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A NEW ROUTE TO OLEFINS FROM DITHIOCARBAMATES VIA S-ALKYLATION-ELIMINATION PROCESS. APPLICATION TO A STEREOSELECTIVE SYNTHESIS OF NATURALLY-OCCURRING TRIENES

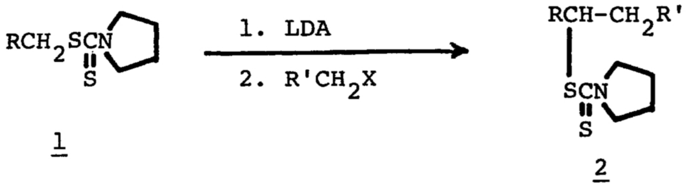
Toshio HAYASHI*, Akio SAKURAI, and Takeshi OISHI
The Institute of Physical and Chemical Research (RIKAGAKU KENKYUSHO)
Wako-shi, Saitama 351

Alkyl 1-pyrrolidinecarbodithioates, when treated with an excess of methyl iodide in hexamethylphosphoric triamide, afforded trans-olefins stereoselectively in high yields. Naturally-occurring 2,4,6- and 1,3,5-undecatrienes and allo-ocimene were prepared.

Pyrolysis of O-alkyl dithiocarbonates or thiocarbamates to give olefins is well known as the Chugaef reaction. With alkyl dithiocarbamates, however, the pyrolysis usually leads to the formation of tar. In the course of our study on synthesis using allylic dithiocarbamates$^{1)-3)}$, we have found that alkyl 1-pyrrolidinecarbodithioates (2) can easily be converted to trans-olefins stereoselectively via S'-methylation-elimination process.

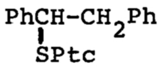
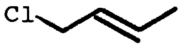
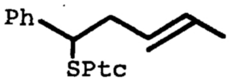
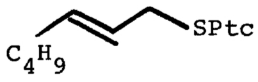
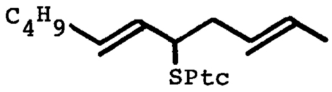
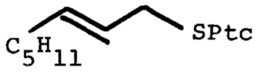
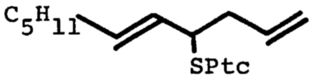
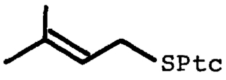
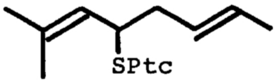
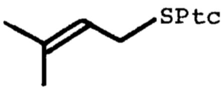
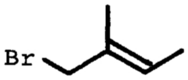
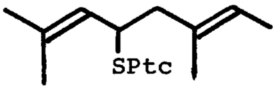
This method consists of the reaction of the alkyl 1-pyrrolidinecarbodithioates (2) with a large excess of methyl iodide in a mixture of hexamethylphosphoric triamide (HMPA), lithium carbonate and fluoride at room temperature, under argon, for 24 hrs. Preliminary experiments revealed that the yields of olefins were much dependent upon the kind of the N-alkyl moiety in the dithiocarbamate. In general, N,N-dimethyl- and N,N-diisopropyldithiocarbamates did not afford olefinic compounds in reasonable yields, whereas 1-pyrrolidinecarbodithioates (2) always gave trans-olefins in fair to excellent yields.

In a representative procedure, 1-pyrrolidinecarbodithioate 2c (10 mmol) was dissolved in a solution of methyl iodide (40 mmol) in HMPA (2 ml) under argon in the dark at room temperature. After the solution was stirred for several hrs, pale yellow crystals began to precipitate from the solution, whereupon lithium carbonate (1.0 g) and lithium fluoride (1.0 g) were added and the mixture was stirred overnight. The product was extracted repeatedly with n-hexane, the combined extracts



