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Nitrosochlorination of Alkenes

P.P.Kadzyauskas and N.S.Zefirov

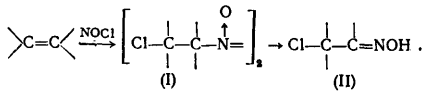
The reaction of nitrosochlorination has recently been attracting the attention of organic chemists, since it provides a ready means of obtaining classes of compounds which are extremely interesting from both theoretical and practical points of view. The laws governing this reaction, including the fine details of the stereochemistry and mechanism of this reaction, have not hitherto been systematised. The present review gives a detailed and systematic survey of the processes involved in nitrosochlorination and of the empirical laws of this reaction. Special attention is paid to published data on the mechanism and the stereochemistry of the reaction; nitrosochlorination is shown to possess features common to other reactions of electrophilic addition. The paper is addressed to a wide circle of organic chemists and undergraduate and postgraduate students. The list of references contains 119 items.

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INTRODUCTION

In 1877 Tilden[1] established that nitrosyl chloride adds at a double bond to form dimeric nitrosochlorides of the type (I), which are able to isomerise to the corresponding oximes (II):



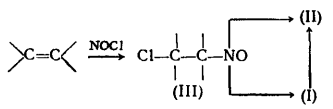
This reaction played an important part in the study of terpene compounds.

Nitrosochlorination has recently attracted the attention of chemists as a method of synthesising aziridine derivatives[2], intermediates in the synthesis of amino-sugars[3,4], amino-steroids[5-7], etc.

Several reviews have been published on methods of preparation, properties, and reactions of nitrosyl chloride[8-12]. The last review[12] covers all publications up to 1949, and fully reveals the preparative value of these reactions. During recent years, however, a large number of papers have appeared which change fundamentally our ideas on the mechanism and the stereochemistry of the nitrosochlorination of alkenes. In our survey, therefore, we have tried to summarise the general features of this reaction, while paying special attention to the stereochemistry and the mechanism of the process. We have used mainly literature which has appeared since 1950, but where necessary reference has been made to earlier work.

1. PRODUCTS OF NORMAL NITROSOCHLORINATION

Tilden[1] was the first to show that compounds containing a carbon–carbon double bond react with nitrosyl chloride usually with the formation of nitrosochlorides (III), which are dark blue oily substances. In most cases the latter are converted further into white crystalline substances—hydroxyimino-compounds (II)—or even into dimeric compounds (I). Henceforward we shall term the reaction leading to compounds of types (I), (II), or (III) normal nitrosochlorination:



It is readily seen that isomerisation to an oxime is possible only in those nitrosochlorides in which hydrogen is attached to the carbon linked to the nitroso-group.

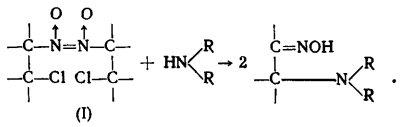
Partial conversion of (III) into (II) or into (I) can occur in the preparation of nitrosochlorides[13-16] or during their recrystallisation[17]. This explains the discrepancies in the early published data on the reaction products obtained from nitrosyl chloride and alkenes. For example, several of the compounds obtained earlier, which were regarded as hydroxyimino-compounds[15,18], have subsequently proved to be dimeric compounds[16,19].

The structure of dimeric nitrosochlorides was for a long time a matter of controversy. The work of Gowenlock[20-23] and also of Smith[24] showed that the dimerisation of nitroso-compounds involves formation of the grouping $-N(\rightarrow O)=N(\rightarrow O)-$. In such a case *syn–anti* isomerism may be expected to appear about the N=N bond even in the nitrosochlorides (in the literature on nitrosochlorination this isomerism is frequently termed *cis–trans* isomerism, although this name is evidently not accurate, and sometimes[25] incorrect terminology leads to misunderstanding).

