Pergamon

Tetrahedron Letters 39 (1998) 2153–2156

TETRAHEDRON
LETTERS

# New Methods for the Preparation of 1-Alkenyl Ethers and Sulfides Using Di- and Tri-thioorthoformates

Md. Abdur RAHIM, Haruhiko TAGUCHI, Mikako WATANABE, Tooru FUJIWARA, and Takeshi TAKEDA*

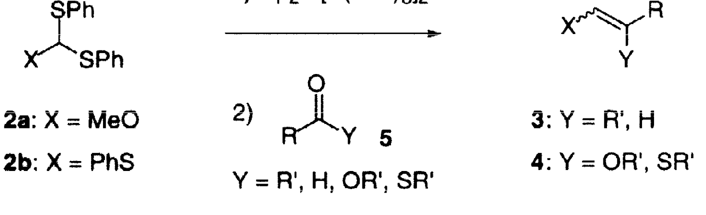
Department of Applied Chemistry, Tokyo University of Agriculture and Technology,
Koganei, Tokyo 184, Japan

Received 10 December 1997; revised 5 January 1998; accepted 6 January 1998

***Abstract:*** The treatment of carbonyl compounds with the organotitanium species formed from methoxybis(phenylthio)methane and low valent titanium species $Cp_2Ti[P(OEt)_3]_2$ gave 1-alkenyl ethers in good yields. 1-Alkenyl sulfides were also obtained by the similar reaction using triphenyl trithioorthoformate. These reactions were successfully applied to carboxylic esters and thiolesters to produce 1,2-diheteroatom substituted 1-olefins.

Since olefination of carbonyl compounds is one of the most important transformations in organic synthesis, various methods are used for this transformation; such as the Wittig reaction using organophosphorous compounds,[1] the Peterson olefination using organosilicon compounds,[2] and alkylidenation using titanium-based reagents.[3] The olefination of carboxylic acid derivatives using the former two methods is generally unsuccessful owing to the preferential formation of acylated products. Therefore the preparations of alkenyl ethers and sulfides have been achieved only by using alkoxymethylene triphenylphosphoranes,[4] methoxy(trimethylsilyl)methyllithium,[5] or their sulfur analogues[4,6] as active intermediates. On the other hand, the alkylidenation of carboxylic acid derivatives using titanium reagents has been developed[3] though the olefination of carbonyl compound with the heteroatom substituted titanium reagent has not yet appeared.

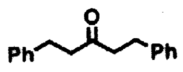
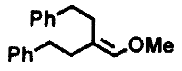
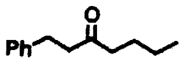
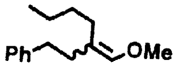
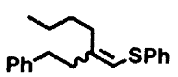
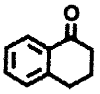
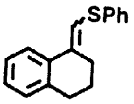
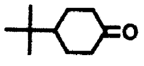
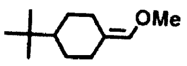
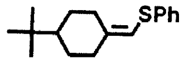
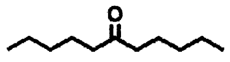
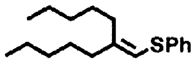
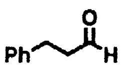
Recently we reported a useful method of carbonyl olefination using thioacetals and titanocene(II) compound $Cp_2Ti[P(OEt)_3]_2$ (**1**).[7] The most striking characteristic of this procedure is that it is capable of being employed for the olefination of carboxylic acid derivatives. This result prompted us to study the desulfurization of di- and tri-thioorthoformates **2a and b** with **1** and the reactions of the resulting organotitanium species with carbonyl compounds (Eq. 1). These reactions provide 1-alkenyl ethers and sulfides **3** and also 1,2-diheteroatom substituted olefins **4** which would not be accessible by the conventional carbonyl olefination procedures.



(1)

*PII:* S0040-4039(98)00083-5

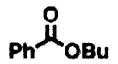
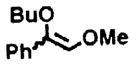
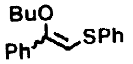
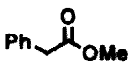
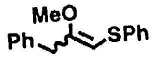
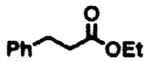
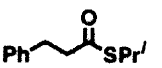
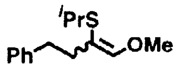
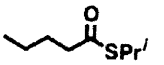
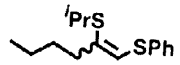
Table 1. Preparation of Alkenyl Ethers and Sulfides 3[a]

