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Electrophilic Amination†

E.Schmitz

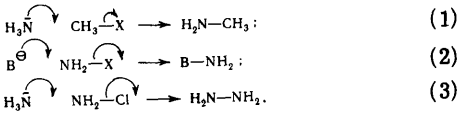
The review is devoted to reactions in which amino-, alkylamino- and acylamino-groups are transferred to nucleophilic agents. Electrophilic aminating agents are chloramine, hydroxylamine-*O*-sulphonic acid, oxaziridines unsubstituted at the nitrogen atom, and *N*-acyloxaziridines. The formation of three-membered rings with two heteroatoms, occurring as intramolecular electrophilic amination, is discussed.
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I. INTRODUCTION

The majority of the reactions with the aid of which amino-nitrogen is introduced into molecules proceed as nucleophilic substitutions. The nucleophilic agent is ammonia or an amine, which substitutes another group, for example, in the interaction of ammonia with alkyl halides [reaction (1)]. These reactions have been known for a long time, have been thoroughly investigated, and are therefore not considered in this review.



(1)

(2)

(3)

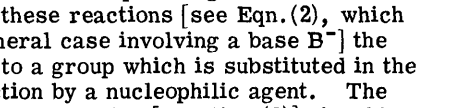
Substitution reactions in which nitrogen-containing compounds behave as electrophilic agents are encountered more rarely. In these reactions [see Eqn.(2), which formulates the general case involving a base B^-] the nitrogen is linked to a group which is substituted in the course of the reaction by a nucleophilic agent. The Raschig synthesis of hydrazine [reaction (3)], in which chloramine aminates an ammonia molecule via an electrophilic mechanism [1], is a prototype of reactions of this kind. Together with chloramine, hydroxylamine-*O*-sulphonic acid later came to be used as an aminating agent [2]. The ability of certain oxaziridines to transfer NH and NCOR groups has been discovered in recent years [3]. Reactions of compounds of this type are very similar and are treated in this review as electrophilic amination. The reactions involving transfer of nitrogen-containing groups in which the intermediate formation of nitrenes has been firmly established or postulated are not discussed. A number of reviews have been devoted to such reactions [4-7]. Reactions in which the intermediate stage proceeds via the solvolysis of chloramines, nitrenium ions, and cations with an electron sextet are likewise disregarded [8].

† Translated into Russian from German by T.A.Burtseva and retranslated into English.

II. REACTIONS OF CHLORAMINE AND SUBSTITUTED CHLORAMINES

An example of electrophilic amination with the aid of chloramine which has been known for a long time and has been most thoroughly investigated is the Raschig synthesis of hydrazine [1]. It has been firmly established that, in contrast to frequently expressed hypotheses, 1,1-elimination from chloramine followed by the interaction of NH with ammonia does not occur and there is instead a synchronous dissociation of the N–Cl bond and the formation of the N–N bond [see Eqn.(3)] [9].

The role of the base in the initial method for the synthesis of hydrazine can be accounted for by partial deprotonation to give the chloramide anion. Thus the formation of hydrazine should be regarded as electrophilic amination in which chloramine and the chloramide anion behave as competing electrophilic agents:

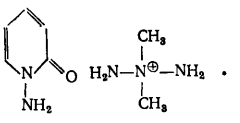


(4)

Later studies of the interaction of chloramine with primary [10], secondary [11], and tertiary [12] amines showed that the presence of a strong base is not a precondition for the formation of the N–N bond: the majority of studies on the synthesis of alkylhydrazines have been carried out with chloramine–ammonia mixtures, obtained by the gas-phase chlorination of ammonia, which were combined with amines without adding a strong base. It has been shown [13] that the amination of tertiary amines by chloramine follows second-order kinetics. The ratios of the rates of interaction of ammonia, n-propylamine, and di-n-propylamine with chloramine are 1 : 140 : 460. [14]

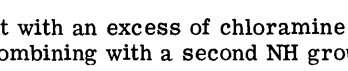
The interactions of chloramine with the most important classes of nucleophilic agents and their anions have been studied in the last 20 years. In base-catalysed amination 2-pyridone gives rise to 1-aminopyridone (I); [15] on interaction with chloramine, *NN*-dialkylhydrazines form triazanium salts (II). [16,17] Phosphites give rise to aminophosphonium chlorides (III), [18] triphenylarsine and stibines are converted into arsonium and stibonium salts (IV) and

(V),[20] while aminosulphinium salts (VI) are formed from thioethers[21].



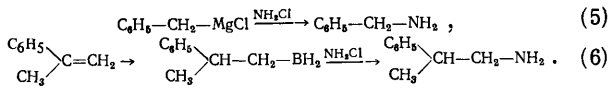
(I) (II)

On treatment with an excess of chloramine, the latter are capable of combining with a second NH group[22,23].



