Tetrahedron Letters, Vol. 33, No. 50, pp. 7789-7792, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Palladium Catalysed Cascade Cyclisation - Carbonylation Processes. Rate Enhancement By Tl(I) Salts.

Ronald Grigg[a,*], Peter Kennewell[b] and Andrew J Teasdale[a].

a.School of Chemistry, Leeds University, Leeds LS2 9JT.

b. Roussel Scientific Institute, Kingfisher Drive, Swindon SN3 5BZ.

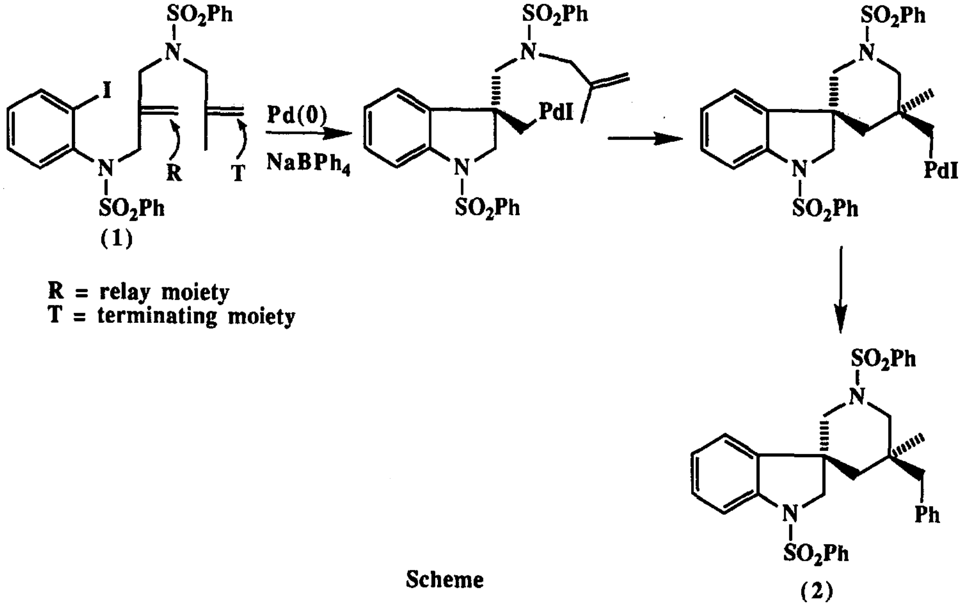
Abstract. The addition of TlOAc (3 mol) promotes a series of cylisation-carbonylation reactions under 1 atm of CO at 65°C. One example of a bis-cyclisation is reported.

We recently introduced a new and powerful palladium catalysed tandem cyclisation-anion capture process whereby a vinyl-, aryl-, alkyl- or π-allyl-palladium (II) intermediate, generated from the corresponding halide or acetate via oxidative addition of Pd(0), undergoes regio- and stereo-specific cyclisation onto a proximate alkene, alkyne or diene moiety followed by interception of the resulting alkyl-, vinyl or π-allyl-palladium (II) species by an "anion" transfer agent[1]. The tandem process has been extended to bis-cyclisation-anion capture processes generating two rings with subsequent anion capture[2] and can be generalised as shown in the Table.

Table1 Potential Combinations for (Poly) Cyclisation-Anion Capture Processes

Starter Species	Relay Species (R)	Terminating Species (T)	Anion Transfer Reagent (Y)
alkyl	alkene	alkene	anionic [H, OAc, CN, SO_2Ph, $CH(CO_2R)_2$]
aryl	alkyne	alkyne	neutral (amines, MeOH/ CO, acrylates)
vinyl	1,2-diene	1,2-diene	
allyl	1,3-diene	1,3-diene	organometallics RM[M=Sn (IV), B(III), Zn (II)]

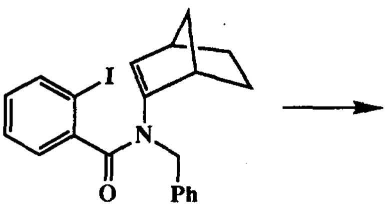
The "anion " transfer reagents listed in the Table are illustrative rather than exhaustive and much further work remains to be done in this area. The Table emphasises the potential of the process for multiple ring formation since any starter can conceptually be combined with any relay moiety, any terminating species, and any transfer reagent. The relay phase can, in principle, incorporate several cyclisations before engaging the terminating moiety. A typical example is shown in the Scheme. The overall conversion of (1) → (2) occurs in 63% and yields a single diastereomer of (2)[1].



