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NUCLEOPHILIC SUBSTITUTION IN NITROARENES. GENERAL MECHANISM

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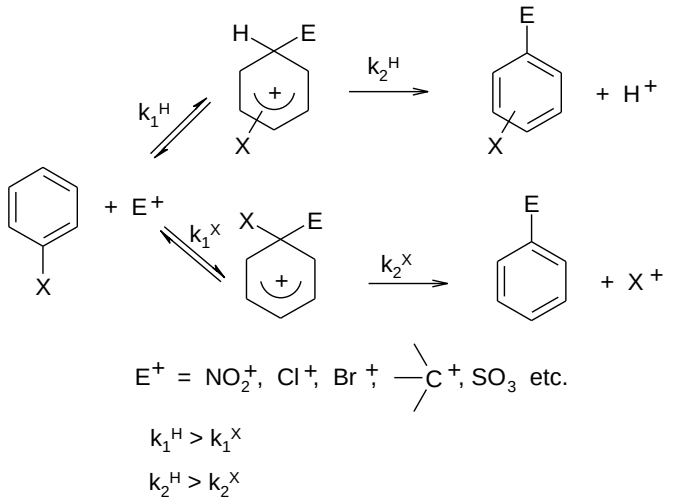
Experimental studies and theoretical calculations revelated that generally accepted mechanism of nucleophilic aromatic substitution needs correction. In the paper general corrected mechanism of nucleophilic substitution in nitroarenes is formulated. Mechanistic analogies between electrophilic and nucleophilic aromatic substitutions are disclosed.

References 33.

Introduction of substituents into aromatic rings are processes of great importance to organic chemistry. Amongst many variants of these processes the most important and frequently used is electrophilic aromatic substitution that proceeds via addition of electrophilic agent to the aromatic ring to form cationic adduct followed by departure of proton giving product of the substitution of hydrogen. Such important processes as nitration, halogenation, sulfonation and particularly many variants of the Friedel-Crafts reaction proceed according to this general mechanistic scheme. Efficiency of the process is due to π^-−electron system of aromatic rings that facilitate addition of electrophilic agents, particularly at positions occupied by hydrogen and mobility of proton departing from the cationic adduct. The reaction can proceeds also via addition of electrophiles at positions occupied by a substituent and departure of this substituent in cationic form. This variant named *ipso*-substitution is much less frequent, but also have found practical application. *Normal* and *ipso* variants of electrophilic aromatic substitution are presented in scheme 1 [1].

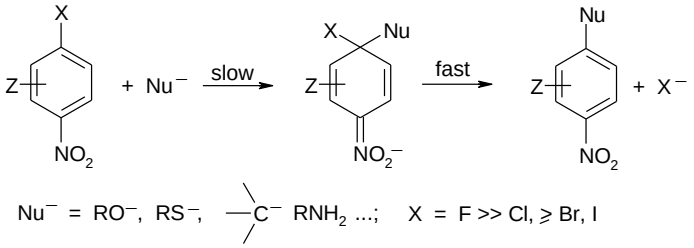
Scheme 1. General scheme of electrophilic aromatic substitution, "*normal*" and "*ipso*"



Introduction of substituents into aromatic rings via a reaction with nucleophilic agents is much more difficult and less obvious.

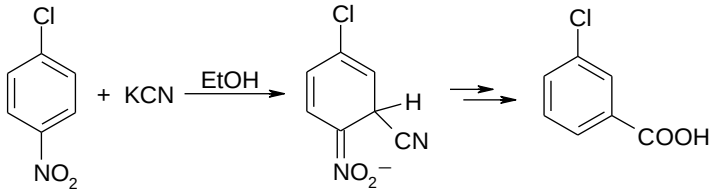
π-electron systems of the rings that facilitate addition of electrophilic agents disfavor addition of nucleophiles. Moreover formation of new bonds between nucleophiles and ring carbon atoms requires that a substituent with an electron pair should depart, hence it should be a nucleofugal group – (halogen anion etc.) not hydrogen, because hydride anion is a very unstable and basic entity. Due to this situation a few mechanisms of nucleophilic aromatic substitution were developed: elimination-addition (via arynes), S_NR^1 via electron transfer and radical-nucleophile coupling, etc. but the most common and important is substitution of halogens and other nucleofugal groups in electron-deficient arenes, particularly nitroarenes. This reaction, S_NAr, is a process of great importance, widely used in laboratory and industrial organic synthesis [2]. According to the mechanism formulated by J.F. Bunnett [3] it proceeds via addition of nucleophiles to *o*- or *p*-halonitroarenes at positions occupied by halogens, X to form σ^X adducts, followed by spontaneous departure of X^- with the formation of products of the substitution. The addition is connected with dearomatization, hence energetically disfavoured, therefore it is a slow, rate limiting step, whereas elimination of X^-, connected with rearomatisation usually proceeds faster. This mechanism was confirmed in thorough mechanistic studies, and it is presently generally accepted and presented in reviews, monographs and text-books [2].

Scheme 2. General picture of nucleophilic aromatic substitution, S_NAr in *p*-halonitrobenzenes.



