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A. N. Mirskova[a]; S. G. Seredkina[a]; M. G. Voronkov[a]
[a] Institute of Organic Chemistry, Siberian Division of the USSR Academy of Sciences, Irkutsk, U.S.S.R.

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(ORGANYLTHIO)CHLOROACETYLENES, NEW POLYFUNCTIONAL REAGENTS FOR ORGANIC SYNTHESIS

A. N. MIRSKOVA, S. G. SEREDKINA and M. G. VORONKOV
Institute of Organic Chemistry, Siberian Division of the USSR Academy of Sciences, SU-664033 Irkutsk, U.S.S.R.

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Data concerning the synthesis, electronic structure, and reactivity of (organylthio)chloroacetylenes are summarized. A recently developed method for the preparation of (organylthio)acetylenes under phase-transfer conditions as well as the unique arrangement of several reactive centers in the molecules of these compounds make them valuable and accessible raw materials for organic syntheses.

The reactivity of (organylthio)chloroacetylenes towards anionic, uncharged, mono- and bifunctional nucleophiles is described. These reactions lead to previously unknown or otherwise difficultly available products. (Organylthio)chloroacetylenes are rather promising polyfunctional reagents.

Key words: (Organylthio)chloroacetylenes, haloacetylenes.

CONTENTS

I. INTRODUCTION

The chemistry of heteroatom-substituted acetylenes has been extensively developing during recent years. Investigations in the field of haloacetylenes are of special interest. This is due to both the high reactivity and diversity of conversions and the great practical value of these compounds.[1-13]

During the two last decades thermostabilizers of fluorine-containing rubbers, metal corrosion inhibitors, polymers for microelectronics as well as bioactive substances of a wide range of action have been prepared from haloacetylenes.[14-25]

Nucleophilic substitution at the sp-hybridized carbon atom is also of great theoretical interest. At present it is one of the least studied reaction types, the existing concepts for

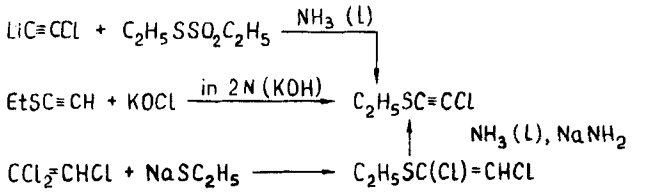
the mechanisms of these processes being rather contradictive. Despite numerous attempts no nucleophilic substitutions of halogen in haloacetylenes had been carried out until recently. The first reliable results were obtained as late as in the nineteen hundred seventies.[5,26-29] Later on the reactivity of haloacetylenes has been shown to depend greatly on the substituents at the triple bond.[5,30] In this connection, activated haloacetylenes containing an aromatic ring, vinyl or heteroatomic group as a second substituent are of great interest. The presence of several reactive centers in the molecule and their high reactivity make these compounds valuable raw materials for organic syntheses. At the same time, the number of heteroatomic haloacetylenes known at present is very small. The synthesis and reactions of nitrogen- and phosphorus-containing derivatives, $R_2NC{\equiv}CX$ and $(RO)_2P(O)C{\equiv}CX$ have been reported.[12,26]

A few sulfur-substituted haloacetylenes have been obtained in pure form and characterized[2,31,32,33] Until recently, however, the synthetic routes to (organylthio)chloroacetylenes have not been properly developed, their reactivity having been illustrated with only a few examples. This gap had to be filled since the development of simple synthetic routes to (organylthio)chloroacetylenes and the investigation of their reactivity in reactions with nucleophiles, first of all, would allow the evaluation of their synthetic possibilities and the application of these compounds as new synthons for the preparation of either unknown or otherwise difficultly accessible S-, N-, O-, and P-containing acetylenic or heterocyclic compounds. Besides, the study of the reactivity of (organylthio)chloroacetylenes containing a combination of reactive centers (a mobile chlorine atom, a triple bond and, conjugated with it, a sulfide bridge) in the molecule provides new information concerning the mechanism of nucleophilic substitution of halogen in activated haloacetylenes.

II. SYNTHESIS AND ELECTRONIC STRUCTURE

Some general methods for the preparation of haloacetylenes have been discussed in detail in reviews[3,4] and further developed in subsequent investigations.[2,20,26,31-40] The synthesis of sulfur-containing haloacetylenes encountered for a long time considerable experimental difficulties[2,31,33] which constrained further work on (organylthio)acetylenes.

The first (organylthio)chloroacetylene, (ethylthio)chloroacetylene, was obtained by Nooi and Arens[32] by three methods in 21–50% yield:



SCHEME 1

Later on, further (organylthio)chloroacetylenes $RSC{\equiv}CCl$ ($R = i\text{-}C_3H_7$, C_4H_9, C_6H_5) were prepared by dehydrochlorination of 2,2-dichlorovinyl organyl sulfides with alkali and heating *in vacuo* in 40–60% yield.

