tensive programme for the production of mineral fertilisers, weed-killers, chemical poisons, and other crop-protecting substances, in order to fulfil the country's economical requirements. It has been estimated that by 1970 the agricultural needs will amount to 70–80 million tonnes of mineral fertilisers, 800–900 thousand tonnes of insecticides, fungicides, and weed-killers. To meet these goals in the production of fertilisers the capacity of the existing plants must be increased by about 20 million tons and 55 new plants must be built, of which 28 are for nitrogeneous fertilisers, 19 for phosphate fertiliers, 6 are potash mines and 2 are for production of phosphate meal [19 for superphosphate and 2 for bone meal ? (Ed. of Translation)].

These goals will be achieved by speeding up the construction of new plants, as well as workshops and individual production units at existing factories. In addition to the increased volume of production of fertilisers and chemical poisons for agricultural purposes their quality and range must also be improved.

At the moment a considerable proportion of the fertilisers supplied to agricultural undertakings are inadequate in terms of nutrient components; for example, of the potassium fertilisers about one-half are crude potassium salts. The situation is similar in the case of phosphate fertilisers.

In future the new plants will be producing mainly highly concentrated mixed fertilisers to enrich the soil with all the necessary nutrient substances in the required amounts and proportions.

The development of agricultural chemistry gives rise to new scientific problems, requiring profound and systematic research into the synthesis of the most effective mineral fertilisers, especially highly concentrated and complex ones, development of economical methods for their manufacture, production of optimal mixtures of fertilisers for the main soil and climatic zones and the most important crops, as well as the production of new effective agents against weeds, pests, and crop diseases.

The Plenary Session has also outlined a comprehensive programme for the development of the manufacture of clothing, footwear, and other consumer goods based on products of the chemical industry. The target production of synthetic fibres for 1970 is 1.35 million tonnes. This will serve as a basis for qualitative changes in the textile industry, with a changeover to extensive production of knitted fabrics, artificial leather goods and non-woven fabrics, with consequent improvement in the quality of the goods, greater efficiency of production and reduction of cost.

The target production of plastics and synthetic resins for 1970 is 3.5–4 million tonnes.

Plastics should largely replace non-ferrous metals whenever it is economically and technologically possible; they should also be widely used for the manufacture of machine components and pipes, and for treating wood, especially for floor coverings, finishing materials, sanitary-technical equipment, etc.

An important goal put forward by the Plenary Session is the organisation of full-value replacements of raw food materials so that by 1967–1968 no grain, sugar, vegetable oils, or other foodstuffs will be used for technological purposes.

Among the tasks of the fine chemicals industry, also considered by the December Plenary Session, are the creation of a pure reagents industry and production of super-purity metals and various equipment needed for further scientific and industrial developments.

An extensive development of theoretical and applied chemical research has been outlined for Soviet science.

Having directed the work of scientific research organisations towards the creation of new materials and the development of more suitable, simple, and economical technological processes, the Plenary Session of the Central Committee of the Soviet Communist Party paid particular attention to the need for completing promptly the development of production methods, of more effective fertilisers and chemical pesticides for crops, new plastics, synthetic fibres, synthetic rubbers, dyestuffs, lacquers, pigments, and other chemical products.

Special stress was laid on the need to ensure rapid incorporation of scientific advances into industry and to attain the highest technological levels in the chemical industry.

It is also most important to develop the fundamentals of chemical technology and to create methods of small-scale testing and calculating technological processes with the help of computers.

The programme for the rapid development of the chemical industry, agriculture, and light industry adopted by the December Plenary Session is of the utmost national importance, with enormous bearing upon communist construction, economic development and reinforcement of the country's might.

The rewarding task of all workers in chemical science and industry is the creative and prompt fulfilment of all the goals of the development of chemical science and the incorporation of chemistry into the national economy.

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ADDITION OF ALCOHOLS AND MERCAPTANS TO COMPOUNDS WITH TRIPLE BONDS

M. F. Shostakovskii, A. V. Bogdanova, and G. I. Plotnikova

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I. INTRODUCTION

Reactions involving the addition of alcohols and mercaptans to acetylenes have been known for a long time. Investigation of the conditions in which these reactions take place led to the development of a method of vinylating alcohols and mercaptans and the preparation of vinyl ethers and sulphides. Apart from acetylene, its various monosubstituted derivatives have been used as vinylating agents.

In recent years many studies have been made on the reaction of diacetylene with various compounds containing reactive hydrogen, including alcohols and mercaptans, which led to the synthesis of ethynyl vinyl and butadienyl ethers and sulphides.

The increasing interest of organic chemists in diacetylene has arisen because this compound is formed as a side-product in the preparation of acetylene by thermal cracking of natural gas; its utilisation as a new starting material is thus one of the urgent problems of synthetic chemistry. The available literature data on the addition of alcohols and mercaptans to compounds containing a triple bond have not been surveyed so far, which makes it difficult to become familiar with the investigations which have been made in the field of acetylene derivatives, and in particular diacetylene. We therefore felt it was timely to review studies dealing with additions of alcohols and mercaptans to acetylenes, diacetylenes, and some of their derivatives.

II. ADDITION OF ALCOHOLS AND MERCAPTANS TO ACETYLENES

1. Addition of Alcohols to Acetylene

In his study of the isomerisation of substituted acetylenes on heating with alcoholic alkali, Favorskii[1] showed that alcohols add on to substituted acetylenes, forming vinyl ethers. A synthesis of vinyl ethers by vinylating acetylene with alcohols was developed on the basis of this reaction[2,3].

At present this is the principal industrial method of manufacturing a wide variety of vinyl ethers in the USSR. The vinylation of alcohols with acetylene is carried out in an autoclave under pressure, at elevated temperatures, and in the presence of strongly alkaline catalysts. In recent years this reaction has been extended to many different alcohols, phenols, naphthols, and other compounds containing reactive hydrogen[3,4].

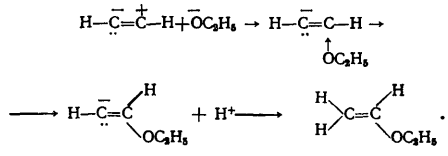
It is noteworthy that in the vinylation of alcohols and phenols some investigators[4] have used acetylene diluted with nitrogen, which in their view prevented explosions and did not interfere with the main reaction. However, Shostakovskii and coworkers[3] showed that dilution of acetylene with nitrogen is not necessary and in many cases slows down the reaction and necessitates an increase in temperature, which gives rise to side-reactions.

The rate of vinylation significantly depends on the structure of the initial alcohol. Holly[5] found that it falls sharply on going from a primary to a tertiary alcohol. For example, in the vinylation of secondary and tertiary alcohols it is necessary to use potassium alkoxides, and not inorganic alkali which causes resinification of the products.

Phenols, cresols, and naphthols are vinylated under more severe conditions than aliphatic alcohols: a larger amount of alkali, the presence of water, and a higher temperature are necessary, probably because of the acidic properties of phenols. Alizarin, for example, has pronounced acidic properties and is not vinylated under the usual conditions[6].