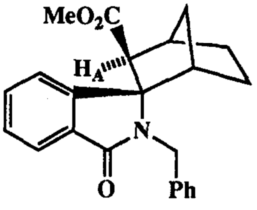
Scheme

Typical "anion" transfer reagents include the anionic, neutral, and organometallic species listed in the table and we have provided illustrative examples of these[3-5]. We now report the utilisation of CO/MeOH as the anion transfer reagent ($Y = CO_2Me$). This process is foreshadowed in the report by Oppolzer of a related metallo-ene cyclisation-carbonylation sequence[6]. The successful realisation of the tandem cyclisation-anion capture processes is predicated on the cyclisation rate(s) being significantly faster than the rate of direct anion capture. The proposed carbonylation sequence turned out to be a case where this was not so and advantage was therefore taken of our observation of the ability of Tl(I) salts to enhance the desired sequence[7].

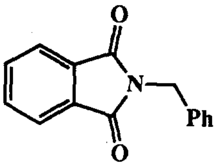
A typical example is provided in the cyclisation of (3) → (4). The reaction [MeOH, 1 atm. CO, 5 mol% $PdCl_2(PPh_3)_2$, 65°C][8] furnishes (4) in 86% yield in the presence of TlOAc (3mol) over 21h. Omitting the TlOAc (NEt_3 as base) results in a very slow reaction (ca. 15% conversion in 17h) and the formation of a ca. 10:1 mixture of (4) and (5). The stereochemistry of (4) is based on our previous demonstration that the 5-exo-trig cyclisation occurs on the exo-face of the norbornene[1], and on the p.m.r. spectrum of (4) in which H_A gives rise to a singlet a δ 2.30.



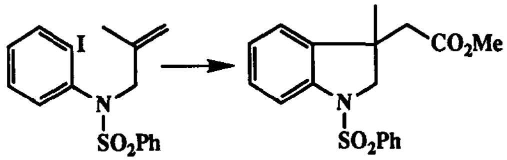
(3)

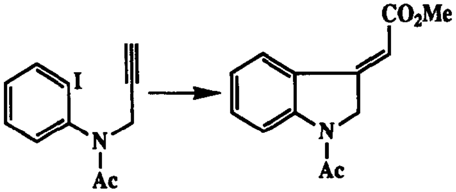


(4)



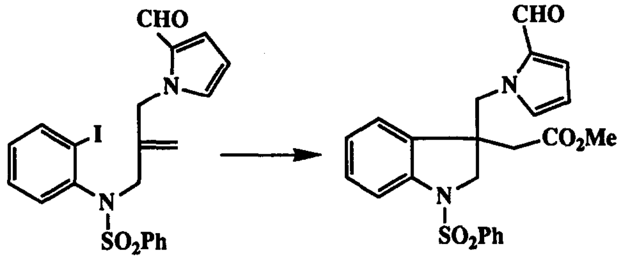
(5)

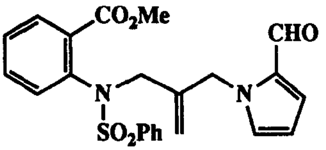

(6) (7)

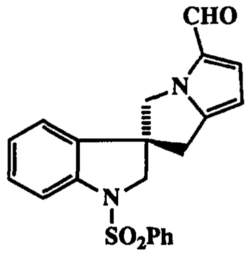

(8) (9)

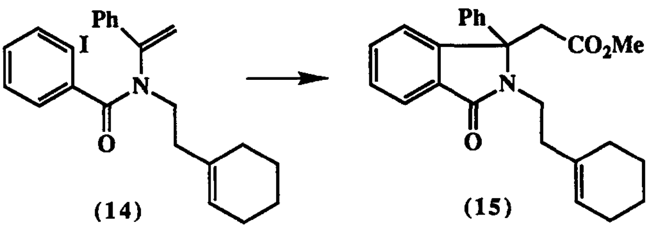
Using identical conditions (6) cyclised to (7) (91%) over 21h. In this case the cyclisation (6) → (7) occurred in 89% yield when the TlOAc was replaced by a combination of triethylamine and titanium tetra isopropoxide (3mol) but the reaction was much slower (66h). Replacing the TlOAc by either triethylamine alone or by potassium acetate or carbonate resulted either in no (7) being formed or very poor yields (<35%). In a similar manner using the standard conditions[8] (8) gave (9) (50%). In this latter case chromatographic (SiO_2) work up was deleterious and is best-avoided. Several related cyclisation-carbonylation processes have been reported recently but these all required temperatures ≥100°C and CO pressures of 20-40 atm[9]. Thus Tl(I) salts offer a significant advantage in such processes.

