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Synthesis and structural characterization of an azatitanacyclobutene: the key intermediate in the catalytic anti-Markovnikov addition of primary amines to α-alkynes†

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Reaction of the imidotitanium complexes [Ti(N^{t}Bu)(N_2N_{py})(py)] (1) and [Ti(N-2,6-$C_6H_3{}^i$Pr$_2$)(N_2N_{py})(py)] (2) with phenyl acetylene and tolyl acetylene in toluene gave the corresponding {2+2} cycloaddition products [Ti(N_2N_{py}){κ^2-N(^{t}Bu)CH=CR}] (R = Ph: 3, Tol: 4) and [Ti(N_2N_{py}){κ^2-N(2,6-$C_6H_3{}^i$Pr$_2$)CH=CR}] (R = Ph: 5, Tol: 6). Complex 6 is the first example of a key intermediate in the anti-Markovnikov addition of a primary amine to a terminal acetylene which has been structurally characterized by X-ray diffraction.

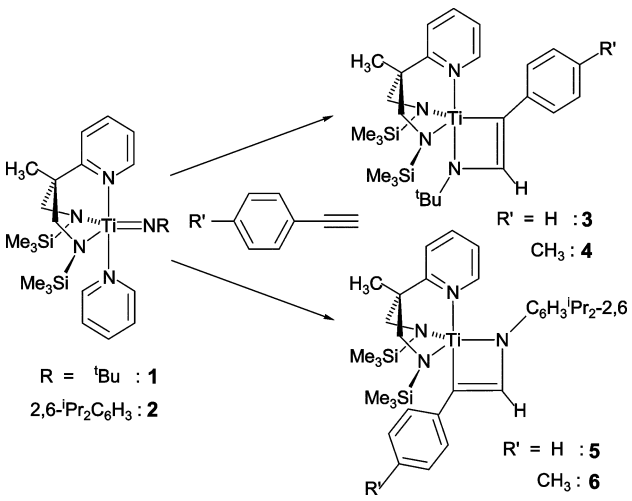
The catalytic hydroamination of carbon–carbon multiple bonds has recently emerged as a potentially powerful tool in chemical synthesis both in an academic and industrial context.[1] Among the catalysts employed, group 4 metal complexes were found to efficiently hydroaminate alkynes giving enamines and imines. Based on early work by Bergman and Livinghouse,[2,3] several novel classes of precatalysts, in particular titanium complexes, have been developed in recent years.[4–6] The crucial reaction step in the catalytic cycle is thought to be the formal {2+2} cycloaddition of a C≡C bond to the M=NR bond of an imidometal intermediate.

In spite of the considerable research efforts undertaken to date, the hydroamination of terminal alkynes, in particular with anti-Markovnikov regioselectivity, remains a challenge. The latter leads to aldimines which are useful synthetic intermediates for a wide range of further transformations, and some progress towards this goal has been made very recently.[7] It is in this context that we have studied the key step of this transformation using the diamido-pyridine supported imidotitanium complexes [Ti(N^{t}Bu)(N_2N_{py})(py)] (**1**) and [Ti(N-2,6-$C_6H_3{}^i$Pr$_2$)(N_2N_{py})(py)] (**2**) (N_2N_{py} = 2-C_5H_4N-C(CH_3)(CH_2NSiMe_3) which we developed previously.[8,9] This has now led to the first isolation and full characterization of the metallacyclic intermediate in an anti-Markovnikov hydroamination of terminal alkynes.

Reaction of the imidotitanium complexes **1** and **2** with phenyl acetylene and tolyl acetylene in toluene gave the corresponding {2+2} cycloaddition products [Ti(N_2N_{py}){κ^2-N(^{t}Bu)CH=CR}] (R = Ph: **3**, Tol: **4**) and [Ti(N_2N_{py}){κ^2-N(2,6-$C_6H_3{}^i$Pr$_2$)CH=CR}] (R = Ph: **5**, Tol: **6**) (Scheme 1).

