ORGANIC LETTERS

2006
Vol. 8, No. 26
6095−6098

Mild Preparation of Alkenes from Phenyl Sulfides: One-Pot Elimination of Phenylthio Group via Sulfilimine at Ambient Temperature

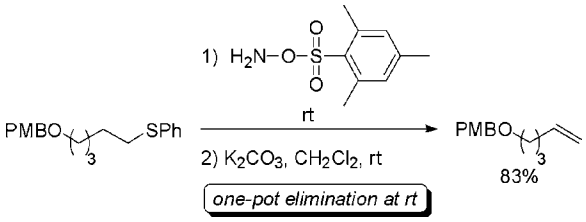
Jun-ichi Matsuo,* Takaaki Kozai, and Hiroyuki Ishibashi*

Division of Pharmaceutical Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma-machi, Kanazawa 920-1192, Japan

jimatsuo@p.kanazawa-u.ac.jp

Received October 25, 2006

ABSTRACT

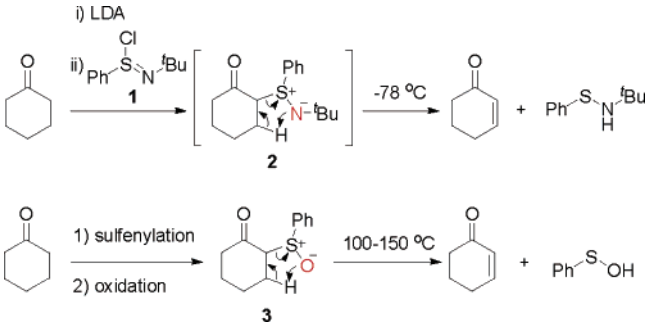


Various alkenes were prepared from phenyl sulfides in a one-pot manner at room temperature by converting them to the corresponding *S*-aminosulfonium salts with *O*-mesitylenesulfonylhydroxylamine, followed by treatment with potassium carbonate. Alkenes were formed by *cis*-elimination of in situ generated phenyl sulfilimines.

Pyrolysis reactions of esters,[1] xanthates,[2] amine oxides,[3] sulfoxides,[4] and selenoxides[5] are important for the synthesis of alkenes.[6] Phenyl sulfides are useful precursors of alkenes since they are relatively tolerant of basic and acidic conditions, and *cis*-elimination of their sulfoxides proceeds at temperatures ranging from 100 to 150 °C.[4] It could be expected that the synthetic utility of the elimination would be enhanced if the elimination could be induced under milder conditions such as at room temperature.

We have been studying the unique reactivity of *N*-*tert*-butylbenzenesulfinimidoyl chloride (**1**)[7] as an oxidizing agent, and we found that **1** dehydrogenated carbonyl compounds to the corresponding α,*β*-unsaturated carbonyl compounds via sulfilimine **2** even at −78 °C in a few minutes (Scheme 1).[8] Compared to the elimination of the α-phenyl-

Scheme 1. Milder Elimination of **2** than **3**



sulfinyl group from **3**, which required reaction temperatures ranging from 100 to 150 °C for several hours,[4] the **1**-mediated dehydrogenation proceeded under surprisingly mild

(1) (a) Hurd, C. D.; Blunck, F. H. *J. Am. Chem. Soc.* **1938**, *60*, 2419−2425. (b) Barton, D. H. R. *J. Chem. Soc.* **1949**, 2174−2178. (c) Curtin, D. Y.; Keiiom, D. B. *J. Am. Chem. Soc.* **1953**, *75*, 6011−6018.

(2) (a) Nace, H. R. *Org. React.* **1962**, *12*, 57−100. (b) Cram, D. J. *J. Am. Chem. Soc.* **1949**, *71*, 3883−3889. (c) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828−5835. (d) Alexander, E. R.; Mudrak, H. *J. Am. Chem. Soc.* **1950**, *72*, 1810−1813.

