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Reactions of anodic and chemical aromatic substitution

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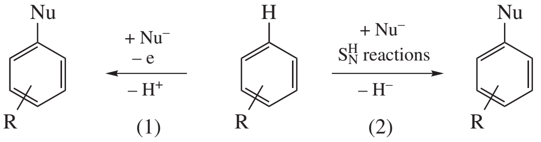
Among anodic (electro-oxidative) aromatic substitution reactions there is a specific group of reactions involving direct nucleophilic replacement of hydrogen atom at the aromatic ring, or S_N^H(An) reactions. These reactions occurring *via* an intermediate σ^+ complex represent a versatile type (the hydrogen atom that is easily removed as a proton) of S_N^H reactions, on the one hand, and are somewhat similar to aromatic electrophilic substitutions, on the other hand.

Anodic substitution reactions represent important area in organic electrosynthesis. Of these, the central place belongs to processes that occur in reactions of arenes with nucleophiles under electrochemical activation of one or both co-reactants simultaneously. Reactions of this kind have been attracting much attention for over fifty years, as shown in numerous reviews and monographs (see, *e.g.*, refs. 1–9). In many cases, the process involves the replacement of a hydrogen atom (Scheme 1, pathway 1.1), which results in the direct formation of C–C, C–O, C–N and other bonds. Such reactions that meet the green chemistry principles[10] are of obvious interest for solving problems in organic synthesis. However, their place among classic aromatic substitution reactions has never been specially discussed in electrochemical literature.



Scheme 1

On the other hand, the nucleophilic replacement of hydrogen (S_N^H reactions, pathway 1.2) is most similar to the type of reactions in question (pathway 1.1). The concept of S_N^H reactions as an important type of nucleophilic aromatic substitution was introduced in chemical literature in the 1970s.[11] To date, these reactions have been developed extensively to become a new approach to the construction of C–C and C–X bonds (X = O, N, P, S, halogen) based on the nucleophilic replacement of aromatic hydrogen.[12,13] In view of this, the reviews that, on the one hand, showed the wide capabilities of S_N^H reactions,[13] and on the other hand, performed a comparative analysis of regularities of aromatic substitution,[14] are of undeniable interest. Unfortunately, anodic substitution was left out of scope even in these publications, though one monograph[12] contains a small chapter devoted to electrochemical methods. In order to fill the vacuum, the current publication outlines a brief discussion of the main features of these reactions and their comparison with aromatic substitution reactions. Thus, the most attention will be given to a systematization of data concerning the anodic substitution mechanisms. The synthetic application of these reactions will be considered rather briefly, mostly with reference to the corresponding reviews.

Aromatic anodic substitution reactions. As a rule, anodic substitution mostly involved such objects as arenes and heteroarenes (including fused ones) with electron-donating substituents and similar non-substituted arenes. A wide range of anions were used as nucleophiles: HO^-, RO^-, $RCOO^-$, NO_2^-, N_3^-, SCN^-, CN^-, OCN^-, $HC(NO_2)_2^-$, $C(NO_2)_3^-$, halide and azolate ions, the series of acids matching these anions: H_2O, ROH, RCOOH, azoles as well as uncharged nucleophiles, *e.g.*, MeCN, pyridine.

The mechanisms of anodic substitution are a matter of discussion for many decades now. This allows us to use the already established concepts, while referring to the original studies only to substantiate certain statements or in those cases where some important information was not reflected in reviews, including studies of the past few years.

Analysis of anodic substitution reactions is generally performed based on the reaction type (cyanation, acetoxylation, *etc.*) or the resulting bond type (C–C, C–O, *etc.*).[1–9] However, in order to analyse data on the mechanisms of these reactions,[†] we suggested a more rational approach[15] based on the facility of the nucleophile

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[†] In the discussion of these issues we are going to use general concepts while avoiding the terminology and notation that are accepted in special literature.

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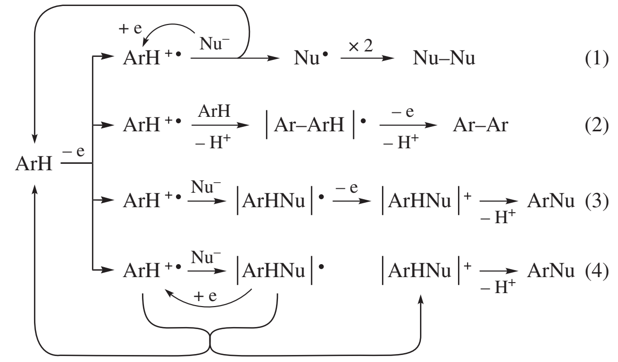
oxidation in comparison with the arene, irrespective of the type of the resulting bonds or the type of the reaction in question. Two main reaction groups may be distinguished from this point of view: reactions involving nucleophiles that undergo oxidation less easily than arenes (Scheme 2) or more easily than arenes (see below).

