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Diacetylene: a candidate for industrially important reactions

I A Maretina, B A Trofimov

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Abstract. The review is devoted to industrially important syntheses based on diacetylene, a side product from electrocracking, oxidative pyrolysis of methane and plasmochemical synthesis of acetylene. Reactions of diacetylene and its derivatives with mono- and dinucleophilic reagents occurring in the chemisorption of diacetylene from industrial gases and resulting in stable reactive compounds which can be used as valuable intermediates for organic synthesis and pharmaceutical industry are described. Some specific features of diacetylene reactions in superbasic media are discussed. The bibliography includes 266 references.

I. Introduction

Preparation of chemical products on the basis of acetylene is one of the most promising trends in basic industrial organic synthesis. The interest in acetylene-related raw materials, which subsided considerably in 1955 – 1975, has now rekindled.[1] The reorientation towards coal and gas as valuable raw materials of the future and the development of new technologies for acetylene production from coal, *e.g.* using plasmochemical reactions, played a crucial role in the revision of the place of acetylene in organic synthesis.[2] The use of acetylene and its derivatives in small-tonnage production of sophisticated and expensive organic compounds holds especially great promise.[1, 2]

The classical studies by A E Favorsky and W Reppe have formed the basis for modern technologies of the chemistry of acetylene, *viz.*, vinylation, ethynylation and carbonylation reactions. A vast body of accumulated data on reactions of acetylene is documented in numerous monographs and reviews.[1 – 40] On the other hand, some technological aspects of the chemistry of acetylene were obviously underestimated. This is particularly true of diacetylene (butadiyne) formed in the manufacture of acetylene. As regards the potential utility of side products derived from acetylene and accompanying compounds (methylacetylene, allene, diacetylene, higher alkynes, phenylacetylene, *etc.*), diacetylene occupies the second place after the methylacetylene – allene fraction.

A significant contribution to the chemistry of diacetylene and its commercial application was made by Russian scientists belonging to the M F Shostakovskii [3, 8, 11 – 32, 34] and A A Petrov [36 – 40] scientific schools. The aim of the present review is to analyse and systematise the published data devoted to industrial syntheses based on diacetylene and to evaluate the prospects for the development of this branch of chemistry.

II. The problem of diacetylene utilisation

Despite the fact that many compounds of the diacetylene series (1,3-diynes) had been known since the XIX century, the development of the chemistry of these compounds began only after 1950 [3] when they were discovered in nature [4, 5] as well as among the products of electrocracking and oxidative pyrolysis of methane.[6]

Under industrial conditions, these two reactions yield, in addition to acetylene, some of its homologues and derivatives among which diacetylene constituting 5% of the whole manufacture of acetylene presents the greatest practical interest.[1]

Utilisation of the accompanying diacetylene presents a serious problem for chemical technology. All industrial methods used for the isolation of acetylene are based on the sorption – desorption principle. Higher alkynes and diacetylene are extracted with the help of selective solvents, *e.g.*, anhydrous ammonia, cooled methanol, *N*-methylpyrrolidone, DMF.[3, 6]

The first solution to this problem was proposed and implemented at the oldest petrochemical plant 'Chemische Werke Huls A.G.' [41] Preparation of 1-methoxybut-1-en-3-yne as a 50% solution in methanol from accompanying diacetylene has been described.[42] However, this method is not industrially acceptable because of extremely high diacetylene concentrations in the reactor. Labour protection laws currently in force in the Russian Federation prohibit the use of industrial technologies based on the use of material (gas or liquid) flows containing more than 10% of diacetylene.[6] Therefore, problems of diacetylene extraction from gases produced by pyrolysis of hydrocarbon raw materials have

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received recently considerable attention, especially with regard to the safety of acetylene extraction due to the ability of diacetylene to undergo polymerisation and decomposition with explosion.

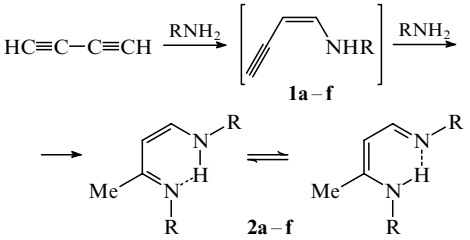
It should be noted in this connection that operations with diacetylene in manufacturing plants and in the laboratory belong to the category of particularly hazardous ones. It is therefore expedient to give due consideration to the vast experience accumulated in this area. The formation of a liquid phase in gas flows containing diacetylene is impermissible. The schemes of chemical conversion of diacetylene into practically valuable compounds should employ exclusively alkaline media, because the polymers formed under these conditions as side products are not hazardous. Manipulations with condensates or products prepared based on industrial diacetylene-containing gases differ substantially from those with pure diacetylene, since the polymerisation processes are more pronounced owing to the presence of higher 1,3-diynes. It is therefore preferable to prepare compounds which can easily be removed by distillation. It is rather difficult to isolate high-boiling products from such mixtures by conventional methods.

The technologies implemented in Russia were developed with due regard for safety for two main types of the processes, *viz.*, those in which liquid ammonia [36, 43, 44] and *N*-methylpyrrolidone [37] were used as selective solvents. A possible approach to diacetylene utilisation is based on its ability to react with alcohols.[36, 37, 41, 42] The products of this reaction can be used in the synthesis of some aromatic and heterocyclic compounds (*e.g.,* monomers, dyes and drugs) as well in the production of plasticisers, herbicides, rubber vulcanisation accelerants, intermediates for electronic industry, broad-spectrum metal corrosion inhibitors, *etc.*[36, 37] Other conversions of diacetylene can be used in the synthesis of otherwise inaccessible heterocyclic compounds.[38–40, 45–47] All this makes diacetylene and its heterofunctional derivatives promising candidates for building blocks in the targeted synthesis of heterocyclic compounds.[11–17, 38–40, 47]

Diacetylene most easily enters into reactions of nucleophilic addition with amines, alcohols and thiols, and high reactivities of the adducts make them promising reagents for practical purposes. In reactions with nucleophilic reagents, diacetylene behaves as a typical alkyne activated by an acceptor group,[47] *i.e.*, in this case the addition occurs at the terminal carbon atom of the acetylene bond, eventually resulting in the formation of 1-heteroalk-1-en-3-ynes.

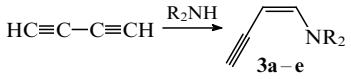
III. Reactions with amines

Tne addition of primary amines to diacetylene occurs readily at 30–40 °C in the absence of a catalyst. Usually, monoadducts of the type **1** cannot be isolated,[48] 1-*tert*-butylaminobut-1-en-3-yne (**1f**) being the only exception.[49] *N*-Alkyl(β-aminovinyl methyl)-ketimines or their tautomers, *e.g.*, *N*-alkyl-3-alkylaminocrotonaldimines **2,** are the reaction products, which are formed in good yields.



R = Me (**a**), Et (**b**), Pr^n (**c**), Pr^i (**d**), Bu^n (**e**), Bu^t (**f**).

According to the published data,[48, 49] the adducts **2** have *s-Z*-conformation which is stabilised by an intramolecular hydrogen bond. The reaction of diacetylene with secondary amines gives 1-dialkylaminobut-1-en-3-ynes (**3**).[3, 47]



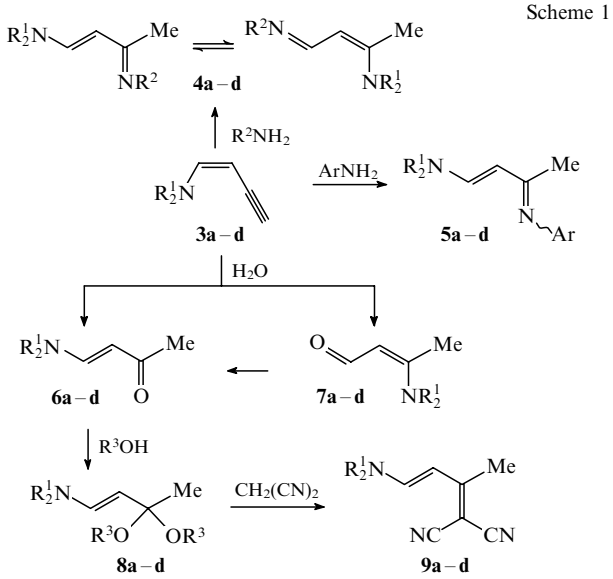
R = Me (**a**), Et (**b**), Pr^n (**c**), Bu^n (**d**); R_2N =  (**e**).

The stereochemistry of the reaction of diacetylene with diethylamine in various solvents and at different temperatures resulting in the formation of the *Z*- and *E*-isomers **3b** has been studied.[50] The *E*:*Z* ratio increases with temperature. The *Z*-isomer prevails in acetonitrile, diethylamine and THF at 0–20 °C, whereas the *E*-isomer is predominantly formed in ethanol at 20 °C. The $Z \rightarrow E$ transition is observed only in the photolysis.

The kinetics of addition of secondary amines to diacetylene in dioxane at 20–80 °C corresponds to that of second-order reactions.[51] The formation of compounds **3b**,**d** was monitored by UV-spectroscopy. The low values of activation entropy ($\Delta S^{\neq} = -55$ e.u.) and enthalpy ($\Delta H^{\neq} = 33.4$ kJ mol^{-1}) for the amine **3b** prompted a conclusion [47] that the addition occurs *via* intermediate products with considerable charge separation (bipolar ions). The final products result from intramolecular (*E*-isomers) or intermolecular (*Z*-isomers) proton transfer. The charge separation in the transition state favours both specific orientation of the amine and dioxane molecules and low values of activation entropy and enthalpy.[47]

1-Dialkylaminobut-1-en-3-ynes **3** with primary alkyl substituents react with primary amines to give potentially tautomeric aminocrotonaldimines **4** due to the exchange of the amino groups. Reactions of compounds **3** with arylamines yield *C*-(2-dialkylaminovinyl)-*C*-methyl-*N*-(aryl)azomethines **5**.[40, 48] Depending on conditions, the hydration of amines **3** gives either 4-dialkylaminobut-3-en-2-ones **6** [3, 46, 52, 53] or 3-dialkylaminobut-2-enals **7** (Scheme 1).[46]

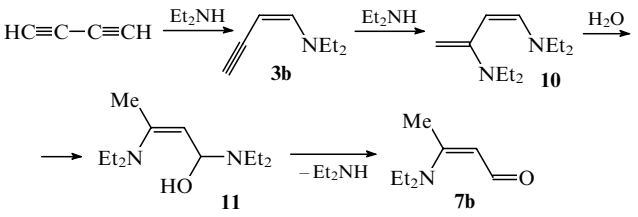
Scheme 1



R^1 = Me (**a**), Et (**b**), Pr^n (**c**), Bu^n (**d**).

The addition of alcohols to enamino ketones **6** which is catalysed by bases gives the vinylogues of aminoacetals **8** [40] which easily react with CH-acids, *e.g.*, malonodinitrile, to give the diene **9** (see Scheme 1).[40] Stepwise *C*-alkylation and hydrogenation of the amines **3** results in *N*-monosubstituted 1-aminoalkanes which represent valuable building blocks for the introduction of the 4-aminobutyl group.[54]

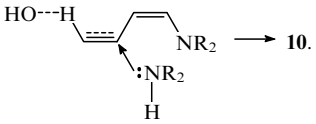
The reaction of diacetylene with an excess of diethylamine in dilute aqueous solutions of acetonitrile, ethanol or THF results in the diadduct, *viz.*, 1,3-bis(diethylamino)buta-1,3-diene (**10**); upon subsequent concentration of the reaction mixture, the latter is hydrated by a residual amount of water to be converted first into the hemiaminal **11** and then into the aldehyde **7b** following splitting-off of diethylamine.[55]



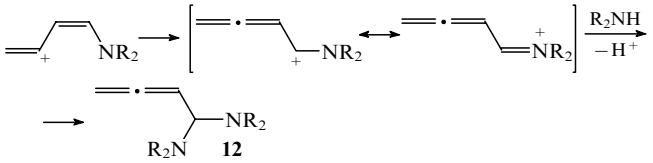
The reaction of the monoadduct **3b** with diethylamine is accompanied by the appearance of a band at 325 nm in the UV spectrum of the reaction mixture; its intensity increases with a simultaneous decrease in the intensity of the band at 275 nm corresponding to the original amine **3b**. After completion of the reaction, the UV spectrum contains only the former band corresponding to the product **10**.[55]

The absorption band of the original enyne **3b** in the IR spectrum is shifted towards the low-frequency region; its intensity decreases simultaneously with the appearance of a band around 1580 cm^{-1}, which corresponds to the product **10** having *Z*-configuration.[55] The intensity of this band increases as the reaction proceeds further. The first diethylamine molecule adds to diacetylene in acetonitrile much faster than the second one.

