

## New Carbonyl Olefination Using Thioacetals

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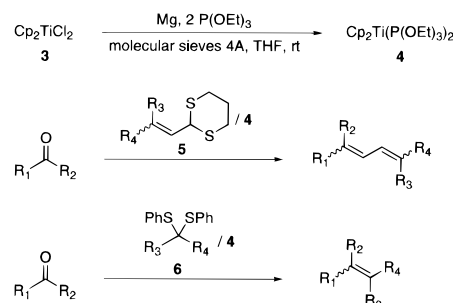
The discovery of active organometallic species presents a constant challenge to the chemists who desire to establish efficient methods for carbon–carbon bond formation. In this context, we have studied the desulfurative metalation of organosulfur compounds<sup>1</sup> and recently reported that vinylcyclopropanes were obtained by the reaction of unsaturated thioacetals **5** and their analogues 1,3-bis(phenylthio)alk-1-enes with titanocene–olefin complexes prepared by the treatment of titanocene dichloride (**3**) with alkylolithiums.<sup>2</sup> Although more work will be required before the reliable reaction path can be proposed, we tentatively assume that the vinylcarbene complex of titanium **1** is a likely intermediate of this reaction.



The titanium methylenide **2** is a well-known chemical species, and its reaction with carbonyl compounds is a useful synthetic tool for the Wittig-like methylenation of carbonyl compounds.<sup>3</sup> Three main preparative routes to **2** have been established using the Tebbe reagent derived from titanocene dichloride and trimethylaluminum,<sup>4</sup> Grubbs' titanacyclobutanes prepared by the reaction of Tebbe reagent with olefins,<sup>5</sup> and dimethyltitanocene.<sup>6</sup>

We expected that the vinylcarbene complexes **1** could react with carbonyl compounds to produce conjugated dienes. In order to effect this transformation, the use of olefin-free titanocene is required to avoid the formation of cyclopropane. The alkaline or alkaline-earth metal reduction of **3** is frequently employed for the preparation of low-valent titanium reagents.<sup>7</sup> Kool et al. first synthesized  $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$  by the reduction of **3** with magnesium<sup>8</sup> (Scheme 1). This low-valent titanium species has been recently employed for the reductive cyclization of enones<sup>9</sup> and seemed to be effective for the desulfurization of thioacetals **5**. However, we thought that the preparation of  $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$  was still problematic since it was too time-

## Scheme 1



consuming (16–20 h) and required an excess amount of expensive  $\text{PMe}_3$ . Then we investigated the preparation of low-valent titanium reagent using  $\text{P}(\text{OEt})_3$  as a ligand.<sup>10</sup> The treatment of **3** with excess magnesium turnings and  $\text{P}(\text{OEt})_3$  in THF for 12 h or more gave a black solution which contained the low-valent titanium species  $\text{Cp}_2\text{Ti}(\text{P}(\text{OEt})_3)_2$  (**4**). It was found, however, that this preparation was not completely reproducible; we sometimes observed no reaction after 2 days. On the basis of the assumption that a trace amount of water would retard the reduction, we examined the use of a drying agent as an additive and found that the reduction of **3** was completed within 3 h in the presence of powdered molecular sieves 4A (100 mg/1 mmol of **3**) using a small excess of magnesium (1.2 equiv) and  $\text{P}(\text{OEt})_3$  (2 equiv) in THF.

As was expected, the reduction of thioacetals **5** (1.1 equiv) with the low-valent titanium species **4** (3 equiv, THF, room temperature, 5 min) and the following treatment with ketones or aldehydes (room temperature, 30 min) produced 1,3-dienes (entries 1–6, Table 1). What is striking is that this reaction is not limited to unsaturated thioacetals **5**. The analogous desulfurative titanation of saturated thioacetals **6**, including the one prepared from ketone **6c**, followed by the treatment with the carbonyl compounds afforded the corresponding olefins in good yields (entries 9, 10, 13, 14, and 16). Methylenation also proceeded using bis(phenylthio)methane (**6d**) under the same reaction conditions although the yield was not satisfactory (entry 18). Furthermore, the present olefination could be successfully applied to carboxylic esters. After reduction of thioacetals with **4**, esters were added dropwise to the mixture and stirred at room temperature for 2 h to produce enol ethers, which could be isolated by chromatography on basic alumina (entries 7, 11, and 15). Lactones were also transformed to cyclic enol ethers in a similar manner (entries 8, 12, and 17). Unlike the olefination products of ketones and aldehydes, these enol ethers had predominantly Z-geometry.

The present reaction is also interesting from a mechanistic point of view. We found that the reaction of thioacetal **5d** with **4** (3 equiv) at room temperature for 5 min and then at 0 °C for 5 min followed by quenching with water at the same temperature gave a mixture of the structurally isomeric olefins **7** (**7a**:**7b** =

(10) The preparation of  $\text{Cp}_2\text{Ti}(\text{P}(\text{OME})_3)_2$  by condensing sodium atoms at  $-100$  °C into the THF solution containing **3** and excess  $\text{P}(\text{OME})_3$  was reported: Chang, M.; Timms, P. L.; King, R. B. *J. Organomet. Chem.* **1980**, *199*, C3.