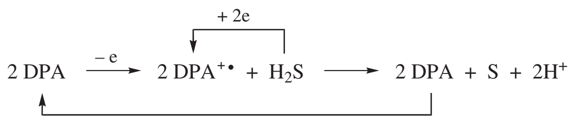
Scheme 2 generalises the main types of reactions typical of arenes with any structures, provided that their oxidation potential is lower than that of the nucleophile.



Scheme 2

Pathways 2.1 and 2.4, where Nu^- and accordingly $ArNu^{\bullet}$ act as reducing agents, have been discussed.[7]

Introduction of such nucleophiles as I^-, CN^- or H_2S to a reaction mixture containing an arene that is oxidised more readily results in a catalytic increase in the arene oxidation current due to the complete recovery of the arene by pathway 2.1.[16,17] In this respect, the example of oxidation of 9,10-diphenylanthracene (DPA) in the presence of H_2S, which acts as a two-electron reducing agent, is of interest (Scheme 3).[17]



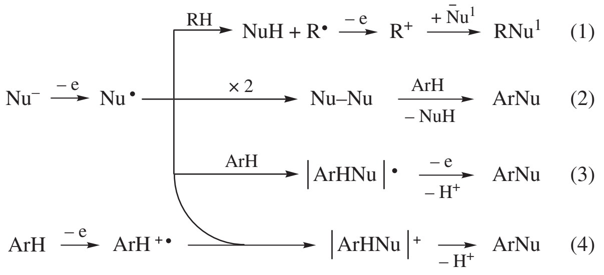
Scheme 3

More often than not, the original arene can act as a nucleophile (pathway 2.2). Such reactions are typical of anodic polymerisation of arenes.

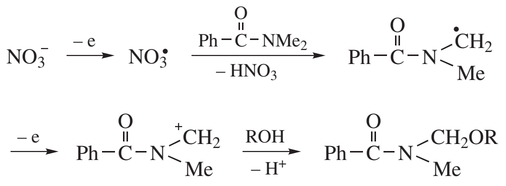
The most interesting reactions that follow pathway 2.3 will be discussed below. It is only to be noted here that these processes can be easily tested by voltammetry: the addition of a nucleophile increases the arene oxidation current, since the intermediate radical adduct is oxidized more easily than the original arene.

Pathway 2.4 is a specific variation of pathway 2.3. Its specific feature is that the radical adduct (which is formed in the reaction of the cation radical of the original arene with the nucleophile) can reduce a second cation radical species. This results in the recovery of the original arene and formation of a cationic adduct, which is stabilised with abstraction of a proton to give the final product. Anodic hydroxylation of 9,10-diphenylanthracene (MeCN with addition of water as a Nu) to give equal amounts of the starting arene and *trans*-9,10-dihydroxy-9,10-diphenyl-9,10-dihydroanthracene[18] is an example of a process that occurs by such a 'semi-regeneration' mechanism.[7]

Pathway 4.1 (Scheme 4) of the electrode reaction group involving nucleophiles that are oxidised more easily than arenes is the main way for the stabilisation of electrochemically generated $Nu^{\bullet}$ radicals, in which the solvent molecules usually act as the RH. The destiny of $R^{\bullet}$ is usually not discussed, except for the cases where the $R^{\bullet}$ intermediate is used for some special purpose. An indirect electrochemical synthesis of RNu^1 can be an example; it occurs by pathway 4.1 in the N-alkoxylation of *N*,*N*-dimethylcarboxamides in nitrate solutions in alcohols ($Nu = NO_3^-$ and $Nu^1 = ROH$),[19] according to Scheme 5.

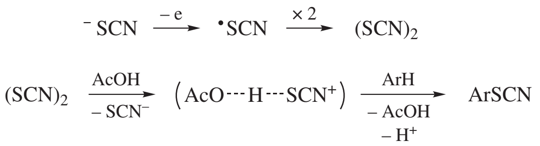


Scheme 4



Scheme 5

Pathway 4.2 gives dimeric products. Nu–Nu species are also used in indirect electrosynthesis processes, *e.g.*, in those cases where the Nu–Nu species electrogenerated at the first stage act as mediators (Br_2 in furan methoxylation[20]) or as co-reagents, which at the second stage chemically react with the arene to give the target product, such as $(SCN)_2$ in indirect thiocyanation of arenes,[21] as shown in Scheme 6.