Thus, the first step of the conversion of diacetylene into the bisadduct **10** is the rate-limiting step. The enhancing effect of the solvent is attributed to incomplete removal of water and hence to electrophilic catalysis by water molecules which attack the terminal atom of the ethynyl group:

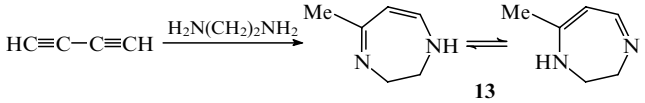


This transition state is in accord with the observed regioselectivity of the reaction and *Z*-configuration of the diene formed as well as with the high negative entropy and low activation energy of the reaction. The proton transfer and the addition of the nucleophile are synchronous processes and are accompanied by the migration of the positive charge to the α-carbon atom as might be expected. Otherwise, the allene **12** would be formed.[55]

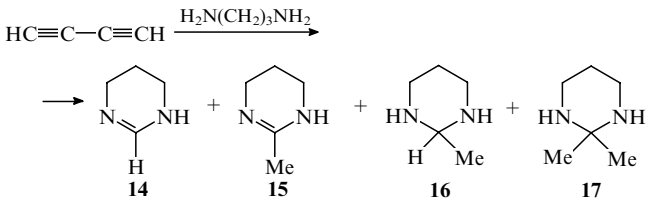


In aqueous solutions, the role of a nucleophile is played by water, which leads to the formation of the enamino ketone **6b**. The calculated rate constants for this reaction in aqueous THF are much lower than the rates of addition of the second diethylamine molecule to the amine **3b**, the enthalpy of activation is also lower. This attests to a concerted process and the involvement of the nucleophile in the limiting stage of both reactions, since water is a much weaker nucleophile than diethylamine.[55]

1,2-Diaminoethane reacts with diacetylene to give a mixture of tautomers of 5-methyl-2,3-dihydro-1,4-diazepine (**13**).[56]

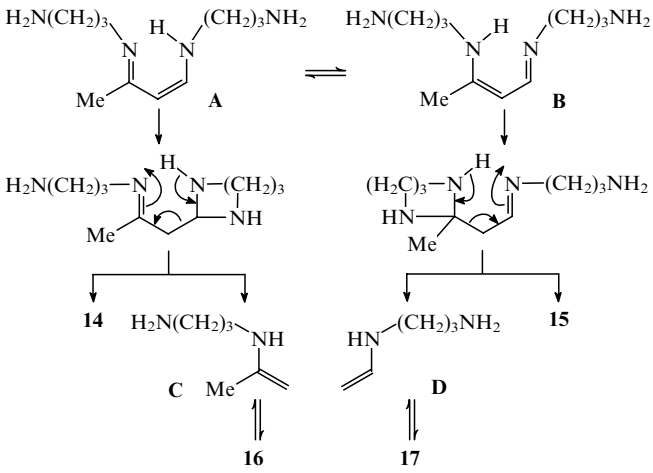


It was expected that the reaction of diacetylene and its homologues with 1,3-diaminopropane would give 1,2,3,4-tetrahydro-1,5-diazocine.[57] However, the reaction product represents a mixture of Δ^1-tetrahydropyrimidine (**14**), 2-methyl-Δ^1-tetrahydropyrimidine (**15**), 2-methyl- (**16**) and 2,2-dimethylhexahydropyrimidines (**17**).



This can be rationalised as the addition of two diamine molecules to one diyne molecule, resulting in the diadducts **A** and **B** which undergo further cyclisation and fragmentation in two directions (Scheme 2).

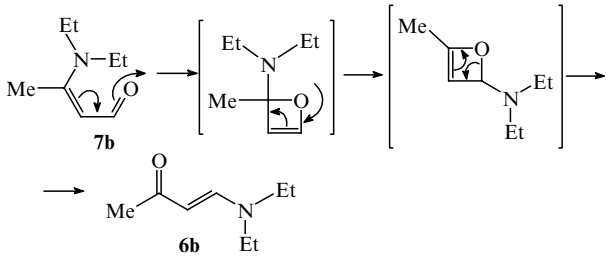
Scheme 2



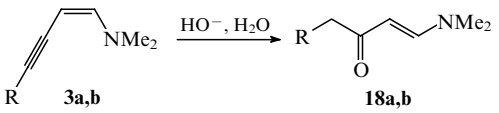
These results are similar to those obtained for the reaction of acetylacetone with 1,3-diaminopropane[57] and formally correspond to the scission of β-diketone derivatives.

As noted above, reactions of diacetylene with solutions of primary and secondary amines in aqueous ethanol produce enamino ketones **6**. It was found, however, that the physical constants of enamino ketones **6** thus prepared do not coincide with those prepared by amination of alkoxy ketones.[58] Later, this discrepancy was explained[59] by the formation of enamino aldehydes **7** along with enamino ketones **6** in reactions of diacetylene with solutions of amines in aqueous ethanol. Depending on the size of the alkyl substituents at the nitrogen atom and the concentration of the aqueous solution of alkali (3%–5%), the content of the aldehyde in the reaction mixture changes and may exceed 40% with respect to the ketone.[59] Thus if 3-dimethylaminobut-2-enal (**7a**) is formed only in trace amounts, the yields of the products **7b** and **7d** amount to 35% and 43%, respectively.[59]

It is believed[46] that the formation of enamino ketones **6** from amines **3** can also occur *via* aldehydes **7**. With an increase in temperature, the ketone : aldehyde ratio increases.[46] Thermal isomerisation occurs quantitatively, probably, *via* the oxetene cycle. The aldehyde **7b** is fully isomerised into the ketone **6b** in 4 h at 150 °C.



The addition of water to amines **3a**,**b** occurs easily in the presence of catalytic amounts of an alkali exclusively at position 3 and results in alkyl 2-dimethylaminovinyl ketones **18**.[60]



R = Me (**a**), Et (**b**).

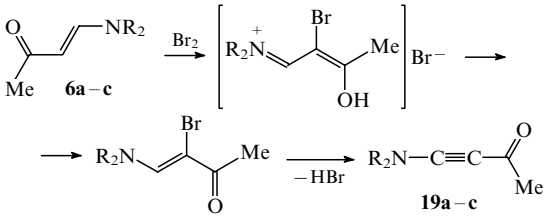
These conversions were used to develop a procedure for chemisorption of diacetylene by aqueous solutions of primary and secondary amines aimed at separation of diacetylene in the manufacture of acetylene by oxidative pyrolysis of methane.[59] This approach has been approved at the Yerevan Industrial Corporation 'Nairite' with both a real abgas † and a diacetylene-enriched condensate. Their compositions are shown in Table 1.[59] The presence of methane, nitrogen, ethylene and some other components in the abgas can be explained by the fact that diacetylene-containing gases are diluted with a cracking gas from which acetylene had previously been removed by absorption down to concentrations of $HC{\equiv}C{-}C{\equiv}CH$ (< 10 vol.%) which ensure their safety upon transportation.[59] Chemisorption of diacetylene is performed by a 25% aqueous solution of dimethylamine. The number of absorption plates and the design of the absorption apparatus ensure the absorption of 92%–94% of diacetylene at its average concentration of 6%–7%. The addition of dimethylamine to diacetylene occurs at 25–30 °C. Since this reaction is exothermic, the temperature of the reaction mass increases slowly to 50 °C.‡ The amine **3a** formed in the first step was isolated from the reaction mixture in its individual state and characterised.[59]

Table 1. The composition of abgases and their condensates.

Component	Content (vol.%)	
	in abgas	in condensate
Hydrogen	35–40	–
Methane	20–25	–
Nitrogen	7.0–11.0	–
Diacetylene	6.0–8.0	36–52
Ethylene	1.0–2.0	–
Methylacetylene	1.0–1.5	5.5–7.5
Benzene	1.0–1.5	5.0–7.0
Allene	0.5–1.0	3.5–5.5
Vinylacetylene	0.5–1.8	4.0–4.5

Then, the reaction mass is loaded into a reactor where the triple bond is hydrated at 60–65 °C. The ketones **6** formed are rather stable and convenient C_4-synthons for the synthesis of heterocyclic compounds.[38–40]

1-Dialkylaminobut-3-yn-2-ones (**19**), which are promising reagents for the synthesis of heterocyclic compounds, are easily prepared by bromination and dehydrobromination of enamino ketones **6**.[62–67]

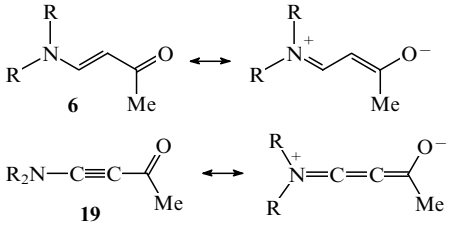


R = Me (**a**), Et (**b**), Pr^n (**c**).

† Abgas is a technical term, which designates an absorption gas.

‡ Among a vast array of products present in diacetylene as admixtures, vinylacetylene ranks second in reactivity after diacetylene. However, even this compound reacts with aqueous solutions of secondary amines at a detectable rate only at 100 °C in an autoclave.[61]

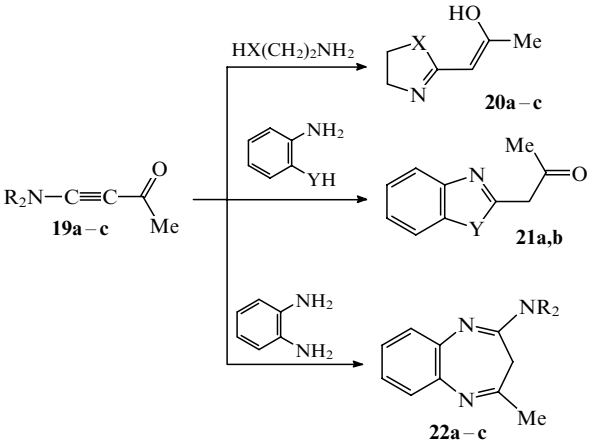
The structures and reactivities of enamino ketones **6, 18** and ynamino ketones **19** were described in numerous publications.[38, 39, 52, 62] The effects of substituents on the distribution of electron density in the molecules of en- and ynaminocarbonyl compounds were studied by ^{13}C-NMR spectroscopy. These studies were aimed at the determination of spin-spin coupling constants (J_{CC}) $^{13}C-{}^{13}C$ at the double and triple bonds.[62] The J_{CC} values were found to be significantly smaller than those calculated according to the additive scheme. This is due to delocalisation of the multiple bonds by direct polar conjugation, through the double (triple) bond involving the lone pair on the nitrogen atom and the π-system of the carbonyl fragment.



The contribution of the bipolar resonance form was estimated to be ~ 30% for enamino ketones **6** and exceeded 50% for ynamino ketones **19**.[62] Comparison of chemical shifts in the ^{13}C NMR spectra of carbon atoms at the triple bond of substituted ynamines with the corresponding values for the C atoms at the double bond of enamines led to a conclusion about cross-polarisation of the orthogonal π-system of the triple bond in ynamines containing acceptor groups.[62]

This effect is manifested in the abnormally low shielding exerted by the dialkylamino group on the carbon atom of the multiple bond nearest to the nitrogen atom. Data on the structures of ynamino carbonyl compounds suggest that the conjugation of the donor and acceptor groups through the multiple bond (the so-called 'push-pull effect') strongly influences the distribution of electron density in the molecules and, as a consequence, their reactivities. As a result, these compounds acquire specific properties which differ radically from those of both ynamines and ketones containing a triple bond.[40]

The behaviour of ynamino ketones **19** in cyclisation reactions differs from that of enamino ketones **6** and **18**.[38, 39, 52] Whereas enamino carbonyl compounds typically 'deliver' three-carbon fragments in cyclisation,[40] ynamino ketones mostly react like simple ynamines, *i.e.*, with a twofold attack by bifunctional reagents on the carbon atoms of the triple bond (1,1-attack).[52]



19, **22**: R = Me (**a**), Et (**b**), Pr^n (**c**); **20**: X = NH (**a**), O (**b**), S (**c**); **21**: Y = O (**a**), S (**b**).

Thus the reaction of ynamino ketones **19** with ethylenediamine, ethanolamine and 2-mercaptoethanol is accompanied by the elimination of the dialkylamino group and the formation of

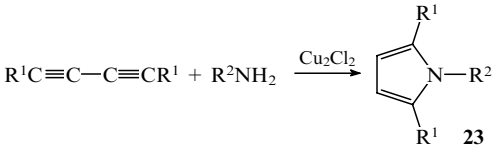
1-(4,5-dihydroimidazol-2-yl)prop-1-en-2-ol (**20a**), 1-(4,5-dihydrooxazol-2-yl)prop-1-en-2-ol (**20b**) and 1-(4,5-dihydrothiazol-2-yl)prop-1-en-2-ol (**20c**), respectively, containing a fully enolised carbonyl fragment.[68,69] The use of derivatives **20** as the X_α-inhibition factor[70] and anticonvulsants, *e.g.,* in the treatment of industrial electronic shock traumas, was described.[71]

The ynamino ketones **19** react with aromatic α,β-bifunctional reagents, *e.g.*, 2-aminophenol and 2-aminobenzenethiol, like ordinary ynamines[72–76] to produce 1-(benzooxazol-2-yl)propan-2-one (**21a**) and 1-(benzothiazol-2-yl)propan-2-one (**21b**), respectively.[77,78] Benzothiazole **21b** has been used in the synthesis of compounds for modulation of information signals[79] and pharmaceutical preparations against acidophilia, bronchial asthma, allergies,[80] diabetes and nephropathies.[81] Benzothiazoles of the type **21b** manifest herbicidal activities[82] and are used in the production of liquid-crystal compositions.[83]

The cyclisation of ynamino ketones **19** with *o*-phenylenediamine results in 2-dialkylamino-4-methyl-3*H*-1,5-benzodiazepines **22**[69] in up to 83% yields.

Photosensitive materials based on benzodiazepines **22** were patented.[84] Compounds of this class are used in the therapy of cholecystitis, gastritis[85] and meningitis[86] as well as squalene synthase inhibitors,[87] atypical neuroleptics[88] and fungicides against *Penicillum notatum*.[89] Thus, benzodiazepines of the type **22**, which have a wide range of practical applications, can also be synthesised from ynamino ketones.

