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**C–C Bond Cleavage**

# Coupling of Titanacyclopentadienes with a Cp Ligand and Elimination of One Substituent

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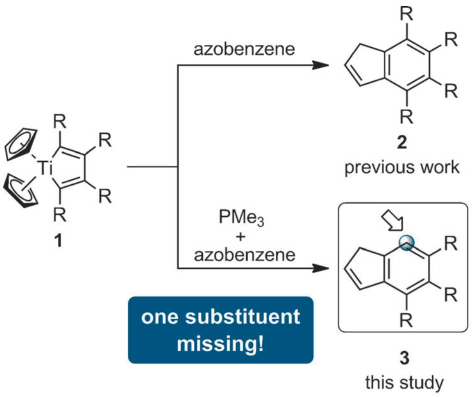
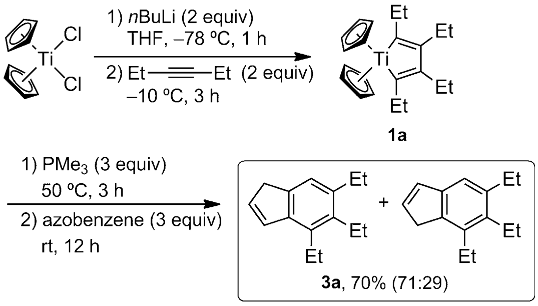
***Abstract:*** *Titanacyclopentadienes, prepared from [$Cp_2TiBu_2$] and either two equivalents of an alkyne or a diyne, were treated with $PMe_3$ (3 equiv) at 50 °C for 3 h and then with azobenzene at room temperature for 12 h to give 4,5,6-trisubstituted indene derivatives with the loss of one substituent in good yields. This reaction contrasts sharply with our previously reported reaction for the formation of 4,5,6,7-tetrasubstituted indene derivatives without the loss of substituents by the treatment of titanacyclopentadienes with azobenzene without $PMe_3$. $^{13}C$ NMR spectroscopy of the product derived from a $^{13}C$-enriched complex revealed that the five carbon atoms originating from a Cp ligand were arranged linearly in the trisubstituted indene derivatives, in contrast to the 4,5,6,7-tetrasubsituted indene derivatives, in which the corresponding five carbon atoms are arranged in a ring.*



***Scheme 1.*** Novel C–C bond-cleavage reaction of a titanocene.

Carbon–carbon bond cleavage with transition metals has long been a challenging target in organic chemistry.[1] Since the Cp ligand has been believed inert for a long time, reactions of the Cp ligand have been very limited.[2–4] Rosenthal et al. reported the first example of the coupling of a Cp ligand with a diene moiety of titanacyclopentadienes and the ring-opening reaction of the Cp ligand on titanium.[3] We confirmed that the Cp-derived moiety was cyclic or linearly arranged in the dihydroindenyltitanium complexes by a $^{13}C$ NMR spectroscopic experiment involving $^{13}C$ enrichment. During our studies, we reported that the treatment of titanacyclopentadienes **1** with azobenzene gave 4,5,6,7-tetrasubstituted indene derivatives **2** (Scheme 1).[4d] However, surprisingly, we found that if **1** was treated first with $PMe_3$ before treatment with azobenzene, the trisubstituted indene derivative **3** was formed. One substituent was missing in the product. Herein we report the synthesis of trisubstituted indene derivatives **3** from titanacyclopentadienes **1** with the loss of one substituent by treatment first with $PMe_3$ and then with azobenzene.

Titanacyclopentadiene **1a** was prepared by the reaction of 3-hexyne (2 equiv) with [$Cp_2TiBu_2$], which was generated by the treatment of [$Cp_2TiCl_2$] with *n*BuLi (2 equiv) in THF at −78 °C for 1 h.[5] The treatment of complex **1a** with $PMe_3$ (3 equiv) at 50 °C for 3 h and then with azobenzene (3 equiv) at room temperature for 12 h gave 4,5,6-triethylindene **3a** as a 71:29 mixture of double-bond positional isomers in 70 % combined yield (Scheme 2). The starting compound **1a** had four ethyl groups on the diene moiety. Thus, during the reaction, one ethyl group was eliminated. To verify the structure of the product, we converted **3a** into **4a** by treatment with tetracyanoethylene (TCNE) to obtain suitable crystals for X-ray crystal-structure analysis (Scheme 3). The crystal structure of **4a** (Figure 1)[6] clearly shows that **4a** has only three ethyl groups.



