Intramolecular Cocyclisation of Carbonyl Groups and Unactivated Alkenes or Alkynes induced by a Low-valent Titanium Complex

Dudley F. Hewlett and Richard J. Whitby*

Department of Chemistry, The University, Southampton SO9 5NH, UK

Treatment of δ-enones or δ-ynones with $[(C_5H_5)_2Ti(PMe_3)_2]$ induces an intramolecular cyclisation to afford 2-bis(cyclopentadienyl)-1-oxa-2-titanabicyclo[3.3.0]oct-anes and -3-enes in reasonable yields.

As part of our studies on the use of early transition metal complexes for the carbometallation of unactivated alkenes and alkynes we were interested in η^2-ketone complexes (metallaoxiranes) of titanium and zirconium prompted by a report by Erker that the complex **1** would insert alkenes to give oxazirconacyclopentanes.[1] In this case, and the extension to aliphatic examples by Grubbs,[2] the complexes were produced by rearrangement of acyl complexes.

We required a route which avoided further organometallic intermediates and the direct addition of a ketone to a metallocene(II) complex seemed reasonable. There is a precedent in the formation of an η^2-diphenylketene titanocene complex by reaction between diphenylketene and $[Cp_2Ti(CO)_2]$ ($Cp = C_5H_5$).[3] The parent metallocenes 'Cp_2M' (M = Ti or Zr) are not stable but the coordinatively saturated bis-trimethylphosphine complexes $[Cp_2M(PMe_3)_2]$ act as

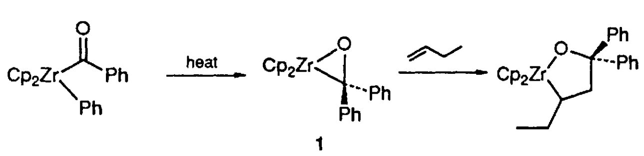
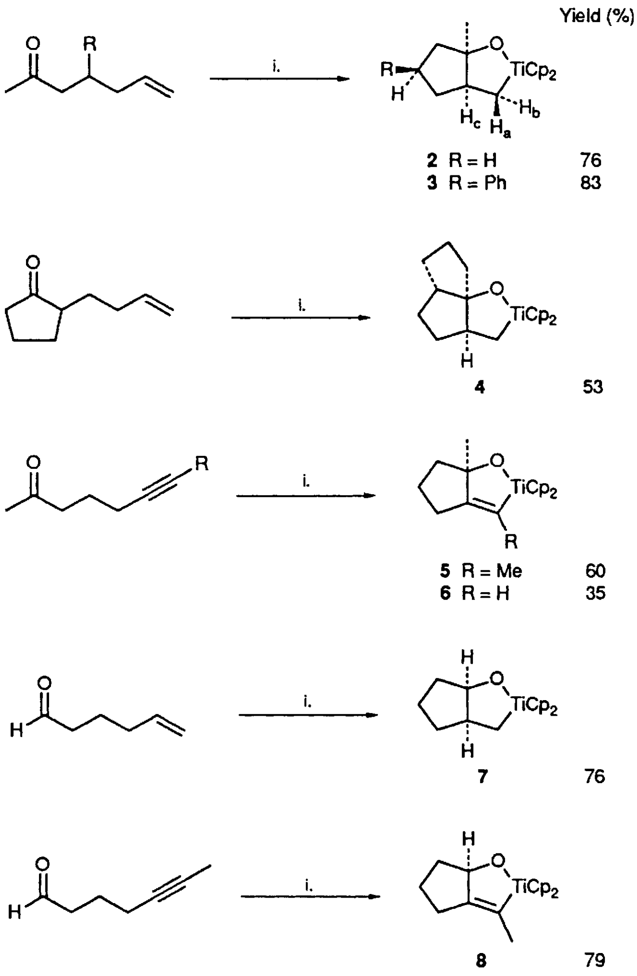


Table 1 Oxatitanabicyclopent-anes and -enes by intramolecular cyclisation[a]



[a] *Reagents and conditions*: i, $[Cp_2Ti(PMe_3)_2]$, hexane, room temp.

equivalents.[4] To improve the prospect of efficient trapping of the supposed η^2-ketone intermediate we initially looked at the intramolecular case, and the results for titanium are now reported. The use of the zirconium complex $[Cp_2Zr(PMe_3)_2]$ has not yet given useful results. The intramolecular cyclisation of α,ω-diynes, -enynes, and -dienes induced by low-valent zirconium and titanium has been known for some time,[5,6] and the intramolecular coupling of hydrazones to alkenes and alkynes induced by a zirconium(II) complex was reported during the course of this work.[7]