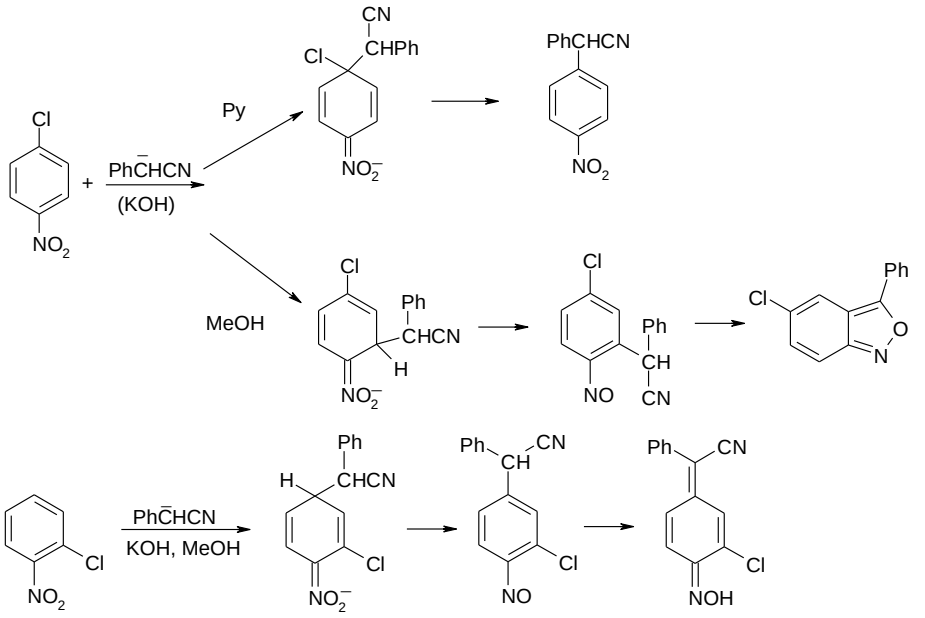
Ability of halonitrobenzenes to add nucleophiles is due to the activating effect of the nitro group, not halogens, thus nucleophiles should be able to add to these arenes also at positions occupied by hydrogen. Indeed there are a few early reports of reactions between nucleophiles and *p*-chloronitrobenzene that proceed via addition of nucleophiles at positions *ortho* followed by further transformations of the intermediate σ^H adducts [4]. For instance von Richter reaction in scheme 3 was reported in 1871 [4a].

Scheme 3. von Richter reaction



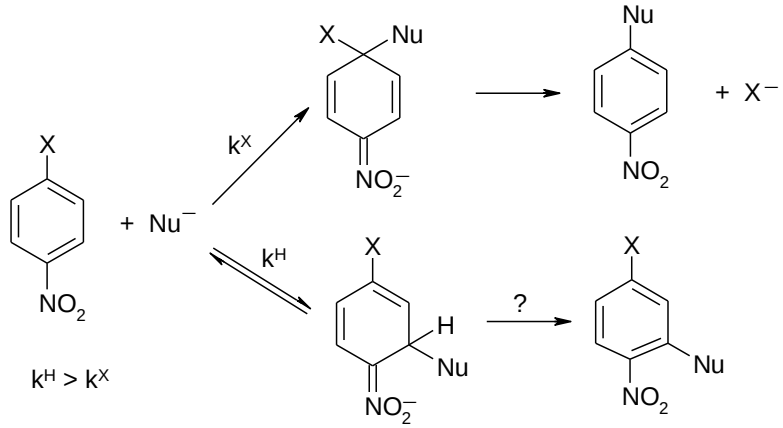
The most instructive is report that carbanion of phenylacetonitrile reacts with *p*-chloronitrobenzene in two different ways. In polar aprotic solvents simple S_NAr of chlorine takes place whereas in protic media phenyl chloro-benzisoxazole is formed via initial formation of σ^H adducts [4b]. Both of these reactions proceed in high yield and selectivity. Formation of benzisoxazole proceeds via conversion of the σ^H adduct into nitrosoarene followed by cyclization. On the other hand addition of this carbanion to *o*-chloronitrobenzene proceeds in position *para* followed by conversion of the σ^H adducts into nitrosoarenes than can be isolated in form of cyano methylene quinonoxime [4c].

Scheme 4. Early examples of reactions proceeding via σ^H adduct.



Since addition at position occupied by chlorine is an irreversible process, formation of the benzisoxazole and quinonoxime can proceed only when rates of the addition at positions occupied by hydrogen is higher than rate of the formation of the σ^{Cl} adducts. On the basis of this observation we put forward a hypothesis that addition of nucleophiles to halonitro-benzenes as a rule proceeds faster at positions occupied by hydrogen than halogens, as shown in scheme 5.

Scheme 5. Relation of the rates of nucleophilic addition to *p*-halonitrobenzenes.



This relation of rates suggest that it should be possible to design processes of fast further conversion of the initially formed σ^H adducts into products of nucleophilic aromatic substitution of hydrogen S_NArH. Indeed a few ways of fast conversion of σ^H adducts were found, hence new possibilities of organic synthesis opened [6, 7]. Moreover these results indicated that generally accepted mechanism

of S_NAr (of halogens) should be corrected namely should include fast and reversible formation of σ^H adducts.

The main goal of this paper is to provide proofs that generally accepted mechanism of S_NAr (of halogens) needs substantial corrections, namely that key step of the reaction, addition of nucleophiles at positions occupied by halogens is a slow process, preceeded by fast and reversible addition at positions occupied by hydrogen to form σ^H adducts. The σ^H adducts, as a rule are short lived species and cannot be observed, but their formation is evidenced via fast conversion into products of nucleophilic substitution of hydrogen S_NArH. In the following part the main variants of S_NArH in *para*- and *ortho*-halonitrobenzenes are described and exemplified hence fast formation of the σ^H adducts is confirmed. There are three major ways of conversion of the σ^H adducts into products of nucleophilic substitution of hydrogen.

a) oxidation of the σ^H adducts by external oxidants – oxidative nucleophilic substitution of hydrogen, ONSH,
b) base induced β-elimination of HL from the σ^H adducts of nucleophiles which contain a nucleofugal group L at the nucleophilic center – vicarious nucleophilic substitution, VNS,
c) conversion of the σ^H adducts into substituted nitrosoarenes that proceeds according to intramolecular redox stechiometry.

Since hydride anion is unable to spontaneously depart from the σ^H adducts the obvious and natural direct way of conversion them into products of substitution of hydrogen is removal of the hydride anions by external oxidants.