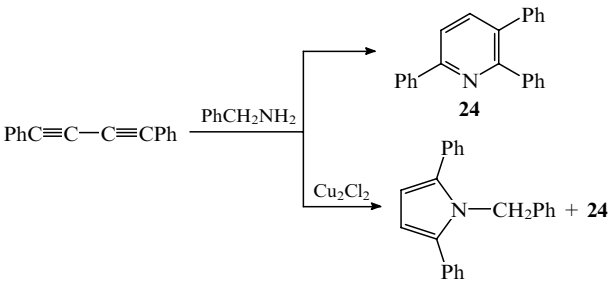
The reaction of diacetylene with primary amines in the presence of copper(I) salts occurs as 1,4-addition and results in the formation of pyrrole or 1-alkylpyrroles.[3] This reaction is carried out at 140–160 °C both in the absence of the solvent and in methanol, ethanol or DMF. In the latter case, the resulting pyrroles have a high degree of purity and are formed in higher yields. The reaction of ammonia and primary alkyl- and arylamines with disubstituted symmetrical 1,3-diynes in the presence of copper(I) chloride affords 1,2,5-trisubstituted pyrroles **23**.[3]



23

R^1 = H, Me, Et, Ph; R^2 = H, Me, Et, Bu^n, Ph.

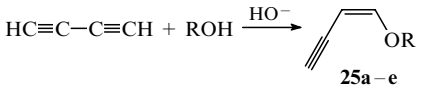
According to Shostakovsky and Bogdanova,[3] the role of a catalyst in this reaction consists in the formation of a non-polar π-complex with one of the triple bonds where the electron density is evenly distributed between both carbon atoms, which facilitates the interaction of the nucleophilic nitrogen with the fourth carbon atom of the conjugated diyne system. The smooth course of this reaction made it possible to develop a general scheme for the synthesis of substituted pyrroles.[3] The practical significance of this class of compounds is documented in numerous monographs and reviews.[13–16,21,29,90–94] In the absence of a catalyst, the reaction of diphenylbutadiyne with benzylamine affords 2,3,6-triphenylpyridine (**24**) in 50% to 70% yield.[95]



The specific feature of this reaction is that in the absence of a catalyst only pyridine **24** is formed; however, in the presence of Cu_2Cl_2 it proceeds simultaneously in two directions. This phenomenon is interpreted by the ability of copper(I) chloride to coordinate both at the nitrogen atom and at the triple bond.[95]

IV. Reactions with alcohols

The synthesis of 1-alkoxybut-1-en-3-ynes **25** by the reaction of diacetylene with alcohols in the presence of a catalyst was described;[3] however, the physical constants obtained by different authors differ.[96] This may be due to the difference in the ratios of *E*- and *Z*-isomers in the specimens prepared under different conditions or due to their contamination with products of further transformations of the ethers **25**.



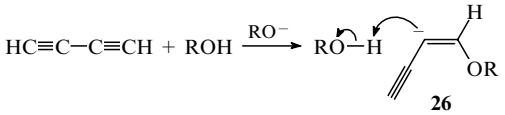
25a–e

R = Me (**a**), Et (**b**), Pr^n (**c**), Bu^n (**d**), n-C_5H_{11} (**e**).

The addition of methanol, ethanol, propan-1-ol, butan-1-ol, 2-methylpropan-2-ol, pentan-1-ol and hexan-1-ol to diacetylene has been studied under identical conditions at the alcohol : diacetylene ratio of 3 : 1 in the presence of catalytic amounts of KOH.[96] The content of *E*- and *Z*-isomers was determined on the basis of ^{1}H NMR spectroscopy and GLC data.

The ethers **25a**,**b** appeared to be pure *Z*-isomers; their homologues **25c**,**d** contained approximately equal amounts of the *E*-isomer (12.8% – 13.3%), whereas compounds **25e**,**f** represented equimolar mixtures of *E*- and *Z*-isomers.[96] It is probable that the rule of *trans*-nucleophilic addition is observed only for lower alcohols. However, if the reaction mixture contains compounds capable of forming complexes with diacetylene, the above rule may not be observed as is the case even with the reaction of diacetylene with methanol, which gives up to 15% of the *E*-isomer with dioxane as a solvent.[96]

Kinetic studies of reactions of diacetylene with lower aliphatic alcohols in the presence of KOH were carried out using UV spectroscopy and GLC.[97,98] The reaction of diacetylene with methanol (5 moles/mole of HC≡C–C≡CH) in the presence of KOH (0.22 moles/mole HC≡C–C≡CH) is described by an equation for a pseudo-unimolecular reaction with the activation enthalpy, $\Delta H^{\neq}$, of 87.8 kJ mol^{-1} and the activation entropy, $\Delta S^{\neq}$, of −19 e.u. The experimental results suggest[47] that the addition of the alkoxide ion to the terminal carbon atom of diacetylene followed by rapid protonation of the carbanionic intermediate **26** formed is the rate-limiting step of this reaction. sp^2-Hybridisation of the carbon atom orbitals at the double bond and spatial hindrances created by bulky alkoxy and ethynyl groups direct the attack of the proton donor to the *trans*-position relative to the alkoxide ion.

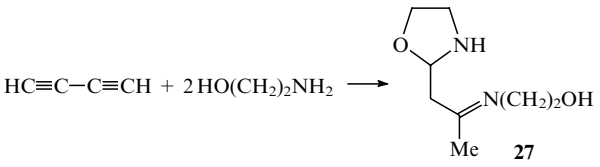


26

UV spectroscopy and GLC were used to study[98] the kinetics of the reaction of diacetylene with methanol and ethanol under conditions close to the industrial ones,[37] in the presence of potassium hydroxide and sodium hydroxide at 50–73 °C and at a 1,3-diyne concentration of 2.5 mass % – 10 mass %. Such a narrow temperature range can be explained by the fact that at lower temperatures diacetylene is predominantly polymerised due to the slow rate of the main reaction. At temperatures above 73 °C, this reaction proceeds further.[98] Since the rate of formation of the ether **25b** is proportional to the concentration of diacetylene in the solution, the reaction should be carried out at the maximally permissible (up to 10 mass %) concentration of HC≡C–C≡CH. The dependence of the rate constant for the formation of the ether **25b** on KOH concentration is more complex. With an increase in KOH concentration from 1% to 5%, the rate constant increases abruptly. Within the concentra-

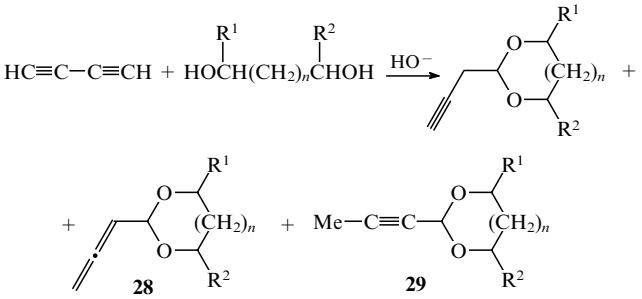
tion range of KOH from 5 mass % to 15 mass %, the reaction rate is not changed (k_{aver} = 2.7–2.8 l mol^{-1} s^{-1}, 60 °C), but this drops drastically after further increase in the catalyst concentration.[98] This is ascribed to the simultaneous effect of several factors. At low concentrations of the catalyst, the increase in the reaction rate is mainly due to an increase in the concentration of the alkoxide ions responsible for this reaction. At 5 mass %–15 mass % of KOH, the concentration of alkoxide ions increases to such an extent that its fluctuations within the indicated range do not influence the reaction rate. At KOH concentrations above 15 mass %, the rate of side reactions increases drastically. From these data, it was concluded that the optimum concentration of KOH is 5 mass %.[98]

When diacetylene was passed through a solution of monoethanolamine in benzene at 0 °C, a crystalline product was formed which represents 2-[2-(2-hydroxyethyl)iminopropyl]oxazolidine (**27**) as can be judged from the ^{1}H and ^{13}C NMR spectral data.



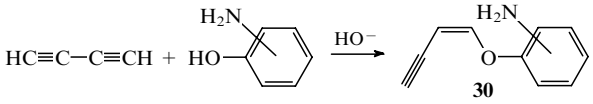
This adduct of diacetylene with ethanolamine is used for stabilisation of biologically active substances in grass fodders.[99]

The binding of 1,2- and 1,3-diols to diacetylene was studied in the presence of catalytic amounts of alkali and resulted in a mixture of cyclic acetals of but-3-ynal, buta-2,3-dienal (**28**) and but-2-ynal (**29**); their ratio changed depending on experimental conditions.[100]



n = 0: R^1 = R^2 = H; n = 1: R^1 = R^2 = H, Me, R^1 = Me, R^2 = H.

Bifunctional derivatives of the aromatic series, such as *o*-, *m*- and *p*-aminophenols, add to diacetylene in the presence of alkalis like ordinary alcohols, *i.e.*, through the hydroxy group, to give 1-aryloxybut-1-en-3-ynes (**30**).[101]



Alcohols (glycols, amino alcohols) and phenols add to diacetylene under much milder conditions than to acetylene and vinylacetylene.[37,98] The vinylation of lower alcohols with acetylene requires the use of superbasic media [19,20,23,28,102] or heating up to 120–140 °C, and their addition to vinylacetylene occurs at temperatures around 100 °C, while the optimum temperature for the reaction of diacetylene with methanol in the presence of KOH (5 mass %) is as low as 72–73 °C.[37,98] This circumstance is extremely important because the substantial difference between the rates of the reaction of methylacetylene, vinylacetylene and diacetylene with lower aliphatic alcohols allows selective chemisorption of diacetylene from gas mixtures produced by acetylene-manufacturing plants [36,37] which contain these particular hydrocarbons. Moreover, extraction of diacetylene from industrial gases allows implementation of technologies for industrial syntheses of isopropenylmethyl ether, acetone and acetylacetone based on the accompanying methylacetylene–allene fraction.[1]

Numerous transformations of the ether **25a** have been described under conditions of alkaline and acid catalysis (Scheme 3).[103] Thus the addition of the second methanol molecule to the ether **25a** in the presence of an alkali results in 1,1-dimethoxybut-3-yne (**31a**). Its analogue, *viz.*, 1-methoxy-1-phenethoxybut-2-yne, is used in perfumery.[104]

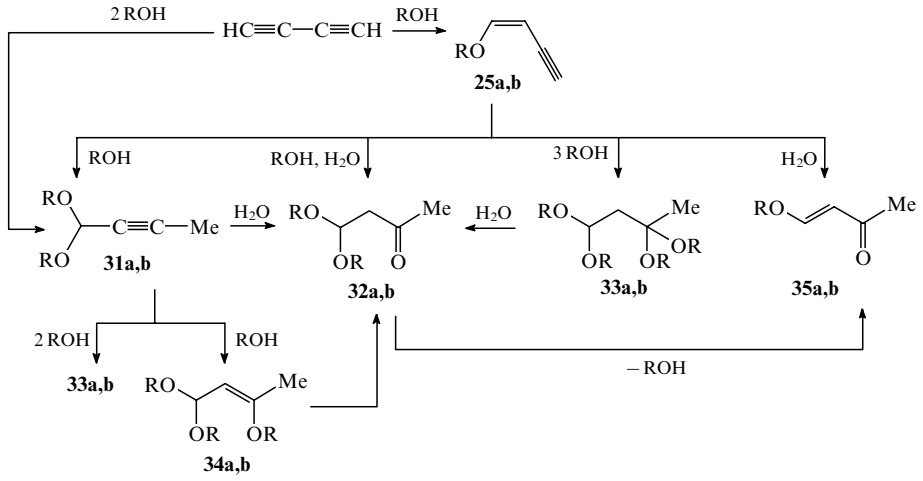
1,1-Dimethoxybutan-3-one (**32a**) is formed in 80% yield as a result of hydration of the triple bond of acetal **31a** under conditions of acid and mercury salt catalysis (H_2SO_4, $HgSO_4$) in boiling aqueous methanol (see Scheme 3). The addition of an alcohol and water to the ether **25a** in the presence of an acid catalyst also results in the acetal **32a** in 85% yield.

