# Unprecedented Elimination of Conjugated Phenylthioether Groups by Low-Valent Titanocene

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*Received 26 August 2010*

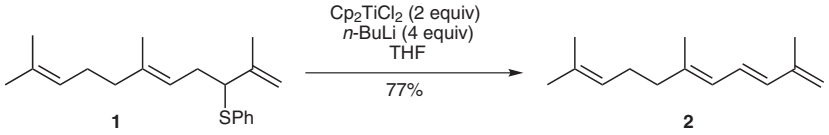
This paper is amicably dedicated to Professor Carmen Nájera on the occasion of her 60th birthday

**Abstract:** The first thioether elimination reaction utilizing a low-valent titanocene has been discovered. This reaction occurs under mild conditions and affords stereospecifically a variety of dienes and styrenes. Our data suggest that this new reaction involves an intermediate of dimerization of titanocene as the reactant responsible for this elimination.

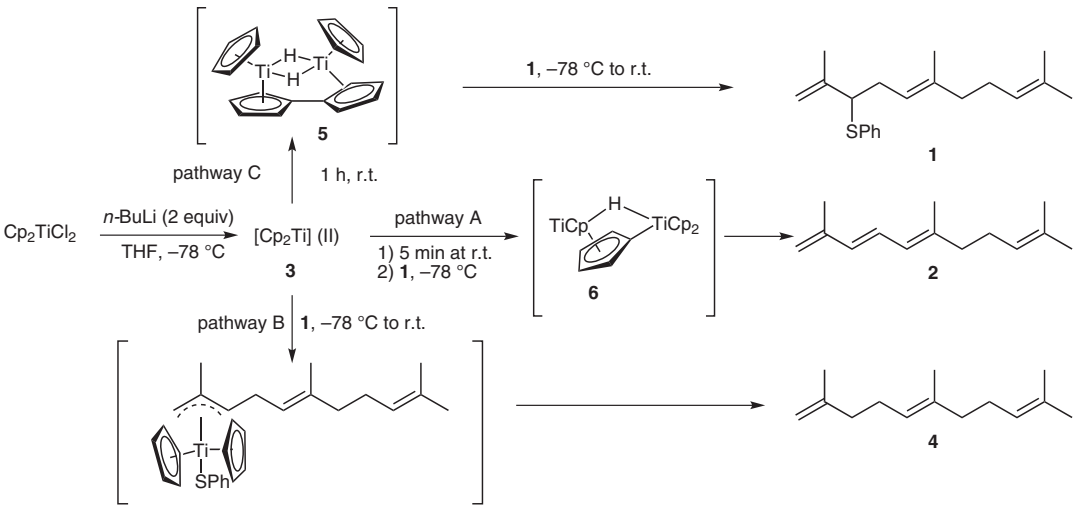
**Key words:** thioethers, titanocene, alkenes, allyl complexes, elimination

A major breakthrough in the field of titanium chemistry came from Whitesides et al. who showed that a titanocene(II) species can be synthesized by addition of *n*-BuLi to $Cp_2TiCl_2$.[1] This convenient method opened the door to the generation of allyltitanocenes from various allylic substrates, including allylthioethers, by Takeda et al.[2] During the course of our study on the use of allylthioethers in organic synthesis,[3] we observed an unexpected elimination of the phenylsulfide group of **1** to give stereospecifically the alkene **2** in 77% yield (Scheme 1), which led to the discovery of an unprecedented elimination of phenylthioethers by a low-valent titanocene species.

The optimal elimination conditions were obtained after the solution of the low-valent titanocene **3** (2 equiv) was left at room temperature for 5 minutes and chilled again at –78 °C prior to the addition of thioether **1** (pathway A, Scheme 2). Indeed, if the solution of **3** was kept at –78 °C before the addition of the thioether **1**, the protonated product **4** was obtained as described by Takeda (pathway B, Scheme 2).[2] If the solution of **3** was left for one hour at room temperature, there was not reaction after addition of **1** at –78 °C (pathway C, Scheme 2). This lack of reactivity can be explained by the instability of the solution of **3** at