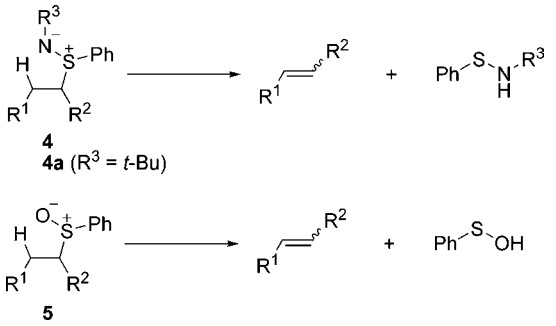
(3) Cope, A. C.; Trumbull, E. R. *Org. React.* **1960**, *11*, 317−493.

(4) (a) Field, L. *Synthesis* **1972**, 101−133. (b) Field, L. *Synthesis* **1978**, 713−740. (c) Trost, B. M.; Salzman, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887−4902. (d) Trost, B. M. *Acc. Chem. Res.* **1978**, *11*, 453−461. (e) Trost, B. M. *Chem. Rev.* **1978**, *78*, 363−382.

10.1021/ol062620w CCC: $33.50
Published on Web 12/01/2006

conditions. It was thought that the differences in reactivity between sulfilimine **2** and sulfoxide **3** arose from the enhanced basicity of the nitrogen in **2** compared to the oxygen in **3**. Along the same lines, we speculated that elimination of sulfilimines **4** would proceed under milder conditions than those for elimination of sulfoxides **5** (Scheme 2). Several

Scheme 2. Comparison between Elimination of **4** and That of **5**

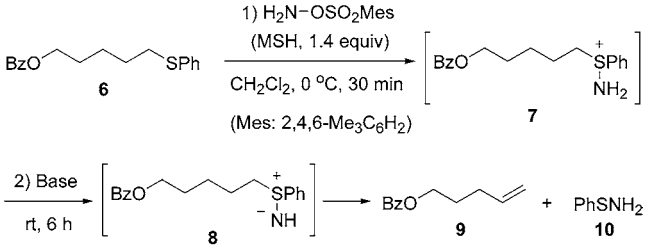


examples of elimination of *N*-substituted sulfilimines,[9] including *N*-ethoxycarbonyl-,[10] *N*-tosyl-,[11] *N*-carbamoyl-,[12] *N*-acyl-,[13] *N*-phenyl-,[14] and *N*-H sulfilimines,[15] have been reported. However, sulfilimines that have an electron-withdrawing group on the nitrogen atom (R^3 of **4** = electron-withdrawing group) required elevated temperatures for elimination. We therefore planned to establish a new method for the efficient and mild elimination of sulfilimines that do not have an electron-withdrawing group (R^3 of **4** ≠ electron-withdrawing group). We describe here a one-pot elimination of phenyl sulfides to alkenes via *N*-H sulfilimines that proceeds at ambient temperature which is also applicable to the synthesis of α,β-unsaturated carbonyl compounds.

First, we investigated elimination of sulfilimines bearing a *tert*-butyl group on the nitrogen atom (R^3 of **4** = *tert*-butyl) expecting mild elimination as observed in the intermediate **2**. However, preparation of *N*-*tert*-butyl phenyl sulfilimines **4a** from phenyl sulfides failed in spite of many trials, and so we then planned to prepare *N*-H sulfilimines from phenyl sulfides. Among some methods known for the preparation of *N*-H sulfilimines from phenyl sulfides,[16,17] the use of *O*-mesitylenesulfonylhydroxylamine (MSH)[18] was chosen as this reagent seemed to allow *N*-H sulfilimines to be prepared under mild conditions.[17]

Phenyl sulfide **6** was treated with MSH at 0 °C in dichloromethane to generate *S*-aminosulfonium salt **7** (Scheme 3). Quantitative formation of **7** was confirmed by ^{1}H NMR