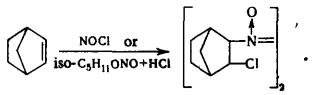
As several workers have shown, the nitrosochlorination of alkenes actually results in the formation of both *syn*- and *anti*-forms of dimeric nitrosochlorides (with respect to the N=N bond)[25-29]. In most cases the *syn*-isomers are unstable, and are readily isomerised into the *anti*-isomers. In several cases such isomerisation can occur so readily that the *syn*-isomers cannot be isolated at all[29-31].

In the molten form or in a hot solvent dimeric nitrosochlorides are in equilibrium with the monomeric form, as is indicated by the dark blue colour of the solution. After prolonged boiling, however, the hydroxyimino-compound (II) can be isolated from solutions of the dimeric nitrosochlorides[17,32,33]. The best method for obtaining oximes is probably to boil the dimeric nitrosochlorides with dilute hydrochloric acid[32,34].

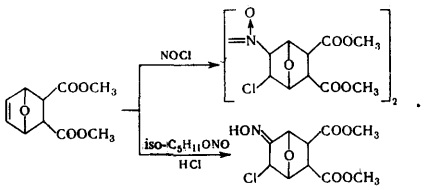
Dimeric nitrosochlorides (I) are decomposed with the formation of oximes by the action of primary or secondary amines[34-37], alkoxides[16,35], or metal phenyl sulphides[37]:



The course of the reaction is substantially influenced by the way in which nitrosochlorination is conducted. Differing results are obtained depending on whether the alkene is treated with pure nitrosyl chloride, with nitrosyl chloride contaminated with hydrogen chloride, or with isopentyl nitrite and hydrochloric acid. Thus the nitrosochlorination of norbornene and norbornadiene, both with pure nitrosyl chloride and with isopentyl nitrite and hydrochloric acid, results in the formation only of dimeric nitrosochlorides[38-40]:



In the nitrosochlorination of dimethyl 7-oxabicyclo[2,2,1]-hept-5-ene-2,3-dicarboxylate, however, pure nitrosyl chloride yields the dimer, whereas the use of isopentyl nitrite and hydrochloric acid gives the hydroxyimino-compound[32,41]:



It is seen from this example that even slight differences in the structure of the alkene strongly affect the course of the reaction.

Sometimes normal nitrosochlorination takes place only in the presence of a catalyst, such as nickel chloride, iron(II) chloride, copper(I) chloride[42], or aluminium chloride[43,44]. Thus ethylene and propene[45] do not form nitrosochlorides on reaction with nitrosyl chloride under the usual conditions of nitrosochlorination. However, good yields of the corresponding nitrosochlorides have been obtained[42] in dichloromethane or in chloroform in the presence of a catalyst (Raney nickel).

2. GENERAL FEATURES OF THE NORMAL NITROSOCHLORINATION OF ALKENES

The nitrosochlorination of unsaturated hydrocarbons shows several general features associated with the effect of substituents adjacent to the carbon–carbon double bond. Published data indicate that nitrosyl chloride adds to alkenes at the double bond more readily the more nucleophilic is this bond. Thus nitrosochlorination takes place more easily with di- and tri-substituted alkenes[13,15,16,18,27,46-51] than with monosubstituted alkenes[50-52].

It is noteworthy that the possibility and the rate of nitrosochlorination depend substantially on the position of the carbon–carbon double bond in the chain. Thus Ogloblin and his coworkers were unable to isolate crystalline dimeric nitrosochlorides by the nitrosochlorination of but-1-ene[52], pent-1-ene, hex-1-ene, hept-1-ene, or oct-1-ene[50], and only in the case of non-1-ene can stable dimeric compounds be obtained[12]. It is interesting to note that nitrosyl chloride reacts with propene at −22°C, whereas with ethylene the reaction is conducted in a nickel autoclave at +40°C.[42]

However, on treating but-2-ene[48] in contrast to but-1-ene with nitrosyl chloride, Ogloblin and Samartsev obtained a 29% yield of a crystalline dimer. Tilden and Forster[53], and subsequently also Thorne[54], isolated monomeric nitrosochlorides of hex-2-ene, hept-2-ene, oct-2-ene, and 4-methylpent-2-ene in low yields. Nevertheless, on the basis of a study of the infrared spectra, Ogloblin and Samartsev consider that pent-2-ene[27] and hex-2-ene[28] form dimeric compounds, though these are liquids.