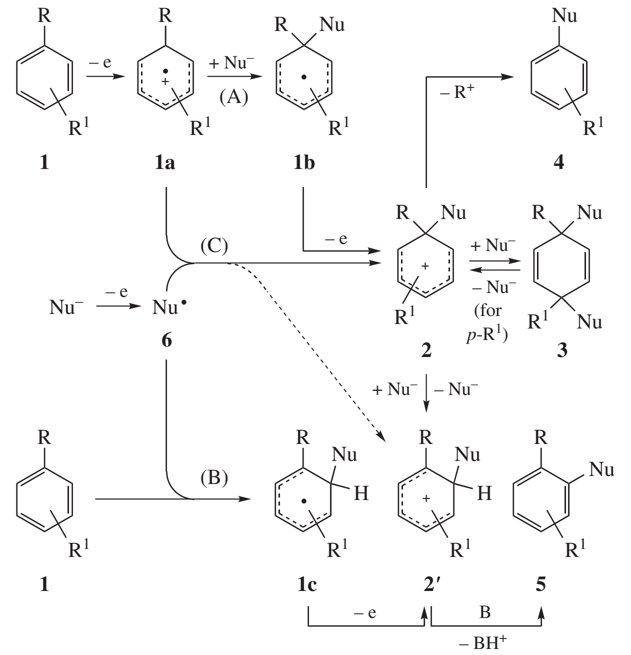
Scheme 6

There are few examples of reactions that occur by pathway 4.3 and have a reliably proven mechanism (Scheme 7, pathway B). The issue is that the competing processes 4.1 and 4.2 usually occur at higher rates. In such cases, electrolysis for arene functionalisation (pathway 4.4) is carried out at high potentials, such that both the Nu^- and the arene are oxidised (see pathway C, Scheme 7).

The brief, and hence far from comrehensive, analysis of the main types of anodic reactions of nucleophiles and arenes performed above still allows one to single out the reactions that result in direct replacement of an aromatic ring hydrogen by a Nu^-. These reactions occurring by pathway 2.3 (Scheme 2) or by pathways 4.3 and 4.4 (Scheme 4) are mostly carried out in alcohols or in aprotic media.

Analysis of literature data and results of our own studies allowed us to understand the mechanisms of such reactions in more detail (Scheme 7).

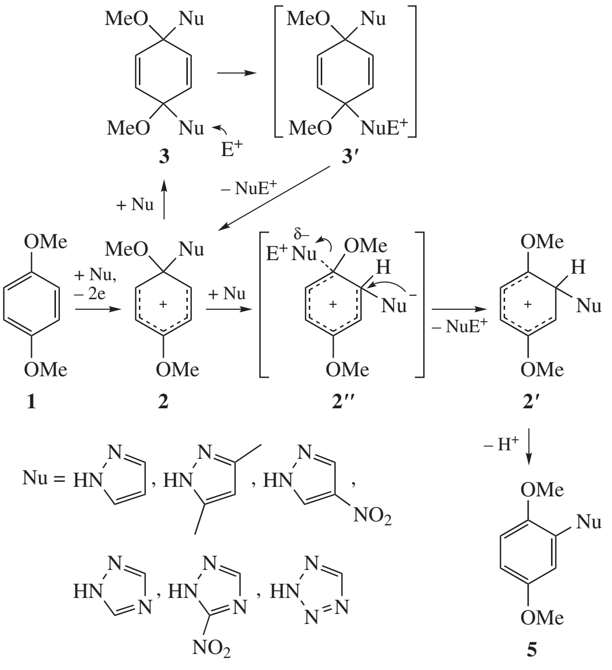
Pathway A. This pathway (Scheme 7) details the mechanism of substitution processes involving arenes that are oxidized more easily than nucleophiles (see pathway 2.3, Scheme 2). Conclusive evidence confirming the validity of this pathway has been obtained in a study of azolation of dimethoxybenzenes,[22–26] which are oxidized much more easily than azole-type nucleophiles. It has been found[22] that substitution occurs by an *ipso*-reaction of an



Scheme 7

azole with radical cation **1a**, whereas implementation of stages **1** → **1a** → **1b** → **2** leads to arenonium cation **2** as the key intermediate of the process.

The subsequent reaction of cation **2** with a nucleophile sometimes affords *ipso*-substitution products (**4**); however, in the electrooxidation of *p*-dimethoxybenzene, the competing *ipso*- and *ortho*-reactions of cation **2** with the azole nucleophile are the main stages that lead to *ipso*-bis-addition (**3**) and *ortho*-substitution (**5**) products, respectively.



