Tetrahedron Letters,Vol.26,No.35,pp 4203-4206,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

A CONVENIENT AND STEREOSELECTIVE SYNTHESIS OF ALLYLIC SULFIDES

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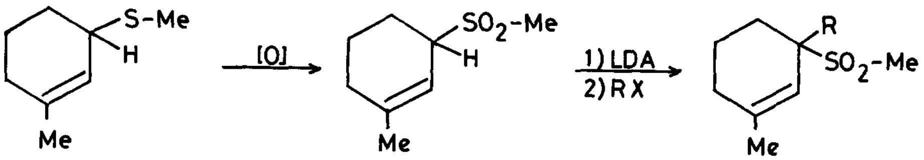
Abstract: The fractional distillation of O-(2-alkenyl or 2-cycloalkenyl) S-alkyl dithiocarbonates (xanthates) affords 2-alkenyl or 2-cycloalkenyl alkyl sulfides. The reaction involves the [3,3]-sigmatropic rearrangement of the xanthates to produce S-(2-alkenyl or 2-cycloalkenyl) S-alkyl dithiocarbonates followed by extrusion of carbon oxysulfide to give 2-alkenyl or 2-cycloalkenyl alkyl sulfides.

Allylic sulfides and their oxidation products (sulfoxides and sulfones) play a significant role in organic synthesis[1)] because of the diversity of their chemical reactions, which reflects the various functionalities in the molecules, namely, an acidic allylic hydrogen, an olefinic group, and a removable sulfur group. An important reaction of allylic sulfides and their oxidation products involves removal of the allylic hydrogen(s) by bases such as lithium diisopropyl amide (LDA) followed by a carbon-carbon bond formation reaction.



However, these methods are not always useful because the general methods for the stereoselective synthesis of the starting allylic sulfides have not yet been established.[2)]

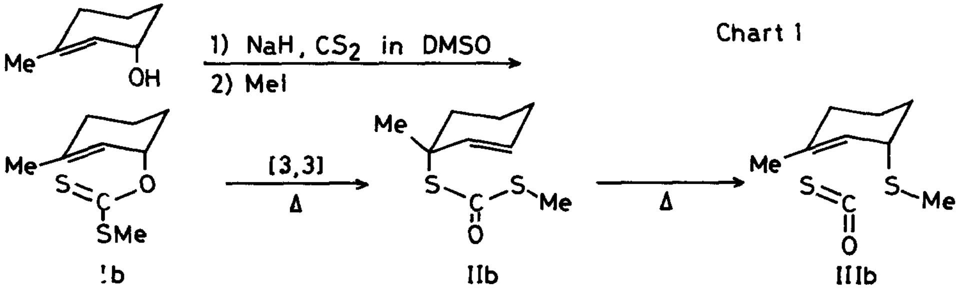


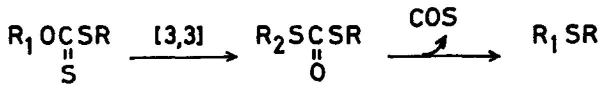
Chart 1

Previously, we have reported the highly stereoselective preparation of S-(2-alkenyl or 2-cycloalkenyl) S-alkyl dithiocarbonates (II) starting from the readily available allylic alcohols via the corresponding O-(2-alkenyl or 2-cycloalkenyl) S-alkyl dithiocarbonates (xanthates).[3] We now describe an extension of this procedure to the stereoselective synthesis of allylic sulfides (III) (Chart 1).

The reaction was carried out by stirring a mixture of an allylic alcohol and carbon disulfide in dimethyl sulfoxide (DMSO) containing a slight excess amount of sodium methylsulfinyl carbanion followed by alkylation.[4] Distillation of the product (I) at reduced pressure gave the corresponding [3,3]-sigmatropy product (II) and distillation at atmospheric pressure led to the doubly rearranged product (III) with extrusion of carbon oxysulfide.

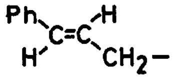
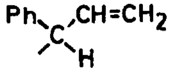
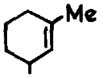
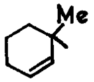
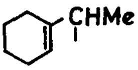
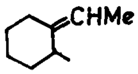
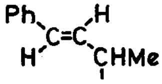
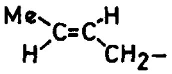
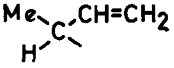
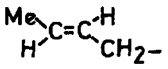
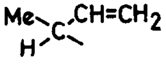
The reaction condition and yields are summarized in Table I.[5]

Table I. 2-Alkenyl or 2-Cycloalkenyl Alkyl Sulfides (III) formed from Thermolysis of the Corresponding Xanthates (I) via Dithiocarbonates (II).



$$R_1O\underset{\overset{\|}{S}}{C}SR \xrightarrow{[3,3]} R_2S\underset{\overset{\|}{O}}{C}SR \xrightarrow{COS} R_1SR$$

