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Nucleophilic Substitution of Hydrogen in Aromatic Systems

O.N.Chupakhin and I.Ya.Postovskii

The literature data on the substitution of hydrogen under the influence of nucleophilic agents in aromatic and heteroaromatic systems and in quinones are reviewed. The absence of anionic stabilisation of the hydrogen substituted with its pair of binding electrons is responsible for the specific nature of the reactions under consideration, which is different from that of the nucleophilic substitution of other species and from that of the electrophilic substitution of hydrogen, necessitating the use of an oxidant in most instances.
The bibliography includes 227 references.

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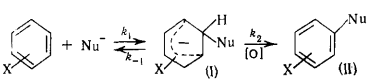
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I. INTRODUCTION

In one form or another the problems of the nucleophilic substitution of hydrogen have been reflected in the literature on nucleophilic aromatic substitution of anionically stabilised groups[1,2] and hydride shifts[3-5], in reviews dealing with aromatic and heteroatomic cations[6-9]. There exists a monograph[10] as well as a series of review articles on the nucleophilic aromatic[11-17] and heteroaromatic[18-21] substitution of anionic bearing groups. Concepts concerning the structures of the intermediate σ complexes[15-17], the involvement of π complexes[21], and the role of one-electron steps in such reactions[22-27] have been developed with the aid of chemical and physical methods. Extensive data have been accumulated, including quantitative measurements of kinetic and thermodynamic parameters, correlations between the rate constants and the influence of the activating or eliminated group, and solvation, catalytic, and isotopic effects. However, these results can by no means always be used to interpret the nucleophilic substitution of aromatically combined hydrogen, because such reactions are different from the electrophilic substitution of hydrogen as well as from the nucleophilic substitution of anionically stabilised species†.

The hydride ion is not involved in the formation of hydrogen bonds, is not solvated, and shows no tendency whatever towards any anionic stabilisation. Anionic or anionoid σ complexes, containing hydrogen at the germinal site, are as a rule more stable than the corresponding structures with a group capable of being stabilised in the form of an anion. For this reason it has come to be accepted[28] that the removal of the hydride ion involves considerable difficulties and requires several conditions. This is probably the case when the hydride ion is removed as such without using an oxidant. A dehydrogenating oxidising agent may be deliberately introduced into the reaction mixture or, for a favourable ratio of the oxidation-reduction potentials of the σ complexes and the starting materials, the substrate itself can serve as the oxidant. In the present review it is shown that the use of an oxidant can lead to low activation energies and to the possibility of carrying out the process under mild conditions.

S_NH reactions probably proceed via a two-stage mechanism in the vast majority of cases with formation of an intermediate. The mechanism shows that, depending on the ratio of the rate constants, the interaction can proceed in different ways:



The constant k_2 depends on the ratio of the oxidation-reduction potentials of the intermediate (I) and the oxidant. When $k_1 \gg k_{-1}$ and k_2 is large, the process is completed with formation of the product (II). When $k_1 \gg k_{-1}$ and k_2 is small, the reaction may stop at the stage of the product (I); when $k_1 \ll k_{-1}$ and k_2 is large, the σ complex (I) is present at a vanishingly low quasistationary concentration and the process can develop only in the presence of an appropriately selected oxidant. In the absence of an oxidant or when its oxidising capacity is inadequate, other processes may be observed—the substitution of other groups when these are present or the dimerisation of the substrate.

The fact that in many instances σ complexes can be isolated in a pure state in S_NH reactions is in all probability responsible for the lack of terminological consistency in the description of such reactions: they are sometimes regarded as addition reactions even in those instances where the intermediate has not been isolated and has not been detected by other methods[29,30]. According to Ingold, the term "bimolecular nucleophilic substitution" can be applied to all such reactions, despite the existence of intermediate addition products[28].

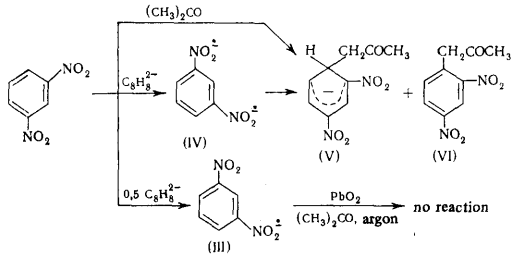
In the present review an attempt has been made to treat from general standpoints the S_NH reactions in various aromatic systems, both activated and not activated by nitro- and aza-groups, and in quinones. Such parallels can be usefully drawn in the treatment of nucleophilic substitution of hydrogen and related phenomena. Particular attention has been devoted to the elucidation of the role of the oxidant in these processes and also to the discussion of the quantitative data characterising the reactions of the S_NH type in the series of aromatic compounds.

†We suggest that nucleophilic substitution of hydrogen be designated by the symbol S_NH, emphasising the specific nature of such reactions.

II. S_NH REACTIONS OF NITRO-COMPOUNDS

The reactions of aromatic compounds activated by a nitro-group with different nucleophiles have all the features of the interaction between an electron donor and acceptor (oxidant and reductant) and depend on the number and positions of the nitro-groups in the substrate, the nature of the nucleophile, and the involvement of the oxidant. The interaction can result in the respective formation of donor–acceptor complexes, anionic σ complexes (Meisenheimer complexes), or products of the nucleophilic substitution of hydrogen. An increasing amount of data is being published, showing that the products obtained as a result of complete electron transfer can play a significant role also in S_NH reactions [23].

As an example, one may quote a study of the reaction of *m*-dinitrobenzene with the carbanion formed from acetone in an alkaline medium (Yanovskii's reaction). Gol'teuzen et al. [31] resorted to the simulation of electron transfer processes using the cyclooctatetraene dianion $C_8H_8^{2-}$ instead of the acetone carbanion:



By adding specific amounts of this dianion, it was possible to control separately the formation of both the radical-anion (III) and the biradical-dianion (IV) from dinitrobenzene. It was established that the radical-anion (III) is not involved in the reaction with the acetone anion, while the dianion (IV) yields the product of Yanovskii's reaction—the σ complex (V), together with the product (VI) of the nucleophilic substitution of hydrogen. This provides a sound basis for the assumption that the biradical-dianion (IV) is located on the reaction coordinate in the formation of the σ complex (V). Other examples indicating that the involvement of electron transfer products in reactions of the S_NH type is quite likely are also known [27,32].

Whether or not the reaction stops at the Meisenheimer addition stage depends to a considerable degree on how effectively the negative charge is delocalised over the electron-accepting groups. The differences between the delocalisation energies on passing from aromatic nitro-compounds to anionic σ complexes (−8 kcal mole^{-1} for nitrobenzene, 1 kcal mole^{-1} for 2,4-dinitrobenzene, and 10 kcal mole^{-1} for 1,3,5-trinitrobenzene) show how strong is the influence of the successive introduction of nitro-groups in the *meta*-positions [33].

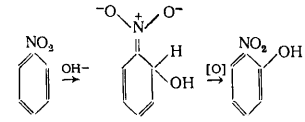
Numerous stable Meisenheimer complexes containing a hydrogen atom at the geminal site have been described[15]. Their oxidation makes it possible to obtain substituted aromatic polynitro-compounds, although in the literature there are only isolated reports on this problem [34–36]. Studies indicating a systematic approach to the investigation of the oxidation of hydride-active hydrogen in anionic σ complexes were only published as late as 1973–1974. [37,38] It has been shown [37] that both two-electron (the tropylium cation, lead tetraacetate, hypohalogenites, and halogens) and one-electron [Fenton's reagent, silver nitrate, and iron(III) chloride] oxidants can be used for the oxidation reaction and that the rate of oxidation depends on the standard potential of the oxidant. The first quantitative data appear to have been obtained [38] (Table 1) for the oxidation potentials of the anionic σ complexes at a rotating platinum electrode. They demonstrate the necessity for the use of a strong oxidant in order to obtain substituted polynitro-compounds.

Table 1. The polarographic oxidation potentials of the σ complexes of nitro-compounds with acetone in 0.1 *N* $(C_4H_9)_4NClO_4$ as the supporting electrolyte (relative to the saturated calomel electrode).

Initial nitro-compound	$E_{1/2}$, V	*E*, mV	No.of electrons	Reversibility
1,3-Dinitrobenzene	0.330	85	2	Irreversible
2,4-Dinitroanisole	0.325	75	2	»
1,3,5-Trinitrobenzene	0.825	80	2	»

The use of optimal conditions ensures a fairly smooth course of the S_NH reactions of nitro-compounds, which makes them important on a preparative scale and in some cases on an industrial scale. Examples of such reactions are considered below.

The treatment of nitrobenzene with dry powdered alkali has been known for a long time as a method for the synthesis of *o*-nitrophenol: [39,40]

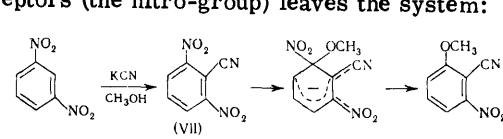


Presumably the residue eliminated here is a free hydride ion, which is accepted by the oxidant. The oxidant may be potassium nitrate or hexacyanoferrate(III). In the absence of an oxidant, nitrobenzene itself plays the role of the hydride ion acceptor, being reduced to azoxybenzene:

$$C_6H_5NO_2 \xrightarrow{H^-} C_6H_5{-}N{=}N{-}C_6H_5 \quad (O)$$

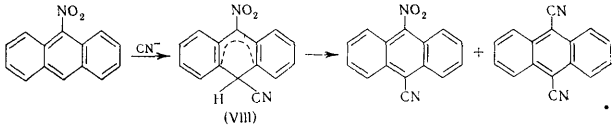
Trinitrobenzene readily exchanges one of its hydrogens for a hydroxy-group, forming picric acid when it is acted upon by an alkaline solution of potassium hexacyanoferrate(III). [41]

The cyanide ion is able to substitute hydrogen in the 2-position of *m*-dinitrobenzene [42]; the nitro-compound present in excess serves as the H^- acceptor. It is of interest that the reaction does not then stop. The dinitrobenzonitrile(VII) formed is so electrophilic that it captures an alkoxide anion, the steady-state concentration of which is undoubtedly very low. Under these conditions, one of the acceptors (the nitro-group) leaves the system:



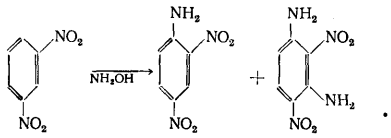
6-Nitroquinoline behaves similarly in this reaction; the heteroatom plays the role of a second nitro-group. [43] Picric acid forms a disubstitution product with KCN, the capture of hydride residues proceeding via an intramolecular mechanism and being completed by the formation of a

hydroxylamine derivative [44]. The reaction of 9-nitroanthracene with the cyanide ion in dimethylformamide leads to the formation of the Meisenheimer complex (VIII), which is then involved in oxidative substitution reactions with formation of 10-cyano-9-nitroanthracene and 9,10-dicyanoanthracene:[45]

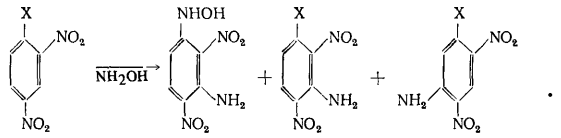


(VIII)

The reaction of dinitrobenzene with hydroxylamine in an alcoholic alkaline solution, discovered by Meisenheimer and Patzig[46], is an interesting example of the direct substitution of hydrogen by a nucleophile:

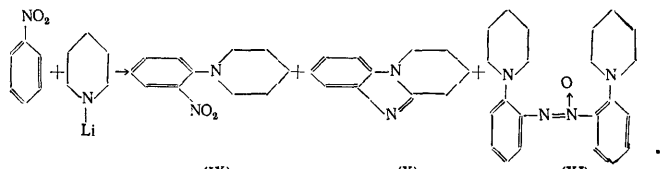


The reaction proceeds under mild conditions and with an almost quantitative yield, which makes it preparatively important. It was established that the introduction of a methyl group lowers the reactivity of dinitrobenzene, while the introduction of a nitro-group increases it. Subsequently Gitis et al.[47] established the mechanism of this reaction; they also made a more detailed study of the influence of the ring substituent on the reactivity of *m*-dinitrobenzene and identified three types of substitution products[48]:



On reaction with hydroxylamine, 2-nitronaphthalene forms 2-nitro-1-naphthylamine, while trinitrobenzene gives rise to picramide.[46]

Alkyl and aryl derivatives of lithium and Grignard reagents reduce nitro-compounds. In contrast to this, organic amides give rise to the substitution of the hydride ion. Thus lithium piperidide reacts with nitrobenzene to form a low yield of the *ortho*-substitution product (IX) together with its ring-closure product [1,2-tetramethylenebenzimidazole (X)] and reduction product [2,2'-dipiperidinoazoxybenzene (XI)]:[49]

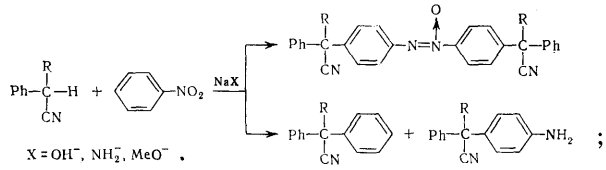


(IX) (X) (XI)

The sodium salts of amines form as a rule *para*-substitution products: on reaction with nitrobenzene, sodium piperidide yields 9-(*p*-nitrophenyl)piperidine [50], while the potassium salt of carbazole forms 9-(*p*-nitrophenyl)carbazole [51]. Sodium diphenylamide is involved in a similar reaction[52].

Contrary to expectation, on being mixed with sodamide in liquid ammonia, nitrobenzene is not involved in a Chichibabin substitution reaction, but forms a complex mixture of unidentified products[50].

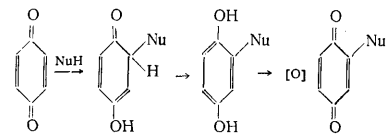
The carbanions formed from CH acids in the presence of bases give rise to Meisenheimer complexes on reaction with polynitro-compounds[15]. These are usually fairly stable products, but can be converted into substitution products by choosing an appropriate oxidant[37,38]. Comparatively recently, it proved possible to make nitrobenzene undergo such reactions[53]:



III. S_NH REACTIONS OF QUINONES

Quinones are not aromatic compounds; they can be classified as unsaturated cyclic $\alpha\beta$-diketones. However, although ketones do not in fact belong to the class of aromatic compounds, they are very close to them genetically and readily regenerate a benzenoid structure. Comparison of similar S_NH reactions of quinones and aromatic (and heteroaromatic) compounds permits a better understanding of the general nature of such processes. The reactions of quinones with nucleophiles are of interest as models of oxidation-reduction processes occurring in organisms with participation of *p*-benzoquinone and 1,4-naphthoquinone derivatives—ubiquinones and tocopherylquinones [54,55].

Quinones are involved in these processes as fairly active electrophiles—their interaction with uncharged nucleophiles involves the simultaneous nucleophilic substitution of hydrogen in the quinone and the electrophilic substitution of hydrogen in the nucleophile:

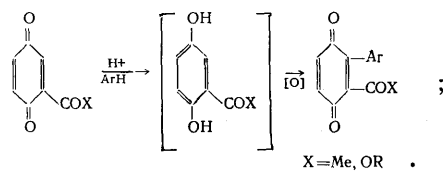


(XII)

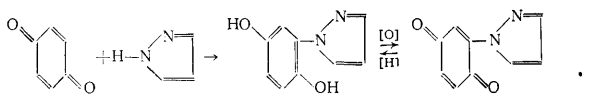
There is an initial 1,4-addition of the nucleophile to the quinone, completed by the formation of adducts having the structure of hydroquinones (XII). In order to convert them into substitution products, it is sometimes necessary to use an oxidant, although in certain instances intermediates of type (XII) have not been detected, the final substituted quinone being formed[29].

Reactions in which quinones form neither addition products nor hydrogen substitution products in the absence of an oxidant, [57] are discussed below.

It has been shown that benzoquinone and its carbonyl derivatives react under conditions of acid catalysis with nucleophiles such as dimethylaniline, phenols, or their ethers, and even alkylbenzenes.[58] With few exceptions, the reactions proceed at room temperature and are completed by the formation of arylbenzoquinones. Ag_2O is used for the oxidation of the adduct:



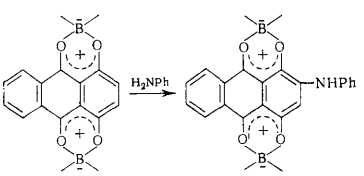
The interaction of quinones with heteroaromatic compounds having an excess of π electrons (pyrrole, furan, etc.) also leads to the formation of products of the substitution of hydrogen in quinones under oxidative conditions[59-61]. Pyrrole forms mono- and di-addition products involving the 2- and 5-positions or the 3-position, when the first two are occupied. Pyrazole reacts at the nitrogen atom and, as in the preceding case, the addition products are readily and reversibly oxidised[61]:



The interaction of benzo- and naptho-quinones with thiophen[62], furan[63,64], enol ethers[61], and CH acids[65] has also been investigated.

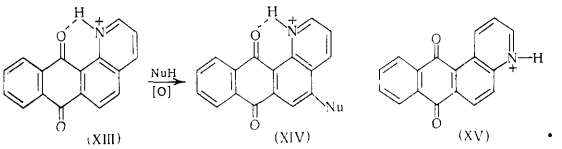
When reactions with diene-like nucleophiles (for example indole) are considered, one must bear in mind the possibility that quinones are involved not only in S_NH reactions but also in Diels–Alder addition reactions[29], which has not always been taken into account [66,67].

Direct nucleophilic attack on the quinone fragment is impossible in 9,10-anthraquinone, its activating effects being merely transmitted to the adjacent benzene ring. For this reason, anthraquinones are relatively inactive in the S_NH reactions characteristic of benzo- and naphthoquinones. For example, anthraquinone-2-sulphonic acid gives rise to alizarin only on being fused with alkali[68]. Anthraquinones containing in the *peri*-position with respect to the carbonyl group a substituent capable of combining with a proton and forming a chelate ring acquire greatly enhanced electrophilic properties and readily react with nucleophiles. Electronic interactions in chelate rings influence the distribution of electron density in the ring with the substituent, which is reflected in the localisation of the $C_{(2)}$–$C_{(3)}$ bond[69]. The influence of chelate formation on the reactivity is also manifested by the fact that 1-hydroxyanthraquinone is much more reactive in hydride-ion substitution reactions than 2-hydroxyanthraquinone. The involvement of boric acid as a catalyst in the arylamination of quinizarin[56] consists in the formation of a chelate ring, which increases sharply the reactivity of the substrate:



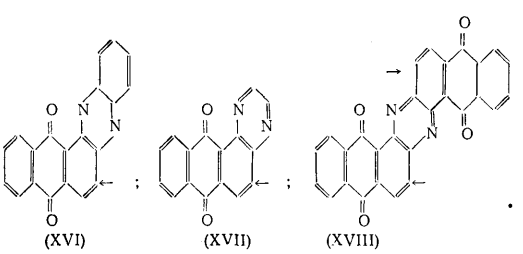
Direct amination with ammonia[70] and secondary amines[57] of 1- and 2-hydroxyanthraquinones and the substitution of hydrogen in the alkyl- and aryl-amine residues in quinizarin[71,72], 1-amino-4-hydroxyanthraquinone, and 1,4-diaminoanthraquinone[73] also belong to reactions of the type under consideration.

In a series of studies by Gorelik and coworkers, the influence of the heteroaromatic ring of the azine or azole type annelated to anthraquinone on the reactivity of the system with respect to a nucleophile was elucidated. The very important problem in the chemistry of anthraquinone discussed above, namely the increase of its electrophilic properties as a result of the involvement of the carbonyl group in chelate formation, is being solved by the synthesis of structures in which a favourable position of the protonated heterocyclic nitrogen permits the formation of a chelate ring with an intramolecular hydrogen bond. Under these conditions, two factors have a synergistic effect: the formation of the ammonium (azinium) cation and the enhancement of the electron-accepting properties of the carbonyl group. For example, the cation (XIII) reacts smoothly with thiophenoxides, sulphinic acids[74], and alkylamines[75], forming the substitution products (XIV):

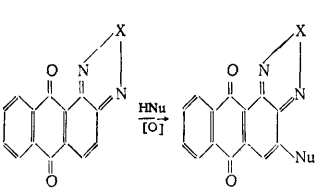


The quinone (XV) does not enter into these reactions[74], which demonstrates the validity of the conclusion[69] that chelate formation plays an important role in the transfer of the positive charge in the chain and that there is conjugation in structures of type (XIII).

The activation of the anthraquinone nucleus by the annelation of an azine has been demonstrated for naphtho[2,3-*a*]phenazine-8,13-dione (XVI) [76-78], naphtho-[2,3]quinoxaline-7,12-diones (XVII) [79], and anthraquinone-azine (XVIII) [80]‡:



Using an azole ring instead of an azine, it proved possible to carry out similar substitution reactions in an activated anthraquinone nucleus [81,87]. Anthraquinone-furazan (X = O) is the most reactive in these processes[81] and anthraquinone-triazole (X = NH) is least reactive[68], in conformity with the electronegativities of the heteroatoms:

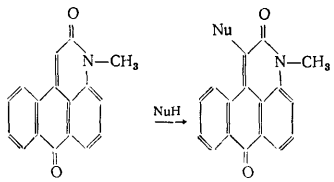


Although in the majority of cases S_NH reactions take place in the anthraquinone nucleus, nevertheless nucleophilic attack involving also the annelated fragment has been described[78], in agreement with the results of quantum-chemical calculations[88].

The substitution of hydrogen atoms in anthrapyridone has been observed on treatment with amines[89], cyanide ions, and hydroxide ions[90]. The distribution of π-electron density and other reactivity indices of anthrapyridone are different[91] from those of the anthraquinones discussed

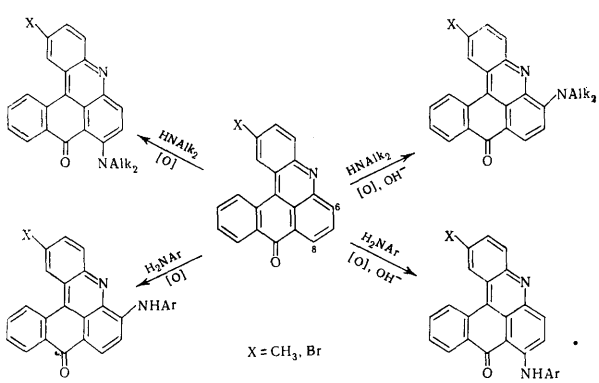
‡The arrows indicate the direction of nucleophilic attack.

above, since substitution takes place in the pyridine fragment. It is of interest that *N*-unsubstituted anthrapyridone does not react with amines, although this finding has not so far been explained:



The so-called ceramidonine—9*H*-naphtho[3,2,1-*kl*]-acridin-9-one—is an analogue of anthrapyridone. In contrast to anthrapyridone, in this case hydrogen is substituted in the anthraquinone part of the molecule[92,93]. The reaction is carried out in solution in pyridine under oxidising conditions, $KClO_3$ or $FeCl_3$ being used as oxidants.

