REDOX TRANSFORMATIONS OF COMPOUNDS OF THE THIOPHENE SERIES (REVIEW)

L. I. Belen'kii and V. P. Gul'tyai

UDC 542.941'943:547.732

Chemical and electrochemical methods for the reduction and oxidation of compounds of the thiophene series that consist in transformations of the substituents or the heteroring and are suitable for preparative use are described.

Thiophene occupies a special position among five-membered heterocycles with one heteroatom. Inasmuch as it is the most resistant of these compounds to the action of acids, in many respects it resembles activated compounds of the benzene series with respect to its ability to undergo substitution reactions. Moreover, its behavior in these reactions, particularly with regard to orientation, as in the case of other heterocycles, is determined by the presence of a heteroatom, which is a unique "internal function." It is not by chance that thiophene compounds are often used as model systems in the study of the reactivities and mechanisms of the reactions of five-membered heterocycles. At the same time, the ability of the thiophene heteroatom and particularly that of substituted thiophenes to undergo oxidation makes it possible to easily convert them to heterocycles that have diene properties. The reductive cleavage of the thiophene ring, which proceeds with retention or elimination of the sulfur atom, leads to diverse compounds of the aliphatic, alicyclic, and heterocyclic series. The interesting possibilities of the production of polyfunctional aliphatic compounds on the basis of thiophene and substituted thiophenes are also opened up by their electrochemical oxidation or reduction. Considering the fact that thiophene compounds can be obtained by the reaction of hydrocarbons with sulfur, H_2S, or SO_2, one can regard the sequence of reactions, including the synthesis of thiophene or its homolog, the introduction of substituents, and, finally, ring cleavage as a pathway for the functionalization of the simplest C_4–C_6 hydrocarbons obtained in the refining of petroleum and used in petrochemical processes.

Thus redox processes are essentially a special area in the chemistry of thiophene. Individual aspects of such reactions in the thiophene series have been reflected in correlating papers (for example, see [1]). An examination of such problems in a broader scale is of great theoretical interest and is linked with their important preparative value.

The present review is also devoted to these problems, and in it, in addition to oxidative and reductive transformations that involve the thiophene ring, we examine the transformations of the substituents, the selective realization of which is fraught with specific difficulties due to the high reactivity of the heteroaromatic ring. For the reasons set forth below, in addition to traditional chemical methods of reduction and oxidation of thiophenes, special attention was directed to preparative electrochemical processes.

In recent years concepts that the formation of a new bond in the course of organic reactions that are usually regarded as heterolytic may be preceded by transfer of one electron have evolved [2]. Whereas the intermediate formation of ion radicals in substitution reactions is hypothetical in many cases, the existence of electron transfer in processes involving the reduction of organic compounds by metals or oxidative and reductive reactions with the participation of cations of metals with variable valences raises no doubts, although the detection of this step is an extremely difficult task. At the same time, in the case of the electrochemical transformations of organic compounds one can frequently unambiguously detect a step involving one-electron transfer that leads, in the case of reactions with the participation of neutral molecules, to the formation of the corresponding ion radicals [3].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow 117913. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 723-743, June, 1981. Original article submitted June 17, 1980.

0009-3122/81/1706-0523$07.50

Several fundamental monographs devoted to the electrochemical transformations of organic compounds (for example, see [3, 4]), including furan derivatives [5], as well as reviews devoted to organic electrosynthesis [6] and the electrochemical behavior of sulfur-containing compounds [7, 8], have been published in recent years; however, thiophene derivatives are virtually disregarded in all of these works. It should be pointed out that preparative electrolysis is still rather rarely used in the synthesis of compounds on the basis of thiophene. This is evidently due to two principal factors: first, the inadequate knowledge of the mechanisms of the electrochemical transformations of compounds of this sort, which are generally based on the use of a polarographic method [7, 8] and, second, the existence of considerable disparity between the results of polarographic (in the general case, electroanalytical) studies and data from the preparative transformation of organic compounds (see [3, pp. 123-127]). In the present review we will therefore present chiefly data on the preparative electrochemical transformation of compounds of the thiophene series without a detailed examination of the results of polarographic and other electroanalytical studies.

Insofar as purely chemical transformations are concerned, the mechanisms of a number of reductive and oxidative reactions still remain unclear. Catalytic hydrogenation processes constitute a large and important group of such reactions. The similar-to-the-latter reductive desulfuration under the influence of Raney nickel (it will be discussed briefly below) occurs through the formation of free radicals (see [1, Ch. 5]) and consequently includes steps involving electron transfer; however, the detailed mechanism of this reaction is unknown. In addition, in the case of reactions for which the mechanisms are apparently known in their general features such as, for example, hydride reduction (the successive addition of a hydride ion and a proton) and electrophilic ionic hydrogenation (protonation accompanied by the addition of a hydride ion [9]), the existence of intermediate steps involving electron transfer has not been established.

In the course of our further exposition we will, for the sake of brevity, generally not discuss the mechanisms of the examined reactions; however, the differences existing here must be taken into account by selecting the most suitable agent for carrying out the desired reaction. The data presented in the review may, it seems to us, be of interest not only to those engaged in research on thiophene, since wherever possible and necessary, the transformations of thiophene compounds are compared with the reactions of their analogs, first and foremost, benzene and furan analogs.

The material contained in this review is divided into three principal sections. In the first two sections we examine reduction and oxidation processes, while in the final section we examine substitution reactions for which the existence of one-electron transfer steps has been proved or is probable. In each section the data on the transformation of the corresponding thiophene derivatives are classified with respect to the reaction pathway (at the side chain, in the ring, or with ring cleavage). To keep the volume of the review within the allowable limits we generally will discuss only the results that pertain to the simplest thiophene derivatives.

1. Reduction

Diverse reductive reactions that are widely used in preparative practice have been described for thiophene compounds. Thiophenes are capable, in principle, of undergoing the same reductive transformations as other aromatic compounds; many reactions of such compounds proceed more readily and more selectively than in the benzene series, and this is due to the activating effect of the sulfur atom on the α position of the thiophene ring and the ability of sulfur to participate in delocalization of not only a positive charge but also a negative charge, as well as the odd electron. There are serious limitations only for hydrogenation processes in the presence of heterogeneous catalysts, most of which are poisoned in the presence of divalent sulfur compounds.

1.1. Reduction of Substituents Bonded to the Thiophene Ring

Hydroxyalkyl-Substituted Compounds. The reduction of the CHOH group in alkylthienylcarbinols to CH_2 is usually realized by the action of lithium aluminum hydride (LAH) in the presence of $AlCl_3$ [10]. Alcohol groups do not, as a rule, undergo electrochemical reduction; however Lund and co-workers [11] have pointed out the possibility of the reduction of mercury of aromatic pinacols, which proceeds through a step involving their dissociation at the C—C bond on the surface of the electrode. Thiophene derivatives have not been investigated under such conditions.

Carbonyl Compounds. The reduction of compounds of this class has been studied in greatest detail and plays an important role in diverse transformations of thiophene derivatives. It is sufficient to point out that the reduction of acylthiophenes, which includes conversion of the CO group to a CH_2 group, is the principal method for the preparation of many compounds of the thiophene series that contain primary alkyl groups. The most important reaction used for preparative purposes are Clemmensen reduction (for example, see [12]) and Kishner reduction, recently in the Huang—Minlon modification [13, 14]. The catalytic reduction of the CO group to a CH_2 group has been realized successfully in the thiophene series in the presence of rhenium heptasulfide [15, 16].

The reduction of aldehydes and ketones is widely used for the preparation of pinacols and alcohols. In particular, pinacols can be obtained from ketones of the thiophene series by the action of zinc in acetic acid [17]. Diverse methods, the description of which can be found in the literature (for example, see [18]), are used for the preparative synthesis of alcohols from carbonyl compounds. In most cases the conditions for the reduction of ketones and aldehydes of the thiophene series do not differ fundamentally from those used in the benzene series. In addition to new reducing agents, traditional reducing agents have been used successfully, particularly for the reduction of aldehydes. For example, 2-thenyl alcohol is obtained in high yield in the reduction of 2-formylthiophene with zinc powder in an alkaline alcohol solution [19] or in aqueous acetic acid [20]; when a modified Cannizzaro reaction is used, the yield of 2-thenyl alcohol is ∿60% [21].

According to the classical concepts [3, 4], the electrochemical reduction of the CO group of aromatic compounds should lead to the corresponding pinacols, alcohols, and in some cases alkyl-substituted compounds. Thus from polarographic studies it was concluded that in the reduction of both 2-formylthiophene [22] and 2-acetothienone [23] in aqueous organic media one can selectively obtain the corresponding pinacols or alcohols, depending on the pH of the medium and the applied potential. However, in practice the preparative electrolysis of such compounds often leads [24, 25] to the formation of resinous and difficult-to-identify products. The results of polarization measurements made by the method of a disk with a ring [26, 27] in the case of the reduction of aromatic carbonyl compounds led Vykhodtseva and Nekrasov [26] and Gul'tyai and co-workers [28] to conclude that the reduction process is more complex than that suggested by the classical scheme. According to [27, 29], the anion radicals formed in the first step of the reduction can react with the participation of both their carbonyl group and the aromatic ring, which also leads to the formation of various products, including resinification products.

As we have already noted, the first attempts to obtain a pinacol in the electrolysis of 2-acetylthiophene in buffer solutions of 30% aqueous tetrahydrofuran (THF) [24] and in acetonitrile with a 0.1 M solution of tetraethylammonium perchlorate as the base electrolyte [25] were unsuccessful. However, by selection of the conditions the authors were able to isolate 2,3-di(2-thienyl)butane-2,3-diol in good yield (up to 70%) from both the acetonitrile solutions (in the presence of weak proton donors) [25] and from 70% aqueous dimethylformamide (DMF) (on a tin cathode) [30]. In the case of the electrical reduction of acetophenone on a mercury cathode it was shown that the nature of the cation of the base electrolyte has a substantial effect on the yield of the corresponding pinacol when the electrolysis is carried out in DMF and CH_3CN [31]. The optimal yield of 1,2-(2-thienyl)ethane-1,2-diol (∿80%) was recently obtained by one of us in a DMF solution containing 0.1 M tetrabutylammonium perchlorate and 0.1 M lithium perchlorate when $E = -1.7$ V (relative to a saturated calomel electrode).