Monitoring the reaction by ^{1}H NMR spectroscopy indicated that in all four cases only one of the two possible regioisomers ("Markovnikov" or "anti-Markovnikov") was being formed. The NMR data of compounds **3–6** are consistent with an overall molecular C_s-symmetry of the complexes. The metallacycle methine proton is observed as a singlet with a rather downfield chemical shift (*ca.* 9.4 ppm for **3** and **4**, *ca.* 9.8 ppm for **5** and **6**). The HMBC NMR spectra indicate the metallacyclic structures represented in Scheme 1 which implies that the acetylene has indeed undergone cycloaddition with the imido bond and not C–H activation. The ^{1}H-^{1}H ROESY NMR spectra of **3** and **4** indicate that the *tert*-butyl resonance has a close proximity to the $SiMe_3$ groups of the N_2N_{py} ligand, but not to the H^6 proton of the pyridyl donor which allows us to suggest that the metallacycle adopts a configuration with the *tert*-butylamido group *trans* to the pyridyl donor. However, the analogous experiments carried out for **5** and **6** indicate a configuration of the metallacycle with the N-aryl group *cis* to the pyridyl donor, whilst retaining the anti-Markovnikov form. Also of note is that the H^6 resonance of the pyridyl donor is shifted upfield of the position in the protio ligand. This is consistent with the proton being shielded by ring currents from the N-aryl ring of the diisopropylanilido substituent. For the latter the internal rotation around the Aryl-C–N bond is assumed to be hindered although the mirror symmetry of the molecule prevented the NMR-spectroscopic observation of this intramolecular motion. The different regiochemistry observed in compounds **5** and **6**, compared to **3** and **4**, may be attributed to unfavourable steric interactions of the diisopropylanilido group with the $SiMe_3$ groups of the ancillary ligand, if the anilido group were oriented *trans* to the pyridyl group.

A single crystal X-ray structure analysis of complex **6** (Fig. 1) confirms the structural proposals derived from the NMR data.‡ The pentacoordinate titanium atom adopts a coordination geometry which is neither trigonal bipyramidal nor square pyramidal but resembles the transition state geometry proposed for the turnstile rearrangement. It is facially tricoordinated by the diamidopyridine ligand combined with the small bite angle chelation of the C(17)–C(16)–N(4) unit which forms a highly distorted azatitanacyclobutene ring together with the metal centre. The principal structural features of the metallacycle are related to the azatitanacyclobutene and azazirconacyclobutene units previously characterized by



Scheme 1 {2+2} Cycloaddition of the arylacetylenes to the imidotitanium complexes giving the metallacyclic products **3–6**.

† Dedicated to Professor Mike Lappert on the occasion of his 75th birthday.

Electronic supplementary information (ESI) available: experimental procedures. See http://www.rsc.org/suppdata/cc/b3/b316383k/

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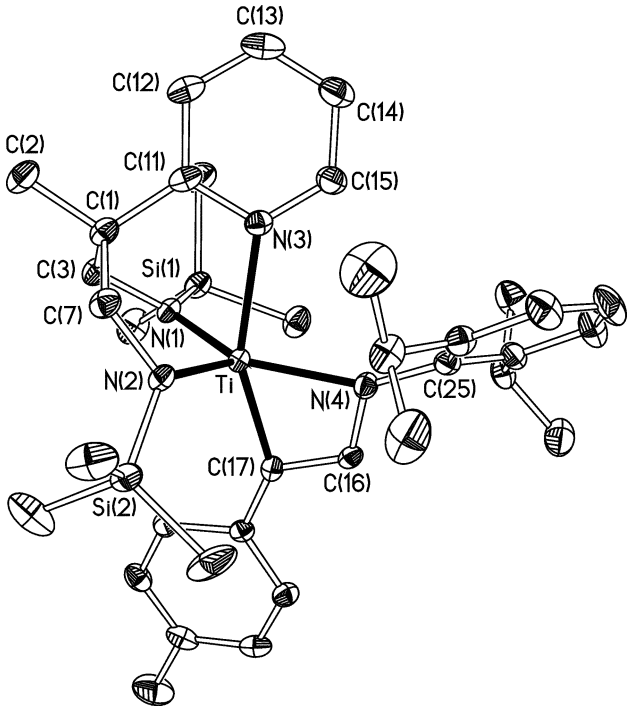
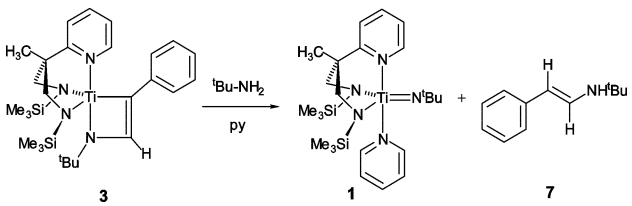