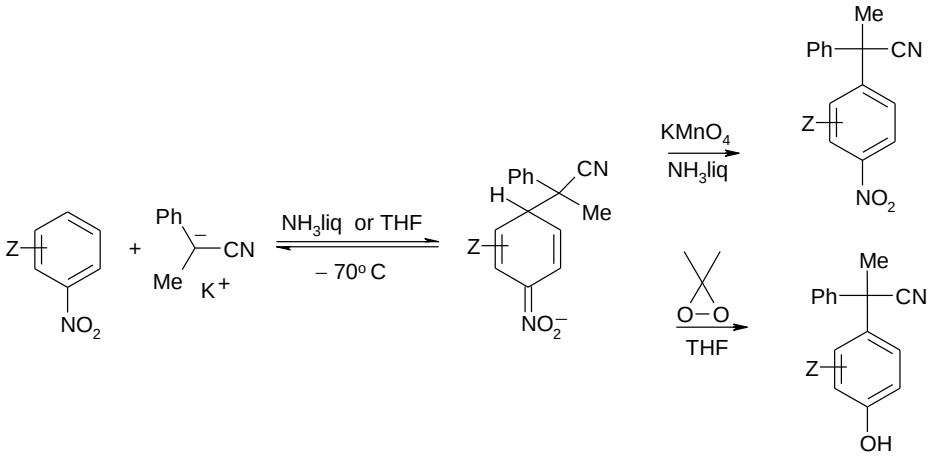
However formation of the σ^H adducts is a reversible process and nucleophiles are, as a rule, sensitive to oxidation so this process is limited to a few general cases: the addition equilibrium is shifted towards the σ^H adducts, oxidation of the σ^H adducts proceeds faster than nucleophiles (or nucleophiles are not oxidized by oxidants used) and the addition is an irreversible process. The most common oxidants used for oxidation of the σ^H adducts are: potassium permanganate [8], dichloro-dicyanoquinone, DDQ [9], and atmospheric oxygen [10]. These oxidants convert the σ^H adducts in products of substitution of hydrogen by nucleophiles in nitroaromatic rings, oxidative nucleophilic substitution, ONSH. On the other hand oxidation of some σ^H adducts by dimethyldioxirane, DMD, gives products of replacement of hydrogen by nucleophiles and the nitro group by hydroxy group [11].

Oxidation of the σ^H adducts by $KMnO_4$ and DDQ probably proceeds as a direct abstraction of the hydride anions, oxidation by oxygen is more complicated and appears to embrace single electron transfer, SET from dianions of the adducts. On the other hand DMD directs its attack on the negatively charged nitro group of the adducts.

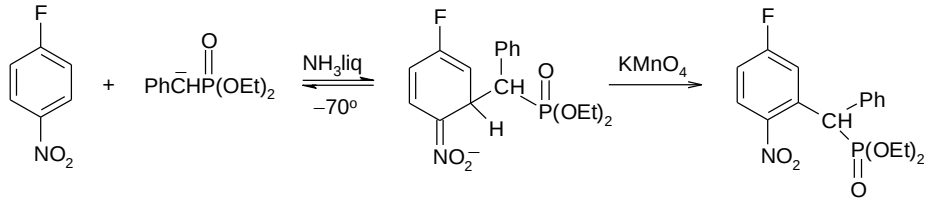
Addition equilibrium of nucleophiles to nitroarenes is shifted towards σ^H adducts provided nucleophiles are highly active and the reactions are carried out at low temperature.

Particularly numerous are examples of ONSH with highly nucleophilic methinic carbanions carried out with strong external oxidants in liquid ammonia at low temperatures.

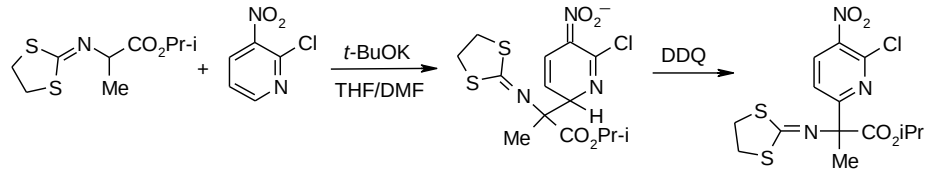
Scheme 6. ONSH by methinic carbanions and various oxidants [8, 11].



Scheme 7. ONSH by methylenic carbanions in *p*-fluoronitrobenzene proceeds faster than S_NAr [9a].



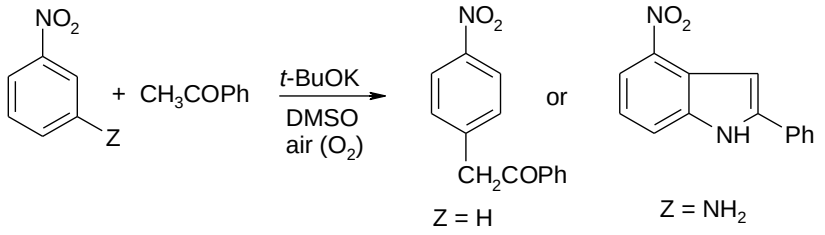
Scheme 8. Nitroarylation of protected alanine via ONSH [9b].



Oxidation of σ^H adducts by oxygen proceeds efficiently when they are formed by addition of methylenic carbanions. It appears that such σ^H adducts are oxidized by oxygen upon deprotonation thus in form of dianions, hence excess of base should be used in these processes [10]. Oxygen is rather mild oxidant, so for ONSH by methylenic carbanions and oxygen full conversion of the carbanions into σ^H adducts is not necessary. For instance enolate anions, generated by deprotonation ketones by potassium *t*-butoxide add to nitroarenes and the produced σ^H adducts are oxidized by atmospheric oxygen to give nitroarylated ketones [10c]. The enolate anions are moderately active nucleophiles and the reaction proceeds at room temperature thus addition equilibrium is not shifted towards adducts. Particularly valuable variant of this reaction is synthesis of nitroindoles via direct reaction of *m*-nitroanilines with

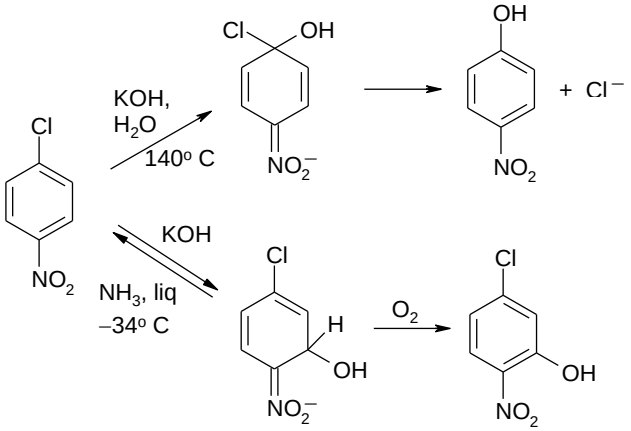
ketones in the presence of *t*-BuOK in DMSO. The reaction proceeds via ONSH in vicinity of the amino group followed by the Bayer type condensation [10b].

