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Novel, stereoselective tricyclization of a dienyne by titanium aryloxide centers†

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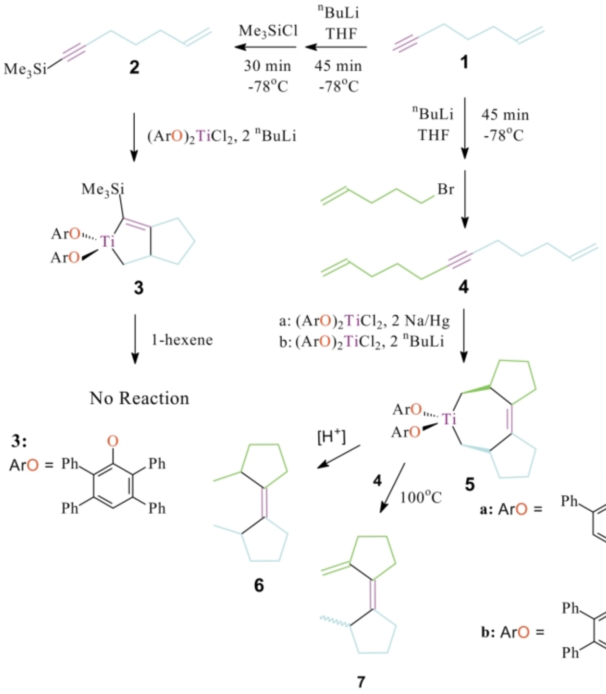
Titanium centers supported by aryloxide ligation mediate the tricyclization of a dienyne *via* intramolecular insertion of an olefin into the titanium–vinyl bond of a titanacyclopent-2-ene.

The metal-mediated bicyclization of enynes has proven to be a powerful synthetic method.[1] Group 4 metal complexes facilitate the construction of unsymmetrical cyclic compounds *via* this methodology[2] and promote further functionalization *via* insertion of carbon monoxide,[3] isocyanides,[4] and aldehydes.[5] However, no report exists of ring expansion *via* insertion of olefins by Group 4 metal complexes.

As part of our continuing studies of the formation and reactivity of titanacyclic compounds supported by aryloxide ligands we have sought routes to titanacyclopent-2-enes for comparison with metallocene analogues. During this work we have discovered the tricyclization of dienynes, a reaction that appears to proceed *via* intramolecular insertion of olefin into the titanium–vinyl bond of an unobserved titanacyclopent-2-ene intermediate.[6,7]

Enynes may be synthesized in two steps from dibromoalkanes.[8] The alkynyl proton may be substituted (Scheme 1) with silyl or alkyl groups in moderate to high yield *via* deprotonation by ^{n}BuLi and subsequent quenching with an appropriate chlorosilane[9] or primary haloalkane.‡ Bicyclization of 1-trimethylsilyl-6-hepten-1-yne (**2**) according to the route in Scheme 1 affords a titanacyclopent-2-ene (**3**) in 64% yield as a yellow powder. This compound does not undergo ring expansion in the presence of excess 1-hexene even at elevated temperatures.



Scheme 1 Reaction pathways

Observed as a byproduct in the synthesis of 6-hepten-1-yne (**1**), 1,11-dodecadien-6-yne (**4**) may be prepared in 40% yield following the procedure outlined in Scheme 1.§ Aryloxide-supported titanium centers will react with **4** to form a tricyclic titanacyclohept-3-ene (**5**). The 2,6-diphenylphenoxide derivative (**5a**) was isolated in greater purity and higher yield (67%) as an orange solid following recrystallization from hot benzene. Slow cooling affords crystals suitable for X-ray diffraction analysis.

Fig. 1 shows the solid-state structure of **5a**. Seven-membered titanacyclic rings are scarce.[10] The structure of **5a** is the first reported for a titanacycloheptene.[11] The geometry is pseudo-tetrahedral about the metal center. The bond lengths Ti–C(16), Ti–C(26), Ti–O(3), and Ti–O(4) are within expected limits, though the O(3)–Ti–O(4) angle is opened and the C(16)–Ti–C(26) angle pinched compared to other structurally characterized aryloxide-supported titanacycles.[11] The molecule exists as a single isomer with the titanacyclic ring adopting the *cis* conformation.