(III) (IV) (V) (VI)

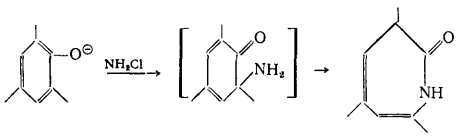
Relatively little is known about amination at a carbon atom. The interaction of chloramine with a Grignard reagent[24], which makes it possible, for example, to obtain a good yield of benzylamine from benzylmagnesium chloride [Eqn.(5)], was achieved comparatively long ago. Subsequently chloramine was used to convert into amines, via reaction (6), the products of the hydroboration of olefins[25]:



(5)

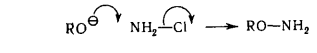
(6)

When polyalkylphenols react with chloramine, amination at the oxygen atom does not occur, as believed previously; instead, the ring is expanded to give a lactam in which the first stage must be regarded as *C*-amination[26]:



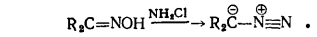
(7)

On the other hand, *O*-amination is possible for alkoxides and it has been suggested for the synthesis of *O*-alkylhydroxylamines[27]:



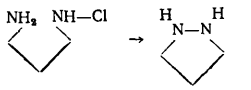
(8)

We may also recall the interaction of chloramine with oximes to form diazo-compounds, which was known previously only for a diketomonoxime[28], was later extended to simpler ketoximes[20], and was used finally to synthesise diazomethane [Eqn.(9)]:[30]



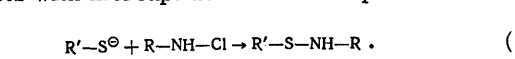
(9)

Analysis of the extensive literature on chloramine leads to the striking observation that only a few reactions of chloramine can be extended to *N*-chloroalkylamines. The formation of the N–N bond between the amine and *N*-chloroalkylamine can be achieved only with simultaneous ring closure[31]:



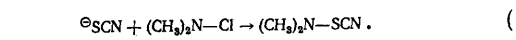
(10)

The interaction of *N*-chloroalkylamines, RNHCl, and *N*-chlorodialkylamines, R_2NCl, via the electrophilic amination mechanism has been described only for powerful nucleophilic agents, in particular for sulphur- and phosphorus-containing compounds. For example, chloramine reacts with mercaptides to form sulphenamides[32]:



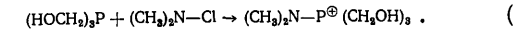
(11)

Thiocyanate is aminated by reaction with *N*-chlorodialkylamines to form *N*-thiocyanatoamines[33]:



(12)

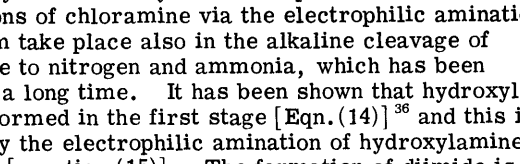
Tri(hydroxymethyl)phosphine reacts with *N*-chlorodimethylamine to form the N–P bond[34]:



(13)

The amination of azide ions to give substituted aminoazides has been reported[33]. The amination of Grignard reagents by *N*-chloroalkylamines is possible[35].

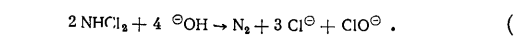
Reactions of chloramine via the electrophilic amination mechanism take place also in the alkaline cleavage of chloramine to nitrogen and ammonia, which has been known for a long time. It has been shown that hydroxylamine is formed in the first stage [Eqn.(14)][36] and this is followed by the electrophilic amination of hydroxylamine to diimide [reaction (15)]. The formation of diimide is confirmed by the powerful hydrogenating effect in the decomposition of chloramine in alkaline solutions; for example, cinnamic acid is hydrogenated under these conditions of hydrocinnamic acid[37]:



(14)
(15)
(16)
(17)
(18)

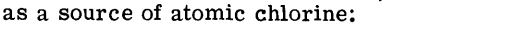
Bearing in mind that, on disproportionation, two diimide molecules form nitrogen and hydrazine and that the latter may be oxidised to diimide, which requires the consumption of yet another chloramine molecule, it is possible to obtain a sequence of reactions [reactions (14)–(17)], which reflects the overall formation of nitrogen and ammonia from three chloramine molecules [Eqn.(18)].

The alkaline decomposition of dichloramine, in which two molecules of the latter decompose with formation of nitrogen, chlorite, and hypochlorite, has been studied recently[38]:



(19)

The pronounced chlorinating effect on substrates, subjected to the action of radicals (for example ethyl ether or cyclohexene), observed in the decomposition of dichloramine in alkaline media, permitted the conclusion that the reaction begins with electrophilic amination and the formation of trichlorohydrazine. The elimination step then results in the formation of dichlorodiimide, which is regarded as a source of atomic chlorine:



(20)

The reactions with *N*-halogenoamines have been recently discussed by Kovacic et al.[39]

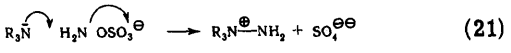
III. REACTIONS OF HYDROXYLAMINE-*O*-SULPHONIC ACID AND *O*-ACYL DERIVATIVES OF HYDROXYLAMINE

Another widely used aminating agent is hydroxylamine-*O*-sulphonic acid (HSA). It was obtained for the first time by Sommer and coworkers[2,40], who also discovered the

ability of HSA to convert primary and secondary aliphatic and aromatic amines into hydrazines.