Scheme 9. σ^H-Adducts of ketone enolates can be oxidized by oxygen [10b, c].



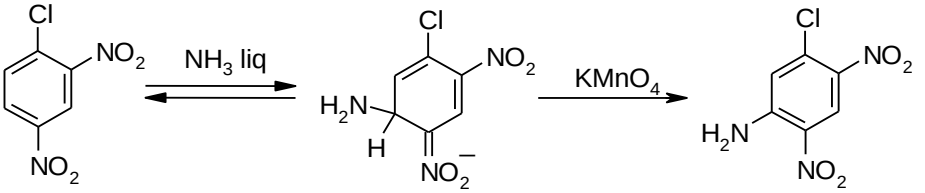
Nucleophiles resistant towards oxidation are exemplified by hydroxide anions and ammonia. In majority of text-books substitution of chlorine in *p*-chloronitrobenzene in the reaction with potassium hydroxide is presented as a typical example of nucleophilic aromatic substitution, S_NAr. This reaction proceeds at elevated temperature whereas at -35^o C in liquid ammonia in the presence of oxygen reaction of nitrobenzene with KOH proceeds exclusively as ONSH [12].

Scheme 10. Reaction of OH^- anions with *p*-chloronitrobenzene: fast ONSH, slow S_NAr [17].



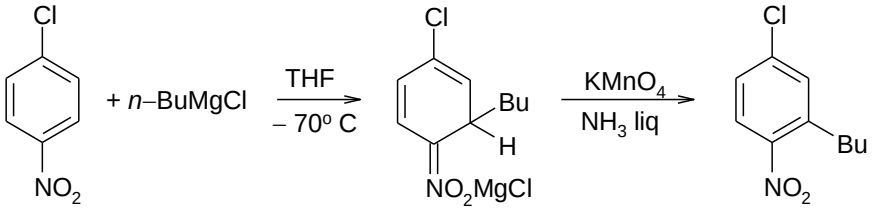
Liquid ammonia is a versatile solvent and moderately active nucleophile, resistant to oxidation able to form stable solutions of potassium permanganate. Introduction of highly electron-deficient arenes e.g. 2,4-dinitrochlorobenzene into such solutions results in fast formation of the σ^H adducts of ammonia that are subsequently oxidized to form product of ONSH 5-chloro-2,4-dinitroaniline. The oxidative nucleophilic substitution of hydrogen with ammonia even in such active chloro-dinitroarene proceeds faster than S_NAr of chlorine [13]. A solution of $KMnO_4$ in liquid ammonia is an efficient system for amination of a variety of electron deficient azines, so called oxidative Chichibabin reactions [14].

Scheme 11. Oxidative amination of 2,4-dinitrochlorobenzene proceeds faster than S_NAr [13].



Addition of primary alkylmagnesium halides tohalonitroarenes proceeds selectively at positions occupied by hydrogen to form σ^H adducts. The addition is fast and irreversible process thus subsequent treatment of these adducts with a strong oxidant resulted in formation of products of ONSH - alkylated nitroarenes [15]. The most efficient oxidant for introduction of primary alkyl groups into nitroaromatic ring is a solution of permanganate in liquid ammonia [16].

Scheme 12. Oxidative nucleophilic alkylation of nitroarenes.

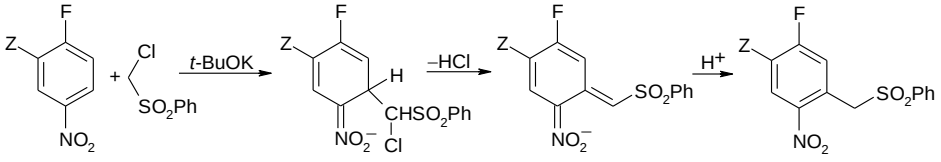


Due to irreversibly of the addition of the Grignard reagents to nitroarenes S_NAr of halogen in *ortho*- and *para*-halonitrobenzenes is not observed.

Removal of hydride anions from the σ^H adducts by external agents – oxidants is intuitively obvious process however somewhat limited. Looking for more general way of further conversion of the σ^H adducts we have found that σ^H adducts of α-halocarbanions to nitroarenes undergo rapid base induced β-elimination of hydrogen halide on the expenses of the ring hydrogen to form products of nucleophilic substitution of hydrogen [5, 17]. We propose the name vicarious nucleophilic substitution VNS, because halogen anions depart from the σ^H adducts instead of hydride anions so they act as vicarious leaving groups.

The most important feature of VNS is that in the reaction of α-halocarbanions with *ortho*- and *para*- halonitroarenes VNS of hydrogen is, as a rule, the only process, much faster than S_NAr of the ring halogens [5, 17]. For instance, carbanion of chloromethyl phenyl sulfone reacts with *p*-fluoronitrobenzene and even 2,4-dinitrofluorobenzene (the Sanger reagent) exclusively via VNS pathway.

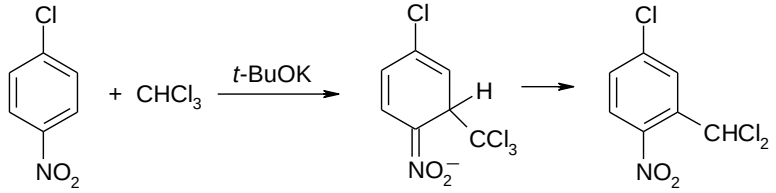
Scheme 13. VNS with α-chlorocarbanion proceeds via addition – base induced β-elimination faster than S_NAr of fluorine [17b, c].



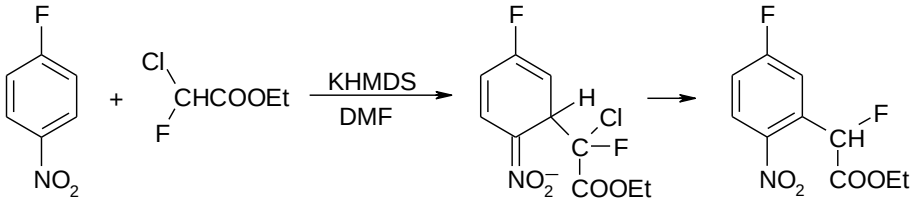
VNS is a general reaction in respect to nitroarenes and α-halocarbanions. Carbanions generated from α-haloalkyl aryl sulfones esters of α-haloacids, α-halonitriles, α-haloketones and even haloforms react with a variety of nitroarenes according to the addition-β-elimination pathway to give products of replacement of hydrogen with α-functionalized carbon substituents [5, 6, 17, 18].