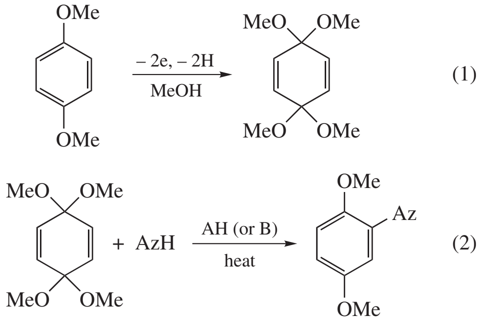
$E^+ = AcOH, ZnCl_2$

Scheme 8

An important characteristic feature of the process in question is that product **3** can turn into product **5** in the course of electrolysis.[22–26] This occurs due to the fact that the conversion of cation **2** to product **3** (Scheme 8) is reversible owing to removal of the nucleophile (catalysis by acidic components present in the reaction mixture) from the *ipso*-position of intermediate **3′**. On the other hand, the electrophilic assistance to the removal of the nucleophile from the *ipso*-position of intermediate **2″** provided by the same components stimulates the irreversible rearrangement of cation **2** to the more stable cation **2′**, which occurs by the *cine*-substitution mechanism.[26] This conclusion is based on the fact that addition of electrophiles (Lewis or Brønsted acids), *e.g.*, in the electrolysis of a 2,5-dimethylpyrazole/1,4-dimethoxybenzene mixture, does not deactivate the nucleophile (as one might have expected) but increases the yield of product **5**, whereas the yield of product **3** decreases; addition of a base (2,4,6-trimethylpyridine) gives an opposite effect.[26]

These regularities show a clear similarity to those of the electrophilic nitration of *p*-cymene with acetylnitrate in a nucleophilic medium (acetic acid or acetic anhydride).[27] The process involves the generation of an intermediate σ-complex of type **2** (Scheme 8) to give isomeric 4-acetoxy-4-isopropyl-1-methyl-1-nitrocyclohexa-2,5-diene, which turns to 2-nitro-*p*-cymene on treatment with H_2SO_4. In view of the above, one may believe that the stages of transformations of this σ-complex are similar to those of arenonium cation **2** (Scheme 8).

The features of arene azolation described above (Scheme 8) served as a base for a new method for synthesising these compounds,[25] as shown in Scheme 9.



AzH = azole, AH = acid, B = base

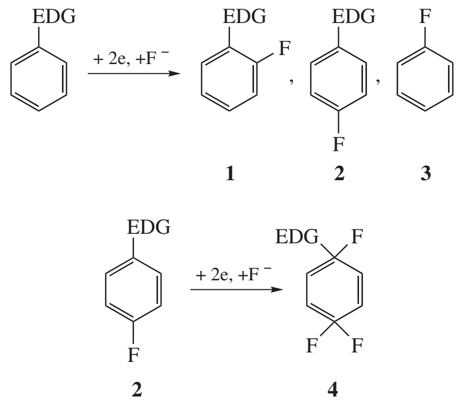
Scheme 9

The first stage of this process is the synthesis of a quinone diketal by the method reported previously,[28] while the second stage involves a chemical formation of an arylazole; in this case, the acidity of the azole defines whether AH or B should be added to the reaction mixture.

Of nucleophiles belonging to the reaction group in question, fluoride is the hardest to oxidise. The regularities of anodic fluorination (dry MeCN, $R_3N\cdot n$HF or $R_4N\cdot n$HF) of arenes with electron-donating substituents[29–31] are almost equivalent to those of the azolation of these compounds. Like with azolation, the electrochemical fluorination of substituted arenes[29] may result in *ortho*- (**1**) or *para*-substitution (**2**) products, as well as to *ipso*-substitution (**3**) or *ipso*-bis-addition (**4**) products (Scheme 10).

Presumably,[30,31] the formation of an *ortho*-isomer results from an initial *ipso*-attack of the fluoride anion to radical cation **1a** (Scheme 7) followed by a 1,2-shift of the substituent in the type-**2** arenonium cation to give cation **2′**. This mechanism agrees with the mechanism represented by pathway A (Scheme 7), the only difference being that the possibility of electrophilic assistance to the cation rearrangement **2** → **2″** → **2′**, which occurs by the *cine*-substitution mechanism (see above, Scheme 8), was not studied in refs. 29–31. Likewise, the possibility of sequential transformations **3** → **3′** → **2** → **2″** → **2′** → **5** (Scheme 8) for the conversion of cyclohexadiene **4** (Scheme 10) into the corresponding *ortho*-substitution product was not studied, either.

Acetate ion, which undergoes oxidation more hardly than a wide range of arenes with electron-donating substituents and fused



EDG = electron-donating group

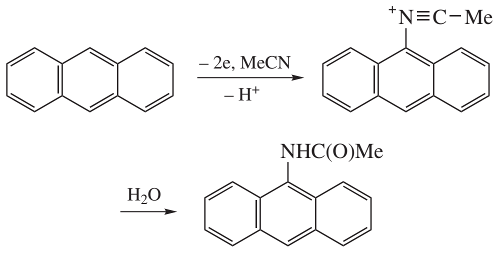
Scheme 10

arenes, should also be attributed to nucleophiles that can be involved in the group of reactions under discussion. Though numerous studies deal with the acetoxylation of arenes and these studies were systematised more than once,[4,5,9] the mechanism of the process has not been examined in detail. However, it is generally believed[9] that the formation of *ortho*- or *para*-substitution products results from an attack by the nucleophile to the corresponding positions of the originally generated arene radical cation (no *ipso*-bis-addition products were detected in the acetoxylation of *para*-substituted arenes).