Optimum conditions have been found for the preparation in good yield of vinyl phenyl, vinyl cyclohexyl, vinyl 2-decalyl, and vinyl 2-naphthyl ethers[7-9]. The vinylation of phenols requires the presence of a large amount of water which prevents the thermal polymerisation of the vinyl ethers[8] and favours the formation of phenoxide ions which accelerate the vinylation[10]. The role of water as a factor favouring the ionisation of phenols during their vinylation has also been considered by Ban *et al.*[11], who confirmed that the reaction depends on the concentration of the $C_6H_5O^-$ ions. They investigated in detail the pH of the medium required for the vinylation of phenols, cresols, and *p*-nitrophenol in aqueous solutions in the presence of alkali, and found that the nature of the alkaline reagent does not affect the rate of reaction provided that the optimum pH is maintained; the reaction does not take place in the absence of alkali. On this basis, they believe, together with Reppe[4] and Miller[10,12], that vinylation of alcohols is a nucleophilic addition reaction.

In view of the electrophilic activity of the triple bond, Müller put forward the following mechanism[13]:



Among recent investigations dealing with the kinetics of vinylation of various alcohols with acetylene in the presence of metal alkoxides are those of Japanese workers[14,15], who proposed a mechanism for this reaction, involving the formation of an intermediate complex of the alcohol, alkoxide, and acetylene, which then breaks down and KOH is liberated under the reaction conditions. However, these workers say nothing about the nature of these complexes.

2. Addition of Mercaptans to Acetylene

Syntheses based on acetylene and mercaptans were first described by Reppe[4,16] in a number of patents, which showed that aliphatic, aromatic, and hydroaromatic mercaptans are vinylated under conditions similar to those

used in the vinylation of alcohols and phenols, the reaction resulting in the formation of the corresponding vinyl sulphides, which can be isolated in good yields[17]:

$$CH{\equiv}CH+RSH \longrightarrow CH_2{=}CH{-}SR.$$

Thus in the reaction with acetylene diluted with nitrogen (2:1) in the presence of butanol and solid KOH at 160°, thiophenol is almost quantitatively converted into vinyl phenyl sulphide in 12 h. In the vinylation of mercaptans, as in the case of alcohols, Reppe used nitrogen, which in the view of Shostakovskii *et al.*[18-23] hinders the reaction.

According to Reppe[4], the reaction of mercaptans with acetylenes takes place as follows:

$$RSH+KOH \longrightarrow RSK+H_2O$$

$$RSK \xrightarrow{CH{\equiv}CH} [RS{-}CH{=}CHK] \xrightarrow{RSH} RS{-}CH{=}CH_2+RSK.$$

Later, this reaction was studied in detail by Shostakovskii and coworkers[18-24], who found optimum conditions for the preparation of vinyl sulphides of different structures. They observed that such conditions for this reaction depend on the structure of the initial mercaptan, and investigated the effect of temperature, catalyst concentration, and various solvents and diluents on the course of the reaction. Particular attention was paid to inhibiting the secondary reaction between the vinyl sulphide formed and the mercaptan, which under the reaction conditions shows anti-Markovnikov addition:

$$RS{-}CH{=}CH_2+RSH \longrightarrow RS{-}CH_2CH_2SR.$$

They showed[21] that a good yield of vinyl sulphide may be obtained in the presence of an excess of acetylene, and recommended dioxan[20], methanol, butanol, formals[25], etc., as solvents. Apart from these, Schneider[26] used aqueous solutions of weak bases for the preparation of vinyl thioethers. Alcohols may be used as solvents in the synthesis of vinyl sulphides because mercaptans are much more readily vinylated.

The higher activity of the mercapto-group compared with the hydroxyl in the vinylation reaction is well illustrated by the reaction of monothioethylene glycol with acetylene[22], which involves only the mercapto-group and results in the formation of 2-hydroxyethyl vinyl sulphide:

$$HO{-}CH_2{-}CH_2{-}SH+CH{\equiv}CH \longrightarrow HO{-}CH_2{-}CH_2{-}S{-}CH{=}CH_2.$$

Phenylacetylene undergoes an exothermic reaction with mercaptoethanol in the presence of catalytic amounts of alkali and here too only the mercapto-group is involved[27]:

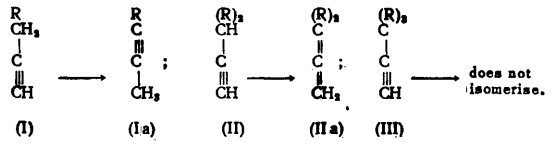
$$C_6H_5C{\equiv}CH+HS{-}CH_2{-}CH_2{-}OH \longrightarrow C_6H_5{-}CH{=}CH{-}S{-}CH_2{-}CH_2{-}OH.$$

Comparison of the conditions for the addition of alcohols and mercaptans to acetylene shows that in general they are similar for both types of reaction. However, the reaction of mercaptans with acetylene is not confined to the addition of one mercaptan molecule, so that the reaction mixture always contains a considerable amount of 1,2-alkylthioethanes. The reaction of acetylene with mercaptans in the presence of free-radical initiators at 130° at a pressure of 13–17 atm in an autoclave has been described in a recent communication[28]. It is suggested that the alkylthio- or arylthio-radical RS$^{\cdot}$ adds on to the acetylene molecule with the formation of a new double-bonded radical, RS–CH=$\dot{C}$H. This radical is stabilised by reaction with a mercaptan molecule, in which the alkylthio-radical is liberated, etc:

$$RS{-}CH{=}\dot{C}H+RSH \longrightarrow RS{-}CH{=}CH_2+RS^{\cdot}.$$

3. Addition of Alcohols to Substituted Acetylenes

The addition of alcohols to substituted acetylenes was first investigated by Favorskii[1] and described in his series of papers on the mechanism of isomerisation of hydrocarbons. Investigating the reaction of various substituted acetylenes (I), (II), and (III) with alcoholic alkali, Favorskii found that monosubstituted acetylenes (I) are then isomerised to disubstituted acetylenes (Ia), disubstituted acetylenes (II) are isomerised to allenes (IIa), whereas acetylene with a tertiary substituent (III) does not isomerise under these conditions.



(I) (Ia) (II) (IIa) (III)

Favorskii[1] also discovered that reaction of methylacetylene with alcoholic potassium hydroxide results in the formation of ethyl isopropenyl ether:

$$CH_3{-}C{\equiv}CH+C_2H_5OH \longrightarrow CH_3{-}\underset{\displaystyle OC_2H_5}{\underset{|}{C}}{=}CH_2.$$

and noted that the reaction involved the isomerisation of methylacetylene to allene:

$$CH_3{-}C{\equiv}CH \rightleftarrows CH_2{=}C{=}CH_2.$$

Shostakovskii *et al.*[29-34] investigated in detail the conditions of the reaction of methylacetylene with other alcohols and phenols, paying particular attention to the equilibrium between methylacetylene and allene. They made a special study of the behaviour of allene under the conditions of this reaction and found that allene, without even a trace of methylacetylene, isomerises almost quantitatively at 200° in 50% potassium hydroxide solution to methylacetylene, which was isolated as the acetylide. Frank-Kamenetskii and Markovich[35] established that at 200° this equilibrium is displaced towards methylacetylene to the extent of 90%.

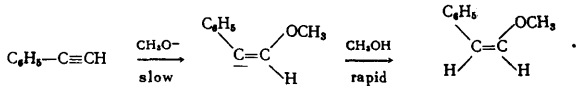
On the basis of this finding and their own experimental results, Shostakovskii *et al.*[29] showed that this temperature is most favourable for the synthesis of isopropenyl ethers from alcohols and methylacetylene. Furthermore, they found that allene or its mixture with methylacetylene can also be used for vinylation. Using various alcohols and phenols, they synthesised different α-substituted vinyl ethers[30-33] and noted that the reaction of alcohols with methylacetylene requires more severe conditions than that with acetylene.

