Preparation of Alkenyl Sulfides by the Olefination of Thiolesters Using Thioacetals

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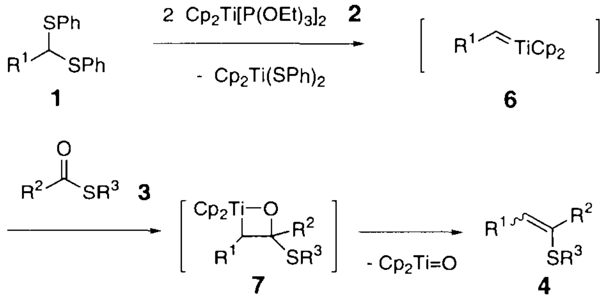
(Received October 8, 1997; CL-970778)

The reaction of thiolesters with titanocene alkylidenes prepared by the treatment of thioacetals with the low valent titanium species $Cp_2Ti[P(OEt)_3]_2$ produced the corresponding alkenyl sulfides in good yields with moderate to good *Z* stereoselectivity.

The preparation of alkenyl sulfides has been extensively investigated[1] since they are useful intermediates in organic synthesis. Recently we reported a new method for the Wittig-type olefination of carbonyl compounds using thioacetals **1** and the titanocene(II) species $Cp_2Ti[P(OEt)_3]_2$ **2**.[2] One of the features of this olefination is its wide range of applicability; not only ketones and aldehydes, but also carboxylic esters and lactones can be transformed into olefins. We further investigated the olefination of carboxylic acid derivatives using the low valent titanium-thioacetal system and found that the olefination of thiolesters **3** with this system is a convenient method for the preparation of alkenyl sulfides **4** (Scheme 1).

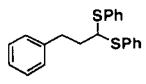
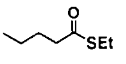
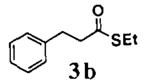
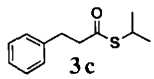
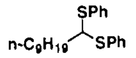
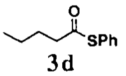
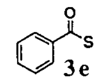
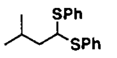
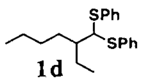
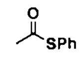
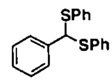
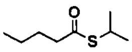


Scheme 1.

The reaction of *S*-ethyl pentanethioate (**3a**) with the organotitanium reagent, prepared by the treatment of a small excess amount of 1-phenyl-3,3-bis(phenylthio)propane (**1a**) (1.1 equiv) with **2**, at room temperature for 4 h, gave the alkenyl sulfide **4a** in 65% yield (run 1). The yield of **4a** increased with increasing the amount of thioacetal used (run 3). The best yield was obtained when the reaction was carried out in refluxing THF (run 4). Under these conditions, the reactions of several thiolesters and thioacetals were performed and the results were summarized in Table 1. In every case examined, the use of higher reaction temperature gave the satisfactory yield of **4** (see runs 6, 7, 11, and 12).

The following is a typical experimental procedure. To a flask charged with finely powdered molecular sieves 4A (225 mg), magnesium turnings (66 mg, 2.7 mmol), and Cp_2TiCl_2 (560 mg, 2.25 mmol) was added THF (4 ml) and $P(OEt)_3$ (0.77 ml, 4.5 mmol) with stirring at room temperature under argon. After 3 h, **1a** (252 mg, 0.75 mmol) in THF (1 ml) was added to the reaction mixture which was further stirred for 10 min. Then **3a** (73 mg, 0.5 mmol) in THF (1.5 ml) was added dropwise over 15 min and the reaction mixture was refluxed for 2 h. After being cooled to room temperature, the reaction was quenched by the addition of 1M NaOH (15 ml) and the resulting insoluble materials were filtered off through Cerite. The filtrate was extracted with ether and the extract was dried over Na_2SO_4. After removal of the solvent, the residue was purified by PTLC (hexane) to yield 105 mg (84%) of 4-ethylthio-1-phenyloct-3-ene (**4a**).

Table 1. Olefination of thiolesters using thioacetals[a]

Run	Thioacetal	Thiolester	Alkenyl sulfide	Yield/%	*E* : *Z*[b]
1[c]			**4a**	65	22 : 78
2[d]			**4a**	64	22 : 78
3[e]			**4a**	72	22 : 78
4	**1a**	**3a**	**4a**	84	19 : 81
5		 **3b**	**4b**	77	29 : 71
6[e]			**4c**	67	26 : 74
7		**3c**	**4c**	78	27 : 73[f]
8	**1b**	 **3d**	**4d**	53	14 : 86
9		 **3e**	**4e**	50	g
10		**3b**	**4f**	66	36 : 64
11[e]		**3c**	**4g**	71	34 : 66
12	**1c**	**3c**	**4g**	77	34 : 66[f]
13	 **1d**	 **3f**	**4h**	65[h]	22 : 78[f]
14		**3a**	**4i**	58	42 : 58
15	**1e**	 **3g**	**4j**	54	46 : 54

[a] All reactions were performed with a similar procedure as described in the text, unless otherwise noted. [b] Determined by NMR spectrum. [c] Carried out using 1.1 equiv of **1a** at room temperature for 4 h. [d] Carried out using 1.1 equiv of **1a**. [e] Carried out at room temperature for 2 h. [f] Determined based on their isolated yields. [g] The NMR spectrum of the corresponding sulfone **5** suggested that the product consisted of a single stereoisomer. Its configuration is assumed to be *Z* on the basis of the chemical shift of vinyl proton. [h] Contaminated with a small amount of 2-ethylhexyl phenyl sulfide. The yield was corrected for the contaminant.

