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SYNTHESIS OF 2-HETEROSUBSTITUTED 1,3-OXATHIANES AND THEIR REACTION WITH *sec*-BUTYLLITHIUM

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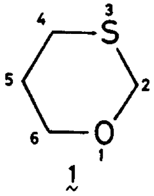
Summary: A series of 2-heterosubstituted 1,3-oxathianes were synthesized and their reactivity toward a strong base, *sec*-butyllithium, was studied. It was shown that *sec*-butyllithium attacked 2-heterosubstituted 1,3-oxathianes in three different ways depending upon the heteroatom at C-2; the removal of the proton at C-2, the nucleophilic attack at the heteroatom, or the nucleophilic attack at C-2 took place.

Umpolung[1] of the normal reactivity by modifying the structural unit has become one of the most prevailing methods of choice in synthetic organic chemistry. Particularly, the importance of the acyl anion equivalents has been well documented,[2] since Corey and Seebach[3] first utilized 1,3-dithiane as an acyl anion equivalent. Moreover, a considerable amount of knowledge on the chemistry of 2-heterosubstituted 1,3-dithianes has been gradually accumulated.[4]



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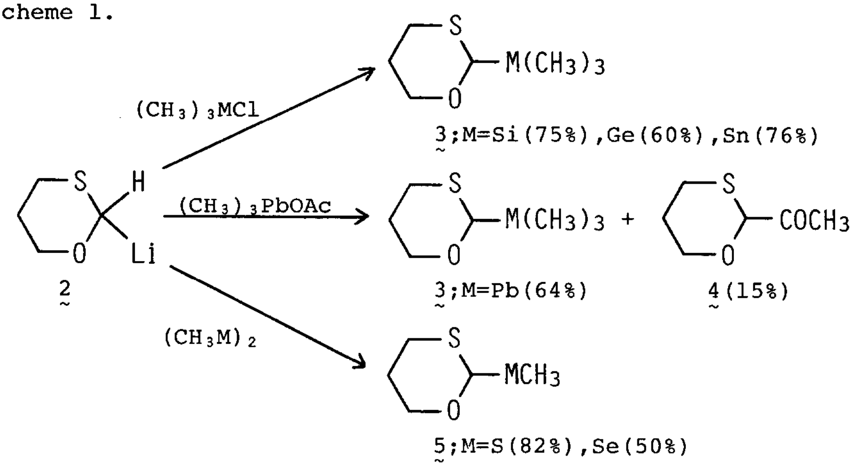
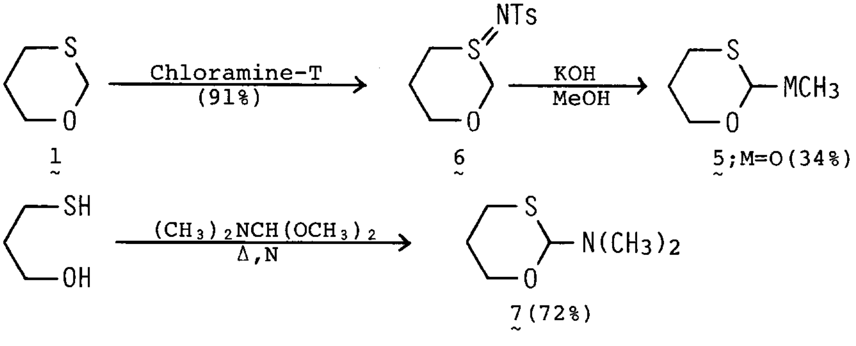
We have reported that 1,3-oxathiane (1) can possibly be utilized as an acyl anion equivalent.[5] As an extention of this work, a number of 2-heterosubstituted 1,3-oxathianes have been synthesized and their reactivity towards the strong base, *sec*-butyllithium, has been studied in hopes of the development of the acyl anion equivalents at higher oxidation stage, an increase in the kinetic acidity of H-2,[6,7] an increase in softness of the resulted anion, and a revelation of the reactivity characteristic to the introduced heteroatoms at C-2.