Reactions involving addition of alcohols to substituted acetylenes containing electron-acceptor groups are particularly interesting[36]. In contrast to alkyl-substituted acetylenes such as methylacetylene, in this case the alkoxy-group of the alcohol adds to the β-carbon atom of the substituted acetylene. Thus phenylacetylene readily reacts

with different alcohols in the presence of alkali at 130–140°, forming the corresponding β-alkoxystyrenes which can be isolated in good yield[10,12,37,38]:

$$R'-C\equiv CH+ROH \longrightarrow R'-CH=CH-OR.$$

According to Miller and Shapenko[12], this too is an ionic nucleophilic reaction which can take place stereospecifically with formation of the *cis*-isomer:



Nitrophenylacetylenes add to alcohols by this mechanism even more vigorously[39]:

$$p\text{-}NO_2C_6H_4-C\equiv CH+ROH \longrightarrow p\text{-}NO_2C_6H_4-CH=CH-OR.$$

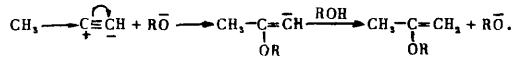
Another substituted acetylene of this type is trifluoromethylacetylene which undergoes an exothermic reaction with ethanol in an alkaline medium[36]:

$$CF_3-C\equiv CH+C_2H_5OH \xrightarrow{C_2H_5ONa} CF_3-CH=CH-OC_2H_5.$$

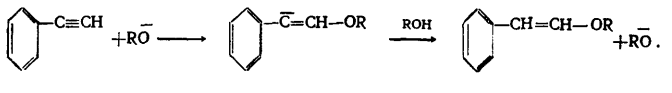
Alcohol adds similarly to the triple bond of the acetal of propiolaldehyde[40]:

$$CH\equiv C-CH(OC_2H_5)_2+C_2H_5OH \xrightarrow{C_2H_5ONa} C_2H_5O-CH=CH-CH(OC_2H_5)_2.$$

The presence of a substituent in the acetylene molecule polarises the triple bond in a way which depends on the electronic properties of the substituent. Electron-donor substituents displace the electrons, thereby polarising the molecule, in such a way that addition of an alkoxide ion to the α-carbon atom is favoured[29]:



Electron-acceptor substituents, on the other hand, polarise the triple bond in the opposite sense, which results in the addition of an alkoxide ion to the β-carbon atom:

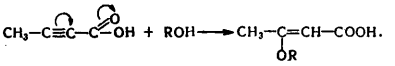


All the above applies to the addition of alcohols to monosubstituted acetylenes, *i.e.* to acetylenes having a reactive hydrogen atom. However, it is known that alcohols can also add to disubstituted acetylenes, which do not have a reactive hydrogen atom; for example, an alcohol can add on to tetrolic acid and acetals of tetrolaldehyde in an alkaline medium with formation of an unsaturated acid[41].

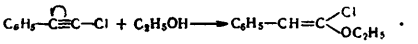
In an alkaline or acid medium in the presence of $HgSO_4$ an alcohol molecule can add to the dibutyl acetal of tetrolaldehyde with formation of an unsaturated ether-acetal:

$$CH_3-C\equiv C-CH(OR)_2+ROH \longrightarrow CH_3-C(OR)=CH-CH(OR)_2.$$

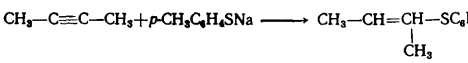
The mechanism of this reaction is probably similar to that of the nucleophilic addition of alcohols to monosubstituted acetylenes. Tetrolic acid has a carboxy-group which lowers the electron density at the triple carbon–carbon bonds thus making possible the addition of an alcohol molecule. The polarisation of the triple bond in this direction is facilitated by the presence of a methyl group:



For this reason, the absence of a reactive acetylenic hydrogen in 1-chloro-2-phenylacetylene does not prevent the addition of alcohol in an alkaline medium with formation of β-chloro-β-ethoxystyrene[42]:



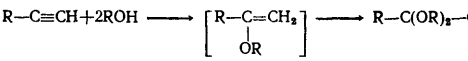
However, addition to the triple bond does not depend solely on the electronic properties of the adjacent substituents. The nature of the adding molecule has a considerable influence on the reaction. Powerful nucleophilic reagents, for example mercaptans, can add, in an alkaline medium, to disubstituted acetylenes without electron-acceptor substituents. The sodium salt of *p*-thiocresol readily adds on to but-2-yne[43]:



The rate of addition to the triple bond depends on how nucleophilic is the attacking ion[44], this property decreasing in the series[45]

$$\bar{S}Alk > \bar{O}Alk > \bar{O}Ar.$$

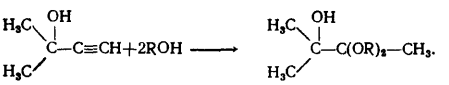
The reactions involving addition to various substituted acetylenes described above were carried out in the presence of alkaline catalysts. However, they have also been investigated under conditions of acid catalysis. Nieuwland and coworkers[46] showed that straight-chain primary alcohols add smoothly to acetylenic hydrocarbons, under the action of boron trifluoride and mercuric oxide, with formation of ketals, which can be isolated in high yields:



Under these conditions three molecules of alcohol add to vinylacetylene forming 1.3,3-trialkoxybutanes[47]:

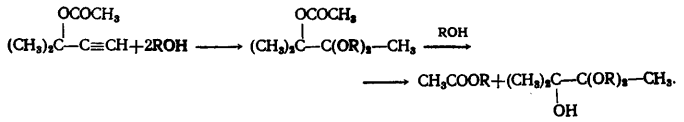
$$CH_2=CH-C\equiv CH+3ROH \longrightarrow RO-CH_2CH_2-C(OR)_2-CH_3.$$

These reactions involve a stage in which α-substituted vinyl ethers, which were not isolated, are formed. Nazarov[48] investigated in detail and described the addition of aliphatic alcohols to a tertiary ethynyl alcohol — ethynyldimethylmethanol. This addition takes place smoothly with formation of the ketal of acetyldimethylmethanol in 60–80% yield and also involves a stage in which the α-substituted vinyl ether is formed:

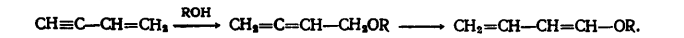


In the presence of BF_3 and HgO three molecules of methanol add to 1,1-dimethylprop-2-ynyl acetate and the latter is quantitatively converted into methyl acetate and

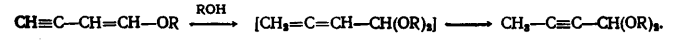
the ketal of acetyldimethylmethanol. The reaction involves two stages:



Among the compounds with the triple bond considered here, vinylacetylene occupies a special place because its multiple bonds are strongly conjugated, which according to Petrov [49] to a large extent determines the mode of the addition reactions. In a detailed review dealing with vinylacetylene and its homologues, Petrov interprets the reaction with alcohol as addition to the conjugated vinylacetylene system. In the presence of potassium alkoxide at the normal pressure alcohols undergo 1,4-addition with formation of 1-alkoxybutadienes, as a result of the subsequent allene-1,3-diene isomerisation [49,50]:



A molecule of alcohol adds to ethynyl vinyl ether on heating in the presence of alkali, acetals of but-2-yn-4-al being formed [51-53]:

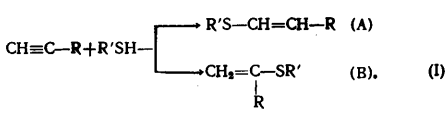


It appears that the 1,4-addition of the alcohol occurs as in the case of vinylacetylene.