The course of the reaction is probably unaffected by conjugation of the double bond with a benzene ring. Thus propenylbenzene forms a nitrosochloride[54], whereas allylbenzene does not react with nitrosyl chloride. Similarly, 1,3,5-trimethylstyrene does not interact with nitrosyl chloride[54], whereas 1,3,5-trimethyl-2-propenylbenzene[55] gives a crystalline nitrosochloride.

Nitrosyl chloride adds readily also to cycloalkenes to

Nitrosyl chloride adds readily also to cycloalkenes to form the normal nitrosochlorination products. For example, cyclohexene[25,26,56-60], cyclo-octene[61], cyclododecatriene[62-64], Δ^9-octahydronaphthalene[65-67], dicyclopentadiene[68], and *endo*- and *exo*-2-oxa-1,2-dihydrodicyclopentadienes[69] readily form dimeric chloro-nitroso-derivatives.

Nitrosochlorination goes still better with alkenes containing more than one alkyl substituent adjacent to the double bond. Thus 2-methylpropene[16,70] and 2-methylbut-2-ene[17,45-47,54] form with nitrosyl chloride dimeric compounds in yields of 60% and 50% respectively. 2,3,3-Trimethylbut-1-ene, 2-methylbut-1-ene, and 2-*p*-tolylpropene give yields respectively of 28%, 19%, and 9% of crystalline dimeric compounds[50]. 2,4,4-Trimethylpent-1(and 2)-enes also give good yields of dimeric nitrosochlorides[54].

A monomeric derivative was isolated from reaction of the tetrasubstituted 2,3-dimethylbut-2-ene with nitrosyl chloride[71]. In this case formation of a dimeric compound is probably made difficult by steric hindrance.

The addition of nitrosyl chloride obeys the Markovnikov rule[15,18,27,28,33,48,50,53,72-75]: the nitroso-group adds to the most hydrogenated carbon atom, which indicates that the double bond is initially attacked by the nitrosyl cation[73].

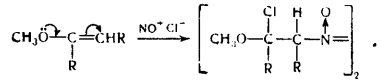
The orienting effect of n-alkyl substituents on the addition of nitrosyl chloride is the same as that of the methyl group. In the case of branched alkyl substituents the nitroso-group adds preferentially to a carbon atom attached to methyl[28], which is explained by the inductive effect of the alkyl groups. The strengthening of the orienting effect of various alkyl groups compared with that of methyl corresponds to the increase in the positive inductive effect of these groups[28], in the sequence $CH_3 < C_2H_5 < CH(CH_3)_2 < C(CH_3)_3$.

Recent kinetic investigations[76] indicate that electron-donor groups influence nitrosochlorination. The accompanying Table shows that the rate of nitrosochlorination decreases as the double bond becomes less nucleophilic.

Rate constants for the nitrosochlorination of alkenes in chloroform at 0°C.[76]