It follows from the research of Caullet and co-workers [25, 32] that the electrochemical production of alcohols from the corresponding ketones of the thiophene series evidently raises no special difficulties. Thus (2-thienyl)phenylcarbinol was obtained in greater than 80% yield from 2-benzoylthiophene when it was electrolyzed in acetonitrile solution with 0.1 M tetraethylammonium perchlorate as the base electrolyte in the presence of a twofold excess of phenol, which acts as an efficient proton donor.

It follows obviously from the data presented above that the preparative electrochemical methods in a number of cases may compete successfully with the chemical reduction of thiophene carbonyl compounds.

Carboxylic Acids and Their Derivatives. Lithium aluminum hydride has been used most often for the reduction of thiophenecarboxylic acids and their derivatives to thienylalkanols in recent years (for example, see [33, 34]). An extremely specific method for the hydride reduction of the carboxy group to a methyl group, which consists in the action of trichlorosilane and a tertiary amine with subsequent hydrolytic cleavage of the resulting thenyltrichlorosilane in an alkaline medium, was applied in [35] to thiophene-2- and thiophene-3-carboxylic acids. However, the corresponding methylthiophenes were obtained in only 20 and 11% yields. Let us note that reduction products could not be isolated at all in the case of acids of the furan series [35], whereas in the benzene series this reaction give high yields of the methyl-substituted compounds [36, 37].

The electrochemical reduction of the carboxy group in thiophene compounds has not been studied. In analogy with the reduction of benzoic and phenylacetic acids (see [3, pp. 294-300]) one might expect, depending on the electrolysis conditions, the production of the corresponding aldehydes or alcohols. Esters undergo electrochemical reduction more readily than carboxylic acids. However, a study of the polarographic behavior of methyl esters of thiophenecarboxylic acids in aqueous buffer solutions led Mikhailov and co-workers [38] to the conclusion that the products of electrical reduction in this case are the corresponding ring-hydrogenated compounds rather than the aldehydes, as follows from the research of Nahaya and co-workers. Thus it should be assumed that the anion radicals formed from carboxylic acid derivatives preferably undergo reduction in the ring rather than in the functional group. This reaction pathway will be discussed in greater detail in section 1.2.

Other Compounds. Of great significance in the preparative chemistry of thiophene is the reduction of halogen, which is often used to prepare difficult-to-obtain β-substituted derivatives; the halogen atom is used as a protective group for the α position. In this connection, let us first of all mention the reduction of 2,3,5-tribromothiophene to 3-bromothiophene, which is an important intermediate in the synthesis of various β-substituted thiophenes. It can be accomplished by various methods, of which the most convenient is evidently the action of zinc in acetic acid [40]. The action of one equivalent of butyllithium with subsequent decomposition of the exchange product with water is used in certain cases in which one is required to remove one of two bromine atoms in the α positions. For example, the conversion of 2,3,5-tribromothiophene to the 2,4-dibromide is realized in precisely this way [41, 42]. The action of copper metal in organic acids (usually in propionic acid) is a specific method for the reduction of halogen in the α position when there is an orienting group of the II type in the α' or adjacent β position [43-45]. Of the heterogeneous catalysts, palladium on charcoal is used for replacement of chloride by hydrogen in thiophene compounds [46].

An interesting new method for the reduction of bromine in the α position of the thiophene ring consists in the action of sodium alkoxides in dimethyl sulfoxide (DMSO) [47]. The mechanism of this reaction, which has also been described for polybromobenzenes [48], is not yet clear. It is possible that this transformation is related to reactions of the $S_{RN}1$ type, which will be examined in the last section of the present review.

Data on the reduction of thiocyanatothiophenes, which are converted to the corresponding thiophenethiols or disulfides, are available. Lithium aluminum hydride and sodium borohydride, [49], as well as the dipotassium salt of cyclooctatetraene [50], have been used as reducing agents. The dipotassium salt [50] and lithium aluminum hydride [51] can be used for the reduction of disulfides of the thiophene series to mercaptans.

The reduction of nitro compounds and other substituted thiophenes that contain nitrogen-containing groups has relatively limited application in the thiophene series. Let us point out, in particular, the possibilities of the hydrogenation of nitro groups in the thiophene ring in the presence of a palladium catalyst [46], as well as the reduction of Schiff bases to the corresponding aminomethylthiophenes, which is realized by the action of $NaBH_4$ [52] or catalytically in the presence of rhenium heptasulfide [53].

The use of the Zinin reaction, which is classical for nitro compounds of the benzene series, is hindered in the thiophene series by the instability of the corresponding amines, which can be isolated only in the form of salts [54, 55].

Insofar as we know, the macroelectrolysis of the thiophene derivatives discussed in this section has not been described. However, concise information regarding the available literature data dealing with their polarographic study may be of use to the reader. Thus the results of a polarographic study of bromo derivatives of thiophene [56] indicate the possibility of complete replacement of the bromine atoms in the ring by hydrogen under electrical-reduction conditions; electrochemical cleavage of the C—Br bond proceeds considerably more readily in the α position than in the β position. The mechanism of the process is evidently similar to the reduction of other aromatic halo derivatives [57]:

$$RBr + 2e \rightarrow R^- + Br^-$$
$$R^- + DH \rightarrow RH + D^- \text{ (}DH \text{ — a proton donor).}$$

In the case of halothiophene [23, 58-60] that have various substituents in the ring the electrode process is complicated by both absorption of the depolarizer and the products of the electrochemical reaction on the electrode and by the possibility of the reduction of the functional group (for example, the carbonyl group) [23]. The existence of certain contradictions between the results in [23, 58] requires additional studies to establish the true mechanism of the reduction of compounds of this class. In this connection, the data in [61, 62], which are devoted to the preparative reduction of bromo-substituted acetophenone and benzophenone in an aprotic medium, are of interest, especially since an attempt has been made [29] to explain these data on the basis of the concept of the dual reactivity of the anion radicals formed in the first step of the reduction of the indicated compounds.

In analogy with the mechanism of the reduction of 2-thiocyanatomethyl-5-carboxyfuran [64], reduction on a dropping mercury electrode of various thiocyanatothiophenes [63] can be described by a scheme that includes the irreversible addition of two electrons with the formation of the corresponding mercaptans.

The polarographic behavior of nitro derivatives of thiophene in aqueous buffer solutions has been studied in a number of papers [65-68]. The reduction of a nitro group over a broad pH range proceeds with the participation of four electrons and should lead to the formation of the corresponding hydroxylamines. On the basis of the results of the preparative electrical reduction of nitro derivatives of the benzene series (see [3, pp. 242-247]), it may be assumed that a broad spectrum of products may be formed in the electrolysis of nitrothiophenes under various conditions; in particular, the possibility of preparing difficult-to-obtain amino derivatives of thiophene is not excluded.

1.2. Reduction of the Thiophene Ring without Ring Opening

Alkylthiophenes. One of the important reactions of alkylthiophenes is hydrogenation of the thiophene ring, which leads to the corresponding di- and tetrahydro derivatives. The catalytic hydrogenation of thiophenes to di- and tetrahydrothiophenes is, as a rule, impossible because of poisoning of the catalysts and simultaneous destruction of the ring. A palladium catalyst is an exception in this respect [46]. Hydrogenation takes place at low temperatures and pressures; however, because of poisoning of the catalyst, it requires a great deal of palladium consumption (by weight, the amount consumed is close to the amount of the compound undergoing hydrogenation), and the process is therefore justified only in special cases such as in the stereospecific synthesis of biotin through the corresponding thiophene precursor [69]. High yields of tetrahydrothiophenes can be obtained when rhenium heptasulfide is used as the catalyst [70, 71]; however, the severe reaction conditions (250-500°C and 100-300 atm) and the high cost of the catalyst prevent its broad application. Hydrogenation of the thiophene ring also occurs with catalysts such as nickel, tungsten, and molybdenum sulfides [72]; however, the reactions take place under severe conditions and give low yields of tetrahydrothiophenes.

There are presently quite convenient methods for the reduction of the thiophene ring that do not involve the use of heterogeneous catalysts. One of them, viz., electrophilic ionic hydrogenation [73, 74], which consists in successive reversible protonation and irreversible addition of a hydride ion under the influence of trialkylsilanes in a protic acid (usually CF_3COOH) medium, proceeds better in the presence of additives such as CF_3 etherate [75], p-toluenesulfonic acid, and lithium tosylate and perchlorate [76]. The process is accelerated markedly in the $HCl—AlCl_3—Et_3SiH$ system due to the effective formation of C-protonation products by the action of HCl and $AlCl_3$ on the alkylthiophenes [77]. The reaction makes it possible to obtain the corresponding tetrahydrothiophenes in up to 80% yields from alkylthiophenes. Thiophene itself upon hydrogenation in the $CF_3COOH—Et_3SiH$ system gives a mixture of di- and tetrahydrothiophenes with predominance of the former. This is due to the low concentration of the corresponding carbonium ions, which should be formed in the second step of the hydrogenation.

It is interesting to note that when the HF—TaF_5 superacid is used, ionic hydrogenation leads to thiophan in 80% yield [78]. Isopentane serves as the hydride ion donor under these conditions.

Reduction with alkali metals in liquid ammonia has been studied rather extensively as applied to thiophene compounds. This reaction is especially interesting in view of its fundamental similarity to electrochemical reduction. When a proton donor (usually an alcohol) is present in the medium, the process reduces to the successive addition of an electron and a proton (see [1, Ch. 5 and the references therein]). By varying the conditions and above all the amount of alkali metal, in a number of cases one can stop the reaction at the step involving the addition of a definite amount of hydrogen. The reaction was first applied to thiophene and its homologs by Birch and McAllan [79], who demonstrated that under the influence of sodium in liquid ammonia thiophene is converted to a mixture of 2,3- and 2,5-dihydrothiophenes. Further reduction of this mixture leads to ring cleavage, regarding which more details will be given in the next section.

