Zirconium-mediated Ring Opening of Cyclopropanes

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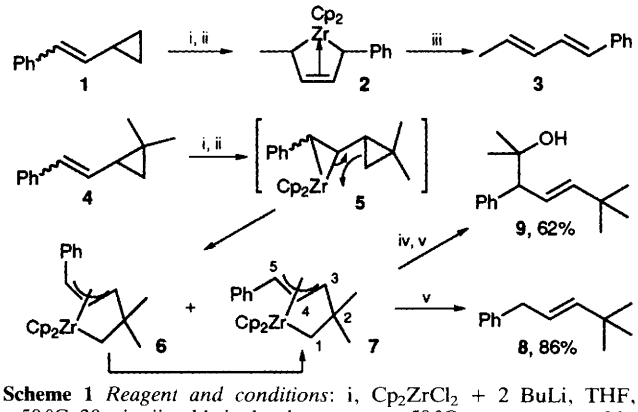
Zirconocene η^2-alkene and η^2-imine complexes with adjacent cyclopropane rings undergo cyclopropane ring cleavage to afford novel η^3-allyl, η^3-azaallyl, and η^1-enamine complexes.

There has been much recent interest in the cleavage of cyclopropanes, particularly vinylcyclopropanes, using transition metal reagents.[1] The rearrangement of titanocene and zirconocene complexes of cyclopropenes to titanocene vinylcarbene and zirconacyclobutene complexes respectively is the only reported example of group 4 transition metal complexes showing this type of reactivity.[2] The cleavage of carbon–heteroatom bonds adjacent to zirconocene η^2-alkene complexes[3] and the ready equilibrium between η^2-diene and η^4-diene complexes of zirconium[4] suggested that the transformation of vinylcyclopropanes to zirconacyclohexenes was reasonable. Our interest was further enhanced because although there are many examples of zircona-cyclopentanes and -pentenes known,[5] the homologous zirconacyclohexanes/enes are rare.[6]

Ligand exchange between *in situ* generated zirconocene–but-1-ene[7] and 2-cyclopropyl styrene **1** gave the complex **2** presumably *via* a cyclopropyl ring opening and a subsequent hydride shift. Related hydride shifts are implicated in the formation of zirconocene diene complexes from non-conjugated dienes.[8] The complex **2** had NMR properties consistent with similar known complexes[4] and gave the diene **3** on work-up with iodine. Although **3** was not the hoped-for product, its isolation confirmed that cyclopropane ring opening had occurred.

The hydride shift was blocked in the dimethylcyclopropane **4**, formed as a 2.8:1 mixture of (*Z*)- and (*E*)-alkene isomers *via* a Wittig reaction. Ligand exchange with zirconocene–but-1-ene gave initially a ≈2.5:1 mixture of two new complexes identified as **6** and **7**. On heating, the major isomer was gradually converted to the minor (first-order rate constant 1.3 × 10^{-4} s^{-1} at 60 °C, <3% **6** after 12 h at 60 °C). Repeating the reaction with pure (*E*)-**4** formed by palladium-catalysed cross coupling between (*E*)-2-bromostyrene and 2,2-dimethylcyclopropylzinc bromide gave only **7** confirming that the isomers are due to (*E*)- and (*Z*)-configuration across the 4,5-C–C bond. The selective formation of the (*E*)-3,4-allyl system follows from the preference for conformation **A** over **B** in the ring cleavage.† The interconversion between **6** and **7** is most likely to take place *via* the zirconacyclohexene **11** which demonstrates that the latter is not a thermodynamically stable form.



Scheme 1 *Reagent and conditions*: i, Cp_2ZrCl_2 + 2 BuLi, THF, −50 °C, 30 min; ii, add vinylcyclopropane, −50 °C to room temp., 2 h, THF; iii, 1.2 equiv. I_2, 0 °C, 1 h; iv, 5 equiv. Me_2CO, 60 °C, 5 h; v, MeOH, room temp., 1 h

NMR assignments for **6** and **7** followed from H–H and C–H COSY experiments (Table 1). The (*E*,*E*)-stereochemistry of the allyl complex **7** follows from the H–H coupling constants. The low chemical shifts of C-1, H-1 and H-1′, and the cyclopentadienyl rings compared to most zirconacycles are due to the uncommon 18 electron configuration of the metal (zirconium complexes generally adopt a 16 electron configuration). Representation as vinyl zirconacyclobutanes **10/12** is not consistent with the low chemical shifts of C-5/H-5 (Table 1).

