Formation of Zirconocene η^2 -Imine Complexes by Rearrangement of Cyclic Iminoacyl Complexes.

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Abstract. Insertion of phenylisocyanide into bicyclic zirconacyclopentanes, obtained from a 1,7-octa- or 1,6-hepta-diene by reaction with dibutylzirconocene, affords initially an iminoacyl complex that rearranges on warming to form a zirconocene n^2 -imine complex which inserts unactivated alkenes and alkynes.

The zirconocene induced bicyclisation of 1,6- or 1,7-dienes is a powerful new ring forming method¹ but has the limitation that the carbon-metal bonds in the so formed zirconacycle (e.g. 1) are relatively unreactive. The only reported C-C bond forming reaction is the insertion of carbon monoxide to afford bicyclic ketones or alcohols². This reaction probably occurs *via* rearrangement of an acyl complex 2 to a η^2 -ketone complex 3, a reaction which has precedent from acyclic cases³.



We are investigating the use of η^2 -heteroalkene complexes of zirconocene as carbometallating reagents in organic synthesis since they readily insert unactivated alkenes and alkynes into the carbon-zirconium bond. Attempts to trap the supposed η^2 -ketone intermediate 3 with alkynes failed despite literature precedent for such an insertion into acyclic analogues³. Zirconocene η^2 -imine complexes, formed by a C-H activation method from amines, are particularly effective carbometallating reagents even in very hindered systems^{4,5}. This suggested that insertion of an isocyanide (isoelectronic with CO) into a zirconacyclopentane followed by rearrangement might illustrate a valuable new synthesis of this useful class of reagents⁶, and also provide a powerful method for elaboration of the zirconacycles.

Treatment of the 1,6-heptadiene 4 with dibutylzirconocene (generated in situ from Cp_2ZrCl_2 and 2 eq. of n-BuLi) and warming to room temperature cleanly gave the *trans*-zirconacyclopentane 5. Addition of BuNC gave

the iminoacyl complex 6 (δ_C 236.6 p.p.m.) but this was thermally stable, no sign of rearrangement to the required η^2 -imine complex being observed even on thermolysis. Much to our surprise however oxidative work-up (Bu¹OOH) gave not the expected monocyclic amide but the bicyclic ketone 11 (48%, m.p. 86-87°C). This is a convenient, though generally lower yielding, alternative to carbonylation / I_2 work-up previously reported². Acidic work-up gave 11 in 25% yield.





Scheme 1.



The insertion of phenyl isocyanide was more successful, the first formed iminoacyl complex 7⁷ smoothy rearranging to the η^2 -imine complex 8 on warming to 40°C. The complex 8 was trapped in situ with 4-octyne to form the azazirconacyclopentene 9a⁸ which gave the bicyclic amine 10a in 48% yield on protonolysis with methanol followed by aqueous work-up and chromatography⁹. The overall yield is reasonable for a one pot reaction in which 4 new carbon-carbon bonds are formed. Either the steric bulk of the tert-butyl group, or conjugation of the phenyl ring with the nitrogen lone pair or with the C=N π -bond (so that it can act as an electron sink) could account for the different results with the two isocyanides.

Though warming the iminoacyl complex 7 in the absence of an alkyne trap gave a species which could be tentatively assigned as 8 on the basis of its n.m.r. properties and its subsequent reaction with 4-octyne to give 9a it was not obtained in a reasonable state of purity. Carrying out the rearrangement in the presence of trimethyphosphine allowed the PMe₃ stabilised complex 12 to be isolated and characterised¹⁰. The complex 12 reacted with 4-octyne to give 9a (67°C, 20 min).

The range of substrates which could successfully insert into the η^2 -imine complex 8 was examined next. A variety of alkynes worked well (Table 1) and showed excellent regioselectivity when the substituents were different, the larger group ending up near zirconium in the metallacyclic intermediates 9c-e. With terminal alkynes a major by-product was the amine 13 presumably arising by protonation of the η^2 -imine complex 8 by the acidic acetylene proton. Carrying out the rearrangement 7 to 8 in the presence of a secondary amine as a proton source gave 13 in 90 % yield. Amines are not strong enough acids to protonate either the zirconacyclopentane precursor 5 or the azazirconacyclopentenes 9. Carrying out the rearrangement in the absence of a trap, followed by protonolysis also gave 13 though in lower yield.

The insertion of alkenes into 8 was examined next. Reaction with 1-heptene gave a single adduct 14a in which the alkene substituent was adjacent to the metal leading to the amine 15a on protolytic work-up. In the same



way 1-bromo-4-pentene gave the adduct 15b illustrating a useful functional group compatibility of these transformations. The regiochemistry of insertion of these terminal alkenes was somewhat unexpected since the closely related ketimine complex 16 gives a 4: 1 ratio in favour of the isomer where the alkene substituent is remote to the metal when reacted with 1-heptene⁴. The reaction of *in-situ* generated 8 with 1-bromo-3-butene was attempted as a direct route to spirocyclic compounds but instead gave the cyclopropane 18, presumably by intramolecular transfer of the bromide to the metal as in 17 (carbon zirconium bonds do not normally react with alkyl halides).



The PhNC insertion / rearrangement / trapping with 4-octyne procedure was extended successfully to other zirconacycles (Table 2) with generally good overall yields.