Thus $[Cp_2TiCl_2]$ (1 mmol) in tetrahydrofuran (THF) was reduced with magnesium amalgam (16 h; room temp.) in the presence of trimethylphosphine (5 mmol) to give a red solution. Solvent was removed and the extremely oxygen- and moisture-sensitive $[Cp_2Ti(PMe_3)_2]$ extracted into hexane.[4] $[Cp_2Ti(PMe_3)_2]$ could also be formed by reducing $[Cp_2TiCl_2]$ with 2 equiv. of BuLi in the presence of PMe_3 (2 equiv.).[8] The solution was filtered and hept-1-en-6-one (0.8 mmol) in hexane added. After 0.5 h $CDCl_3$ (0.1 ml) was added to destroy any excess of $[Cp_2Ti(PMe_3)_2]$, the mixture filtered and solvent removed from the filtrate to afford the oxatitanacycle **2** as an orange solid.† This could be further purified by filtration of a hexane solution through Celite to afford a pale orange powder in 65% yield. The structure rests on the full assignment of proton and carbon resonances in the high-field NMR spectra assisted by H-H and C-H COSY experiments. Most characteristic were the protons H_a, H_b and H_c appearing at δ 3.01 (dd, *J* 12.1, 10.6 Hz), 0.926 (dd, *J* 10.6, 6.2 Hz) and 3.456 (dtd, *J* 12.1, 6.2, 2 Hz) respectively. The *cis*-stereochemistry of the ring junction was proved by comparison of the *trans*-1,2-dimethylpentan-1-ol produced by acid hydrolysis with an independently synthesised sample.[9]

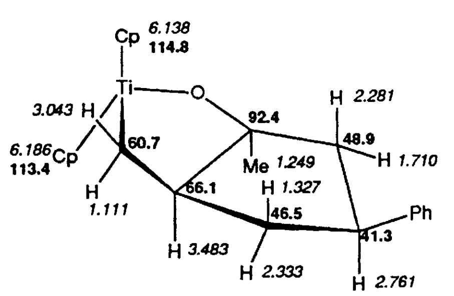


Fig. 1 NMR assignments for **3**: δ_H in *italics*, δ_C in **bold**

We then examined a range of other substrates (Table 1). Substitution of a phenyl ring at the 4-position gave excellent relative diastereocontrol, only the isomer **3** shown being detected. The stereochemistry indicated rests on full assignment of the ^1H and ^{13}C NMR spectra of the metallacycle [H-H, C-H COSY and nuclear Overhauser enhancement (NOE) experiments] (Fig. 1). The analogous cyclisation to form the tricycle **4** gave a poor yield. The intramolecular addition to a substituted alkyne to form the unsaturated titanoxacycle **5** worked well, but with a terminally unsubstituted alkyne the yield of **6** was low. This is in accord with literature precedent where bicyclisation of enynes fails with terminally unsubstituted alkynes.[5] δ-Ethylenic and -acetylenic aldehydes also cyclise under these conditions for example to form **7** and **8**. The intramolecular titanocene induced cocycli-

---

† Selected NMR data for the titanacycles (270 or 360 MHz ^1H and 67.5 or 90 MHz ^{13}C, both in $CDCl_3$; *J* in Hz). They were also characterised by mass spectrometry[12] and IR spectroscopy, and by their hydrolysis products.

2: δ_H 6.20 (5H, s), 6.14 (5H, s), 3.456 (1H, dtd, *J* 12.1, 6.2, 2), 3.010 (1H, dd, *J* 12.1, 10.6), 2.10 (1H, m), 1.9–1.7 (2H, m), 1.45–1.3 (2H, m), 1.17 (3H, s), 1.16 (1H, m) and 0.926 (1H, dd, *J* 10.6, 6.2); δ_C 114.52 (d), 113.25 (d), 92.94 (q), 66.89 (d), 58.61 (t), 40.47 (t), 36.91 (t), 28.13 (q) and 21.35 (t).

5: δ_H 6.21 (5H, s), 6.18 (5H, s), 1.14–2.1 (9H, m) and 1.21 (3H, s); δ_C 186.24 (s), 152.69 (s), 115.44 (d), 114.87 (d), 85.95 (s), 37.45 (t), 24.30 (t), 23.87 (q), 23.78 (t) and 20.69 (t).

6: δ_H 6.23 (6H, s), 6.18 (5H, s), 1.5–2.1 (6H, m) and 1.29 (3H, s). C–H COSY indicates that the vinylic proton appears directly beneath the cyclopentadienyl proton resonance signal at δ 6.23; δ_C 176.61 (d), 158.87 (s), 115.64 (d, Cp), 114.95 (d, Cp), 89.15 (s), 37.62 (t), 29.17 (t), 23.65 (q) and 21.09 (t).