***Scheme 2.*** Formation of trisubstituted indene derivative **3a** from titanacyclopentadiene **1a**.

Trisubstituted indene derivatives **3a–d** were formed in this way from various titanacycles **1a–d** (Table 1). The same reaction proceeded for **1b** and **1c** to give **3b** and **3c** (Table 1, entries 2 and 3). In the case of the bicyclic titanacycle **1d**,

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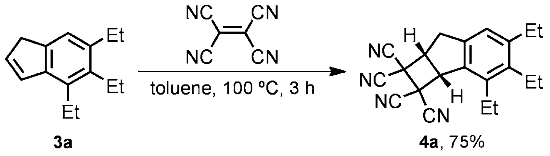


***Scheme 3.*** Reaction of compound **3** with TCNE.

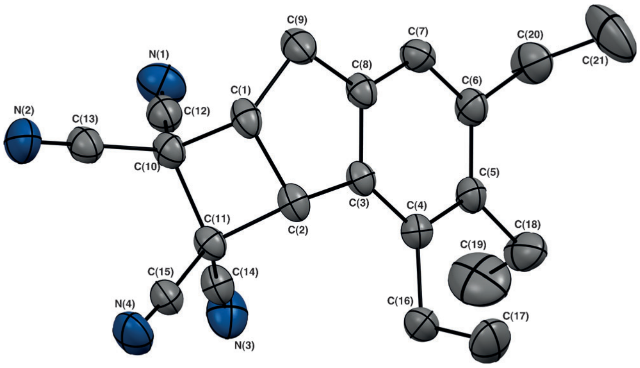
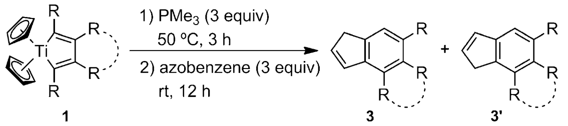
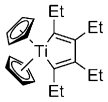
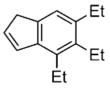
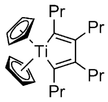
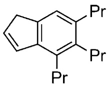
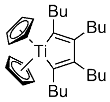
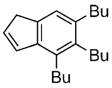
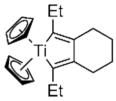
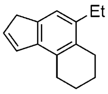


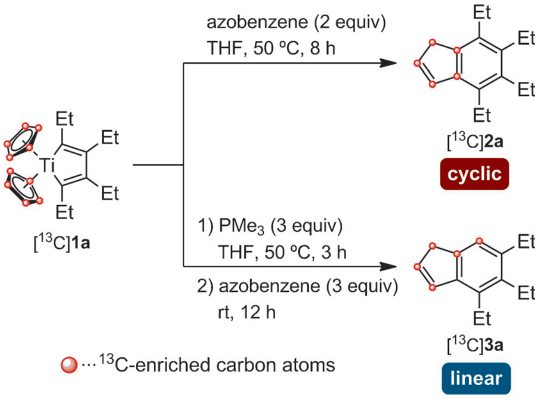
***Figure 1.*** Molecular structure of compound **4a**. All hydrogen atoms are omitted for clarity.

***Table 1:*** Formation of 4,5,6-trisubstituted indene derivatives with the loss of one substituent.



| Entry | Titanacycle | Product | Yield [%][a] | 3/3′ |
|---|---|---|---|---|
| 1 |  |  | 70 (61) | 71:29 |
| 2 |  |  | 61 (50) | 74:26 |
| 3 |  |  | 68 (56) | 74:26 |
| 4 |  |  | 72 (60) | 34:66 |

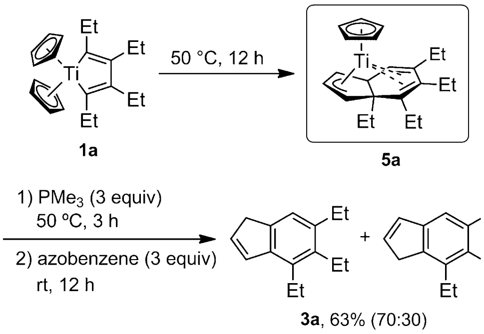
[a] Combined yield of the two double-bond isomers, as determined by NMR spectroscopy. The yield of the isolated product is given in parentheses.