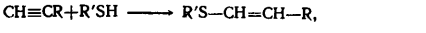
4. Addition of Mercaptans to Substituted Acetylenes

Most of the detailed investigations of the addition of mercaptans to substituted acetylenes have been made in the last decade, those of Truce and coworkers [43,54,55] being particularly important. Apart from its practical importance (this reaction serves as a basis for the development of a method of synthesing a wide variety of unsaturated sulphides), it is also of considerable theoretical interest. It made it possible to investigate the variation in the properties of the triple bond with the nature of the substituents in the acetylene, the influence of the mercaptan which adds on, and the influence of the mechanism on the mode of the reaction. Furthermore, by investigating the stereochemistry of the addition of mercaptans to substituted acetylenes, Truce and coworkers were able to find the conditions under which this reaction is stereospecific, to observe some of the rules governing it, and to formulate the so-called "rule of *trans*-nucleophilic addition" which is general for substituted acetylenes [55].

Depending on the reaction conditions, the addition of mercaptans to substituted acetylenes can take place differently, resulting in the formation of α- or β-substituted vinyl sulphides:

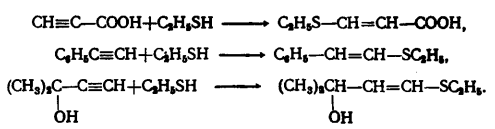


Truce and coworkers [43,54-60] showed that reactions with mercaptans and acetylenes having electron-acceptor substituents result in the formation of β-substituted vinyl sulphides, which were isolated in good yields:

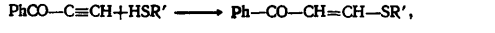


where R = C_6H_5, Cl, p-$CH_3C_6H_4$, COC_6H_5, COC_2H_5, or COOH, and R′ = p-$CH_3C_6H_4$, CH_3, C_6H_5, or mesityl. The reaction takes place when an alcoholic alkaline solution of acetylene and the mercaptan is boiled for 15–23 h. Truce and coworkers found that in some cases the reaction can occur in two ways, (A) and (B), for example, in the case of butylacetylene and p-thiocresol [56].

Other workers, who investigated the free-radical addition of mercaptans to acetylenes with electron-acceptor substituents, discovered that this too results in β-substituted vinyl sulphides. Thus Kohler and Potter [61] found that thiocresol undergoes an exothermic reaction with phenylacetylene forming 1-phenyl-2-tolylthioethylene which was isolated in quantitative yield. Blomquist and Wolinsky [62] showed that in the presence of benzoyl peroxide and on irradiation with ultraviolet light ethanethiol yields β-substituted vinyl sulphides when it reacts with phenylacetylene, propiolic acid, and 2-methylbut-3-yn-2-ol:

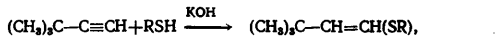


Ethynyl ketones [63], to which mercaptans add quantitatively with formation of β-substituted vinyl sulphides, can also be regarded as acetylenes with electron-acceptor substituents:



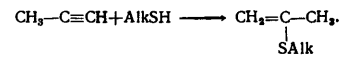
where R′ = Ph or C_2H_5.

Shostakovskii *et al.* [64] investigated the addition of mercaptans to t-butylacetylene in the presence of alkali, and discovered that the reaction also results in the formation of β-substituted vinyl sulphides:



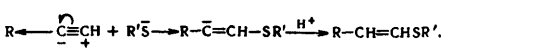
where R = C_2H_5, C_3H_7, or C_4H_9. According to these workers, this course of reaction can be explained either by steric hindrance due to the t-butyl group in the acetylene or by a radical mechanism of the process, since the reaction was carried out in an autoclave in the presence of atmospheric oxygen.

Addition of mercaptans to acetylene with electron-donor substituents yields α-substituted vinyl sulphides, *i.e.* the reaction is similar to the addition of alcohols [29] to these acetylenes. Shostakovskii *et al.* [65,66] studied the conditions of the reaction of methylacetylene and mercaptans in an alkaline medium and found that in the reaction with alkanethiols isopropenyl alkyl sulphide is the main reaction product:

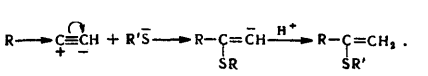


The addition of thiophenol to methylacetylene under these conditions results in the formation of two compounds, isopropenyl phenyl and propenyl phenyl sulphides, according to reactions (A) and (B). Shostakovskii *et al.* [66] were unable to suppress reaction (A) even in the presence of hydroquinone in the medium. On the basis of this reaction, they developed a method of synthesing isopropenyl alkyl (aryl) sulphides (temperature 120–170° depending on the mercaptan, elevated pressure, and alkaline medium).

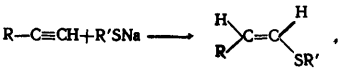
It may be assumed that the activation of the triple bond in this reaction results from the displacement of the electrons towards the electron-donor substituent, which facilitates nucleophilic attack on the triple bond:

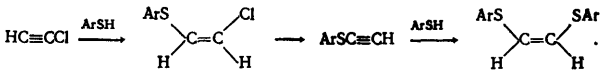


In the case of an electron-acceptor substituent, the electrons are displaced in the opposite direction, and α-substituted vinyl sulphides are formed:



Truce and coworkers [43,54-60] and Montanari [67-69] investigated the stereochemistry of the addition of mercaptans to acetylenes having different electronegative substituents. In their study of the addition of mercaptans to phenylacetylene, but-2-yne, chloroacetylene, and *p*-toluenesulphonylmesitylthioacetylene as examples they discovered [43,44,55] that the addition results in the formation of *cis*-isomers in 73–79% yield:



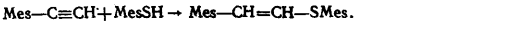


On the basis of a detailed examination of the reaction conditions, Truce and coworkers [43,54,57] concluded that the reaction of mercaptans with monosubstituted acetylenes having electronegative groups takes place stereospecifically under ionic conditions and obeys the *trans*-nucleophilic addition rule. In the view of these workers [43,57], the addition involves a stage in which an intermediate carbanion is formed:

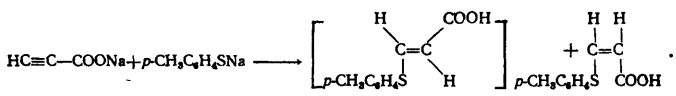


From a comparison of the results of these investigations, Truce [57] concluded that the formation of *cis*-products is the result of both electronic and steric factors.