α-Halocarbanions are usually unstable entities hence in some cases VNS proceeds more efficiently with carbanions that contain RO or RS as nucleofugal groups able to undergo base induced β-elimination. Versatility of VNS in respect to carbanions and nitroarenes is illustrated in schemes 11-14 [5, 17, 18].

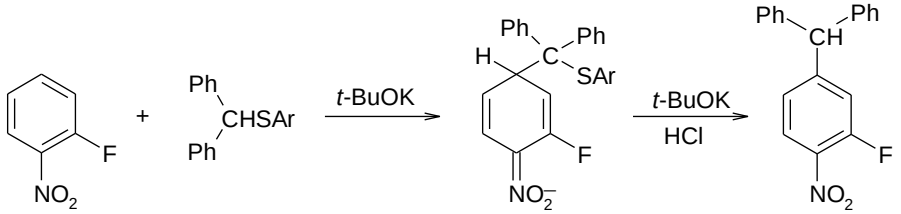
Scheme 14. Nucleophilic dichloromethylation of nitroarenes [18a].



Scheme 15. Synthesis of ethyl α-nitroaryl-α-fluoroacetate via VNS [18b].

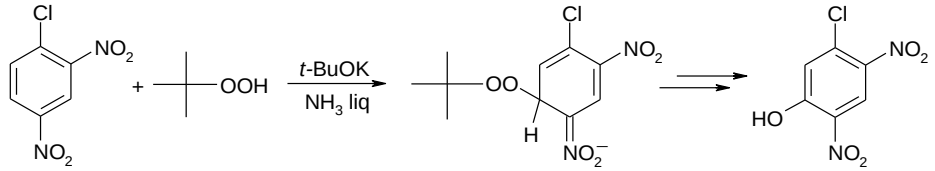


Scheme 16. VNS with sulfides proceeds via β-elimination of thiophenol [18c].



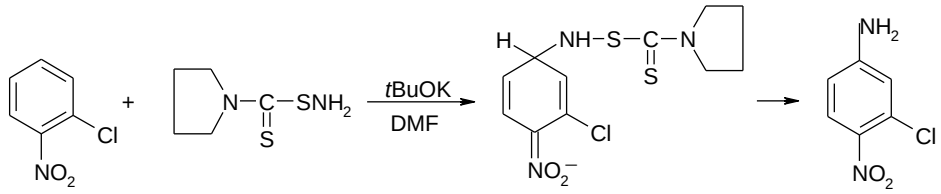
VNS proceeds also with *O*- and *N*-nucleophiles. For instance, *t*-butyl hydroperoxide reacts with 2,4-dinitrochlorobenzene in the presence of *t*-BuOK to form 2,4-dinitro-5-chlorophenol. The reaction proceeds via fast addition at position occupied by hydrogen followed by base induced β-elimination of *t*-butanol [19].

Scheme 17. VNS hydroxylation of 2,4-dinitrochlorobenzene is much faster than S_NAr.



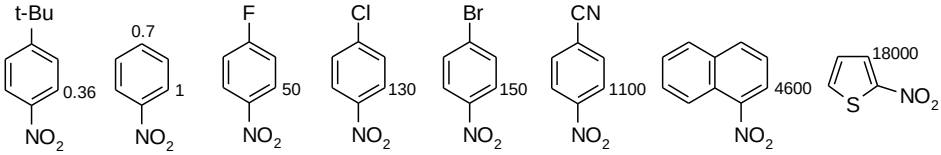
Similarly VNS amination of nitroarenes proceeds with a variety of aminating agents [20].

Scheme 18. Amination of *o*-chloronitrobenzene with sulfenamide.



Besides of great value of VNS for organic synthesis this reaction provides unambiguous proof of the corrected, general mechanistic picture of nucleophilic aromatic substitution. Substitution of halogens in ortho- and para-halonitrobenzenes is preceeded by fast and reversible addition at positions occupied by hydrogen. VNS was also used as a tool for determination of effects of substituents and structural features on electrophilic activity of nitroarenes. Electrophilic activities of nitroarenes can be defined as rate constants of the addition of a standard nucleophile under standard conditions. Effects of substituents on rates of S_NAr in halonitroarenes was thoroughly studied [2], however the results, although useful for organic synthesis, cannot be considered as a measure of electrophilic activity of nitroarenes for two reasons: the rates of S_NAr depend on the nature of leaving groups e.g. fluorine vs, chlorine and particularly, because it is a secondary process, preceded by reversible formation of the σ^H adducts. Direct measurements of the absolute rate constants of the formation of the σ^H adducts is a difficult task because addition is a fast and reversible process thus we have determined relative rate constants of the addition using competitive experiments in which two nitroarenes competed for VNS with carbanion of chloromethyl phenyl sulfone as the standard nucleophile, under conditions that assure faster β-elimination of HCl than dissociation of the σ^H adducts. In these experiments position *ortho* in nitrobenzene was used as the standard [21, 22]. Value of the rate constants of the nucleophilic addition of selected nitroarenes are shown in scheme.

Scheme 19. Relative rate constants of the nucleophilic addition as measure of electrophilicity of nitroarenes [21, 22].



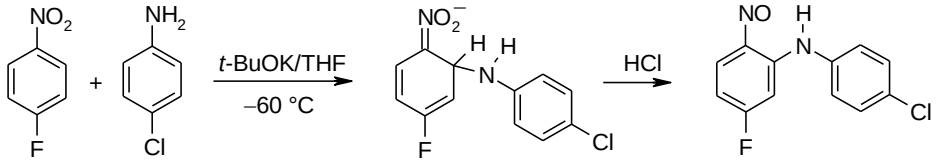
σ^H-Adducts of some nucleophiles under proper conditions can be converted into nitrosoarenes according to intramolecular redox stoichiometry. This third way of conversion of the σ^H adducts proceeds in protic media, upon action of Lewis acids or silylation. The most known examples are reactions of arylacetonitriles with nitroarenes and nitroheteroarenes in alcoholic KOH. Thus the reaction of phenylacetonitrile with *o*- and *p*-chloronitrobenzene in alcoholic solutions of KOH proceeds via initial addition of the carbanions at positions *p*- and *o*- respectively followed by conversion of the σ^H adducts into nitroso arenes that can be isolated in

tautomeric form of methylenequinones or react further to produce benzisoxazoles scheme 3 [4b, c].