***Scheme 4.*** $^{13}$C-Labeling experiment for the formation of indenes **2a** and **3a**.

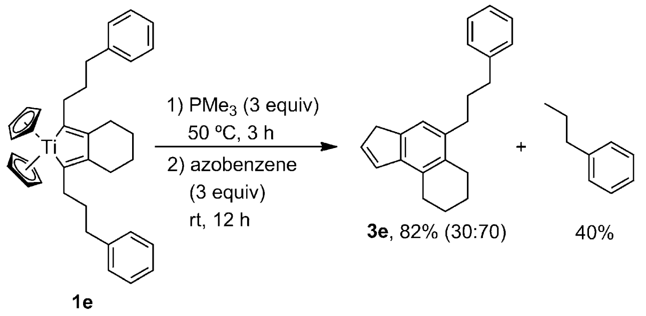
compound **3d** was obtained in 72 % yield (Table 1, entry 4). Interestingly, compound **3d** was not a linear tricyclic compound. The bent-type tricyclic structure suggests that the five carbon atoms originating from one of the Cp ligands are not in a cyclic arrangement in the indene derivative **3d**. To make clear this point, an experiment with $^{13}$C-enriched Cp ligands was carried out for the formation of indene **3a** (Scheme 4). As we reported previously, in the case of the reaction of titanacyclopentadiene [$^{13}$C]**1a** with azobenzene; the five carbon atoms originating from a Cp ligand were in a cyclic arrangement in the indene derivative [$^{13}$C]**2a**.[4d] However, the treatment of titanacycle [$^{13}$C]**1a** with PMe$_3$ and the subsequent addition of azobenzene gave indene [$^{13}$C]**3a**, in which five carbon atoms derived from a Cp ligand were linearly arranged.

This result reminded us of dihydroindenyltitanium complexes **5** with a substituent at the bridgehead carbon atom (Rosenthal-type complex). In these complexes, the five carbon atoms originating from a Cp ligand were linearly arranged in the dihydroindenyl moiety.[3b] We already made clear the position of the linearly arranged five carbon atoms in complexes **5** by $^{13}$C-labeling experiments.[4d] When complex **5a** was treated under the same conditions, first with PMe$_3$ and then with azobenzene, the same trisubstituted indene derivative **3a** was obtained as a mixture of isomers in 63 % combined yield. This result suggests that complex **5a** is the intermediate for the formation of **3a** from **1a** (Scheme 5).



***Scheme 5.*** Formation of complex **5a** from **1a** and reaction of **5a** with PMe$_3$ and azobenzene.

To enable detection of the eliminated substituent after the reaction, titanacyclopentadiene **1e** with a relatively large substituent was prepared from the corresponding diaryl diyne. Under the same conditions, **1e** was treated successively with PMe$_3$ and azobenzene. Propylbenzene was detected in



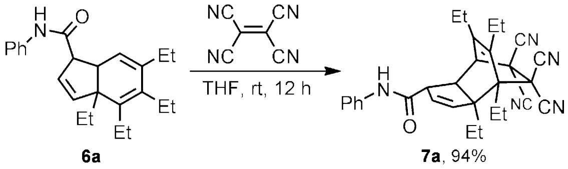
*Scheme 6.* Reaction of titanacyclopentadiene **1e** with PMe$_3$ and azobenzene, and detection of the eliminated substituent.

the reaction mixture in 40 % yield along with indene **3e** in 82 % yield (Scheme 6). This result reveals that the eliminated phenylpropyl group abstracted a proton from the reaction mixture to become propylbenzene.

It was important to know whether the treatment of **1a** with PMe$_3$ induced the elimination of the substituent at the bridgehead carbon atom of the dihydroindenyltitanium complex **5a**. To trap the intermediate after the addition of PMe$_3$, we quenched the reaction of **1a** with PMe$_3$ by treatment with phenylisocyanate (2 equiv) at 50 °C for 12 h. Interestingly, the dihydroindenyltitanium complex **5a** with one ethyl substituent at the bridgehead of the dihydroindene was trapped as the coupling product **6a** in 37 % yield. Thus, the allyltitanium moiety in **5a** reacted with phenylisocyanate to give **6a**.[7] Compound **6a** was not detected after the addition of azobenzene. We can therefore conclude that after the addition of azobenzene, the allyltitanium moiety disappeared, and one substituent was eliminated from the bridgehead carbon atom of the dihydroindenyl moiety (Scheme 7).

