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Chemoselective Phosphination of Titanacyclobutene: A Convenient Method for Synthesis of Allylphosphine Derivatives

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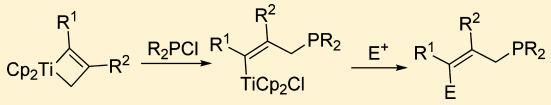
Supporting Information

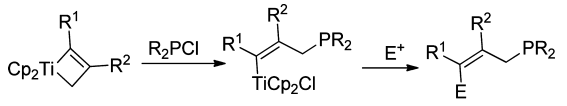
ABSTRACT: Titanacyclobutenes reacted with chlorophosphine to afford titanoallylphosphines with high chemoselectivity, and the resulting titanoallylphosphine could be converted into functionalized allylphosphine sulfides via reactions with various electrophiles.



Allylphosphine and its derivatives are an important class of organic compounds that are widely employed both as ligands in transition-metal complexes and as substrates in various organic synthesis processes.[1,2] Conventionally, protocols for the preparation of allylphosphines included the reactions of chlorophosphine and allyl Grignard reagents or allyl chlorides and lithium diphenylphosphanide[3] and other related methods.[4] Other ways to prepare allylphosphines are by Michaelis–Arbuzov and Pudovik rearrangements.[5] Nonetheless, it is often difficult to prepare substituted allylphosphines by these methods. Consequently, the development of a versatile and general method for the preparation of functionalized allylphosphines is a necessity. Titanacyclobutenes which can be easily prepared by the reaction of alkyne and Cp_2TiMe_2[6] have two markedly different sites of reaction in the sp^2- and sp^3-hybridized titanocene–carbon bonds with an allyl skeleton. Reactions occurring selectively at either site and at both sites have been reported.[7] Among them, the groups of Knobler' and Harlow have reported the reaction of titanacyclobutenes with $PhPCl_2$ or $PhAsCl_2$ to afford phosphacyclobutenes or arsacyclobutenes.[7b,c] In these cases, both sp^2 carbon–titanocene and sp^3 carbon–titanocene bonds reacted with two P–Cl or As–Cl moieties. It is interesting to compare the reactivities of sp^2 carbon–titanocene and sp^3 carbon–titanocene bonds in titanacyclobutene toward the P–Cl moiety, which potentially affords acyclic monophosphine reagents. Herein, we report the reaction of titanacyclobutenes with a chlorophosphine (R_2PCl) that has one P–Cl moiety. The reaction occurred at the sp^3 carbon–titanocene bond, which provides a novel preparative method for the preparation of allylphosphine derivatives (Scheme 1). Furthermore, the resulting intermediate **2** can be converted into other functionalized allylphosphines via reaction with electrophiles.

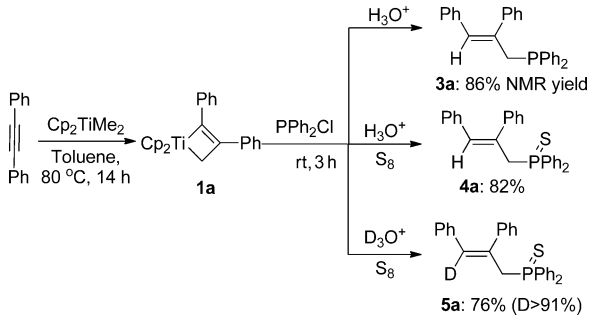
A typical procedure is as follows. To a toluene solution of titanacyclobutene **1a** (3 mL), prepared from Cp_2TiCl_2 (150 mg, 0.6 mmol), MeLi (3 M in diethoxymethane solution, 0.4 mL, 1.2 mmol), and diphenylacetylene (107 mg, 0.6 mmol) in the dark (wrapped in aluminum foil) according to the reported procedure,[6d] was added 1 equiv of diphenylchlorophosphine at 0 °C. Then the reaction mixture was warmed to room temperature and stirred at the same temperature for 3 h. The reaction mixture was quenched with 3 M HCl, and allylphosphine **3a** was obtained in 86% NMR yield. Purification of **3a** directly by column chromatography led to the formation of a complex inseparable mixture. Since the trivalent phosphine **3a** was sensitive to oxygen, the product of **3a** was isolated as phosphine sulfide **4a** in 82% isolated yield after treatment of the reaction mixture with elemental sulfur. Deuteriolysis of the reaction mixture instead of hydrolysis afforded the deuterated compound 3-deuterio-2,3-diphenylallylphosphine sulfide (**5a**) in 76% isolated yield with 91% deuterium incorporation (Scheme 2). This result showed that the product of the reaction of titanacyclobutene with chlorodiphenylphosphine before hydrolysis contains one titanocene–sp^2 carbon bond.

Scheme 1



1 **2**

Scheme 2



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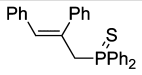
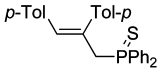
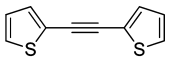
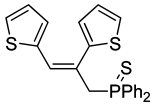
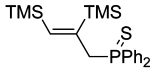
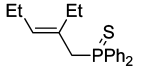
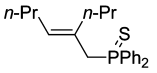
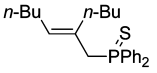
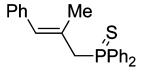
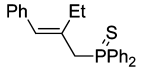
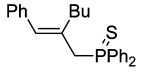
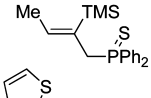
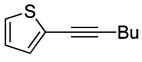
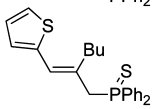
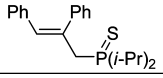
The result also indicates that the reaction shows good selectivity for phosphination of titanacyclobutene.