Addition of a methinic carbanion of 2-phenylpropionitrile to nitroarenes proceeds at position *para* to form σ^H adducts. Silylation of these σ^H adduct, followed by elimination of silanol produces substituted nitrosobenzene that can be isolated in high yield [8].

Particularly interesting results, that convincingly confirm faster nucleophilic substitution of hydrogen than halogens, even fluorine, are reactions of anilines with *p*-halonitrobenzenes in the presence of strong base at low temperature. The initially formed σ^H adducts upon protonation form *o*-nitrosodiarylamines [23].

Scheme 20. Substitution of hydrogen by anilide anion in *p*-fluoronitrobenzene proceeds faster than S_NAr [23].

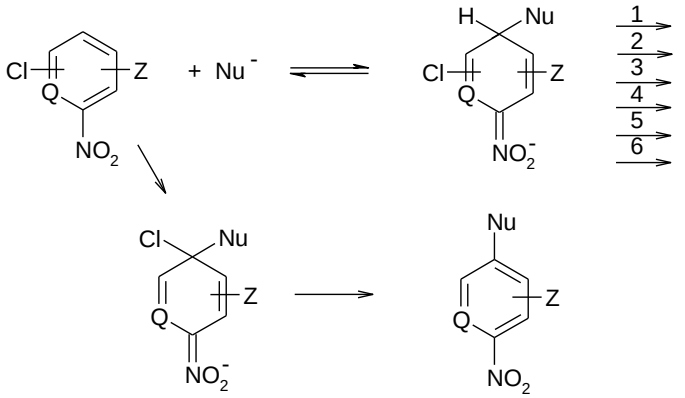


Under such conditions well known replacement of halogens by anilines proceeds much slower. It should be stressed that in text-books and monographs only S_NAr of halogen in these nitroarenes by anilines is mentioned.

Numerous examples of S_NArH in nitroarenes and particularly halonitroarenes have shown that these reactions are general and versatile tool in organic synthesis. They also provide unambiguous proof that addition of nucleophiles to halonitroarenes proceeds faster at positions occupied by hydrogen than halogen.

Besides of these three main pathways of conversion of the anionic σ^H adducts into products of nucleophilic substitution of hydrogen S_NArH, there are a few less known and general such as cine-substitution, tele-substitution etc. Thus general picture of nucleophilic aromatic substitution can be presented as in scheme 21.

Scheme 21. General picture of nucleophilic aromatic substitution.



The initial reaction between nucleophiles and halonitroarenes (carbo- and heterocycloc) is addition at positions occupied by hydrogen to form σ^H adducts. The rapidly formed σ^H adducts can be converted into products of S_NAr on many ways,

three of them are discussed in the paper. Only when due to structure of the nucleophiles and nitroarenes and conditions fast further concersion of the σ^H adducts does not proceed they dissociate and slower addition at positions occupied by haloogen and S_NAr of halogens can proceed. It is therefore evident that S_NAr of halogens is preceded by reversible formation of the σ^H adducts and generally accepted mechanism of S_NAr should be corrected.

It is really surprising that in numerous kinetic studies of mechanism of nucleophilic aromatic substitution this situation was not discovered.

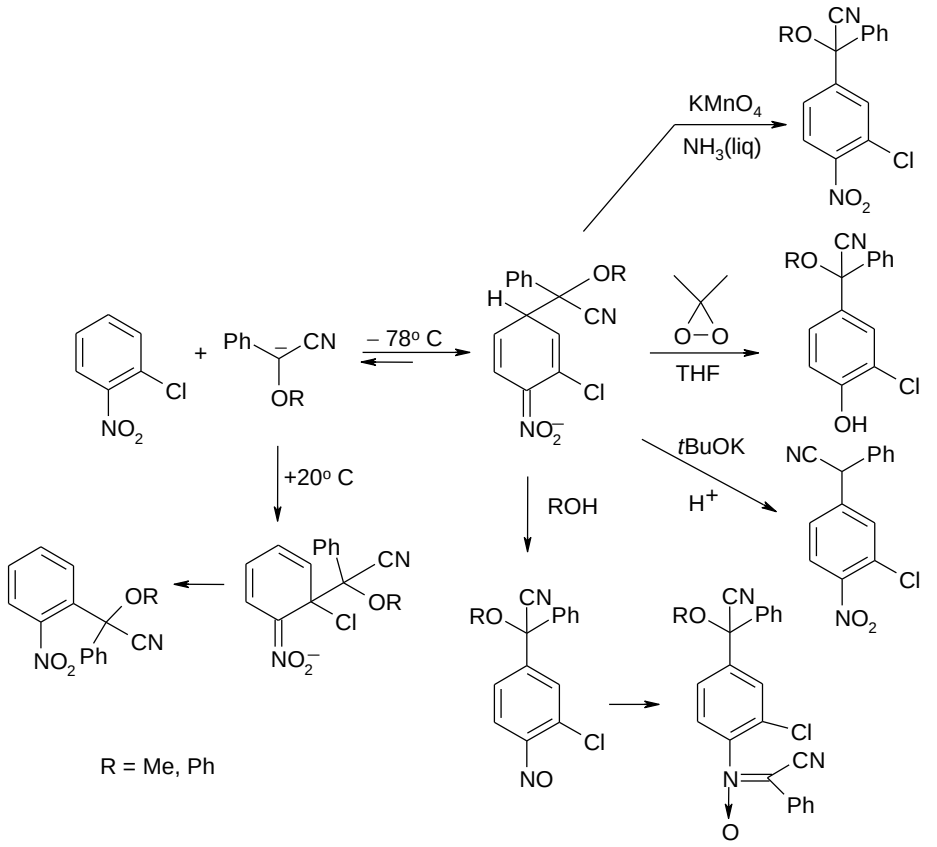
Moreover we have recently calculated energy profiles of the nucleophilic addition of carbanion of chloromethyl phenyl sulfone to nitrobenzene, *p*-chloro- and *p*-fluoronitrobenzenes and have found that calculated rates of nucleophilic addition at positions *ortho* of these *p*-halonitrobenzenes occupied by hydrogen are higher than at positions *para*, in good correlation with experimental results [24]. Recently published calculations of the relation of S_NAr and VNS reactions are also in full agreement with experimental results [25]. It should be mentioned than there are many reports of *ab initio* calculations of reactions between nucleophiles and halonitroarenes. It is really surprising that in these calculations only addition at positions occupied by halogens were considered. The additions at positions occupied by hydrogen and formation of the σ^H adducts, although proceeds via transition states of lower free energy was ignored [26]. Thus we can formulate a general mechanism of nucleophilic substitution in nitroarenes and other electron-deficient arenes.