The structure of **6a** was verified by X-ray crystal-structure analysis after the conversion of **6a** with TCNE into **7a** in 94 % yield (Scheme 8). Compound **7a** was isolated in crystalline form. Its crystal structure (Figure 2)[8] clearly shows that the intermediate of the reaction of **1a** after treatment with PMe$_3$ has four ethyl groups.

On the basis of the results described herein, the following possible mechanism is proposed (Scheme 9). First, the coupling of one Cp ligand of the titanacyclopentadiene with a diene moiety of **1** proceeds to form intermediate **8**. In fact, the reaction product of **8a** with phenylisocyanate was obtained, since intermediate **8** also has the allyltitanium moiety. The complex was then converted into complex **5** (Rosenthal-type complex), in which the ring of five carbon atoms originating from the Cp ligand is changed to a linear arrangement of five carbon atoms in **5** by metathesis, as we reported before.[4d] Compound **5** is stable, since the diene moiety of the dihydroindene coordinates to titanium. Coordination of PMe$_3$ to the titanium metal center of **5** kicks out the coordinated diene moiety from titanium to give **9**, and the dihydroindene moiety becomes unstable and reactive. The reaction of complex **5** with PMe$_3$ was monitored by $^{31}$P NMR spectroscopy, and a new broad resonance at $\delta = 28$ ppm was observed that indicated the coordination of PMe$_3$ to titanium. If **5** is treated with azobenzene



*Scheme 8.* Reaction of compound **6a** with TCNE.

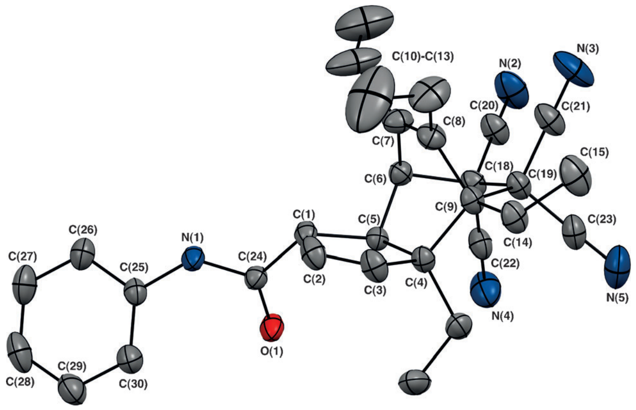
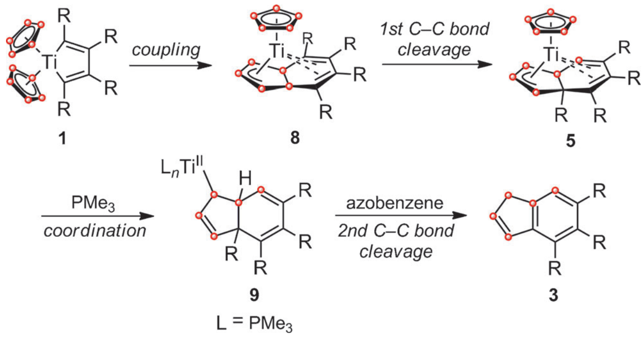
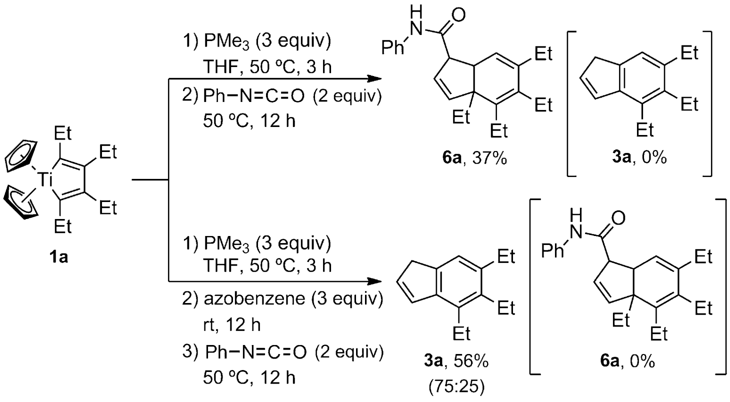


*Figure 2.* Molecular structure of compound **7a**. All hydrogen atoms are omitted for clarity.