The solid-state structure and stereochemistry are retained in solution, as confirmed by NMR spectroscopy. In the ^{1}H NMR spectrum, the product has a distinct upfield resonance (**5a**: δ −0.06 ppm; **5b**: δ −0.47 ppm) appearing as a sharp doublet. ^{1}H-^{1}H COSY correlations allow unambiguous assignment of the upfield peak to the pseudo-equatorial protons on C(16) and C(26). The protons are coupled (^2J = 10.5–10.8 Hz) to the corresponding axial protons. Fig. 1 demonstrates that the pseudo-equatorial protons are in position to experience diamagnetic anisotropy from the phenyl substituents of the aryloxides.

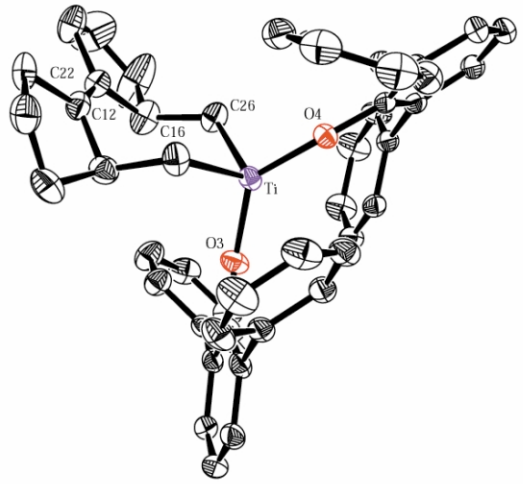


Fig. 1 ORTEP view of **5a**. Selected bond distances (Å) and angles (°): Ti–O(3) 1.821(2), Ti–O(4) 1.815(2), Ti–C(16) 2.067(4), Ti–C(26) 2.073(4), C(12)–C(22) 1.322(5), O(3)–Ti–O(4) 132.30(11), C(16)–Ti–C(26) 97.41(16), O(3)–Ti–C(16) 104.73(15), O(3)–Ti–C(26) 108.11(14), O(4)–Ti–C(16) 104.48(13), O(4)–Ti–C(26) 104.51(14).

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† Electronic supplementary information (ESI) available: synthesis of compounds **1**–**6** and spectroscopic data for **1**–**3**. See http://www.rsc.org/suppdata/cc/b2/b209889j/

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The *cis* conformation is also confirmed by the appearance in the ^{13}C NMR spectrum of two sets of aryloxide peaks, including two well resolved resonances for the *ipso* Ti–O–C carbons of the inequivalent phenoxides.

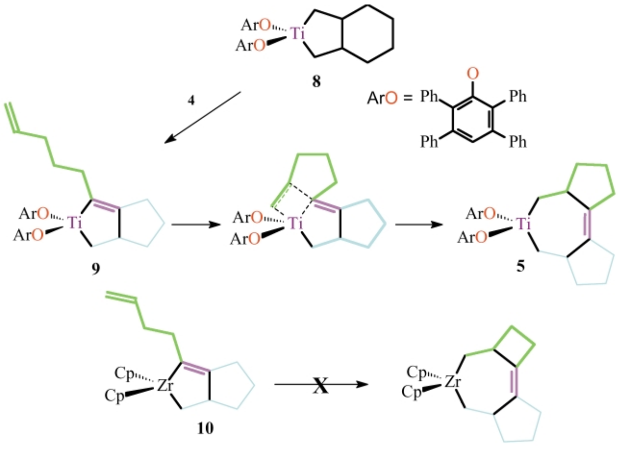
Reactive titanium centers are also supplied by precursor titanacycles such as **8** (Scheme 2). The presence of substrate (**4**) induces retrocyclization of **8** to release 1,7-octadiene. Clean formation of **5b** follows. This reaction may be monitored by ^{1}H NMR. Conversion to **5b** occurs rapidly at 100 °C, slowly at room temperature, but at no point can intermediates be observed. We hypothesize a mechanism involving intermediate formation of titanacyclopent-2-ene (**9**) followed by rapid intramolecular insertion of olefin into the titanium–vinyl bond (Scheme 2).