The synthesis of (arylthio)bromoacetylenes involves bromination of terminal ethynyl sulfides:[33]

$$ArSC{\equiv}CH \xrightarrow{NaOBr} ArSC{\equiv}CBr$$

SCHEME 2

A method for preparing (organylthio)chloroacetylenes[2] consisting of the dehydrochlorination of 2,2-dichlorovinyl propyl or phenyl sulfide with potassium *t*-butoxide in tetrahydrofuran at $-30 + -40$ °C in yields of 26 and 35%, respectively, has been suggested by Japanese scientists:[2] This method is not suitable, however, for large-scale

$$RSCH{=}CCl_2 \xrightarrow{t\text{-}BuOK} RSC{\equiv}CCl$$

SCHEME 3

application since it requires low temperatures, highly flammable solvents and metallic potassium and produces low yields. The use of DMSO as the solvent in the alkali-assisted dehydrochlorination of 2,2-dichlorovinyl organyl sulfides allows the process to be carried out at 0–5 °C and atmospheric pressure[41,42] which provides higher yields and a greater variety of (organylthio)chloroacetylenes. The starting 2,2-dichlorovinyl organyl

$$RSCH{=}CCl_2 \xrightarrow{KOH,\ DMSO} RSC{\equiv}CCl \qquad (1)$$

SCHEME 4

sulfides are obtained in high yields in a one-pot procedure from commercial thiols and trichloroethylene.[43]

$$RSH + CCl_2{=}CHCl \xrightarrow[-HCl]{h\nu} RSCH{=}CCl_2$$

SCHEME 5

We have suggested a very simple process for preparing (organylthio)chloroacetylenes in yields up to 95–98% by dehydrochlorination of 2,2-dichlorovinyl organyl sulfides with alkali at 20–22 °C and atmospheric pressure in an aqueous medium using a phase transfer catalyst, triethylbenzylammonium chloride, (TEBAC):[44–46]

$$RSCH{=}CCl_2 \xrightarrow[TEBAC]{KOH,\ H_2O} RSC{\equiv}CCl \qquad (2)$$

1

SCHEME 6

The (organylthio)chloroacetylenes obtained are mobile colorless or light-yellow liquids with a specific odor and a slight lachrymatory effect. The haloacetylenes synthesized by us do not form explosive mixtures with air and are stable while kept in the cold for two days. The physicochemical parameters and yields of (organylthio)chloroacetylenes are presented in Table 1.

With the use of IR, ^{13}C NMR, X-ray fluorescence spectroscopy, and quantum chemical calculations the electronic structure of (organylthio)chloroacetylenes has been inves-

Table 1. Physicochemical Constants and Yields of (Organylthio)chloroacetylenes

Formula	Yield, %	B.p., °C (mm Hg)	n_D^{20}	d_4^{20}	Ref.
$C_2H_5SC{\equiv}CCl$	80	44 (12)	1.5105	1.1063	42
	92	44 (12)	1.5105	1.1063	44
$C_3H_7SC{\equiv}CCl$	65	49 (12)	1.4913	1.1075	42
	94	49 (12)	1.4913	1.1075	44
	26	47–49 (13)	1.4913	1.1075	2
$C_4H_9SC{\equiv}CCl$	72	62 (11)	1.5050	1.0823	42
	95	62 (11)	1.5050	1.0823	44, 45
i-$C_4H_9SC{\equiv}CCl$	68	65 (14)	1.5020	1.0681	42
	90	65 (14)	1.5020	1.0681	45
t-$C_4H_9SC{\equiv}CCl$	70	23 (3)	1.5000	1.0777	42
	92	23 (3)	1.5000	1.0777	44, 45
$C_6H_5SC{\equiv}CCl$	78	78–80 (1)	1.6118	1.1095	42
	94	78–80 (1)	1.6118	1.1095	44, 45
	35	78–80 (1)	1.6118	1.1095	2
$C_6H_5CH_2SC{\equiv}CCl$	90	81–82 (1)	1.6134	1.1081	45

Table 2. ^{13}C NMR Spectral Parameters of (Organylthio)chloroacetylenes, $RSC^{\beta}{\equiv}C^{\alpha}Cl$

Formula	Chemical shifts, δ, ppm		
	R	C^{α}	C^{β}
$C_2H_5SC{\equiv}CCl$	15.26; 23.73	69.57	59.71
$C_3H_7SC{\equiv}CCl$	14.07; 24.36; 38.56	70.03	61.69
$C_6H_5SC{\equiv}CCl$	126.55; 126.87; 129.25	74.70	57.47

Table 3. $\Delta SK\alpha$ and $\Delta ClK\alpha$ and Charges on the Chlorine and Sulfur Atoms in (Organylthio)chloroacetylenes According to X-Ray Fluorescence Spectroscopy*