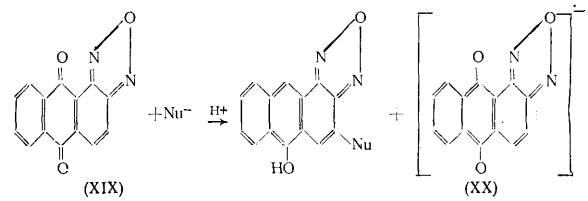
The direction of nucleophilic attack depends significantly on the nature of the amine and the presence of a base[92]. In the absence of bases, alkylamines substitute hydrogen in the 8-position and arylamines in the 6-position. The introduction of an alkali metal or tetraethylammonium hydroxide into the reaction mixture alters the orientation of the nucleophile and under these conditions an aromatic amine is directed to the 8-position and an aliphatic amine to the 6-position. A rare instance of the substitution of hydrogen rather than the halogen has been noted in the reaction of cyclohexylamine with 5-chloroanthraquinone-thiadiazole, in which the chlorine is activated with respect to nucleophilic substitution, according to current views, by both anthraquinone and thiadiazole components[94]:



A change in the direction of nucleophilic attack has also been observed in the amination of 1-hydroxyanthraquinone[72] by secondary alkyl amines. In aqueous solutions of dimethylamine and piperidine, the alkylamine residue substitutes hydrogen exclusively in the 2-position, while in pyridine solution substitution in the 2- and 4-positions takes place with formation of a mixture of products. In the absence of a solvent, 1-hydroxyanthraquinone gives rise to 1-hydroxy-2,4-dipiperidinoanthraquinone. The different modes of reaction have been explained by the characteristics of the solvation of both the initial amine and of the transition state arising when the 2- and 4-positions are attacked.

The role of the oxidant in the reactions of anthraquinone derivatives discussed above is exceptionally important. It determines the mode of reaction and the yield of products. In the oxidation of the unstable intermediate formed reversibly[95], the reaction is directed towards the nucleophilic substitution of hydrogen. In the absence of atmospheric oxygen or another oxidant, there is a possibility of several types of interaction of quinones with nucleophiles: (a) the reaction proceeds via the abstraction of a hydride ion from the intermediate by the initial quinone[82]; (b) the substitution reaction does not occur, the dimerisation of the substrate with formation of the corresponding bianthraquinonyl being observed[72,95]; (c) when the molecule contains a group capable of anionic stabilisation, it is substituted (for example, a hydroxy-group)[57].

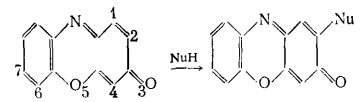
The interaction of anthraquinones with nucleophiles can occur during the initial period as a donor–acceptor process and instances of complete charge transfer have been noted. Thus radical-anions have been detected in the reactions of hydroxide ions with quinones[96] and of anthraquinones with sulphite ions[97,98], in the direct amination of quinizarin[57], and also in the nucleophilic substitution of hydrogen by CN^-, OH^-, and $OAlk^-$ ions in anthraquinone-furazan [84]:



(XIX) (XX)

Most of the initial quinone (**XIX**) is converted into the stable radical-anion (**XX**). It is believed that the formation of charge-transfer complex does not constitute an intermediate stage but proceeds as a parallel reaction[86]. On the other hand, it has been suggested that the radical-anions may precede the formation of σ complexes[97,98].

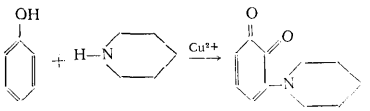
A series of studies have been made on the S_NH reactions of phenoxazinone derivatives[99–107]. In the fractions investigated, phenoxazinone, which contains the quinone imine fragment in its structure, exhibits much similarity with quinones:



Like quinones, phenoxazinones are capable of having their hydrogen substituted under oxidising conditions by residues of nucleophiles such as thiophenols[100], alkylamines[101], arylamines[102], arenesulphinic acids[103], and mercapto-compounds[104]. Hydrogen is apparently substituted always via a stage involving the formation of an intermediate addition product, which can be isolated when the experiment is carried out in the absence of air[105].

A systematic study has been made of the influence of the annelation of benzene rings on the electrophilic properties of phenoxazinone[106,107]. Analysis of the electronic structures of 2-phenoxazinone and its derivatives by the LCAO-MO method in the Hückel approximation showed[106] that benzophenoxazinones in which benzene is not annelated to the quinone imine component, contain, apart from the 7-position, a second electrophilic centre—the *peri*-position with respect to the heterocyclic nitrogen in the quinonoid ring. The calculated data were confirmed experimentally; a mixture of three compounds was found in the reactions of 3-phenoxazinone with thiophenols: 7-substituted, 1-substituted, and 1,7-disubstituted 3-phenoxazinone derivatives[107]. The method of oxidative amination of phenols discovered in 1955 by Brackman and

Havinga[108] has considerable synthetic possibilities. The above workers established that amino-*o*-quinones can be obtained by oxidising phenol and 2-naphthol with oxygen in the presence of the copper complex of morpholin.



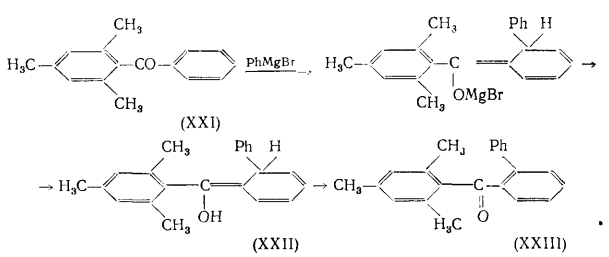
Phenol is initially oxidised to *o*-quinone, which then undergoes the S_NH reaction. Still earlier it was shown that catechol is involved in the oxidative amination reaction[109]. Sodium iodate in alcohol can also be used as the oxidant in this reaction[110].

Subsequently this method was successfully extended to phenols containing annelated azine[111-115] and azole[116,117] rings. In the oxidation of heterocyclic phenols in the presence of the copper(II) complex of a secondary amine, the corresponding *o*-quinones are usually formed with the amine residue in the quinonoid component[118], although in certain cases the heterocyclic fragment of the molecule is aminated[114,117]. Annelation of the quinone ring leads to a redistribution of electron density in the heterocyclic part of the molecule and alters significantly the nature of its reactivity. Isoquinoline quinones, for example, are aminated in the 3-position, although nucleophilic agents usually attack the $C_{(1)}$ atom of isoquinoline.[18]

IV. OTHER INSTANCES OF S_NH REACTIONS

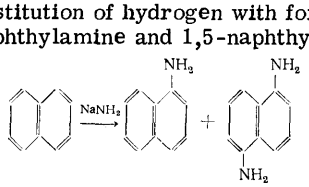
As far as we are aware there are no examples in the literature of the activation of the nucleophilic substitution of hydrogen by SO_2R, CN, and $\overset{+}{N}R_3$ groups. The explanation is probably the tendency of the groups themselves to be split off in the form of anions on treatment with nucleophilic agents.

However, there are examples of S_NH reactions in systems activated by the carbonyl or carboxy-group. Thus phenylmagnesium bromide attacks the *o*-position relative to the carbonyl group in the reaction with benzoylmesitylene (**XXI**), forming 2′-phenylbenzoymesitylene (**XXIII**). The dihydro-compound (**XXII**) can be sometimes isolated in small amounts as a side product[119]:



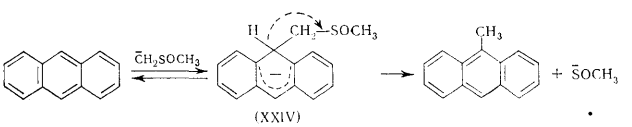
p-Hydroxybenzoic acid mixed with salicyclic acid can be obtained by fusing potassium benzoate with potassium hydroxide[120].

In 1901, Sachs[121] discovered the reaction which is a unique instance of an S_NH process in a non-activated aromatic system: fusion of naphthalene with sodamide leads to the substitution of hydrogen with formation of a mixture of 1-naphthylamine and 1,5-naphthylenediamine:



It is even more surprising that naphthols and naphthylamines, which occur in an anionic form in the presence of bases and should be highly deactivated with respect to nucleophilic attack, undergo similar reactions. However, 1- and 2-naphthols form 5-amino-derivatives, while 1- and 2-naphthylamines give rise to 1,5- and 2,5-naphthylenediamines respectively in yields of 20–50%.

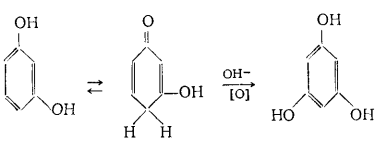
The nucleophilic alkylation of anthracene and phenanthrene by dimethyl sulphoxide and methyl phenyl sulphone[122-124], the carbanions of which are formed under the influence of sodium hydride in hexamethylphosphoramide, was reported in 1966. According to the authors[124], the formation of the final methyl derivatives takes place as a result of a hydride shift and the removal of the sulphinate residue from the anionic σ complex (**XXIV**):



(XXIV)

It is striking that systems with reduced aromaticity undergo this reaction, while benzene, naphthalene, and thionaphthene do not.

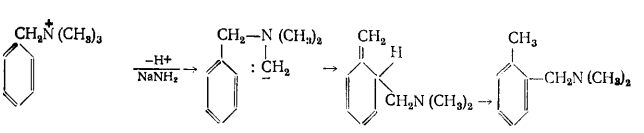
The nucleophilic substitution of hydrogen in the system activated more with respect to electrophilic attack than with respect to nucleophilic attack is represented by the reactions of phenols with alkalis, which lead to the formation of polyphenols with evolution of hydrogen. For example, when resorcinol is fused with alkali, phloroglucinol is formed[120]. This is explained by the fact that a tautomeric form of resorcinol (**XXV**) enters into the reaction and the latter reduces intrinsically to the substitution of hydrogen in a quinonoid system[50]. The reaction occurs only in the presence of an oxidant[125,126].



(XXV)

Certain intramolecular octet rearrangements and anomalous reactions can probably be classified as S_NH processes. Such intramolecular substitution of the hydride ion occurs, for example, in the Sommelet–Hauser rearrangement[127-129].

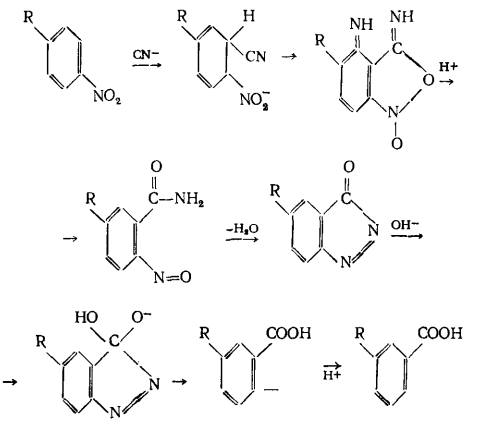
When quaternary benzylammonium salts are treated with strong bases, a proton is abstracted with formation of the ylid (**XXVI**). The free electron pair then attacks the aromatic ring, which has been activated by the ammonium group whose influence is transmitted via the methylene bridge:



(XXVI) (XXVII)

If the product (**XXVII**) is remethylated and again subjected to the rearrangement, it is possible to introduce another methyl group into the ring and continue in this way until the hexasubstituted benzene derivative is obtained[129].