Turning to the electrochemical reduction of alkylthiophenes we note that their reduction potentials are very high and that direct reduction is fraught with considerable difficulties [80]. It therefore became necessary to investigate their indirect reduction by means of carriers, i.e., electrochemically generated anion radicals of organic compounds that are capable of transfer of an electron to a molecule that is difficult to reduce [81]. Electrolysis of solutions of thiophene and methylthiophenes in dimethylformamide (DMF) in the presence of diphenyl as the carrier and 10% water (by volume) leads to the formation of the 2,5-dihydro derivative in 50% yield and tetrahydro derivatives in 45% yield [80]. The percentage of water in the reaction medium and the presence of Zn^{2+} ions, which, in the opinion of Mairanovskii and co-workers [82], increase the rate of protonation by water of the intermediately formed thiophene anion radicals, have a substantial effect on the yields of the hydrogenation products. The further development of these studies may lead to the formulation of a new and promising method for the preparation of hydrogenated thiophenes.

The reduction of the thiophene ring by electrochemically generated solvated electrons may be of doubtless interest. This method has thus far been used in the reduction of a number of aromatic compounds (see [3, pp. 594-603]) in order to obtain products of partial or complete hydrogenation. In this case the process takes place through the intermediate formation of the corresponding anion radicals and free radicals, methods for the generation and the reactivities of which in the thiophene series have recently been the subject of intensive study by means of EPR spectroscopy [83, 84].

Compounds of the Thiophene Series that Contain Oxygen-Containing Substituents. The preparation of functional substituted tetrahydro- and, particularly, dihydrothiophenes is of interest from the point of view of the search for physiologically active compounds [85-87] and their conversion to compounds of other classes such as isoprenoids [88]. Since the action of reducing agents often leads either to reduction of the functional group or to profound reduction of the thiophene ring with the formation of tetrahydrothiophenes or products of cleavage of the C—S bond, a number of multistep methods for the synthesis of dihydrothiophenes by means of cyclization of aliphatic sulfur-containing compounds have been developed [85-87, 89, 90].

Considering the urgent need for the development of methods for the direct reduction of the thiophene ring in compounds with oxygen-containing substituents, let us examine some peculiarities and limitations of the existing chemical methods.

Ionic hydrogenation, which makes it possible to easily obtain various alkyltetrahydrothiophenes (see above), is fraught with certain difficulties on passing to functional compounds. If the thiophene ring contains electron-acceptor substituents such as NO_2 and COOH, ionic hydrogenation does not occur. However, thienylalkanoic acids in which the carboxy group is remote from the thiophene ring, behave like alkylthiophenes: The reaction proceeds smoothly and leads to the corresponding tetrahydro derivatives [74]. Other thiophenes, the functional group of which is separated from the ring by a polymethylene chain, are also hydrogenated similarly [91]. Under ionic hydrogenation conditions alkylthienyl ketones are initially converted to alkylthiophenes, which are subsequently hydrogenated to alkyltetrahydrothiophenes [74]. 2-Formylthiophene gives (through the di-2-thenyl ether) the corresponding hydrogenated ether [74].

The use of sodium amalgam is convenient in some cases. Thus the reduction of thiophene-2-carboxylic acid with excess 2.5% sodium amalgam in aqueous sodium hydroxide solution leads to tetrahydrothiophene-2-carboxylic acid in 60% yield [92]. The reduction of thiophene-2-carboxylic acid by lithium in liquid ammonia, which leads to 2,5-dihydrothiophene-2-carboxylic acid, was recently described [93].

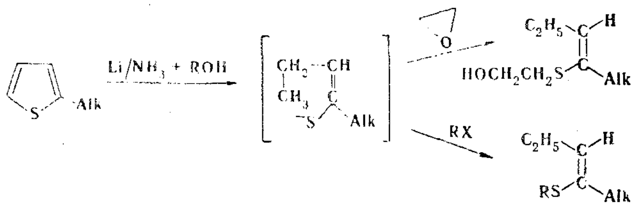
Electrochemical reduction is a promising method for the preparation of dihydro derivatives of the type under consideration. Thus, when the starting compound does not contain a rather strong electron-acceptor group (for example, in the case of hydroxy compounds), it is expedient to use catalysts, viz., electron carriers of various types, in the reduction [81, 94], the regeneration of which can be accomplished by the electric current. However, in the case of carboxy-substituted thiophenes a convenient method [88, 95] has been developed for the direct electrochemical reduction, which leads in the case of thiophene-2-carboxylic and 4- and 5-methylthiophene-2-carboxylic acid to the corresponding 2,5-dihydro derivatives in yields that exceed 90%. It is proposed in [88] that the high selectivity of the process is associated with the favorable orientation on the surface of the mercury cathode (under conditions for the formation of a lithium amalgam) of intermediate particles that are formed under conditions of stepwise electron transfer to the anion of the starting acid. If one takes into account the fact that dihydro derivatives of thiophene readily undergo desulfuration, including transformations under photochemical conditions [89], the electrochemical method for the preparation of dihydro derivatives may assume substantial significance in the synthesis of isoprenoids on the basis of compounds of the thiophene series.

1.3. Reduction with Opening of the Thiophene Ring

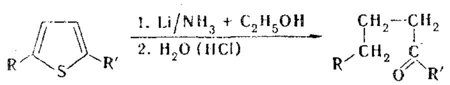
As we noted in the preceding section, the action of reducing agents frequently leads to cleavage of the thiophene ring. The products of such transformations are aliphatic and carbo- and heterocyclic (O- and N-containing) compounds. Since the character of the substituents most often does not have a decisive effect on the reductive cleavage of the thiophene ring, in this section such reactions will be classified only with respect to the types of agents.

The catalytic desulfuration of thiophene derivatives (see [1, Ch. 5] for data on this process) has not assumed preparative value because of the difficulty involved in retention of the functional groups and the production of individual compounds under severe reaction conditions. Reductive desulfuration by means of Raney nickel and reductive cleavage of thiophene compounds by the action of alkali metals in liquid ammonia have found preparative application.

Birch and McAllan have shown [79] that the mixture of 2,3- and 2,5-dihydrothiophenes formed by the action of sodium in liquid ammonia on thiophene is converted by further reduction to a mixture of butenethiols and butenes. This reaction was recently studied in detail by Gol'dfarb and Zakharov, who showed, in particular, that the reduction of 2-alkylthiophenes with lithium metal in liquid ammonia in the presence of ethanol as a proton donor leads, after treatment with an alkyl halide or an α-oxide, to α,β-unsaturated sulfides [96-98]:

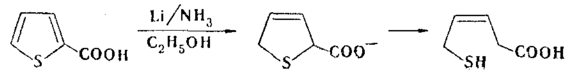


If the mixture formed as a result of the action of lithium in ammonia is subjected to hydrolysis, dialkyl ketones are obtained [99]; ω-(2-thienyl)alkanoic acids under the same conditions are converted to aliphatic keto acids [100], while ω-(2-thienyl)alkanols [101] and 2-(ω-diethylaminoalkyl)thiophenes [102] are converted to keto alcohols and amino ketones in 70-80% yields:



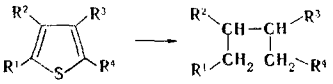
R=H, R'=Alk; R=R'=Me; R=H, R'=$(CH_2)_nCOOH$ (n=3—5,9); R=H, R'=$(CH_2)_nOH$ (n=2—6); R=H, R'=$(CH_2)_nNEt_2$ (n=2—6)

Reduction by alkali metals in liquid ammonia proceeds even more readily in the case of thiophene compounds that contain electron-acceptor substituents, since the first step in the reduction consists in attack by the nucleophile (the electron) at the aromatic ring. In particular, the action of lithium in liquid ammonia on thiophene-2-carboxylic acid leads, depending on the number of equivalents of the alkali metal, to 2,5-dihydrothiophene-2-carboxylic acid or the cis-mercapto acid, which is formed as a result of ring cleavage [93].



This process, as demonstrated in [103] for thiophene-2-carboxylic acid and its 3-, 4-, and 5-methyl-substituted derivatives, is regiospecific and stereospecific. The Z isomers of β,γ-unsaturated δ-mercapto acids are obtained in all cases.

The reduction of thiophene compounds with the elimination of sulfur is realized by the action of Raney nickel and some other skeletal metals, which are used in amounts that several times exceed the weight of the thiophene compound. This type of transformation has been studied particularly extensively by Gold'farb and co-workers.

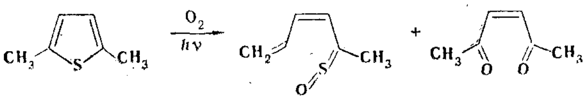


Thus diverse functional compounds of the aliphatic and cycloaliphatic series can be obtained on the basis of thiophene and its homologs (see [1, Ch. 5-7]). Let us note in particular the methods for the preparation of amino acids with various structures and substituted 7- and 8-membered lactams (see [1, Ch. 6; 104]), numerous cyclic ketones that have a musklike odor, and ketolactones that are related with respect to their skeleton to aglycones of macrolide antibiotics [1, Ch. 7, p. 105].

The available data on the electrochemical desulfuration of thiophene compounds is still scanty. The fundamental possibility of the electrochemical desulfuration of methyl thiophene-2-carboxylate when the electrolysis is carried out on mercury (H_2S is obtained in ~5% yield) is noted in [106]. There is also an indication [80] of the formation of thiophene in DMF in the presence of a "carrier," viz., diphenyl. These processes require more detailed study in order to solve the problem of the expediency and possibility of their use in synthetic practice.

2. Oxidation

Thiophene is a "π-electron-surplus" heterocycle and therefore is oxidized more easily than, for example, benzene. In particular, complete disruption of the ring with the formation of oxalic and maleic acids in the case of unsubstituted thiophene is possible under the influence of strong oxidizing agents such as HNO_3 [107]. The action of singlet oxygen on alkyl- and arylthiophenes is accompanied by cleavage of the heteroring and the formation of a mixture of unsaturated carbonyl compounds and sulfides [108, 109].



Nevertheless, the thiophene ring is quite stable with respect to a number of oxidizing agents. This makes it possible to carry out selective oxidation of the substituents.

2.1. Oxidation of Substituents without Involvement of the Thiophene Ring

Alkylthiophenes. As in the benzene series, the oxidation of alkyl groups with retention of the aromatic ring is possible. For example, 3-methylthiophene can be converted to thiophene-3-carboxylic acid in ~80% yield by the action of an aqueous solution of sodium dichromate [110].