Formula	$\Delta SK\alpha$ eV × 1000	qS e × 100	$\Delta ClK\alpha$ eV × 1000	q(Cl) e × 100
$C_2H_5SC{\equiv}CCl$	33 (7)	3 (2)	−42 (25)	−3 (2)
n-$C_4H_9SC{\equiv}CCl$	34 (4)	3 (1)	+5 (12)	−1 (1)
i-$C_4H_9SC{\equiv}CCl$	33 (3)	3 (1)	−49 (4)	−3 (1)
t-$C_4H_9SC{\equiv}CCl$	0 (8)	−1 (1)	−38 (10)	−2 (1)
$C_6H_5SC{\equiv}CCl$	46 (7)	5 (2)	−17 (44)	−1 (1)

*Values in brackets correspond to mean-square errors in the last significant digit in a 95% confidence interval by the Student criterion.

tigated. This allows their reactivity to be explained and the most likely mechanism for the nucleophilic substitution of the chlorine atom to be proposed.[47–49]

The organylthio group in acetylenic sulfides is known[50] to be both an electron donor and an electron acceptor. On the other hand, the presence in the (organylthio)chloroacetylene of a chlorine atom capable of exerting an +M effect (depending on the second substituent in the acetylene) together with an −I effect contributes much to the

electron density distribution in the molecule. Therefore, the polarization of the triple bond in (organylthio)chloroacetylenes is possible in two directions:

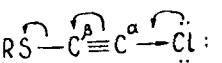
SCHEME 7

In the IR spectra of (organylthio)chloroacetylenes an absorption band of medium intensity corresponding to be triple bond is observed at 2150–2170 cm^{-1}. It should be noted that the triple bond frequency does not depend much on the nature and structure of the substituent R of (organylthio)chloroacetylenes. The upfield $\nu_{C\equiv C}$ shift for (organylthio)acetylenes[51] may be due to both differences in the elastic properties of the C≡C bond and effects of the kinematic and dynamic parameters of the C–CCl bond. Based on calculations[52] of normal vibrations of monosubstituted acetylenes of the type X–C≡CH with X = Cl, Br, I the C–X bond is shown to participate in the triple bond vibrations (approximately by 60% in amplitude). This suggests that the higher $\nu_{C\equiv C}$ in (organylthio)chloroacetylenes may be explained in terms of a specific donor effect of the chlorine atom and an acceptor effect of the SR group.

The ^{13}C NMR spectra of the compounds studied are characterized by the presence of two signals corresponding to the acetylenic carbons (see Table 2) which, when compared with the analogous signals of (ethylthio)acetylene ($C_2H_5SC^1 \equiv C^2H$, δC^1 = 72.8 ppm, δC^2 = 81.6 ppm), reveal considerable electron counterpolarization effects.[53]

In the ^{13}C NMR spectra of (alkylthio)chloroacetylenes run without proton decoupling, the sp-hybridized C signal lying in the upper field is split into a triplet with J = 6.1 Hz. The signal of the second acetylenic carbon is not split which allows it to be assigned to the atom adjacent to the chlorine.

Carbon-13 chemical shifts are known to be a fairly adequate measure of the general charge density on the resonating carbon nucleus. From this point of view the ^{13}C chemical shifts of the acetylenic carbons in (organylthio)chloroacetylenes have been compared with the ^{13}C chemical shifts in alkylhaloacetylenes.[54] The decrease in C^{α}-shielding as compared with that for C^{β} in the (organylthio)chloroacetylenes is likely to be due to competing pπ-bonding between the sulfur atom and the triple bond. The chlorine lone pair is also involved in the conjugation with the multiple bond:

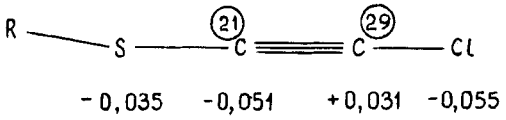


SCHEME 8

As seen by X-ray fluorescence spectroscopy (Table 3) the chlorine atom in (organylthio)chloroacetylenes is negatively charged which makes it a hardly possible site of nucleophilic attack.

The analysis of CNDO/2 (spd-basis set) quantum chemical calculations carried out with the simplest perturbation theory method approximated for an isolated molecule[55]

indicates stereoselectivity of nucleophilic attack on compound **1**. The results of these quantum chemical calculations are presented in the molecular diagram below:



SCHEME 9

The following bond lengths of the linear fragment of RSC≡CCl (R = C_2H_5, C_6H_5) were chosen: S–C = 1.85 Å, C≡C = 1.25 Å, C–Cl = 1.78 Å.[56] In the calculations the valence angle R–S–C was taken to be 128°. The substitutent R framework and the linear chain SC≡C–Cl were arranged in the same plane. On the molecular diagram the numerals below the atoms indicate the effective charge on the atom, the encircled numerals correspond to the AO contribution (%) to the LOMO. From the molecular diagram analysis it follows that for reactions taking place in the plane of the molecular framework it is the acetylenic carbon atom attached to the chlorine atom that is the preferred site of attack for both hard and soft reagents. However, in the case of charge-controlled reactions the dominating terms in the perturbation theory equation[57] are those with orbital populations corresponding to the direction of attack, $q_{px}^{C\alpha,\beta}$ and $q_{pz}^{C\alpha,\beta}$, the values of which are $q_{px}^{C\alpha} = 0.082$, $q_{px}^{C\beta} = 0.028$, $q_{pz}^{C\alpha} = -0.017$, $q_{pz}^{C\beta} = 0.052$. Therefore, when the nucleophilic attack takes place orthogonally the hard site is reactive and hard nucleophiles preferably attack the carbon atom bound to the sulfur atom.

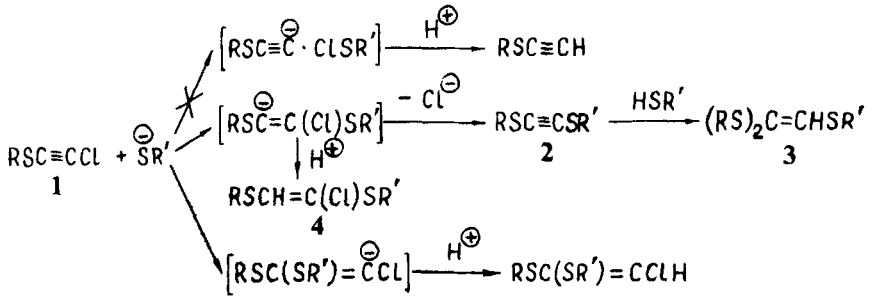
Thus, the chemical shifts of the triple bond carbon atoms in ^{13}C NMR, IR, and X-ray fluorescence spectroscopy, as well as quantum chemical calculations indicate electronic interactions involving the organylthio group, the π-electrons of the triple bond and the p-electrons of the chlorine atom. The organylthio group acts as an acceptor of electron density with the minimum at the carbon atom bound to the chlorine atom which makes it the most favorable site for nucleophilic attack.

III. REACTIVITY

3.1 Reactions with Thiolate Anions

The reaction of haloacetylenes with thiolate anions has been studied in detail and found wide application in organic synthesis.[3,5,27,28,29,30,31,58] The reaction of (organylthio)-chloroacetylenes **1** with thiolate anions parallels the nucleophilic substitution of the halogen in haloacetylenes with the anion attacking the carbon atom adjacent to the chlorine (unlike the reaction of ClC≡CH with RSH[29]). This is implied by the formation of 1-chloro-1,2-di(organylthio)ethenes **4** and the absence of terminal acetylenes when the reaction is carried out in a protic solvent.

Symmetrically substituted alkenes and alkynes were believed until recently not to be subjected to phosphorylation with PCl_5. Acetylenic sulfides **2**, however, react readily with phosphorus pentachloride to form organyltrichlorophosphonium hexachlorophosphates **5** in quantitative yield. Treatment of the adducts **5** with sulfur dioxide leads



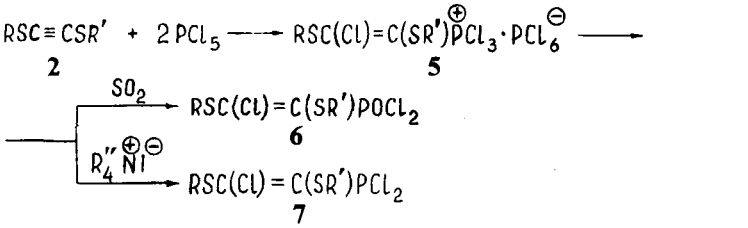
(3)

$R = C_2H_5$, C_3H_7, i-C_3H_7, n-C_4H_9, C_6H_5, p-$CH_3C_6H_4$;

$R' = C_2H_5$, i-C_3H_7, n-C_4H_9, C_6H_5, $C_6H_5CH_2$.

SCHEME 10

to dichlorides of alkenephosphonic acids **6** and their reduction with a tetraorganylammonium iodide affords the corresponding alkenyldichlorophosphines **7**:[41,59]



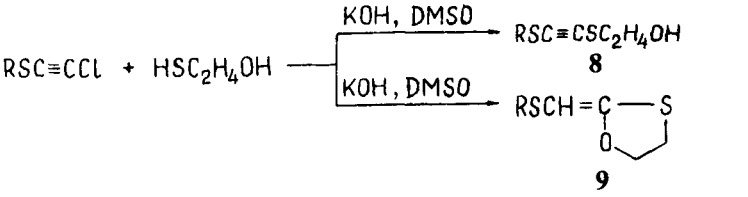
(4)

$R = C_2H_5$, C_3H_7, n-C_4H_9, i-C_4H_9, C_6H_5, p-$CH_3C_6H_4$;

$R' = C_2H_5$, C_3H_7, n-C_4H_9, i-C_4H_9, C_6H_5, $R'' = n$-C_4H_9.