| Run | Carbonyl Compound | | Thioorthoformate (equiv) | Time (h) | Product | | Ratio of Stereoisomers[b] | Yield (%) |
|---|---|---|---|---|---|---|---|---|
| 1 |  | **5a** | **2a** (1.5) | 3 |  | **3a** | - | 63 |
| 2 |  | **5b** | **2a** (1.5) | 3 |  | **3b** | 54 : 46 | 64 |
| 3 |  | **5c** | **2a** (1.5) | 3 |  | **3c** | 52 : 48 | 65 |
| 4 | **5c** | | **2b** (1.2) | 2.5 |  | **3d** | 51 : 49 | 65 |
| 5 |  | **5d** | **2b** (1.2) | 2 |  | **3e** | 58 : 42[c] | 78 |
| 6 |  | **5e** | **2a** (1.5) | 3 |  | **3f** | - | 62 |
| 7 | **5e** | | **2b** (1.2) | 1.5 |  | **3g** | - | 76 |
| 8 |  | **5f** | **2b** (1.2) | 2 |  | **3h** | - | 74 |
| 9 |  | **5g** | **2b** (1.2) | 2 |  | **3i** | 55 : 45[d] | 42 |

a) All the reactions were carried out at room temperature. b) Determined by NMR analysis. c) *E* : *Z* determined by NOE experiment. d) *E* : *Z* determined on the basis of coupling constant of vinyl proton.

A small excess amount (1.2 equiv) of triphenyl trithioorthoformate (**2b**) was treated with the low valent titanium **1**, and the progress of the reaction was monitored by TLC. After 10 min, the disappearance of **2b** was observed with a slight change of color of the reaction mixture. The treatment of various ketones with the resulting organotitanium reagent produced the corresponding alkenyl sulfides **3d**, **e**, **g**-**i** in good yields (Table 1). Using an aldehyde as a carbonyl component, the olefination product was obtained only in a moderate yield (run 9). Under a similar set of operating conditions, the reaction of the dithioorthoformate **2a** with 1,5-diphenylpentan-2-one (**5a**) was performed, and 1-methoxy-4-phenyl-2-(2-phenylethyl)but-1-ene (**3a**) was obtained in 50% yield. The yield was increased by increasing the amount of **2a** used (run 1). The starting material **2b** is commercially available, and methoxybis(phenylthio)methane (**2a**) is easily obtained by the reaction of commercial dichloromethyl methyl ether with potassium thiophenoxide in THF in 85% yield.

Table 2. Preparation of 1,2-Diheteroatom Substituted 1-Olefins 4[a]

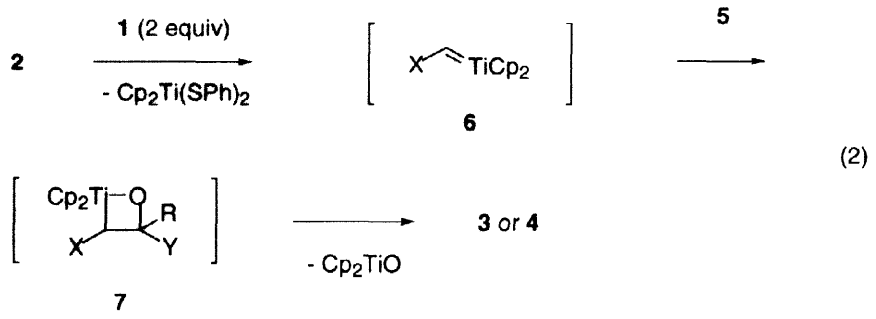
| Run | Carbonyl Compound | | Thioorthoformate (equiv) | Time (h) | Product | | Ratio of Stereoisomers[b] | Yield (%) |
|---|---|---|---|---|---|---|---|---|
| 1 |  | **5h** | **2a** (2.0) | 3 |  | **4a** | c | 56 |
| 2 | **5h** | | **2b** (1.5) | 3 |  | **4b** | 19 : $81^{d,e}$ | $80^{f}$ |
| 3 |  | **5i** | **2b** (1.5) | 3 |  | **4c** | 58 : $42^{e}$ | 87 |
| 4 |  | **5j** | **2a** (2.0) | 3 |  | **4d** | 53 : 47 | 78 |
| 5 |  | **5k** | **2a** (2.0) | 3 |  | **4e** | 58 : 42 | 78 |
| 6 | **5k** | | **2b** (1.5) | 3 |  | **4f** | 63 : $37^{e}$ | 88 |
| 7 |  | **5l** | **2a** (2.0) | 1.5 |  | **4g** | 17 : $83^{e}$ | 82 |
| 8 |  | **5m** | **2b** (1.5) | 2 |  | **4h** | 69 : $31^{e}$ | 85 |

a) All the reactions were performed in refluxing THF. b) The two stereoisomers were separated each other by using preparative TLC. The ratio was determined based on their isolated yields. c) Only the one stereoisomer was obtained. d) Determined by NMR analysis. e) *E* : *Z* determined by NOE experiment. f) Contaminated with a small amount of bis(phenylthio)methane. The yield was corrected for the contaminant.