Nevertheless, one may believe that the acetoxylation of arenes, similarly to the azolation and fluorination of these compounds discussed above, proceeds by pathway A (Scheme 7) through initial *ipso*-attack of the arene radical cation by the nucleophile. This is suggested by the data on the anodic acetoxylation of mono- and disubstituted arenes (MeCN, $MeCOO^-Alk_4N^+$),[32,33] according to which acetoxylation products are only formed upon addition of acids [AcOH, $H_2C(CO_2Me)_2$ or $ZnCl_2$] to the reaction mixture. This is due to the fact[33] that addition of acids electrophilically assist the rearrangement of unstable cation **2** to cation **2′** by the *cine*-substitution mechanism (Scheme 8) followed by the conversion of the latter to an *ortho*-substitution product.

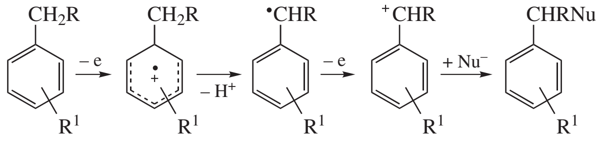
In general, the possibility to remove a substituent from the *ipso*-position of arenonium cation **2** (Scheme 8) by the *cine*-substitution mechanism[26,32,33] is of special interest. This allows us, on the one hand, to specify the factors that stimulate the 1,2-shift of a substituent under these conditions, and on the other hand, to assume that the formation of *para*-substitution products in the anodic substitution of arenes occurs by a similar mechanism (see Scheme 8) due to the attack of the nucleophile to the *para*-position of cation **2** involving *tele*-substitution.

The above reactions that occur by the mechanism represented by pathway A are not exceptional examples. The acetamidation in MeCN as a hardly-oxidizable solvent acting as the nucleophile is widely used in practical electrosynthesis. The electrochemical acetamidation of anthracene[34] (Scheme 11) can serve as an example.



Scheme 11

The specific character of Nu and radical cations of some substituted arenes interactions should be pointed out. Electrolysis involving alkyl-substituted arenes can give, along with products of substitution into the aromatic ring, also products of substitution into the side chain[6,9] according to Scheme 12.

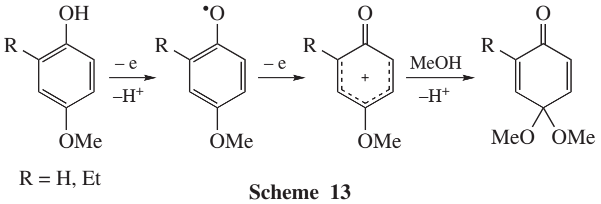


Scheme 12

Generally, for example, in $MeOH/MeO^-$ (ref. 35) or AcOH/AcO^- systems,[36] the stronger nucleophile (MeO^-, AcO^-) forms products of substitution into the ring, whereas the weaker one (MeOH, AcOH) gives products of substitution into the side chain.

The formation of side chain substitution products is also typical of the electrooxidation of phenyl-, alkyl- or benzylamines in the presence of nucleophiles.[9] These processes occur by a similar mechanism (see Scheme 12). Meantime, it has been noted[7,9] that functionalisation of arylamines directly into the aromatic ring is possible.

The oxidation of phenols proceeds in a special way, which involves the loss of aromaticity. For example,[37] the reaction of methanol with phenoxonium cation formed upon oxidation of *p*-methoxyphenol affords the synthetically useful quinone monoketals (Scheme 13).

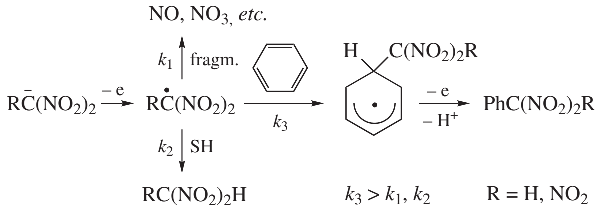


Scheme 13

<u>*Pathway B (Scheme 7).*</u> The majority of nucleophiles studied (NO_2^-, SCN^-, CN^-, Cl^-, Br^- *etc.*) are oxidised much more easily than many arenes. However, the radicals generated at the oxidation potentials of such nucleophiles generally have a too low electrophilicity to efficiently attack an aromatic substrate that is not oxidizable under the experimental conditions, so they are deactivated by dimerisation or in reactions with the medium (pathways 4.1 and 4.2, Scheme 4).