Table 2. Formation of bicyclic amines from 1,n-dienes *.

a. Conditions: i. Cp₂ZrCl₂ 2BuLi, THF, -78°- 20°C; ii. PrC=CPr, PhNC, THF, 20°C, 1 h then 67°C, 3 h; iii. MeOH; iv. H₂O.

b. Isolated yield based on starting diene.

c. Obtained as a readily separable 55: 45 mixture of diastereomers.

d. Obtained as a 1.8 : 1 mixture of cis : trans isomers. Only one of the two possible cis isomers was formed

e. Obtained as an inseparable mixture of isomers in which one of the cis-fused isomers predominates (66%). The other components were characterised by g.c. - MS.

Conclusion.

Insertion of phenyl isocyanide into zirconacyclopentanes affords η^2 -imine complexes which insert a variety of unactivated alkenes and alkynes in an efficient route to elaborated bicyclo[3.3.0]octylamines. The formation of four new carbon-carbon bonds in a one-pot reaction is notable. This transformation considerably extends the scope of the zirconocene induced bicyclisation of 1,6- and 1,7-dienes and illustrates a novel route to zirconocene η^2 -imine complexes.

Experimental procedure.

To a stirred solution of Cp_2ZrCl_2 (584 mg, 2 mmol) in THF (8 ml) under argon at -78°C was added dropwise n-BuLi (1.6 ml of a 2.5M soln. in hexanes, 4 mmol) and the reaction mixture stirred at this temperature for 1 h. A solution of the diene 4 (392 mg, 2 mmol) in THF (2 ml) was added and the mixture allowed to warm slowly to room temperature over 2 h. To the resulting light orange solution of the zirconacycle 5 was added 4-octyne (276 mg, 2.5 mmol) followed by a solution of freshly Kugelrohr distilled PhNC (234 mg, 2 mmol) in THF (2 ml). After boiling under reflux for three hours the dark red reaction mixture was quenched with methanol (2 ml) then poured onto water (50 ml) and extracted with ether (3 x 50 ml). Removal of solvent, chromatography (SiO₂, 10% ether in 40-60 petrol), and recrystallisation (ether) gave the bicyclic amine **10a** (414 mg, 48%) m.p. 138-140°C.

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- 7. 7: ¹H NMR (270 MHz, C_6D_6) δ 7.44-6.90 (5H, m), 5.59 (5H, s), 5.43 (5H, s), 3.63-3.88 (4H, m), 2.34 (1H, dd, J = 13.1, 6.8 Hz), 2.10 (1H, dd, J = 12.6, 6.6 Hz), 1.90-0.91 (8H, m), 1.75 (6H, s); ¹³C NMR (67.5 MHz, C_6D_6) δ 248.26 (C), 145.50 (C), 130.20 (CH), 124.50 (CH), 114.07 (CH), 107.56 (CH, Cp), 106.90 (CH, Cp), 98.46 (C), 70.93 (CH₂), 70.82 (CH₂), 50.09 (CH), 49.94 (CH), 48.67 (CH₂), 47.55 (s),43.81 (CH₂), 41.30 (CH₂), 31.51 (CH₂), 24.86 (CH₃), 22.99 (CH₃).
- 8. **9a**: ¹H NMR (270 MHz, C₆D₆) δ 7.34-6.74 (5H, m), 5.95 (5H, s), 5.75 (5H, s), 3.46 (2H, d, J = 10.4 Hz), 3.26 (2H, d, J = 10.4 Hz), 2.54-0.86 (18 H, m), 1.73 (6H, s), 1.12 (3H, t, J = 7.2 Hz), 1.05 (3H, t, J = 7.2 Hz); ¹³C NMR (67.5 MHz, C₆D₆) δ 184.22 (C), 151.77 (C), 146.64 (C), 131.09 (CH), 126.94 (CH), 114.16 (CH), 112.60 (CH, Cp), 112.14 (CH, Cp), 98.20 (C), 90.00 (C), 71.02 (CH₂), 70.84 (CH₂), 52.33 (CH), 51.21 (CH), 48.36 (CH₂), 41.33 (C), 41.16 (CH₂), 40.50 (CH₂), 36.90 (CH₂), 33.47 (CH₂), 26.47 (CH₂), 25.15 (CH₃), 25.01 (CH₂), 24.69 (CH₂), 24.51 (2 x CH₃), 16.57 (CH₃), 16.48 (CH₃).
- 9. All organic compounds were characterised by high field ¹H and ¹³C n.m.r., IR, and mass spectroscopy, and either combustion analysis or HRMS on M⁺.
- 10. 12: ¹H NMR (270 MHz, $C_{6}D_{6}$) δ 7.517 (2H, dd, J = 7.5, 7.0 Hz), 7.174 (2H, d, J = 7.5 Hz), 6.874 (1H, t, J = 7.0 Hz), 5.456 (5H, d, J_{HP} = 1.9 Hz), 5.364 (5H, d, J_{HP} = 1.7 Hz), 3.6 (4H, m), 2.4 (2H, m), 1.95 (3H, m), 1.2 1.8 (5H, m), 1.480 (6H, s), 0.940 (9H, d, J_{HP} = 6.0 Hz); ¹³C NMR (67.5 MHz, $C_{6}D_{6}$) δ 155.51 (C, d, J_{CP} = 1.9 Hz), 130.11 (CH), 116.23 (CH), 114.79 (CH), 106.81 (CH, Cp), 106.57 (CH, Cp), 98.39 (C), 71.58 (CH₂), 71.08 (CH₂), 54.35 (C, d, J_{CP} = 18.6 Hz), 52.72 (CH), 52.29 (CH), 39.01 (CH₂), 38.62 (CH₂), 37.904 (CH₂), 37.60 (CH₂), 25.28 (CH₃), 24.70 (CH₃), 17.06 (CH₃, d, J_{CP} = 15.6 Hz).

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