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$P(MeNCH_2CH_2CH_2)_3N$: An Efficient Promoter for the Generation of Nonstable and Somewhat Stable Sulfur Ylides From Sulfonium Salts

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ABSTRACT: *The commercially available nonionic strong base $P(MeNCH_2CH_2)_3N$ promotes the formation of stable and nonstable sulfur ylides from sulfonium salts at room temperature without competing [2,3] sigmatropic rearrangement. The ylides generated in situ reacted with aldehydes to give the corresponding oxiranes in high yield.* © 1999 John Wiley & Sons, Inc. Heteroatom Chem 10: 538–540, 1999

INTRODUCTION

Sulfur ylides are useful in organic synthesis, functioning as nucleophilic alkylidene transfer agents in reactions with electron-deficient functional groups. With carbonyls, epoxides are formed, and with Michael acceptors, either carbonyl addition with epoxide formation or conjugate addition with cyclopropanation occurs depending on the structure of the Michael acceptor [1]. The most common method of sulfur ylide generation consists of proton abstraction from the corresponding sulfonium salt in the presence of base. Stable sulfur ylides are generally generated by ionic bases such as KOH [2], NaH [3] and RO^- [4] from the corresponding sulfonium salts at room temperature, whereas the generation of nonstable sulfur ylides requires stronger bases such as *n*-BuLi [5] or LDA [6] at low temperature. $P(MeNCH_2CH_2)_3N$ (**1**) is a commercially available bicyclic nonionic strong base that has been utilized for a variety of organic transformations [7]. Here, we report that somewhat stable and nonstable sulfur ylides generated in the presence of **1** are captured by aromatic aldehydes to give oxiranes.

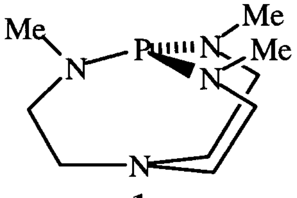

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TABLE 1 Reaction of Stable Sulfur Ylides from **2** with Aldehydes to Produce Oxiranes **3**

R¹	*R²*	*Yield of* **3** *(%)*	*trans/cis*[a]
PhCH=CH	*p*-MeC_6H_4	91	90/10
PhCH=CH	*p*-$MeOC_6H_4$	82	92/8
PhCH=CH	*p*-FC_6H_4	95	76/24
PhCH=CH	*p*-ClC_6H_4	93	91/9
PhCH=CH	Ph	85	75/25
Ph	*p*-MeC_6H_4	84	73/27
Ph	Ph	92	90/10
Ph	*p*-ClC_6H_4	96	65/35
Ph	*p*-$MeOC_6H_4$	81	70/30
CH_2=CH	Ph	87	69/31
CH_2=CH	*p*-$MeOC_6H_4$	80	60/40
CH_2=CH	*p*-MeC_6H_4	89	73/27
CH_2=CH	*p*-ClC_6H_4	91	75/25
CH_2=CH	*p*-FC_6H_4	93	71/29

[a] Determined by 300 MHz ^1H nmr spectroscopy.

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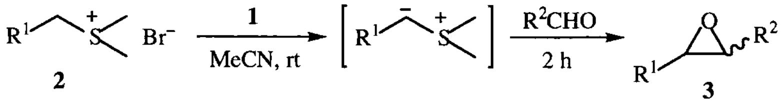
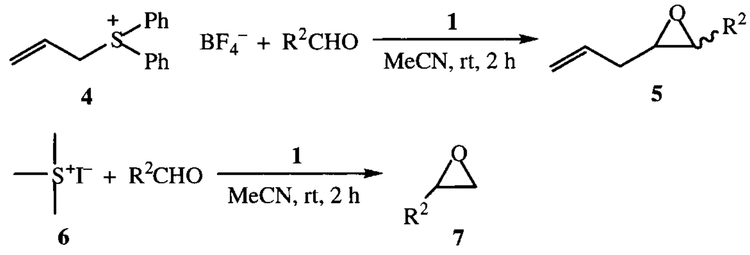
Dedicated to Alfred Schmidpeter on the occasion of his 70th birthday.



SCHEME 1



SCHEME 2

TABLE 2 Reaction of Nonstable Ylides from **4** and **6** with Aldehydes to Produce Oxiranes **5** and **7**

Sulfonium Salt	*R²*	*Yield of* **5** *and* **7** *(%)*	*trans/cis*[a]
4	Ph	96	57/43
4	*p*-FC_6H_4	92	71/29
4	*p*-ClC_6H_4	91	77/23
4	*p*-MeC_6H_4	90	82/18
4	2-Naphthyl	88	68/32
6	2-Naphthyl	87	—
6	*p*-MeC_6H_4	79	—
6	*p*-ClC_6H_4	83	—
6	*p*-FC_6H_4	75	—

[a] Determined by 300 MHz ^1H nmr spectroscopy.

TABLE 3 Reaction of Sulfonium Salt and Aldehyde in THF and Et_2O

Sulfonium Salt	*R²*	*Solvent*	*Yield (%)*	*trans/cis*[a]
2 (R^1 = Ph)	*p*-MeC_6H_4	THF	81	85/15
2 (R^1 = CH_2CH_2)	*p*-MeC_6H_4	THF	70	66/34
4	*p*-MeC_6H_4	THF	63	87/13
4	2-naphthyl	THF	75	60/40
2 (R^1 = PhCH=CH)	*p*-MeC_6H_4	Et_2O	65	93/7
2 (R_1 = Ph)	*p*-FC_6H_4	Et_2O	54	89/11
4	*p*-ClC_6H_4	Et_2O	78	53/47

[a] Determined by 300 MHz ^1H nmr spectroscopy.

Under mild conditions, **1** generates the corresponding somewhat stable sulfur ylides from cinammyl, benzyl, and allyl dimethylsulfonium bromide. These ylides then react in acetonitrile at room temperature with a variety of aldehydes to give the corresponding epoxides, as shown in Scheme 1. The results are summarized in Table 1.

Base **1** also promotes the in situ generation of the corresponding nonstable sulfur ylides from salts **4** and **6** in Scheme 2. These ylides were trapped with aldehydes to give the corresponding oxiranes **5** and **7** (Table 2). It is noteworthy that unlike *n*-BuLi [1,8], base **1** does not induce [2,3] sigmatropic rearrangement in the ylides generated from **4**.

The effect of solvent was also investigated in this reaction (Table 3). Although THF and Et_2O could be used as reaction solvents, it was found that the product yields in these solvents were not as high as in MeCN.

It was found that **1** could be recovered from the reaction mixtures. The precipitated hydrohalide salts were collected by filtration and treated with *t*-BuOK in THF to give **1** for recycling.

A general procedure for the generation of the sulfur ylides and their reactions with aldehydes follows. To a mixture of aldehyde (1 mmol) and sulfonium salt [8] (1.2 mmol) in 5 mL of dry MeCN, **1** (1.2 mmol), which was dissolved in 5 mL dry MeCN, was added by syringe under N_2. After the reaction mixture was stirred at room temperature for 2 hours, removal of the solvent from the reaction mixture under vacuum was followed by the addition of Et_2O (10 mL). The mixture was stirred for 0.5 hours and filtered. The solid hydrohalide salt of **1** was collected, dried, and treated with *t*-BuOK in THF to regenerate **1**, [9]. The liquid phase was concentrated and purified by chromatography on a basic Al_2O_3 column with a mixture of hexane, EtOAc, and NEt_3 (8:1:1) as eluent to give pure product.

Extension of this work to other carbonyl substrates is in progress.

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