

# Titanocene(II)-promoted reaction of thioacetals with alkynes: highly stereoselective preparation of conjugated dienes

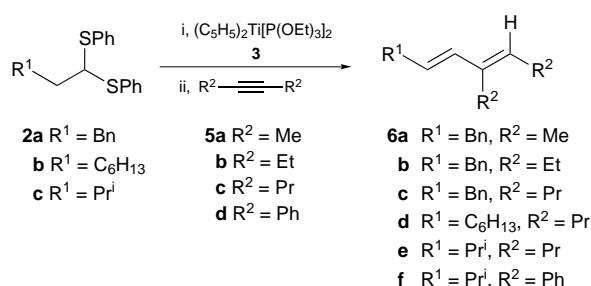
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The reaction of organotitanium species, prepared by the desulfurizative titaniation of thioacetals using  $(C_5H_5)_2Ti[P(OEt)_3]_2$ , with alkynes gives conjugated dienes in good yields with high stereoselectivity.

Titanacyclobutene **1** is a useful intermediate for the synthesis of homoallyl alcohols,<sup>1</sup>  $\beta,\gamma$ -unsaturated ketones,<sup>1,2</sup> conjugated dienes<sup>3</sup> and substituted pyridines.<sup>2</sup> The titanium species **1** is generally prepared by the reaction of Tebbe reagent  $[(C_5H_5)_2Ti-CH_2-AlMe_2Cl]$  or dimethyltitanocene with an alkyne,<sup>4,5</sup> which is believed to proceed *via* methylidenetitanocene. Recently we have shown that the treatment of  $\beta,\gamma$ -unsaturated thioacetals or their analogues with titanocene(II)-alkene complexes produces vinylcyclopropanes.<sup>6</sup> Olefination of a variety of carbonyl compounds also proceeds using the organotitanium species formed from thioacetals **2** and the alkene-free titanocene(II),  $(C_5H_5)_2Ti[P(OEt)_3]_2$  **3**.<sup>7</sup> Since we assumed that the intermediate of these reactions was alkylidenetitanocene **4**, we have also studied the formation of titanacyclobutene **1** by the treatment of the organotitanium intermediate **4** with an alkyne **5**.

It was found that the reaction of hydrocinnamaldehyde diphenyl thioacetal **2a** with **3** at room temperature for 3 h followed by treatment with oct-4-yne **5c** for 20 h gave 1-phenyl-4-propylocta-2,4-diene **6c** in 72% yield. The reaction proceeded with high stereoselectivity and the *2E,4E* isomer was produced with 99% selectivity (Scheme 1).<sup>†</sup> The use of higher reaction temperature reduced the reaction time (Table 1, entry 3).<sup>‡</sup> Similar reactions of several thioacetals **2** with alkynes **5** afforded the corresponding conjugated dienes **6** in good yields.



Scheme 1

Table 1 The reaction of thioacetals **2** with alkynes **5**

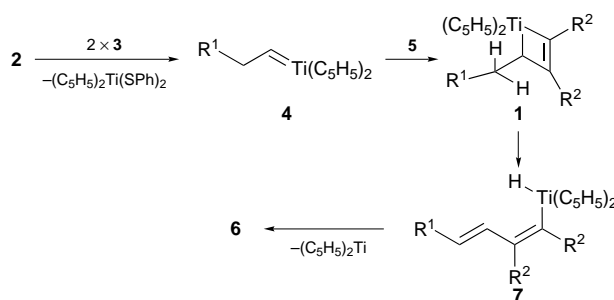
Entry	<b>2</b>	<b>5</b>	<b>6</b> (% yield) <sup>a</sup>	<i>E:Z</i> <sup>b</sup>
1 <sup>c</sup>	<b>2a</b>	<b>5a</b>	<b>6a</b> (72 <sup>d</sup> )	98:2
2	<b>2a</b>	<b>5b</b>	<b>6b</b> (71)	99:1
3	<b>2a</b>	<b>5c</b>	<b>6c</b> (80)	99:1
4	<b>2b</b>	<b>5c</b>	<b>6d</b> (72)	99:1
5	<b>2c</b>	<b>5c</b>	<b>6e</b> (76)	100:0
6	<b>2c</b>	<b>5d</b>	<b>6f</b> (50)	2:98

<sup>a</sup> Isolated yields based on quantity of **5** used. <sup>b</sup> The configuration of trisubstituted double bond. As for the disubstituted double bond, only the *E* isomers were produced. <sup>c</sup> The reaction was carried out using 1.2 equiv. of **5a**. <sup>d</sup> Isolated yield based on quantity of **2a** used.