The liquid-phase oxidation of alkylthiophenes in glacial acetic acid with air oxygen in the presence of Co(II) and "activator" additives, viz., 9,10-dibromoanthracene or NaBr, is a very promising method for the preparation of carbonyl compounds and acids of the thiophene series [111]. The corresponding mono- and dicarboxylic acids were obtained in up to 90% yields in the oxidation of mono- and dimethylthiophenes under the indicated conditions

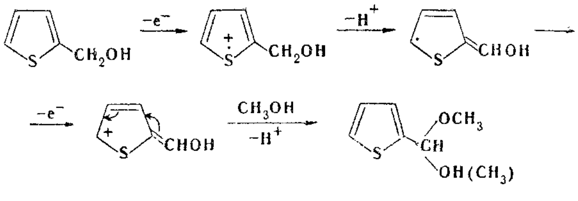
[111, 112]. The intermediate formation in these reactions of aldehydes has been demonstrated; in a number of cases oxidation may stop at the aldehyde-formation step. 2-Acetothienone and 2-thienylmethylcarbinol acetate were obtained in satisfactory yields in the oxidation of 2-ethylthiophene [113]. 2-Benzylthiophene is oxidized to phenyl-2-thienylcarbinol (in up to 80% yield) and 2-benzoylthiophene (11-14%) [114]. It is interesting to note that under the indicated conditions homologs of selenophene are oxidized with greater difficulty than alkylthiophenes, and alkylfurans do not undergo oxidation at all [111].

Insofar as we know, the electrochemical oxidation of alkyl groups of thiophene derivatives has not been studied. However, there are a number of studies devoted to the electrochemical oxidation of alkylbenzenes, which is a promising method for the preparation of aromatic aldehydes [116], particularly in the presence of carriers [117] and acids (see [4, p. 269]).

Hydroxyalkylthiophenes. It is well known that the mild chemical oxidation of aromatic alcohols leads to the production of the corresponding aldehydes or ketones. In the thiophene series this transformation can be accomplished by the action of various reagents. The preparation of ketones from secondary alcohols is, of course, a simpler task. As an example of the oxidation of secondary alcohols that is complicated by the presence of labile substituents, one can cite the conversion of thienylbutynylcarbinols to the corresponding ketones under the influence of chromic anhydride in sulfuric acid [118] in 40-70% yields. The oxidation of primary thienylcarbinols to the corresponding aldehydes required careful selection of the conditions. For example, the oxidation of 2-thenyl alcohol to 2-formylthiophene can be carried out by the action of potassium persulfate [119]. Concentrated nitric acid (at 30-35°C) [120] and N-bromosuccinimide [121] have been described as reagents for the conversion of 2-nitro-3-thenyl alcohol, which contains a deactivating nitro group, to an aldehyde. High yields of carbonyl compounds are obtained in the oxidation of thienylcarbinols with silver carbonate adsorbed on Celite [122]. The more profound oxidation of 2-thenyl alcohol to thiophene-2-carboxylic acid is carried out by, for example, the action of potassium permanganate [92].

The electrochemical oxidation of benzyl alcohols takes place in acetonitrile on platinum or graphite anodes to the corresponding aldehydes (see [4, p. 272]). However, this process is complicated by chemical transformations of the cation radicals formed during detachment of the first electron from the substrate [123, 124]. The presence of proton acceptors (pyridine or quinoline) in the system has a substantial effect on the pathway of the preparative synthesis.

Janda and co-workers [124] have shown that 2-thenyl and benzyl alcohols behave similarly under the conditions of electrical oxidation in methanol in the presence of H_2SO_4, in which case they are converted to the corresponding aldehydes. This result is unexpected, since the principal pathways of anode processes for an entire series of thiophene compounds are transformations in the heteroring rather than in the side chain [125]. Methoxylation and subsequent ring cleavage are also the principal pathways in the electrochemical oxidation of furfuryl alcohol and other furan derivatives [126, 127]. Janda and co-workers [124] propose the following mechanism for the oxidation of 2-thenyl alcohol with the formation of acetals.



In their establishment of the differences in the behavior of furfuryl, thenyl, and benzyl alcohols Janda and co-workers [124, 125] assume that the pathway of the second step in the process (nucleophilic attack on the ring by the MeO^- anion or splitting out of a proton from the side chain) is determined by the nucleophilic superdelocalization (S_N) due to the different reactivities of the cation radicals of the aryl- and hetarylcarbinols under consideration. Deprotonation prevails for compounds of the benzene and thiophene series, while attack on the cation radical by the anion is preferable in the case of the oxidation of furfuryl alcohol and other furan derivatives. This explanation is not specific, does not make it possible to predict the pathway of the process, and does not take into account the role of the medium in the transformations of the intermediates in the electrolysis. From the position of this explanation it is difficult to understand, in particular, the reasons for the fact that, in contrast to 2-thenyl alcohol (the preceding scheme), the principal pathway in the electrical oxidation of 3-(1-acetoxyethyl)thiophene and methyl-3-thienylcarbinol [128, 129], as in the case of thiophene homologs, is ring cleavage, i.e., attack on the ring by the MeO$^-$ anions.

In examining the effect of the medium on the pathway of the anode oxidation of alcohols one should first take into account the factors that affect the reactivity of the cation radicals that are formed in the first step. Unfortunately, a quantitative estimate of the effect of these factors is as yet impossible because of the scantiness of the available experimental data. One can only state that the pathways of the subsequent transformations of the cation radicals should be affected by both their acid–base properties and the solvating capacity of the medium. This can be illustrated by data on the electrical oxidation of benzyl alcohol in various media: Smooth oxidation to benzaldehyde is observed in a methanol solution of sulfuric acid [124], while a polymer is formed in acetonitrile [123]; oxidation to an aldehyde in acetonitrile can be realized only in the presence of a strong proton acceptor, whereas when an acceptor of this type is absent, one observes [123] the formation of intermediates, the further transformation of which evidently takes place in the aromatic ring.

Aldehydes, Ketones, and Acids of the Thiophene Series. The oxidation of carbonyl compounds to the corresponding acids is widely used in the thiophene series. In our subsequent discussion we will restrict ourselves only to individual examples that demonstrate the synthetic possibilities created by the use of various oxidizing agents. Thus the oxidation of aldehydes with silver oxide was used in [130] to obtain 4-substituted thiophene-2-carboxylic acids. Let us also point out the selective (in higher than 80% yield) oxidation of 5-methyl-2-acetylthiophene-2-carboxylic acid with sodium hypobromite to the corresponding 2,4-dicarboxylic acid [131]. It is interesting to note that only the $(CH_3)_2N_6CH_2$ group is oxidized by the action of potassium permanganate in a neutral medium on 5-dimethylaminomethyl-2-methyl-3-acetylthiophene, while the acetyl group is not affected [131], whereas it is well known that an alkaline solution of $KMnO_4$ oxidizes 2-acetothienone to 2-thienylglyoxylic acid [132]. A more convenient method that gives 2-thienylglyoxylic acid in high yield consists in the oxidation of 2-acetothienone with nitrous acid [133].

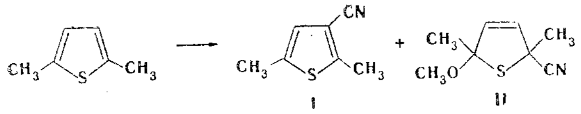
Judging from the oxidation of other aromatic aldehydes on a mercury electrode [134], the electrochemical transformations of aldehydes of the thiophene series on the anode do not have advantages over the methods for their chemical oxidation to the corresponding acids. At the same time, electrical oxidation to the corresponding glyoxals is possible in the case of aromatic ketones (electrolysis of acetophenone derivatives on a copper anode [135]).

In discussing the anode behavior of carboxylic acids we should first of all examine their participation in the Kolbe reaction. Prior to the research of Mirkind and co-workers [136] it was known that "anomalous" carboxylates (including aromatic species) form the corresponding dimers in very low yields. Mirkind and co-workers [136], on the basis of the assumption of heterogeneous character of the radical transformations under the conditions of anode condensation of carboxylates, demonstrated that the electrolysis of benzoic acid in the presence of unsaturated hydrocarbons that are capable of being adsorbed on a Pt anode leads to a fivefold to eightfold increase in the yield of diphenyl. The possibility of realization of the Kolbe reaction for thiophenecarboxylic acids has not been studied. Let us note, however, that the data in [137] on the anode conversion of thiophene-, selenophene-, and furan-2-carboxylic acids in DMF on a Pt anode enabled Konstantinov and co-workers to propose the formation of thiophenecarboxy radicals under electrolysis conditions. The oxidation mechanism examined in [137] was based on the establishment of the structures of the electrolysis products, viz., $C_4H_3XCOOCH_2N(CH_3)CHO$ (X = S, Se, O), which, in the opinion of the authors, are formed as a result of reaction of $C_4H_3XCOO^{\cdot}$ radicals with solvent molecules. In the case of thiophene-2-carboxylic acid this product is obtained in 21% yield. It is interesting to note that no transformations of the investigated substrates whatsoever on the anode are observed in a DMSO medium.

2.2. Oxidative Processes that Lead to Disruption of the Aromatic Character of the Thiophene Ring

A number of oxidative transformations of this type are well known in the chemistry of thiophene. Thus 2,5-disubstituted thiophenes are converted by the action of hydrogen peroxide [138-140] or perbenzoic acid [141] to the corresponding sulfones, which display diene properties [140, 142]. A small amount of a sulfoxide is formed in addition to the sulfone by the action of m-chloroperbenzoic acid on 2,5-di-tert-butylthiophene [143]. As pointed out in [143] (see also [144]), the difficulty in isolating sulfones and sulfoxides with free α positions is associated with the fact that they readily undergo self-condensation via a type of Diels—Alder reaction.

The preparation of substituted ring-hydrogenated thiophene derivatives through the addition of anions (or neutral nucleophiles) to the cation radicals via a type of anode synthesis of the analogous derivatives in the furan series [126] is very promising from a synthetic point of view. However, in this case one must bear in mind the anode potential at which oxidation of both the substrate and the anions of the base electrolyte may occur [145]. Thus in methanol solution discharge of bromide ions on a Pt anode to give bromine occurs when $E = 0.6$ V, while CH_3O^- is discharged when $E = 1.1$ V, and ClO_4^-, NO_3^-, AcO^-, and CN^- are discharged when $E \approx 1.5$ V (relative to a saturated calomel electrode). Thus 3-bromo- or 3-cyano-2,5-dimethylthiophene (I), 2-methoxymethyl-5-methylthiophene, and 2-cyano-5-methoxy-2,5-dimethyldihydrothiophene (II) may be formed in the electrolysis of a methanol solution of 2,5-dimethylthiophene ($E_{discharge} = 1.1$ V), depending on the nature of the base electrolyte anion [145]. The preparation of 2,5-dihydro derivatives is of greatest interest in this section.