For these reasons, only a few examples of homolytic substitution by pathway B, whose mechanism has been proven, were reported. The anodic polynitroalkylation of arenes is among these examples. The electrooxidation of *gem*-polynitroalkane salts results in the generation of a highly electrophilic polynitroalkyl radical (Scheme 14), which is unstable and undergoes partial fragmentation (k_1) to give NO, NO_3^- *etc.* (as detected by voltammetry), but mostly abstracts a hydrogen atom from the solvent SH (k_2) to give the corresponding acid.[38]

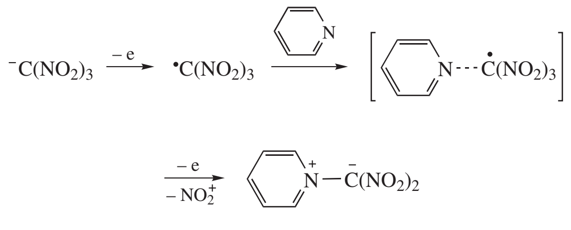
However, the reaction of the electrogenerated polynitroalkyl radical with an arene added to the reaction solution occurs much



Scheme 14

faster. This confirms the fact that in the presence of arenes (PhMe, PhH, PhCl, PhCN) the height of the polynitrocarbanion oxidation wave increases noticeably (due to the contribution of the current of the easily oxidizable radical adduct): the maximum effect is observed with PhMe and the minimum effect, with the weakly-nucleophilic PhCN, which correlates well with the yields of the polynitroalkylation products. This occurs as a one pot process to give *ortho*- and *para*-substituted polynitroalkylarenes[39–40] (the method previously reported for the chemical preparation of such compounds involved a number of stages[41]).

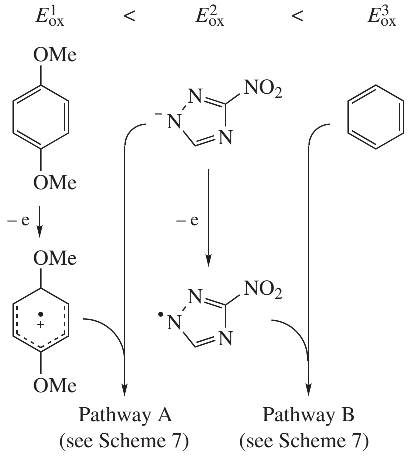
The high electrophilicity of the trinitromethyl radical allows functionalization to be performed even for $PhNO_2$, which is inactive for electrophilic attack. In the case of heteroarenes, it allows a selective attack of the heteroatom's electron pair to proceed (Scheme 15) giving the corresponding dinitromethylides,[42] whereas no C-attack occurs.



Scheme 15

Note that the electrooxidation of dinitromethylides generates dinitrocarbene,[43,44] which proved to be a more efficient dinitroalkylating agent[45,46] than the corresponding radical.

One more example of processes that occur by pathway B is given by the formation of 3-nitro-1-phenyl-1,2,4-triazole isomers in the electrooxidation of a 3-nitro-1,2,4-triazole–Alk_4N^+ salt in the presence of benzene that is not oxidised under the experimental conditions.[47] It should be noted that the same 3-nitro-1,2,4-triazole anion, which does not undergo oxidation under the electrolysis conditions, efficiently reacts with the radical cation of the readily oxidisable 1,4-dimethoxybenzene (Scheme 16) to yield an *ortho*-substitution product through a different mechanism (pathway A).[48]



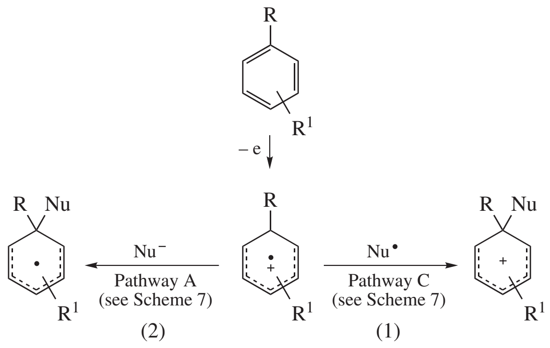
Scheme 16

These examples well demonstrate the efficiency of the approach suggested for analysing the regularities of anodic substitution in arenes: depending on the arene nature (*p*-dimethoxybenzene or benzene), the same nucleophile (3-nitro-1,2,4-triazolate anion) belonging to the hardly-oxidisable group moves to the easily-oxidisable group, whereas the substitution mechanism typical of one group changes to the mechanism typical of the other group.

Pathway C (Scheme 7). With few exceptions (see above), electrolysis at oxidation potentials of nucleophiles in the presence of more hardly oxidisable arenes gives no substitution products. This question was specifically considered in a monograph,[7] where it was noted in particular that it is expedient to perform anodic substitution processes involving easily oxidisable nucleophiles at sufficiently high anodic potentials that ensure that not only the nucleophile but also the arene are oxidised.

Without dwelling on specific examples of halogenation, alkoxylation, cyanation, nitration and other processes that have been systematised in a number of monographs (see, *e.g.*, refs. 6, 7, 9) let us note the general conclusion: electrolysis performed at potentials that ensure the oxidation of not only the nucleophile but also the arene gives products of direct replacement of aromatic ring hydrogen by the nucleophile.

This result can be a consequence of two principally possible reactions (Scheme 17) involving an electrogenerated arene radical cation.