**Scheme 1** Unexpected synthesis of the triene **2**



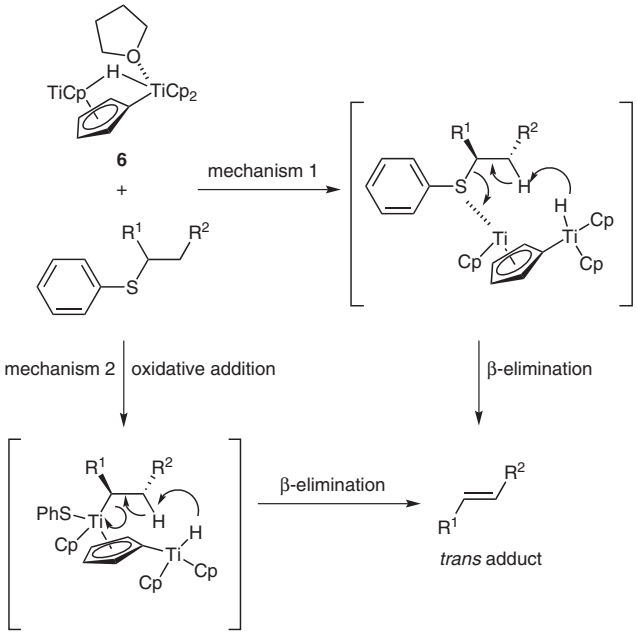

**Scheme 2** Proposed mechanistic pathways for the reaction of thioether **1** with species generated from $Cp_2Ti(II)$ **3** at different temperatures

*SYNLETT* 2010, No. 19, pp 2928–2930
Advanced online publication: 14.10.2010
DOI: 10.1055/s-0030-1259009; Art ID: G26110ST

room temperature, which dimerized to give the inactive fulvalene **5**.[4]

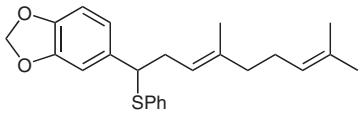
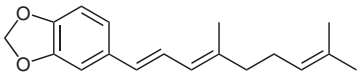
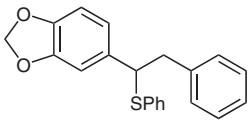
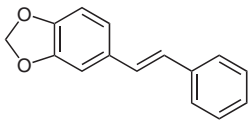
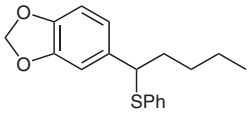
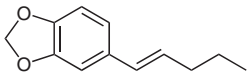
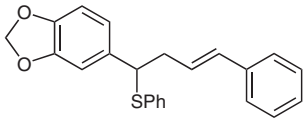
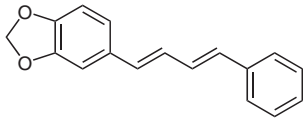
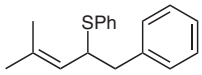
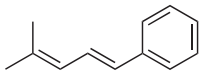
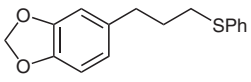
Although we have no direct evidence for the mechanistic pathway, two mechanisms can account for the origin of this reactivity and stereoselectivity (Scheme 3). In 2001, Harrod et al. had demonstrated that the species **6** was an intermediate in the rearrangement of **3** to the unreactive fulvalene **5**.[5] The involvement of **6** is suspected and may corroborate why two equivalents of dichlorotitanocene are required for this reaction. Indeed, **6** may coordinate to the thiophenyl group and induce a β-elimination involving the titanocene hydride (mechanism 1, Scheme 3). Another pathway may invoke the oxidative addition of **6** to the thioether moiety, followed by a β-elimination (mechanism 2, Scheme 3). The *trans* stereoselectivity may arise from the steric hindrance between $R^1$ and $R^2$ groups during the transition state of the reaction.

With the optimized conditions in hand, we performed the reaction on thioethers **7**, **9**, **11**, **13**, **15**, **17**, and **18** (Table 1). Allylic and benzylic phenyl thioethers **7**, **9**, **11**, **13**, and **15** gave stereospecifically the corresponding *trans*-alkenes in moderate to excellent yield (entries 1–5).