The interaction of halogenonitrobenzens with KCN in ethanol at 150°C (the Richter reaction) [130,131] also constitutes essentially an S_NH reaction. Formally, this involves the substitution of the nitro-group, but the COOH group is not found at the site previously occupied by the nitro-group. The mechanism of this reaction has been the subject of a prolonged discussion; the mechanisms proposed by Rosenblum [132] are supported at the present time. It has been incontrovertibly demonstrated that the first stage involves the formation of an anionic σ-complex followed by the removal of hydride-active hydrogen from the latter:



V. S_NH REACTIONS OF AZA-ACTIVATED SYSTEMS

The substitution of a hydrogen atom with its binding electrons in the aromatic cyclopropenylium and tropylium carbonium ions and also in oxa-, thia-, and selena-activated heteroaromatic compounds is described in reviews published in 1974–1975. [6,133]

Aza-activation plays an exceptionally important role in the above processes. In the simplest azine (pyridine), the aza-group exhibits a polarising activity as powerful as that of the exocyclic nitro-group in nitrobenzene. The enhanced reactivity of azine compounds is observed in the *o*-(α-) and *p*-(γ-)positions, where the entropy of activation for electrostatic attraction is greatly enhanced. The nitro-group is known to have a stronger activating influence than the aza-group in the nucleophilic substitution of anionically stabilised species in aromatic systems ($k_{NO_2}/k_{aza} > 1$). [18] However, the intrinsic nucleophilic properties of the aza-group are responsible for its tendency to undergo specific proton solvation, which leads to an increase of reactivity and the reversal of the reactivity sequence: $k_{NO_2}/k_{aza} < 1$.

Only rare instances of S_NH reactions in aromatic aza-systems where neither the reactant nor the substrate is charged are so far known. In the vast majority of cases, the substitution of hydrogen may be achieved by the additional activation by the charge of either the attacking reactant (nucleophile) or the substrate (azine). The papers published up to 1960–1965 were devoted to reactions involving the anionic form of the attacking reactant (H_2N^-, CN^-, and OH^-) and also to organometallic compounds in which the carbon–metal bond is to a large extent polar. These studies have been described in a number of reviews and monographs [2,18,19,134,135]. Whereas only isolated studies using the cationic activation of the azine by its conversion into the *N*-acylammonium form have been made up to that time [136-140], in the last ten–fifteen years systematic investigations have been made and considerable advances have been achieved in the field of the nucleophilic reactions of acylammonium cations [7,9] and also cations arising on formation of azine *N*-oxides [8,141].

This section deals with problems of the activation of aromatic aza-compounds by quaternisation and protonation and also the involvement of nucleophilic substitution of systems not activated by a charge, which have not so far been dealt with in the reviews already published.

1. Quaternary and Protonated Salts

Quaternary and protonated azine salts are on the whole less electrophilic than the corresponding *N*acyl salts [7] or *N*-oxide ethers [8]. Their reduced reactivity is undoubtedly a consequence of the fact that the alkyl group and the proton exhibit electron-donating properties, in contrast to the electron-accepting properties of the acyl or ether residues. Aryl residues occupy an intermediate position between these two types. The use of quaternary and protonated salts is preparatively simpler and in addition makes it possible to introduce them into compounds containing OH, NH_2, and NHR groups, which cannot be done with acyl salts, owing to the transacylation which occurs under these conditions.

It has been frequently postulated that the mechanism of the S_NH reactions of azines involves "addition–elimination" [1,7-10], but kinetic data [142,143] confirming the validity of these hypotheses have been obtained only in recent years.

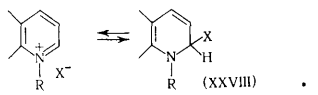
The formation of intermediate addition products on substitution of hydrogen in azinium cations can be observed experimentally, as in the corresponding processes with participation of nitro-activated systems and quinones. The profile of the potential energy surface of the delocalisation of the negative charge following the introduction of additional aza-groups or benzo-annelation constitutes a favourable factor, stabilising σ complexes, lowers the energy of their formation and thereby increases the reactivity of the initial azinium cations. For this reason, the manifestation of the higher reactivity of aza- and benzo-azines compared with the simplest azine (pyridine) is to be expected in S_NH reactions and in the substitution of the groups eliminated.

Quaternary salts constitute a very convenient object for study, since the addition product formed is uncharged and is therefore more stable than the classical Meisenheimer anionic complexes. This makes it possible to investigate in detail the structures of such compounds, including X-ray diffraction analysis, which is particularly important for the understanding of the stereochemistry of the transition state [12].

Reactions leading to the substitution of hydrogen under the influence of anionic and anionoid reagents are known in the series of quaternary and protonated salts of azines. Reactions with negatively charged species have been studied in greatest detail. A tendency towards interaction with nucleophilic agents is manifested by the azinium cations within the quaternary salts themselves. A classical example of such an interaction between the cation and anion, accompanied by charge transfer, is provided by alkylpyridinium iodide and its analogues [144-146].

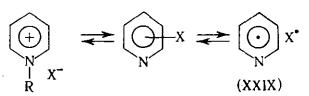
The enhancement of the nucleophilic properties of the counterion in the series $ClO_4^- < C_6H_5SO_3^- < NO_3^- < CH_3COO^- < OCH_3^- < Cl^- < Br^- < N_3^- < OH^- < SCN^- < I^- < CN^- < S_2O_3^-$ [147,148] leads to an equilibrium between anions such as CN^-, SH^-, and OH^- and covalent structures,

which is strongly displaced to the right [149-151]. The stability of covalent compounds of type (XXVIII) also increases in the sequence pyridine < quinoline < acridine.



(XXVIII)

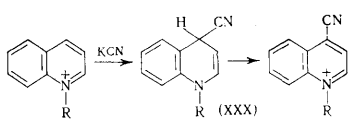
Complexes with partial charge transfer and biradical species, usually arising in an excited state, occupy an intermediate position between the purely ionic salts (X = ClO_4 or NO_2) and covalent structures—the so called "cryptosalts" [149] (X = CN or OH).



(XXIX)

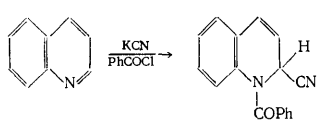
Charge-transfer complexes similar to compound (XXIX) can in all probability play in important role in the mechanism of S_NH reactions.

Alkylpyridinium salts and their analogues readily react with potassium cyanide in an aqueous medium [152-154], forming initially the dihydro-compounds (XXX), which may be oxidised by iodine to the corresponding nitriles [152], for example:



(XXX)

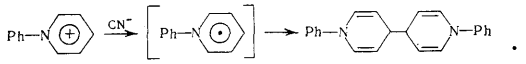
Dihydroquinoline (XXX) is an analogue of Reissert's compounds [155], which arises in the reaction of an acylquinolinium salt with the cyanide ion:



(XXXI)

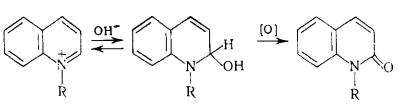
The causes of the formation of the 4-addition [compound (XX)] and 2-addition [compound (XXXI)] products when alkyl- and acyl-quinolinium cations are attacked respectively have not been elucidated [156]. The reactions of the cyanide ion with alkylacridinium [157] and phenanthridinium [158] salts occur similarly. The micellar catalysis by surfactants of the reaction of cyanide with a quaternary salt of nicotinamide [159] has been investigated and it has been established that the rate constants increase in the presence of low concentrations of the detergent and following the addition of zwitterionic compounds.

Certain data concerning the mechanism of the reaction of the cyanide ion with azinium cations have now been obtained. In particular, it has been established that the product of addition in the 2-position is formed initially and then rearranges to the corresponding 4-derivatives [160], which resembles the formation of Servis complexes in the series of aromatic nitro-compounds [15]. When phenylpyridinium chloride was allowed to react with the cyanide ion in an inert atmosphere in an aqueous acetone solution, *N*-phenylpyridyl radicals were detected [161] and the reaction led to the isolation of a dimeric product without nitrile groups:



This led the authors to the hypothesis that the interaction of quaternary pyridinium salts with CN^- proceeds via a one-electron mechanism: in the absence of air, it is completed by the recombination of the intermediate radicals. The presence of oxygen is responsible for another course of the reaction: an addition product is formed, which can then be subsequently oxidised with elimination of the nitrile residue [157].

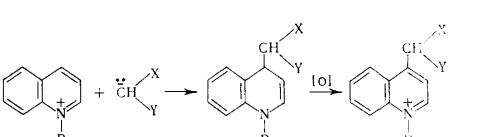
Pozharskii et al. recently demonstrated the substitution by the amide ion of the hydrogen in methylacridinium iodide, which is so far the only example of the involvement of a quaternary salt in the Chichibabin reaction [162]. The final product of the familiar interaction of azinium cations with the hydroxide ion may be regarded as a result of the substitution of hydrogen when the reaction is carried out in the presence of an oxidant, for example potassium hexacyanoferrate(III):



In the absence of an oxidant, there is also a possibility of the formation of oxo-compounds mixed with an equal amount of the dihydro-compound as a result of the disproportionation of pseudobases [163]. Such disproportionation of pyridine and quinoline proceeds via the open-chain form of the pseudobase (derivatives of glutaconaldehyde [164]).

The reactions of carbanions of the type $\bar{C}H_2$–COX include the interaction of pyridinium and benzopyridinium salts with methyl ketones, β-dicarbonyl compounds, cyanoacetic ester, etc. in the presence of strong bases [165-170].

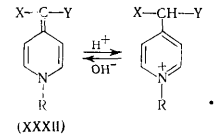
The reactions of CH-active compounds with azinium cations are of interest as models of the addition of acetone and hydroxyketones to diphosphopyridine dinucleotide [171], discovered in 1954. Pyridinium and quinolinium cations usually form 4-substituted products [165,167,169,170], while isoquinolinium [165,172] and acridinium [166,173,174] cations form 1- and 9-substituted products respectively:



Here X = H, $COOCH_3$ or CN and Y = NO_2, CN, $COOCH_3$, or COC_6H_5.

Adducts, which are probably intermediate in the formation of substituted products although this has not been demonstrated kinetically, can be frequently isolated from the reaction mass. The stability of the addition products increases with decrease of the aromaticity of the initial azines: pyridine < quinoline < acridine. Dihydro-compounds are readily oxidised in air [173] and can be dehydrogenated by other oxidants: lead tetra-acetate in benzene, permanganate in acetone, chloranil, etc. [174,175]. In the presence of alkalis, the oxidation of adducts leads to the

formation of coloured "dihydrocompounds" (XXXII) of the quinonoid type, which are rearomatised on treatment with acids [165]:



(XXXII)

The methyl groups in the α- and γ-positions relative to the aza-group in heteroaromatic compounds are known to exhibit some CH acidity. It has been shown that these compounds are able to react with the acridinium in the absence of base catalysis [176-179]. However, one cannot rule out the possibility that the catalytic effect is shown by the reactants themselves, which are bases. Methylated heterocycles, both in the form of bases and quaternary or protonated salts, can be made to react with the acridinium cation. In its turn, the substrate can be used also in the form of the protonated salt and, in the presence of active nucleophiles (quinaldine and lepidine), hydrogen can be substituted in the acridine base too. The condensation takes place under oxidising conditions; suitable oxidants are sulphur (melt) and atmospheric oxygen bubbled through a solution in a polar solvent.

Table 2. The rate constants for the methylation of heterocycles by acridine hydrochloride (in DMF, 120°C, bubbling with air).

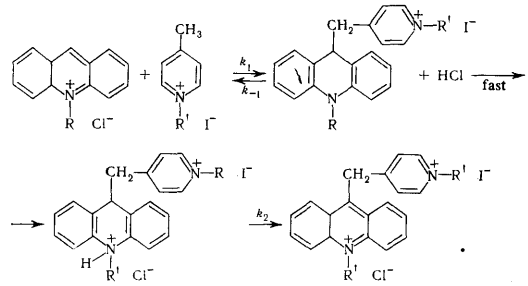
Heterocycle	10^3k, litre mole^{-1} s^{-1}
4-Picoline methiodide	0.50±0.01
4-Picoline ethiodide	0.51±0.01
4-Picoline N-2-propiodide	0.47±0.01
2-Picoline methiodide	0.132±0.007
4-Methylquinoline methiodide	0.50±0.002
2-Methylquinoline methiodide	0.248±0.016
2-Methylbenzothiazole methiodide	0.183±0.003
2-Methylbenzimidazole methiodide	0.031±0.002
Acridine + 4-picoline methiodide	0.062±0.003

This reaction is unusual because it proceeds only in the presence of an oxidant and the addition products characteristic of acridine in an inert atmosphere cannot be detected even in the ultraviolet spectra of the reaction mixtures [142].