Scheme 3. One-Pot Elimination of **6** to **9** Using MSH



analysis of a mixture of **6** and MSH in $CDCl_3$.[19] Then suitable bases needed for the in situ generation of sulfilimine **8** from **7** were screened (Table 1). The use of DBU directly gave

Table 1. Effect of Bases on One-Pot Elimination of Phenyl Sulfide **6** to Alkene **9**[a]

entry	base (equiv)	yield (%)[b]	recovered **6** (%)[b]
1	*i*-Pr_2NEt (2)	0	0
2	DBU (2)	42	16
3	*t*-BuOK (1.5)	78	8
4	K_2CO_3 (10)	80	6
5	K_2CO_3 (10) + MS4A	80	10
6	CsF (5)	83	6

[a] For reaction conditions, see Scheme 3. [b] Determined by ^{1}H NMR analysis.

alkene **9** in 42% yield even at room temperature, while diisopropylethylamine did not give **9** (entries 1 and 2). The use of potassium *tert*-butoxide improved the yield of alkene **9** to 78% yield (entry 3). Inorganic bases such as potassium carbonate and cesium fluoride were found to be effective, and the presence of molecular sieves 4A did not affect the efficiency of the elimination (entries 4−6). As described

(5) (a) Clive, D. L. J. *Tetrahedron* **1978**, *34*, 1049−1132. (b) Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22−30. (c) Paulmier, C. In *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986.

(6) Review: (a) Depuy, C. H.; King, R. W. *Chem. Rev.* **1960**, *60*, 431−457. (b) Astles, P. C.; Mortlock, S. V.; Thomas, E. J. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Heathcock, C. H., Eds.; Pergamon Press: New York, 1991; Vol. 6, pp 1011−1039.

(7) Matsuo, J. *J. Synth. Org. Chem. Jpn.* **2004**, *62*, 574−583.

(8) (a) Mukaiyama, T.; Matsuo, J.; Kitagawa, H. *Chem. Lett.* **2000**, 1250−1251. (b) Matsuo, J.; Aizawa, Y. *Tetrahedron Lett.* **2005**, *46*, 407−410.

(9) Gilchrist, T. L.; Moody, C. J. *Chem. Rev.* **1977**, *77*, 409−435.

(10) Whitfield, G. F.; Beilan, H. S.; Saika, D.; Swern, D. *J. Org. Chem.* **1974**, *39*, 2148−2152.

(11) (a) Oae, S.; Tsujihara, K.; Furukawa, N. *Tetrahedron Lett.* **1970**, 2663−2666. (b) Tsujihara, K.; Furukawa, N.; Oae, S. *Tetrahedron* **1971**, *27*, 4921−4930. (c) Tsujihara, K.; Harada, K.; Furukawa, N.; Oae, S. *Tetrahedron* **1971**, *27*, 6101−6108. (d) Oae, S.; Harada, K.; Tsujihara, K.; Furukawa, N. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3482−3486. (e) Furukawa, N.; Hatanaka, T.; Harada, K.; Oae, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2337−2338.

(12) Oae, S.; Masuda, T.; Tsujihara, K.; Furukawa, N. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3586−3590.

(13) (a) Papa, A. J. *J. Org. Chem.* **1970**, *35*, 2837−2840. (b) Kise, H.; Whitfield, G. F.; Swern, D. *J. Org. Chem.* **1972**, *37*, 1125−1128.

(14) Gassman, P. G.; Gruetzmacher, G. D. *J. Am. Chem. Soc.* **1974**, *96*, 5487−5495.

(15) Appel, R.; Büchner, W. *Chem. Ber.* **1962**, *95*, 855−866.

(16) Furukawa, N.; Omata, T.; Yoshimura, T.; Aida, T.; Oae, S. *Tetrahedron Lett.* **1972**, 1619−1622.

(17) Tamura, Y.; Sumoto, K.; Minamikawa, J.; Ikeda, M. *Tetrahedron Lett.* **1972**, 4137−4140.