Since oxidation of the substrate occurs at a lower potential than, for example, CN^-, one may imagine that the mechanism of the process includes attack by the CN^- anion of the cation radical formed in the electrochemical step; the yield with respect to the current of dihydrothiophene derivative II is $\sim$30%, while I is formed in $\sim$7% yield. This may serve as an illustration of the assumption expressed above, according to which the electrolysis pathway depends on both the properties of the reaction intermediates and on the nucleophilicity of the components of the medium. Thus by changing only the nature of the electrolyte one can change the pathway of the anode oxidation and obtain various thiophene and dihydrothiophene derivatives. For comparison, let us point out a series of similar studies in the furan series [146-148].

2.3. Oxidation Leading to Opening of the Thiophene Ring

As we have already pointed out, purely chemical oxidative processes that are accompanied by opening of the thiophene ring are not selective enough. Below we will examine in greater detail data on the anode opening of the thiophene ring that leads to desulfuration products.

Alkylthiophenes. Electrochemical desulfuration of thiophene was first realized by Janda [149] in 1963; however, the method under consideration has become of preparative value only recently [150]. These studies have opened up a new route to the synthesis of α,β-unsaturated 1,3-dicarbonyl compounds on the basis of thiophene homologs. Let us present the results of anode desulfuration of thiophene and alkylthiophenes that may be of interest to organic chemists specializing in synthesis (Table 1).

Srogl, Janda, and Valentova [150] have noted that the use of thiophene derivatives for the synthesis of γ-dicarbonyl compounds may prove to be preferable to the preparation of such compounds from furan analogs when the starting alkylthiophenes are more accessible than the corresponding alkylfurans or when the dihydrofuran derivatives obtained by anode oxidation are not cleaved under acid methanolysis conditions.

In our opinion, the formation of various products of the anode oxidation of 2- and 3-methylthiophenes [150], like the differences in the anode behavior of thiophene [145] and furan [151] derivatives, can be explained if one takes into account the participation of the

TABLE 1. Anode Desulfuration of Thiophene and Its Homologs

Substrate	Principal reaction products	Yield with respect to the substance, %
Thiophene	$(CH_3O)_2CH—CH{=}CH—CH(OCH_3)_2$ [149]	20
2-Methylthiophene	$(CH_3O)_2CHCH(OCH_3)CH_2CH(OCH_3)_2$ [150]	2
	$CH_3COCH_2CH_2COOCH_3+$ $+CH_3COCH_2CH(OCH_3)CH(OCH_3)_2$ [150]	40
3-Methylthiophene	$(CH_3O)_2CHCH_2CH(CH_3)COOCH_3$ [150]	20
2,5-Dimethylthiophene*	trans-$CH_3COCH{=}CHCOCH_3$ [150]	50

---

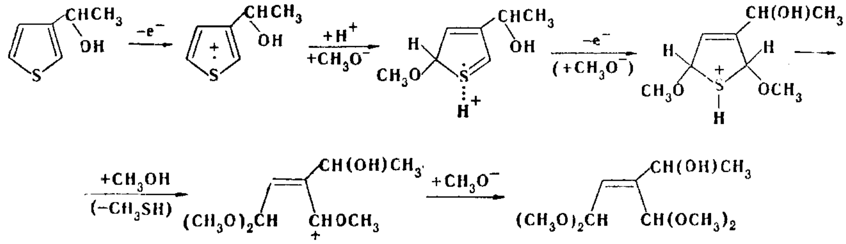
*Oxidation with bromine in methanol in the presence of K_2CO_3.

heteroatom in stabilization of the positive charge and the odd electron in the corresponding cation radicals and the possibility of protonation of the sulfur atom due to the sulfuric acid present in the medium, which facilitates nucleophilic attack by the methoxide anion on the ring, as well as by the ability of the products of two-electron oxidation to split out the elements of methyl mercaptan during solvolysis (methanolysis).

Two electrons are evidently detached in the oxidation of 2,5-dimethylthiophene with subsequent methanolysis of the dication and the primary formation of an unsaturated diketone (see Table 1), while unsubstituted thiophene gives all types of reaction products.

In concluding this subsection we should note that the ability of thiophene to undergo electrochemical oxidation was used by Nechiporenko in the purification of benzene to remove carbon disulfide and thiophene impurities by electrolysis of the corresponding solutions on a Pt anode in a medium consisting of H_2SO_4 and $(NH_4)_2SO_4$ [152].

Oxygen-Containing Compounds. As in the case of alkylthiophenes, electrochemical oxidation with desulfuration proceeds more specifically in the case of oxygen-containing compounds of the thiophene series, and in some cases [128] it proceeds stereospecifically. We note above that the corresponding acetal is formed in the anode oxidation of 2-thenyl alcohol, while the oxidation of 3-(1-hydroxyethyl)thiophene under the same conditions (MeOH + H_2SO_4) makes it possible to obtain desulfuration products, viz., unsaturated dicarbonyl compounds, in up to 40% yields [129]. In our opinion, the presence of an electron-donor grouping in the 3 position of the thiophene ring promotes protonation of the sulfur atom of the cation radical and addition of MeO^- in the α position of the ring:



In the case of 2-thenyl alcohol removal of a second electron with subsequent deprotonation of the dication and attack on the stable carbonium ion by the MeO^- anion seems more likely.

The anode oxidation of methyl thiophene-3-carboxylate with the formation of methyl 2,2',5,5'-tetramethoxy-3-pentenoate proceeds even more selectively [153]. The electrochemical oxidation of thiophene-2-carboxylic acid esters made it possible to develop a method for the preparative synthesis of α-ketoglutaric acid in the form of the diester ketal $ROOCCH_2CH_2C(OR)_2COOR$ (R = Me, Et, tert-Bu), the subsequent catalytic dehydrogenation of which over PdO_2 leads to derivatives of the corresponding unsaturated acid $ROOCCH{=}CHC(OR)_2COOR$ [154]. To obtain reliable data regarding the mechanism of such processes one must make polarization measurements under conditions of electrolysis at a controllable potential, and one must study the effect of the composition of the medium and various physical factors (temperature and pressure) on the yields of the electrolysis products.

3. Substitution Reactions in the Heteroaromatic Ring

The introduction of electrophilic agents in the aromatic ring can be formally regarded as an oxidative reaction, while the introduction of nucleophilic agents can be formally regarded as a reductive reaction. Although for processes of this sort one usually does not observe the formation in the first step of a cation radical by means of detachment of an electron from the neutral molecule or, respectively, from the anion radicals that arise as a result of the addition of an electron to the substrate, there is, nevertheless in a number of cases a definite similarity between substitution reactions that take place under the conditions of anode transformations and by the action of electrophilic agents and reactions that take place on the cathode and by the action of nucleophiles.

As we mentioned above, the possibility of one-electron transfer in the course of heterolytic reactions, particularly aromatic substitution, has often been discussed in the literature [2, 3, 155-157]; however, the experimental evidence for the reaction course under discussion is still clearly inadequate. In particular, we know of no such evidence for electrophilic substitution reactions in the thiophene series. Nevertheless, there is a basis for the assertion that a one-electron process is extremely likely in some reactions of thiophene and substituted thiophenes that contain electron-donor groupings. Such compounds display a wide variety of peculiarities in electrophilic substitution reactions [158]. In particular, it was found that thiophene and certain activated compounds of the benzene series do not differ from one another with respect to the rate of nitration, which is determined by the frequency of collision or the rate of mixing [159, 160]. In this connection it is difficult to explain the primary formation of α-substituted compounds, despite the fact that the rate of nitration appears to be controlled by the frequency of collisions; the ratio of, for example, α- and β-nitrothiophenes formed in the nitration of thiophene is 84:16 [161].

An interesting attempt to explain the indicated disparity between the high positional and low substrate selectivity was made by Perrin [162], who showed that for a number of activated compounds that do not differ from one another with respect to the rate of nitration and are more active than toluene (naphthalene, anisole, mesitylene, and o-xylene) their oxidation potentials (in CH_3CN relative to $Ag/AgClO_4$) are lower than the oxidation potential of NO_2 (1.8 V). This is responsible in the case of activated compounds for the exothermic character of the step involving electron transfer from the substrate to the electrophilic agent (NO_2^+), in the course of which the $ArH^{+\cdot}$ cation radical and the NO_2 molecule), which has an unpaired electron are formed:

$$ArH + NO_2^+ \rightarrow ArH^{+\cdot} + NO_2 \cdot$$

It has been established experimentally [162] that the cation radicals of the indicated compounds generated by electrochemical means react with nitrogen dioxide to give the same ratio of isomeric nitro-substituted compounds as the corresponding aromatic compounds under ordinary nitration conditions. Thus the primary production of 2-nitrothiophene is explained by the fact that the formation of a σ complex, which is known to be a real intermediate in electrophilic substitution and particularly in nitration, is not realized in the case of direct reaction of an aromatic compound with the nitronium ion, which, as we have already mentioned, may be controlled by the frequency of collisions, but rather is realized in the process of "collapse" of the radical pair formed by the $ArH^{+\cdot}$ cation radical and the NO_2 molecule, which contains an odd electron. It is essential in this case to emphasize that for the nitration of compounds that are less active than toluene the one-electron transfer step is evidently excluded, and they react via the classical scheme of electrophilic substitution (an ionic mechanism). Taking into account the criticism of Perrin, which was based, in particular, on the experimental data in [163, 164], it should be assumed that the scheme proposed by him for activated compounds is possible; however, it does not exclude the parallel formation of a σ complex in the case of direct attack on the aromatic compound by the electrophile, and the role played by one-electron transfer in the overall process may be insignificant [165].