Alkene	$10^{-4}k_2$, $M^{-1}\,s^{-1}$	Alkene	$10^{-4}k_2$, $M^{-1}\,s^{-1}$
Methylallyl chloride	0.29	2,3-Dimethylbut-1-ene	20
3,3-Dimethylbut-1-ene	0.32	2-Methylpent-1-ene	23
4,4-Dimethylpent-1-ene	0.52	β-Methylstyrene	26
cis-Stilbene	0.64	Cyclohexene	29
3-Methylbut-1-ene	0.69	2-Methylpropene	30
3-Methylpent-1-ene	1.0	2-Methylbut-1-ene	33
4-Methylpent-1-ene	1.2	But-2-ene	52
But-1-ene	1.5	Hex-3-ene	66
Hex-1-ene	1.6	*cis*-Pent-2-ene	77
Oct-1-ene	1.8	*trans*-Pent-2-ene	108
Dodec-1-ene	1.8	Cycloheptene	135
trans-Stilbene	2.9	Cyclopentene	>1000
Styrene	6.5	2-Methylbut-2-ene	>1000
1,1-Diphenylethylene	9.8	2,3-Dimethylbut-2-ene	>1000
α-Methylstyrene	17	Norbornene	>1000

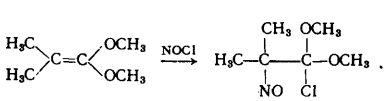
The nucleophilic character of the double bond is enhanced also in vinyl ethers owing to the effect of conjugation between the oxygen electrons and the π-electrons of the double bond. Such compounds therefore react vigorously with nitrosyl chloride[30,77]:



On the other hand, allyl methyl ether, where conjugation of this type is absent, does not form normal nitrosochlorination products[19].

Methylated and methoxylated styrenes give higher yields of the crystalline dimeric nitrosochlorides than do the unsubstituted styrenes. Thus the nitrosochlorination of α-methylstyrene[54], *p*-methylstyrene[45,56,57], *o*-methylstyrene[54], and *m*-methylstyrene[54] gave 71%, 66%, 52%, and 32% respectively of the dimers, whereas unsubstituted styrene[45,54,56,57] forms only 30% of the dimeric compound.

The nucleophilic character of the carbon–carbon double bond in the acetals of ketens is still more intensified by the electron-donor effect of the two alkoxy-groups. In this case, therefore, nitrosochlorination is rapid, and is probably immediately followed by instantaneous isomerisation of the nitrosochloride into an oxime[78]. As Ogloblin and his coworkers have shown[78], nitrosyl chloride easily interacts also with 1,1-dimethoxy-2-methylpropene, but the sole product of this reaction is 1-chloro-1,1-dimethoxy-2-methyl-2-nitrosopropane[78]:



On the other hand, electron-acceptor substituents in the α-position with respect to the double bond strongly retard nitrosochlorination[54,72,79]. Thus maleic and fumaric acids are recovered unchanged[53] from treatment with nitrosyl chloride. Similarly, crotonic and vinylacetic acids[53] also

do not react with nitrosyl chloride, but on prolonged treatment in sealed tubes are decarboxylated[44].

According to Thorne neither 5-phenylpent-4-enoic nor 6-phenylhex-5-enoic acid forms a nitrosochloride[54], although in the former case the double bond is separated from the carboxyl by two methylene groups. Published data do not indicate what is the minimum number of methylene groups necessary between the double bond and the carboxyl for reaction to occur. However, it is known that oleic acid does form a nitrosochloride[53,80].

An ester group has a similar effect. Thus Ogloblin and Semenov were unable to obtain a nitrosochloride by the action of nitrosyl chloride on methyl acrylate[81] or methyl methacrylate[44].

Chlorinated ethylenes do not form nitrosochlorides because of the strong influence of the chlorine atom[43,72,79,82,83].

The presence of a nitro-group near the double bond also prevents nitrosochlorination. Thus neither β-nitrostyrene[54] nor 2-nitropropene[83] gives a normal nitrosochlorination product.

Ogloblin and Potekhin showed[84-86] that, with αβ-unsaturated ketones, nitrosochlorination goes fairly smoothly, in spite of the presence of a strong electron-acceptor group. It is interesting that a dimer or an oxime is obtained depending on the reaction conditions or the structure of the αβ-unsaturated ketone[87,88].