The study of the kinetics of the reaction of acridine hydrochloride with the quaternary salts of methylated heterocycles under the conditions of a zero-order reaction with respect to oxygen showed that it is of second order overall and of first order with respect to each reactant. The rate constants are listed in Table 2. The reactions proceed with low activation energies (9-13 kcal mole^{-1}).

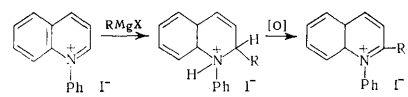
The reactivities of the heterocycles in this reaction (4-methylquinoline > 4-picoline > 2-methylquinoline > 2-methylbenzothiazole > 2-picoline > 1,2-dimethylbenzimidazole) are consistent with the acidities of the protons of the methyl groups based on deuterium-exchange data [180]. Protonation of acridine increases the rate of reaction and the electron-donating properties of the alkyl chain hardly influence the rate.

In many instances the kinetic curves are S-shaped owing to an induction period, which decreases with increase of temperature and the concentrations of the reactants. This shows that the reaction proceeds via an intermediate compound, which is present at a vanishingly low quasistationary concentration.



The example discussed demonstrates the decisive role of the oxidant in both S_NH reactions, where the σ complex is formed at a quasistationary concentration and the substitution of hydrogen can be achieved only in the presence of an oxidant.

As already mentioned, the carbon-metal bond in organometallic compounds, including Grignard reagents, is highly polarised and approaches a linkage of the ionic type. The reactions of alkyl- and aryl-azinium cations with organometallic compounds constitute an example intermediate between their reactions with anions and uncharged species. Quaternary pyridinium salts and their benzo-derivatives combine with Grignard reagents to form dihydro-compounds [181-185], which are mainly unstable and are readily oxidised to the corresponding substitution products [182]:



The analogous interaction of benzylpyridinium chloride with cyclopentadienyl-lithium is completed by the substitution of the hydride ion [186].

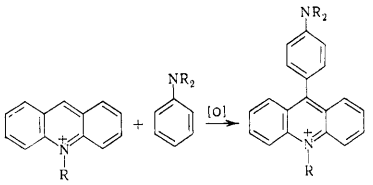
Among the uncharged nucleophiles used to substitute hydrogen in heteroaromatic cations, mention should be made of alkyl- and aryl-amines and their derivatives, heterocycles with an excess of π electrons, and phenols [187-198]. These are undoubtedly much weaker nucleophiles than anionic reagents. Whereas in the series of acyl salts [7] and *N*-oxide ethers [8], the S_NH reactions of anionoid reagents can be achieved even with pyridine, among the quaternary salts those of quinoline and isoquinoline are inactive [199], although their protonated salts can be made to react in this way [200,201]. The cations whose activity has been increased by benzoannelation (acridine [187]) or by an additional aza-group (diazanaphthalenes [198,202,203]) react smoothly with uncharged nucleophiles, forming adducts or hydrogen substitution products depending on the nature of the substrate.

The quaternary salts derived from acridines, both unsubstituted and containing substituents in the 9-position [204], instantly combine with alkylamines, forming the corresponding acridans. Acridans, containing hydrogen at the geminal site, may be oxidised by an acridinium salt as a result of an intermolecular hydride transfer [205].

The hydride ion is abstracted and substituted in the *N*-alkylacridinium cation following attack by arylamines under oxidising conditions (melt with sulphur, bubbling of air through a solution in dimethylformamide or dimethyl sulphoxide). It has been shown that in the melt with sulphur the reaction does not proceed via a stage involving the

preliminary thionation of acridine, sulphur behaving merely as an oxidant[189]. The yields of aminoarylacridinium salts are 80–90%. The side products are acridinone or thioacridinone depending on the experimental conditions.

Arylamines containing various substituents in the ring and in the aminogroup, including arylhydrazones of aldehydes and ketones and carboxylic acid arylhydrazides, may be used in these reactions[206]:



Halogens exhibiting an appreciable $-I$ effect lower the reactivity of arylamines; groups with a $-M$ effect fully deactivate the nucleophile when they are introduced both in the ring and in the amino-group (Table 3). The basicity of aromatic amines may serve as an indirect criterion of their nucleophilic properties. Amines with a high basicity ($pK_a > 4$) readily react with the acridinium cation; amines with $pK_a = 3.5–2.5$ react but under more severe conditions; compounds with $pK_a < 2.5$ are not reactive.

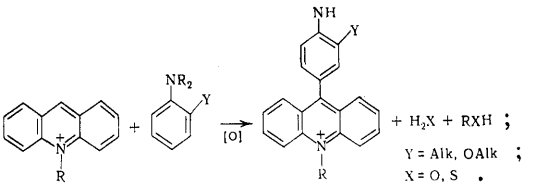
Table 3. The reactions of arylamines with acridine hydrochloride.

Initial arylamine	pK_a	Reaction conditions		Yield, %	
		temperature, °C	time, h	9-aminoaryl-acridine	thio-acridinone
Aniline	4.58	130	2	95	4
N-Monoethylaniline	5.11	120	1.5	92	5
NN-Dimethylaniline	5.06	130	2	94	4
NN-Dipropylaniline	5.29	120	2	90	8
o-Toluidine	4.39	125	2	90	8
m-Toluidine	4.69	120	2	70	20
p-Toluidine	5.13	130	7	25	43
NN-Dimethyl-*m*-toluidine	5.24	135	4	66	28
NN-Dimethyl-*p*-toluidine	—	140	7	*	40
o-Aminophenol	4.47	135	1	85	—
m-Aminophenol	4.30	135	1	95	4
o-Anisidine	4.49	125	2	84	4
NN-Dimethyl-*m*-anisidine	—	125	2	91	—
o-Phenetidine	4.47	125	2	84	10
o-Phenylenediamine	4.74	135	1	80	—
m-Phenylenediamine	4.98	130	1	91	5
o-Chloroaniline	2.64	140	4	25	20
m-Chloroaniline	3.5	135	4	32	34
1-Naphthylamine	3.92	120	1,5	85	5
2-Naphthylamine	3.4	120	2	60	20
m-Nitroaniline	2.47	140	4	*	20
o-Aminoacetophenone	2.22	140	4	*	20
Acetanilide	—	140	4	*	15

*The reaction does not occur; 9-aminoarylacridine was not detected chromatographically in the reaction mixture.

A number of anomalies have been noted in the interaction of arylamines with acridinium salts. Thus phenylhydrazine causes dimerisation of the acridine residues with formation of *NN*-dialkyl-9,9′-biacridanyls[207]. Sterically hindered arylamines behave in an unusual manner. *ortho*-Substituted dialkylanilines undergo dealkylation and monoalkyl derivatives are formed instead of the expected *NN*-dialkylaminoacridinium salts.

The alkyl group split off does not pass to the ring but is eliminated and converted into an alkanethiol when the reaction is carried out in a melt with sulphur or into an alcohol when the oxidant is oxygen[204,208]. The reactions of *NN*-dialkylanilines containing bulky residues give rise to complexes containing three iodine atoms and not to the usual 9-aminoarylacridinium iodides[209]. Such unexpected formation of tri-iodides is probably associated with electron transfer from the electron-donating reactant to the electron-accepting reactant, although one cannot rule out the possibility also of other oxidation-reduction processes, which may lead to the formation of free iodine.



Some data have been obtained for the mechanism of the reactions with arylamines. The primary interaction of the acridinium cation with a dialkylaniline results in the formation of a 1 : 1 charge transfer complex[210], which may be located on the reaction coordinate[199].

The study of the rates of the process demonstrate the absence of base catalysis, the kinetic isotope effect in the reaction with 2,4,6-trideuteroaniline being reduced approximately by a factor of three: $k_H/k_D = 2.28$ (Table 4).[143] Together with the NMR studies on the reaction mixtures, these data show that, as in the reaction with reactive methyl-substituted heterocycles, the oxidative substitution of hydrogen by arylamines proceeds via a stage involving the formation of an intermediate, which probably has the structure (XXXIII)§.

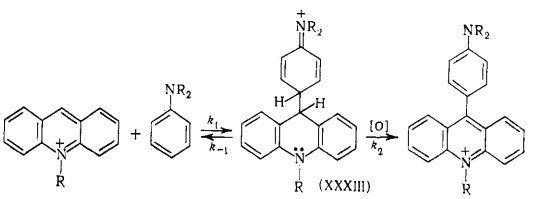


Table 4. The rate constants of the reactions of acridine methiodide with arylamines in DMF on bubbling with air.

Arylamine	Reaction temp., °C	10^2k, litre mole^{-1} h^{-1}	Arylamine	Reaction temp., °C	10^2k, litre mole^{-1} h^{-1}
Aniline	100	0.081	*NN*-Dimethylaniline	100	0.047
Aniline	110	0.124	*NN*-Dimethylaniline	120	0.118
Aniline	120	0.216	*NN*-Dimethylaniline	130	0.180
Aniline	130	0.293	*N*-Methylaniline	120	0.170
2,4,6-Tri-deutero-aniline	120	0.095	*o*-Toluidine	120	0.198

The activation energies are also low in this case. The appearance of a kinetic isotope effect can be explained by the high value of k_{-1}. The steric hindrance arising on

§The formation of the analogous σ complex of trinitrobenzene with phenol, in which the two species are connected via a C–C junction, has been demonstrated recently by NMR.[211]

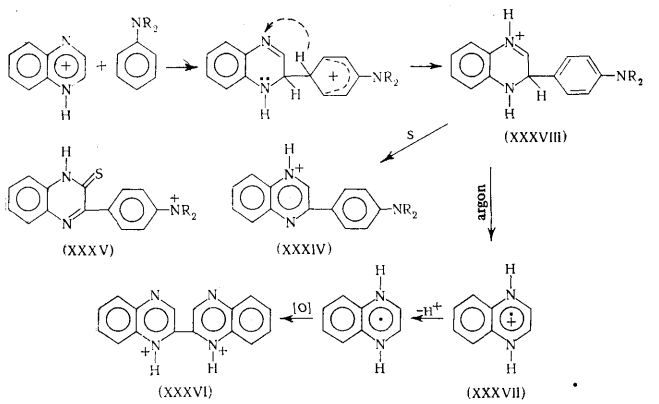
formation of the state (XXXIII) in *ortho*-substituted dialkylanilines can explain their cleavage in these reactions. The dynamics of the interaction of the alkylacridinium cation with five-membered heterocycles, such as indole, with phenols [196] is probably similar to that already discussed.

It was noted above that the introduction of an additional aza-group into the azine molecule activates it with respect to participation in S_NH reactions. Indeed, using quaternary quinoxalinium salts, it is possible to carry out the oxidative subtitution of hydrogen by residues of nucleophilic heterocycles such as pyrrole and indoles [202]. The corresponding 3-methylquinazolinium salts give rise to anomalously stable σ complexes, which are not dehydrogenated by oxidants such as chloranil, iron(III), and sulphur [198]. This manifests the tendency of the 3-alkylquinazolinium cation towards its preferential existence in the form of dihydro-compounds, for example, covalent hydrates [212]. The 1-methylquinazolinium cation does not exhibit a tendency towards interactions of this type [203].