1,1,3,3-Tetramethoxybutane (**33a**) and a small amount of 1,1,3-trimethoxybut-2-ene (**34a**) are formed under identical conditions but in the presence of dry methanol (3 equiv.). Upon mild hydrolysis at room temperature, this mixture is converted into the acetal **32a**; its complete hydrolysis yields 1,3,5-triacetylbenzene, which was first observed by Claisen.[105]

Thus, the acetals **32a**,**b** appear to be the most convenient and stable intermediates prepared from diacetylene.[106]

Thermal or catalytic elimination of methanol from the acetal **32a** gives 4-methoxybut-3-en-2-one (**35a**);[106] a mixture of compounds **32a** and **35a** (7 : 3) is formed in the presence of catalytic amounts of acids or alkalis. Its homologue **32b** (R = Et) yielded

Scheme 3

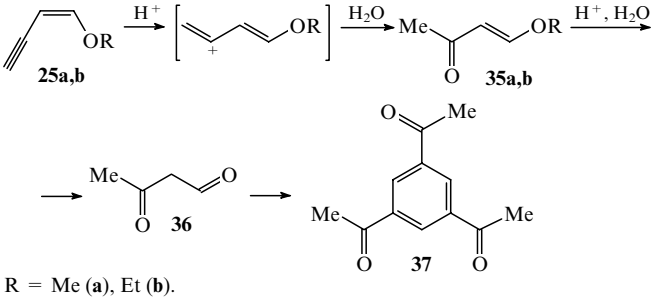


R = Me (**a**), Et (**b**).

an equilibrium mixture of **32b** and **35b** in a 7.5 : 2.5 ratio upon storage under conditions close to those employed in industry.[98]

The structure of the ketone **35a** was studied in detail using UV, IR and NMR spectroscopy.[107] Analysis of thermochemical and ^{1}H NMR spectral data revealed[108] that this compound has *E*-configuration.[108]

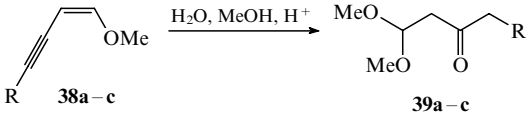
A kinetic analysis of acid-catalysed hydrolysis of the ethers **25a**,**b** by polarography[109,110] provided support for the initial rapid hydration of the triple bond with subsequent slow protonation of ketones **35a**,**b**, which are further decomposed to 3-oxobutanal (**36**); the latter undergoes self-cyclisation into 1,3,5-triacetylbenzene (**37**). In water, the rate of this reaction is an order higher than in 25% aqueous DMF.



R = Me (**a**), Et (**b**).

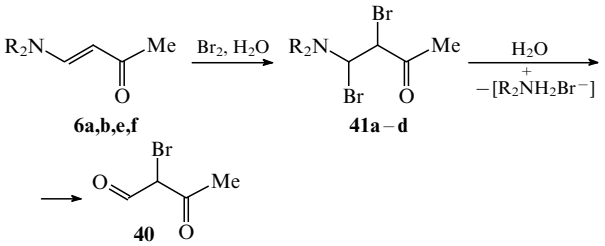
Evidence for primary hydration of the ethers **25a**,**b** was also obtained in kinetic studies of formation of 1,1-dialkyloxybutan-3-ones by GLC.[111–113]

The reaction of 1-methoxypent-1-en-3-yne (**38a**), 1-methoxyhex-1-en-3-yne (**38b**) and 1-methoxyhept-1-en-3-yne (**38c**) with methanol and water under conditions of acid catalysis gave 1,1-dimethoxyalkan-3-ones **39a–c**, respectively.[114]



R = Me (**a**), Et (**b**), Pr^n (**c**).

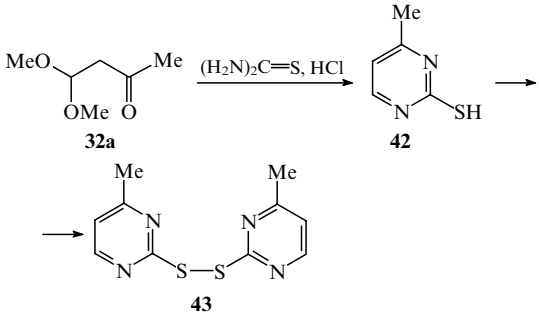
Derivatives of the aldehyde **36** containing functional groups in the methylene group have been synthesised. The synthesis of 2-bromo-3-oxobutanal (**40**) by direct bromination of the acetal **32** was described.[115] However, reproduction of the experiments and structural analysis of the reaction products by GLC revealed the formation of three compounds, which suggests that bromination of the original acetal occurs in all the three possible directions.[115] The bromosubstituted ketone **40** was synthesised in ~ 60% yield by bromination of enamino ketones **6a,b** in an aqueous medium. This reaction is accompanied by hydrolysis of 4-dialkylamino-3,4-dibromobutan-2-one **41** formed with elimination of the secondary amine and dehydrohalogenation.[115]



R = Me (**6a**, **41a**), Et (**6b**, **41b**); R$_2$N = (CH$_2$)$_4$N (**6e**, **41c**), (CH$_2$)$_5$N (**6f**, **41d**).

Intensive development of the chemistry of β-functionalised vinyl ketones has begun following synthesis of β-chlorovinyl methyl ketone by addition of acetyl chloride to acetylene.[116] The synthetic potentialities of β-chlorovinyl ketones have been reviewed.[116–118] The transfer of the acetylvinyl residue was named by A N Nesmeyanov and N K Kochetkov as 'ketovinylation'.[119] The synthetic potential of this reaction was further expanded owing to the involvement of other β-substituted vinyl ketones RCOCH=CHY (Y = OR, NR$_2$, SR, NO$_2$, N$_3$, SO$_2$R);[120] the activities and the selectivities of their reaction centres C(1) and C(3) can be altered by using different solvents.[121]

A pilot plant for the synthesis of the acetal **32b** based on dilute diacetylene-containing industrial gases accompanying manufacture of acetylene by electrocracking of methane (see Scheme 3) was installed at the Scientific-and-Industrial Association 'Azot' (Saratov) in 1974. The ether **25b** was obtained as a by-product.[37,122] This version of diacetylene utilisation was implemented on an industrial scale with DMF and *N*-methylpyrrolidone as selective solvents. A pilot-plant unit for isolation of diacetylene formed as a side product in the manufacture of acetylene by oxidative pyrolysis of methane and preabsorption with ammonium was installed at the Scientific-and-Industrial Association 'Azot' (Novomoskovsk) in 1980.[36,43,44,123–127] The technological process[36,123] involved isolation of diacetylene from the bottoms of an ammonium preabsorption unit followed by the synthesis of the ether **25a**. Its hydration and methoxylation in the presence of catalytic amounts of H_2SO_4 yield the acetal **32a**, which is further used in the synthesis of 4-methylpyrimidine-2-thiol (**42**) by the reaction with thiourea in the presence of HCl and its oxidation product, *viz*., bis(4-methylpyrimidin-2-yl) disulfide (**43**).[36,123]



The pyrimidinethiol and disulfide thus prepared accelerate the vulcanisation of rubbers having a unique spectrum of action.[127,128] Their addition to rubber mixtures increases the resistance of the compositions to prevulcanisation by 150%. The disulfide **43** is a novel accelerant having a retarded initial period of action. The use of such accelerants prevents early cross-linking in processing of rubbers.[128–130] Pyrimidinethiol **42** was used in the preparation of antitumour drugs[131] and novel nematocides.[132] It is also used as a lustre-enhancing coating in the production of electrolytic copper foils.[36,133] The addition of small (0.003–0.03 g litre^{-1}) concentrations of this compound to electrolytes for the production of copper foil increases its yield by 60% and improves its physico-mechanical properties. The use of pyrimidinethiol **42** in the production of photographic materials for thermal development is widely known.[134]

Thus, the interest in the practical use of diacetylene is determined by industrial demands, on the one hand, and by broad potentialities of the syntheses on the basis of 1,3-bifunctional compounds, on the other hand. The latter are the nearest derivatives of diacetylene and offer promising approaches to the synthesis of various classes of organic compounds. The list of products which can be prepared from diacetylene is given below.

Compound	Price per kg /USD[a]
1,1-Dimethoxybutan-3-one	201.75
(*E*)-4-Methoxybut-3-en-2-one	1716
1,3,3-Trimethoxybutane	1600
4-Diethylaminobutan-2-one	1290
Thiophene	236
5-Methylisoxazole	660
3-Methylpyrazole	2566
4-Methylpyrimidine	5200
2-Amino-4-methylpyrimidine	2117.5
4-Methylpyrimidine-2-thiol hydrochloride	770

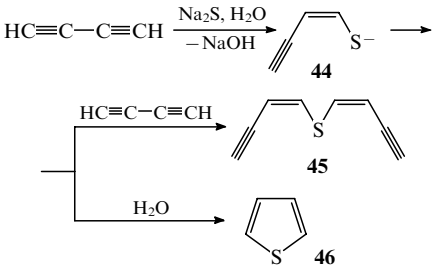
[a]The prices of 1997 are taken from Ref. 135.

V. Reactions with sulfur-containing nucleophiles

1. Reactions with hydrogen sulfide and sulfide ions

Systematic studies of reactions of acetylene and its derivatives with hydrogen sulfide and sulfide ions [12, 17, 20, 23, 26–32, 136–138] have been extended to diacetylene.[12]

The reaction of diacetylene with hydrated sodium sulfide occurs through the formation of the ethynylvinylthiolate anion (**44**) and results in both di(2-ethynylvinyl) sulfide (**45**) and thiophene (**46**),[12, 136–138] which is the product of cyclisation of the anion **44** or the corresponding thiol.



Earlier, an attempt was made [139] to synthesise thiophene from diacetylene by reaction of hydrated sodium sulfide with diacetylene in aqueous ethanol at pH 8–10; however, in this case the yield of the target product did not exceed 20%. When this reaction was carried out in a superbasic medium (KOH–DMSO), thiophene was obtained in high yields (up to 94%) and with high selectivity.[12, 136] The sulfide **45** is not formed under these conditions. If the reaction is carried out in dimethyl sulfoxide, the addition of an alkali is unnecessary, since it is liberated in this reaction, but the yield of thiophene does not exceed 55%. The effect of reaction conditions on the yield of thiophene is demonstrated in Table 2.

Table 2. The effect of conditions of the reaction of diacetylene with sodium sulfide on the yield of thiophene (solvent, DMSO).

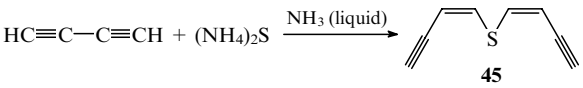
T /°C	Time /min	Concentration of reagents/mol		Yield of thiophene (%)
		C_4H_2	$Na_2S \cdot 9H_2O$	
20	90	0.054	0.108	44.1
55	75	0.038 [a]	0.083	93.9
70	90	0.120	0.061	54.9
100	75	0.072	0.14	40.0

[a] In the presence of 0.08 mol of KOH.

It should be emphasised that the addition of alkali is only necessary to trigger the synthesis, since the alkali liberated accelerates further the reaction. High selectivity of this reaction is worthy of note, *viz*., the purity of raw thiophene distilled from the reaction mixture without additional purification reaches 99.9%.

Since this reaction represents nucleophilic addition of the sulfide ion to diacetylene with subsequent cyclisation of the intermediate product,[140] its rate should be higher in the solvents which do not suppress the activity of anions owing to their solvation. By virtue of their high dielectric permittivity, aprotic dipolar solvents (*e.g*., DMSO, hexamethylphosphoric triamide) enhance electrolytic dissociation of sodium sulfide and sharply increase the concentration of the weakly solvated sulfide ion.[140] *N*-Methylpyrrolidone was also used as a solvent, and the reaction was carried out under identical conditions (55 °C, equimolar amounts of KOH and sodium sulfide). At 70 °C, the reaction of diacetylene with sodium sulfide carried out in an aqueous medium in the presence of an alkali gives thiophene in 52.5% yield.[12]

The conditions of the reaction of diacetylene with the sulfide ion giving exclusively the sulfide **45** (yields up to 89.5%) have been found.[140] In this reaction, liquid ammonia is used as a solvent and sulfide ions are generated from ammonium sulfide formed *in situ* from ammonia and hydrogen sulfide:



The product **45** has *Z*,*Z*-configuration, which points to high *trans*-stereoselectivity of this reaction.[140]

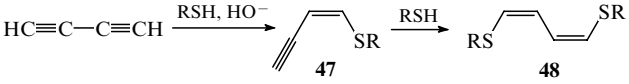
Among reactions of diacetylene with sulfur-containing compounds, synthesis of thiophene undoubtedly presents the greatest interest from the practical point of view. This stimulated the development of a procedure for continuous synthesis of thiophene from diacetylene and sodium sulfide in aqueous-alkaline media[12] with continuous removal of thiophene and replenishment of the reaction mixture with the starting reagents. Circulation of diacetylene lasted for 6 h at 70 °C; the yield of thiophene of 99% purity exceeded 70%. The results were reproducible. An increase in temperature caused a dramatic decrease in the yield of thiophene.

It should be noted that polymers formed from diacetylene in these media are not explosive. However, the synthesis performed in DMSO is more efficient, since it results in thiophene of high purity (99.9%) and in 94% yield.[136] The obvious advantages of this method include its simplicity, one-step procedure and wastelessness as well as high yields and high purity of the final product. Presumably, diacetylene present in waste gases from acetylene-manufacturing plants can also be used in large-scale productions, since the activities of the accompanying products (*e.g*., methylacetylene, vinylacetylene) in the reaction with sulfide ions is much lower.[12]

2. Reactions with thiols

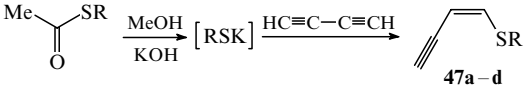
The addition of thiols to diacetylenes has been carried out under diverse conditions.[3] In the presence of catalytic amounts of an alkali, thiols are easily added to one of the triple bonds of diacetylene to form 1-organylthiobut-1-en-3-ynes **47**.[3]

This reaction is neither accelerated by free-radical initiators nor is decelerated by antioxidants, which suggests its heterolytic mechanism.[3] Like many other ionic reactions of nucleophilic reagents with alkynes, it occurs as *trans*-addition and results in the *Z*-isomers **47**. However, this reaction is complicated by the addition of thiol to the sulfide **47** and the formation of 1,4-bis(organylthio)buta-1,3-dienes **48,** which significantly diminishes the yield of the primary adduct **47**.