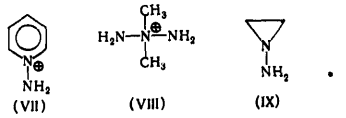
It follows from the data of these investigators, who later studied the preparative use of HSA, that the rate of reaction depends on the nature of the compound aminated. For example, secondary amines react with HSA at 0°C in the course of several hours and tertiary amines react in a few minutes[41]. Evidently, the nucleophilic agent is involved in the rate-limiting stage of the reaction.

The preliminary decomposition of HSA to NH and sulphate, which has been sometimes suggested, is therefore unlikely. Furthermore, it has been shown that the reversible decomposition to NH and sulphate does not occur either: partial decomposition of HSA in dilute NaOH solution in the presence of labelled sulphate does not result in the formation of radioactive HSA.[42] Therefore, an electrophilic mechanism in which a new linkage is formed and sulphate is displaced synchronously, must be adopted for all amination reactions with the aid of HSA, which are faster than the decomposition of HSA in the absence of a nucleophilic agent:



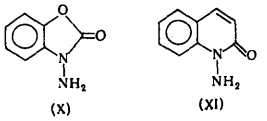
(21)

Subsequently amination by HSA was developed into a preparative method for the synthesis of substituted hydrazines. Gever and Hayes[43] obtained ethyl-, propyl-, isopropyl-, n-butyl-, n-pentyl-, and 2-hydroxyethylhydrazines by the amination of primary amines. An excess of the amine is usually employed in order to suppress the self-decomposition of HSA in an alkaline medium and the subsequent reaction of the resulting hydrazine with HSA. Gösl and Meuwsen[41] and Sisler et al.[44] reported almost simultaneously the synthesis of hydrazine from HSA. The former investigators were able to aminate primary, secondary, and tertiary aliphatic amines to give the corresponding hydrazines. Sisler et al. aminated in accordance with Eqn.(21) tertiary aliphatic amines and dimethylaniline to form hydrazinium salts. Under suitable conditions, aniline is converted into phenylhydrazine in 80% yield[41]. Pyridine gives rise to the *N*-aminopyridinium cation (VII). The corresponding products are obtained from alkylpyridines and quinoline. *NN*-Dimethylhydrazine is aminated to give the dimethyltriazanium cation (VIII):[45]



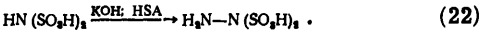
(VII) (VIII) (IX)

The amination of aziridine to an *N*-amino-derivative (IX) has been described[46], but the yield is low. In certain cases an acylated nitrogen atom is sufficiently nucleophilic after deprotonation to be aminated by HSA. Thus, cyclic acid amides, for example compounds (X) and (XI), have been converted into hydrazides with the aid of HSA.[47] Evidently, simple acid amides have not, as yet, been made to undergo this type of reaction.



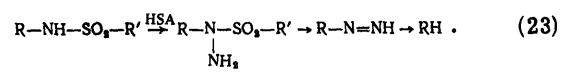
(X) (XI)

Hydrazineisodisulphonate is obtained comparatively easily in accordance with Eqn.(22):[48]



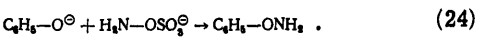
(22)

In the presence of a large excess of HSA, the *N*-alkyl group is split off from sulphonamides in the form of a hydrocarbon. Under these conditions, *N*-amination probably takes place with subsequent elimination of the sulphinate residue[49]:



(23)

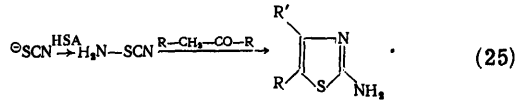
Alkoxides react via the electrophilic amination mechanism with formation of *O*-alkylhydroxylamines. *O*-Alkylhydroxylamines have been obtained from simple C_2–C_4 alcohols and benzyl alcohol in yields of 27–49%.[50] In the presence of KOH, phenol is aminated by HSA to *O*-phenylhydroxylamine[51]:



(24)

Similarly to the reaction employing chloramine, triphenylphosphine and thioethers can be aminated with the aid of HSA.[52] In the latter case only one NH group adds on. Xanthates also react with formation of the S–N bond[53].

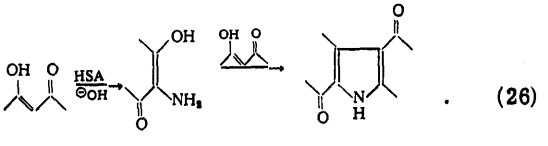
Thiocyanate is smoothly aminated in an aqueous alkaline solution. The thiocyanatoamine formed is of interest because it converts ketones into aminothiazoles in satisfactory yields[54]:



(25)

The olefin hydroboration products can be converted by the Brown reaction into amines by a treatment not only with chloramine but also with HSA.[24]

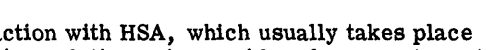
Relatively little is known about the electrophilic amination of carbanions, although in the instances described the reaction proceeds very smoothly. In dilute NaOH solution, acetylacetone reacts with HSA below room temperature in the course of several minutes. If two moles of the diketone per mole of HSA are used, the amination product condenses with the excess diketone into a pyrrole derivative[55,56]:



(26)

Acetoacetic ester derivatives also give rise to pyrrole compounds.