Further study involving the use of various substituted titanacyclobutenes bearing alkyl, aryl, and TMS groups resulted in all cases in the formation of allylphosphines in good yields. Representative results are summarized in Table 1. The

Table 1. $CpTiMe_2$-Mediated Reaction of Alkynes with Chlorophosphines Leading to Formation of Allylphosphine Derivatives

Entry	alkyne	Product		Yield (%)[a]
1	Ph—≡—Ph		**(4a)**	82
2	*p*-Tol—≡—Tol-*p*		**(4b)**	78
3			**(4c)**	69
4	TMS—≡—TMS		**(4d)**	55
5	Et—≡—Et		**(4e)**	54
6	*n*-Pr—≡—*n*-Pr		**(4f)**	58
7	*n*-Bu—≡—*n*-Bu		**(4g)**	47
8	Ph—≡—Me		**(4h)**	57[b]
9	Ph—≡—Et		**(4i)**	62[b]
10	Ph—≡—Bu		**(4j)**	68[b]
11	TMS—≡—Me		**(4k)**	42[c]
12			**(4l)**	66[c]
13[d]	Ph—≡—Ph		**(4m)**	48

[a]Isolated yield. [b]A 3:1 mixture of two regioisomers; major isomer is shown. [c]A 4:1 mixture of two regioisomers; major isomer is shown. [d]$ClP(i\text{-}Pr)_2$ was used, and the reaction was carried out at 80 °C for 8 h.

titanacyclobutenes prepared from symmetrical alkynes afforded single allylphosphine sulfide products (entries 1−7). Aryl-substituted titanacyclobutenes afforded the desired products in excellent yields (entries 1−3). A single-crystal X-ray analysis of **4b** verified the formation of allylphosphine, as shown in Figure 1. When a thienyl-substituted titanacyclobutene was used, allylphosphine sulfide **4c** was obtained in good yield (entry 3). Reaction of a trimethylsilyl-substituted titanacyclobutene with chlorodiphenylphosphine also afforded the desired product **4d**

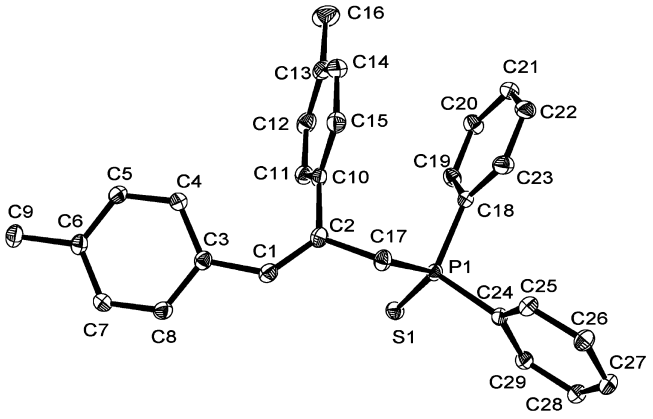
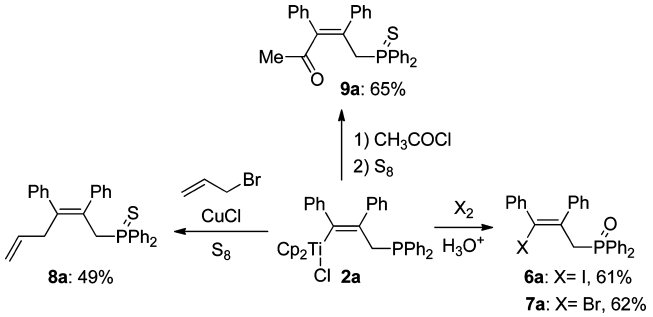


Figure 1. ORTEP drawing of **4b** with 30% probability thermal ellipsoids. Hydrogen atoms are omitted for clarity.

in 55% yield (entry 4). Alkyl-substituted titanacyclobutenes afforded the desired products in moderate yields (entries 5−7). The titanacyclobutenes prepared from unsymmetrical alkynes gave allylphosphine sulfides as a mixture (entries 8−12). When PhC≡CMe, PhC≡CEt, and PhC≡CBu were used (entries 8−10), respectively, two isomers were obtained in a 3:1 ratio on the basis of NMR analysis. When TMSC≡CMe and ThC≡CBu were used, the ratio of two isomers was 4:1, respectively (entries 11 and 12). It should be noted that when chlorodiisopropylphosphine was used instead of chlorodiphenylphosphine, the reaction also proceeded smoothly and the product was obtained in 48% yield at 80 °C for 8 h (entry 13). In all the above reactions, we did not observe any alkenylphosphorus compounds. Therefore, it is interesting to compare the reactivities of Ti−C(sp^3) and Ti−C(sp^2) bonds in titanacyclobutenes toward the P−Cl moiety.

The remaining Ti−C(sp^2) bond of titanoallylphosphine **2** was further treated with electrophiles to give functionalized allylphosphine derivatives (Scheme 3). Treatment of **2a** with

Scheme 3



iodine and bromine gave the iodo- and bromoallylphosphine oxides **6a** and **7a** in 61% and 62% yields after hydrolysis, respectively. The reaction of **2a** with allylic bromide in the presence of CuCl gave the corresponding cross-coupling product **8a** in 49% yield. When acetyl chloride was added directly to a solution of **2a** in situ, product **9a** was obtained in 65% isolated yield.

In summary, we have developed a novel reaction for the direct preparation of substituted metalloallylphosphines via the highly chemoselective phosphination of titanacyclobutene. The resulting titanoallylphosphines could be converted into various functionalized allylphosphine derivatives.

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■ ASSOCIATED CONTENT

Supporting Information

Text, figures, and a CIF file giving experimental details and characterization data for all compounds and crystallographic data for **4b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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