Fig. 1 Molecular structure of complex **6**. Principal bond lengths (Å) and angles (°): Ti–N(4) 2.087(3), Ti–C(17) 2.031(4), C(16)–N(4) 1.368(4), C(16)–C(17) 1.362(4), Ti–N(1) 1.911(3), Ti–N(2) 1.898(3), Ti–N(3) 2.273(3), C(17)–Ti–N(4) 68.3(1), N(3)–Ti–C(17) 155.1(1), N(4)–C(16)–C(17) 115.8(3), N(3)–Ti–N(4) 90.7(1), N(1)–Ti–N(2) 100.9(1), C(16)–N(4)–C(25) 122.8(3), C(16)–C(17)–C(18) 128.1(3).

Bergman *et al.*[2a,4a] The C(16)–C(17) distance of 1.362(4) Å is consistent with there being a double bond between these two carbon atoms in the metallacycle, while the Ti–C(17) and Ti–N(4) bond lengths indicate sp^2-type single bonding to the metal centre, thus supporting the representation of the compound in Scheme 1. The case at hand is the first example of a structurally characterized imido-acetylene {2+2} cycloaddition product corresponding to the key intermediate in the anti-Markovnikov addition of a primary amine to a terminal acetylene.

It is notable that the reaction pattern with terminal aryl acetylenes differs markedly from that observed for non-terminal C≡C bonds,[10] an observation which we are currently studying more closely.

In order to assess whether the cycloaddition products **3–6** may be protonated by the primary amine from which the imido starting material was derived, and thus complete the hydroamination cycle, complex **3**, which had been generated *in situ* from **1** and phenyl acetylene, was reacted with 1 molar equivalent of ^{t}BuNH$_2$ (Scheme 2). Over a period of 16 h the metallacyclic complex **3** was



Scheme 2 Reconversion of **3** to **1** and generation of the hydroamination product **7**.

reconverted to **1** liberating *trans*-cinnamyl(*tert*-butyl)amine **7**. Carrying out the same reaction with ^{t}BuNH$_2$ and phenyl acetylene in the presence of 20 mol% of the imido complex at ambient temperature led to several reaction cycles of product formation as well as partial degradation of the Ti complex (mainly due to partial desilylation of the ancillary amido ligand). Here again the only hydroamination product, which could be detected, was the anti-Markovnikov isomer **7**. We are currently modifying the ancillary ligand to increase the catalyst lifetime and to allow for higher reaction temperatures and thus turn-over frequencies.

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Notes and references

‡ *Crystal data* for [Ti(N_2N_{py}){κ²-N(2,6-$C_6H_3{}^iPr_2$)CH=CTol}] **6** : *n* $C_{36}H_{54}N_4Si_2Ti$, orange blocks, crystal dimensions 0.2 × 0.20 × 0.04 mm, M = 646.93, monoclinic, space group $P2_1/c$, a = 9.9150(2), b = 20.6148(4), c = 18.9685(5) Å, β = 104.045(5)°, U = 3761.2(1) Å, Z = 4, D_c = 1.14 g cm^{-3}, F(000) = 1392, μ = 0.320 mm^{-1}, Trans. min and max: 0.938/0.987, T = 173 K, MoKα, 0 < h < 13, 0 < k < 28, −26 < l < 25, 11205 reflections collected (2.5 < θ < 29.99°) using a Nonius Kappa CCD diffractometer, 4494 (I > 3σ(I)) used in the structure refinement (388 parameters refined). R = 0.054, Rw = 0.071, GOF = 1.262. Largest peak 0.323 e Å^{-3}.CCDC 227108. See http://www.rsc.org/suppdata/cc/b3/b316383k/ for crystallographic data in .cif format.