7: δ_H 6.22 (5H, s), 6.12 (5H, s), 4.860 (1H, ddd, *J* 4.6, 7.8, 6.9 Hz), 3.70 (1H, m), 2.91 (1H, t, *J* 10.2 Hz), 1.1–1.6 (6H, m), 0.92 (1H, dd, *J* 7.4, 10.3 Hz). δ_C 114.2 (d), 112.5 (d), 86.1 (d), 63.6 (d), 58.7 (t), 40.1 (t), 37.6 (d), 23.4 (t).

sation of a ketone to both alkenes and alkynes failed in attempts to form 6-membered rings, *e.g.* with oct-7-en-2-one, 4,4-dimethyloct-7-en-2-one, oct-7-yn-2-one and non-7-yn-2-one. Monocyclic titanoxacycles similar to those described above have been formed by the addition of ketones to $[(Me_5C_5)_2Ti(CH_2{=}CH_2)]$ and $[Cp_2Ti(PhC{\equiv}CPh)]$.[10]

The cyclisation of δ-ethylenic and -acetylenic ketones has previously been induced by a variety of single-electron reducing agents,[9,11] probably *via* cyclisation of a ketyl radical. It is significant that these give the opposite stereochemistry of ring formation to that described herein. A further advantage of the titanium-induced cyclisation for use in organic synthesis is the presence of the remaining carbon–metal bond in the product metallacycles which should allow further functionalisation. Unfortunately, while reaction with iodine, *N*-bromosuccinimide and *m*-chloroperbenzoic acid allowed the introduction of I (45%), Br (34%) and OH (56%) at this position, conditions for new carbon–carbon bond formation have not yet been found.

In conclusion we have described a novel intramolecular cyclisation which produces a range of interesting metallacycles in acceptable yields. It is the first example both of the use of ketones, and of titanium in such intramolecular heteroalkene cyclisations. While significant limitations have been delineated it should find use in organic synthesis.

We thank the SERC for an earmarked studentship, Dr. John Langley for mass spectra, Mrs. Joan Street for NMR studies, Mr. Dorian Lewis for some preliminary experiments and the Nuffield foundation for financial support.

Received, 28th August 1990; Com. 0/03870I

References

1 G. Erker and F. Rosenfeldt, *J. Organomet. Chem.*, 1982, **224**, 29.
2 R. M. Waymouth, K. R. Clauser and R. H. Grubbs, *J. Am. Chem. Soc.*, 1986, **108**, 6385.
3 G. Fachinetti, C. Birani, C. Floriani, A. Chiesi-Villa and C. Guastini, *J. Am. Chem. Soc.*, 1978, **100**, 1921.
4 L. B. Kool, M. D. Rausch, H. G. Alt, M. Herberhold and U. Thewalt, *J. Organomet. Chem.*, 1987, **320**, 37.
5 E. Negishi, S. J. Holmes, J. M. Tour, J. A. Miller, F. E. Cederbaum, D. R. Swanson and T. Takahashi, *J. Am. Chem. Soc.*, 1989, **111**, 3336.
6 C. J. Rousset, D. R. Swanson, F. Lamaty and E. Negishi, *Tetrahedron Lett.*, 1989, **30**, 5105; W. A. Nugent and D. F. Taber, *J. Am. Chem. Soc.*, 1989, **111**, 6435; T. V. Rajan Babu, W. A. Nugent, D. F. Taber and P. J. Fagan, *J. Am. Chem. Soc.*, 1988, **110**, 7128; G. W. Parshal, W. A. Nugent, D. M.-T. Chan and W. Tam, *Pure Appl. Chem.*, 1985, **57**, 1815; P. J. Fagan and W. A. Nugent, *J. Am. Chem. Soc.*, 1988, **110**, 2310; K. I. Gell and J. Schwartz, *J. Chem. Soc., Chem. Commun.*, 1979, 244; W. A. Nugent, D. L. Thorn and R. L. Harlow, *J. Am. Chem. Soc.*, 1987, **109**, 2788; S. M. Yousaf, M. F. Farona, R. J. Shively and W. J. Youngs, *J. Organomet. Chem.*, 1989, **363**, 281.
7 M. Jensen and T. Livinghouse, *J. Am. Chem. Soc.*, 1989, **111**, 4495.
8 P. Binger, P. Muller, R. Benn, A. Rufinska, B. Gabor, C. Kruger and P. Betz, *Chem. Ber.*, 1989, **122**, 1035.
9 T. Shono, I. Nishiguchi, H. Ohmizu and M. Mitani, *J. Am. Chem. Soc.*, 1978, **100**, 545.
10 V. B. Shaw, V. V. Burlakov and M. E. Vol'pin, *J. Organomet. Chem.*, 1988, **347**, 77; S. A. Cohen and J. E. Bercaw, *Organometallics*, 1985, **4**, 1006.
11 G. A. Molander and C. Kenny, *Tetrahedron Lett.*, 1987, **28**, 4367, and references therein.
12 G. Langley, D. F. Hewlett and R. J. Whitby, Proc. of the 18th Meeting of the British Mass Spectrometry Association, University College, London, September 1990.