The initial step is fast and reversible addition of nucleophiles at positions occupied by hydrogen. The produced σ^H adducts can be converted into products of S_NArH or dissociate, thus slower addition at positions occupied by halogens and S_NAr can proceed.

It should be stressed that thanks to proper understanding of the reaction pathways between nitroarenes and nucleophiles scope of nucleophilic aromatic substitution is expanded and embraces also electron-deficient arenes that do not contain leaving groups [27].

According to the general mechanism nucleophiles can react with halonitroarenes in a few ways depending on their nature and conditions, hence there are cases that the same pair of reactants can react in two or more ways. For instance, carbanions of α-methoxy and α-phenoxyphenylacetonitriles can react with *o*-chloronitrobenzene in **five** different ways to give five products with high yields and selectivity (sic!) [28].

Scheme 22. Five different reactions of carbanions of α-alkoxyacetonitriles with *o*-chloronitrobenzene.

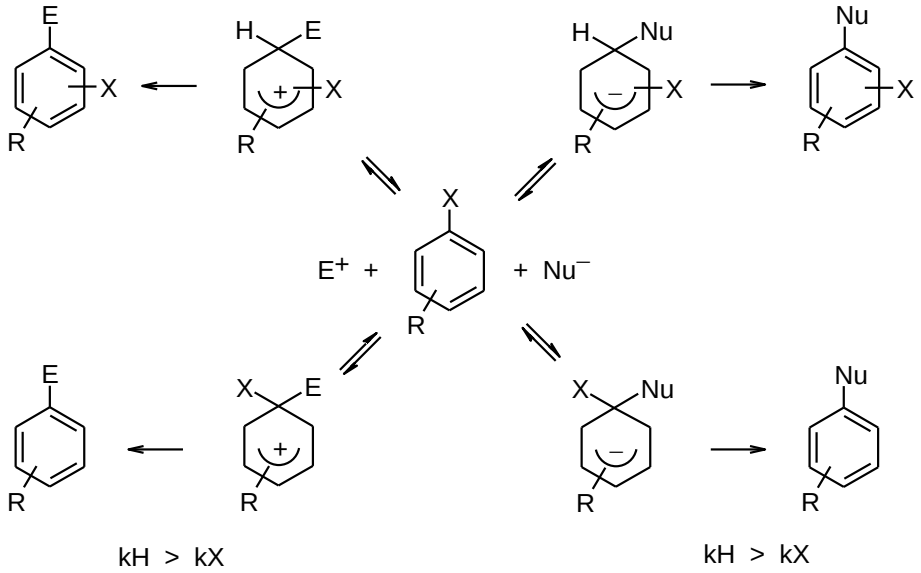


Full general corrected mechanism of nucleophilic aromatic substitution in electron deficient arenes is presented in recent short review [29].

The general mechanism of nucleophilic aromatic substitution is somewhat similar to mechanism of electrophilic substitution. Indeed addition of electrophilic agents to aromatic rings proceeds faster at positions occupied by hydrogen than those occupied by other substituents, nevertheless the latter addition mode often takes place. Initially formed cationic σ^H adducts undergo fast conversion into products of substitution via spontaneous departure of proton. This is the *normal* substitution. Cationic σ adducts of electrophiles at positions occupied by other substituents can also loose these substituents in cationic form to produce products of *ipso* substitution. Similar situation is in reactions of nucleophiles with electron-deficient arenes, particularly halonitroarenes. Fast addition proceeds at positions occupied by hydrogen to form σ^H adducts. Contrary to the cationic σ^H adducts from which spontaneous departure of proton proceeds rapidly, spontaneous departure of hydride anions from anionic σ^H adducts does not proceed, so a few indirect ways to remove the hydride anion were designed. Thus, provided such ways are available, substitution of hydrogen is the fast primary reaction hence it should be considered as *normal* process. On the other hand slower addition of nucleophiles at positions

occupied by halogens X is followed by fast departure of X^- from the σ^H adducts. Thus substitution of halogen is slower, secondary process – *ipso* substitution.

Scheme 23. Electrophilic and nucleophilic aromatic substitution – *normal* substitution of hydrogen and *ipso* – substitution of a substituent.

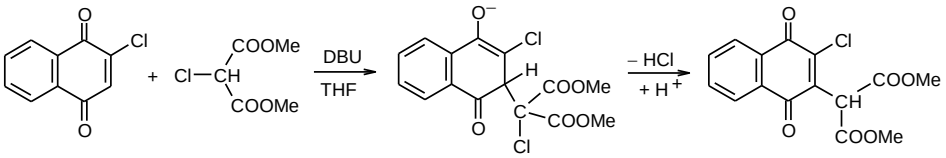


We certainly hope that the corrected general mechanism of nucleophilic aromatic substitution will find way to text-books and academic classrooms.

Observation that addition of nucleophiles to halonitroarenes proceeds, as a rule, faster at positions occupied by hydrogen leads to paradoxical conclusion that halogens in nitroaromatic rings protects positions they occupy against nucleophilic addition. This conclusion has found some applications e.g. in synthesis of indoles. Presence of Cl or Br in nitroaromatic rings activates the ring for VNS cyanomethylation and simultaneously protects positions they occupy against substitution, so synthesis of desired *o*-cyanomethyl nitroarenes proceeds in high yields and selectivity. Subsequent hydrogenation results in formation of indoles and can simultaneously remove of the protecting/activating halogen substituents [30].