1 Reviews: (*a*) T. E. Müller and M. Beller, *Chem. Rev.*, 1998, **98**, 675; (*b*) M. Novis and B. Driessen-Hölscher, *Angew. Chem., Int. Ed.*, 2001, **40**, 3983; (*c*) J. Seayad, A. Tillak, C. G. Hartung and M. Beller, *Adv. Synth. Catal.*, 2002, **344**, 795; (*d*) F. Pohlki and S. Doye, *Chem. Soc. Rev.*, 2003, **32**, 104; (*e*) I. Bytschkov and S. Doye, *Eur. J. Org. Chem.*, 2003, 935; (*f*) P. W. Roesky and T. E. Müller, *Angew. Chem., Int. Ed.*, 2003, **42**, 2708.

2 (*a*) P. J. Walsh, A. M. Baranger and R. G. Bergman, *J. Am. Chem. Soc.*, 1992, **114**, 1708; (*b*) A. M. Baranger, P. J. Walsh and R. G. Bergman, *J. Am. Chem. Soc.*, 1993, **115**, 2753.

3 (*a*) P. L. McGrane, M. Jensen and T. Livinghouse, *J. Am. Chem. Soc.*, 1992, **114**, 5459; P. L. McGrane and T. Livinghouse, *J. Am. Chem. Soc.*, 1993, **115**, 11485.

4 (*a*) J. L. Polse, R. A. Andersen and R. G. Bergman, *J. Am. Chem. Soc.*, 1998, **120**, 13405; (*b*) J. S. Johnson and R. G. Bergman, *J. Am. Chem. Soc.*, 2001, **123**, 2923.

5 (*a*) E. Haak, I. Bytschkov and S. Doye, *Angew. Chem., Int. Ed.*, 1999, **38**, 3389; (*b*) I. Bytschkov and S. Doye, *Eur. J. Org. Chem.*, 2001, 4411; (*c*) F. Pohlki and S. Doye, *Angew. Chem., Int. Ed.*, 2001, **40**, 2305; (*d*) E. Haak, H. Siebeneicher and S. Doye, *Org. Lett.*, 2000, **2**, 1935.

6 (*a*) Y. Shi, C. Hall, J. T. Ciszewski, C. Cao and A. L. Odom, *Chem. Commun.*, 2003, 586; (*b*) Y. Shi, J. T. Ciszewski and A. L. Odom, *Organometallics*, 2001, **20**, 3967; (*c*) C. Cao, J. T. Ciszewski and A. L. Odom, *Organometallics*, 2001, **20**, 5011; (*d*) L. Ackermann, R. G. Bergman and R. N. Loy, *J. Am. Chem. Soc.*, 2003, **125**, 11956.

7 (*a*) A. Tillack, I. Garcia Castro, C. G. Hartung and M. Beller, *Angew. Chem., Int. Ed.*, 2002, **41**, 2541; (*b*) Z. Zhang and L. L. Shafer, *Org. Lett.*, 2003, **5**, 4733.

8 (*a*) A. J. Blake, P. E. Collier, L. H. Gade, M. McPartlin, P. Mountford, M. Schubart and I. J. Scowen, *Chem. Commun.*, 1997, 1555; (*b*) A. J. Blake, P. E. Collier, L. H. Gade, P. Mountford, M. Schubart, M. E. G. Skinner and D. J. M. Trösch, *Inorg. Chem.*, 2001, **40**, 870.

9 Reviews: (*a*) L. H. Gade, *Chem. Commun.*, 2000, 173; (*b*) L. H. Gade and P. Mountford, *Chem. Soc. Rev.*, 2001, **216/217**, 65; (*c*) P. Mountford, *Chem. Commun.*, 1997, 2127.

10 A. Bashall, P. E. Collier, L. H. Gade, M. McPartlin, P. Mountford and D. J. M. Trösch, *Chem. Commun.*, 1998, 2555.