The interaction of protonated salts of azines with uncharged nucleophiles does not differ in principle from the reactions of the quaternary salts. However, one should bear in mind that in this instance there is a possibility of proton transfer from the substrate to the basic reactant, for example an arylamine, and the reactions then proceed with participation of equilibrium concentrations of the reactants. When the reactant is appreciably basic, this can probably constitute an obstacle to such reactions. The principles of additional activation are in this case the same as for quaternary salts and for this reason here too the most reactive compounds are acridine salts—hydrochlorides, sulphates, nitrates, phosphates [191], and salts with organic acids. The yields of the aminoarylation products are nearly quantitative when the oxidant is sulphur or air in dimethylformamide solution, while the yield of the reaction in nitrobenzene, which probably behaves as an acceptor of hydride ions, is about 46% [205]; the yields of acridinylindoles are 64–68% [213] and those of acridinylphosphonates are 70%. [214] In the series of quinoline derivatives nucleophilic hydrogen substitution reactions proceed less satisfactorily; aminoaryl derivatives are formed in yields of about 50% [200] and the yields of quinolinylindoles are 5%. [215] Derivatives of pyridine have not been obtained from its hydrochloride in these reactions.

In the reactions of both protonated and quaternary salts, the successful occurrence of the S_NH processes depends on the correct choice of oxidant. Quinoxaline hydrochloride reacts with dimethylaniline in a melt with sulphur; together with the normal hydrogen substitution product (XXXIV) (14%), this involves the formation of the thiono-derivative (XXXV) (60%). Under argon in dimethylformamide solution, the same reactants give rise to 2,2'-diquinoxaline (XXXVI) only. When the reaction is carried out in air, no products are detected. The appearance in the reaction mass of the radical-cation (XXXVII), detected by ESR, can be explained by the homolytic decomposition of the σ complex (XXXVIII). The inhibition of the reaction by oxygen is most probably associated with chain termination via the formation of a peroxide from the radical-cation (XXXVII). [216]

The different mode of reaction in the presence and absence of oxygen in the present instance and in the cases considered previously [95,157] suggests that many of the reactions, which are usually carried out in air, may lead to other results when they are performed in an inert atmosphere.

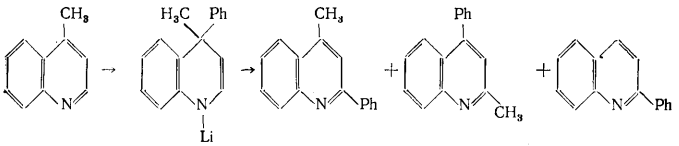


2. Azines which Are Not Activated by a Charge

The vast majority of examples of the substitution of hydrogen in aromatic aza-compounds which are not additionally activated by a charge refer to the interaction of these systems with nucleophiles having a negative charge or with very powerful uncharged nucleophiles such as organometallic compounds. These include in the first place the well known substitution of hydrogen in aza-activated compounds by the amide anion (the Chichibabin reaction) and on fusion with alkalis. These reactions have been considered in detail in a number of reviews and books [134,135]. We shall merely mention that, until recently, the Chichibabin reaction was regarded [217] as a process characteristic of six-membered nitrogenous heterocycles. Simonov and Pozharskii established that many imidazoles containing annelated benzene rings are capable of being aminated by sodamide [135]. This shows that studies on other S_NH reactions in the series of azoles and related systems would be useful.

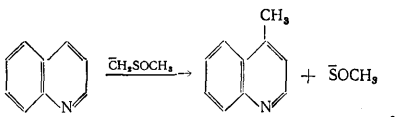
There is a considerable similarity between the Chichibabin amination and the reactions of aromatic aza-compounds with organometallic reagents. Examples of reactions of azines with organometallic nucleophiles have been discussed in a number of reviews [18,218]. Studies were published in 1967–1971 where the reaction mechanisms were investigated by infrared spectroscopy and NMR [219–222] and the addition products of organolithium compounds, whose formation had been previously postulated, were identified.

Interesting results were obtained in a study of the reactions of lepidine with phenyl-lithium [219]:



In this case 2-methyl-4-phenylquinoline (XL) (yield 0.5%) and 2-phenylquinoline (XLI) (yield 3%) are formed together with the main product—2-phenyl-lepidine (XXXIX) (yield 96.5%). A mechanism has been proposed according to which the addition product 1-lithio-4-methyl-4-phenylquinoline (XLII) is formed initially and then rearranges to compound (XXXIX) as a result of the nucleophilic substitution of hydrogen in the 2-position. The nucleophilic substitution of the 4-methyl group leads to compound (XL). Finally the displaced hydride ion may substitute the methyl group in the 4-position with formation of compound (XLI).

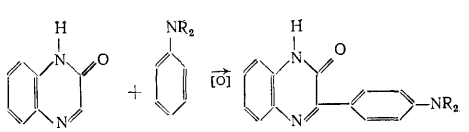
The interaction of free azines with carbanions has been described. Certain instances of such interaction were discussed above [175,176]. Almost all the reactions involve the reactive acridine, which has been shown to form addition products with aliphatic and aromatic methyl ketones in the presence of sodium methoxide[166,174]. The reactions of methyl sulphones [123] and methyl sulphoxides[122,124] with quinoline, isoquinoline, acridine, phenanthridine, and benzoxazole in the presence of sodium hydride are of interest as methods for the preparation of the corresponding methylated azines:



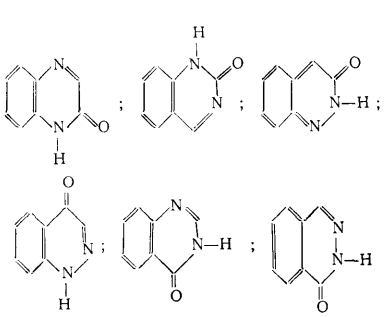
As already mentioned, even the non-activated anthracene and phenanthrene systems are involved in this reaction [122]; however, pyridine, which is more aromatic, proved to be unreactive.

The instances of the nucleophilic substitution of hydrogen where neither the attacking reactant or the substrate are activated by a charge are the rarest reactions in the heteroaromatic series. Whereas the substitution of hydrogen by uncharged nucleophiles (amines, phenols, systems with an excess of π electrons) are usual in the series of quinones, among heteroaromatic compounds these reactions appear to be the privilege of the less aromatic systems with low π-binding energies.

Thus acridine [187] and phenazine activated by the nitro-group [223] are capable of undergoing direct substitution of hydrogen by arylamines in the presence of an oxidant. The involvement of certain diazanaphthalenones in reactions with arylamines and heterocycles having an excess of π electrons [224,225] has been recently demonstrated, for example:



According to Katritzky [226], diazanaphthalenones satisfy all the criteria of aromaticity, like other azinones, and therefore the instances under consideration can be quite justifiably classified as aromatic nucleophilic substitution reactions. Of the six isomeric diazanaphthalenones



only the first three (quinoxalinone, 2-quinazolinone, and 3-cinnolinone) are capable of undergoing reactions involving the substitution of their hydrogen on treatment with uncharged anionoid agents. Quantum-chemical analysis of the structures of these isomers and the study of the chemical shifts of the substituted protons indicate the absence of any correlation between the chemical shifts and the charge densities, on the one hand, and the reactivities of these compounds, on the other. However, calculations have shown that their reactivities vary in opposition to the energies of radical localisation and are determined by the degree of departure of the system from aromaticity [227].

Examination of literature data shows that these are as yet insufficient to give a complete idea about the criteria of the reactivity and the mechanisms of S_NH reactions, nevertheless the considerable preparative scope of these reactions, which makes it possible to obtain compounds belonging to a wide variety of classes, should stimulate further theoretical and synthetic studies in this field.

REFERENCES

1. J. F. Bunnet and R. E. Zahler, Chem. Rev., 49, 273 (1951).
2. J. Sauer and R. Huisgen, Angew. Chem., 72, 294 (1960).
3. Z. N. Parnes and D. N. Kursanov, "Reaktsii Gidridnogo Peremeshcheniya v Organicheskoi Khimii" (The Hydride Shift Reactions in Organic Chemistry), Izd. Nauka, Moscow, 1969.
4. D. N. Kursanov, Z. N. Parnes, and N. M. Loim, Synthesis, 633 (1974).
5. Z. N. Parnes, D. N. Kursanov, and D. I. Lyakhovetskii, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 19, 324 (1974).
6. S. V. Krivun, O. F. Alferova, and S. V. Sayapina, Uspekhi Khim., 43, 1739 (1974) [Russ. Chem. Rev., No. 10 (1974)].
7. A. K. Sheinkman, S. I. Suminov, and A. N. Kost, Uspekhi Khim., 42, 1415 (1973) [Russ. Chem. Rev. No. 8, (1973)].
8. M. Khamana, Khim. Geterotsikl. Soed., 1155 (1973).
9. A. K. Sheinkman, Khim. Geterotsikl. Soed., 3 (1974).
10. J. Miller, "Aromatic Nucleophilic Substitution", Elsevier, Amsterdam, 1968.
11. J. F. Bunnet, Quart. Rev., 12, 1 (1958).
12. P. Rys, P. Skrabal, and H. Zollinger, Angew. Chem., 84, 921 (1972).
13. S. D. Ross, in "Sovremennye Problemy Fizicheskoi Organicheskoi Khimii" (Modern Problems in Physical Organic Chemistry) (Translated into Russian), Izd. Mir, Moscow, 1967, p. 37.
14. F. Pietra, Quart. Rev., 23, 504 (1969).
15. M. Strauss, in "Metody i Dostizheniya v Fizicheskoi Organicheskoi Khimii" (Methods and Advances in Physical Organic Chemistry) (Translated into Russian), Izd. Mir, Moscow, 1973, p. 422.
16. R. Foster and C. A. Fyfe, Rev. Pure Appl. Chem., 16, 61 (1966).
17. K. L. Servis, J. Amer. Chem. Soc., 89, 1508 (1967).
18. G. Illuminati, "Advances in Heterocyclic Chemistry", New York, 1964, Vol. 3, p. 285.
19. R. G. Shepherd and J. L. Fedric, "Advances in Heterocyclic Chemistry", New York, 1965, Vol. 4, p. 145.
20. V. P. Mamaev, O. A. Zagulyaeva, and S. M. Shein, Khim. Geterotsikl. Soed., 723 (1973).
21. D. V. Banthorpe, Chem. Rev., 70, 295 (1970).
22. O. Yu. Okhlobystin, "Perenos Elektrona v Organicheskikh Reaktsiyakh" (Electron Transfer in Inorganic Reactions), Izd. Rostov. Univ., Rostov-on-Don, 1974.

