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Tetrahedron Letters 45 (2004) 1283–1285
Tetrahedron Letters

A new, efficient, and simple method for the synthesis of thiiranes from epoxides under solvent-free conditions

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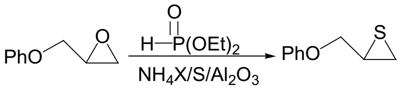
Received 29 September 2003; revised 8 November 2003; accepted 21 November 2003

Abstract—A simple, efficient, and new method has been developed for the synthesis of thiiranes from epoxides through a one-pot reaction of epoxides with diethyl phosphite in the presence of ammonium acetate or ammonium hydrogen carbonate/sulfur/ and acidic alumina under solvent-free conditions using microwave irradiation.

Since organic sulfur compounds have become increasingly useful and important in organic synthesis, the development of convenient and practical methods for the preparation of thiiranes are desirable. Thiiranes are the simplest sulfur heterocycles and occur in Nature. They have been used advantageously in the pharmaceutical, polymer, pesticide, and herbicide industries.[1] The most important method for the synthesis of thiiranes is the conversion of alkene oxides (epoxides) to thiiranes with thiourea, thioamides, phosphine sulfide, or dimethylthioformamide in the presence of trifluoroacetic acid or using inorganic thiocyanates or related compounds.[2] Although there are many classical methods for synthesizing thiiranes, these involve long reaction times, the use of strongly acidic or oxidizing conditions, high-temperature reaction conditions, expensive reagents, give poor yields, involve the formation of several by-products due to rearrangement or polymerization of the oxiranes and use moisture sensitive, and foul smelling reagents, which must be handled with care.[3] On the other hand, thiiranes cannot be prepared from some alkene oxides such as styrene oxide, stilbene oxide, and cycloalkene oxides using thiourea and thiocyanates.[4] Recently the use of recyclable ionic liquids for the conversion of oxiranes to epoxides has been reported.[5] Despite a wide range of synthetic methods for the conversion of epoxides to thiiranes, no attempt has been made to use readily accessible sulfur for this conversion. In recent years, the use of reagents and catalysts immobilized on solid supports has received considerable attention. Such reagents not only simplify purification processes but also help prevent release of reaction residues into the environment. Reagents supported on organic polymers and within and/or on the surface of inorganic matrices have all been reported.[6]

Recently we reported a new method for the synthesis of phosphorothioates of alkyl halides using a mixture of alumina/ammonium acetate/sulfur in the presence of diethylphosphite under microwave irradiation.[7] Here we report a new procedure for the conversion of epoxides into thiiranes using a mixture of alumina/ammonium acetate or ammonium hydrogen carbonate/sulfur in the presence of diethylphosphite under microwave irradiation. Initially, we carried out the experiment with 2-phenoxymethyl oxirane in a mixture of alumina/ammonium acetate/sulfur in the presence of diethylphosphite under microwave irradiation to afford the corresponding episulfide in 78% yield after 2 min (Scheme 1). When this reaction was carried out in ethanol for 3 h it afforded the corresponding thiirane in 56% yield. Ammonium formate (NH_4CO_2H) was not as



Scheme 1.

Keywords: Thiiranes; Epoxides; Diethylphosphite; Ammonium acetate; Microwave.

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0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2003.11.099

Table 1. The reaction of 2,3-epoxypropyl phenyl ether with diethyl phosphite in the presence of ammonium salts/sulfur/alumina

Entry	Ammonium salt	Reaction conditions	Reaction time (min)	Yield (%)[a]
a	NH_4OAc	Microwave	2	78
b	NH_4OAc	Reflux-EtOH	180	56
c	NH_4CO_2H	Microwave	5	—
d	NH_4HCO_3	Microwave	3	58
e	NH_4NO_3	Microwave	4	—
f	NH_4I	Microwave	4	5
g	NH_4Cl	Microwave	4	—
h	NH_4PF_6	Microwave	4	—
i	NH_4Br	Microwave	4	—

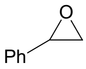
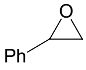
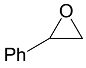
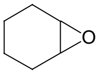
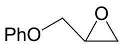
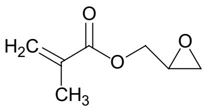
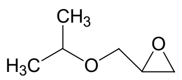
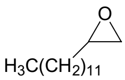
[a] Isolated yields.

effective as ammonium acetate or ammonium hydrogen carbonate and failed to give the required product (Table 1). Other ammonium salts (NH_4Cl, NH_4Br, NH_4PF_6, and NH_4NO_3) were not effective and did not give any product. The reaction with ammonium iodide gave only 5% of the desired product.

