SYNTHESIS OF SULFUR-CONTAINING HETEROCYCLES BY THERMOLYSIS OF α-ALKYLTHIO-*N*-AZIRIDINYLIMINES

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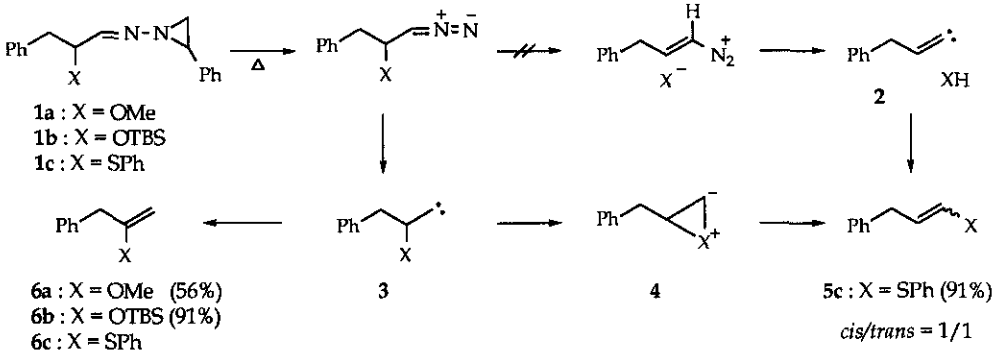
Abstract - Thermolysis of α-alkylthio substituted *N*-aziridinylimines in refluxing toluene gave various structurally different sulfur-containing heterocycles in high yields.

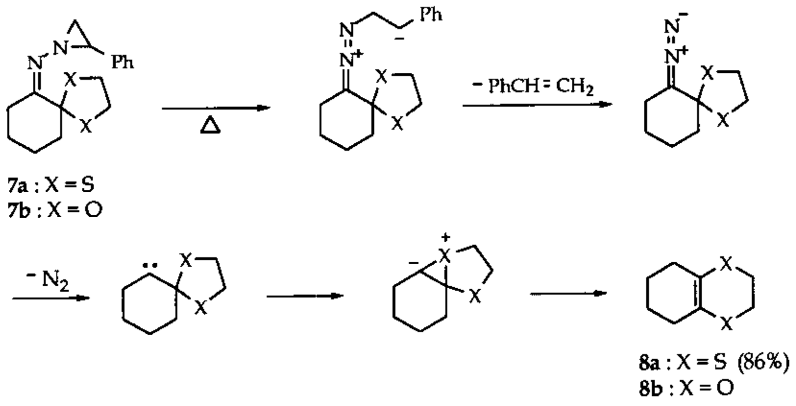
After the thermal reaction of α,β-epoxy-*N*-aziridinylimines to formyl-alkynes was discovered by Eschenmoser,[1] *N*-aziridinylimines have been utilized to generate both diazoalkanes[2] and carbenes[3] under mild conditions. In connection with our interest in the synthetic usefulness of *N*-aziridinylimines,[4] we have initially examined the possibility of generation of the alkylidenecarbene (**2**) with **1** as shown in Scheme 1. However, when **1a** was refluxed in toluene for 8 h, **6a** was isolated in 56% yield as a sole product. Apparently, the alkylidenecarbene (**2**) was not generated under the present conditions, probably due to the poor leaving ability of the alkoxy group. **6a** would be produced by 1,2-H shift of **3**, indicating that 1,2-H shift is much faster than the formation of the oxonium ylide (**4**). Since it is known that sulfur ylides are readily formed by the reaction of carbenes with the sulfides,[5] we turned our attention to the thermolysis of α-alkylthio substituted *N*-aziridinylimines. Thermal reaction of **1c** in refluxing toluene for 8 h gave **5c** in 91% yield as a 1:1 mixture of the *cis*- and *trans*- isomers and there is no indication of the formation of **6c** and 3-phenylpropyne resulting from 1,2-hydrogen shift of **2**. Thus, the reaction may proceed *via* the intermediacy of the sulfur ylide (**4c**). Moreover, intramolecular participation of sulfur linkage in α-alkylthio substituted alkylcarbenes was previously reported.[6]



Scheme 1

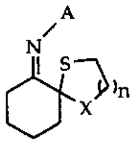
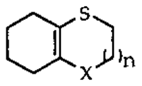
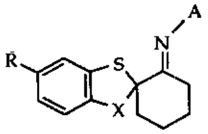
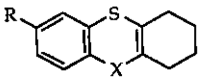
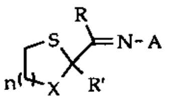
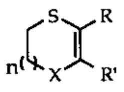
Since sulfur-containing heterocycles such as 1,4-dithiins and 1,4-oxathiins have exhibited promising biological activities,[7] various synthetic methods for their preparations have been developed.[8] In general, ring expansion reactions involving 1,2-sulfur migration[9] or the heterocyclic sulfoxide[10] were widely utilized. We applied the thermal reaction of α-alkylthio substituted *N*-aziridinylimines for the synthesis of sulfur-containing heterocycles.

Our approach is outlined in Scheme 2 and involves the intermediacy of carbenes generated from thermolysis of *N*-aziridinylimines and the subsequent formation of sulfur ylides. When **7a** was refluxed in toluene for 12 h, **8a** was isolated in 86% yield. To further examine the scope of the synthesis of sulfur-containing heterocycles, we prepared several additional substrates as shown in the Table. The substrates were prepared from 1,2-dicarbonyl compounds by the routine operations. When the reactions were carried out under the similar conditions, the reactions were normally clean, yielding sulfur-containing heterocycles in high yields and complete within 12 h in refluxing toluene. The generality and versatility of the present method are demonstrated by the formation of a variety of structurally different sulfur-containing heterocycles including 1,4-dithiins (Entries 1, 4 and 6), 1,4-oxathiins (Entries 3 and 8), and 1,4-thiazines (Entry 5). Moreover, the present method is also applicable to the formation of 1,4-dithiepines (Entries 2 and 7). We briefly studied the possibility of extending the present method to synthesize **8b**. When **7b** was refluxed in toluene for 8 h, the reaction was very messy and we were unable to detect an observable amount of **8b**. The reason for this observation may be due in part to the inefficient formation of the oxygen ylide, as compared with the formation of the sulfur ylide.[11]



Scheme 2

Table. Synthesis of Sulfur-containing Heterocycles

Entry	Substrate[a]	Time, h	Yield, % [b]
			
1	X=S, n=1	12	86
2	X=S, n=2	12	88
3	X=O, n=1	12	81
			
4	X=S, R=Me	12	75
5	X=NH, R=H	10	65
			
6	X=S, n=1, R=H, R' = Me	8	76
7	X=S, n=2, R=H, R' = H	8	80
8	X=O, n=1, R=PhCH$_2$CH$_2$, R'=H	12	65

[a] All substrates are a mixture of *syn*- and *anti*-isomers A = 2-phenylaziridinyl group

[b] The yield refers to the isolated yield.

The advantages of the present method over the previously reported methods are as follows. (i) The reaction occurs under mild conditions. (ii) The present method is operationally simple and does not usually require aqueous workup or chromatographic separation because readily removable styrene and nitrogen gas are generated. (iii) The present method can be generally applied for the synthesis of several kinds of sulfur-containing heterocycles in high yields.

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