SCHEME 11

The reaction of (organylthio)chloroacetylenes **1** with 2-mercaptoethanol has been carried out in the presence of alkali in DMSO. With an equimolar ratio of chloroacetylene, alkali, and 2-mercaptoethanol only (organylthio)ethynyl (2-hydroxyethyl) sulfides **8** are formed whereas with two-fold excess of alkali the products of an intramolecular cyclization, the 2-(organylthiomethylene)-1,3-oxathiolanes **9**, are obtained:[60]



(5)

SCHEME 12

With charged bifunctional nucleophiles the softer anion ($HOC_2H_4S^-$ > $HSC_2H_4O^-$) rather than the more basic one ($HSC_2H_4O^-$ > $HOC_2H_4S^-$) is most reactive towards the reacting carbon atom of an (organylthio)chloroacetylene.

The interaction of chloroacetylenes **1** with 2-mercaptoethylamine in DMSO at 20–22 °C and in an equimolar ratio of the reagents leads to organylthioethynyl 2-aminoethyl sulfide hydrochlorides 10 the IR spectra of which contain a triple bond absorption band at 2080–2090 cm^{-1} and the ^1H NMR spectra signals of the NH_2 protons (8 ppm), SCH_2, and NCH_2 groups (3.3 ppm). There are no signals corresponding to the protons of vinyl, SH, and ketenimine (CH=C=N) groups.[61]

$$RSC{\equiv}CCl + HSC_2H_4NH_2 \longrightarrow \underset{\mathbf{10}}{RSC{\equiv}CSC_2H_4NH_2{\cdot}HCl} \quad (6)$$

SCHEME 13

This reaction course is explained by the formation between the mercapto and amino groups of hydrogen bonds which reduces the NH_2 group basicity. The accompanying redistribution of electronic density in 2-mercaptoethylamine results in the electrophilic center in the chloroacetylenes **1** being attacked by the sulfur atom to afford acetylenic sulfides. The HCl liberated prevents the addition of the amino group to the triple bond of the alkynyl sulfide formed.

3.2 Reactions with Ammonia and with Primary, Secondary and Tertiary Amines

It is known[4,5,12,62,63] that in reactions of haloacetylenes with nucleophiles possessing mobile hydrogen atoms the substitution of halogen usually involves rearrangement with migration of hydrogen and multiple bonds.

(Organylthio)chloroacetylenes have been shown[64] not to react with gaseous ammonia. With sodium amide in liquid ammonia, however, they form (organylthio)acetonitriles **11** in quantitative yield:

$$\underset{\mathbf{1}}{RSC{\equiv}CCl} + NaNH_2/NH_3 \longrightarrow \underset{\mathbf{11}}{RSCH_2C{\equiv}N} \quad (7)$$

SCHEME 14

The reaction of acetylenes **1** with primary alkylamines gives hydrochlorides of (organylthio)acetic acid *N,N'*-dialkylamidines **12**. This can be explained as follows: nucleophilic substitution of the chlorine atom in **1**, prototropic isomerization, and addition of the second amine molecule to the ketenimine multiple bond:

$$\underset{\mathbf{1}}{RSC{\equiv}CCl} \xrightarrow{H_2NR'} \left[RSC{\equiv}\overset{\oplus}{C}NH_2R'\cdot\overset{\ominus}{Cl}\right] \longrightarrow \left[RSCH{=}C{=}\overset{\oplus}{N}HR'\cdot\overset{\ominus}{Cl}\right]$$
$$\xrightarrow{H_2NR'} \underset{\mathbf{12}}{RSCH_2{-}C{=}NR'\ \ \overset{\oplus}{N}H_2R'\cdot\overset{\ominus}{Cl}} \quad (70\text{-}80\,\%) \quad (8)$$

SCHEME 15

The suggested mechanism is in agreement with the fact that in the case of sterically hindered amines (such as *t*-butylamine) the only reaction products are (organylthio)ketenimines **13** to which it was impossible to add a second *t*-butylamine molecule, evidently due to steric hindrance at the nitrogen atom:

$$RSC{\equiv}CCl + H_2NC_4H_9\text{-}t \xrightarrow[-HCl]{} \underset{\mathbf{13}}{RSCH{=}C{=}NC_4H_9\text{-}t} \xrightarrow{H_2NCH_3}$$
$$\longrightarrow \underset{\mathbf{14}}{RSCH_2\text{-}\overset{\displaystyle NHCH_3}{\overset{|}{C}}{=}NC_4H_9\text{-}t} \xrightarrow{HCl} \underset{\mathbf{15}}{(RSCH_2\text{-}\overset{\displaystyle NHCH_3}{\overset{|}{C}}{=}NC_4H_9\text{-}t)\cdot HCl} \qquad (9)$$