Hieber and Buetner[57] aminated the hydrogen tetracarbonylferrate anion:



(27)

When the reaction with HSA, which usually takes place in aqueous alkaline solutions, is considered, account must be taken of the competing alkaline decomposition of HSA. In the case of chloramine this decomposition leads to the formation of a mole of NH_3 and N_2. This overall result [see Eqn.(32)] can also be represented by a series of

amination stages [Eqns.(28)–(31)].[58] The reaction begins with the amination of the hydroxide ion; it has been shown with the aid of ^{18}O that the oxygen in the hydroxylamine produced originates from water[59]. The amination of hydroxylamine to diimide has been demonstrated by the fact that double bonds are hydrogenated both in the alkaline decomposition of HSA and in the reaction occurring in a mixture of HSA and hydroxylamine[58]:

$$HO^{\ominus} + HSA \rightarrow HO{-}NH_2 , \quad (28)$$

$$HONH_2 + HSA \rightarrow HN{=}NH , \quad (29)$$

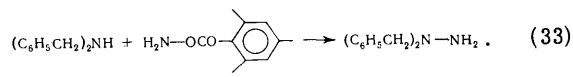
$$2\,HN{=}NH \rightarrow N_2 + N_2H_4 , \quad (30)$$

$$N_2H_4 + HSA \rightarrow H_2N{-}NH{-}NH_2{-}HN{=}NH{+}NH_3 , \quad (31)$$

$$3\,HSA \rightarrow N_2 + NH_3 . \quad (32)$$

The hypothesis of the formation of triazane at an intermediate stage in reaction (31) has been proved by the fact that the reaction of [^{15}N]hydrazine with HSA results in the formation of some labelled NH_3.[58]

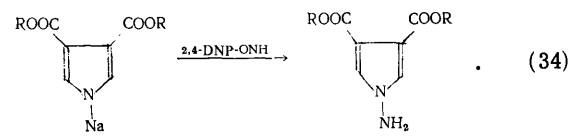
There has been no lack of attempts to discover other electrophilic aminating agents. These began with hydroxylamine containing an active group capable of being eliminated. The first studies were carried out by Carpino[60], who found that *O*-mesitoylhydroxylamine aminates dibenzylamine to dibenzylhydrazine:



(33)

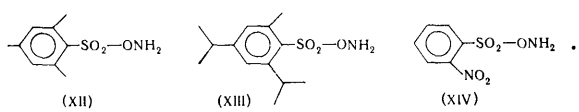
The same investigator reported later[51] the amination of carbazole to *N*-aminocarbazole (in 60% yield), of naphthalimide to *N*-aminonaphthalimide (in 81% yield), of benzylbenzamide to the corresponding hydrazine, of *N*-tosylated 1-aminomethylnaphthalene to the *N*-amino-derivative, and of t-butyliminodicarboxylate to the corresponding hydrazine derivative[62].

Sheradski[63] discovered the effective aminating activity of *O*-(2,4-dinitrophenyl)hydroxylamine. He was able to aminate in 88–95% yield sodium phthalimide, *N*-tosylbenzylamine, and pyrrole-3,4-dicarboxylate ester[63]:



(34)

CH acids, such as methyl fluorene-9-carboxylate and diethyl phenylmalonate, are also aminated[64]. Tamura and coworkers[65–67] achieved electrophilic amination with the aid of *O*-mesitylenesulphonylhydroxylamine (XII), *O*-picrylhydroxylamine, and two other *O*-sulphonated hydroxylamines [compounds (XIII) and XIV)]:

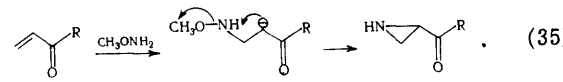


(XII) (XIII) (XIV)

It proved possible to aminate tri-n-butylamine, diphenyl sulphide, diphenyl sulphoxide, triphenylphosphine, quinoline, pyridazine, pyridine, and substituted pyridines. The amination of tertiary amines takes place particularly smoothly and is used to synthesise *N*-amino-derivatives of alkaloids[68].

IV. THE SYNTHESIS OF THREE-MEMBERED RINGS WITH TWO HETEROATOMS

The formation of a new bond in electrophilic amination plays an insignificant role in the syntheses of three-membered rings with a single heteroatom. Of the large number of syntheses of aziridines, mention should be made only of the reaction of $\alpha\beta$-unsaturated ketones with *O*-alkylhydroxylamines, which may be regarded as electrophilic amination[70]:

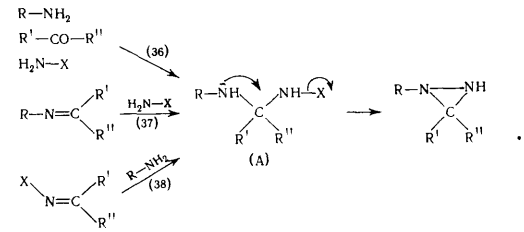


(35)

However, electrophilic amination is a dominant process in the synthesis of three-membered rings with two heteroatoms. If one disregards certain photochemical reactions, the three-membered ring is formed in this case always with the closure of the bond between the two heteroatoms. In the synthesis of diaziridines this bond is always formed as a result of electrophilic amination.