Formation of **9** has some precedent. Negishi *et al.* have reported the *in situ* synthesis of a zirconacyclopent-2-ene (**10**) from 1,10-undecadien-5-yne.[3] Insertion of olefin does not occur due to the strain of the resulting fused cyclobutane, the electronics of the cyclopentadienyl zirconium center, or a combination of these factors. The reactivity of **10** toward free olefins was not investigated.

Why this mechanism precludes formation of the *trans* isomer cannot currently be explained. Preference for the *cis* conformation may arise from the steric demands of the aryloxide ligands. To test this theory, experiments are being conducted with less sterically hindered metal centers.

Simple reactivity of **5** has been investigated. Hydrolysis of the metallacycle yields a novel cyclopentylidene-cyclopentane **6** (Scheme 1). It may be isolated by exposure of a C_6D_6 solution of **5** to ambient atmosphere followed by preparative-scale TLC. Only one isomer is isolated. Compound **5** also displays thermal reactivity. The metallacycle is unstable at high temperatures (75–100 °C) over long periods. **5a** appears to disproportionate into tetraphenoxy titanium and unknown organic products. However, both derivatives of **5** undergo catalysis in the presence of excess dienyne. ^{1}H NMR studies show **5** converts several equivalents of **4** into organic products. We believe the main product to be **7**, which forms *via* β-H abstraction and elimination. However, GC/MS identifies at least five additional C_{12} and C_{24} catalytic products. Further elucidation of this reaction will be communicated in due course.

In conclusion, we have synthesized a novel aryloxide-supported titanacyclohept-3-ene *via* tricyclization of a dienyne. We believe this transformation proceeds through an unprecedented insertion of olefin into the titanium–vinyl bond of a titanacyclopent-2-ene. In addition, the tricyclized organometallic product shows interesting reactivity and synthetic usefulness in forming novel organic molecules by hydrolysis and thermal catalysis. Investigations into further reactivity and all aspects of the chemistry discussed herein are currently underway.



Scheme 2 Intramolecular insertion of olefin to give tricyclized product.

Notes and references

‡ Attempts to synthesize an organometallic compound by reaction of **1** with titanium–aryloxide centers failed. Other researchers have reported difficulty in the cyclization reaction of terminal enynes.[2,3] Our system gives a trisubstituted (1-pentenyl)benzene arising from cyclotrimerization as the only isolable product.

§ *Selected spectroscopic data.* For **4**: ^{1}H NMR (C_6D_6): δ 5.73–5.60 (m, 2 H), 5.02–4.91 (m, 4 H), 2.08–2.01 (m, 8 H), 1.46 (quin, 4 H); ^{13}C ($CDCl_3$): δ138.24, 115.14, 80.25, 33.04, 28.57, 18.51. HRMS calcd. for $C_{12}H_{17}$ [M − H]: 161.1330, found: 161.1325. For **5a**: ^{1}H NMR (C_6D_6): δ 7.47–6.89 (aromatics), 2.84 (dd, 2 H), 2.01–1.85 (m, 4H), 1.58 (t, J = 12 Hz, 2H), 1.50–1.31 (m, 6H), 1.29–1.21 (m, 4H), 0.86–0.82 (m, 4H), −0.062 (d, J = 10.5 Hz, 2H); ^{13}C NMR (C_6D_6): δ 160.23, 159.78 (Ti–O–*C*); 137.17, 103.13 (Ti*C*H$_2$), 43.52, 38.71, 31.90, 24.52. For **5b**: ^{1}H NMR (C_6D_6): δ 7.39–6.85 (aromatics), 2.85 (dd, 2 H), 2.06–1.82 (m, 4H), 1.50 (t, 2H), 1.46–1.32 (m, 6H), 1.22 (m, 4H), 0.87 (m, 4H), −0.47 (d, J = 10.8 Hz, 2H); ^{13}C NMR (C_6D_6): δ 160.77 (Ti–O–*C*; 2 nearly overlapping peaks), 142.46, 104.64 (Ti*C*H$_2$), 43.76, 38.83, 32.02, 24.51. For **6**: ^{1}H NMR (C_6D_6): δ 2.67–2.63 (m, 2 H), 2.14–2.10 (m, 4 H), 1.74–1.57 (m), 1.39–1.35 (m), 1.06 (d, J = 6.9 Hz, 6 H), 0.92–0.89 (m). HRMS calcd. for $C_{12}H_{20}$: 164.1565. Found: 164.1558.