Reactions involving anode substitution are widely used in electroorganic synthesis [4-6]. As applied to compounds of the thiophene series, one may point out a study of electrochemical bromination [166], cyanation [145], fluorination [167], and nitration [168]. If the oxidation potential of the substrate (RH) is lower than the potential of anode discharge of the electrolyte anions or nucleophilic additives (Nu), an electron detaches from the organic molecule to give the corresponding cation radical, which subsequently undergoes chemical and electrochemical transformations [166]:

$$RH \xrightarrow{-e^-} RH^{+\cdot}$$

$$RH^{+\cdot} + Nu \longrightarrow [RHNu]^{+\cdot}$$

$$[RHNu]^{+\cdot} \xrightarrow[-e^-]{-H^+} RNu$$

Nemec and co-workers [166] have developed a method for the electrochemical bromination of 2- and 3-methylthiophenes using platinum or graphite as the working electrode and a 0.35 M solution of NH_4Br in methanol as the base electrolyte. Under galvanostatic conditions they obtained as the principal products 5-bromo-2-methylthiophene in 80-100% yields, depending on the temperature (in the case of 2-methylthiophene), and 2-bromo-3-methylthiophene in 55-80% yields on graphite and in 95% yield on platinum (in the case of 3-methylthiophene).

3-Methylthiophene and some tetrahydrothiophenes have been subjected to anode fluorination on an Ni anode [167]. Abe and co-workers [167] note that in connection with the considerable destruction of the five-membered ring, the yields of the corresponding perfluro derivatives do not exceed 11%.

When the electrochemical cyanation of 2,5-dimethylthiophene is carried out in CH_3CN [143], the expected product, viz., 3-cyano-2,5-dimethylthiophene, is formed in only low yield; however, the principal process, as noted above, is directed to favor the formation of 2-cyano-5-methoxy-2,5-dimethyl-2,5-dihydrothiophene.

In the case of functional compounds of the thiophene series, anode substitution has not yet been adequately studied. Let us point out some possibilities of carrying out such reaction on the basis of data on similar processes for other heterocycles and compounds of the benzene series (see [3] pp. 551-555, and [4], pp. 335-384).

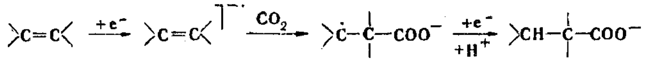
Among the nucleophilic substitution reactions, those that pass through a step involving an anion radical are presently known. One such reaction that is of particular interest in connection with the theme of this review is radical-nucleophilic substitution ($S_{RN}1$). The initiation step of this reaction, which has been studied in detail by Bunnett and co-workers (see [169], as well as an earlier review [170]), consists in the addition of one electron to the halo aromatic compound to give an anion radical, which then reacts via a chain mechanism:

$$[ArX]^{-\cdot} \rightarrow Ar^{\cdot} + X^-$$

$$Ar^{\cdot} + Nu^- \rightarrow [ArNu]^{-\cdot}$$

$$[ArNu]^{-\cdot} + ArX \rightarrow ArNu + [ArX]^{-\cdot}$$

Examples of such reactions are also known for compounds of the thiophene series [171, 172]. Ultraviolet irradiation and the action of alkali metals in liquid ammonia have been used for their initiation. It is interesting to note that the electrochemical initiation of transformations that were formally regarded as reactions of the $S_{RN}1$ type has been realized in the benzene series [61, 62, 173]. However, a pathway involving the reaction of anion radicals with neutral molecules is also possible in the case of cathode processes. A well-known example of reactions of this type is the incorporation of CO_2 in molecules of activated olefins [174] during the reduction of the latter in nonaqueous media, i.e., the formation of carboxylic acids in the reaction of stable anion radicals with CO_2:



$$>C{=}C< \xrightarrow{+e^-} \left[>C{=}C<\right]^{-\cdot} \xrightarrow{CO_2} >\dot{C}-C-COO^- \xrightarrow[+H^+]{+e^-} >CH-C-COO^-$$

Similar reactions are also observed in the reaction of electrochemically generated anion radicals of anthracene [175] and ketones [176] with alkyl halides, as a result of which the corresponding alkyl-substituted compounds are formed. As noted in [29], a reaction of the $[ArX]^{-\cdot} + Z \rightarrow [ArXZ]^{-\cdot}$ type, where Z is a neutral molecule (particularly DMSO or thiophenol), may occur in the electrochemical reduction in nonaqueous media of bromo ketones of the aromatic series [61, 62]. Precisely this point of view [29] with respect to the mechanism of the electrode process made it possible to explain the formation of a whole number of products in the case of electrolysis in DMSO of p-bromobenzophenone.

There is no doubt that a more thorough study of the role of electron transfer in oxidation, reduction, or substitution reactions with the aid of electrochemical concepts and methods will make it possible to extend the use of such transformations for synthetic purposes, including syntheses in the thiophene series.

The authors sincerely thank Professor Ya. L. Gol'dfarb and Master of Chemical Sciences F. M. Stoyanovich for their fruitful discussion of the manuscript of this review and for their valuable advice.

LITERATURE CITED

1. L. I. Belen'kii, E. P. Zakharov, M. A. Kalik, V. P. Litvinov, F. M. Stoyanovich, S. Z. Taits, and B. P. Fabrichnyi, New Directions in the Chemistry of Thiophene [in Russian], Ya. L. Gol'dfarb, ed., Nauka, Moscow (1976).
2. K. A. Bilevich and O. Yu. Okhlobystin, Usp. Khim., 37, 2162 (1968).
3. M. Baizer (editor), The Electrochemistry of Organic Compounds [Russian translation], Mir, Moscow (1976).
4. A. P. Tomilov, M. Ya. Fioshin, and V. A. Smirnov, The Electrochemical Synthesis of Organic Substances [in Russian], Khimiya, Moscow (1976).
5. Ya. P. Stradyn', in: Advances in the Chemistry of Furan [in Russian], É. Ya. Lukevits, ed., Zinatne, Riga (1977), p. 66.
6. V. G. Mairanovskii, Zh. Vses. Khim. Ova., 22, 334 (1977).
7. A. Khodair, A. Swelim, and F. El Sheiku, Int. J. Sulfur Chem., B6, 195 (1971).
8. A. Swelim, A. Khodair, and F. El Sheiku, Int. J. Sulfur Chem., B6, 213 (1971).
9. D. N. Kursanov, Z. N. Parnes, N. M. Loim, and M. I. Kalinkin, Ionic Hydrogenation [in Russian], Khimiya, Moscow (1979).
10. D. W. H. MacDowell and A. W. Springsteen, J. Org. Chem., 41, 3046 (1976).
11. H. A. Michel, G. Mousset, J. Simonet, and H. Lund, Electrochim. Acta, 20, 143 (1975).
12. Ya. L. Gol'dfarb, S. Z. Taits, and V. N. Bulgakova, Izv. Akad. Nauk SSSR, Ser. Khim., No. 7, 1299 (1963).
13. W. J. King and F. F. Nord, J. Org. Chem., 14, 638 (1949).
14. L. I. Belen'kii, S. Z. Taits, and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR. Otdel. Khim. Nauk, No. 9, 1706 (1961).
15. M. A. Ryashentseva, O. A. Kalinovskii, Kh. M. Minachev, and Ya. L. Gol'dfarb, Khim. Geterotsikl. Soedin., No. 6, 694 (1966).
16. M. A. Ryashentseva, Kh. M. Minachev, E. P. Belanova, B. P. Fabrichnyi, and Yu. B. Vol'kenshtein, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 2152 (1977).
17. M. R. Kegelman and E. V. Brown, J. Am. Chem. Soc., 75, 5961 (1953).
18. C. Buehler and D. E. Pearson, Survey of Organic Syntheses, Wiley (1970).
19. T. Mizutani, Y. Ume, and T. Matsuo, Japanese Patent No. 135932; Chem. Abstr., 82, 155744 (1975).
20. T. Mizutani, Y. Ume, and T. Matsuo, Japanese Patent No. 135933; Chem. Abstr., 82, 155745 (1975).
21. F. W. Dunn and K. Dittmer, J. Am. Chem. Soc., 68, 2561 (1946).
22. E. Laviron and J. Tirouflet, Adv. Polarogr., 2, 727 (1960).
23. S. G. Mairanovskii, N. V. Barashkova, and Yu. B. Vol'kenshtein, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 1539 (1965).
24. C. Caullet, M. Salaün, and H. Hebert, Compt. Rend., C264, 228 (1967).
25. P. Foulatier and C. Caullet, Compt. Rend., C279, 25 (1974).
26. L. I. Vykhodtseva and L. N. Nekrasov, Élektrokhimiya, 13, 1239 (1977).
27. L. I. Vykhodtseva and L. N. Nekrasov, Élektrokhimiya, 15, 741 (1979).
28. V. P. Gultyai, S. G. Mairanovskii, T. Ya. Rubinskaya, I. V. Proskurovskaya, and N. P. Rodionov, Élektrokhimiya, 15, 851 (1979).
29. V. P. Gul'tyai and A. M. Moiseenkov, Zh. Org. Khim., 16, 1026 (1980).
30. E. V. Kryukova and A. P. Tomilov, Élektrokhimiya, 5, 869 (1969).
31. J. H. Stocker and R. H. Jenevein, Collect. Czech. Chem. Commun., 36, 925 (1971).
32. P. Foulatier, J.-P. Salaün, and C. C. Caullet, Compt. Rend,m C279, 779 (1974).
33. S. Z. Taits, F. D. Alashev, and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 402 (1969).