Syntheses of Diaziridines

Numerous versions of the synthesis of $\overbrace{C-N-N}$ rings are known. It proceeds as the reaction between a carbonyl compound, an amine, and an aminating agent, and it is frequently immaterial whether all three reactants are made to react simultaneously [Eqn.(36)], or whether the carbonyl compound and the amine form initially a Schiff base which then reacts with the aminating agent [Eqn.(37)], or whether the product of the condensation of the carbonyl compound and the aminating agent is made to react with the amine [Eqn.(38)]. Ring closure via the geminal stage (A) is an intramolecular analogue of the Raschig hydrazine synthesis.



The synthesis of diaziridines with three substituents R, R′, and R″ is restricted to aliphatic compounds but is of general importance in this field. The nitrogen of the aminating agent can also carry an additional alkyl group.

The following versions of the synthesis of diaziridines, which usually takes place with satisfactory yields, have been described.

1. Ketone + NH_3 + $ClNH_2$. In this process ammonia is subjected to gas-phase chlorination and is made to react with acetone[71] or a stream of NH_3 + $ClNH_2$ is passed through the liquid ketone[72].

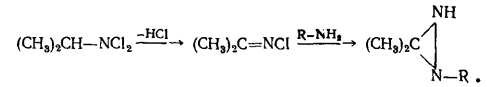
2. Schiff base + $ClNH_2$.[73] The reaction is carried out in an organic solvent. In this case *N*-chloroalkylamines react just as effectively as chloramine, which may be used to synthesise *NN′*-dialkylated diaziridines.

3. Ketone + NH_3 + HSA.[74]

4. Ketone + imine + HSA.[75]

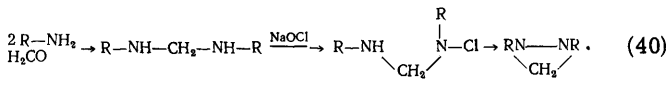
5. *N*-Chloramino-derivative of ketone + NH_3 or amine[76].

This method may be simplified when the *N*-chloriminoderivative of the ketone (XVI) can be obtained during the synthesis by eliminating HCl from *NN*-dichloramine (XV):[77]



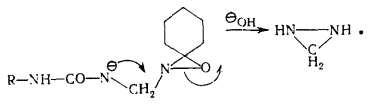
(39)

6. Oxime-*O*-sulphonic acid ($R_2C{=}N{-}OSO_3H$) + amine[78].
7. Schiff base + 3,3-dialkylaziridine[79].
8. Alkaline solutions of formaldehyde and a primary amine, in which the presence of methylenediamines may be postulated, react with hypochlorite to form diaziridines[80]:



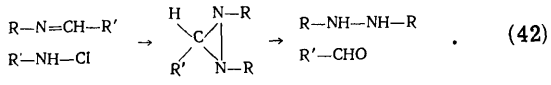
(40)

9. The diaziridine skeleton is formed in a reaction in which it is possible to isolate a geminal intermediate stage corresponding to the intermediate stage postulated in Eqns. (36)–(38) and (40):[81]



(41)

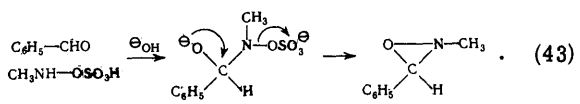
The particular importance of the synthesis of diaziridines consists in the fact that their formation is a stage in the economical syntheses of mono- and di-substituted hydrazines, which are readily formed on acid hydrolysis of diaziridines. For example, *NN*-dialkylhydrazines, which cannot be obtained by direct interaction of an amine and an *N*-chloroalkylamine, can be easily synthesised via a diaziridine by the reaction of primary amines (in the form of Schiff bases) and an *N*-chloroalkyl amine[82]:



(42)

Syntheses of Oxaziridines

In certain cases the two-component reaction of a carbonyl compound and an aminating agent leads to the formation of the oxaziridine ring[83]:

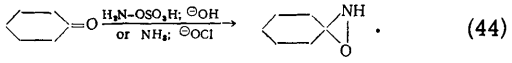


(43)

In this case it is also possible to postulate the formation at an intermediate stage of a product resulting from addition to the carbonyl group; this is indicated, for example, by the observation that in a series of cyclic ketones the maximum yield corresponds to the six-membered ketone. Ring closure is again represented as electrophilic amination. As was to be expected for electrophilic amination, ring closure has to be catalysed by a strong base, since oxygen becomes sufficiently nucleophilic only after deprotonation.

Such syntheses of oxaziridines have been achieved using simple aliphatic ketones, cyclohexanone, and certain aromatic aldehydes. *N*-Chloromethylamine or methylhydroxylamine-*O*-sulphonic acid are usually employed as aminating agents. For higher alkyl substituents, the yields are sharply reduced.