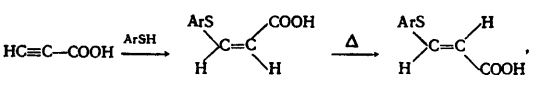
Attempts to circumvent the *trans*-nucleophilic addition rule by introducing the bulky mesityl group into acetylene and then adding to the product 2,4,6-trimethylbenzenethiol in an alkaline medium were unsuccessful [57]. *cis*-1-Mesityl-2-mesitylthioethylene was isolated as the principal product:



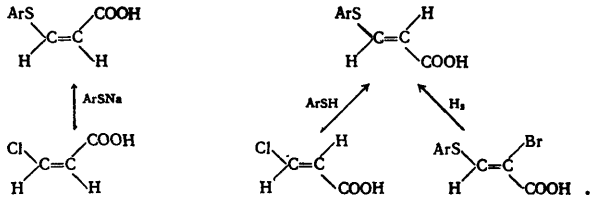
Truce and coworkers [54-57] thought that they had found a partial exception from the nucleophilic addition rule in the addition of *p*-thiocresol to sodium propiolate, but Montanari and coworkers [67-69] showed that this conclusion was erroneous:



The Italian workers [67-69] were the first to prepare *cis*- and *trans*-β-arylthioacrylic acids in different ways: by the reaction of thiophenol with propiolic acid



by nucleophilic substitution of the chlorine by arylthio-groups in *cis*- and *trans*-β-chloroacrylic acid, and by the reduction of *trans*-β-arylthio-α-bromoacrylic acid



The structure of the isomers was confirmed by infrared spectroscopy, reduction, isomerisation, nuclear magnetic resonance, and by the investigation of the analogous *cis*- and *trans*-isomers of acids derived from the corresponding chloroacrylic acids.

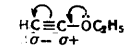
On the basis of a study of the reactivity of the triple bond in acetylene derivatives containing negatively charged groups in nucleophilic addition reactions, Truce and coworkers [58] arranged the substituents in the following sequence:

III. ADDITION OF ALCOHOLS AND MERCAPTANS TO ETHYNYL ETHERS AND SULPHIDES

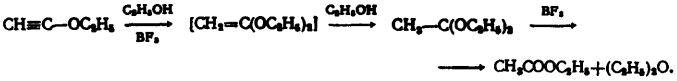
Ethynyl ethers and sulphides with the general formula CH≡C–OR(SR) may be regarded as monosubstituted acetylenes. It is interesting to investigate the reactivity of the triple bond in these compounds as a function of the nature of the heteroatom and the R radical.

1. Addition of Alcohols to Ethynyl Ethers and Sulphides

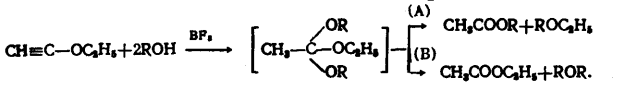
The effect of the nature of substituents adjacent to a multiple bond on its polarisation and consequent mode of reaction were discussed above. The direction of polarisation in ethynyl ethers may be represented as follows:



Arens and coworkers [70], who investigated the behaviour of ethynyl ethers and sulphides in electrophilic and nucleophilic addition reactions adopted this mechanism. In his investigation of the addition of alcohols and phenols to ethoxyacetylene, Arens found that this reaction is greatly facilitated by the presence of BF_3 in the reaction mixture [70-72]. He represents the addition of ethanol to ethoxyacetylene as follows:



If instead of ethanol other alcohols are used in the reaction, a mixed orthoester is formed and can break down into ester and ether molecules containing different radicals:



Since the acetate and the ethyl ether of the given alcohol (or phenol) are the main reaction products the above investigators believe reaction (A) to be the main one. The addition of alcohol to ethoxyhept-1-yne in the presence of boron trifluoride and mercuric oxide has also been investigated. The reaction takes place at room temperature and results in the formation of ethyl heptanoate[73]:

$$C_6H_{11}-C\equiv C-OC_2H_5+2C_2H_5OH \longrightarrow [C_6H_{11}-CH_2-C(OC_2H_5)_3] \xrightarrow[HOH]{BF_3\cdot HgO} C_6H_{11}CH_2-COOC_2H_5+2C_2H_5OH.$$

In earlier investigations[72,74] it was shown that alcohols can add to ethoxyacetylene also under the influence of their alkoxides. However, this reaction is slower than in the presence of acid reagents and terminates in the formation of the ortho-ester which does not decompose under conditions of alkaline catalysis:

$$CH\equiv C-OC_2H_5 \xrightarrow{C_2H_5O^-} [CH=C(OC_2H_5)_2] \xrightarrow{H^+} CH_2=C(OC_2H_5)_2 \xrightarrow{C_2H_5OH} CH_3-C(OC_2H_5)_3.$$

Arens[70] therefore regards the alkoxide-catalysed addition of an alcohol to ethoxyacetylene as nucleophilic addition of the alkoxide ion to the α-carbon atom of the ether, followed by scission and addition of a proton. The final stage is addition of yet another alcohol molecule.

The electron-donor properties of ethoxy-groups in ethynyl ethers are also shown in electrophilic addition reactions. For example, in the reaction of water with ethoxyacetylene[70,74,75], the latter can be hydrated under the influence of both acid (mineral acids) and alkaline catalysts. Arens[75] regards the base-catalysed addition of water to ethoxyacetylene as nucleophilic addition. These studies show that nucleophilic and electrophilic addition reactions of ethynyl ethers are due to the electron-donor properties of the OR groups and take place more readily under the influence of acid catalysts.

Ethylthioacetylene behaves quite differently in electrophilic and nucleophilic additions to the triple bond. Thus, in contrast to the very rapid hydration of ethoxyacetylene in the presence of acid, the corresponding reaction with ethylthioacetylene is very slow and its completion requires prolonged boiling[70], the principal products being acetic acid and the mercaptan:

$$CH\equiv C-SC_2H_5 + H^+ \longrightarrow CH_2=\overset{+}{C}-SC_2H_5 \xrightarrow{H_2O} CH_3-\underset{\underset{O}{\|}}{C}-SC_2H_5 + H^+$$
$$\downarrow H^+,\ H_2O$$
$$CH_3COOH + C_2H_5SH.$$

In terms of Ingold's theoretical ideas[76], Arens[70] expressed this by saying that the "conjugative displacement" of electrons from the RS group in ethylthioacetylene takes place in the same direction as in ethoxyacetylene but to a much lesser extent, and therefore the hydration is more difficult.

Arens[75] showed that, in contrast to the electrophilic reactions of ethylthioacetylene, its nucleophilic additions (even those involving alcohols) do not cause polarisation of the triple bond in the manner characteristic of ethoxyacetylene. Nucleophilic groups always add at the β-carbon atom of ethylthioacetylene, which shows that the latter is polarised as follows[70,75]:

$$HC\overset{\delta-}{\equiv}C\overset{\delta+}{-}SC_2H_5.$$

Addition of alcohols and phenols to ethyl sulphides takes place in the presence of alkoxides[77,78], this process also being slow. On being boiled with sodium ethoxide for 7 h in a stream of nitrogen, ethylthioacetylene forms *cis*- and *trans*-1,2-substituted ethylenes in good yield[77]:

$$CH\equiv C-SC_2H_5+C_2H_5ONa \longrightarrow C_2H_5O-CH=CH-SC_2H_5.$$

The addition of sodium ethoxide to ethylthiopropyne takes place on heating the mixture to 140° for 24 h, the β-adduct being formed in good yield[78]:

$$CH_3-C\equiv C-SC_2H_5+C_2H_5ONa \longrightarrow CH_3-C(OC_2H_5)=CH-SC_2H_5.$$

On the basis of the experimental data, Volger and Arens[70,75] concluded that the alkylthio-group has a twofold effect on the polarisation of the adjacent triple bond, by virtue of the capacity of sulphur to adapt readily to the electronic requirement of the approaching group. This behaviour of the alkylthio-group and its consequent influence on the polarisation of the neighbouring triple bond arises from the capacity of sulphur in the alkylthio-group to extend its octet of valence electrons to ten or to give them up[70].