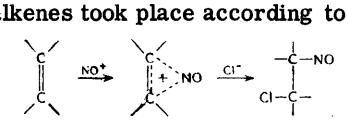
Nitrosochlorination also takes place relatively easily in the presence of a nitrile group. As Ogloblin and Semenov showed, at ordinary temperatures acrylonitrile gives β-chloro-α-hydroxyiminopropionitrile (yield 48%):[81]

$$CH_2{=}CH{-}CN \xrightarrow{NOCl} \underset{Cl}{\overset{}{CH_2{-}C{-}CN}} \underset{NOH}{\overset{}{\parallel}} .$$

3. MECHANISM AND STEREOCHEMISTRY OF THE NITROSOCHLORINATION OF ALKENES

As already stated above, the addition of nitrosyl chloride follows the Markovnikov rule, which indicates that the nitroso-group adds as an electrophilic species in the form of the nitrosyl cation.

On this Ingold[73] suggested that the reaction of nitrosyl chloride with alkenes took place according to the scheme



which is usual for electrophilic additions at a double bond. According to this, nitrosochlorination should result in the formation of *trans*-addition products. An analogous mechanism has been suggested in several other papers[30,43,54,75,77-78,89]. It must be emphasised, however, that the stereochemistry of the reaction has not been studied in any of the work on the addition of nitrosyl chloride to a double bond, with the exception of a few recent investigations[3-7,32,67].

The proposed mechanism is consistent with results for the infrared spectra[90], the electrical conductivity of the solutions[10,91-93], and isotopic exchange in liquid nitrosyl chloride[94-97], from which it follows that nitrosyl chloride dissociates according to the equation†:

$$NOCl \rightleftarrows NO^+ + Cl^- .$$

The concentration of the chloride ion and hence of the nitrosyl cation is 10^{-8} g-ion litre^{-1} at 18°C.[45]

† It must be remarked that sometimes the unjustified opinion is expressed that nitrosyl chloride dissociates into a chlorine cation and a nitrosyl anion[98].

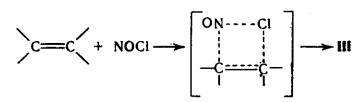
Kinetic investigations of the rate of nitrosochlorination have shown that overall it is of the second order, being of the first order with respect to each component. In the nitrosochlorination of styrene and cyclohexene in various solvents[76] the following sequence of reaction velocity

$$CH_3OH < (C_2H_5)_2O < CCl_4 < C_6H_5CH_3 \simeq n\text{-}C_7H_{16} < C_6H_5Cl < C_6H_4Cl_2 < C_6H_5CN < CH_2Cl_2 < C_6H_5NO_2 < CHCl_3$$

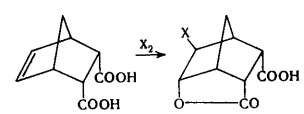
has been observed, which is difficult to explain. Unfortunately, no published data are available on the rate of reaction in liquid sulphur dioxide, where recent work[99] has shown that the course of the reaction is probably most unambiguous.

Nitrosochlorination is characterised by high entropies of activation: thus the values for styrene in chloroform and for cyclohexene are respectively −43.0 and −36.9 cal mole^{-1} deg^{-1}.[76] Unfortunately, data are lacking on the entropy of activation for nitrosochlorination in sulphur dioxide, which makes it impossible to compare the kinetic data with results of a stereochemical study (see below).

All this suggests that the transition state of the reaction is characterised by a definite and rigid orientation of the alkene and nitrosyl chloride molecules, and provides indirect evidence of the possibility of cyclic transfer of electrons, e.g. according to the scheme



There are also several experimental facts showing that nitrosochlorination does not always occur as a two-stage electrophilic addition at the double bond. It is well known that electrophilic addition to *endo*-carboxylic derivatives of norbornene involves the carboxyl and results in the formation of lactones[100,101]. For example, bromination of *endo*-adducts of diene synthesis from cyclopentadiene and maleic anhydride takes place according to the scheme

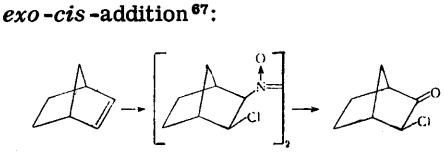


An analogous scheme is valid not only for bromination but also for the addition of mercury salts[102], 2,4-dinitrophenylsulphenyl chloride[103,104], and water[105], for opening an epoxide ring[106], etc.