Treatment of suitable aldehydes or ketones in an alkaline medium by aminating agents without alkyl groups leads to oxaziridines unsubstituted at the oxygen atom. The reaction has been thoroughly investigated for cyclohexanone, which gives rise to 3,3-pentamethyleneoxaziridine in 50% yield on treatment with HSA in dilute NaOH solution[79]:

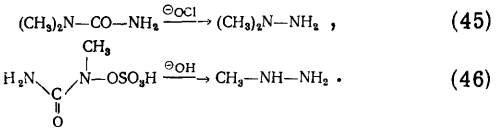


(44)

The synthesis of 3,3-pentamethyleneoxaziridine can be achieved even more simply by treating cyclohexanone with NH_3 and sodium hypochlorite[84]. The yield is about 70%. Both reactions are extremely fast. The interaction of cyclohexanone with NH_3 and hypochlorite takes place at 0° in 30 s and is at least 1000 times faster than the alkaline decomposition of chloramine in the absence of ketone. Thus the latter is involved in the rate-limiting stage of the process. One can also assume the addition of chloramine (or HSA) to the carbonyl group, which is followed by intramolecular electrophilic amination.

Diaziridinones, Iminodiaziridines, and Thiadiaziridine 1,1-Dioxides

The formation of hydrazine on treatment of urea with hypochlorite has been known for a long time[85]. To account for the course of the reaction, it is insufficient to employ the analogy with the Hofmann degradation of amides, since Ohme and Preuschhof were able to show that, although the reaction of asymmetric dimethylurea with hypochlorite yields *NN*-dimethylhydrazine [Eqn. (45)], *N*-hydroxy-*N*-methylurea-*O*-sulphonic acid (XVII) acted upon by alkali also reacts with formation of the N–N bond and gives rise to methylhydrazine [Eqn. (46)][86,87]:



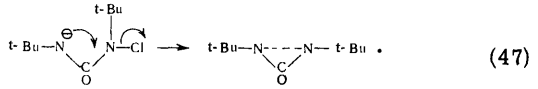
(45)

(46)

(XVII)

The first compound may be deprotonated by *N*-chlorination at the nitrogen atom, which is already linked to chlorine, creating thereby the structural precondition for the Hofmann amide degradation. In compound (XVII) only the unsubstituted nitrogen is deprotonated, which makes it more likely that the N–N bond is formed by intramolecular closure to give an intermediate three-membered ring.

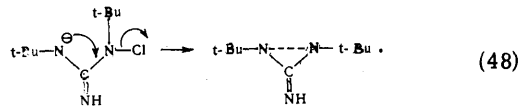
Indeed, in the presence of t-alkyl substituents at both nitrogen atoms of urea, stable diaziridinones were obtained[88]:



(47)

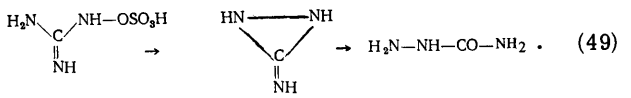
Later it was possible to obtain similarly iminodiaziridines.

N-Chlorination of t-alkylguanidines and base-catalysed ring closure result in the formation of a three-membered ring[89]:



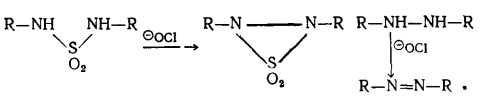
(48)

Before this, experiments with ^{15}N showed that semicarbazide is formed from hydroxyguanidine-*O*-sulphonic acid via an intermediate symmetrical stage, for which the structure of an iminodiaziridine was postulated[90]:



(49)

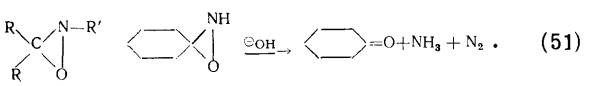
The formation of dialkylhydrazines and isoalkanes from dialkylsulphonamides by reaction with hypochlorite also proceeds via a three-membered cyclic stage, which has been recently demonstrated by the isolation of stable thiadiaziridine 1,1-dioxide[92]:



(50)

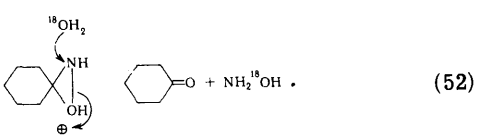
V. AMINATION BY OXAZIRIDINES UNSUBSTITUTED AT THE NITROGEN ATOM

While *N*-alkyloxaziridines (XVIII) are incapable of transferring their nitrogen to other molecules, such ability is shown to a marked extent by oxaziridines (XIX) unsubstituted at the nitrogen atom, which are comparable as regards effectiveness to aminating agents known for a long time, such as chloramine and HSA. All three types of compounds are decomposed by sodium hydroxide in the same way—with formation of NH_3 and N_2:



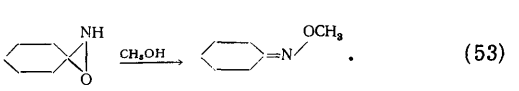
(XVIII) (XIX) (51)

Although cleavaged by aqueous acid solution, which in the case of *N*-alkyloxaziridines is of the same type as the cleavage of acetals and leads to the formation of a carbonyl compound and an alkylhydroxylamine, has the same preparative result for compound (XIX) (the formation of a ketone and hydroxylamine), the reaction proceeds via an amination mechanism: acid hydrolysis of compound (XIX) in the presence of $H_2^{18}O$ yields hydroxylamine containing the ^{18}O isotope (52.6%). Thus amination of water competes with cleavage via the acetal mechanism[93]:



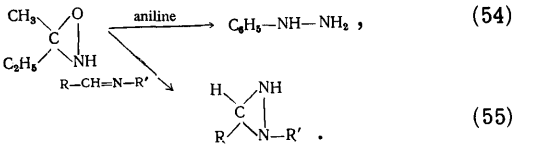
(52)

The occurrence of electrophilic amination when suitable nucleophilic agents are employed has been confirmed by the reaction products. Methanol is aminated by 3,3-pentamethyleneoxaziridine (XX) with formation of the O–N bond when the reaction is catalysed by both methoxide and strong acids[94]:



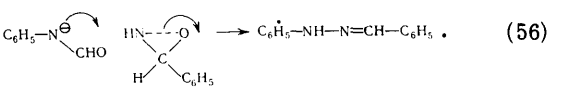
(XX) (53)

Aniline gives rise to phenylhydrazine [Eqn(54)], albeit in a yield of only 20%.[79] Aliphatic Schiff bases are aminated to diaziridines in satisfactory yields [Eqn.(55)]:[79]



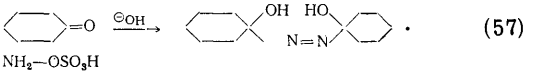
(54) (55)

Acid amides are aminated only in the presence of strong bases as catalysts (this has been observed also for other aminating agents); after deprotonation, the amide nitrogen becomes sufficiently nucleophilic. Thus treatment of formanilide with 3-phenyloxaziridine results in the formation of benzaldehyde phenylhydrazone [reaction (56)][94]. It is remarkable that, when 3-phenyloxaziridine is decomposed by ethoxide in the absence of formanilide, a small amount of benzaldehyde phenylhydrazone is also formed. Evidently, 3-phenyloxaziridine rearranges to formanilide under the influence of the base (the two compounds are isomeric), this being following by amination in accordance with Eqn.(56):



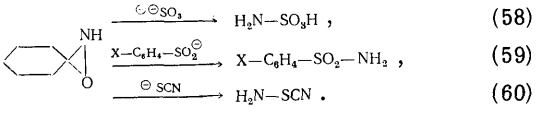
(56)

The intermediate formation of 3,3-pentamethyleneoxaziridine as the aminating agent can also be postulated in the synthesis of 1,1-dihydroxyazocyclohexane from cyclohexanone and HSA:[94]



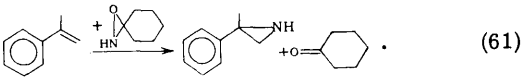
(57)

As was to be expected, strongly nucleophilic sulphur compounds are readily aminated by 3,3-pentamethyleneoxaziridine. For example, the reduction with sodium sulphite solution proceeds as amination of sulphur: sulphamic acid was isolated from the reaction mixture [Eqn.(58)][93]. The reaction with sulphinate anions also proceeds smoothly. Neutralised solutions of toluene-*p*-sulphinic acid or of *p*-chlorobenzenesulphinic acid react fully at room temperature in the course of several minutes. Sulphonamides have been isolated in 85% yield [Eqn.(59)][93]. Thiocyanate is also aminated at room temperature [Eqn.(60)][95].



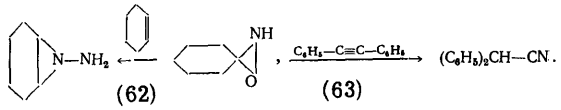
(58) (59) (60)

It has been recently observed that 3,3-pentamethyleneoxaziridine can transfer its NH groups to olefins. For example, *p*-chlorostyrene and 1-methyl-1-phenylethylene have been converted in the course of several hours at 110°C into the corresponding aziridines in accordance with Eqn.(61), the respective yields being 58% and 46%.[96] This reaction, which has been called "enamination", is the nitrogen analogue of epoxidation. The reaction mechanism has not as yet been elucidated, but the occurrence of active intermediate stages is unlikely:



(61)

On treatment with 3,3-pentamethyleneoxaziridine, cyclohexene becomes doubly aminated; *N*-aminoaziridine was isolated as the reaction product [Eqn. (62)]:



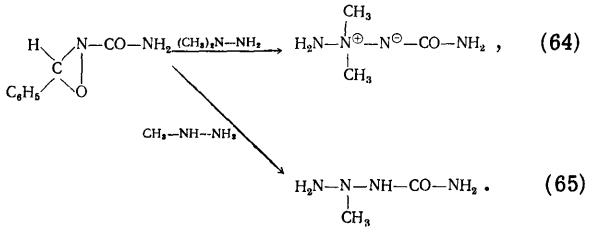
(62) (63)

Diphenylacetylene also reacts formally with addition of the NH group; after rearrangement of the phenyl groups, the reaction product is diphenylacetonitrile [reaction (63)].