As would be expected, the present reactions were found to be applicable to carboxylic esters and thiolesters (Table 2). The reaction of **2b** with methyl phenylacetate (**5i**) at room temperature for 3 h gave 2-methoxy-1-alkenyl sulfide **4c** in 65% yield, and the yield increased to 72% when the reaction was carried out under reflux. Increasing the amount of **2b** (1.5 equiv) and the use of refluxing temperature gave the best yield (87%) (run 3). Similarly 2-alkoxy-1-alkenyl ethers were obtained in good yields by the olefination of carboxylic esters using excess **2a** in refluxing THF. The alkylthio group substituted alkenyl ether and sulfide **4g** and **h** were also prepared by the olefination of thiolesters (runs 7 and 8).

The following is a typical experimental procedure. To a flask charged with finely powdered molecular sieves 4A (300 mg), magnesium turnings (87 mg, 3.6 mmol), and $Cp_2TiCl_2$ (747 mg, 3 mmol) were added THF (5 ml) and $P(OEt)_3$ (1.0 ml, 6 mmol) with stirring at room temperature under argon. After 3 h, methoxybis(phenylthio)methane (**2a**) (262 mg, 1 mmol) in THF (1 ml) was added to the reaction mixture which was further stirred for 10 min. Then ethyl caprylate (**5k**) (86 mg, 0.5 mmol) in THF (1.5 ml) was added dropwise over 15 min, and the reaction mixture was refluxed for 3 h. After cooling, the reaction was quenched by the addition of 1M NaOH (15 ml) and the resulting insoluble materials were filtered off through Celite. The filtrate was extracted with ether and the extract was dried over $K_2CO_3$. After removing the solvent, the residue was purified by using preparative TLC (hexane) to give 78 mg (78%) of 2-ethoxy-1-methoxynon-1-ene (**4e**).

At present, the exact reaction mechanism is still uncertain. However, similarly to the desulfurization of thioacetals of aldehydes,[8] it is reasonable to assume that the Schrock type metal carbene complex **6** having a heteroatom substituent is formed by the reduction of thioorthoformate **2**. The subsequent reaction with a carbonyl compound affords the oxatitanacyclobutane **7** which, in turn, decomposes to produce a heteroatom substituted olefin as depicted in the following equation.



In conclusion, the present study demonstrated that a variety of heteroatom substituted olefins are easily prepared by the titanocene(II)-promoted olefination of carbonyl compounds using thioorthoformates. These compounds are useful synthetic intermediates as not only precursors of ketones and aldehydes, but also highly nucleophilic olefins. Further study on the applications of this new olefination using the titanocene(II)-thioacetal system is now in progress.

This work was supported by a Grant-in-aid for Scientific Research on Priority Area No. 09231213 from the Ministry of Education, Science, Sports and Culture, Japan.

## REFERENCES AND NOTES

1. Maercker, A. *Org. React.* **1965**, *14*, 270.
2. Ager, D. J. *Org. React.* **1990**, *38*, 1.
3. Pine, S. H. *Org. React.* **1993**, *43*, 1.
4. Wittig, G.; Schlosser, M. *Chem. Ber.* **1961**, *94*, 1373. Levine, S. G. *J. Am. Chem. Soc.* **1958**, *80*, 6150. Wittig, G.; Knauss, E. *Angew. Chem.* **1959**, *71*, 127. Wittig, G.; Böll, W.; Krück, K. H. *Chem. Ber.* **1962**, *95*, 2514.
5. Magnus, P.; Roy, G. *J. Chem. Soc., Chem. Commun.* **1979**, 822. Magnus, P.; Roy, G. *Organometallics* **1982**, *1*, 553. Kende, A. S.; Blacklock, T. J. *Tetrahedron Lett.* **1980**, *21*, 3119.
6. Gröbel, B.-T.; Seebach, D. *Chem. Ber.* **1977**, *110*, 852.
7. Horikawa, Y.; Watanabe, M.; Fujiwara, T.; Takeda, T. *J. Am. Chem. Soc.* **1997**, *119*, 1127; Takeda, T.; Watanabe, M.; Nozaki, N.; Fujiwara, T. *Chem. Lett.* in press.
8. On the basis of the titanocene(II)-promoted reactions of thioacetals with carbon-carbon multiple bonds, we have assumed that titanocene alkylidenes are formed by the reduction of thioacetals with the low valent titanium species **1**: Horikawa, Y.; Nomura, T.; Watanabe, M.; Fujiwara, T.; Takeda, T. *J. Org. Chem.* **1997**, *62*, 3678. Takeda, T.; Shimokawa, H.; Miyachi, Y.; Fujiwara, T. *Chem. Commun.* **1997**, 1055. Takeda, T.; Takamori, M.; Fujiwara, T. *Chem. Commun.* in press.