34. L. I. Belen'kii, I. B. Karmanova, Yu. B. Vol'kenshtein, and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., No. 5, 956 (1971).
35. J. Srogl, M. Janda, I. Stibor, and H. Prochazka, Z. Chem., 11, 421 (1971).
36. R. A. Benkeser and J. M. Gaul, J. Am. Chem. Soc., 92, 720 (1970).
37. R. A. Benkeser, H. M. Foley, and J. M. Gaul, J. Am. Chem. Soc., 92, 3232 (1970).
38. V. S. Mikhailov, S. G. Mairanovskii, and V. P. Gul'tyai, Électrokhimiya, 7, 1206 (1971).
39. J. Nahaya, H. Kinoshita, and S. Ono, J. Chem. Soc. Jpn., Pure Chem. Sect., 78, 935 (1957).
40. S. Gronowitz, Acta Chem. Scand., 13, 1045 (1959).
41. S.-O. Lawesson, Ark. Kem., 11, 317 (1957).
42. I. O. Shapiro, L. I. Belen'kii, I. A. Romanskii, F. M. Stoyanovich, Ya. L. Gol'dfarb, and A. I. Shatenshtein, Zh. Obshch. Khim., 38, 1998 (1968).
43. B. P. Fabrichnyi, I. F. Shalavina, and Ya. L. Gol'dfarb, USSR Inventor's Certificate No. 170521; Byul. Izobret., No. 9, 26 (1965).
44. B. P. Fabrichnyi, I. F. Shalavina, Ya. L. Gol'dfarb, Dokl. Akad. Nauk SSSR, 162, 120 (1965).
45. B. P. Fabrichnyi, I. F. Shalavina, S. M. Kostrova, and Ya. L. Gol'dfarb, Khim. Geterotsikl. Soedin., No. 10, 1358 (1971).
46. R. Mozingo, S. A. Harris, D. E. Wolf, C. E. Hoffhine, W. R. Easton, and K. Folkers, J. Am. Chem. Soc., 67, 2092 (1945).
47. J. C. Barker, J. F. C. Coutts, and P. R. Huddleston, Chem. Commun., No. 10, 615 (1972).
48. J. F. Bunnett, and R. R. Victor, J. Am. Chem. Soc., 90, 810 (1968).
49. F. M. Stoyanovich, G. I. Gorushkina, and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 387 (1968).
50. Z. V. Todres, F. M. Stoyanovich, Ya. L. Gol'dfarb, and D. N. Kursanov, Khim. Geterotsikl. Soedin., No. 5, 632 (1973).
51. Ya. L. Gol'dfarb, G. P. Pokhil, and L. I. Belen'kii, Dokl. Akad. Nauk SSSR, 167, 823 (1966).
52. B. P. Fedorov, G. I. Gorushkina, and Ya. L. Gol'dbarb, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 2049 (1967).
53. M. A. Ryashentseva, O. A. Kalinovskii, Kh. M. Minachev, Ya. L. Gol'dfarb, Zh. Org. Khim., 1, 1004 (1965).
54. W. Steinkopf, Ann. Chem., 403, 17 (1914).
55. D. L. Eck and G. W. Stacy, J. Heterocycl. Chem., 6, 147 (1969).
56. S. G. Mairanovskii, N. V. Barashkova, and Yu. B. Vol'kenshtein, Éleketrokhimiya, 1, 72 (1965).
57. É. S. Levin and Z. N. Fodiman, Zh. Fiz. Khim., 28, 601 (1954).
58. M. Person, R. Guilard, and P. Fournari, Compt. Rend., C264, 1727 (1967).
59. S. G. Mairanovskii and A. D. Filonova, Elektrokhimiya, 1, 1044 (1965).
60. V. S. Mikhailov, V. P. Gul'tyai, and S. G. Mairanovskii, Élektrokhimiya, 8, 138 (1972).
61. F. M. Halla, J. Pinson, and J. M. Saveant, J. Electroanal. Chem., 89, 347 (1978).
62. W. van Tilborg and C. J. Smit, Tetrahedron Lett., No. 41, 3651 (1977).
63. F. M. Stoyanovich, S. G. Mairanovskii, Ya. L. Gol'dfarb, and I. A. D'yachenko, Izv. Akad. Nauk SSSR, Ser. Khim., No. 7, 1439 (1971).
64. Ya. P. Stradyn', A. Yurashek, and G. Raikhmanis, Zh. Obshch. Khim., 35, 768 (1965).
65. J. Tirouflet and J.-P. Chane, Compt. Rend., 253, 500 (1956).
66. J. Tirouflet and P. Fournari, Compt. Rend., 246, 2003 (1958).
67. L. I. Belen'kii, É. I. Novikova, I. A. D'yachenko, and Ya. L. Gol'dfarb, Zh. Org. Khim., 7, 1736 (1971).
68. P. Zuman, Substitution Effects in Organic Polarography, Plenum Press, New York (1967).
69. P. N. Confalone, G. Pizzoloto, and M. R. Uskokovic, J. Org. Khim., 42, 135 (1966).
70. H. Broadbent, L. H. Staush, and N. L. Jarvis, J. Am. Chem. Soc., 76, 1516 (1954).
71. M. A. Ryashentseva and Kh. M. Minachev, Usp. Khim., 38, 2050 (1969).
72. G. B. Hatch, U.S. Patent No. 2648675; Chem. Abstr., 48, 8264 (1954).
73. D. N. Kursanov, Z. N. Parnes, G. N. Bolestova, and L. I. Belen'kii, USSR Inventor's Certificate No. 408950; Byull. Izobret., No. 48, 68 (1973).
74. D. N. Kursanov, Z. N. Parnes, G. I. Bolestova, and L. I. Belen'kii, Tetrahedron, 31, 311 (1975).
75. Z. N. Parnes, G. I. Bolestova, and D. N. Kursanov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 478 (1976).

76. Z. N. Parnes, Yu. I. Lyakhovetskii, S. N. Dolgova, A. S. Pakhomov, and D. N. Kursanov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 11, 2526 (1977).
77. Z. N. Parnes, Yu. I. Lyakhovetskii, M. I. Kalinkin, L. I. Belen'kii, and D. N. Kursanov, Tetrahedron, 34, 1703 (1978).
78. J. Wrister, J. Am. Chem. Soc., 5051 (1977).
79. S. F. Birch and D. T. McAllan, J. Chem. Soc., No. 10, 2556 (1951).
80. S. G. Mairanovskii, L. I. Kosychenko, and S. Z. Taits, Izv. Akad. Nauk SSSR, Ser. Khim., No. 6, 1382 (1980).
81. H. Lund, M.-A. Michel, and L. Simonet, Acta Chem. Scand., B28, 900 (1974).
82. S. G. Mairanovskii, L. I. Kosychenko, and S. Z. Taits, Élektrokhimiya, 13, 1250 (1977).
83. P. Cavalieri d'Oro, A. Mangini, G. F. Pedulli, P. Spangnolo, and M. Tiecco, Tetrahedron Lett., No. 48, 4179 (1969).
84. V. Galassó and N. Trinajstic, J. Chim. Phys. Phys. Chim. Biol., 70, 1489 (1973).
85. J. M. McIntosh and H. B. Goodbrand, Tetrahedron Lett., No. 34, 3157 (1973).
86. R. M. Kellogg, S. Wassenaar, and J. Buter, Tetrahedron Lett., No. 54, 4689 (1970).
87. J. M. McIntosh and R. S. Steevensz, Can. J. Chem., 52, 1934 (1974).
88. V. P. Gul'tyai, I. V. Proskurovskaya, T. Ya. Rubinskaya, A. V. Lozanova, A. M. Moiseenkov, and A. V. Semenovskii, Izv. Akad. Nauk SSSR, Ser. Khim., No. 7, 1576 (1979).
89. R. M. Kellogg, J. Am. Chem. Soc., 93, 2344 (1971).
90. B. D. Tilak, H. S. Desai, and S. S. Gupta, Tetrahedron Lett., No. 24, 1609 (1964).
91. G. I. Bolestova, E. P. Zakharov, S. P. Dolgova, Z. N. Parnes, and D. N. Kursanov, Khim. Geterotsikl. Soedin., No. 9, 1206 (1975).
92. N. I. Putokhin and V. S. Egorova, Zh. Obshch. Khim., 18, 1866 (1948).
93. Ya. L. Gol'dfarb, A. V. Semenovskii, E. P. Zakharov, G. V. Davydova, and F. M. Stoyanovich, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 480 (1979).
94. I. A. Avrutskaya and G. A. Kokarev, Electrosynthesis and Bioelectrochemistry. Progress in the Electrochemistry of Organic Compounds [in Russian], Nauka, Moscow (1975), p. 34.
95. V. S. Mikhailov, V. P. Gul'tyai, S. G. Mairanovskii, S. Z. Taits, and I. V. Proskurovskaya, Elektrokhimiya, 11, 888 (1975).
96. Ya. L. Gol'dfarb and E. P. Zakharov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1909 (1975).
97. Ya. L. Gol'dfarb and E. P. Zakharov, Khim. Geterotsikl. Soedin., No. 3, 377 (1977).
98. E. P. Zakharov and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1877 (1978).
99. Ya. L. Gol'dfarb and E. P. Zakharov, Khim. Geterotsikl. Soedin., No. 12, 1633 (1971).
100. Ya. L. Gol'dfarb and E. P. Zakharov, Zh. Org. Khim., 6, 1757 (1970).
101. Ya. L. Gol'dfarb and E. P. Zakharov, Izv. Akad. Nauk SSSR, Ser. Khim., No. 9, 2160 (1973).
102. Ya. L. Gol'dfarb and E. P. Zakharov, Khim. Geterotsikl. Soedin., No. 11, 1499 (1975).
103. Ya. L. Gol'dfarb, E. P. Zakharov, A. S. Shashkov, and F. M. Stoyanovich, Zh. Org. Khim., 16, 1523 (1980).
104. Ya. L. Gol'dfarb, B. P. Fabrichnyi, and I. F. Shalavina, Tetrahedron, 18, 21 (1962).
105. Ya. L. Gol'dfarb, S. Z. Taits, and L. I. Belen'kii, Tetrahedron, 19, 1851 (1963).
106. V. S. Mikhailov, Master's Dissertation, Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow (1972).
107. J. Joule and G. Smith, Heterocyclic Chemistry, Van Nostrand Reinhold (1972).
108. C. N. Skold and R. H. Schlessinger, Tetrahedron Lett., No. 10, 791 (1970).
109. W. van Tilborg, Rev. Trav. Chim., 95, 140 (1976).
110. L. Frierman, D. H. Fisher, and H. Shechter, J. Org. Chem., 30, 1453 (1965).
111. P. A. Konstantinov, T. V. Shchedrinskaya, I. V. Zakharov, and M. N. Volkov, Zh. Org. Khim., 8, 2590 (1972).
112. P. A. Konstantinov, T. V. Shchedrinskaya, and I. V. Zakharov, USSR Inventor's Certificate No. 335248; Ref. Zh. Khim., 6N220 (1973).
113. T. V. Shchedrinskaya, P. A. Konstantinov, V. P. Litvinov, É. G. Ostapenko, I. V. Zakharov, and M. N. Volkov, Zh. Obshch. Khim., 44, 837 (1974).
114. M. N. Volkov, O. A. Kazakova, É. G. Ostapenko, P. A. Konstantinov, and R. I. Shunik, Zh. Org. Khim., 15, 1199 (1979).
115. T. V. Shchedrinskaya, P. A. Konstantinov, and M. N. Volkov, Khim. Geterotsikl. Soedin., No. 1, 57 (1977).