These results prompted us to extend this process to other epoxides. Interestingly, aryl, alkyl, and sterically hindered epoxides reacted smoothly with sulfur under these reaction conditions to produce the corresponding thiiranes in good to excellent yields (Table 2 and Scheme 2). As shown in Table 2, epoxides in the presence of ammonium acetate or ammonium hydrogen carbonate/sulfur/alumina reacted with diethyl phosphite to give the required products in good to excellent yields. Similarly, cyclohexyl oxide was converted into the corresponding thiirane in a good yield. Styrene oxide in the presence of ammonium acetate or ammonium hydrogen carbonate/sulfur/alumina reacted with diethyl phosphite, giving the corresponding thiirane in an excellent yield.[8]

In summary, simple work-up, low use of solvents, fast reaction rates, mild reaction conditions, good yields, and the relatively clean reactions with no tar formation make this method an attractive and a useful contribution to present methodologies. Indeed, a wide range of epoxides was converted into the corresponding thiiranes using this method.

Table 2. Conversion of epoxides to thiiranes using diethyl phosphite in the presence of ammonium acetate or ammonium hydrogen carbonate/sulfur/alumina with or without microwave irradiation

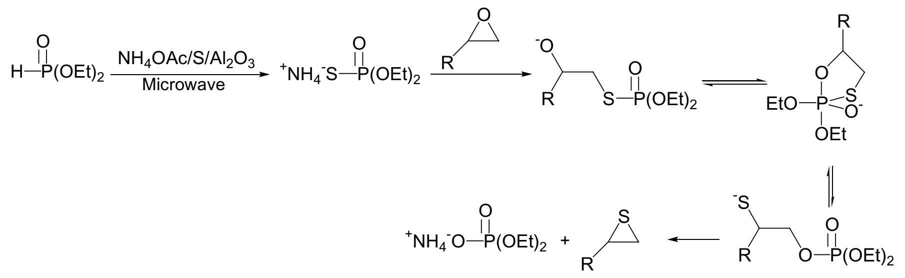
Entry	Epoxide	Conversion[a] (%)	NH_4OAc		NH_4HCO_3	
			Time (min)	Yield[b] (%)	Time (min)	Yield[b] (%)
a		98	0.5	82	0.5	80
b		98	30[c]	83	—	—
c		98	180[d]	80	—	—
d		77	3	69	3	61
e		87	2	78	3	58
f		71	4	62	4	57
g		48	3	42	4	40
h		65	4	60	4	57

[a] Conversions were determined by GC analysis.

[b] Yields refer to the isolated pure products after column chromatography.

[c] Shaking without microwave irradiation.

[d] Reflux in ethanol or methanol.



Scheme 2.

Acknowledgements

The Institute for Advanced Studies in Basic Sciences (IASBS) is thanked for supporting this work.

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8. This solvent-free reaction is operationally simple. The reagent (10 mmol) was prepared by the combination of ammonium acetate (10 mmol, finely ground), sulfur (10 mmol), and alumina (Al_2O_3, acidic, 2.5 g) in a mortar and pestle by grinding them together until a fine, homogeneous, powder was obtained (5–10 min). Diethyl phosphite (10 mmol) was added to this mixture and the mixture was irradiated in a microwave for 1 min using 720 W. The epoxide (9 mmol) was added to this reagent and the mixture was irradiated in a microwave for 0.5–4 min using 300–450 W. (A kitchen-type microwave was used in all experiments.) The mixture was then washed with 200 mL $CHCl_3$. All of the ammonium salts were removed by washing with an aq solution of sodium carbonate and then water. Chromatography through a plug of silica gel with EtOAc/*n*-hexane (1:9) and evaporation of the solvent under reduced pressure gave the pure products in 42–83% yields. The procedure was the same in the case of ammonium hydrogen carbonate. All the products gave satisfactory spectral data in accordance with the assigned structures.