Nevertheless, the interaction of *endo*-norbornenecarboxylic acid either with isopentyl nitrite and hydrochloric acid or directly with nitrosyl chloride results in the formation of dimeric nitrosochlorides, not lactones[38,67].

It should be noted that the nitrosochlorination of norbornene does not involve skeletal rearrangement of the Wagner–Meerwein type, while that of norbornadiene does not involve the second double bond[38,39].

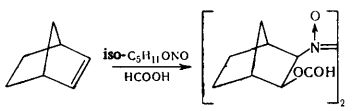
In 1964 Meinwald et al. showed that these reactions are cases of *exo-cis*-addition[67]:



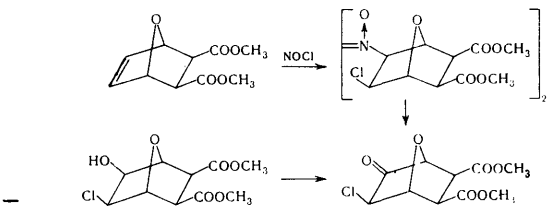
The stereochemical course of the nitrosochlorination of norbornene was elucidated by a chemical method: the dimeric nitrosochloride was converted into an *exo*-chloroketone described previously. The *cis*-configuration of the nitrosochloride of norbornene has since been confirmed by spectroscopy[3]. Miller[39] has also described the nuclear

magnetic resonance (n.m.r.) spectra, which provide unambiguous evidence of the *exo-cis*-configuration of the addition product, but he did not draw this conclusion.

It is interesting that the nitrosoformylation of norbornene[107] is also an *exo-cis*-addition:

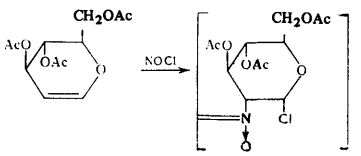


Zefirov et al. have shown[32] that the nitrosochlorination of dimethyl 7-oxabicyclo[2,2,1]hept-5-ene-2,3-dicarboxylate proceeds as an *exo-cis*-addition. This was proved by converting the dimeric nitrosochloride into a chloroketone, which was identified by comparing it with chloroketones obtained from chlorohydrins of known configuration[108]:



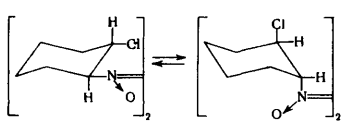
On the other hand, it has been shown in the case of hydroxymercuration[102] that the addition of weak electrophilic reagents to these bicyclic systems may lead to the formation of *cis*-addition products. Therefore it is not possible to draw general stereochemical conclusions concerning nitrosochlorination on the basis of data on the reactions of bicyclic alkenes.

The reaction of nitrosyl chloride with 3,4,6-tri-*O*-acetyl-D-glucal, 3,4-di-*O*-acetyl-D-arabinal, tri-*O*-acetyl-D-glucal, and di-*O*-acetyl-D-xylal takes place as *cis*-addition with the formation of dimeric nitrosochlorides[3,4]:



However, the stereochemical course of additions of D-glucal may also be anomalous. Thus data on the hydroxymercuration of D-glucal are contradictory: Inglis and Schwarz[109] interpret methoxymercuration as *trans*-addition, whereas results obtained by Manolopoulos et al.[110] indicate that this reaction is a *cis*-addition. The chlorination of D-glucal also takes place predominantly as *cis*-addition[3].