In contrast to alkylthio-groups, which can behave both as electron donors and acceptors, alkoxy-groups in ethynyl ethers exhibit only electron-donor properties in the above reactions, polarising the molecule only in the following way:

$$CH\overset{\delta-}{\equiv}C\overset{\delta+}{-}OC_2H_5.$$

2. Addition of Mercaptans to Ethynyl Ethers and Sulphides

Mercaptans react with ethynyl ethers and sulphides by a free-radical mechanism, β-substituted products being formed[70,75]:

$$CH\equiv C-OR(SR)+R'SH \longrightarrow R'S-CH=CH-OR(SR).$$

Arens and coworkers[79] showed that mercaptans readily add to ethoxy- and ethylthio-acetylene when the mixture is heated slightly. According to Arens[70], the mechanism of this reaction involves the formation of an intermediate radical $C_2H_5S-CH=\dot{C}-OC_2H_5(SC_2H_5)$, the orientation of the molecule during the reaction being determined by the approaching SC_2H_5 group and the relative stability of the radical.

The reaction of ethanethiol with ethoxy- and ethylthio-acetylene results in a mixture of *cis*- and *trans*-isomers of 1,2-disubstituted ethylenes. An experiment carried out under conditions excluding the possibility of isomerisation yielded only the *cis*-isomer, which was converted into the *trans*-isomer on distillation. Arens and coworkers[79] concluded from these results that the addition of ethanethiol to ethynyl ethers and sulphides is stereospecific and takes place in accordance with the "*trans*-addition rule". All attempts to carry out this reaction under ionic conditions in the presence of additives inhibiting the free-radical reaction failed. Free-radical addition occurs also in the reaction of ethoxyacetylene with propane-1-thiol, thiophenol, and thiocresol.

Disubstituted acetylenes react similarly with mercaptans. In all cases the RS group adds at the β-carbon atom of the ether or sulphide[75]:

$$R-C\equiv C-OR(SR)+RSH \longrightarrow R-C(SR)=CH-OR(SR).$$

However, the addition of mercaptans to disubstituted acetylenes is slow and requires prolonged boiling and the

presence of free-radical initiators. The following reactions belong to this group: the reaction of ethoxypropyne with ethanethiol:

$$C_2H_5O-C\equiv C-CH_3+C_2H_5SH \longrightarrow C_2H_5O-CH=\underset{\displaystyle SC_2H_5}{C}-CH_3,$$

the reaction of ethoxy- and ethylthio-ethynylmethanols with ethanethiol[29]:

$$RR'C(OH)-C\equiv C-R''+C_2H_5SH \longrightarrow RR'C(OH)-\underset{\displaystyle SC_2H_5}{C}=CH-R'',$$

where $R'' = OC_2H_5$ or SC_2H_5, and the reaction of the ethylthiopropiolate ester with ethanethiol[80]:

$$ROOC-C\equiv C-SC_2H_5 \xrightarrow{C_2H_5S^{\cdot}} \left[ROOC-\underset{\displaystyle SC_2H_5}{\dot{C}}=\dot{C}-SC_2H_5\right] \xrightarrow{C_2H_5SH}$$

$$\longrightarrow ROOC-\underset{\displaystyle SC_2H_5}{C}=CH-SC_2H_5+[C_2H_5\dot{S}].$$

The slower rate of the reactions with substituted ethynyl ethers compared with the similar reactions of unsubstituted ethynyl ethers and sulphides[75] can be understood from an examination of the polarisation of their molecules. Bonnema and Arens[80] believe that the reactions of the substituted ethers are slower because of the reduction of electron density at the second carbon atom resulting from the withdrawal of electrons to the carbonyl group:

$$\overset{\curvearrowleft}{O}=C-\underset{\displaystyle OC_2H_5}{\overset{\curvearrowleft}{O}}-\overset{\curvearrowleft}{C}\equiv\overset{\curvearrowleft}{C}-\overset{\curvearrowleft}{S}C_2H_5.$$

In unsubstituted ethynylsulphides the electron density is concentrated at the second carbon atom by virtue of the free electron pair of the sulphur atom, which favours the formation of a new bond:

$$H-\overset{\curvearrowleft}{C}\equiv\overset{\curvearrowleft}{C}-\overset{\curvearrowleft}{S}C_2H_5.$$

In one of their latest studies, Arens and coworkers[70] were able to carry out the nucleophilic addition of sodium ethanethiolate to ethoxyacetylene. It is known[75] that the ethoxy-group exhibits its electron-donor properties in nucleophilic and electrophilic addition reactions. In reactions of ethoxyacetylene with primary and secondary amines, alcohols, water, etc. the nucleophilic group always adds at the β-carbon atom of the ethoxyacetylene.

Accordingly, Alkema and Arens[79] were able to add sodium ethanethiolate (a nucleophilic reagent) to ethoxyacetylene in liquid ammonia. They found that under these conditions the addition also results in the formation of a 1,1-disubstituted ethylene:

$$CH\equiv C-OC_2H_5 \xrightarrow{C_2H_5SNa} CH_2=\underset{\displaystyle SC_2H_5}{\overset{\displaystyle OC_2H_5}{C}},$$

i.e. the ethylthio-group adds at the β-carbon atom in conformity with other nucleophilic addition reactions. Here too the alkoxy-group of the ethynyl ether exhibits its characteristic electron-donor properties.

Alkema and Arens were able to prove convincingly the structure of their products by infrared spectroscopy, hydrolysis, and the addition of ethanethiol followed by treatment with potassium hydrogen sulphate:

$$CH_2=\underset{\displaystyle SC_2H_5}{\overset{\displaystyle OC_2H_5}{C}} \xrightarrow{C_2H_5SH} C_2H_5S-CH_2-CH(OC_2H_5)(SC_2H_5) \xrightarrow{KHSO_4} C_2H_5S-CH=CH-SC_2H_5.$$

These results invalidate Truce's conclusion[55,60] that nucleophilic addition of mercaptans to acetylenic compounds results in the formation of 1,2-substituted ethylenes. Arens' attempts[79] to isolate the ethylenes which Truce obtained in this reaction were unsuccessful.

It follows that free-radical addition of mercaptans to ethynyl ethers and sulphides yields β-substituted sulphides. Under ionic conditions the reaction is stereospecific, in accordance with the "*trans*-addition rule", resulting in the formation of *cis*-ethylenes. Under very mild conditions it is possible to carry out nucleophilic addition of a mercaptan to ethynyl ethers and obtain α-substituted sulphides.

IV. ADDITION OF ALCOHOLS AND MERCAPTANS TO DIACETYLENES

1. Addition of Alcohols to Diacetylene

The addition of alcohols to diacetylene was first described in a patent[81] dealing with the preparation of ethynylvinyl ethers by this reaction. Then Franke[51,52] and Herberts[82] prepared methyl ethynylvinyl ether and investigated some of its properties. These investigations were the starting point of the development of the chemistry of unsaturated ethers synthesised by addition of alcohols to diacetylenes.

A systematic and detailed investigation of this reaction has been carried out since 1956 in the Laboratory of Vinyl Compounds of the Institute of General Chemistry of the USSR Academy of Sciences[53,83]. Aliphatic, alicyclic, and aromatic alcohols and other compounds containing reactive hydrogen, mercaptans[83-92], amines[93-95], lactams[96], etc., have been used in the reaction.

