

Formation of conjugated dienes by the reaction of titanocene alkenylidene complexes with alkynes

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Abstract—Titanocene alkenylidene complexes, generated by the reductive metallation of 1,1-dichloro-1-alkenes with the titanocene(II) species $\text{Cp}_2\text{Ti}[\text{P}(\text{OEt})_3]_2$, reacted with alkynes to produce conjugated dienes.

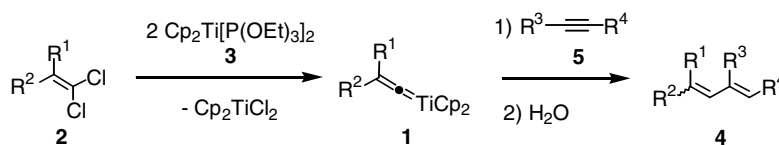
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Various alkenylidene complexes of transition metals are prepared and their reactivities have been well investigated.¹ Concerning the preparation of titanocene alkenylidene complexes, several methods such as the carbotitanation of 1-alkynyl dimethylalanes with $\text{Cp}_2\text{TiCl}_2\text{-AlMe}_3$,² metathesis between titanocene methylenide and allenes,³ and thermolysis of dialkenyltitanocenes⁴ have been reported. These preparations, however, suffer serious limitation on the availability of starting materials. Nonetheless, titanocene alkenylidene complexes thus formed are useful for organic synthesis because they exhibit unique reactivity to multiple bonds.

Recently we found that titanocene alkenylidene complexes **1** are readily prepared by the reductive titaniation of 1,1-dichloro-1-alkenes **2** with $\text{Cp}_2\text{Ti}[\text{P}(\text{OEt})_3]_2$ **3**. These active species were successfully employed for olefination of ketones and aldehydes to afford a variety of allenes and vinylallenes.⁵ Our new procedure is advantageous over the above conventional methods in that the

precursors of the carbene complexes, *gem*-dichlorides **2**, are readily available by the dichloromethylenation of aldehydes and ketones.⁶ We anticipated that these organotitanium species were reactive towards organic molecules having a multiple bond as well as carbonyls similarly to titanocene-alkylidene complexes.⁷

Beckhaus et al. reported that the titanocene vinylidene complex $\text{Cp}_2^*\text{Ti}=\text{C}=\text{CH}_2$, prepared by ethylene or methane elimination from methylenetitanacyclobutane and methylvinyltitanocene, respectively, reacts with alkynes to form methylenetitanacyclobutenes.⁸ Although Hawkins and Grubbs reported the stereochemical outcome of the formation of alkylidenetitanacyclobutenes by the reaction of a certain unsymmetrically substituted alkenylidene complex with 3-hexyne,⁹ the reaction of higher homologues of titanocene vinylidene complexes with alkynes has not been fully studied yet. We found that the reaction of alkenylidene complexes **1**, prepared from *gem*-dichlorides **2**, with alkynes **5** gave conjugated dienes **4** (Scheme 1).



Scheme 1.

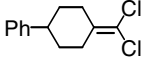
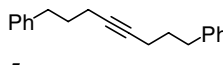
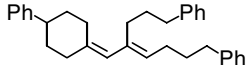
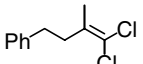
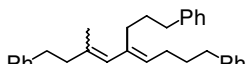
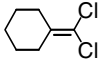
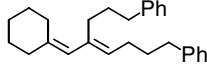
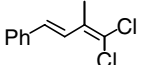
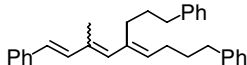
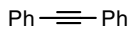
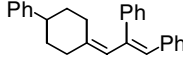
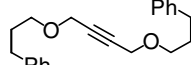
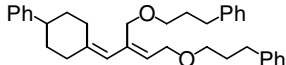
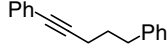
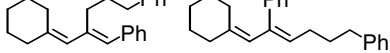
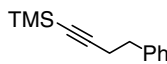
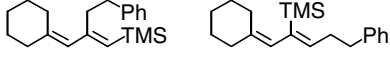
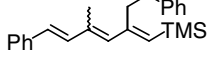
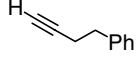
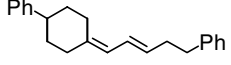
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The organotitanium species **1**, prepared by the reaction of 1-(dichloromethylidene)-4-phenylcyclohexane **2a** (2 equiv) with the titanocene(II) reagent **3** (5 equiv) for 3 h, was treated with 1,8-diphenyl-4-octyne **5a** to afford the conjugated diene **4a** in 68% yield after aqueous