R = Alk, Ar, Het.

The *in situ* generation of the thiolate anion from *S*-alkylisothiouronium salts [141] or thioacetates [142] under the action of alkalis prevents competitive free-radical addition of the free thiol thus reacting to sulfides **47** in high yields. The reaction of diacetylene with thioacetates is carried out in the presence of KOH (1.2 moles per mole of the starting acetate) with methanol as a solvent. This reaction gives sulfides **47** in up to 80% yields.[141, 142]



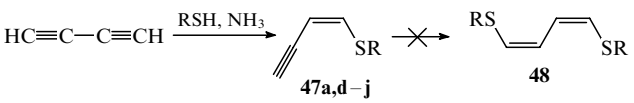
R = Et (**a**), Pr^n (**b**), Pr^i (**c**), Bu^n (**d**).

The IR spectra of sulfides **47a–d** contain characteristic absorption bands at 3290 (≡CH), 2100 (C≡C) and 1560 cm^{-1} (C=C–S). In ^{1}H NMR spectra, the spin-spin coupling constant of vicinal protons (J_{HH}) is 10 Hz, *i.e.,* it is characteristic of the *cis*-arrangement of vinylic protons.

The use of liquid ammonia or of aqueous ammonia for nucleophilic thiylation of 1,3-diynes opens up new prospects for

the synthesis of unsaturated sulfides and practical utilisation of diacetylene in those technological processes where liquid ammonia is used as a selective solvent.[36]

The reaction of diacetylene with thiols was studied [143] both in liquid ammonia and in aqueous ammonia at concentrations of ammonia varying from 25% to 70% within the temperature range of −33 to +20 °C. The aim of these studies was to reach the maximum use of the high solubilising capacity of ammonia with respect to diacetylene, which is determined by its moderate dielectric permittivity and polarity as well as by its relatively high basicity and ability to form hydrogen bonds and ammonium salts with thiols, which exist in ammoniacal solutions as contact ionic pairs and free ions. These factors altogether enhance the reactivity of thiolate ions, which are weakly solvated by ammonia. In fact, the reaction of diacetylene with thiols in liquid ammonia occurs under mild conditions (−33 °C) and is completed immediately after mixing of the reactants. Irrespective of the diacetylene : thiol molar ratio (1.0 : 0.5, 1 : 1, 1.0 : 1.2, 1 : 2), the selectivity of the reaction is not changed and the reaction results exclusively in sulfides **47** in 84% to 98% yields. This suggests that the secondary reaction leading to disulfides **48** is completely excluded in this case.[143]



47a,d–j **48**

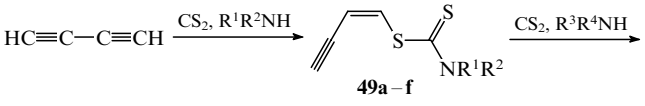
R = Et (**a**), Bu^n (**d**), n-C_6H_{13} (**e**), $(CH_2)_2OH$ (**f**), $CH_2CH(OH)CH_2OH$ (**g**), $CH_2Si(OMe)_3$ (**h**), $(CH_2)_2Si(OMe)_3$ (**i**), $CH_2Si(OEt)_3$ (**j**).

In this reaction, ammonia activates both the thiolate ion and diacetylene due to the formation of hydrogen bonds. The violation of the stereospecificity of the addition of thiols to diacetylene in liquid ammonia is attributed to the formation of diacetylene–ammonium complexes.[143] The adducts **47a**,**d–j** represent mixtures of *E*- and *Z*-isomers; the spin-spin coupling constants for the protons of *E*- and *Z*-ethylene fragments in the ^{1}H NMR spectra have characteristic values (15 and 10 Hz, respectively). The proportion of the *Z*-isomer increases with an increase in the bulk of the radical R, reaching a maximum (30%) in the case of compounds **47h–j**, *i.e.*, at the highest branching in the immediate vicinity of the sulfur atom. This suggests a significant contribution of spatial effects to the stereochemistry of this reaction, which seems to be predominantly kinetic, for the ratio of *E*- and *Z*-isomers is not changed after thermal treatment of the reaction products.

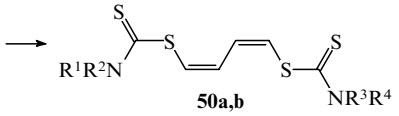
High reactivity of diacetylene with respect to thiols in liquid ammonia [143] permits, in principle, its quantitative isolation from gas mixtures in the form of sulfides **47**. Mild conditions of this reaction allow the involvement of thiols containing various functional groups.

3. The reaction with dithiocarbamate ions

Reactions of diacetylene with carbon disulfide and secondary amines or its direct reaction with ammonium dithiocarbamate in protic or aprotic solvents represent an efficient utilisation of diacetylene as a valuable product.[144] This reaction proceeds very easily in the absence of a catalyst when gaseous diacetylene is passed through a solution of a mixture of a secondary amine and carbon disulfide in MeOH, EtOH, Et_3N, THF, DMSO, acetone, benzene or ether or through a solution of dithiocarbamate at 20–50 °C and results in *s*-(*Z*)-(but-1-en-3-ynyl) *N,N*-dialkyldithiocarbamates **49** and 1,4-bis-(*N,N*-dialkylthiocarbamoylthio)-buta-1,3-dienes **50** in up to 94% yields.



49a–f



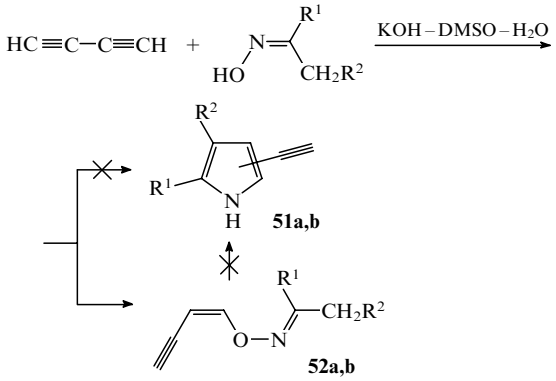
50a,b

49: $R^1 = R^2$ = Et (**a**), Pr^n (**b**); $R^1–R^2 = (CH_2)_5$ (**c**), $(CH_2)_2O(CH_2)_2$ (**d**); $R^1 = R^2$ = H (**e**), R^1 = H, R^2 = Me (**f**);
50: $R^1 = R^2 = R^3 = R^4$ = Et (**a**); $R^1 = R^2$ = Et, $R^3–R^4 = (CH_2)_5$ (**b**).

Mild conditions of this reaction are determined by high nucleophilicities of dithiocarbamate ions. The reaction products are *Z*-isomers.[144] However, the reaction of diacetylene with ammonium *N,N*-diethyldithiocarbamate is not stopped at the addition of one mole of dithiocarbamic acid and is complicated by further conversions resulting in the formation of bis(dithiocarbamate) **50**. Dithiocarbamates are used as nematocides and flotation agents [145, 146] as well as in the production of photosensitive materials. The information about the use of alkynes in the synthesis of such esters is scarce.[147]

VI. Reactions with ketoximes and amidoximes

It might be expected that the extension of the reaction of ketoximes with alkynes, which results in pyrroles (the Trofimov reaction),[13, 15, 16, 22, 29, 90, 93] to diacetylene [13] would open a route to the synthesis of ethynylpyrroles of the type **51** which could be regarded as promising monomers and reagents in fine organic synthesis. However, the route resulting in *O*-adducts, *e.g.*, *O*-(but-1-en-3-ynyl)ketoximes **52**, proved to be preferable due to the high reactivity of triple bonds of diacetylene with respect to nucleophilic reagents.[13, 148, 149]



51a,b

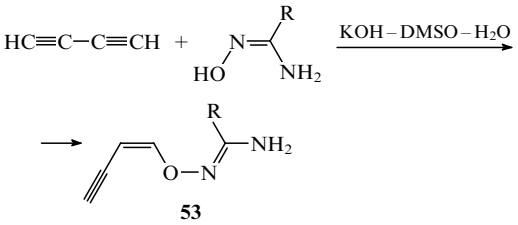
52a,b

R^1 = Me, R^2 = H (**a**); $R^1–R^2 = (CH_2)_4$ (**b**).

In aqueous DMSO, diacetylene exothermally adds to ketoximes in the presence of catalytic amounts of alkalis resulting in vinylketoximes **52**.[148, 149] It was of interest to find out whether more drastic conditions, which are normally used in the synthesis of pyrroles from ketoximes and acetylene, would result in cyclisation of vinylketoximes **52** through a [3,3]-sigmatropic shift characteristic of simple *O*-vinylketoximes.[13] However, under different reaction conditions diacetylene reacted with ketoximes to give either vinylketoximes **52** or black-coloured insoluble polymers formed upon more profound transformations of diacetylene itself and its adducts.[13] Ethynylpyrroles **51** were not found. The best yields of the adducts **52** (36%–41%) were obtained in the presence of ~10%–30% of water in DMSO and at a concentration of KOH 1%–2%. A decrease in the reagent's concentration increased the yield of the adduct, since polymerisation is inhibited under these conditions. An increase in the alkali concentration has a negative effect on the reaction yields. In neither case were bisadducts formed. The reaction of ketoximes with diacetylene is stereospecific and occurs as *trans*-addition. According to the ^{1}H NMR spectroscopic data, the adducts formed have *Z*-configuration (J_{HH} = 6.5–6.7 Hz), which corresponds to the nucleophilic addition to the triple bond with concerted attachment of a

proton from the reaction medium. Vinylketoximes **52** are rather unstable mobile fluids, these do not withstand heating up to 70–90 °C, being rapidly and quantitatively converted into a black insoluble powder even in solution. Thermolysis products largely contained polymers formed with involvement of the triple bonds. Pyrroles were not detected, either.

The reaction of diacetylene with amidoximes in the presence of KOH in aqueous DMSO gives *O*-adducts **53**. Their rearrangement into the corresponding ethynylimidazoles was not observed.[150]

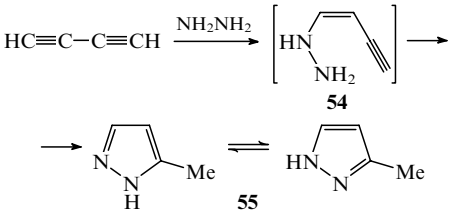


R = Me, Ph.

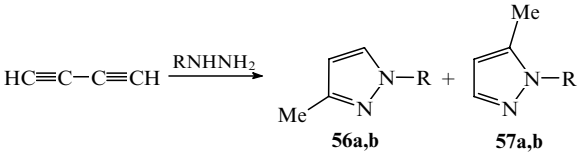
VII. Reactions with hydrazines and semicarbazide

In the syntheses of heterocyclic systems, 1,3- and 1,4-dicarbonyl compounds are widely used.[151] The role of such C_3- and C_4-synthons can be played by 1,3-diynes.[12, 13, 16, 17, 38–40]

Three independent groups of investigators reported simultaneously on the synthesis of pyrazole derivatives by addition of hydrazines to diacetylene and its mono- and disubstituted homologues.[38, 39, 49, 56, 152–155] Apparently, hydrazine reacts with diacetylene as a primary amine to give an intermediate **54**; further intramolecular attack of the second amino group at the C(3) atom results in the formation of the pyrazole ring **55**.[48]



Z-Configuration of the adduct favours the cyclisation. The condensation of methyldiacetylene with hydrazine hydrate gives 3,5-dimethylpyrazole together with 3(5)-ethylpyrazole,[155] which confirms the feasibility of another type of attack at the conjugated diyne system. In anhydrous media, the reactions of diacetylene with monosubstituted hydrazines result in 1,3-dialkylpyrazoles **56**, whereas 1,5-dialkylpyrazoles **57** are formed in the presence of water. The reaction of diacetylene with methylhydrazine in an ethanolic solution gives a mixture of pyrazoles **56a** and **57a** (4 : 1), which corresponds to the predominant attack of hydrazine at the carbon atom bearing the hydrogen atom.[156]

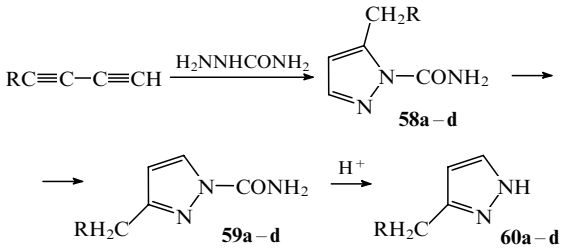


R = Me (**a**), Et (**b**).

Pyrazole **55** has become accessible due to the reaction of diacetylene with hydrazine.[152, 154, 155] Direct synthesis of pyrazoles seems to be one of possible clues to the practical solution of the problem of diacetylene utilisation;[155] the resulting pyrazoles with various substituents are used as starting compounds in the synthesis of *C*- and *N*-vinylpyrazoles.[155]

Syntheses of vinylpyrazoles and their homo- and copolymerisation acquired further development.[157–159] Syntheses of biological additives to polymeric materials based on pyrazoles prepared from diacetylene were also described.[157, 158] The synthesis of *C*-vinylpyrazoles from pyrazole **55** was carried out.[159] Vinyl derivatives of some azoles, including pyrazole, were used in various branches of industry, such as production of plastics and synthetic fibres, radio engineering and medicine.[159] Some novel herbicides,[160–162] pesticides,[163,164] antidiabetic drugs,[165] immunostimulators[166] and perfume compositions[167] prepared from pyrazoles **55**–**57** have been covered by patents. Synthesis of polychelating agents of the pyrazole series designed for solidification of epoxide resins was described.[157] The possibilities of extractive isolation of noble metals (Pd, Au, Ag) with pyrazole **55** hydrochlorides,[168, 169] of preparation of complex-forming ion-exchange resins,[170, 171] absorbents for concentration of platinum metals,[172] nitration catalysts[173] and disproportionation catalysts in the synthesis of monoalkyl- and monoaryl-halogenosilanes[174] were demonstrated.