The reaction of diacetylenes with alcohols takes place in the presence of alkaline catalysts even when diacetylene is merely passed into the alcohol at 60–110° (depending on the alcohol), resulting in the formation of ethynylvinyl ethers and 1,1-dialkoxybut-2-yne:

$$CH\equiv C-C\equiv CH+ROH \longrightarrow CH\equiv C-CH=CH-OR \xrightarrow{ROH} CH_3-C\equiv C-CH(OR)_2.$$

Shostakovskii *et al.*[53] established that the reaction takes place in stages and that the yields of the ethynylvinyl ether and the acetal depend on the initial ratio of the reactants, the nature of the alcohol, the amount of catalyst, and especially on the reaction temperature. Thus on heating to 100–110°, only one alcohol molecule adds and the ethynylvinyl ether is formed; when the mixture is heated to 130° and above, a second alcohol molecule adds to the ethynylvinyl ether and the acetal is formed.

Later[86,88], this reaction was extended to benzyl alcohol and phenol, the corresponding ethynylvinyl ethers being obtained. A patent application[81] describes the preparation of an ethynylvinyl ether from phenol and diacetylene, but repeated attempts[86] to repeat this synthesis were unsuccessful, and the method is therefore doubtful.

In considering the mechanism of addition to diacetylene, the molecule of the latter can be regarded either as a conjugated system of triple bonds or as a substituted acetylene molecule in which one ethynyl group behaves as an electron-acceptor substituent in relation to the other, under the conditions of this reaction. Nieuwland and Bohlmann regarded the vinylacetylene and diacetylene molecules in terms of the first concept, this being apparently valid for alcohol addition reactions.

Adopting Nieuwland's hypothesis [47] of the formation of an intermediate allene structure when methanol adds to vinylacetylene,

$$CH_2{=}CH{-}C{\equiv}CH \xrightarrow{CH_3OH} [CH_3O{-}CH_2{-}CH{=}C{=}CH_2] \longrightarrow CH_3O{-}CH_2{-}C{\equiv}C{-}CH_3,$$

Bohlmann [97,98] proposed the following mechanism for the reaction of diacetylene with methanol:

$$CH{\equiv}C{-}C{\equiv}CH \rightleftarrows [HC^{+}{=}C{=}C{=}CH^{-}] \xrightarrow{RO^-} [RO{-}CH{=}C{=}C{=}CH^{-}] \xrightarrow{H^+} RO{-}CH{=}CH{-}C{\equiv}CH.$$

The action of the alkoxide results in the formation of an intermediate polar compound with a cumulative system of double bonds to which the alkoxy-group undergoes addition. The resulting complex anion is converted into an ethynylvinyl ether molecule after addition of a proton and subsequent isomerisation.

Bohlmann [98] also found that the formation of an allene structure is facilitated by an increase in the number of triple bonds, which accelerates the addition of the alcohol. Comparison of the conditions under which alcohols react with acetylene and diacetylene is instructive in this connection. Vinylation of alcohols with acetylene requires heating to 140–160° and an elevated pressure [3], while the addition of the same alcohols to diacetylene takes place at 60–125° under normal pressure [53].

Bohlmann [97,98] explained the formation of the intermediate with a cumulative system of double bonds by the tendency of the π electrons of the triple bonds to interact with one another whereby the electrons are uniformly distributed throughout the system, which can be represented as follows [13]:

$$CH{\equiv}C{-}C{\equiv}CH \longleftrightarrow H{-}\overset{+}{C}{=}C{=}C{=}\overset{-}{C}{-}H \text{ etc.}$$

Physical investigations confirm this. Examination of the C–C, C=C, and C≡C bond lengths in diacetylene, vinylacetylene, and acetylene molecules shows that single C–C bonds included between double and triple bonds are somewhat shorter [13]:

$HC{\equiv}C{-}C{\equiv}CH$	$CH_2{=}C{-}C{\equiv}CH$	$HC{\equiv}CH$	$CH_3{-}CH_3$.
1.19; 1.36; 1.19	1.36; 1.42; 1.20	1.20	1.54

The shortening of these bond lengths shows that in the above molecules there is partial double bond character. However, the similarity to olefinic compounds is very superficial, because pure cumulative polyenes do not add alcohols under the same conditions. For example, aliphatic cumulative pentaenes do not react with alcohol [97]. It is also known that the triple bond is more reactive with respect to nucleophilic reagents (alcohol, water, amines) than is the double bond, whereas with respect to electrophilic reagents (halogens, per-acids, ozone) the opposite is true [13].

2. Addition of Alcohols to Substituted Diacetylenes

Substituents in diacetylene have a major effect on its reactivity and the mode of the reaction. Monosubstituted diacetylenes are more reactive in alcohol addition reactions than are disubstituted acetylenes. Herberts [99,100] showed that the addition of methanol to methyl- or ethyl-diacetylene takes place when the mixture is heated in the presence of NaOH:

$$R{-}C{\equiv}C{-}C{\equiv}CH + CH_3OH \longrightarrow R{-}C{\equiv}C{-}CH{=}CH{-}OCH_3.$$

Dimethyldiacetylene virtually does not react under conditions in which alcohols add on diacetylene itself. More severe conditions are required for this reaction than in the case of alkyldiacetylenes: the mixture must be heated in a bomb under pressure for 14 h at 120°:[97]

$$CH_3{-}C{\equiv}C{-}C{\equiv}C{-}CH_3 \xrightarrow{CH_3OH} CH_3{-}C(OCH_3){=}CH{-}C{\equiv}C{-}CH_3.$$

This finding confirms Bohlmann's mechanism. In his view the electron-donating methyl groups hinder the formation of an intermediate structure with accumulative systems of double bonds and thereby inhibit the addition of the alcohol. However, the effect of the substituents diminishes with increase in the number of triple bonds. Thus ethanol adds much more easily to dimethyltriacetylene than to dimethyldiacetylene and its addition to dimethyltetraacetylene takes place on simple refluxing of the mixture in a flask for 2 h: [97]

$$CH_3[C{\equiv}C]_4CH_3 \xrightarrow[CH_3OH]{Na} CH_3[C{\equiv}C]_2{-}CH{=}C(OCH_3){-}CH_3.$$

The existing data on the reactions of polyynes [98] indicate that the terminal atom with a partial positive charge is responsible for the ease of the nucleophilic reactions.

3. Addition of Mercaptans to Diacetylene

Up to 1958 [85] only the preparation of an ethynylvinyl sulphide as the sole product of the reaction of diacetylene with butanethiol and toluene-ω-thiol under the influence of alkali, described in patents [84], was known. The reaction of diacetylene with mercaptans takes place in stages,

$$CH{\equiv}C{-}C{\equiv}CH + RSH \longrightarrow CH{\equiv}C{-}CH{=}CH{-}SR \xrightarrow{RSH} RS{-}CH{=}CH{-}CH{=}CH{-}SR,$$

and results in the formation of ethynylvinyl sulphides and dialkylthio(arylthio)buta-1,3-dienes. The reaction begins on mixing the starting materials in the presence of alkali and a diluent at room temperature and is accompanied by a rise in temperature. When gaseous acetylene is passed into a mixture of the mercaptan and alcoholic alkali, the latter must be heated to 50–55°. With ethane- and isopropane-thiol the second method of synthesis is more convenient, since the reaction takes place more smoothly without a jump in temperature.