The derivatives of group IVB elements (Si, Ge, Sn, Pb) and group VI elements (S, Se) were synthesized in moderate yields by the reaction of 1,3-oxathianyllithium (2)[8] with the pertinent electrophiles (Scheme 1). 2-Methoxy-1,3-oxathiane (5, M = O) was synthesized by the methanolysis of N-tosylsulfilimine 6 in 31% overall yield from 1,3-oxathiane (1) according to the reported method for the preparation of dithioorthoformate.[4b] Transacetalization between 3-mercapto-1-propanol and N,N-dimethylformamide dimethylacetal afforded 2-dimethylamino-1,3-oxathiane (7) in 72% yield. The substituent attached to the heteroatom was unified to the methyl group in order to avoid the complication arising from the different steric bulk of the substituents during the reactions.

Scheme 1.



Scheme 2.

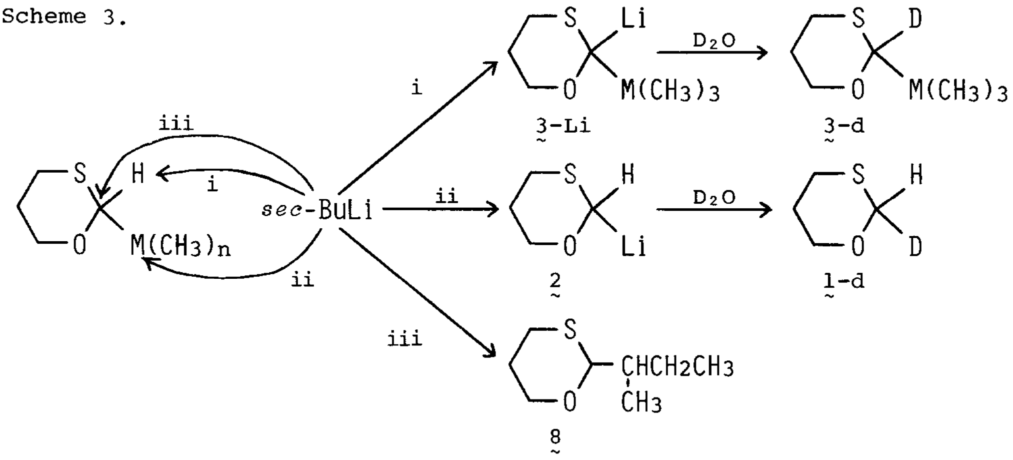


General procedure for the reaction of 2-heterosubstituted 1,3-oxathianes with *sec*-butyllithium is as follows: To a stirred solution of a given substrate in tetrahydrofuran was added a hexane solution of *sec*-butyllithium under nitrogen at -78°C until the solution was colored faint yellow.[9] After being stirred for a few minutes the reaction mixture was quenched with deuterium oxide and the products were analyzed. The results are shown in Scheme 3 and the Table.

With the group IVB derivatives **3** *sec*-butyllithium abstracted the proton at C-2 to give the lithiated species **3**-Li (for Si, Ge) or attacked the heteroatom at C-2 to leave 1,3-oxathianyllithium (**2**) (for Sn, Pb) depending upon the heteroatom. The nucleophilic displacement at C-2 giving 2-*sec*-butyl-1,3-oxathiane (**8**) was observed in the reaction of the group VI derivatives **5**. In the case of 2-methylseleno-1,3-oxathiane (**5**, M = Se) the nucleophilic attack at the metal was also recognized.

From the consideration of our present results we have chosen 2-trimethylsilyl-1,3-oxathiane (**3**, M = Si) as the most plausible acyl anion equivalent at least partially to meet the conditions mentioned earlier. Evaluation of synthetic utility of the silyl derivative **3** (M = Si) is being undertaken.

Scheme 3.



Table

M	n	Type of Reaction	Product	Yield, %	Incorporation of deuterium
C	3	Recovery of starting material			
Si	3	i	3-d	79	~100%
Ge	3	i	3-d	86	~98%
Sn	3	ii	1-d	95	~100%
Pb	3	ii	1-d	95	~100%
O	1	iii	8	57	-
S	1	iii	8	14	-
Se	1	ii	1-d	54	~100%
		iii	8	26	-
N	2	A complex mixture including starting material			

References and Notes

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8. It is easily obtained from 1,3-oxathiane (1) with *sec*-butyllithium in tetrahydrofuran under nitrogen at -78°C.
9. The color is a distinct indication of a slight excess of *sec*-butyllithium in the reaction mixture when the reaction is carried out in tetrahydrofuran.

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