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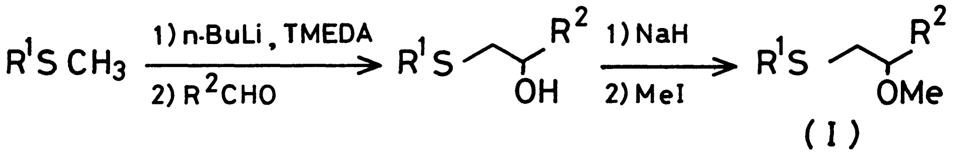
A CONVENIENT METHOD FOR THE PREPARATION OF 1-(METHYLTHIO) AND 1-(PHENYLTHIO)VINYLLITHIUM REAGENTS

Takeshi TAKEDA*, Hiroyuki FURUKAWA, and Tooru FUJIWARA
Department of Industrial Chemistry, Fuculty of Technology,
Tokyo University of Agriculture and Technology, Koganei, Tokyo 184

1-(Methylthio) and 1-(phenylthio)vinyllithiums were prepared by the treatment of the corresponding 2-methoxyethyl sulfides with twice molar amounts of butyllithium in the presence of N,N,N',N'-tetramethylethylenediamine (TMEDA). β-Alkylthio-β,γ-unsaturated alcohols were obtained in good yields by the reaction of the lithium salts with aldehydes.

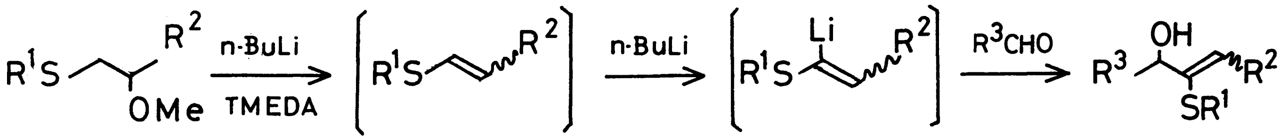
The α-lithiated alkyl vinyl sulfide is one of the most useful acyl anion equivalents and frequently employed in the synthesis of carbonyl compounds. Several methods were reported for the preparation of the vinyl anion from vinyl sulfide$^{1)}$ which was generally synthesized by the reaction of aldehyde with the phosphonate anion or phosphorous ylide that has an alkylthio group at the α-carbon atom$^{2)}$, treatment of aldehyde with thiol in the presence of acid catalyst$^{3)}$, dehydration of β-hydroxy sulfide$^{4)}$, or reduction of β-hydroxy thioacetal with low valent titanium compound.$^{5)}$ In this communication, we wish to report a convenient method for the preparation of 1-(methylthio) and 1-(phenylthio)vinyllithiums (II) utilizing 2-methoxyethyl sulfides (I) which were easily obtained by the addition of alkylthiomethyllithium to aldehydes$^{6)}$ followed by methylation with methyl iodide (eq-1).



(I-a); R^1=Me R^2=H
(I-b); R^1=Me R^2=Alkyl
(I-c); R^1=Ph R^2=Alkyl
(I-d); R^1=Me R^2=Ph

(eq-1)

When 2-methoxyethyl methyl sulfide (I-a) was treated with twice molar amounts of butyllithium in the presence of TMEDA, elimination of lithium methoxide and metallation of the resulting vinyl sulfide$^{7)}$ proceeded successively to form 1-(methylthio)vinyllithium (II-a) which reacted with aldehydes at the same temperature to give β-methylthio-β,γ-unsaturated alcohols (III-a) in good yields (eq-2).



(I) (II) (III)

(eq-2)

The typical experimental procedure is as follows: To a THF (5 ml) solution of the sulfide (I-a) (212 mg, 2 mmol) and TMEDA (511 mg, 4.4 mmol) was added a hexane solution of butyllithium (4.4 mmol) at -30° and stirred for 1 h. Benzaldehyde (233 mg, 2.2 mmol) in THF (1 ml) was added to the solution at -30°, and the reaction mixture was warmed up to room temperature. After addition of a phosphate buffer solution (pH-7) to the reaction mixture, the organic layer was extracted with AcOEt. The extract was dried over Na_2SO_4 and condensed under reduced pressure. The residue was chromatographed on silica gel (AcOEt - hexane) and 3-hydroxy-2-methylthio-3-phenylpropene (III-a) (289 mg) was obtained in 80% yield.

In a similar manner, the various allylic alcohols (III-a) were synthesized (Table-1).