Quenching the reaction with methanol gave only the (*E*)-alkene **8** irrespective of the composition of the starting mixture of **6** and **7**. Reaction with acetone followed by aqueous work-up gave the alcohol **9** in good yield. In both cases the reactions are best considered as occurring *via* the η^1-bound forms **10** or **12**, the oxygenation of methanol or the ketone coordinating to the metal and the proton or ketone addition occurring *via* a six-membered transition state with allylic rearrangement. Complexes **6** and **7** comprise a novel type of zirconacycle although homologues are known.[9,4c] 1,2-Unsaturated analogues of **6** and **7** have been formed by rearrangement of zirconabicyclo[3.1.0]hexenes.[10]

In an attempt to form azazirconacyclohexenes by cyclopropane ring cleavage the zirconocene η^2-imine complexes

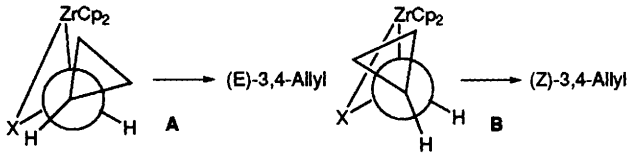


Fig. 1 View along what will become the 3,4-bond. X = CHPh or NPh.

Table 1 NMR[a] assignments for complexes **6**, **7**, **15**, **16** and **21**

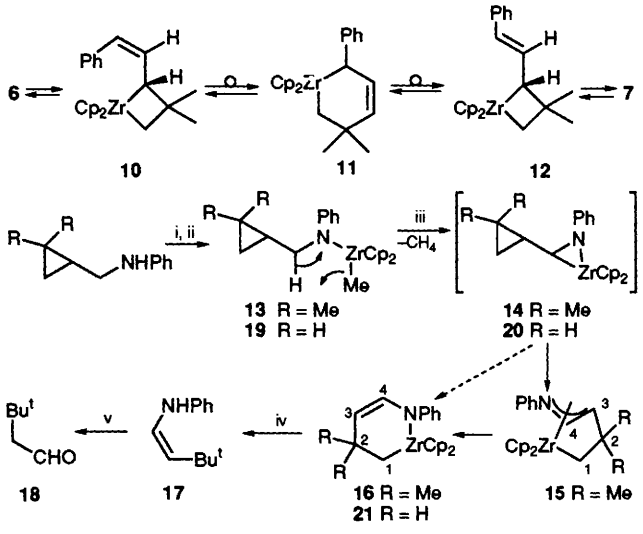
δ_H	6	7	15	16	21
Cp	5.322	5.363	5.684	5.89	5.78
Cp′	5.108	5.086	5.359	—	—
H-1	−0.706	−0.744	−0.252	1.01	0.99
H-1′	−0.884	−0.781	−0.470	—	—
H-2/Me-2	1.12	1.11	1.356	1.37	2.98
H-2′/Me-2′	1.44	1.43	1.200	—	—
H-3	4.21 to 4.35	3.270 to 4.974	3.802 to 5.041	4.93 to 5.68	4.87 to 5.96
H-4					
H-5		3.149	—	—	—
$J_{1,1}$	10.4	10.2	9.5	—	—
$J_{3,4}$	—	16.1	12.3	8.3	8.3
$J_{4,5}$	—	14.3	—	—	—
δ_C					
Cp	105.58	105.59	107.83	110.54	110.4
Cp′	107.22	105.82	106.24	—	—
C-1	−11.37	−12.55	−4.51	33.49	28.4
C-2	34.88	33.89	34.73	37.15	33.6
Me-2	26.95	25.27	36.40	35.08	—
Me-2′	37.02	37.83	24.56	—	—
C-3	62.76	62.64	84.49	128.11	113.1
C-4	101.36	101.47	105.82	134.11	137.6
C-7	89.98	78.33	—	—	—

[a] All spectra were recorded on a 300 MHz (proton) Bruker spectrometer in C_6D_6 and referenced with respect to an external standard (proton) or solvent peak (carbon). $J_{H,H}$ values are in Hz.