SCHEME 16

At the same time, ketenimines **13** readily add methylamine to form (organylthio)acetic acid amidines **14**. The latter give with hydrogen chloride stable hydrochlorides **15**.[64]

In the reaction of chloroacetylenes **1** ethanolamine, along with chlorine substitution and triple bond migration, one can observe intramolecular cyclization leading to 2-[(organylthio)methyl)]-4,5-dihydro-1,3-oxazoles **16**:[65]

$$RSC{\equiv}CCl + H_2NC_2H_4OH \longrightarrow \left[RSC{\equiv}\overset{\oplus}{C}\overset{\ominus}{N}H_2C_2H_4OH\cdot Cl\right] \xrightarrow[-HCl]{}$$
$$\longrightarrow \left[RSCH{=}C{=}NC_2H_4OH\right] \longrightarrow \underset{\mathbf{16}}{RSCH_2\text{-}\overset{\displaystyle O}{\overset{|}{C}}{=}N\text{-}CH_2CH_2\text{-}O} \qquad (10)$$

SCHEME 17

As is well known, the reactions of most haloacetylenes with secondary amines do not lead to *N*-substituted acetylenes.[5,36,66-68] At the same time, haloacetylenes with strongly electron-withdrawing substituents are susceptible to nucleophilic substitution by secondary amines to form ynamines.[69-74]

(Organylthio)chloroacetylenes **1** readily react with secondary amines to afford [(organylthio)ethynyl]amines **17** in 50–80% yield:[75-77] The reactivity of amines towards

$$RSC{\equiv}CCl + HNR'R'' \xrightarrow[20\text{-}22\ ^\circ C]{(C_2H_5)_2O} \underset{\mathbf{17}}{RSC{\equiv}CNR'R''} \xrightarrow{H_2O} \underset{\mathbf{18}}{RSCH_2C(O)NR'R''} \qquad (11)$$

SCHEME 18

(organylthio)chloroacetylenes **1** depends on their basicity. Diphenylamine, *N*-methylaniline, *N*-ethylaniline, and imidazole fail to react with acetylenes **1** due to the low basicity of the amino group, whereas piperazine reacts *via* only one amino group. When reaction

(11) is carried out in the presence of water (organylthio)acetic acid amides **18** are formed. The structure of **18** was proven by independent synthesis *via* hydration of [(ethylthio)ethynyl]-morpholine in alkaline medium.[75]

The reaction of chloroacetylenes **1** with secondary 2-hydroxyethylamines leads only to acid amides **19**.[75] This provides evidence for the reaction of compounds **1** with β-aminoalcohols to involve the formation of ynamines which are very easily hydrated in the presence of alcohols and hydrogen halides thus impeding intramolecular cyclization of the intermediate ynamine:

$$RSC{\equiv}CCl + R'NHC_2H_4OH \xrightarrow[-HCl]{(C_2H_5)_2O} [RSC{\equiv}CN(R')C_2H_4OH] \xrightarrow{R'NHC_2H_4OH,\ HCl} RSCH_2C(O)NR'C_2H_4OH + R'NHC_2H_4Cl \quad (12)$$

19 (50–60%)

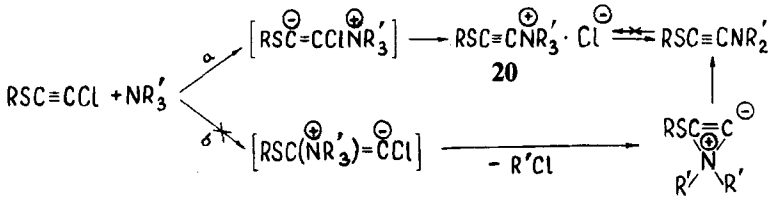
SCHEME 19

(Organylthio)chloroacetylenes **1** readily react with trialkylamines in diethyl ether at 20–22 °C to give stable water-soluble (organylthioethynyl)trialkylammonium chlorides **20** in 95–97% yield:[65,78]

$$\underset{\mathbf{1}}{RSC{\equiv}CCl} + NR'_3 \longrightarrow \underset{\mathbf{20}}{RSC{\equiv}C\overset{\oplus}{N}R'_3 \cdot Cl^{\ominus}} \quad (13)$$

SCHEME 20

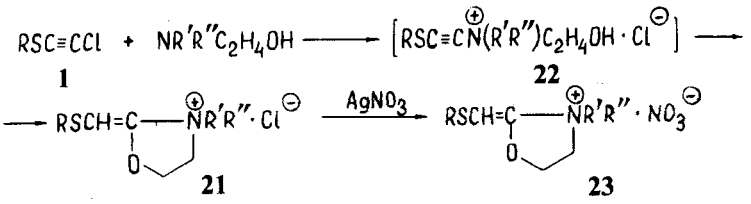
Investigations of the reaction mechanism were also performed with ethanol as a proton source. Also in this case the salts **20** were formed, (alkylthio)acetylenes being absent, which excludes the possibility of the chlorine atom being attacked by the nucleophile. When the tertiary amine attacks the sp-hybridized acetylenic carbon attached to the sulfur atom (route 'b', Scheme 21) it is not possible to obtain the salt **20** since the tertiary amine is a stronger nucleophile than ynamines.