Interestingly, similar relations the rates of the nucleophilic addition at positions occupied by hydrogen and chlorine were found in electron-deficient alkenes. For instance, ONSH and VNS in 2-chloronaphthoquinone with carbanions of dimethyl malonate and dimethyl chloromalonate proceeds faster than nucleophilic vinylic substitution of the chlorine [31].

Scheme 24. Vicarious nucleophilic substitution of hydrogen in chloronaphthoquione [31].



Thorough kinetic measurements revealed that amines add to 2,5-dichlorobenzoquinone faster at positions occupied by hydrogen than chlorine [32].

Similarly addition of carbanions to esters of chlorofumaric and chloromaleic acids proceeds faster at positions occupied by hydrogen [33]. These results raise the question "does chlorine at electron-deficient sp^2 carbon indeed hinder (decelerate) nucleophilic addition?" Observations that in *o*- and *p*-chloronitroarenes, chloroquinones and chloromaleates addition at positions occupied by hydrogen proceeds faster than at those occupied halogens are insufficient to support this hypothesis, because halogens in the rings or in vicinal positions activate positions occupied by hydrogen towards nucleophilic addition, whereas hydrogen does not exert activating effects. To find unbiased answer of this question one should compare rates of the nucleophilic addition at position occupied by hydrogen and chlorine that are not affected by additional effects. In our opinion comparison of the rates of nucleophilic addition at positions *para* of nitrobenzene and *p*-chloronitrobenzene meet this criterion. Relation of rates of the addition at positions *para* of nitrobenzene and *p*-chloronitrobenzene of the methinic carbanion of 2-phenylpropionitrile (for steric reason it adds selectively at positions *para*) was determined using competitive experiments (ONSH versus S_NAr). It was found that the addition to nitrobenzene proceeds faster $k_H/k_{Cl} \approx 6$, thus chlorine indeed protects position it occupies against nucleophilic addition.

Conclusions

General, corrected mechanism of nucleophilic aromatic substitution in nitroarenes was formulated. According to this mechanism reactions between nucleophiles and nitroarenes are not limited to replacement of leaving groups e.g. halogens, but can proceed as nucleophilic replacement of hydrogen. Moreover it was documented that nucleophilic substitution of hydrogen proceeds faster than substitution of halogens thus one can consider that nucleophilic substitution of hydrogen in nitroarenes is the fast, primary "*normal*" reaction whereas conventional substitution of halogen secondary "*ipso*" substitution. In this respect there is a peculiar analogy between electrophilic and nucleophilic aromatic substitution.

Reactions of nucleophiles with nitroarenes form therefore very rich chapter of aromatic chemistry. It was shown that, against to the common believe, chlorine at electron-deficient sp^2 carbon centers declerates nucleophilic addition at this positions.

Acknowledgments

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ՆՈՒԿԼԵՈՖԻԼ ՏԵՂԱԿԱԼՈՒՄ ՆԻՏՐՈԱՐԵՆՆԵՐՈՒՄ. ԸՆԴՀԱՆՈՒՐ ՄԵԽԱՆԻԶՄ

ՄԻՉԻՍԼԱՎ ՄԱԿՈՇԱ

Փորձարարական հետազոտությունները և տեսական հաշվարկները ցույց են տվել, որ ընդունված նուկլեոֆիլ արոմատիկ տեղակալման մեխանիզմը ճշգրտման կարիք ունի: Հոդվածում սահմանված է նիտրոարեններում նուկլեոֆիլ արոմատիկ տեղակալման ճշգրտված ընդհանուր մեխանիզմը: Համաձայն ռեակցիայի, այդ մեխանիզմի նուկլեոֆիլների և նիտրոարենների միջև ընթացող փոխազդեցությունները սկսվում են նուկլեո-

ֆիլների առաջնահերթ արագ ընթացող միացմամբ այն դիրքերում, որոնք զբաղեցված են ջրածնի ատոմներով: Առաջացած σ^H-ադուկտները կարող են փոխարկվել ջրածնի փոխանակման արգասիքների մի քանի ճանապարհներով: Այն դեպքերում, երբ նման փոխարկումները անհնարին են, σ^H-ադուկտները դիսոցվում են և σ^X-ադուկտների դանդաղ առաջացումը բերում է հալոգենների տեղակալմանը SNAr մեխանիզմով: Բացի այդ, արձանագրվել է, որ ջրածնի նուկլեոֆիլ տեղակալումը ընթանում է ավելի արագ, քան հալոգենների տեղակալումը: Կարելի է համարել, որ ջրածնի նուկլեոֆիլ տեղակալումը նիտրոարեններում արագ ընթացող առաջնային նորմալ ռեակցիա է, մինչ դեռ հալոգենների սովորական «իփսո»-տեղակալումը՝ երկրորդական է:

Այսպիսով, բացահայտվել են մեխանիստիկական նմանություններ էլեկտրոֆիլ և նուկլեոֆիլ արոմատիկ տեղակալման ռեակցիաների միջև:

НУКЛЕОФИЛЬНОЕ ЗАМЕЩЕНИЕ В НИТРОАРЕНАХ. ОБЩИЙ МЕХАНИЗМ

МИЧИСЛАВ МАКОША

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Экспериментальные исследования и теоретические расчеты показали, что общепринятый механизм нуклеофильного ароматического замещения нуждается в корректировке. В статье сформулирован общий скорректированный механизм нуклеофильного замещения в нитроаренах. В соответствии с этим механизмом реакции между нуклеофилами и нитроаренами протекают путем первоначального быстрого присоединения нуклеофилов в позициях, занятых водородом, а σ^H-аддукты могут превратиться в продукты нуклеофильного замещения водорода несколькими путями. Когда эти способы недоступны, аддукты σ^H диссоциируют, и медленное образование аддуктов σ^X ведет к конвенциональному замещению галогенов по механизму S_NAr. Кроме того, зарегистрировано, что нуклеофильное замещение водорода протекает быстрее, чем замещение галогенов, поэтому можно считать, что нуклеофильное замещение водорода в нитроаренах является быстрой первичной «нормальной» реакцией, тогда как обычное замещение галогенов («*ipso*»-замещение) — вторично.

Таким образом, выявлены механистические аналогии между реакциями электрофильного и нуклеофильного ароматического замещения.

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