14 and **20** were required as intermediates. The cleanest route proved to be *via* a C–H activation from the corresponding amines.[11–13] Deprotonation of *N*-(2,2-dimethylcyclopropylmethyl)aniline with butyllithium followed by addition to zirconocene–methyl chloride gave the methyl zirconocene amide **13**. On standing at room temperature this underwent slow conversion to a new compound identified as the (*E*)-azaallyl[13] complex **15**.† The presumed intermediate η^2-imine complex **14** was not observed showing that the rate of cyclopropane ring opening was much faster than the β-hydrogen activation. Even at room temperature small amounts of a second complex **16** were observed to be formed before complete consumption of **13**. Heating at 60 °C for 2 h completed the β-hydrogen activation of **13** and isomerised **15** to the azazirconacyclohexene form **16** (*ca.* 95% pure) (first order rate constant $\approx 8 \times 10^{-4}$ s^{-1} at 60 °C). The change in coupling constant between H-3 and H-4 from 12.3 to 8.3 Hz is consistent with isomerisation about the 3–4 bond in the transformation of **15** to **16**. The large change in the chemical shifts of C-3 and C-4, and their attached protons, is indicative of the change from η^3-azaallyl to η^1-enamine coordination. The dramatic change in the chemical shift of the remote carbon C-1 (+38 ppm) on the isomerisation of **15** to **16** is notable and reflects the change from an 18 to a 16 electron configuration at the metal. Most, if not all, of **16** is formed *via* **15**. For example, after 6 h at room temperature the reaction contained a 20 : 20 : 1 mixture of **13**, **15** and **16**. Methanolysis of **16** gave initially the *cis*-enamine **17**,‡ further aqueous hydrolysis giving the known aldehyde **18**.

The methyl zirconocene amide **19** formed from cyclopropylmethylaniline slowly gave the azazirconacyclohexene **21** at room temperature, no intermediates being observed by NMR spectroscopy. Heating at 50 °C for 2 h gave clean conversion to **21** (>90% pure) It is notable that **21** does not isomerise to the azadiene complex[14] analogous to **2**. It is likely that the failure to observe an intermediate azaallyl complex analogous to **15** is due to a faster rate of isomerisation to the η^1-bound form.

We have shown that cyclopropane rings are rapidly cleaved by adjacent zirconocene η^2-alkene or η^2-imine moieties to give initially (*E*)-allyl or -azaallyl complexes. In the former case these are the thermodynamically stable form, but in the later facile isomerisation to (*Z*)-azazirconacyclohexenes occurs.



Scheme 2 *Reagent and conditions*: i, BuLi, THF, −10 °C, 10 min; ii, add to $Cp_2ZrMeCl$ at −50 °C; iii, room temp. −60 °C, THF or benzene; iv, MeOH; v, H_2O

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Footnotes

† The high selectivity for both (*E*)-3,4-bond geometry and insertion into the C–CH_2 cyclopropyl bond in the formation of **6** and **7** is surprising. The initial η^2-alkene complex **5** may be formed as a mixture of diastereoisomers (ignoring the phenyl stereochemistry), one of which should give either (*E*)-3,4-bond geometry and insertion into the C–CMe_2 cyclopropyl bond, or (*Z*)-3,4-bond geometry and insertion into the C–CH_2 bond. The non-observance of these products could be due to any one of several factors including: selective formation of one diastereoisomer of **5**; interconversion of the two diastereoisomers of **5** with selective ring cleavage in one form; a non-concerted ring opening, probably *via* a diradical, which would allow an *anti*-ring cleavage in **5**; or rapid isomerisation of any (*Z*)-3,4-allyl complex formed to the (*E*)-isomer. The same comments apply to the formation of **15** but here the initial formation and isomerisation of the (*Z*)-3,4-isomer can be ruled out since **16** is the more stable form.

‡ **17**: δ_H (300 MHz, C_6D_6) 7.17 (2H, t, *J* 7.8 Hz), 6.84 (1H, t, *J* 7.8 Hz), 6.58 (2H, d, *J* 7.8 Hz), 6.20 (1H, dd, *J* 11.6, 9.5 Hz, PhNHC*H*CHBu^t), 5.69 (1H, br d, *J* 11.6 Hz, NH), 4.39 (1H, d, *J* 9.5 Hz, PhNHCHC*H*Bu^t), 1.20 (9H, s); δ_C (90 MHz, C_6D_6) 143.95 (s), 129.67 (d), 124.17 (d, PhNH*C*HCHBu^t), 119.46 (d), 114.45 (d, PhNHCH*C*HBu^t), 113.63 (d), 31.01 (q), missing-*C*Me$_3$ probably obscured by the δ 31.01 signal.

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