Table-1

R^3	Yield of III-a(%)[8]
Ph	80
	88
$Ph(CH_2)_2$	81
CH_3CH_2	65
$(CH_3)_2CHCH_2$	70
Acetophenone	67

Table-2

R^2	R^3	Yield of IV(%)[8]
$Ph(CH_2)_2$	Ph	47
$Ph(CH_2)_2$	$Ph(CH_2)_2$	39
$Ph(CH_2)_2$	CH_3CH_2	27
$(CH_3)_2CHCH_2$	Ph	32

In the case of the sulfide (I-b) which possesses an alkyl group at β-position, the best result was obtained when the preparation of the vinyllithium (II-b) was carried out at 0° for 30 min followed by the treatment with aldehyde at -30°, although the product was a mixture of the allylic alcohol (III-b) and an unknown by-product and they could not be separated each other. Therefore the yield of III-b was determined after isomerization of III-b to α-methylthio ketone (IV) by the treatment with hydrochloric acid in CH_3CN[9] (Table-2).

On the other hand, the allylic alcohols (III-c) were obtained in good yields regardless of β-substituent when 2-methoxyethyl phenyl sulfide (I-c) was employed (Table-3).

Table-3

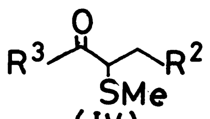
(Yield of III-c(%)[8])

R^2 \ R^3	Ph		$Ph(CH_2)_2$	CH_3CH_2	$(CH_3)_2CHCH_2$	Acetophenone
$Ph(CH_2)_2$	84	92	74	64	58	55
$(CH_3)_2CHCH_2$	63	72	62	61	67	54
H	44					

Contrary to the above results, the allylic alcohol (III-d) could not be isolated under the similar reaction conditions when 2-methoxy-2-phenylethyl methyl sulfide (I-d) was employed. Further, it was found that a Michael-type addition of butyllithium to the olefinic bond of the resulting vinyl sulfide occured and the vinyl anion (II-d) was not formed in this case. But this difficulty was overcome by the use of lithium diisopropylamide (LDA) instead of butyllithium as a base (Table-4). The typical reaction procedure is described for the preparation of 3-hydroxy-2-methylthio-1,5-diphenyl-1,4-pentadiene (III-d): To a THF (0.5 ml) solution of diisopropylamine (111 mg, 1.1 mmol) was added a hexane solution of butyllithium (1.1 mmol) at 0° and stirred for 10 min. To the reaction mixture cooled to -30°, the sulfide (I-d) (182 mg, 1 mmol) in THF (1 ml) was added. After stirring for 40 min, HMPA (0.6 ml) and a THF (0.5 ml) solution of LDA which was prepared from diisopropylamine (121 mg, 1.2 mmol) and butyllithium (1.2 mmol) were added successively at -60° and stirred for 2.5 h. After addition of cinnamaldehyde (159 mg, 1.2 mmol) in THF (1 ml), the reaction mixture was warmed up to room temperature. The usual work-up gave 3-hydroxy-2-methylthio-1,5-diphenyl-1,4-pentadiene (III-d) (174 mg, 67%).

Table-4

R^3	yield of III-d(%)[8]
	67
$Ph(CH_2)_2$	40
CH_3CH_2	28
$(CH_3)_2CHCH_2$	33



(IV)

In conclusion, various 1-(methylthio) and 1-(phenylthio)vinyllithiums can be prepared easily from 2-methoxyethylsulfides (I) under suitable reaction conditions. The reactions of the thus prepared anion with other electrophiles are now under investigation and will be reported soon.

References

1) H. W. Gschwend and H. R. Rodriguez, Organic Reactions, J. Wiley and Sons, N. Y., 26, 32 (1979).
2) a) I. Shahak and J. Almog, Synthesis, 1969, 170.
   b) T. Mukaiyama, T. Kumamoto, S. Fukuyama, and T. Taguchi, Bull. Chem. Soc. Jpn., 43, 2870 (1970).
   c) E. J. Corey and J. I. Shulman, J. Org. Chem., 35, 777 (1970).
   d) J. I. Grayson and S. Warren, J. Chem. Soc., Perkin Trans.1, 20, 2263 (1977).
3) T. Mukaiyama and K. Saigo, Chem. Lett., 1973, 479; and references cited therein.
4) W. Dumont and A. Krief, J. Chem. Soc., Chem. Commun., 1980, 673.
5) T. Mukaiyama, M. Shiono, and T. Sato, Chem. Lett., 1974, 37.
6) a) D. J. Peterson, J. Org. Chem., 32, 1717 (1967).
   b) E. J. Corey and D. Seebach, J. Org. Chem., 31, 4097 (1966).

7) It was confirmed that the treatment of 2-methoxy-1-methylthio-4-phenylbutane (I-b) and 2-methoxy-4-phenyl-1-phenylthiobutane (I-c) with an equimolar amount of butyllithium under the same reaction conditions gave the corresponding vinyl sulfides in 89% and 90% yields, respectively.

8) All compounds exhibited ir and nmr spectrum data in accordance with assigned structures.

9) R. C. Cookson and P. J. Parsons, J. Chem. Soc., Chem. Commun., 1978, 821.

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