work-up (Table 1, entry 1). Similarly various conjugated dienes were obtained by the reaction of dichlorides **2** with alkynes **5**. Although the formation of the double bond originated from alkyne was highly stereoselective,¹⁰ no stereoselectivity was observed in the formation

Table 1. Preparation of conjugated dienes **5**^a

| Entry | Dichloride 2 | Alkyne 5 | Conjugated diene 4 (yield/%) ^b |
|-----------------|--|--|--|
| 1 |  2a |  5a |  4a (68) |
| 2 |  2b | 5a |  4b (69, 54:46 ^c) |
| 3 |  2c | 5a |  4c (55) |
| 4 |  2d | 5a |  4d (85, 53:47 ^c) |
| 5 ^d | 2a |  5b |  4e (77, 99:1 ^c) |
| 6 | 2a |  5c |  4f (70) |
| 7 | 2c |  5d |  4g (55, 85:15 ^c) |
| 8 ^d | 2c | 5d | 4g (64, 85:15 ^c) |
| 9 | 2c |  5e |  4h (51, 78:22 ^c) |
| 10 ^d | 2c | 5e | 4h (51, 100:0 ^c) |
| 11 ^d | 2d | 5e |  4i (63, 51:49 ^c) |
| 12 | 2a |  5f |  4j (35) |

^a All the reactions were performed with a similar procedure as described in the text using 2 equiv of **2** and 5 equiv of **3**, unless otherwise noted.

^b Based on **5**.

^c Ratio of stereoisomers.

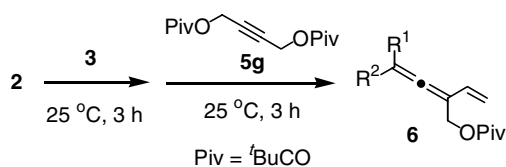
^d Carried out under reflux for 3 h.

^e Ratio of regioisomers.

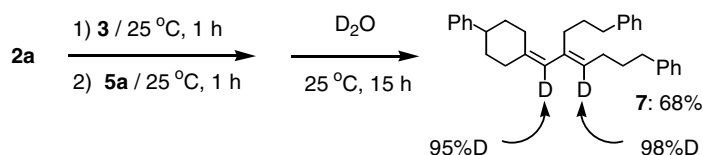
of another double bond. The conjugated triene **4d** is also obtained in good yield by using the 1,1-dichloro-1,3-alkadiene **2d** (entry 4). The reactions of unsymmetrical alkynes **5d** and **5e** at 25 °C ended up with the formation of mixtures of two regioisomers (entries 7 and 9). It is of interest that the conjugated diene **4h** was obtained as a single regioisomer when the reaction of **2c** with **5e** was carried out under reflux in THF (see entries 9 and 10). The regioselective formation of triene **4i** was also observed in the reaction of **2d** with **5e** at higher temperature. The reaction of terminal alkyne **5f** proceeded regioselectively to give the diene **4j**, which is in sharp contrast with the reaction of titanocene vinylidene complex with terminal alkynes that afford alkynylvinyl-titanocenes selectively.⁹

The typical experimental procedure is as follows: finely powdered molecular sieves 4 A (150 mg), magnesium turnings (37 mg, 1.5 mmol) and Cp₂TiCl₂ (374 mg, 1.5 mmol) were placed in a flask and dried by heating with a heat gun under reduced pressure (2–3 mmHg). After cooling, THF (3 mL) and P(OEt)₃ (0.51 mL, 3.0 mmol) were added successively with stirring at 25 °C under argon. After 3 h, **2a** (145 mg, 0.6 mmol) in THF (1 mL) was added to the mixture, and stirring was continued for 3 h. A THF (1 mL) solution of **5a** (79 mg, 0.3 mmol) was added, and the mixture was further stirred for 16 h. The reaction was quenched by addition of 1 M NaOH, and the insoluble materials were filtered off through Celite and washed with ether. The layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by TLC (hexane) to afford **4a** (89 mg, 68%).