Scheme 17

Reaction (1) (Scheme 17) is due to a combination of a radical cation and radical species that are generated simultaneously. This mechanism, which is generally accepted at the moment (pathway C, Scheme 7)[9] and involves stages (**1a** + **6**) → **2** → **3**, was first considered in refs. 35, 49, 50. However, this process can also occur through stages **2** → **2′** → **5**. For example, it has been shown recently[51] that direct thiocyanation of arenes occurs by this mechanism, though it was believed previously that electrochemical thiocyanation was only possible by indirect electrosynthesis (see Scheme 6). In principle, it may not be ruled out that pathway C can include stages (**1a** + **6**) → **2′** → **5**, but this requires additional studies.

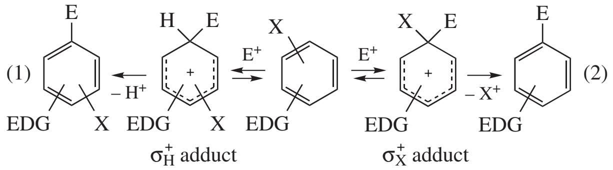
Reaction (2) (Scheme 17) is realized owing to the fact that even under conditions of electrolysis, at high potentials the arene radical cation can 'intercept' an easily-oxidisable anion that is approaching the anode. The resulting radical adduct undergoes further transformations by pathway A.

Thus, under conditions of joint oxidation of a nucleophile and an arene, the process can occur through parallel pathways A and C, but it is difficult to judge which of the mechanisms would be preferred.

However, it is much more important that the reaction mechanisms presented in Scheme 7 well reflect the specifics of anodic nucleophilic replacement of hydrogen in arenes, which mostly proceeds *via* arenonium cation **2**. The reaction of this cation with a nucleophile that is present in excess in the reaction mixture determines the nature and ratio of the reaction products. It should be noted that cations with structure **2** are the key intermediates in electrophilic aromatic substitution, and that generation of these cations under anodic substitution conditions has two specific features: first, the stage of the formation of these cations (**1b** → **2**, Scheme 7) is most likely to be irreversible; second, they are always generated in nucleophilic media.

Overall, this was only a principal analysis of data on the regularities of anodic substitution, many aspects of which deserve a more detailed discussion.

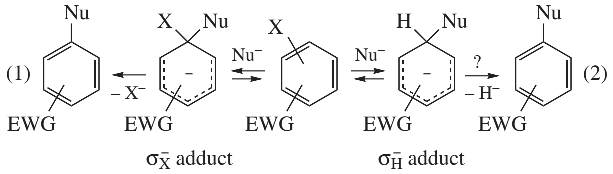
Anodic replacement of the hydrogen atom in the aromatic ring as a versatile type of S_N^H reactions. Reactions of electrophilic (S_EAr) and nucleophilic (S_NAr) aromatic substitution are of fundamental importance in the chemistry of electron-enriched and electron-deficient aromatic systems, respectively. These varieties of substitution reactions covering the entire scope of aromatic substitution processes have certain specific features.



EDG = electron-donating group

Scheme 18

The vast majority of S_EAr reactions occur by reversible addition of an electrophile to give a cationic σ_H^+ adduct with violated aromaticity (pathway 18.1, Scheme 18). The subsequent removal of the hydrogen atom that is eliminated as H^+ restores aromaticity to give the substitution product. The much rarer *ipso*-substitution reactions (pathway 18.2) involve the elimination of cationoid groups (NO_2^+, $^+Pr^i$, $^+Bu^t$ *etc.*).[52]



EWG = electron-withdrawing group

Scheme 19

Conversely, in S_NAr reactions, the classical process (pathway 19.1, Scheme 19) occurs as *ipso*-replacement of function X by a nucleophile; the former is readily removed as an anionic particle, such as NO_2^-, Hal^- *etc.* from the intermediate anionic σ_X^- adduct. It is only in the past years (see ref. 13 and the references cited therein) that reactions of nucleophilic replacement of a hydrogen atom in the aromatic ring were developed intensely; such reactions were designated as S_N^H (ref. 11) in order to distinguish them from the classical *ipso*-substitution that was designated as S_N^{ipso}Ar. It is quite obvious that a direct S_N^H process is unlikely since it would involve hydrogen abstraction from a σ_H^- adduct as a hydride ion (pathway 19.2). However, a number of 'indirect' methods for performing this task are known, the main ones[13] involving the addition–oxidation S_N^H(AO) (pathway 20.1, Scheme 20) and addition–elimination S_N^H(AE) processes (pathway 20.2).

It is this group of hydrogen nucleophilic substitution reactions that is similar (with 'opposite sign') to hydrogen electrophilic substitution, as noted in a review[14] that gives an excellent analysis of regularities characterising the S_EAr and S_NAr reactions.