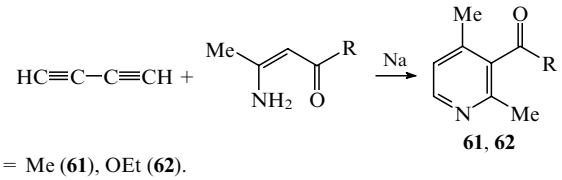
The reaction of diacetylene with semicarbazide, which manifests much weaker basic properties than hydrazines, yields a mixture of 3- and 5-alkylpyrazolecarboxamides (**58**, **59**).[175] The amides **58**, which are irreversibly isomerised into the adducts **59** under these conditions, are the main reaction products.[175] Other 1,3-diynes produce exclusively amides of the type **59**.[175]



R = H (**a**), Me (**b**), Et (**c**), Pr^n (**d**).

The presence of a pyrazole ring was confirmed[175] by acid hydrolysis of the adducts **59**, which was accompanied by decarboxylation and formation of pyrazoles **60**. Synthesis of 1-guanyl-3-methylpyrazole (yield 86%) from pyrazole **55** was described.[176] Pyrazole-1-carboxylic acid derivatives are used as pesticides[177] and insecticides.[178]

Functionalised pyridines were prepared based on diacetylene and compounds containing a weakly nucleophilic nitrogen atom and an active CH-component (*e.g.*, acetylacetoneimine and ethyl β-aminocrotonate).[176–178] The reaction products are 3-acetyl-2,4-dimethylpyridine (**61**) and ethyl 2,4-dimethylnicotinate (**62**), respectively.



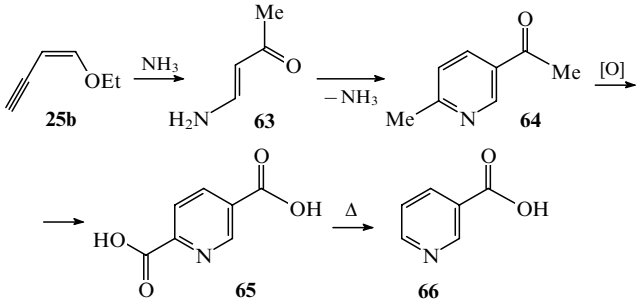
R = Me (**61**), OEt (**62**).

Since the nucleophilicity of the nitrogen atom in the starting enamino ester and the enamino ketone is lowered, the reaction with diacetylene occurs in the presence of metallic sodium.

The formation of one of two possible isomers in both reactions was confirmed by ^{1}H NMR and IR spectroscopy as well as by chromatography. Moreover, pyridine **62** was obtained independently by oxidation of ethyl 2,4-dimethyl-1,4-dihydronicotinate synthesised from crotonaldehyde and ethyl β-aminocrotonate.[178] The IR spectra of compounds **61** and **62** contain bands corresponding to stretching vibrations of the pyridine ring (1560, 1580 cm^{-1}), ester (1076 cm^{-1}) and carbonyl (1721 cm^{-1}) groups.[176, 178] The protons of the pyridine ring in the ^{1}H NMR spectrum of compound **62** resonate as two doublets in the low-field region at δ 8.24 and 6.84 (J = 5.2 Hz). The former belongs to the proton at the C(6) atom, which is especially strongly

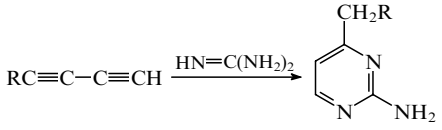
deshielded by the nitrogen atom of the pyridine ring, while the latter corresponds to the proton at the C(5) atom.

Pyridines prepared from diacetylene are candidates for the synthesis of nicotinic acid. However, the above-described reaction is inefficient because of low yields of the target products. A promising procedure for large-scale synthesis of nicotinic acid was developed [37, 130] on the basis of 4-aminobut-3-en-2-one (**63**) obtained by transamination of the ether **25b**.[58] Aminobutenone **63** cyclises spontaneously into 5-acetyl-2-methylpyridine (**64**),[179] which is further oxidised to pyridine-2,5-dicarboxylic (isocinchomeronic) acid (**65**), which in turn is decarboxylated into nicotinic acid (**66**) at 200 °C.[37]



VIII. Reactions with guanidine

The reaction of diacetylene and monosubstituted 1,3-diynes with guanidine in the presence of equimolar amounts of metallic sodium yields 4-alkyl-2-aminopyrimidines **67**.[180, 181]

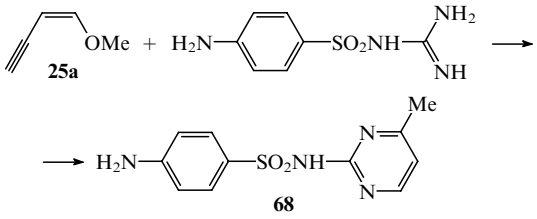


67a–d

R = H (**a**), Me (**b**), Et (**c**), Pr^n (**d**).

The structure of cyclisation products was established by a comparison of physical constants of isolated compounds and their picrates with those of known compounds obtained by independent synthesis.[180, 181]

Amines of the pyrimidine series are widely used in large-scale organic synthesis, particularly, in the pharmaceutical industry.[182] Some of them are intermediates in the synthesis of sulfonylamide drugs, *e.g*, sulfomerazine 2-(*p*-aminophenylsulfonylamido)-4-methylpyrimidine (**68**),[182] which can be prepared in high yields from the acetal **32a** or the ether **25a**.[130]

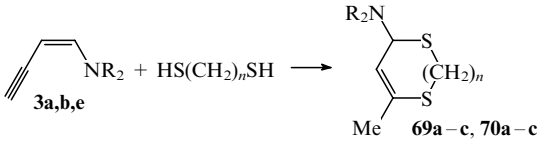


68

Sulfomerazine (**68**) is less toxic and more easily accessible (one-step procedure, high yields) than the well-known drug sulfodimezine [2-(*p*-aminophenylsulfonylamido)-4,6-dimethylpyrimidine] prepared from 2-amino-4,6-dimethylpyrimidine by a six-step procedure. Sulfomerazine is manufactured by the pharmaceutical company 'Polfa' and is used in the treatment of streptococcal and pneumococcal infections. Some derivatives of the pyrimidine **67a**, which include protein tyrosine kinase inhibitors,[183] vitronectin receptor antagonists,[184] potent psychotropic drugs,[185] novel fungicides[186] and perfume compositions,[187, 188] were patented.

IX. 1-Dialkylaminobut-1-en-3-ynes as building blocks for the synthesis of heterocyclic compounds

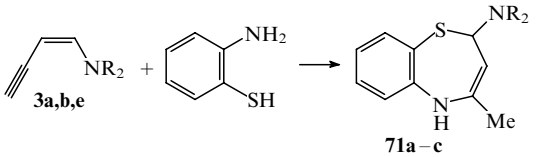
Some cyclisation reactions occur exclusively with the amines **3**. Their reaction with 1,2-ethanedithiol and 1,3-propanedithiol result in 5-dialkylamino-7-methyl-5*H*-2,3-dihydro-1,4-dithiepines **69a–c** and 2-dialkylamino-4-methyl-2,6,7,8-tetrahydro-1,5-dithiocines **70a–c**, respectively.[189, 190]



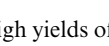
69a–c, 70a–c

R = Me (**3a**, **69a**, **70a**), Et (**3b**, **69b**, **70b**); R$_2$N = (**3e**, **69c**, **70c**); *n* = 2 (**69a–c**), 3 (**70a–c**).

The condensation of 2-aminobenzenethiol with the amines **3a**,**b**,**e** is performed at room temperature in the absence of a catalyst and gives 2-dialkylamino-4-methyl-2,5-dihydro-1,5-benzothiazepines **71a–c** in up to 90% yields.[190, 191]

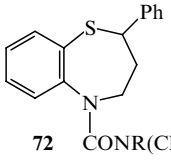


71a–c

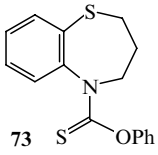
R = Me (**3a**, **71a**), Et (**3b**, **71b**); R$_2$N =  (**3e**, **71c**).

High yields of the reaction products and the absence of routes to their direct synthesis from diacetylene makes this method for the preparation of thiazepines promising.

1,4-Dithiepine derivatives are biologically active and can be used as tranquillisers.[192, 193] 1,5-Benzothiazepines manifest antiarrhythmic activity [194] and are used as regulators of the cardiovascular function.[195, 196] Compounds **72** are tranquillisers,[197] and 1,5-benzothiazepines **73** possess antifungal activity.[198]



72



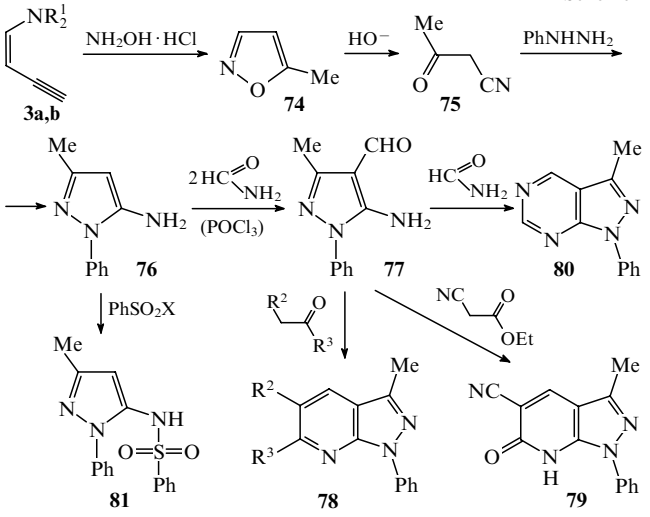
73

n = 2, 3.

The salient advantage of 1-dialkylaminobut-1-en-3-ynes over diacetylene and its other derivatives as building blocks becomes especially obvious in the synthesis of isoxazoles. The latter cannot be obtained by the reaction of diacetylene with hydroxylamine hydrochloride.[47] 1-Alkoxy- and 1-alkylthiobutenynes give a mixture of 3- and 5-methylisoxazoles.[37, 38, 47] On the other hand, 1-dialkylaminobut-1-en-3-ynes **3** give exclusively 5-methylisoxazole (**74**) in reaction with hydroxylamine (Scheme 4).[37, 47] The latter yields cyanoacetone (**75**) upon alkaline treatment.[199] Cyanoacetone reacts with phenylhydrazine to give the cyclisation product, *viz*., 5-amino-3-methyl-1-phenylpyrazole (**76**).[37] The latter is subjected to Wilsmeyer–Haack formylation to give 5-amino-3-methyl-1-phenylpyrazole-4-carbaldehyde (**77**),[200] which is used in the construction of fused pyrazolopyridines **78** and **79** and pyrazolopyrimidines **80** (see Scheme 4).[201, 202]

Novel long-acting sulfonylamide drugs of the type **81** can be prepared from the isoxazole **74**.[202] Aminopyrazole **76** is used in the synthesis of pharmacologically active compounds (*e.g*., antidepressants, anticonvulsants, analgesics, *etc*.),[203] biologically active reagents, some key synthons,[204] diazo dyes for colour offset,[205] heterocyclic anionic monoazo dyes [206] and compositions for colour photography.[207–209]

Scheme 4

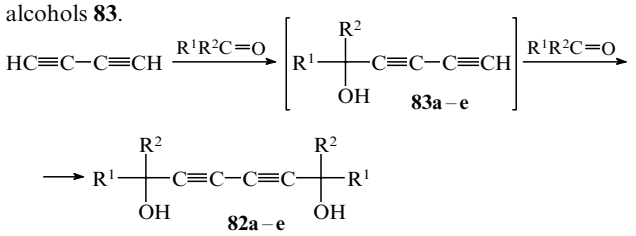


$R^2 = R^3$ = Me, Et.

X. Reactions with carbonyl compounds

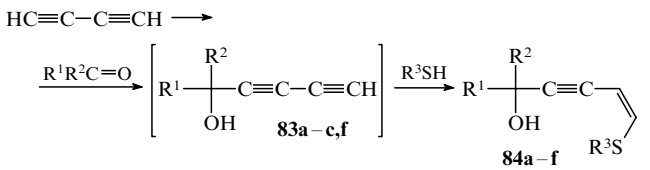
General methods for the synthesis of diacetylene alcohols and glycols include the reaction of sodium derivatives of 1,3-diynes with carbonyl compounds in liquid ammonia, condensation of mono- and bis(bromomagnesium) derivatives of 1,3-diynes with aldehydes and ketones in THF, the Favorsky condensation of 1,3-diynes with carbonyl compounds in the presence of KOH powder in ether or THF, oxidative condensation of α-acetylenic alcohols in the presence of copper salts and the Hodkevich–Kadyo condensation of monoacetylenic alcohols.[3]

This review provides a detailed description of reactions of diacetylene with carbonyl compounds which are applicable to industrial diacetylene and result in the formation of valuable products. Since some technological schemes used in acetylene production include selective extraction of diacetylene with liquid ammonia,[36] its extraction with ammoniacal and aqueous ammoniacal solutions also seems to be efficient. A one-step procedure was developed for the synthesis of bis-tertiary diacetylenic glycols by the reaction of diacetylene with ketones in the presence of a catalytic system (ammonia–water–alkali).[210] The use of a small excess of the ketone allows preparation of glycols **82** in nearly quantitative yields without the formation of the diacetylenic alcohols **83**.