(18) (a) Tamura, Y.; Minamikawa, J.; Sumoto, K.; Fujii, S.; Ikeda, M. *J. Org. Chem.* **1973**, *38*, 1239−1241. (b) Johnson, C. R.; Kirchhoff, R. A.; Corkins, H. G. *J. Org. Chem.* **1974**, *39*, 2458−2459.

(19) We observed that phenyl sulfide **6** hardly reacted with hydroxylamine-*O*-sulfonic acid (HAS) even at room temperature, while Appel reported that dimethylsulfide and diethylsulfide reacted with HAS to give the corresponding *S*-aminosulfonium salts. See: Appel, R.; Buchiner, W. *Chem. Ber.* **1962**, *95*, 849−854.

above, phenyl sulfide **6** was completely converted to **7** by the reaction of MSH, but phenyl sulfide **6** was regenerated in 6−16% yield after treating **7** with bases (entries 2−6). These results are in accordance with results of a previous report mentioning that *N*-H sulfilimines decompose readily to sulfide, NH_3, and N_2 at room temperature.[16] Our results suggest that the regeneration of **6** was influenced by the bases employed and that bases such as potassium carbonate and cesium fluoride minimize the decomposition of **8** to **6**.

The effects of solvents were next examined using potassium carbonate as a base (Table 2). It was found that the present elimination proceeded smoothly in both polar and nonpolar solvents except diethyl ether. In the case of diethyl ether, **9** was formed in only 18% yield, probably due to the low solubility of *S*-aminosulfonium salt **7** in diethyl ether (entry 3). Dichloromethane was generally employed as a solvent in this elimination since it was observed that *S*-aminosulfonium salts were sometimes insoluble in toluene when another phenyl sulfide was employed. Alkene **9** was isolated by thin-layer column chromatography on silica gel after organic extracts were washed with diluted NaOCl solution in order to oxidize benzenesulfenamide **10** and regenerated phenyl sulfide **6** (entries 2 and 7).

Next, the scope and limitations of the present elimination via sulfilimines were examined using MSH, potassium carbonate, and dichloromethane (Table 3). Longer reaction times were sometimes needed for converting *S*-aminosulfonium salts to alkenes. Protecting groups such as PMB, BOM, and TBDPS groups were tolerant of the MSH-mediated elimination of phenyl sulfides (entries 1−3). It should be noted that enamide **12e** was obtained in good yield as in the case of generating *N*-allyl amide **12d** (entries 3−4). Thus, the present method would be applicable to the preparation of labile olefinic compounds.

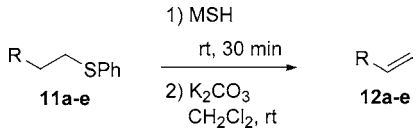
In order to investigate the stereochemistry of the present elimination reaction, diastereoisomeric phenyl sulfides **13** and **16** were subjected to the present elimination reaction (Scheme 4). Phenyl sulfide **13** gave **14** in 85% yield, and isomer **15** was not detected by ^{1}H NMR analysis. On the other hand, phenyl sulfide **16** afforded **14** and **15** in a ratio of 1:40 after 3 h. It was found that **15** isomerized to **14** since

Table 2. Effect of Solvents on One-Pot Elimination of Phenyl Sulfide **6** to Alkene **9**[a]

entry	solvent	yield (%)[b]
1	toluene	82
2	CH_2Cl_2	80 (77)
3	Et_2O	18
4	THF	75
5	CH_3CN	79
6	$MeNO_2$	77
7	DMF	80 (76)

[a] For reaction conditions, see Scheme 3. [b] Determined by ^{1}H NMR analysis. Numbers in parentheses are isolated yields.

Table 3. Mild One-Pot Elimination of Phenyl Sulfides **11a−e** to Alkenes **12a−e**



entry	R		reaction time (h)	product	yield (%)[a]
1	$PMBO(CH_2)_3$	**11a**	6	**12a**	83
2	$BOMO(CH_2)_3$	**11b**	6	**12b**	76
3	$TBDPS(CH_2)_3$	**11c**	24	**12c**	77
4	$BzNHCH_2$	**11d**	12	**12d**	78
5	BzNH	**11e**	12	**12e**	65

[a] Isolated yield.