116. M. I. Usanovich, A. V. Solomin, and E. I, Kryuchkova, Elektrokhimiya, 6, 894 (1970).
117. R. Clarke, A. Kuhn, and E. Okah, Chem. Br., 11, 59 (1975).
118. L. V. Timokhina, A. S. Nakhmanovich, and T. P. Shcherbina, Izv. Akad. Nauk SSSR, Ser. Khim., No. 12, 2851 (1974).
119. Z. Horii, K. Sakurai, K. Tomino, and T. Homishi, J. Pharm. Soc. Jpn., 76, 1101 (1956).
120. W. J. Raich and C. S. Hamilton, J. Am. Chem. Soc., 79, 3800 (1957).
121. H. R. Snyder, L. A. Caprino, J. F. Zack, and J. F. Mills, J. Am. Chem. Soc., 79, 2556 (1957).
122. M. Fetizon, F. Gomez-Parra, and J.-M. Louis, J. Heterocycl. Chem., 13, 525 (1976).
123. H. Lund, Acta Chem. Scand., 11, 491 (1957).
124. M. Janda, J. Srogl, and M. Synackova, Collect. Czech. Chem. Commun., 37, 2584 (1972).
125. M. Janda, J. Srogl, M. Nemec, and I. Stibor, International Symposium on Low-Molecular-Weight Sulfur-Containing Natural Products, Poland (1976).
126. K. Yoshida and T. Fueno, J. Org. Chem., 36, 1523 (1971).
127. H. Tanaka, Y. Kobayasi, and S. Torii, J. Org. Chem., 41, 3482 (1976).
128. J. Srogl, M. Janda, and I. Stibor, Collect. Czech. Chem. Commun., 39, 185 (1974).
129. M. Janda and L. Paviensky, Collect. Czech. Chem. Commun., 32, 2675 (1967).
130. M. Nemec, M. Janda, J. Srogl, and I. Stibor, Collect. Czech. Chem. Commun., 39, 3527 (1974).
131. A. P. Yakubov, L. I. Belen'kii, and Ya. L. Gol'dfarb, Zh. Org. Khim., 7, 525 (1971).
132. A. Peter, Chem. Ber., 18, 537 (1885).
133. M. G. Johnson, J. P. Turnbull, and H. A. Crige, West German Patent Application No. 2528786 (1976); Chem. Abstr., 84, 150492 (1976).
134. O. Manousek and J. Volke, J. Electroanal. Chem., 43, 365 (1973).
135. W. Boardman and G. Edwards, J. Electroanal. Chem., 33, 95 (1971).
136. L. A. Mirkind, M. Ya. Fioshin, and L. V. Aniskova, Dokl. Akad. Nauk SSSR, 219, 1127 (1974).
137. P. A. Konstantinov, I. V. Shelepin, and P. M. Kolesnikova, Khim. Geterotsikl. Soedin., No. 7, 915 (1971).
138. Ya. L. Gol'dfarb and M. S. Kondakova, Izv. Akad. Nauk SSSR, Otd. Khim. Nauk, No. 6, 1131 (1952).
139. Ya. L. Gol'dfarb and I. S. Korsakova, Dokl. Akad. Nauk SSSR, 89, 301 (1953).
140. Ya. L. Gol'dfarb and M. L. Kirmalova, Dokl. Akad. Nauk SSSR, 91, 539 (1953).
141. J. L. Melles and H. J. Baker, Rec. Trav. Chim., 72, 314 (1953).
142. J. L. Melles, Rec. Trav. Chim., 71, 869 (1952).
143. W. L. Mock, J. Am. Chem. Soc., 92, 7610 (1970).
144. K. Torssell, Acta Chem. Scand., B30, 353 (1976).
145. K. Yoshida, T. Saeki, and T. Fueno, J. Org. Chem., 36, 3673 (1971).
146. N. L. Weinberg and H. R. Weinberg, Chem. Rev., 68, 449 (1968).
147. I. Stibor, J. Srogl, and M. Janda, Chem. Commun., No. 10, 397 (1975).
148. S. Torii, H. Tanaka, T. Anoda, and Y. Simizu, Chem. Lett., No. 5, 495 (1976).
149. M. Janda, Collect. Czech. Chem. Commun., 28, 2524 (1963).
150. J. Srogl, M. Janda, and M. Valentova, Collect. Czech. Chem. Commun., 35, 148 (1970).
151. N. Clauson-Kaas, F. Limborg, and K. Gleus, Acta Chem. Scand., 6, 531 (1952).
152. N. N. Nechiporenko, Zh. Prikl. Khim., 29, 1337 (1956).
153. M. Janda, J. Srogl, M. Nemec, and A. Janosova, Collect. Czech. Chem. Commun., 38, 1221 (1973).
154. M. Janda, J. Srogl, and M. Nemec, Czechoslovakian Patent No. 155895; Chem. Abstr., 83, 27613 (1975).
155. O. Yu. Okhlobystin, Electron Transfer in Organic Reactions [in Russian], Izd. Rostovsk. Gos. Univ. (1974).
156. Z. V. Todres, Usp. Khim., 47, 260 (1978).
157. L. A. Blyumenfel'd, L. V. Bryukhovetskaya, G. V. Fomin, and S. M. Shein, Zh. Fiz. Khim., 44, 931 (1970).
158. L. I. Belen'kii, Izv. Akad. Nauk SSSR, Ser. Khim., No. 2, 344 (1975).
159. J. H. Hoggett, R. B. Moodie, and K. Shofield, J. Chem. Soc., B, No. 1, 1 (1969).
160. J. H. Ridd, Acc. Chem. Res., 4, 248 (1971).
161. B. Ostman, Ark. Kem., 19, 499 (1962).
162. C. L. Perrin, J. Am. Chem. Soc., 99, 5576 (1977).
163. M. R. Draper and J. H. Ridd, Chem. Commun., No. 10, 445 (1978).
164. L. Eberson, L. Jonsson, and F. Radner, Acta Chem. Scand., B32, 749 (1978).

165. I. P. Beletskaya and A. N. Kashin, Zh. Vses. Khim. Ova., 24, 148 (1979).
166. M. Nemec, M. Janda, and J. Srogl, Collect. Czech. Chem. Soc., 38, 3857 (1973).
167. T. Abe, S. Nagase, and H. Baba, Bull. Chem. Soc., Jpn., 46, 3845 (1973).
168. M. Libert and C. Caullet, Compt. Rend., C278, 439 (1974).
169. J. K. Kim and J. F. Bunnett, J. Am. Chem. Soc., 92, 7463 (1970).
170. I. P. Beletskaya and V. N. Drozd, Usp. Khim., 48, 793 (1979).
171. J. F. Bunnett and B. F. Gloor, Heterocycles, 5, 377 (1976).
172. Ya. L. Gol'dfarb, A. P. Yakubov, and L. I. Belen'kii, Khim. Geterotsikl. Soedin., No. 8, 1044 (1979).
173. J. Pinson and J.-M. Saveant, J. Am. Chem. Soc., 100, 1055 (1978).
174. S. Wawzonek and A. J. Gunderson, J. Electrochem. Soc., 111, 324 (1964).
175. J. Simonet, M. A. Michel, and H. Lund, Acta Chem. Scand., B29, 489 (1975).
176. L. H. Kristensen and H. Lund, Acta Chem. Scand., 33, 735 (1979).

THE CHEMISTRY OF sym-TETRACYANOETHANE.

1. CONDENSATION OF sym-TETRACYANOETHANE WITH ALDEHYDES AND KETONES

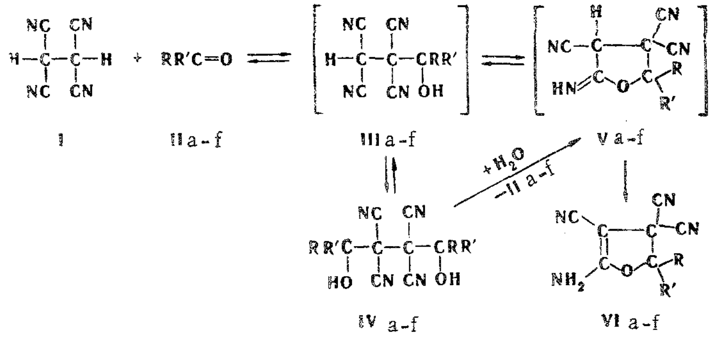
O. E. Nasakin, V. V. Alekseev,
V. K. Promonenkov, A. Kh. Bulai,
and S. Yu. Sil'vestrova

UDC 547.722.3

In an aqueous dioxane solution sym-tetracyanoethane adds to aldehydes and ketones with subsequent cyclization to 3,3,4-tricyano-5-amino-2,3-dihydrofurans.

Very little study has been devoted to sym-tetracyanoethane (I) and its derivatives, probably in connection with the complexity involved in the preparation of I [1]. We have developed a number of relatively accessible methods for the preparation of I [2], which makes it possible to begin a systematic study of its chemistry in order to search for potentially physiologically active preparations and amino nitrile monomers.

The reactions of I with aliphatic and aromatic aldehydes and ketones were investigated. Compound I reacts exothermally with acetaldehyde in the presence of water to give 3,3,4-tricyano-5-amino-2,3-dihydrofuran (VIa) as the final product. Chloral hydrate reacts similarly. Aliphatic ketones and aromatic and heterocyclic aldehydes react with I in the form of the bisulfite compounds or under basic catalysis conditions. The characteristics of VIa-f are presented in Table 1. The probable reaction scheme is given below:



II—VI a R=H, R'=CH_3; b R=H, R'=CCl_3; c R=H, R'= 3-nitrophenyl; d R=H, R'=2-furyl ; e R=R'=CH_3; f R=CH_3, R'=$CH_2C(O)CH_3$

The intermediately formed tetracyanoglycol IVa was obtained by the reaction of I with 2 moles of IIa in absolute alcohol. Its IR spectrum contains a band of medium intensity at 3290

I. N. Ul'yanov Chuvash State University, Cheboksary 428015. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 744-746, June, 1981. Original article submitted June 10, 1980.

0009-3122/81/1706-0541$07.50