SCHEME 21

The reaction of chloroacetylenes **1** with tertiary 2-hydroxyalkylamines in ether at 20–22 °C leads to 2-[(organylthio)-methylene]-3,3-dialkyl-1,3-oxazolidinium chlorides

21. The simplicity and high yields (90–98%) of the above reaction allows it to be employed as a convenient preparative route to **21**:[78–80]



(14)

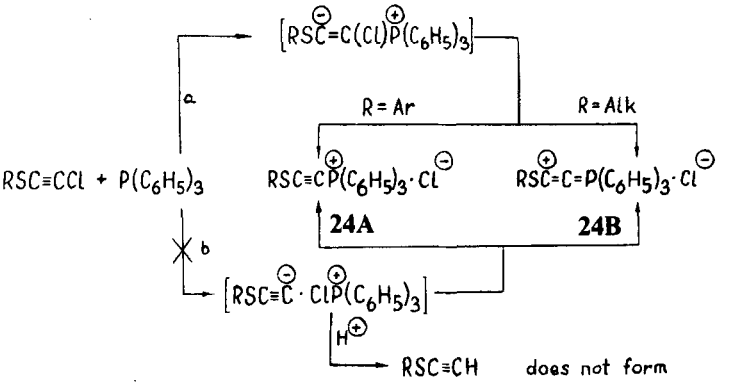
SCHEME 22

As shown by IR and UV spectroscopy compounds **21** exist as two conformers with *s*-cis and gauche orientation of the organothio group relative to the double bond, the gauche conformer being predominant.[81] The formation of an acyclic intermediate **22** was detected by IR spectroscopy. The salt character of compounds **21** reveals itself in their water solubility and the possibility of chloride-nitrate exchange to form the salts **23**.

3.3 Thioethynylation of Tertiary Phosphines and of Trialkyl Phosphites

Organylphosphorus compounds containing a thioethynyl group are of practical interest as potential bioactive substances. The substitution of the chlorine atom in chloroacetylenes by phosphorus-containing nucleophiles represents one possible route to the above compounds.

The present authors have carried out the reaction[45] of (organylthio)chloroacetylenes **1** with triphenylphosphine to afford [(organylthio)ethynyl]triphenylphosphonium chlorides **24** in quantitative yield. With alkyl substituents attached to the sulfur atom the formation of a ketenephosphonium structure of type **B** (Scheme 23) takes place as shown by IR and ^{31}P NMR spectroscopy. The IR spectra of compounds **A** contain an absorption band of the triple bond at 2100 cm^{-1}, those of compounds **B** an absorption band at 1980 cm^{-1} corresponding to the C=C=P bond.



(15)

SCHEME 23

The experimental data obtained when the reaction was carried out in ethanol suggest a reaction mechanism analogous to that of the nucleophilic chlorine substitution in the interaction of chloroacetylenes **1** with tertiary amines, which involves nucleophilic attack at the carbon atom bound to the chlorine atom.

(Organylthio)chloroacetylenes **1** react readily with trialkyl phosphites to form in good yields the normal products of the Arbuzov rearrangement, [(organylthio)ethynyl]phosphonates **25**:[45,82]

$$\underset{\mathbf{1}}{RSC{\equiv}CCl} + P(R'O)_3 \longrightarrow \underset{\mathbf{25}\ (57\text{-}72\%)}{RSC{\equiv}CP(O)(OR')_2} \qquad (16)$$

SCHEME 24

The similarity of the chemical shifts and the spin–spin coupling constants in the ^{31}P NMR spectra of **25** to those of $RC{\equiv}CP(O)(OR)_2$ with R = Alk[12] indicates an insignificant polarizing effect of the organylthio group in the acetylenes **25**.

From the above-said it follows that the reaction of (organylthio)chloroacetylenes with di- and trialkylamines, trialkylphosphines, triarylphosphines and alkali metal thiolates in an aprotic solvent proceeds by nucleophilic substitution of the chlorine atom and presents a new general route to otherwise difficultly accessible derivatives of acetylenic sulfides with $RSC{\equiv}CX$ where X = $N(Alk)_2$, $^+NAlk_3 \cdot Cl^-$, $P(O)(OR)_2$, $^+PAr_3 \cdot Cl^-$, SAr, SAlk, SC_2H_4OH, and $SC_2H_4NH_2 \cdot HCl$.