Scheme 4. Stereochemistry

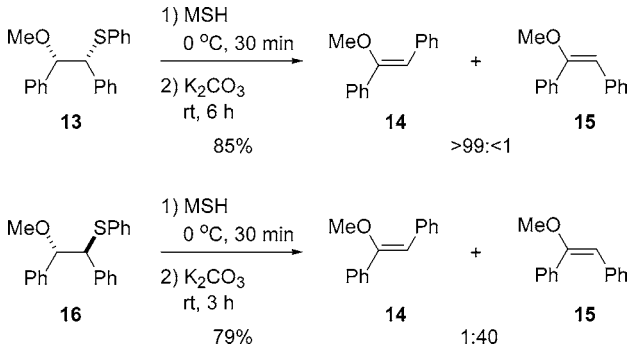
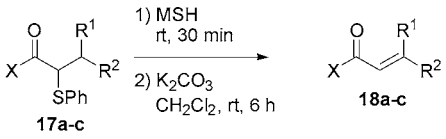
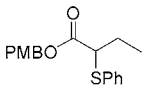
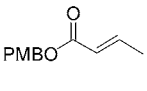
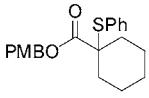
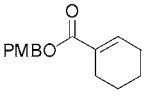
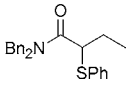
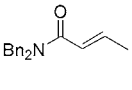


Table 4. Elimination of the α-Phenylthio Group of **17a−c** to α,β-Unsaturated Carbonyl Compounds **18a−c** Using MSH and K_2CO_3



entry	α-phenylthio carbonyl compound		α,β-unsatureated carbonyl compound		yield (%)[a]
1		**17a**		**18a**	87
2		**17b**		**18b**	81
3		**17c**		**18c**	86

[a] Isolated yield.

a longer reaction time (6 h) changed the ratio of **14**/**15** = 1:40 to **14**/**15** = 1:3.6. Therefore, it was confirmed that the present elimination of sulfilimine proceeded by *cis*-elimination. Moreover, the present elimination gave **15** more stereoselectively than elimination of *N*-Ts sulfilimine of **16** (80 °C, 5 h, **14**/**15** = 1:17).[11c]

Finally, the present method was applied to conversion of α-phenylthio carbonyl compounds to obtain α,*β*-unsaturated carbonyl compounds (Table 4). The elimination proceeded in a one-pot manner at ambient temperature to afford α,*β*-unsaturated esters (**18a**, **b**) and amide (**18c**) in high yields. It should be noted that only (*E*)-isomers were obtained in the case of acyclic substrates and that MSH-mediated elimination of α-phenylthio carbonyl compounds gave the corresponding α,*β*-unsaturated carbonyl compounds more efficiently than that of phenyl sulfides to alkenes (Tables 3 and 4).

In summary, various alkenes were prepared from phenyl sulfides in a one-pot manner at room temperature using MSH and potassium carbonate. It was previously thought that the intermediates, *N*-H sulfilimines, were unstable and decomposed to sulfides;[16] however, we found that *cis*-elimination took place as the major reaction pathway by the present procedure. The mildness and efficiency of the present elimination reaction would be useful for introduction of carbon−carbon double bonds in various kinds of molecules.

Acknowledgment. We are grateful for the financial support from Takeda Science Foundation, and this work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

Supporting Information Available: Experimental procedures for elimination and spectral data for phenyl sulfides (**6**, **11a**−**e**, **13**, **16**, and **17a**−**c**) and elimination products (**9**, **12a**−**e**, and **18a**−**c**). This material is available free of charge via the Internet at http://pubs.acs.org.

OL062620W