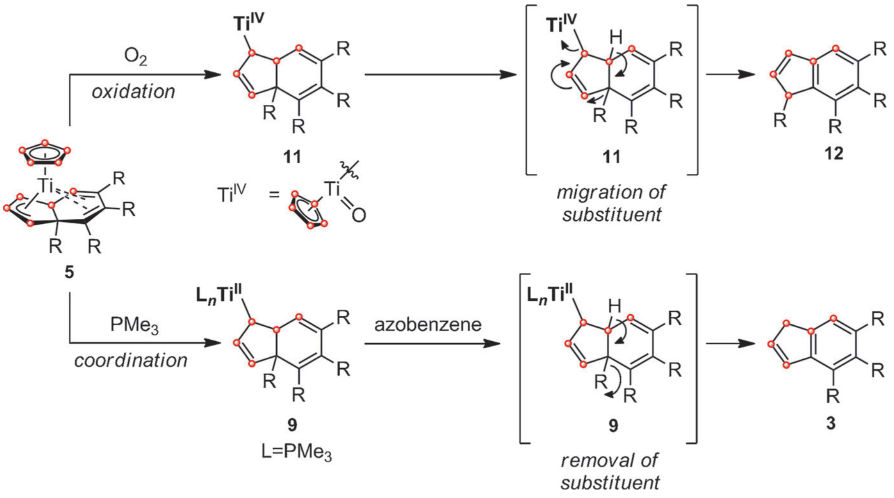
*Scheme 9.* Plausible reaction mechanism.



*Scheme 7.* Trapping of the intermediate with phenylisocyanate after the addition of PMe$_3$ or azobenzene to **1a**.

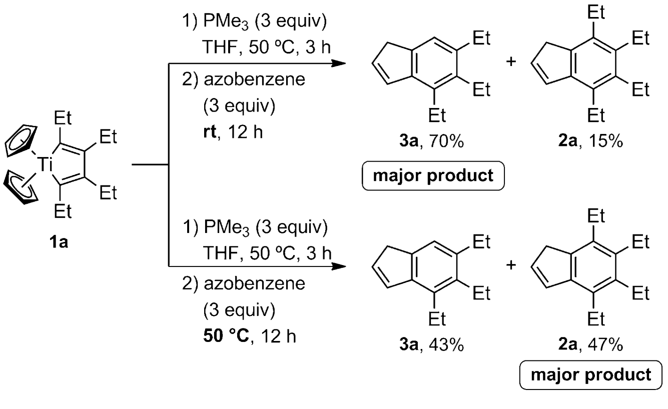
directly without $PMe_3$, azobenzene coordinates to the titanium metal center to convert **5** into **8**, followed by hydrogen abstraction by an additional azobenzene molecule to give a tetrasubstituted indene **2**.[9] Coordination of $PMe_3$ prevents the conversion of **5** into **8** and gives **9**, and an additional azobenzene molecule abstracts the bridgehead hydrogen atom from **9**.[10] For aromatization of the dihydroindene moiety, one of the carbon–carbon bonds at the opposite bridgehead has to be cleaved. One substituent was thus eliminated to give the trisubstituted indene **3**.[11]

The ratio of **2** and **3** formed was found to depend on the reaction temperature of the second step with azobenzene (Scheme 10). At a higher temperature, some of the $PMe_3$ on titanium is replaced with azobenzene, and then complex **9** is converted into **8**. Therefore, the relative amount of **2** formed increased with respect to **3**.

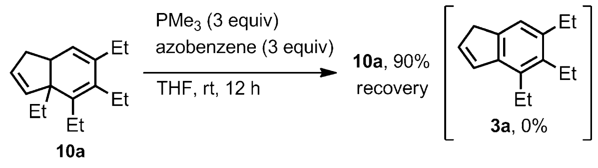


*Scheme 12.* Two types of allyltitanium species with different reactivity: migration of one substituent or elimination of one substituent at the bridgehead.

Interestingly, the treatment of dihydroindene **10a**, which has no titanium moiety, with $PMe_3$ and azobenzene did not give the aromatized compound **3a** at all (Scheme 11). This result suggests that the existence of the titanium metal center is important for the abstraction of the proton from the bridgehead carbon atom of the dihydroindene moiety by azobenzene. Azobenzene interacts with the titanium center in **9** and comes to closer to the hydrogen atom at the bridgehead carbon atom. The proton is then abstracted by azobenzene, and the aromatization proceeds.