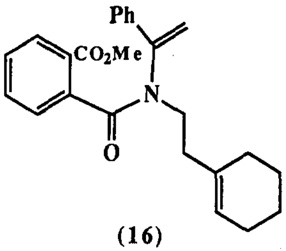
Attempts to achieve bis-cyclisation-carbonylation of (10) were unsuccessful. Under standard conditions[8] (10) furnished a ca. 2:1:1 mixture of (11), (12) and (13)(87%). Replacing TlOAc by triethylamine (4 mol) and increasing the carbon monoxide pressure to 120 psi furnished a 6:1 mixture (70%) of (12) and (11).


(10) (11)

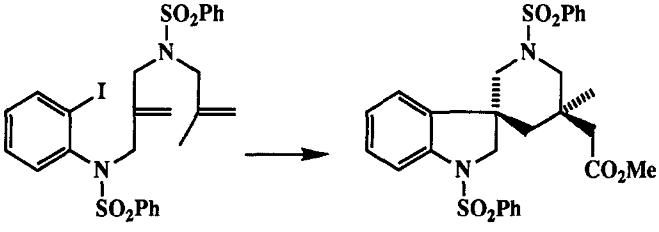

(12)


(13)


(14) (15)



(16)



(17) (18)

The iodo-compound (14) failed to cyclise under our standard conditions[8] but replacing TlOAc by NEt_3 (4 mol) and under more forcing conditions (MeOH, 106°C, 280 psi CO, 3h) it furnished a ca. 2:1 mixture (97%) of (15) and (16). However, the iodo-compound (17) did undergo a bis-cyclisation-carbonylation sequence under our standard conditions and afforded (18) in moderate yield (43%) as a single diastereomer.

Further Studies of these and analogous processes are underway.

We thank Leeds University and Roussel for support.

References and notes

1. Burns, B; Grigg, R.; Santhakumar, V.; Sridharan, V.; Stevenson, P.; Worakun, T. *Tetrahedron*, in press.

2. Grigg, R.; Dorrity, M.J.; Malone, J.F.; Sridharan, V.; Sukirthalingam, S. *Tetrahedron Lett.* 1990, 31, 1343-1346.

3. Burns, B.; Grigg, R.; Sridharan, V.; Worakun, T.; *Tetrahedron Lett.* 1988, 29, 4325-4328; Burns, B.; Grigg, R.; Ratanukul, P.; Stevenson, P.; Sridharan, V.; Worakun, T. *ibid*, 1988, 29, 4329-4332; Grigg, R.; Sridharan, V.; Sukirthalingam, S.; Worakun, T. *ibid*, 1989, 30, 1139-1142.

4. Burns, B; Grigg, R.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S.; Worakun, T. *Tetrahedron*, Lett. 1989, 30, 1135-1138.

5. Burns, B; Grigg, R.; Ratanukul, P.; Sridharan, V.; Stevenson, P.; Sukirthalingam, S.; Worakun, T. *Tetrahedron*, Lett. 1988, 29, 5565-5568.

6. Oppolzer, W.; Keller, T. H.; Bedoya-Zuria, M.; Stone, C. *Tetrahedron Lett.* 1989, 5883-5886.

7. Grigg, R.; Loganathan, V.; Sridharan, V.; Sukirthalingam, S. *Tetrahedron Lett.* 1990, 31, 6573-6576; Grigg, R.; Loganathan, V.; Santhakumar, V.; Sridharan, V.; Teasdale, A. *ibid*, 1991, 32, 687-690.

8. This combination and quantities of catalyst, solvent, carbon monoxide and temperature was used throughout unless otherwise stated.

9. Wu, G.; Shimoyama, I.; Negishi, E.-I.; *J. Org. Chem.* 1991, 56, 6506-6507; Negishi, E.-I.; *Pure Appl. Chem.* 1992, 64, 323-334; Kalinin, V. N.; Shostaovsky, M. V.; Ponomaryov, A. B.; *Tetrahedron Lett.* 1992, 33, 373-376; for a milder carbonylation sequence see Torii, S.; Okumoto, H.; Xu, L.H. *Tetrahedron Lett.* 1991, 32, 237-240.

(Received in UK 21 September 1992)