In the case of the reaction of 1,4-dipivaloyloxy-2-butyne **5g** with the dichlorides **2**, not the dienes **4** but the vinylallenes **6** were produced (Scheme 2 and Table 2). The results indicate that the process involves the elimination of pivaloyloxy group from certain organotitanium intermediate formed from the carbene complex **1** and alkyne **5**.



Scheme 2.



Scheme 3.

Table 2. Preparation of vinylallenes **6**^a

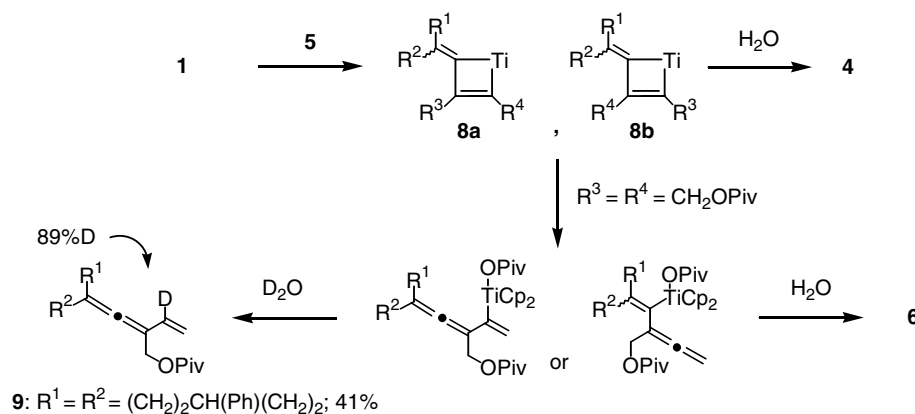
| Entry | Dichloride 2 | Vinylallene 6 | Yield/% ^b |
|-------|---------------------|----------------------|----------------------|
| 1 | 2a | 6a | 59 |
| 2 | 2b | 6b | 64 |
| 3 | 2e | 6c | 63 |
| 4 | 2f | 6d | 59 |

^a All the reactions were performed using 2 equiv of **5g** and 5 equiv of **3**.

^b Based on **5g**.

In order to elucidate the reaction pathway, the deuteration of organotitanium intermediate was performed. After successive treatments of **2a** with **3** and **5a** at 25 °C, the reaction was quenched with D₂O (Scheme 3). The formation of dideuterated diene **7** indicates that the present reaction proceeds via the alkylidenetitanacyclobutene **8** as shown in Scheme 4. The conjugated diene **4** is produced by hydrolysis of the intermediate **8**. Since the 2-deuterio-1,3,4-triene **9** was isolated when the reaction of **2a** with **5g** was quenched with D₂O, the formation of vinylallene **6** is also rationalized by the elimination of a pivaloyloxy group from the titanacycle **8** followed by protonation. The fact that only the sterically preferred regioisomer of **4h** was produced by the reaction carried out at elevated temperature implies that the two regioisomers of titanacycle **8a** and **8b** may be equilibrated with dissociation to the vinylidene complex **1** and alkyne **5** at higher temperature. This is in contrast with the fact that the formation of alkyl groups substituted alkylidenetitanacyclobutene from 3-hexyne is irreversible.⁹

In conclusion, we have demonstrated that the titanocene alkenylidene complexes generated by the reductive metalation of 1,1-dichloro-1-alkenes with the titanocene(II) reagent react with alkynes to form 4-alkylidenetitanacyclobutenes, which afford conjugated dienes on hydrolysis. Further study on the reactions of these carbene complexes with organic molecules having a multiple bond is now in progress.



Scheme 4.

Acknowledgement

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References and notes

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- The configuration of double bond derived from acetylene in **4a–i** was confirmed by NOE experiment. The coupling constant of vinyl protons of **4j** (15 Hz) suggests that its configuration is *E*.