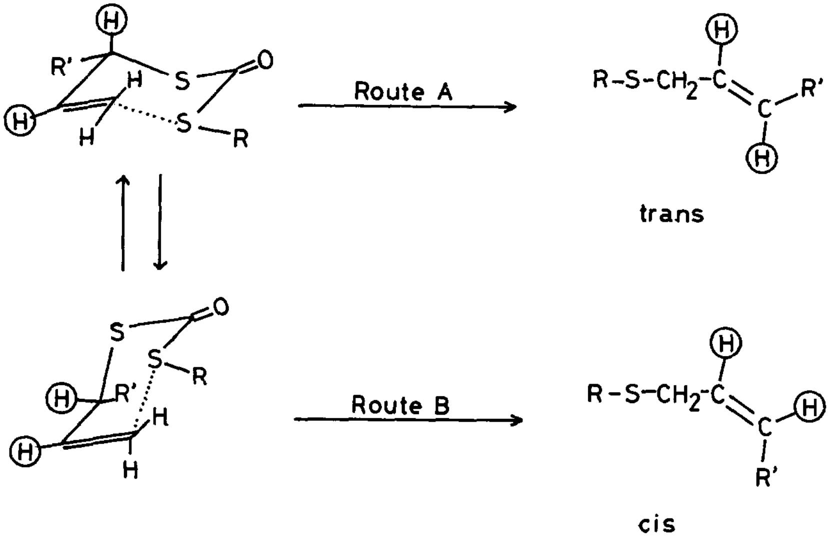
I II III

Entry NO.	I R$_1$	I R	II R$_2$	Pyrolysis Temp(°C)	bp (°C/mmHg)	Yield[a)] (%)
a		Me		200	164/760	85
b		Me		190	100/55	81
c		Me		180	121/60	74
d		Me	—	bp	100/27	67[b)]
e	$CH_2{=}CMeCH_2{-}$	Bz	R$_1$	220-230	99/4	70
f		Me		210	86/87	52[c)]
g		Bz		215-225	109/5	78

a) Calcd based on II. b) Calcd based on I. c) 1:1 Mixture of cis- and trans-isomers.

The reaction proceeded with high selectivity giving rise only to the allylic isomer. As the reaction involves an allylic shift, two geometrically isomeric products (cis and trans isomers) are possible in the pyrolysis of α-substituted allyl derivatives(Chart 2). As the result, the presence of bulky group such as phenyl in the molecule has a marked effect on the product distribution.
For example, S-(1-methylallyl) S-methyl dithiocarbonate (II$_f$) gave the cis and trans sulfides (III$_f'$ and III$_f$) in a nearly 1:1 ratio; in contrast, S-(1-methylallyl) S-benzyl dithiocarbonate (II$_g$) gave exclusively the trans isomer (III$_g$). In addition, in case of S-(1-phenylallyl) S-methyl dithiocarbonate, the trans isomer (IIIa) was exclusively formed. Thus, steric factors appear to play a major role in determining the geometry of the product.

Chart 2



IIa (R' = Ph , R = Me) IIIa (trans)
IIf (R' = Me , R = Me) IIIf (trans) , IIIf'(cis)
IIg (R' = Me , R = CH_2Ph) IIIg (trans)

The reactions (IIa, IIb and IIc) obeyed first-order rate laws and were only weakly accelerated by an increased polarity of the solvent.$^{6)}$ Thus a four-fold increase in rate was observed for the pyrolysis of S-(1-phenylallyl) S-methyl dithiocarbonate (IIa) in going from n-hexadecane to nitrobenzene.$^{7)}$ Furthermore, the activation entropies of these pyrolyses are highly negative.

These data indicate a tight transition state with little charge-separation in the rate-determining step. These reaction behaviors fall into category of *SNi* mechanism reaction and may be rationalized in terms of the four system interaction by frontier molecular orbital theory.[8]

The reaction is particularly valuable for the conversion of sensitive allylic alcohols to the corresponding sulfides without rearrangement of the carbon skeleton. As have been known, the preparative method of allylic sulfides by replacement reactions of 2-alkenyl derivatives are usually ready to produce isomeric sulfides regarding to the double bond and moreover to result in poor yields by side reaction (oxidation or polymerization) due to prolonged operation. In this sense, this pericyclic procedure is superior to the known method in terms of yield and simplicity of operation.

The procedure developed here can be carried out in a one-pot procedure and provides a new convenient method for the synthesis of allylic sulfides which might be otherwise difficult to prepare.

References and Notes

1) J. F. Biellmann and J. B. Ducep,"Organic Reactions", Vol. 27, ed. by W. G. Dauben, John Wiley and Sons, Inc., New York, 1982, Chapter 1.
2) T. L. Wardell, "The chemistry of the thiol group: Preparation of thiols" ed. by S. Patai, John Wiley & Sons, Ltd, New York, 1974 Chapter 4.
3) a) K. Harano and T. Taguchi, Chem. Pharm. Bull., 23, 467(1975): b) Idem Ibid., 20, 2348 and 2357(1972).
4) Primary 2-alkenols can be xanthated by using solid KOH in DMSO solution containing carbon disulfides (see ref. 3a).
5) For all new compounds, correct analytical and spectral data were obtained.
6) The rate constants were determined by measuring evolution of carbon oxysulfide (COS) gas (for IIa: Ea 18.5 Kcal/mol; $\Delta S^{\ddagger}$ -31 e.u.).
7) The reaction were found to be accelerated by phenolic solvents such as p-chlorophenol indicating the hydrogen-bonding to the carbonyl group to facilitate the reaction rate.
8) S. Inagaki, H. Fujimoto and K. Fukui, J. Am. Chem. Soc., 98, 4693(1976): In the cyclic D(donor)-D(donor)-A(acceptor)-A(acceptor) system, the HOMO-HOMO interaction between D's should be out of phase and the LUMO(A)-LUMO(A) and LUMO(A)-HOMO(D) interactions in-phase for the stabilization.

(Received in Japan 20 April 1985)