82, **83**: $R^1 = R^2$ = Me (**a**); R^1 = Me, R^2 = Et (**b**); $R^1-R^2 = (CH_2)_5$ (**c**); R^1 = Me, $R^2 = Bu^n$ (**d**); R^1 = Me, R^2 = n-C_6H_{13} (**e**).

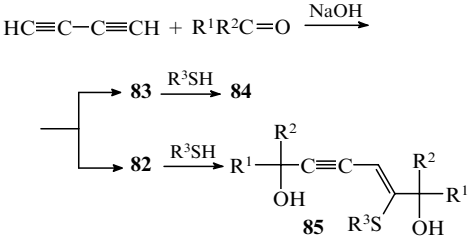
A simple and efficient one-pot synthesis of tertiary alkylthioenyne alcohols **84** from diacetylene, ketones and thiols in liquid ammonia has been developed.[211–214]



Diacetylenic alcohols **83**	R^3 in the thiol R^3SH	Thioalcohol **84**
83a ($R^1 = R^2$ = Me)	Et	**84a**
	Pr^n	**84b**
	Bu^n	**84c**
83b (R^1 = Me, R^2 = Et)	Et	**84d**
83c ($R^1-R^2 = (CH_2)_5$)	Et	**84e**
83f ($R^1-R^2 = (CH_2)_4$)	Et	**84f**

The alcohols **84a–f** are characterised by a broad spectrum of biological activities and exhibit interest as monomers and intermediates for fine organic synthesis and for the pharmaceutical industry.[215]

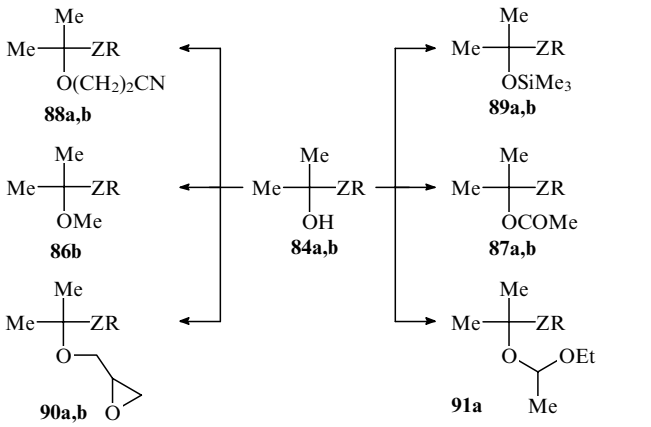
Condensation of diacetylene with ketones in the presence of catalytic amounts of an alkali (0.01–0.1 moles per mole of HC≡C–C≡CH) in liquid ammonia with subsequent addition of a thiol was studied with the aim of developing a reliable procedure for the synthesis of alkylthioenyne alcohols **84** and glycols **85**.[213] This reaction is carried out with a 6%–10% diacetylene solution in liquid NH_3 at the temperature of liquid ammonia and at the diacetylene : ketone : thiol molar ratio of 1.0 : 0.5 : 1.2. Alkali metal cations catalyse the condensation of diacetylene with ketones and simultaneously accelerate the reaction of diacetylenic alcohols **82** with thiols resulting in compounds **84** (yields 83%–96%).[213] An excess of diacetylene (relative to the ketone) directs the reaction towards the formation of diacetylenic alcohols. Alkylthioenyne glycols **85** are formed in 89% to 95% yields at the diacetylene : ketone : thiol molar ratio of 1.0 : 2.0 : 1.3.[213,216]



R^1 = Me: R^2 = Me, Et; $R^1-R^2 = (CH_2)_4$;
R^3 = Et, Pr^n, Pr^i, Bu^n, Bu^i.

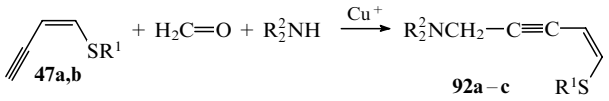
The sulfides **84** can also be synthesised by the condensation of enynyl sulfides **47** with acetone under conditions of the Favorsky reaction.[217] Since the presence of the hydroxy functional group often excludes the possibility of selective attack at other reaction centres, Volkova *et al.*[211] have converted alcohols **84a**,**b** into ethers (**86b**), esters (**87a**,**b**), β-cyanoethyl (**88a**,**b**), trimethylsilyl (**89a**,**b**) and glycidyl (**90a**,**b**) derivatives and acetals (**91a**) (Scheme 5).

Scheme 5



ZR = C≡C–CH=CH–SR, where R = Et (**a**), Pr^n (**b**).

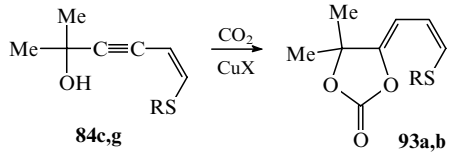
The functionalisation of the thioethers **47a–c** was described.[142] These sulfides, contrary to the published data,[3] enter into the Mannich reaction with secondary amines on heating in dioxane in the presence of copper(I) chloride to give 1-alkylthio-5-dialkylaminopent-1-en-3-ynes **92a–c**.



47: R^1 = Et (**a**), Pr^n (**b**);
92: R^1 = R^2 = Et (**a**); R^1 = Pr^n, R^2 = Et (**b**); R^1 = Et; R^2 = $(CH_2)_2OH$ (**c**).

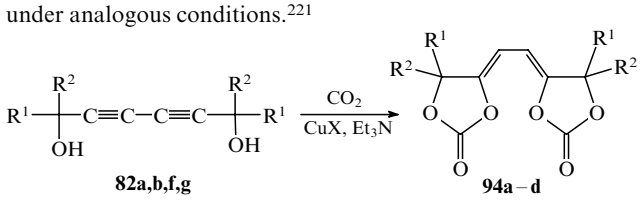
The reaction of 2-methyl-6-phenylhexa-3,5-diyn-2-ol with alcohols and ketones[218] was used to obtain the corresponding ethynylvinyl ethers and dioxolanes which contain an enyne fragment in the side chain and manifest pharmacological activities.[219]

An unusual reaction of tertiary alkylthioenyne alcohols **84** with CO_2 was carried out under a pressure of 70–73 atm at 70–75 °C in the presence of catalytic amounts of copper(I) salts and triethylamine without solvents.[220,221] The products of this reaction are 5-(3-alkylthioprop-2-enylidene)-4,4-dimethyl-1,3-dioxolan-2-ones **93a**,**b**.[220]



R = Bu^n (**84c**, **93a**), Me (**84g**, **93b**); X = Cl, OAc.

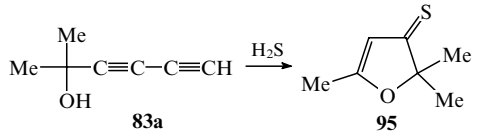
Stable 1,2-bis(1,3-dioxolan-2-on-5-ylidene)ethanes **94a–d** are formed from diacetylenic glycols **82a–d** in more than 90% yields under analogous conditions.[221]



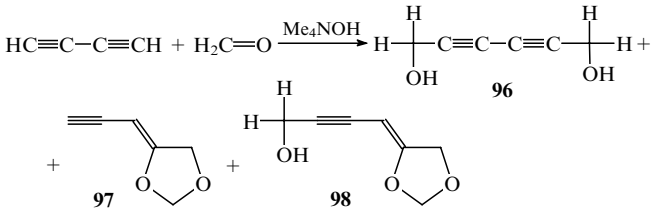
X = Cl, OAc.

R^1	R^2	Glycol **82**	Product **94**
Me	Me	**82a**	**94a**
Me	Et	**82b**	**94b**
Pr^n	Pr^n	**82f**	**94c**
$(CH_2)_4$		**82g**	**94d**

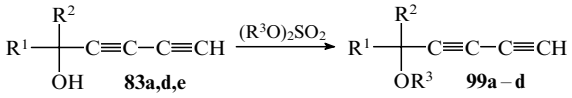
The reaction of the tertiary diacetylenic alcohol **83a** or the bis-tertiary diacetylenic glycol **82a** with hydrogen sulfide[222] in the presence of alkaline catalysts result in dihydrofuranthione **95**.



Condensation of diacetylene with carbonyl compounds was carried out under conditions close to the industrial ones.[223–225] 2,7-Dimethylocta-3,5-diyne-2,7-diol (**82a**) was obtained in 72% yield (acetone, 25% aqueous NH_3, 0.01–0.04 mole of KOH or NaOH per mole of acetone, 10-fold excess of diacetylene).[224] A decrease in the catalyst's concentration to 0.01 mole decreases the yield of glycol to 11% and simultaneously increases the yield of 2-methylhexa-3,5-diyn-2-ol (**83a**) from 9% to 61%. An increase in the ammonia concentration in the reaction mixture directs the reaction exclusively towards the formation of glycol **82a**; its yield reaches 94%. Butylmethyl- and hexylmethyl ketones react with diacetylene in the presence of an alkali (0.3 mole per mole of ketone) to form diacetylenic alcohols **83** (yields ~ 60%).[224] It was shown that the anion-exchange resin AB-17-8P (OH) catalyses the condensation of diacetylene with carbonyl compounds.[226] Tetramethylammonium hydroxide also catalyses the reaction of diacetylene with formaldehyde.[227] The reaction with formaldehyde occurs smoothly at 20–40 °C and yields, in addition to hexa-2,4-diyne-1,6-diol (**96**), 1,3-dioxolanes **97** and **98** which are the products of subsequent reaction of formaldehyde with the diol **96** and 2,4-pentadiynol.[227]

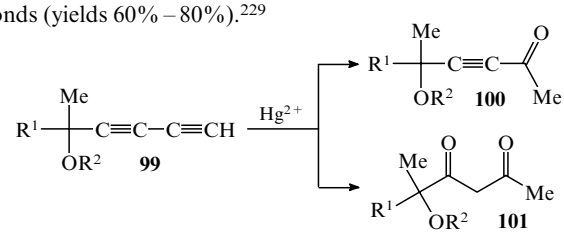


Alkylation of alcohols **83a–d** (dialkyl sulfate, 5–15 °C, 2 h) was used to prepare ethers of tertiary diacetylenic alcohols **99** in up to 80% yields.[228]



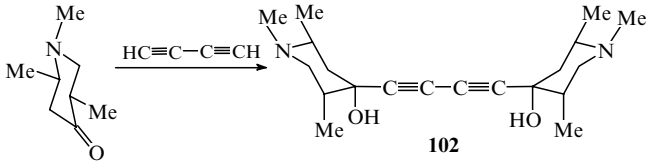
R^1	R^2	R^3	Alcohol **83**	Ether **99**
Me	Me	Me	**83a**	**99a**
Me	Me	Bu^n	**83a**	**99b**
Me	n-C_6H_{13}	Me	**83e**	**99c**
Me	Bu^n	Et	**83d**	**99d**

β-Diketones and acetylenic ketones were synthesised from ethers **99**.[229] In the presence of $HgSO_4$ (1 h, 65–70 °C), the hydration of the terminal triple bond of the ethers **99** gives ketones **100** in up to 93% yields.[229] β-Diketones **101** are formed with an increase in temperature to 80 °C and with larger amounts of $HgSO_4$ in 8–10 h as a result of total hydration of both triple bonds (yields 60%–80%).[229]



A number of papers are devoted[230–237] to the synthesis of potentially physiologically active compounds based on acetylenic and diacetylenic alcohols and glycols as well as to the analysis of biological activities of reaction products and their applications in agriculture.

