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Preparation of alkynylcyclopropanes by the titanocene(II)-promoted reaction of 1,1-bis(phenylthio)-2-alkynes with 1-alkenes

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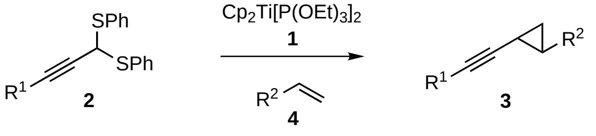
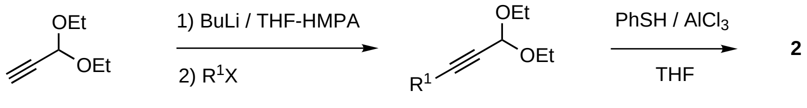
Abstract—The desulfurization of 1,1-bis(phenylthio)-2-alkynes with the titanocene(II) species $Cp_2Ti[P(OEt)_3]_2$ in the presence of 1-alkenes produced 1-alkyn-1-ylcyclopropanes in good yields. © 2002 Elsevier Science Ltd. All rights reserved.

Vinylcyclopropanes are useful synthetic intermediates and are easily transformed into cyclopentenes or dienes by thermal-, transition-metal catalyzed-, or photo-isomerization.[1] Therefore, synthetic routes to these compounds have been extensively studied. Their counterparts, alkynylcyclopropanes, are of interest as synthetic intermediates[2] and are found in structures of certain biologically active substances.[3] However, their synthetic utility is largely restricted because of the difficulty in preparing these compounds. Although several reports on the synthesis of alkynylcyclopropanols[4] and alkynylcyclopropanes possessing an additional alkenyl[5] or alkynyl[6] substituent have appeared, only a limited number of methods for the preparation of unfunctionalized alkynylcyclopropanes have been reported. For example, cyclopropylacetylene is prepared from cyclopropyl methyl ketone via the formation of the corresponding *gem*-dichloride.[7] The cyclopropanation of pent-3-en-1-yne with diazomethane gives the corresponding alkynylcyclopropane.[8] The yields of these reactions, however, were not satisfactory for synthetic purposes. Synthesis of various alkynylcyclopropanes by the thermal reaction of tetrachlorocyclopropene with 1-alkenes and the successive treatment of the resulting 1-chloro-1-(trichlorovinyl)cyclopropanes with butyllithium and electrophiles was studied by de Meijere and coworkers.[9]



Scheme 1.

During the course of our study on the desulfurization of organosulfur compounds with titanocene(II) species,[10] we found that alkenylcyclopropanes were produced by treatment of thioacetals of α,β-unsaturated aldehydes or 1,3-bis(phenylthio)-1-alkenes with the low-valent titanium species $Cp_2Ti[P(OEt)_3]_2$ **1** in the presence of 1-alkenes.[11] The organotitanium species formed in the above reaction is assumed to be vinylcarbene complexes of titanium. We further studied the preparation of analogous alkynylcarbene complexes from 1,1-bis(phenylthio)-2-alkynes **2**. In this communication, we describe a facile method for the preparation of alkynylcyclopropanes **3** by the titanocene(II) **1**-promoted reaction of **2** with terminal olefins **4** (Scheme 1).



Scheme 2.

Keywords: cyclopropanation; olefins; organosulfur compounds; titanocene(II).

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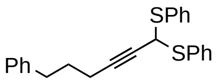
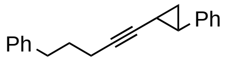
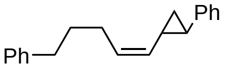
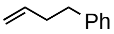
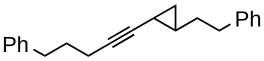
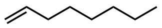
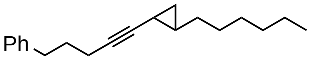
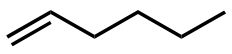
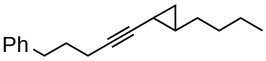
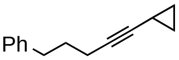
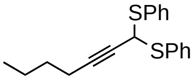
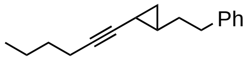
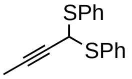
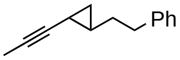
The starting materials **2** were prepared by the reaction of the lithium salt of propiolaldehyde diethyl acetal (BuLi; 1.1 equiv./THF-HMPA/−78°C/0.7–1.5 h) with appropriate alkylating agents (1.1 equiv.) (−78°C–room temperature/overnight, $Ph(CH_2)_3Br$; 87%, CH_3-$(CH_2)_3OTs$; 76%, CH_3I; 71%) and the treatment of

Table 1. Preparation of alkynylcyclopropanes[a]