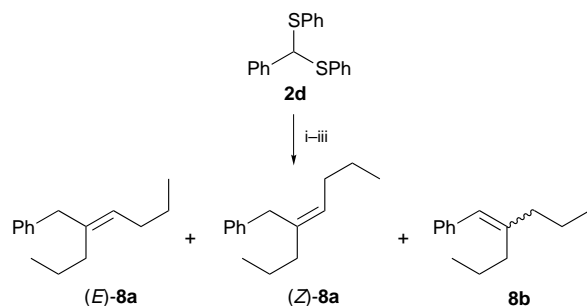
When an unsymmetrical alkyne was employed, the reaction proceeded with mixed regioselectivity. For example, 3-pentylundeca-2,4-diene and 7-methylpentadeca-6,8-diene were formed in 69% total yield by the reaction of oct-2-yne with **2b** carried out at room temperature for 20 h. The ratio of the two regioisomers was found to be 57:43, respectively.

The stereoselective formation of conjugated dienes **6** is explained by the reaction pathway depicted in Scheme 2. As would be expected, the reaction of alkylidenetitanocene **4**, formed by the desulfurizative titaniation of thioacetal **2**, with an alkyne **5** produces the titanacyclobutene intermediate **1**. Then  $\beta$ -hydride elimination proceeds to afford the vinyltitanium species **7**. Subsequent reductive elimination gives the diene **6** with retention of configuration of the trisubstituted double bond. This reaction pathway was substantiated by the fact that the reaction of benzaldehyde diphenyl thioacetal **2d** with **5c** gave the structurally isomeric alkenes **8a** and **8b** [*E*-**8a**: (*Z*)-**8a**: **8b** = 81:1:18] in 58% yield (Scheme 3). It is reasonable to assume that these alkenes are formed by protonation of the intermediate titanacyclobutene **1**.

Preparation of higher homologues of methylidenetitanocene *via* titanium-aluminium metallacycles was not successful, owing to decomposition by  $\beta$ -hydride elimination.<sup>8</sup> Although it has been suggested that the alkylidenetitanocenes are produced by thermolysis of dibenzyl-,<sup>9</sup> bis[(trimethylsilyl)methyl]-,<sup>10</sup> dicyclopropyl-,<sup>11</sup> dialkenyl-<sup>5b,d</sup> and alkylalkenyl-titanocene,<sup>5d,12</sup> the formation of simple alkylidene complexes from dialkyltitanocene is improbable because of the preferential formation of titanocene(II)-alkene complexes.<sup>13</sup> The present



Scheme 2



Scheme 3 Reagents and conditions: i, **3**, room temp., 10 min; ii, **5c**, room temp., 20 h; iii, 1 M NaOH

work is the first example of formation of titanacyclobutene **1** from an alkylidenetitanocene possessing a  $\beta$ -hydrogen bonded to an  $sp^3$  carbon atom and shows that **1** thus formed easily decomposes by  $\beta$ -hydride elimination. In conclusion, the titanocene-promoted reaction of thioacetals with alkynes is an excellent method for the stereoselective preparation of conjugated dienes. Further aspects of this reaction will be reported in due course.

#### Footnotes

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† The configuration of **6** was determined by a NOE experiment.

‡ *Typical experimental procedure:* to a flask charged with finely powdered molecular sieves 4 Å (150 mg), magnesium turnings (1.8 mmol) and titanocene dichloride (1.5 mmol) were added THF (4 ml) and triethyl phosphite (3 mmol) successively with stirring. After 3 h, a THF (2 ml) solution of **2** (0.6 mmol) was added and stirring was continued for 10 min. Then **5** (0.5 mmol) in THF (1 ml) was added dropwise over 15 min. After being refluxed for 3 h, the reaction was quenched with 1 M NaOH, and the insoluble materials were filtered off through Celite. The organic materials were extracted with diethyl ether, dried ( $Na_2SO_4$ ) and concentrated. Purification was accomplished by PTLT providing **6** as a clear, colourless oil.

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Received in Cambridge, UK, 20th March 1997; Com. 7/01952A