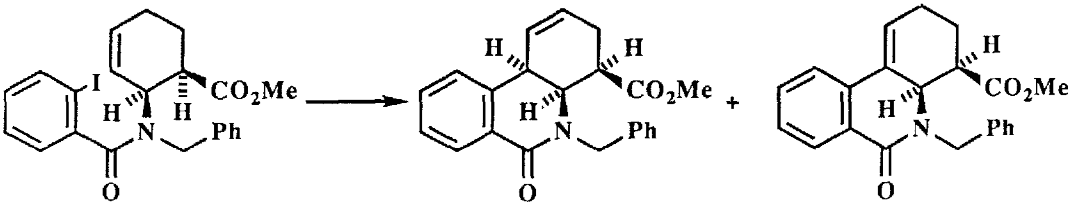


(5) (6) (7)

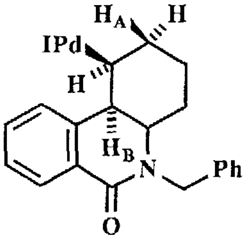


(8) (9) (10) (11)

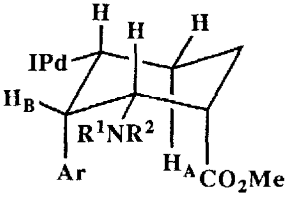
Cyclisation of (8) in the absence of additives gives a 1.45:1.27:1 mixture of (9)-(11).[8] Repeating the reaction (MeCN, 80°C, 4dy) in the presence of TlOAc(2 5 mol) afforded only (9) (65%).



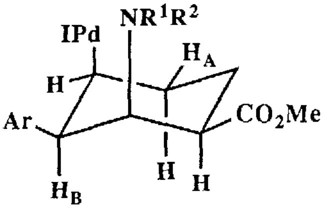
(12) (13) (14)



(15)

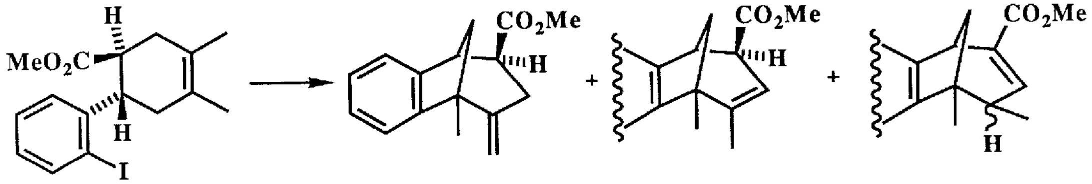


(16)



(17)

Catalytic cyclisation (MeCN, 80^{0}C) of (12) in the absence of additives affords a 1.8 1 mixture of (13) and (14).[8] In the presence of 1 mol of $AgNO_3$ or Ag_2CO_3 the cyclisation is very slow (24 h, 36% conversion) but gives only (13).[8] However, the cyclisation is complete in 22 h in the presence of Tl_2CO_3(2 mol) and affords only (13) (78%). β-Hydride elimination in the intermediate (15) could involve H_A or H_B giving (13) and (14) respectively. Formation of (14) implicates conformer (16) (Pd/H_B dihedral angle *ca.* 60^{0}) rather than (17) (Pd/H_B dihedral angle 180^{0}) since β-hydride elimination normally occurs with cis-stereochemistry.[9]



(18) (19) (20) (21)

Catalytic cyclisation [anisole, KOAc(2 mol), 148^{0}C] of (18) gives a 1:5.5:7.4 mixture of (19)-(21) (80%). Addition of TlOAc(1 2 mol) suppresses (21)[10] and gives a 1:1 4 mixture of (19) and (20). Increasing the amount of TlOAc to 4 mol (reaction temperature 120^{0}C) affords a 4:1 mixture of (19) and (20) whilst AgOAc(4 mole) reverses the selectivity (reaction temperature 135^{0}C) and affords a 1:5 mixture of (19) and (20)!

In summary, Tl(I) salts have a marked affect on both the direction of β-hydride elimination and on subsequent double bond isomerisation in the product. The mechanism by which this effect is exerted is unclear but anion exchange (RPdI + TlX → RPdx + TlI) is clearly an important factor.[11]

Further studies of the influence of Tl(I) salts are in hand.

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6 All catalytic processes discussed in this paper employed 10 mol% Pd(OAc)$_2$ and 20 mol% PPh$_3$ as the catalytic system

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10 (21) is obtained as a single stereoisomer whose stereochemistry has yet to be determined

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