23. Z. V. Todres, Zhur. Vses. Khim. Obshch. im Mendeleeva, 19, 294 (1974).
24. G. B. Sergeev, 19, 285 (1974).
25. J. K. Kim and J. F. Bunnet, J. Amer. Chem. Soc., 92, 7463 (1970).
26. S. M. Shein, L. V. Bryukhovetskaya, A. D. Khmelinskaya, V. F. Starichenko, and T. M. Ivanova, Reakts. Sposobnost' Org. Soed., 6, 1078 (1969).
27. G. B. Russel, E. G. Janzen, and E. T. Strom. J. Amer. Chem. Soc., 86, 1807 (1964).
28. C. K. Ingold, in "Teoreticheskie Osnovy Organicheskoi Khimii" (Theoretical Principles of Organic Chemistry) (Translated into Russian), Izd. Mir, Moscow, 1973, pp. 641, 328.
29. K. K. Prasad, Tetrahedron Letters, 1361 (1974).
30. M. V. Gorelik and V. I. Lomzakova, Khim. Geterotsikl. Soed., 1278 (1974).
31. E. E. Gol'teuzen, Z. V. Todres, A. Ya. Kaminskii, S. S. Gitis, and D. N. Kursanov, Izv. Akad. Nauk SSSR, Ser. Khim., 1083 (1972).
32. L. A. Blyumenfel'd, L. V. Bryukhovetskaya, G. V. Fomin, and S. M. Shein, Zhur. Fiz. Khim., 44, 931 (1970) [Russ. J. Phys. Chem., No. 4 (1970)].
33. P. Buck, Angew. Chem., 81, 136 (1969).
34. A. Rezmick and M. J. Strauss, Tetrahedron Letters, 4439 (1970).
35. M. Nilsson, C. Ullemius, and O. Wennerström, Tetrahedron Letters, 2713 (1971).
36. C. Möberg and O. Wennerström, Acta Chem. Scand., 25, 2871 (1971).
37. M. I. Kalinkin, Z. N. Parnes, V. E. Puzanov, A. D. Khmelinskaya, S. M. Shein, and D. N. Kursanov, Zhur. Org. Khim., 9, 2354 (1973).
38. I. M. Sosonkin and G. L. Kalb, Zhur. Org. Khim., 10, 133 (1974).
39. A. Wohl, Ber., 32, 3486 (1899).
40. A. Wohl and W. Aue, Ber., 34, 2442 (1901).
41. P. Hepp, Annalen, 215, 344 (1882).
42. C. A. Lobry de Bruyn, Rec. Trav. chim., 2, 205 (1883).
43. R. Huisgen, Annalen, 559, 101 (1948).
44. W. Borsche and E. Böcker, Ber., 37, 4388 (1904).
45. R. G. Landoldt and H. R. Snyder, J. Org. Chem., 33, 403 (1968).
46. J. Meisenheimer and E. Patzig, Ber., 39, 2533 (1906).
47. S. S. Gitis, A. I. Glaz, V. V. Grigor'ev, A. Ya. Kaminskii, A. S. Martynenko, and R. S. Sadkov, Zhur. Org. Khim., 3, 1617 (1967).
48. N. A. Lakomova, S. S. Gitis, Yu. D. Grudtsyn, A. V. Ivanov, and A. Ya. Kaminskii, "Tezisy I Vsesoyuznogo Simpoziuma po Organicheskomu Sintezu" (Abstracts of Reports at the First All-Union Symposium on Organic Synthesis), Moscow, 1974, p. 9.
49. R. Huisgen and H. Rist, Annalen, 594, 159 (1955).
50. W. Bradley and R. Robinson, J. Chem. Soc., 1254 (1932).
51. G. de Montmollin and M. de Montmollin, Helv. Chim. Acta, 6, 94 (1923).
52. F. W. Bergstrom, J. M. Granera, and V. Erickson, J. Org. Chem., 7, 98 (1942).
53. M. Makosza, Chem. Comm., 648 (1970).
54. A. N. Nesmeyanov and N. A. Nesmeyanov, "Nachala Organicheskoi Khimii" (Principles of Organic Chemistry), Izd. Khimiya, Moscow, 1970, Vol. II, p. 728.
55. R. B. Ivanova and M. L. Khidekel', Izv. Akad. Nauk SSSR, Ser. Khim., 222 (1967).
56. T. N. Kurdyumova, Zhur. Org. Khim., 4, 1683 (1968).
57. S. A. Russkikh, Candidate's Thesis, Institute of Organic Chemistry, Siberian Division of the USSR Academy of Sciences, Novosibirsk, 1974.
58. P. Kuser, M. Inderbitzin, J. Brauchli, and C. H. Eugster, Helv. Chim. Acta, 54, 980 (1971).
59. P. Pratesi, Gazzetta, 66, 215 (1936).
60. H. Fischer, A. Treibs, and E. Zanker, Ber., 92, 2026 (1959).
61. P. Kuser, E. Frauenfelder, and C. H. Eugster, Helv. Chim. Acta, 54, 969 (1971).
62. N. Baumann, S. Fumigalli, G. Weisgerber, and C. H. Eugster, Helv. Chim. Acta, 49, 1974 (1966).
63. C. H. Eugster and P. Bosshard, Helv. Chim. Acta, 46, 815 (1963).
64. P. Bosshard, S. Fumigalli, R. Grood, W. Trueb, and C. H. Eugster, Helv. Chim. Acta, 47, 769 (1964).
65. S. Fumigalli and C. H. Eugster, Helv. Chim. Acta, 54, 959 (1971).
66. J. M. Buce, J. Chem. Soc., 2366 (1959).
67. J. D. Bu'Lock and J. Harley-Mason, J. Chem. Soc., 703 (1951).
68. German P. 186526 (1904); Frdl., 8, 327.
69. M. V. Gorelik, Symposium, "Organicheskie Poluprodukty i Krasiteli" (Organic Intermediates and Dyes), Izd. Khimiya, Moscow, 1969, p. 5.
70. N. S. Dokunikhin and L. I. Egorova, Dokl. Akad. Nauk SSSR, 67, 1033 (1949).
71. V. V. Russkikh, S. A. Russkikh, and E. P. Fokin, Zhur. Org. Khim., 7, 2409 (1971).
72. E. P. Fokin, V. V. Russkikh, S. A. Russkikh, and V. G. Mazur, Zhur. Prikl. Khim., 44, 2271 (1971).
73. S. A. Russkikh, V. A. Loskutov, and V. V. Russkikh, Zhur. Obshch. Khim., 44, 642 (1974).
74. M. V. Gorelik, M. I. Evstratova, and I. Ya. Koshcheeva, Zhur. Org. Khim., 4, 1465 (1968).
75. M. V. Gorelik and M. I. Evstratova, 4, 758 (1969).
76. M. V. Gorelik and T. F. Bezrukova, Khim. Geterotsikl. Soed., 1139 (1971).
77. M. V. Gorelik and T. F. Bezrukova, Zhur. Org. Khim., 5, 1840 (1969).
78. M. V. Gorelik and T. F. Bezrukova, Zhur. Org. Khim., 5, 1836 (1969).
79. M. V. Gorelik and T. F. Bezrukova, Geterotsikl. Soed., 1271 (1974).
80. M. V. Gorelik and T. F. Bezrukova, Geterotsikl. Soed., 1570 (1971).
81. M. V. Gorelik, B. E. Zaitsev, T. P. Kononova, and N. S. Dokunikhin, Geterotsikl. Soed., 780 (1968).
82. M. V. Gorelik and S. V. Dantsman, Geterotsikl. Soed., 447 (1968).
83. M. V. Gorelik, T. P. Kononova, and N. S. Dokunikhin, Geterotsikl. Soed., 463 (1968).
84. M. V. Gorelik and V. V. Puchkova, Zhur. Org. Khim., 5, 1695 (1969).
85. M. V. Gorelik, O. S. Zhdamarov, E. S. Levin, B. E. Zaitsev, and L. A. Chetkina, 7, 1044 (1971).
86. M. V. Gorelik and M. S. Kharash, Khim. Geterotsikl. Soed., 1574 (1971).
87. M. V. Gorelik and R. E. Smurova, Zhur. Vses. Khim., Obshch. im. Mendeleeva, 14, 476 (1969).
88. G. G. Dyadyusha and E. A. Ponomareva, Ukrain. Khim. Zhur., 29, 1279 (1963).
89. M. V. Kazankov and V. N. Ufimtsev, Zhur. Obshch. Khim., 34, 4124 (1964).

90. M. V. Kazankov and V.N. Ufimtsev, Khim.Geterotsikl. Soed., 315 (1966).
91. B. E. Zaitsev and T. A. Mikhailova, Khim.Geterotsikl. Soed., 812 (1974).
92. E. P. Fokin and R. P. Shishkina, Izv. Sibir. Otd. Akad. Nauk SSSR, No. 5, 104 (1969).
93. R. P. Shishkina, L. I. Shchegoleva, and L. V. Ektova, Izv. Sibir. Otd. Akad. Nauk SSSR, No. 6, 62 (1971).
94. S. B. Lantsman, Candidate's Thesis, NIOPiK, Moscow, 1969.
95. E. P. Fokin, S. A. Russkikh, and V. V. Russkikh, Izv. Sibir. Otd. Akad. Nauk SSSR, No. 5, 109 (1969).
96. N. N. Katmazovskii and G. V. Fomin, Zhur. Fiz. Khim., 46, 2427 (1972). [Russ. J. Phys. Chem., No. 9 (1972)].
97. G. V. Fomin, N. S. Dokunikhin, and A. N. Struve, Zhur. Fiz. Khim., 44, 1330 (1970) [Russ. J. Phys. Chem., No. 5 (1970)].
98. N. S. Dokunikhin, A. N. Struve, and G. V. Fomin, Zhur. Fiz. Khim., 45, 2651 (1971) [Russ. J. Phys. Chem., No. 10 (1971)].
99. N. P. Shimanskaya, G. B. Afanas'eva, K. I. Pashkevich, L. A. Kotok, I. Ya. Postovskii, and V. D. Bezuglyi, Zhur. Obshch. Khim., 41, 1106 (1971).
100. G. B. Afanas'eva, K. I. Pashkevich, I. Ya. Postovskii, V. G. Vykhristyuk, N. P. Shimanskaya, and V. D. Bezuglyi, Khim. Geterotsikl. Soed., 1345 (1972).
101. T. S. Viktorova, G. B. Afanas'eva, I. Ya. Postovskii, and L. V. Ivanova, Khim. Geterotsikl. Soed., 1196 (1974).
102. G. B. Afanas'eva and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 167 (1969).
103. G. B. Afanas'eva and I. Ya. Postovskii, Zhur. Obshch. Khim., 34, 3893 (1964).
104. G. B. Afanas'eva and I. Ya. Postovskii, Zhur. Org. Khim., 1, 1163 (1965).
105. G. B. Afanas'eva and I. Ya. Postovskii, Zhur. Obshch. Khim., 34, 1741 (1964).
106. K. I. Pashkevich, G. B. Afanas'eva, E. G. Kovalev, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 1316 (1970).
107. K. I. Pashkevich, G. B. Afanas'eva, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 746 (1971).
108. W. Brackman and E. Havinga, Rec. Trav. Chim., 74, 1107 (1955).
109. F. Kehrmann and M. Cordone, Ber., 46, 3009 (1913).
110. V. B. Barry, J. G. Belton, F. O. Sullivan, and D. Towney, J. Chem. Soc., 859 (1958).
111. M. M. Joullûe and I. P. Puthenpurayal, J. Heterocycl. Chem., 6, 697 (1960).
112. Yu. S. Tsizin and M. V. Rubtsov, Khim. Geterotsikl. Soed., 637 (1970).
113. Yu. S. Tsizin, Khim. Geterotsikl. Soed., 1253 (1974).
114. Yu. S. Tsizin and N. B. Karpova, Khim. Geterotsikl. Soed., 1698 (1971).
115. Yu. S. Tsizin and M. V. Rubtsov, Khim. Geterotsikl. Soed., 687 (1969).
116. A. V. Luk'yanov, V. G. Voronin, and Yu. S. Tsizin, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 15, 238 (1970).
117. A. V. Luk'yanov, V. G. Voronin, and Yu. S. Tsizin, Khim. Geterotsikl. Soed., 196 (1971).
118. N. B. Karpova and Yu. S. Tsizin, Khim. Geterotsikl. Soed., 1376 (1970).
119. R. C. Fuson and R. Gaertner, J. Org. Chem., 13, 496 (1948).
120. G. Barth and H. Schreder, Monatsh., 3, 799 (1882).
121. F. Sachs, Ber., 39, 3006, 3023, 3081 (1906).
122. H. Nozaki, Y. Yamamoto, and R. Noyuri, Tetrahedron Letters, 1123 (1966).
123. H. Nozaki, Y. Yamamoto, and T. Nisimara, Tetrahedron Letters, 4625 (1968).
124. G. A. Russel and S. A. Weiner, J. Org. Chem., 31, 248 (1966).
125. G. Barth and H. Schreder, Ber., 12, 417 (1879).
126. B. C. Boswell and J. Dickson, J. Amer. Chem. Soc., 40, 1786 (1918).
127. M. Sommelet, Compt. rend., 205, 56 (1937).
128. Ch. R. Hauser and S. W. Kantor, J. Amer. Chem. Soc., 73, 4122 (1951).
129. Ch. R. Hauser, J. K. Lindsey, and D. Lednicer, J. Org. Chem., 23, 358 (1958).
130. V. von Richter, Ber., 4, 21, 451, 553 (1871).
131. J. F. Bunnet, J. F. Cormac, and F. C. McKay, J. Org. Chem., 15, 481 (1950).
132. M. Rosenblum, J. Amer. Chem. Soc., 82, 3797 (1960).
133. V. G. Kharchenko, S. N. Chalaya, and T. M. Konovalov, Khim. Geterotsikl. Soed., 147 (1975).
134. R. A. Abramovitch, and J. G. Saha, "Advances in Heterocyclic Chemistry", New York, 1966, Vol. 6, p. 229.
135. A. F. Pozharskii and A. M. Simonov, "Amilirovanie Geterotsiklov po Chichibabinu" (The Chichibabin Amination of Heterocycles), Izd. Rostov. Univ., Rostov-on-Don, 1971.
136. E. Koenigs and E. Ruppelt, Annalen, 509, 142 (1934).
137. W. E. McEwen, R. H. Terss, and I. W. Elliott, J. Amer. Chem. Soc., 74, 3605 (1952).
138. H. von Dobeneck, H. Deubel, and F. Heilhell, Angew. Chem., 71, 310 (1959).
139. H. Adkins and O. Thompson, J. Amer. Chem. Soc., 71, 2242 (1949).
140. W. Doering and W. E. McEwen, J. Amer. Chem. Soc., 73. 2104 (1951).
141. M. Colonna and P. Bruni, Atti. Sci. Ist. Bologna Cl. Sci. Fis., 3, 11 (1968); Chem. Abs., 71, 49660 (1969).
142. V. E. Kirichenko and O. N. Chupakhin, Khim. Geterotsikl. Soed., 658 (1974).
143. O. N. Chupakhin and V. L. Rusinov, Khim. Geterotsikl. Soed. (1976) (in the Press).
144. K. Nakamura, N. Jasuoka, N. Kasai, and H. Mikawa, Chem. Comm., 1175 (1970).
145. E. M. Kosower, J. Amer. Chem. Soc., 82, 3253, 3261, 3267 (1958).
146. R. S. Mulliken and W. B. Person, "Molecular Complexes", John Wiley, New York, 1969.
147. C. G. Swain and C. Scott, J. Amer. Chem. Soc., 75, 141 (1953).
148. J. Edwards, J. Amer. Chem. Soc., 78, 1819 (1956).
149. K. W. Wallenfels and H. Schüly, Annalen, 621, 86 (1959).
150. K. Wallenfels and H. Schüly, Annalen, 621, 178 (1959).
151. K. Wallenfels and H. Schüly, Annalen, 621, 188 (1959).
152. A. Kaufmann and A. Albertini, Ber., 42, 3776 (1909).
153. M. Marti, M. Viskontini, and P. Karrer, Helv. Chim. Acta, 39, 145 (1956).
154. A. Kaufmann, Ber., 51, 116 (1918).
155. K. Reissert, Ber., 38, 1905, 1603, 3415 (1905).
156. F. Popp, "Advances in Heterocyclic Chemistry", New York, 1968, Vol. 9, p. 1.
157. J. W. Happ, E. Janzen, and B. C. Rudy, J. Org. Chem., 35, 3882 (1970).
158. C. Tinkler, J. Chem. Soc., 856 (1906).
159. J. Baumrucker, J. Phys. Chem., 74, 1152 (1970).