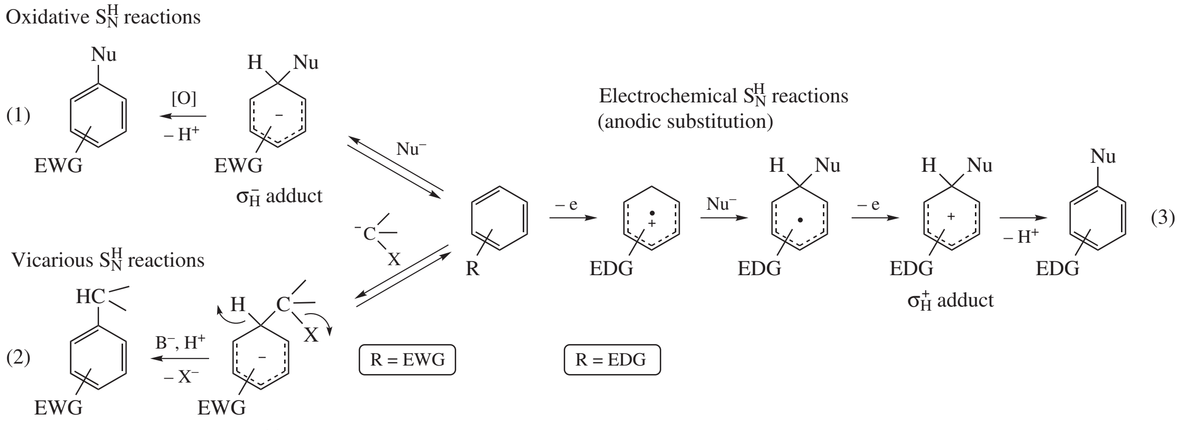
However, in comparison with the S_EAr process that occurs by pathway 18.1, the S_N^H(AO) reactions, which follow pathway 20.1, have certain limitations[14] due to the fact that the oxidation of σ_H^- adducts requires that they be present at high concentration along with a minimum concentration of the nucleophile, which is not always possible. Furthermore, it is necessary to find an oxidant that selectively oxidizes σ_H^- adducts, but not a nucleophile that usually readily undergoes oxidation.

Reactions that belong to the S_N^H(AE) group also have certain drawbacks. Implementation of such reactions requires involving either specially selected nucleophiles that contain nucleofugal groups X at the nucleophilic center (vicarious S_N^H reactions, Scheme 20) or specially selected starting arenes containing nucleofugal groups at a position adjacent to the site of the attack (*cine*-substitution) or at a more distant position (*tele*-substitution). Furthermore, S_N^H(AE) reactions are not perfect from the green chemistry standpoint,[10] since the leaving nucleofugal group (mostly Cl^-) appears in the reaction mixture as a result.

Taking this into consideration, the electrochemical S_N^H reactions discussed above (pathway 20.3, Scheme 20) are more promising. They occur *via* intermediate σ_H^+ rather than σ_H^- adducts, hence the hydrogen that is replaced is easily removed as a proton. It is expedient to designate these reactions by a special symbol, S_N^H(An), since they are referred to as anodic substitution reactions in electrochemical literature. The S_N^H(An) reactions meet the green chemistry principles to a higher extent, since they do not involve the removal of nucleofugal groups [*cf.* S_N^H(AE) reactions] and the electron transfer successfully works instead of an oxidant [S_N^H(AO) reactions] that is often used just once.

It should be noted that S_N^H(An) reactions, similarly to S_EAr reactions, use arenes with electron-donating substituents that are prone to addition of electrophilic reagents as the main starting compounds. However, due to the polarity inversion ('Umpolung'), which is easily achievable by electrochemical means, the starting nucleophilic arene is converted to a radical cation (pathway 20.3) to become an electrophile, which, in turn, efficiently adds nucleophilic reagents. This fact expands considerably the scope of arenes that can undergo S_N^H reactions.

Thus, a unique feature of S_N^H(An) reactions considered above is that, while being reactions of nucleophilic substitution of arenes (according to Ingold's classification 'based on the reagent'[53]),



Scheme 20

they occur *via* a key intermediate of electrophilic aromatic substitution. This allows the hydrogen being replaced to be removed as a proton, the scope of the starting arenes in nucleophilic substitution to be expanded considerably, and, finally, opens up broad possibilities for studying the reactivity of arenonium cations in the presence of nucleophiles, which has still almost not been studied in chemical substitution reactions. In general, S_N^H(An) reactions provide a good illustration to the main idea of the review[14] devoted to electrophilic and nucleophilic substitution of hydrogen as similar and complementary processes.

It should be noted in conclusion that comparative analysis of the main features of anodic substitution of arenes and of aromatic substitution reactions allowed a special group of reactions to be singled out, namely, anodic aromatic replacement of hydrogen [S_N^H(An)], which is a versatile version of S_N^H reactions. Unfortunately, the currently known examples of processes of this kind mostly involve the simplest nucleophiles. It may be hoped that this fact will attract the attention of researchers and encourage a further development of S_N^H(An) reactions, the synthetic potential of which is far from being exhausted.

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