*Scheme 10.* Formation of indene derivatives with $PMe_3$ and azobenzene at various temperatures.



*Scheme 11.* Reaction of compound **10a** with $PMe_3$ and azobenzene.

Previously, we reported the migration of one substituent at the bridgehead carbon atom of **5** to the next atom of the five-membered ring of the dihydroindene upon oxidation.[4b] In this reaction, titanium is oxidized from oxidation state II to IV. However, in the reaction reported herein, the elimination of the substituent at the bridgehead occurred as shown in Scheme 12. The oxidation state of the titanium center remained II. When titanium is oxidized to oxidation state IV, the allyltitanium moiety aids the migration of a substituent at the bridgehead. However, a low-valent titanium species stabilized with $PMe_3$ does not accept a nucleophilic attack on the allyltitanium moiety. This factor may control the fate of the substituent at the bridgehead of the dihydroindene moiety.

In summary, we have developed a novel carbon–carbon bond-cleavage reaction in titanocene complexes. The reaction involving two types of C–C bond cleavage and the formation of a C–C bond gave 4,5,6-trisubstituted indene derivatives **3**. One substituent on the diene moiety was cleaved by the effect of $PMe_3$ coordination to the titanium center to avoid the coordination of azobenzene. In this way, the conversion of **5** into **8** is prevented. The abstraction of a bridgehead hydrogen atom causes aromatization with the elimination of one substituent, in sharp contrast to the formation of 4,5,6,7-tetrasubstituted indene derivatives **2**,[4d] in which no elimination of a substituent occurred.

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**Keywords:** C–C activation · C–C coupling · cleavage reactions · cyclopentadienyl ligands · titanocenes

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[1] For general reviews of the C–C cleavage of unstrained organic molecules as mediated or catalyzed by transition-metal compounds, see: a) T. Takahashi, K. Kanno, in *Metallocenes in Regio- and Stereoselective Synthesis*, *Vol. 8* (Ed.: T. Takahashi), Springer, Berlin, **2005**, pp. 217–236; b) B. Rybtchinski, D. Milstein, *Angew. Chem.* **1999**, *111*, 918–932; *Angew. Chem.*

*Int. Ed.* **1999**, *38*, 870 – 883; c) M. Murakami, Y. Ito in *Activation of Unreactive Bonds and Organic Synthesis* (Ed.: S. Murai), Springer, Berlin, **1999**, pp. 97 – 129; d) R. H. Crabtree, *Chem. Rev.* **1985**, *85*, 245 – 269.

[2] For reactions of the Cp ligand, see: a) D. M. Giolando, T. B. Rauchfuss, *J. Am. Chem. Soc.* **1984**, *106*, 6455; b) W. E. Crowe, A. T. Vu, *J. Am. Chem. Soc.* **1996**, *118*, 5508; c) T. L. Dzwiniel, N. Etkin, J. M. Stryker, *J. Am. Chem. Soc.* **1999**, *121*, 10640; d) T. L. Dzwiniel, J. M. Stryker, *J. Am. Chem. Soc.* **2004**, *126*, 9184.

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[5] Titanacyclopentadienes **1** were prepared according to a previously described procedure: K. Sato, Y. Nishihara, S. Huo, Z. Xi, T. Takahashi, *J. Organomet. Chem.* **2001**, *633*, 18.

[6] CCDC 1001391 (**4a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[7] For a review of the general reactivity of allyltitanium derivatives, see: J. Szymoniak, C. Moïse in *Titanium and Zirconium in Organic Synthesis* (Ed.: I. Marek), Wiley-VCH, Weinheim, **2002**, pp. 451 – 474.

[8] CCDC 1001392 (**7a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[9] There is an equilibrium between complexes **5** and **8** via a titanium carbene complex (see Ref. [4d] for details).

[10] The formation of 1,2-diphenylhydrazine was observed (see Ref. [4d] for details).

[11] After workup of the two reactions shown in Scheme 12, formation of the monocyclopentadienyl titanium complex was observed. The complex obtained from the top reaction ($O_2$ oxidation) was characterized by X-ray crystal-structure analysis. See the Supporting Information.