The configurations of the alkenyl sulfides **4a**, **i**, and **j** were determined by NOE experiments. Then all the alkenyl sulfides obtained were transformed into the corresponding alkenyl sulfones **5** by the treatment with potassium peroxymonosulfate (OXONE®) (6 ~ 8 equiv / 0 °C ~ room temperature / overnight) or MCPBA (10 equiv / 0 °C ~ room temperature / overnight). The stereochemistry of these compounds was assigned on the basis of the chemical shifts of their vinyl protons. The range of vinyl proton of one isomer of **5** was fairly downfield (δ 6.67 ~ 7.59) compared with that of the corresponding alkenyl sulfide **4** (δ 5.34 ~ 6.48). On the other hand, in the case of the other stereoisomer, a smaller difference in chemical shifts (δ 0.11 ~ 0.58) between the vinyl protons of sulfide **4** and sulfone **5** was observed.[3] These results indicate that the former is the *E* isomer and the latter should be assigned to *Z*. The fact that the configurations of **4a**, **i**, and **j** thus determined are consistent with those determined by NOE experiments proves the reliability of the above way of assignments. As shown in Table 1, the *Z* isomers were always predominant in the present reaction.[4] The extent of stereoselectivity is clearly dependent on the substituents of both thioacetals and thiolesters; the loss of stereoselectivity was observed when benzaldehyde diphenyl thioacetal **1e** was employed (runs 14 and 15).

As for the mechanism of olefination of carbonyl compounds, we have proposed the two reaction pathways in which the *gem*-dititanium species or the carbene complex of titanium **6** is formed as an active intermediate.[2] The recent results of titanocene(II)-promoted reactions of thioacetals with carbon-carbon multiple bonds[5] suggest that the present carbonyl olefination proceeds through the oxatitanacyclobutane **7** which is formed by the reaction of **6** with a thiolester **3** as depicted in Scheme 1.

In conclusion, the present study showed that thiolesters could be olefinated by the treatment with titanocene alkylidenes formed from thioacetals. Although the Zn-*gem*-dibromoalkane-$TiCl_4$-TMEDA system effects the olefination of thiolesters,[4] the present reaction enjoys an advantage that the starting materials, thioacetals, are accessible from various starting materials.

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

References and Notes

1 For examples; B. M. Trost and A. C. Lavoie, *J. Am. Chem. Soc.*, **105**, 5075 (1983), and references cited therein; T. Takeda, H. Furukawa, M. Fujimori, K. Suzuki, and T. Fujiwara, *Bull. Chem. Soc. Jpn.*, **57**, 1863 (1984); H. Kuniyasu, A. Ogawa, K. Sato, I. Ryu, N. Kambe, and N. Sonoda, *J. Am. Chem. Soc.*, **114**, 5902 (1992); T. Ishiyama, K. Nishijima, N. Miyaura, and A. Suzuki, *J. Am. Chem. Soc.*, **115**, 7219 (1993).

2 Y. Horikawa, M. Watanabe, T. Fujiwara, and T. Takeda, *J. Am. Chem. Soc.*, **119**, 1127 (1997).

3 The chemical shifts (δ in $CDCl_3$) of vinyl protons of alkenyl sulfides **4** and sulfones **5** are as follows: **4a** (*E*; 5.34, *Z*; 5.64); **5a** (*E*; 6.70, *Z*; 6.13); **4b** (*E*; 5.40, *Z*; 5.58); **5b** (*E*; 6.71, *Z*; 6.01); **4c** (*E*; 5.59, *Z*; 5.64); **5c** (*E*; 6.69, *Z*; 6.03); **4d** (*E*; 5.85, *Z*; 5.89); **5d** (*E*; 6.91, *Z*; 6.00); **4e** (*Z*; 6.00); **5e** (*Z*; 6.33); **4f** (*E*; 5.44, *Z*; 5.60); **5f** (*E*; 6.75, *Z*; 6.04); **4g** (*E*; 5.62, *Z*; 5.65); **5g** (*E*; 6.72, *Z*; 6.07); **4h** (*E*; 5.64, *Z*; 5.51); **5h** (*E*; 6.67, *Z*; 5.73); **4i** (*E*; 6.30, *Z*; 6.55); **5i** (*E*; 7.59, *Z*; 7.13); **4j** (*E*; 6.48, *Z*; 6.59); **5j** (*E*; 7.56, *Z*; 7.12). The similar spectroscopic data of a series of 1-arylalkenyl phenyl sulfides were obtained; T. Takeda, F. Kanamori, M. Masuda, and T. Fujiwara, *Tetrahedron Lett.*, **32**, 5567 (1991).

4 K. Takai, O. Fujimura, Y. Kataoka, and K. Utimoto, *Tetrahedron Lett.*, **30**, 211 (1989).

5 Y. Horikawa, T. Nomura, M. Watanabe, T. Fujiwara, and T. Takeda, *J. Org. Chem.*, **62**, 3678 (1997); T. Takeda, H. Shimokawa, Y. Miyachi, and T. Fujiwara, *J. Chem. Soc., Chem. Commun.*, **1997**, 1055.