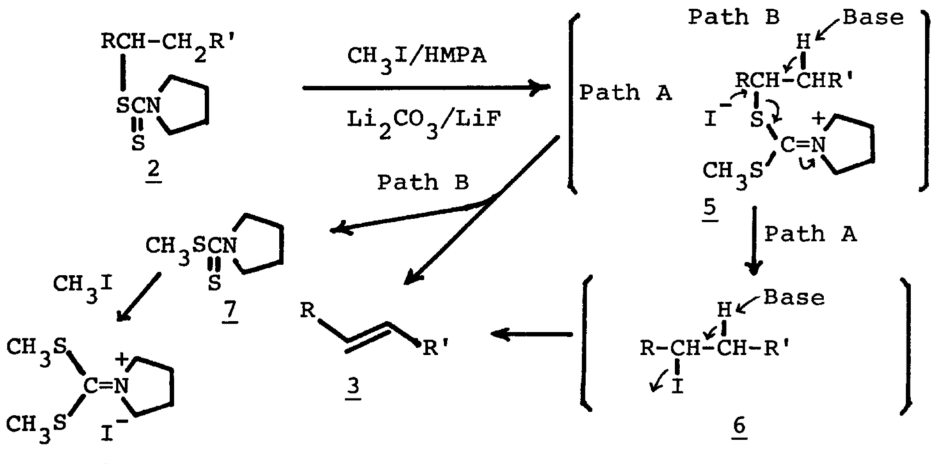
Scheme 1

Table 1. Reactions of allylic or benzyl dithiocarbamates with halides

Entry	RCH_2SPtc (1)[a]	$R'CH_2X$	Yield (%)	Product (2)[b]
a	$PhCH_2SPtc$	$PhCH_2Cl$	100	 $\underset{SPtc}{PhCH}-CH_2Ph$
b	$PhCH_2SPtc$		100	
c			90	
d			98.6	
e			99	
f			99	

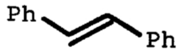
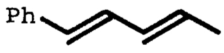
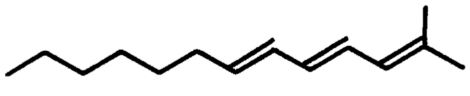
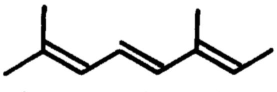
a) Ptc = 1-pyrrolidinylthiocarbonyl group. b) All products were characterized spectrally and by combustion analysis.

were washed with a 5% sodium sulfite solution, and dried (Na_2SO_4) under argon. After the evaporation of the solvent in vacuo, the residue was chromatographed on silica gel using n-hexane to give 3c; 1.172 g (78%): colorless oil, which, when exposed to the air, turned pale yellow. A part of it was further purified by distillation under reduced pressure: bp 90°C at 20 mmHg (Table 2). All the trienes prepared in the work (Table 2) were sensitive to oxidation in the air and underwent the Diels-Alder reaction or polymerization even at -20°C[4]. The dienyl 1-pyrrolidinecarbodithioate 2d having the terminal double bond afforded a mixture of 3d and 3c (3d:3c = 55:45). All attempts to prepare 3d free from 3c were unsuccessful. However, 3d was isolated in a pure form, using preparative liquid chromatography. Recently,



Scheme 2

Table 2. Preparations of olefins from dithiocarbamates (2)

Dithiocarbamate (2)	Yield (%)[a]	Product (3)[b]	mp or bp
2a	95		mp 123-125°C
2b	84.7		Solidified at -20°C
2c	78		bp 90°C/20mmHg
2d	77[c]		bp 98°C/20mmHg
2e	72		liquid
2f	75.6	 (allo-ocimene)	bp 89°C/20mmHg[5]

a) Yields were of the products chromatographed on silica gel using n-hexane.
b) All products were characterized spectrally and by combustion analysis. The analysis by Hplc were made on a Waters Associates ALC-244, equipped with two 30 cm X 4 cm columns packed with μ porasil using 9:1(v/v) n-hexane/ether. c) Isomerization occurred during the reaction to give a mixture of 3d and 3c (3d:3c = 55:45).

3c and 3d were found in marine algae by Moore and coworkers[6]. Glpc and Hlpc analyses proved that allo-ocimene (3f) prepared was almost free from other geometric isomers.

An advantage of this method over the pyrolytic reactions such as the Chugaef and Cope eliminations is that the reaction is easily carried out and proceeds under mild conditions to give, in general, high yields of trans-olefins. However, when the reaction is carried out with primary allylic dithiocarbamates of the $RCH=CHCH_2$-$SCSNR'_2$ type, the corresponding allylic iodides are obtained in high yields[7]. The pale yellow crystals (mp 100-103°C) which precipitated during the reaction, was isolated in a pure state and its structure was determined by direct comparison with an authentic sample as 1-bis(methylthio)methylenepyrrolidinium iodide(8). A possible reaction sequence is illustrated in Scheme 2. Presumably, the reaction proceeds through the intermediary of the iminium salt 5, which subsequently reacts with bases directly (path B) or with an iodide ion via the formation of an iodide 6 (path A) to give an olefin.

Another advantage of this method is that the dithiocarbamates (2c-2f) used for the triene synthesis can be easily prepared in excellent yields by the reaction of allylic halides with allylic dithiocarbamates (1) (Scheme 1 and Table 1)[8], which are also easily available from allyl or 2-methylallyl dithiocarbamates[1].

Further investigation on the scope and limitation of this method and application to the synthesis of carotenoids are now in progress.

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8) The lithiation of the allylic dithiocarbamate 1 was achieved with lithium diisopropylamide (LDA) in tetrahydrofuran at -78°C. To the lithio compound was added at -78°C a slight excess of an allylic halide. The product (2) was chromatographed on silica gel using dichloromethane.

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