Crystal data for **5a**: $TiC_{48}H_{44}O_2$, M = 700.78, triclinic, space group $P\bar{1}$ (no. 2), a = 11.9946(4), b = 11.7706(4), c = 13.7377(6) Å, α = 73.1412(15), β = 77.5151(14), γ = 84.8318(15)°, V = 1811.51(18) Å^3, D_c = 1.285 g cm^{-3}, Z = 2, T = 150 K. Of the 8326 unique reflections collected ($5 \leq \theta \leq 28°$) with Mo-Kα (λ = 0.71073 Å), the 8313 with $F_o^2 > 2.0\ \sigma(F_o^2)$ were used in the final least-squares refinement to yield R = 0.085 and R_W = 0.179. CCDC 197519. See http://www.rsc.org/suppdata/cc/b2/b209889j/ for crystallographic data in CIF or other electronic format

1 See the following, and references therein: (*a*) E.-i. Negishi, in *Comprehensive Organic Synthesis,*, ed. B. M. Trost, Pergamon, Oxford, 1991,**vol. 5**, p., 1163; (*b*) B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 259; (*c*) N. E. Schore, *Chem. Rev.*, 1988, **88**, 1081–1119.
2 See, for example: (*a*) S. L. Buchwald and R. B. Nielsen, *Chem. Rev.*, 1988, **88**, 1047; (*b*) R. D. Broene and S. L. Buchwald, *Science*, 1993, **261**, 1696; (*c*) T. V. RajanBabu, W. A. Nugent, D. F. Taber and P. J. Fagan, *J. Am. Chem. Soc.*, 1988, **110**, 7128; (*d*) E.-i. Negishi, S. J. Holmes, J. M. Tour and J. A. Miller, *J. Am. Chem. Soc.*, 1985, **107**, 2568; (*e*) F. Sato, H. Urabe and S. Okamoto, *Chem. Rev.*, 2000, **100**, 2835; (*f*) H. Urabe, T. Hata and F. Sato, *Tetrahedron Lett.*, 1995, **36**, 4261–4264.
3 E.-i. 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.
4 S. C. Berk, R. B. Grossman and S. L. Buchwald, *J. Am. Chem. Soc.*, 1994, **116**, 8593.
5 H. Urabo and F. Sato, *J. Org. Chem.*, 1996, **61**, 6756.
6 For insertion of olefins into titanacyclopent-3-ene, see: (*a*) J. E. Hill, P. E. Fanwick and I. P Rothwell, *Organometallics*, 1991, **10**, 3428; (*b*) J. E. Hill, G. J. Balaich, P. E. Fanwick and I. P. Rothwell, *Organometallics*, 1993, **12**, 2911; (*c*) G. J. Balaich, J. E. Hill, S. A. Waratuke, P. E. Fanwick and I. P. Rothwell, *Organometallics*, 1995, **54**, 14265.
7 For insertions of olefins into titanacyclopenta-2,4-dienes, see: E. S. Johnson, G. J. Balaich and I. P. Rothwell, *J. Am. Chem. Soc.*, 1997, **119**, 7685.
8 (*a*) Synthesis of ω-bromo-1-enes: G. A. Kraus and K. Landgrebe, *Synthesis*, 1984, 885; (*b*) Synthesis of ω-ene-1-yne: W. Novis Smith and O. F. Beumel, *Synthesis*, 1974, 441.
9 M. Shipman, H. R. Thorpe and I. R. Clemens, *Tetrahedron*, 1998, **54**, 14265.
10 Titanacycloheptanes formed by reaction of dilithio- or bis-Grignard reagent with Cp_2TiCl_2 have been reported : L. M. Engelhardt, Wing-Por Leung, R. I. Papasergio, C. L. Raston, P. Twiss and A. H. White, *J. Chem. Soc., Dalton Trans.*, 1987, 2347.
11 Hetero-titanacycloheptanes have been synthesized. See: M. G. Thorn, J. E. Hill, S. A. Waratuke, E. S. Johnson, P. E. Fanwick and I. P. Rothwell, *J. Am. Chem. Soc.*, 1997, **119**, 8630.