160. R. Lille and G. Gawthier, Tetrahedron Letters, 4615 (1965).
161. L. Winters, N. Smith, and M. Cohen, Chem. Comm., 642 (1970).
162. A. F. Pozharskii, V. V. Kuz'mina, I. S. Kashparov, V. I. Sokolov, and M. M. Medvedeva, Khim. Geterotsikl. Soed., (1976) (in the press).
163. A. Pictet and N. Patry, Ber., 35, 2534 (1902).
164. H. Decker, Ber., 25, 3326 (1892).
165. F. Kröhnke and K. Ellegast, Annalen, 600, 176 (1956).
166. O. Dimroth and R. Griege, Ber., 90, 2207 (1957).
167. F. Kröhnke and I. Vogt, Annalen, 600, 211 (1956).
168. E. Hayashi, J. Pharm. Soc. Japan, 79, 969 (1959); Chem. Abs., 53, 21934 (1959).
169. T. Severin, H. Lerche, and D. Bätz, Ber., 102, 2163 (1969).
170. T. Severin, D. Bätz, and H. Lerche, Ber., 101, 2731 (1968).
171. R. M. Burton and N. O. Kaplan, J. Biol. Chem., 206, 283 (1954).
172. H. J. Leonard, H. A. De Walt, and G. M. Leubner, J. Amer. Chem. Soc., 73, 3325 (1951).
173. F. Kröhnke and H. L. Honig, Annalen, 624, 97 (1959).
174. E. Hayashi and T. Naruka, J. Pharm. Soc. Japan, 87, 570 (1969); Chem. Abs., 67, 64228 (1967).
175. F. Kröhnke and H. L. Honig, Ber., 90, 2215 (1957).
176. V. E. Posazhennikova, O. N. Chupakhin, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 1384 (1970).
177. O. N. Chupakhin, V. E. Kirichenko, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 1116 (1974).
178. O. N. Chupakhin, V. Poushkareva, J. Ya. Postovskii, V. A. Trofimov, V. Je. Posajennikova, and V. L. Rusinov, "Proceedings of the Third International Congress on Heterocyclic Chemistry, Sendai, Japan, 1971", p. 311.
179. V. E. Kirichenko, Candidate's Thesis, the Polytechnic Institute, Sverdlovsk, 1972.
180. N. N. Zatsepina and I. S. Tupitsyn, Khim. Geterotsikl. Soed., 1587 (1974).
181. R. Grewe and A. Mondon, Ber., 81, 279 (1948).
182. R. F. Stadnilchuk, G. D. Pilyugin, and O. E. Petrenko, Zhur. Obshch. Khim., 40, 1834 (1970).
183. W. Bradley and S. Jeffey, J. Chem. Soc., 2770 (1954).
184. J. Knabe and H. Holtje, Tetrahedron Letters, 433 (1969).
185. N. B. Eddy, J. G. Murky, and E. L. May, J. Org. Chem., 22, 1370 (1957).
186. D. N. Kursanov and N. K. Baranetskaya, Izv. Akad. Nauk SSSR, Ser. Khim., 1763 (1961).
187. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, Dokl. Akad. Nauk SSSR, 188, 376 (1969).
188. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, Khim. Geterotsikl. Soed., 954 (1969).
189. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, Khim. Geterotsikl. Soed., 1674 (1970).
190. V. A. Trofimov, O. N. Chupakhin, and Z. V. Pushkareva, Khim. Geterotsikl. Soed., 653 (1971).
191. V. A. Trofimov, O. N. Chupakhin, Z. V. Pushkareva, and V. L. Rusinov, Khim. Geterotsikl. Soed., 112 (1971).
192. V. L. Rusinov, O. N. Chupakhin, N. I. Kollegova, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 216 (1972).
193. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, USSR P. 215999; Byul. Izobret, No. 28 (1968).
194. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, USSR P. 271697; Byul. Izobret., No. 18 (1970).
195. V. A. Trofimov, O. N. Chupakhin, and Z. V. Pushkareva, USSR P. 292976; Byul. Izobret., No. 15 (1971).
196. O. N. Chupakhin, V. I. Shilov, I. Ya. Postovskii, and V. A. Trofimov, Khim. Geterotsikl. Soed., 1975.
197. G. T. Pilyugin, A. A. Malakhova, O. M. Stashkevich, and V. V. Stashkevich, Zhur. Vses. Khim. Obshch. im. Mendeleeva, 14, 263 (1963).
198. T. L. Pilicheva, O. N. Chupakhin, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 561 (1975).
199. V. A. Trofimov, Candidate's Thesis, The Polytechnic Institute, Sverdlovsk, 1969.
200. S. Kitaura, Proc. Faculty Sci. Tokai Univ., 1, 63 (1965).
201. A. A. Deikalo, Candidate's Thesis, The State University, Donetsk, 1971.
202. O. N. Chupakhin, E. O. Sidorov, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 1433 (1975).
203. T. L. Pilicheva, Candidate's Thesis, The Polytechnic Institute, Sverdlovsk, 1975.
204. V. L. Rusinov, Candidate's Thesis, The Polytechnic Institute, Sverdlovsk, 1973.
205. A. K. Sheinkman, S. G. Potashnikova, and S. N. Barnov, Khim. Geterotsikl. Soed., 614 (1970).
206. O. N. Chupakhin, V. L. Rusinov, I. Ya. Postovskii, and V. N. Charushin, Khim. Geterotsikl. Soed., 387 (1975).
207. O. N. Chupakhin, V. L. Rusinov, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 284 (1972).
208. I. Ya. Postovskii, O. N. Chupakhin, and V. L. Rusinov, Dokl. Akad. Nauk SSSR, 209, 122 (1973).
209. O. N. Chupakhin, V. N. Charushin, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 1578 (1975).
210. V. A. Trofimov, O. N. Chupakhin, and Z. V. Pushkareva, Dokl. Akad. Nauk SSSR, 191, 1302 (1970).
211. E. Buncell and J. G. K. Webb, J. Amer. Chem. Soc., 95, 8470 (1973).
212. A. Albert, Angew. Chem., 21, 913 (1967).
213. A. K. Sheinkman, S. G. Potashnikova, and S. N. Baranov, Khim. Geterotsikl. Soed., 1295 (1970).
214. D. Redmore, J. Org. Chem., 34, 1420 (1969).
215. A. K. Sheinkman, A. N. Kost, S. G. Potashnikova, A. O. Ginzburg, and S. N. Baranov, Khim. Geterotsikl. Soed., 640 (1971).
216. O. N. Chupakhin, E. O. Sidorov, I. I. Bil'kis, and S. M. Shein, Zhur. Org. Khim. (1976) (in the Press).
217. A. R. Surrey, "Name Reactions in Organic Chemistry" (Translated into Russian), GKhI, Moscow, 1962, p. 214.
218. K. Blaha and O. Cervinka, "Advances in Heterocyclic Chemistry", New York, 1966, Vol. 6, p. 84.
219. Y. Otsuji, K. Yutani, and F. Unoto, Bull. Chem. Soc. Japan, 44, 520 (1971).
220. G. Fraekel and J. C. Cooper, Tetrahedron Letters, 1825 (1968).
221. R. A. Foster and C. A. Fyfe, Tetrahedron, 25, 1489 (1969).
222. C. S. Gian and J. L. Shout, Chem. Comm., 142 (1969).
223. S. Pietra and G. Casiraghi, Gazzetta, 100, 138 (1970).
224. I. Ya. Postovskii, O. N. Chupakhin, T. L. Pilicheva, and Yu. Yu. Popelis, Dokl. Akad. Nauk SSSR, 212, 1125 (1973).
225. O. N. Chupakhin, E. O. Sidorov, and I. Ya. Postovskii, Khim. Geterotsikl. Soed., 993 (1974).
226. A. R. Katritzky, Chimia (Switz.), 24, 134 (1970).
227. E. O. Sidorov, Candidate's Thesis, The Polytechnic Institute, Sverdlovsk, 1975.

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