**Scheme 3** Proposed mechanisms for the β-elimination

**Table 1** Elimination of Conjugated Phenylthioethers by Low-Valent Titanocene

| Entry | Thioether | Product | Yield (%)[a] |
|---|---|---|---|
| 1 |  **7** |  **8** | 71 |
| 2 |  **9** |  **10** | 91 |
| 3 |  **11** |  **12** | 79 (95 brsm)[b] |
| 4 |  **13** |  **14** | 27 (45 brsm)[b] |
| 5 |  **15** |  **16** | 68 |
| 6 |  **17** | – | 0[c] |
| 7 | $PhS(CH_2)_{10}COOMe$ **18** | – | 0[c] |

[a] Isolated yields.
[b] Yield based on recovery of the starting material.
[c] The starting material was recovered.

However, nonconjugated thioethers **17** and **18** were unreactive, and the starting materials were recovered (Table 1, entries 6 and 7). The temperature plays an important role in order to achieve high yield and *trans* stereoselectivity. After the addition of the thioether, the reaction should be warmed slowly from –78 °C to room temperature over 2 or 3 hours. On the contrary, if the temperature increases suddenly to room temperature, the substrate **9** gives **10** with only 48% yield and an equimolar ratio of *E*/*Z*.

In conclusion, we reported an unprecedented elimination of conjugated phenyl thioether groups by a low-valent titanocene species. The study of this new reactivity and mechanism are now under investigation, and the results will be reported in due course.

**Typical Procedure**

Dichlorotitanocene (298 mg, 1.2 mmol) was diluted in 3 mL of anhydrous THF and cooled to –78 °C, and then *n*-BuLi (1.6 M in hexane, 2.4 mmol) was added dropwise. After 30 min at –78 °C, the solution was left at r.t. for 5 min, and then chilled again to –78 °C. A solution of the thioether **9** in anhydrous THF (2 mL) was added dropwise. The reaction was then slowly warmed to r.t. and stirred overnight. The reaction was stopped by addition of distilled $H_2O$ (10 mL) and extracted twice with $Et_2O$. The cumulated organic phase were dried over $MgSO_4$, and the crude was purified on silica gel column with pentane–$Et_2O$ (95:5) as eluant to yield 123 mg of the expected product **10**.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 5.86 (s, 2 H), 6.70 (d, *J* = 8 Hz, 1 H), 6.84 (d, *J* = 16 Hz, 1 H), 6.85 (d, *J* = 9 Hz, 1 H), 6.93 (d, *J* = 16 Hz, 1 H), 6.97 (s, 1 H), 7.14 (t, *J* = 7.2 Hz, 1 H), 7.25 (t, *J* = 7 Hz, 2 H), 7.38 (d, *J* = 8 Hz, 2 H). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 101.3 ($CH_2$), 105.7 (CH), 108.6 (CH), 121.6 (CH), 126.5 (CH), 127.2 (CH), 127.5 (CH), 128.5 (CH), 128.8 (CH), 132.1 (C), 137.6 (C), 147.5 (C), 148.3 (C).

**Product 2**

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.61 (s, 3 H), 1.68 (s, 3 H), 1.80 (s, 3 H), 1.89 (s, 3 H), 2.12 (s, 4 H), 4.93 (d, *J* = 6.0 Hz), 5.11 (m, 1 H), 5.90 (d, *J* = 10.8 Hz, 1H), 6.24 (d, *J* = 15.3 Hz, 1 H), 6.42 (dd, *J* = 15.3, 10.8 Hz, 1 H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 16.8 ($CH_3$), 17.7 ($CH_3$), 18.6 ($CH_3$), 25.7 ($CH_3$), 26.6 ($CH_2$), 40.1 ($CH_2$), 115.5 ($CH_2$), 123.9 (CH), 125.0 (CH), 125.6 (CH), 131.7 (C), 133.1 (CH), 139.7 (C), 142.5 (C).

## Acknowledgment

N.R. and S.S. have been funded by a doctoral fellowship from the Ministry of Research and Technology (MRT, France).

## References

(1) McDermott, J. X.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 947.
(2) Takeda, T.; Miura, I.; Horikawa, Y.; Fujiwara, T. *Tetrahedron Lett.* **1995**, *36*, 1495.
(3) Streiff, S.; Ribeiro, N.; Désaubry, L. *J. Org. Chem.* **2004**, *69*, 7592.
(4) Brintzinger, H.; Bercaw, J. E. *J. Am. Chem. Soc.* **1970**, *92*, 6182.
(5) Shu, R.; Harrod, J. F.; Lebuis, A. M. *Can. J. Chem.* **2002**, *80*, 489.