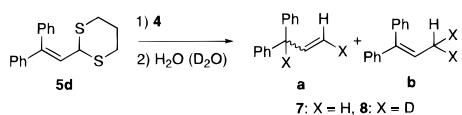
(11) The configurations of dienes, dienol ethers, and trisubstituted olefins were determined by NOE experiments. The stereochemistry of 2-benzylidene-2,3-dihydrobenzofuran (entry 12) was assigned by the comparison of its <sup>1</sup>H NMR spectrum with that of the authentic sample prepared by the method reported by Petasis and Bzowej (see ref 15a). As for the other enol ethers, the configurations were assigned on the basis of their <sup>13</sup>C-NMR chemical shifts of the carbon β to the alkoxy group: (a) Huet, J. *Tetrahedron* **1978**, *34*, 2473. (b) Strobel, M. P.; Andrieu, C. G.; Paquer, D.; Vazeux, M.; Pham, C. C. *Nouv. J. Chem.* **1980**, *4*, 101. (c) Huet, J. *Tetrahedron* **1981**, *37*, 731.

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**Table 1.** Olefination of Carbonyl Compounds

Entry	Thioacetal	Carbonyl Compound	Product	Yield(%) <sup>a</sup> (E : Z ratio) <sup>b</sup>
1				74 (60 : 40)
2	5a			77
3	5a			63 (56 : 44)
4				84 (79 : 21)
5				79 (47 : 53)
6	5c			88
7	5c			73 (23 : 77)
8	5c			64 (38 : 62)
9				80 (54 : 46)
10	6a			52 (56 : 44)
11 <sup>c</sup>	6a			61 (23 : 77)
12 <sup>c</sup>	6a			75 (<1 : >99)
13				69
14	6b			48 (69 : 31)
15 <sup>c</sup>	6b			75 (14 : 86)
16				63
17 <sup>c</sup>	6c			64
18				22

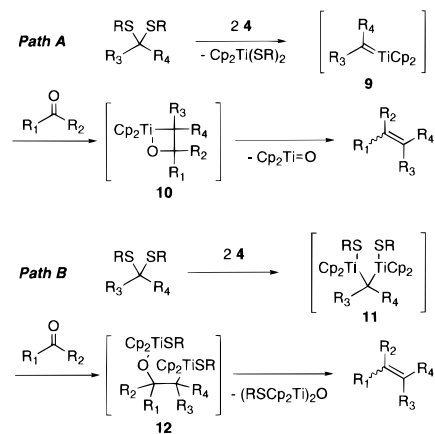
<sup>a</sup> Isolated yields based on the carbonyl compounds used. <sup>b</sup> Determined by <sup>1</sup>H- and <sup>13</sup>C-NMR spectroscopies. <sup>c</sup> 4 equiv of **4** was used.

**Scheme 2**

84 : 16) in 86% yield (Scheme 2). Furthermore, the dideterio compounds **8**<sup>12</sup> were obtained when the reaction was quenched with D<sub>2</sub>O.

On the basis of the above observation, the following two principal reaction pathways should be considered. The first one involves the carbene complex of titanium **9** as a key intermediate, which reacts with a carbonyl compound to form an olefin *via* the oxatitanacyclobutane **10** (path A, Scheme 3). An alternative mechanism involves the addition of *gem*-dimetallic species **11** to a carbonyl carbon. The adduct **12** then eliminates (RSCp<sub>2</sub>Ti)<sub>2</sub>O to produce an olefin (path B).

(12) The formation of **8a** took place with ca. 90% deuterium incorporation. Although the extent of deuterium incorporation was not determined, the formation of **8b** was confirmed by <sup>13</sup>C NMR spectroscopy.

**Scheme 3**

Olefination of carbonyl compounds is one of the most important processes for the construction of organic molecules. A variety of methods such as Wittig and related reactions using organophosphorous compounds,<sup>13</sup> Peterson olefination using organosilicon compounds,<sup>14</sup> and the olefination using the aforementioned titanium-based reagents<sup>15</sup> are employed for this transformation. The related olefinations using *gem*-dihaloalkane-Zn-TiCl<sub>4</sub><sup>16</sup> and *gem*-dihaloalkane-CrCl<sub>2</sub><sup>17</sup> systems were investigated by Utimoto, Takai, and their co-workers. Although a practical method for the transformation of ketones and aldehydes to *gem*-dibromides has been recently developed by us,<sup>18</sup> thioacetals seem to be superior to dihalides as olefination agents because they are more stable than *gem*-dihalides and a variety of congeners are easily prepared from carbonyl compounds. The present olefination also has advantages that the reaction is operationally simple and requires neither a strong base nor a pyrophoric reagent.

In conclusion it should be noted that the desulfurative titanation of thioacetals and the following treatment with carbonyl compounds constitute a useful method for the reductive olefination having a wide range of application.

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**Supporting Information Available:** Typical experimental procedures and characterization of all products in the paper (6 pages). See any current masthead page for ordering and Internet access instructions.

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