The optimum temperature for the formation of ethynylvinylethyl and ethynylvinyl isopropyl sulphides is 50–55° and for ethynylphenyl sulphide 35–40°. The addition of the first mercaptan molecule to diacetylene yields an ethynylvinyl sulphide and the addition of the second molecule a 1,4-dialkyl(aryl)thiobuta-1,3-diene. The reviewers have shown that both stages have their own optimum conditions, for the maximum yield of the final product, and that they can take place independently.

When it is desired to obtain the ethynylvinyl sulphide, solvents must be used to increase its yield and to suppress the second stage. Since the reaction of diacetylene with mercaptans takes place more readily than with alcohols, the latter may be used as diluents, their hydroxyl hydrogen not being involved in the reaction. Methanol is particularly suitable for this purpose [90], but dioxan has also been used [85]. The reaction of diacetylene with mercaptans takes place vigorously, with rise in temperature, only in the presence of alkali. Azodiisobutyronitrile or heating alone do not

initiate the reaction, the yield of the ethynylvinyl sulphide not exceeding 10% under these conditions. We must therefore conclude that the addition of the first mercaptan molecule to diacetylene takes place by an ionic mechanism.

The action of alkali results in the formation of alkyl- or aryl-sulphide ions which cause a shift of electrons in the diacetylene molecule thereby facilitating the nucleophilic addition of the ions to the carbon atom having the least electron density:

$$CH{\equiv}C{\longleftarrow}\overset{\oplus}{C}{\equiv}CH + R\bar{S} \longrightarrow CH{\equiv}C{-}\bar{C}{=}CH{-}SR \xrightarrow{RSH} CH{\equiv}C{-}CH{=}CH{-}SR + R\bar{S}.$$

The addition of mercaptans to diacetylene under ionic conditions is stereospecific. Like other ionic reactions involving the addition of nucleophilic reagents, it takes place according to the "*trans*-nucleophilic addition rule", *cis*-isomers being formed[89,92,95].

The addition of a second mercaptan molecule requires more severe conditions. The reaction is not accelerated by alkaline catalysts (in "catalytic" amounts), requires heating in the presence of free-radical initiators (benzoyl peroxide, azodiisobutyronitrile), and is inhibited by antioxidants[91] (hydroquinone, triethanolamine, SO_2), *i.e.* the addition takes place by a free-radical mechanism.

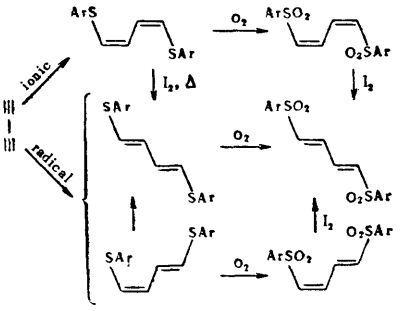
In considering the mechanism of the addition of mercaptans to diacetylene, the latter may be regarded as a monosubstituted acetylene. The available data show that the reaction is similar to that involving acetylenes with electron-acceptor substituents[43,44,55,68] in which the addition to the triple bond takes place across the 1,2-positions.

V. STEREOSPECIFIC SYNTHESES BASED ON DIACETYLENE AND MERCAPTANS

The problem of the stereochemistry of reactions involving the addition of mercaptans to diacetylene is still obscure. Studies of the conditions of the reaction between diacetylene and mercaptans and amines in the Laboratory of Vinyl Compounds[89,92,95] showed that the addition of the first mercaptan or amine molecule is an ionic reaction while the addition of the second molecule is a free-radical reaction. Thorough investigation of the products of this reaction showed that it is stereospecific, the stereospecificity depending on the mechanism.

It has been shown, for the addition of various mercaptans to diacetylene[89,92], that stereospecific synthesis of *cis*-*-cis*-1,4-dialkylthio(arylthio)buta-1,3-dienes is possible under ionic conditions, while under free-radical or mixed conditions the addition results in a mixture of all three isomers, their proportions depending on the reaction temperature.

To establish the geometrical configuration of the stereoisomers obtained from butanethiol, the reaction mixture was oxidised and the resulting sulphones were separated by fractional crystallisation, whereby all three isomers were isolated[92]. Since in the case of thiophenol the resulting diphenylthiobuta-1,3-dienes are crystalline, the *cis*-*cis*-*-*isomer was isolated directly from the reaction mixture and the remaining two isomers were isolated after oxidation of their mixtures to the corresponding sulphones[89]. The geometrical configurations of the stereoisomeric dialkylthio- and diarylthio-buta-1,3-dienes were assigned on the basis of their physical properties and isomeric transformations. The isomeric transformations of 1,4-diarylthiobuta-1,3-dienes are shown below:



The stereochemistry of the addition of alkylamines to diacetylene has also been investigated. Shostakovskii *et al.*[95] found that the addition of one diethylamine molecule to diacetylene under ionic conditions is stereospecific resulting in the formation of *cis*-diethylaminobutenyne whilst butylamine and diacetylene form a di-adduct with *cis-cis* configuration. Analysis of the available data shows that in an investigation of the stereochemistry of the addition of mercaptans and amines to diacetylene, the molecule of the latter must be regarded not as a system of conjugated multiple bonds but as a molecule of monosubstituted acetylene[90,92,95]. Consequently the reaction of diacetylene with mercaptans consists in the addition of two molecules of the latter to both triple bonds, as in the addition to mono- and di-substituted acetylenes, *i.e.* in accordance with the "*trans*-nucleophilic addition" rule; under ionic conditions the reaction is stereospecific with the formation of the corresponding *cis-cis*-isomers.

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CHEMISTRY OF 19-NORSTEROIDS

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1. INTRODUCTION

In the production of highly active steroidal compounds, it has been found that their hormonal activity can be increased (*i*) by introducing into the steroid molecule additional substituents, such as halogens, alkyl groups, and hydroxy-groups not normally present in the natural compounds, or (*ii*) by preparing compounds in which certain structural units present in natural steroids are missing. This class of compounds includes the 19-norsteroids, which do not have the methyl group at $C_{(10)}$ of the steroid skeleton.

Some 19-nor-compounds have a considerably higher activity than their 19-methyl analogues. For practical application, however, it is not so much the generally higher level of physiological activity of 19-norsteroids which is of importance, as their highly specific action in comparison with the natural steroids. Thus compounds have been prepared having high anabolic or anti-oestrogenic activity but practically no androgenic action; highly active gestagens, hypotensive and contraceptive agents, etc., have also been obtained. The high physiological activity of 19-norsteroids has led to their rapid introduction into medical practice and to an increased number of preparative studies in this field. It is difficult to find a section of organic chemistry which has developed so rapidly in the last 5–10 years as the study of modified steroid hormones, and of 19-norsteroids in particular. The index to *Chemical Abstracts* for 1950 contains only three references to 19-norsteroids, while for 1960 there are about 200. The only existing review of the chemistry of 19-norsteroids[1], which covers work appearing up to 1958, is thus considerably out of date.

Because of limitations of space, we have used only reviews and the most important original papers in discussing the pharmacology and clinical use of 19-norsteroids, but the literature on their chemistry will be reviewed as fully as possible.

2. DERIVATIVES OF 19-NORANDROSTANE

(*a*) 19-Nortestosterone and Its Isomers

19-Nortestosterone (I) has been obtained by the Birch reduction of oestrone and oestradiol, alkaline treatment of 19-hydroxytestosterone, and various total syntheses.