3.4. (Organylthio)chloroacetylenes in Reactions with Oxygen-Containing Nucleophiles

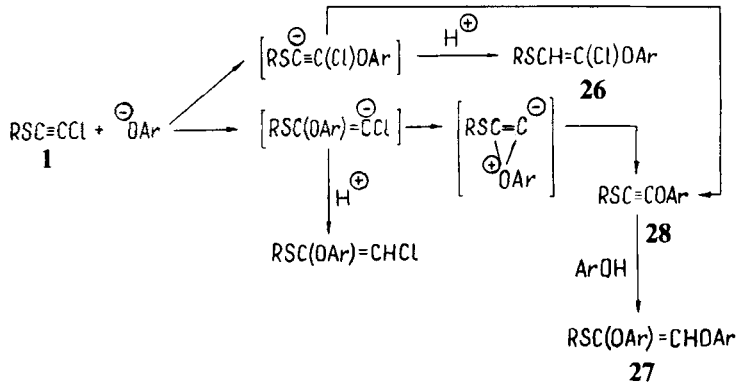
Japanese scientists[2] have described the reaction of 2,2-dichlorovinyl organyl sulfides with potassium *t*-butoxide in tetrahydrofuran to (organylthio)chloroacetylenes. They have been isolated and characterized. The *t*-butoxide anion has been shown capable of substituting the chlorine atom in chloroacetylenes to form acetylenic ethers:

$$RSCH{=}CCl_2 \xrightarrow{t\text{-}BuOK} [RSC{\equiv}CCl] \xrightarrow{t\text{-}BuO^{\ominus}} RSC{\equiv}COBu\text{-}t \qquad (17)$$

SCHEME 25

We have found that the reaction of chloroacetylenes **1** with alkali metal phenoxides in DMSO gives a mixture of two products, 1-chloro-1-aryloxy-2-(alkylthio)ethenes **26** and 1,2-diaryloxy-2-(alkylthio)ethenes **27**; their formation may be represented as in Scheme 26.

The preparation of the diaryloxyethenes **27** provides evidence for the formation of the acetylenic adducts **28**, followed by addition of phenol to the latter. However, as shown by quantum chemical calculations (see Section 1), hard anionic nucleophiles are able to attack **1** in the direction orthogonal to the molecular plane at the carbon atom bound to the sulfur atom. Indeed, from the products of the reaction of (organylthio)chloroacetylenes **1** with alcohols in the presence of their sodium derivatives it was possible to isolate 1-alkoxy-1-(alkylthio)-2-chloroethenes **29** the formation of which can be



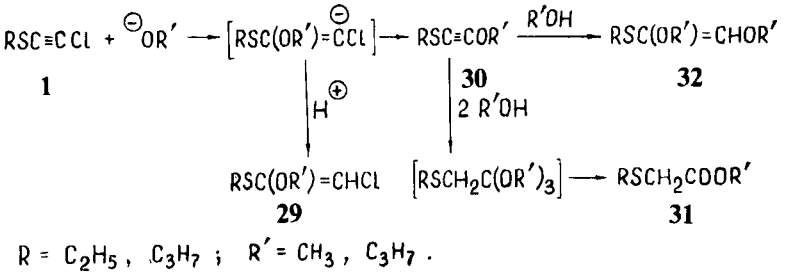
(18)

R = C_3H_7, n-C_4H_9, C_6H_5;

Ar = C_6H_5, p-ClC_6H_4, p-BrC_6H_4, p-FC_6H_4, m-$CH_3C_6H_4$.

SCHEME 26

explained by attack of the alkoxide anion at the sp-hybridized carbon atom attached to sulfur. Besides, acetylenic ethers **30** and the products of nucleophilic addition of alcohols **31** and **32** (Scheme 27) are present in the reaction mixture. The formation of the product **30** can be detected by IR spectroscopy.



(19)

R = C_2H_5, C_3H_7; R′ = CH_3, C_3H_7.

SCHEME 27

Thus, alcohols, thiols and phenols in the presence of their sodium or potassium derivatives are able either to substitute the chlorine atom in (organylthio)chloroacetylenes or to add regiospecifically to the triple bond. It has been established that the phenoxide and thiolate anions attack the acetylenic carbon attached to the chlorine atom wheras the alkoxide anions attack the carbon atom bound to the sulfur.

Systematic investigations of the reactivity of (organylthio)chloroacetylenes **1** have shown them to be highly active with respect to anionic and uncharged mono- and bifunctional nucleophiles and revealed a relationship between the direction of the attack and the nature of the attacking nucleophile. They also have provided new data on the mechanism of nucleophilic substitution of the halogen in activated haloacetylenes.

IV. CONCLUSION

In conclusion, it is necessary to emphasize that (organylthio)chloroacetylenes are new, promising sulfur-containing synthons with a wide range of reactivity. Their high activity in reactions with nucleophiles opens a synthetic route to S-, N-, P- and O-containing acetylenic and heterocyclic compounds.

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