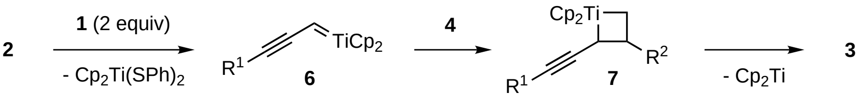
Entry	2	4 (equiv)	Temp / °C	Time / h	Product 3 (Yield / %; Ratio of stereoisomers[b])
1[c]	 **2a**	 **4a** (2)	0	3	 **3a** (27; >99 : 1)  **5** (16; >99 : 1)
2[c]	**2a**	**4a** (4)	25	2	**3a** (54; >99 : 1)
3	**2a**	**4a** (4)	25	3.5	**3a** (65; >99 : 1)
4	**2a**	 **4b**(8)	25	3.5	 **3b** (59; 68 : 32)
5	**2a**	 **4c** (8)	25	3.5	 **3c** (58; 63 : 42)
6	**2a**	 **4d** (8)	25	3.5	 **3d** (65; 60 : 40)
7[d]	**2a**	 **4e**	25 / reflux	3 / 0.5	 **3e** (56)
8	 **2b**	**4a** (4)	25	3.5	 **3f** (73; >99 : 1)
9[c]	**2b**	**4b** (8)	25	3.5	 **3g** (65; 60 : 40)
10	**2b**	**4b** (8)	25	3.5	**3g** (77; 57 : 43)
11[c]	 **2c**	**4b** (8)	25	3.5	 **3h** (58; 57 : 43)
12	**2c**	**4b** (8)	25	3.5	**3h** (70; 56 : 44)

[a] All reactions were performed by a similar procedure as described in the text, unless otherwise noted.

[b] Determined by NMR analysis.

[c] Carried out in the absence of additional triethyl phosphite.

[d] The titanocene(II) species prepared in the presence of an equimolar amount of triethyl phosphite under ethylene was used.



Scheme 3.

the alkylated acetals with thiophenol (2.2 equiv.) in the presence of aluminum chloride (2.2 equiv.) (THF/0°C–room temperature/2 days, **2a**; 70%, **2b**; 72%, **2c**; 97%) (Scheme 2). When the thioacetal **2a** was treated with the low-valent titanium reagent **1** (2 equiv.) in the presence of styrene (**4a**) (2 equiv.) at 0°C for 3 h, the alkynylcyclopropane **3a** was produced in 27% yield (Table 1, entry 1). The major byproduct isolated was the *cis*-alkenylcyclopropane **5**, which would be produced by the further reduction of **3a** with **1** via the formation of titanacyclopropene.[12] The formation of **5** was absolutely suppressed and **3a** was obtained in 54% yield by use of higher reaction temperature (entry 2). It was found that the yield of **3a** was increased when the reaction was carried out in the presence of additional 4 equiv. of triethyl phosphite (entry 3).

In a similar manner, the reactions of several unsaturated thioacetals **2** with terminal olefins **4** were performed, and the alkynylcyclopropanes **3** were produced in good yields using excess triethyl phosphite (see entries 9, 10, 11, and 12). The cyclopropanes **3** were obtained as single isomers by the reactions using styrene,[13] whereas mixtures of stereoisomers were produced in all the other cases examined. The alkynylcyclopropane **3e** possessing no substituent on the cyclopropane ring was produced only in poor yield under the reaction conditions described above. However, **3e** was obtained in moderate yield when the reaction was carried out at 25°C and then at reflux using the titanocene(II) reagent prepared by the reduction of titanocene dichloride with magnesium in the presence of an equimolar amount of triethyl phosphite under ethylene (entry 7).

The typical experimental procedure is as follows: Magnesium turnings (24 mg, 1 mmol; purchased from Nacalai Tesque Inc. Kyoto, Japan) and finely powdered molecular sieves 4 Å (100 mg) were placed in a flask and dried by heating with a heat gun under reduced pressure (2–3 mmHg). After the mixture was stirred for 15 h under argon at room temperature, Cp_2TiCl_2 (249 mg, 1 mmol) was added to the mixture and dried by heating under reduced pressure. After cooling, THF (2 ml), $P(OEt)_3$ (0.69 ml, 4 mmol), and **4a** (0.23 ml, 2 mmol) were added successively with stirring at 25°C under argon. After 3 h, **2a** (187 mg, 0.5 mmol) in THF (1.5 ml) was added to the mixture, and stirring was continued for 3.5 h. The reaction was quenched by addition of 1 M NaOH (10 ml), and the resulting insoluble materials were filtered off through Celite and washed with ether (10 ml). The organic materials were extracted with ether (3×30 ml), and the extract was dried (Na_2SO_4). After removal of the solvent, the residue was purified by PTLC (hexane:AcOEt = 98:2) to give **3a** (85 mg, 65%).

Although we have no corroborating evidence for the reaction pathway, we tentatively assume that the present reaction proceeds via the initial formation of an unprecedented alkynylcarbene complex of titanium **6** by the desulfurization of the thioacetal **2** with the titanocene(II) species. The cyclopropane **3** would be produced by the formation of titanacyclobutane **7** with terminal olefin and the subsequent reductive elimination (Scheme 3).

Since the starting materials **2** are readily available, this reaction provides a practical way for the synthesis of different alkynylcyclopropanes. Further study on the reaction of titanium–alkynylcarbene complexes is currently underway.

Acknowledgements

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13. Since an NOE between the propargyl proton in the cyclopropane and the orth proton on the benzene ring was observed, the configuration of **3a** was assumed to be *trans*.