VI. THE TRANSFER OF ACYLAMINO-GROUPS WITH THE AID OF *N*-ACYLOXAZIRIDINES

It has already been stated that oxaziridines alkylated at the nitrogen atom do not exhibit the aminating activity characteristic of the compounds in which the nitrogen atom is unsubstituted. On the other hand, *N*-acyloxaziridines are powerful aminating agents. Under suprisingly mild conditions, they frequently transfer the R—CON group to a nucleophilic agent.

For example, the strongly nucleophilic aliphatic hydrazines react fully even at room temperature in the course of several minutes. Triazaniumbetaine is formed in 80% yield from 2-carbamoyl-3-phenyloxaziridine and *NN*-dimethylhydrazine [Eqn. (64)][97]. Under the same conditions, methylhydrazine gives rise to triazanecarbonamide [Eqn. (65)]:



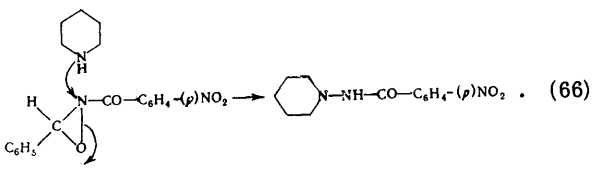
(64)

(65)

The corresponding compounds have been obtained from adducts of phenyl isocyanate or *p*-nitrophenyl isocyanate and 3-phenyloxaziridine by reaction with dialkyl- and monoalkyl-hydrazines.

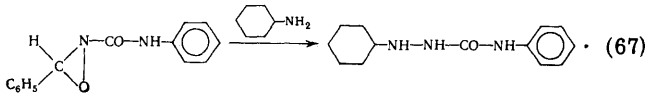
However, a precondition for the reaction is the presence of a phenyl group at the carbon atom of oxaziridine. The triazine derivatives obtained are very unstable: at room temperature they exist for several minutes. They can be obtained only by virtue of the extremely high reactivity of *N*-acyloxaziridines. The formation of the N—N bond must be again regarded as electrophilic amination. The oxaziridine is not cleaved to benzaldehyde and acylnitrene, since in the absence of a nucleophilic agent acyloxaziridines are completely stable under the reaction conditions.

Aliphatic amines react similarly to hydrazines[98]. As a result of the closure of the N—N bond, acid hydrazides or semicarbazides are formed. For example, an acid hydrazide is formed from 2-(*p*-nitrobenzoyl)-3-phenyloxaziridine and piperidine at 0°C in 92% yield in the course of several minutes:



(66)

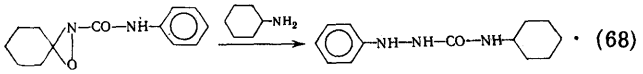
The corresponding reactions take place with high yields when the adducts of cyanic acid or phenyl isocyanate and 3-phenyloxaziridine are made to react with NH_3, cyclohexylamine, or piperidine. For example, cyclohexylamine is aminated to a cyclohexylhydrazine derivative:



(67)

A precondition for these amination reactions is the presence of a phenyl group at the carbon atom of the oxaziridine ring.

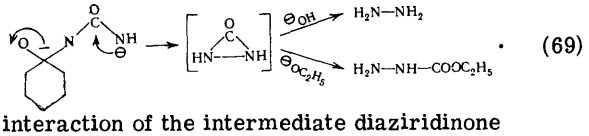
A fundamentally different result is obtained when the oxaziridine derived from cyclohexanone is made to react with cyclohexylamine[99]:



(68)

It is very remarkable that the interaction of analogous compounds with the same reagent in accordance with Eqns. (67) and (68) yields isomeric semicarbazides, where the two substituents change places. Evidently, yet another N—N bond, joining the two nitrogen atoms of the acyloxaziridine, is formed.

This second reaction is catalysed by bases. After deprotonation, the amide nitrogen probably attacks the nitrogen in the three-membered ring [Eqn. (69)]. A new three-membered ring (diaziridinone) is then formed from the oxaziridine ring. The formation of hydrazine [Eqn. (69)] in the presence of sodium hydroxide and the formation of hydrazinecarboxylate ester in the presence of sodium ethoxide are extremely likely and have indeed been observed when the above compounds were used.



(69)

The interaction of the intermediate diaziridinone [according to Eqn. (68)] following the addition of cyclohexylamine would have led to the formation of phenylcyclohexylsemicarbazide, whose substituents would have been in the positions observed for the final product.

---o0o---

Comparison of electrophilic amination, which can also be regarded as nucleophilic substitution at a nitrogen atom, with reactions involving nucleophilic substitution at a carbon atom, shows that the latter reactions have been investigated in very great detail, including their mechanisms, while the mechanisms of nucleophilic substitution at a nitrogen atom have been very little studied.

The kinetics of the reactions of chloramine and certain alkylchloramines in the Raschig synthesis of hydrazine have been investigated. The studies of the reactions involving hydroxylamine-*O*-sulphonic acid have been concerned with syntheses on a preparative scale. The available information about amination with the aid of oxaziridines is based largely on synthetic studies and a few superficial kinetic investigations. Despite this, in the present review an attempt has been made to survey the available information from a single standpoint concerning the mechanism of electrophilic amination. This is justified to some extent by the fact that the majority of the studies discussed have been carried out in recent years and have been stimulated by definite ideas about the mechanism of the process.

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