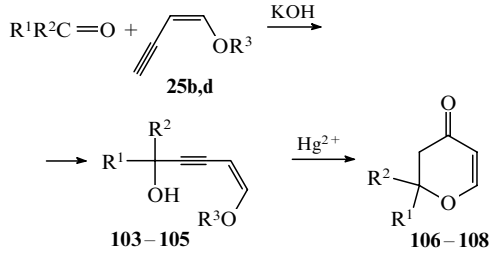
It was shown that diacetylene and diynes containing terminal triple bonds add to the carbonyl group of 1,2,3-trimethylpiperidin-4-one under conditions of the Favorsky reaction to yield a mixture of isomeric alcohols and glycols containing predominantly epimers **102**, the products of axial addition of diynes to the C=O bond.[230–237]



A correlation was found between the biological activity and chirality of asymmetrical diacetylenic glycols.[230] Acpinol, which represents a product of exhaustive hydrochlorination of a mixture of isomers of the glycol **102,** was recommended for use in agriculture.[236–240] A method of manufacture of acpinol employs diacetylene present in the abgases from acetylene-manufacturing

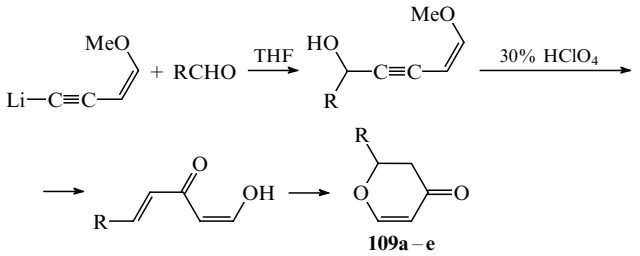
plants. The purity of the product depends on the composition of the abgas.[230]

The cyclohydration of alkoxyvinylacetylenic alcohols **103–105** obtained from ethoxybutenyne (**25b**) and butoxybutenyne (**25d**)[241,242] under conditions of the Kucherov reaction or in dilute H_2SO_4 at room temperature results in dihydropyran-4-ones **106–108**.[243,244]



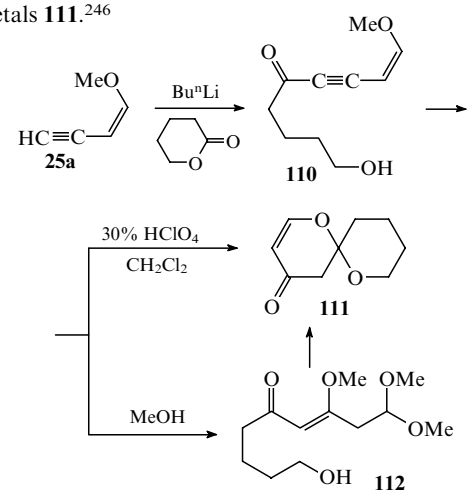
$R^1 = R^2 = Me$ (**103**, **106**); $R^1 - R^2 = (CH_2)_5$ (**104**, **107**);
$R^1 - R^2 = (CH_2)_2NMe(CH_2)_2$ (**105**, **108**); R^3 = Et (**b**), Bu^n (**d**).

The synthesis of 2-alkyl-2,3-dihydro-γ-pyrones **109** from the ether **25a** and aldehydes was described.[245] Condensation of lithium methoxybutenynide with various aldehydes (from MeCHO to iso-$C_5H_{11}CHO$) in THF at −78 °C yields secondary alcohols which undergo hydration at the triple bond with subsequent cyclodehydration to give dihydropyrones **109a–e**.[245]



R = Me (**a**), Et (**b**), Pr^n (**c**), Pr^i (**d**), iso-C_5H_{11} (**e**).

The yield of the reaction products increases with an increase in the length of the alkyl radical. Thus pyrones **109a** and **109e** are formed in 40% and 80% yields, respectively. The reaction of the lithium derivative of the ether **25a** with lactones affords spiroketals **111**.[246]



For example, the hydroxy ketone **110** was obtained from δ-valerolactone in THF at −78 °C in 98% yield. Its conversion into the spiroketal **111** can be carried out in two ways,[246] *viz*., by direct conversion under the action of 30% $HClO_4$ in CH_2Cl_2 (yield 58%) or *via* an intermediate trimethoxy ketone **112** (yield 86%). These dihydropyrones are used as fungicides.[247]

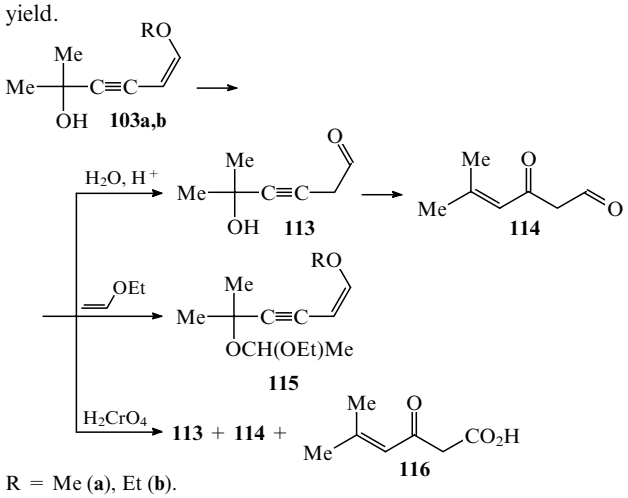
A general method for the synthesis of functionalised spiroketals from lactones and (*Z*)-lithium derivatives of the ether **25a** was proposed.[248]

Some novel antiinflammatory drugs and a pharmaceutically stable inhibitor of LTA_4-hydrolase based on the *E*-isomer of the ether **25a** were patented.[249] These compounds are used as constituents of composite fuels for stabilisation of combustible mixtures.[250]

Ethynylation with diacetylene was used in the synthesis of additives to perfume compositions, *e.g*., 2,6,11,15-tetramethylhexadecane-6,11-diol[251] or 6,11-dihydroxycrocetane and crocetane.[252] A commercial synthesis of squalane by ethynylation of geranylacetone with a diacetylene–*N*-methylpyrrolidone complex (1 : 1) in the presence of KOH with subsequent reduction over Raney nickel was described.[253]

The alkoxy- and alkylthioenyne alcohols prepared from diacetylene can be used in the synthesis of various polyfunctional unsaturated compounds.[254]

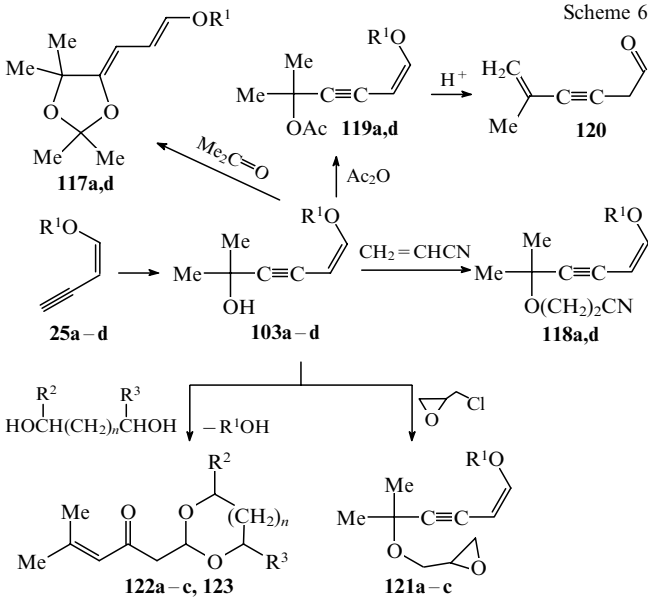
Hydrolytic scission of vinyl ethers **103a**,**b** by dilute acids results in acetylenic hydroxy aldehydes **113**, which are readily isomerised into oxoaldehydes **114** in up to 75% yields.[254] The reaction of vinyl ethers **103a**,**b** with ethyl vinyl ether was used to obtain acetals **115** (yield 80%). The oxidation of vinyl ethers **103a**,**b** with chromic acid in acetone gives a mixture of aldehydes **113** and **114** in a total yield of 61% and the oxo acid **116** in 10% yield.



R = Me (**a**), Et (**b**).

Reactions of tertiary alcohols **103a–d** with acetone, acrylonitrile, acetic anhydride, epichlorohydrin and glycols (Scheme 6) were studied.[255]

Scheme 6



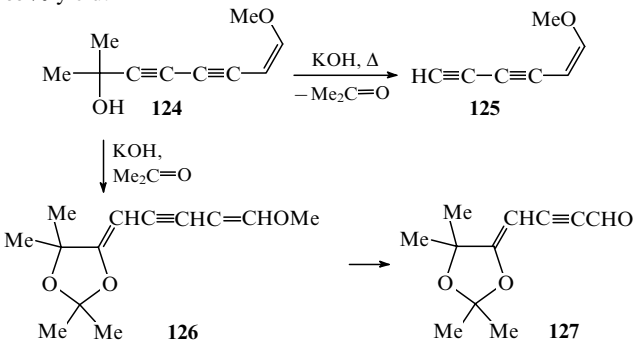
R^1 = Me (**a**), Et (**b**), Pr^n (**c**), Bu^n (**d**);
R^2, R^3 = H, Me; *n* = 0 (**122**), 1 (**123**).

The reactions of the vinyl ether **103a**,**d** with acetone result in 5-(3-alkoxyallylidene)-2,2,4,4-tetramethyl-1,3-dioxolanes **117a**,**d**.[255] Cyanoethylation of these ethers with acrylonitrile occurs in the presence of an 40% aqueous solution of KOH or MeONa in *tert*-butyl alcohol and results in 1-alkoxy-5-(2-cyanoethoxy)-5-methylhex-1-en-3-ynes **118a**,**d** in up to 50% yields. Acetylation of the alcohols **103a**,**d** with acetic anhydride in pyridine at 70–90 °C results in 5-acetoxy-1-alkoxy-5-methylhex-1-en-3-ynes (**119a**,**d**) in 21% to 49% yields.[255] During distillation, acetates undergo deacetylation and dehydration to give the enynal **120**.[255] The reaction of epichlorohydrin with ethers **103a–c** in an alkaline medium afforded glycidyl ethers **121a–c** in 60%–65% yields (see Scheme 6).[256] The resulting products are candidates for epoxy-containing monomers.[215]

The reaction of bisprimary and primary-secondary α- and β-glycols with ethers **103a**,**b**,**d** in the presence of the Newland catalyst ($HgO-BF_3$) results in 2-(4-methyl-2-oxopent-3-enyl)-1,3-dioxolanes **122** in up to 64% yields (see Scheme 6).[257] Presumably, this reaction begins with isomerisation of the alkoxy-enyne alcohol into an unstable alkoxydivinyl ketone. The latter adds a glycol molecule to give an asymmetrical hydroxy acetal, which easily loses the alcohol molecule and cyclises into 1,3-dioxolanes **122** or 1,3-dioxanes **123**.[257] Moderate neuroactivity of 1,3-dioxolanes and 1,3-dioxanes prepared on the basis of alkoxy-enyne tertiary alcohols was established.[258]

It is worth noting that the most reactive compounds of this series manifest both general depressant activity and a stimulating effect on the central adreno- and dopaminergic systems of the brain, which makes them similar to antidepressants.[258]

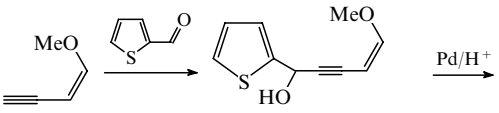
Base-catalysed thermolysis (the retro-Favorsky reaction) of 8-methoxyoct-7-ene-3,5-diyn-2-ol (**124**) was studied.[259] In organic media, this is accompanied by different reactions the direction of which depends on the nature of the solvent.[259] In benzene or THF, the thermolysis at the boiling temperature of the reaction mixture results in the formation of 1-methoxyhex-1-ene-3,5-diyne (**125**) in 85% yield.[259]

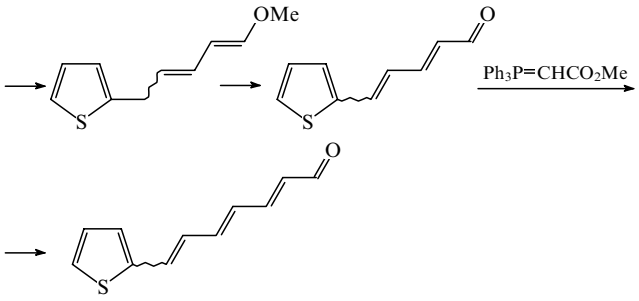


The formation of 2,2,4,4-tetramethyl-5-(5-methoxypent-4-en-2-ynylidene)-1,3-dioxolane (**126**) isolated from the reaction mixture as a side product can be attributed to the reaction of the original alcohol with acetone in the presence of KOH. In air, the product **126** is oxidised to 2,2,4,4-tetramethyl-5-(3-formylpropynylidene)-1,3-dioxolane (**127**).[259]

Vinyl ethers **103** react with nitrogen bases (hydrazine, methylhydrazine, hydroxylamine) in acid and alkaline media with the formation of heterocyclic compounds of the pyrazole and isoxazole series.[260]

Some natural thiophene derivatives (*e.g.*, 7-thienylheptatrienal) were synthesised from (*E*)-methoxybutenyne and thiophene-2-carbaldehyde.[261]





XI. Conclusion

The data accumulated thus far demonstrate the possibility of utilisation of diacetylene in industrial syntheses of valuable products, reagents, starting compounds for pharmaceutical industry, materials for new technologies, *etc*.

The processes aimed at acetylene production based on pyrolysis of hydrocarbon raw materials will long be used as a source for large-tonnage synthesis of diacetylene the utilisation of which is still a challenge for chemists and also common sense, since combustion of hydrocarbon gases is most senseless in this case. As D I Mendeleev used to say, 'one can fire a furnace with banknotes'.[262]

It has now become quite clear that diacetylene can be used for small-capacity, profitable manufacture of thiophene, vitamins A and PP, geraniol and phytol derivatives, pyrazoles, pyrimidines and pyridines. Studies of diacetylene polymerisation reactions present special interest. The first example of polyacetylene synthesis from a diacetylenic monomer has been described recently.[263]

The diacetylene present in industrial gases enters into reactions of nucleophilic addition selectively. In this review, it is these transformations which encompass only some of possible applications of diacetylene and its derivatives that are analysed in detail. Thus copolymers of diacetylenic glycols and their derivatives are used as a basis in the preparation of stereoregulatory membranes mimicking cell liposomes[14] and thermochromic polymeric layers[264,265] for laser image recording and observations over conformational transitions in polymers at ambient temperatures.

The role of compounds produced from diacetylene will be increasing with the development of new technologies. The synthesis of reagents based on diacetylene can be the first step towards its commercial utilisation. This, in turn, will give an impetus to the development of new procedures for the synthesis of a vast variety of useful compounds from inexpensive industrial raw materials using reactions discussed in the present review.[266]

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