In this connection it is most interesting to study the stereochemistry of nitrosochlorination on simple models. Zefirov et al. have shown[111] that the reaction of cyclohexene with isopentyl nitrite and hydrochloric acid produces a dimeric nitrosochloride, which the n.m.r. spectra indicate to have a *trans*-configuration and which exists predominantly in the diequatorial form:



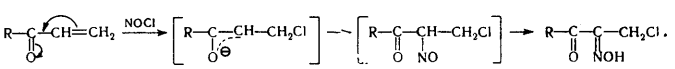
At the same time Ohno et al.[99] showed that the reaction of nitrosyl chloride with cyclohexene in liquid sulphur dioxide gives a nitrosochloride which is a *trans*-isomer. In chloroform, however, this reaction results in the formation of a dimeric nitrosochloride, to which a *cis*-configuration was attributed.

Thus the stereochemistry of nitrosochlorination depends fundamentally not only on the structure of the alkene but also on the method of preparing the nitrosochloride and on the solvent employed. The most plausible hypothesis is that the addition of nitrosyl chloride in non-polar solvents may involve an intermediate four-centre transition state. In polar solvents, however, a two-stage *trans*-addition is possible. The relative proportions of these mechanisms may depend not only on the solvent but also on the nature of the alkene, the reaction temperature, etc. It may be expected theoretically that catalysts of the aluminium chloride type will have a substantial effect on these proportions.

In 1963 Titov[43] reported the anomalous addition of nitrosyl chloride to halogenoethylenes. In order to accomplish smooth and rapid nitrosochlorination, solutions of Lewis acids (aluminium chloride, tin(IV) chloride, zinc chloride, iron(III) chloride, antimony(V) chloride) in excess of liquid nitrosyl chloride were used in this case at low temperatures. These aprotic acids form[10] with nitrosyl chloride complexes of the type $NO^+[MCl_x]^-$, which are strongly dissociated into the ions NO^+ and $[MCl_x]^-$. The use of complexes of nitrosyl chloride with Lewis acids should eliminate the possibility of a four-centre cyclic mechanism of addition of nitrosyl chloride at the double bond. Titov suggested an ionic mechanism for this process of nitrosochlorination, essentially analogous to that proposed earlier by Ingold[73].

However, data on the influence of catalysts on nitrosochlorination are contradictory. Thus Beier et al.[76] found that the use of Lewis acids produces no increase in the rate of nitrosochlorination, whereas Ogloblin and Semenov established[44] that the reaction between nitrosyl chloride and methyl methacrylate is far more rapid in the presence of aluminium chloride. Further results are evidently required, which would enable the effect of Lewis acids on nitrosochlorination to be assessed with complete clarity. Perhaps such acids will be found to accelerate the reaction only in the case of alkenes having a certain structure, in particular those containing electron-acceptor groups.

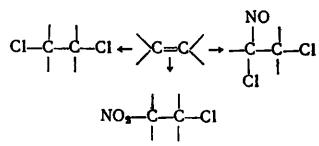
Ogloblin and Potekhin consider it possible that in several cases nitrosyl chloride adds by a nucleophilic mechanism:



Thus they showed[84] that $\alpha\beta$-unsaturated ketones form β-chloro-α-hydroxyimino-ketones very smoothly, in spite of the fact that the presence of a strongly electron-acceptor group adjacent to the double bond makes electrophilic addition difficult. Study of the reaction between nitrosyl chloride and $\alpha\beta$-unsaturated aldehydes also led the authors to the conclusion that such nucleophilic addition was possible. Thus under comparable conditions nitrosyl chloride reacts more vigorously with unsaturated aldehydes[31] than with the corresponding ketones[84]. A nucleophilic mechanism of nitrosochlorination is supported in this case by the effect of electron-donor substituents at the carbon–carbon double bond, which greatly lower the reaction velocity[31,84].

4. ANOMALOUS PRODUCTS OF NITROSOCHLORINATION

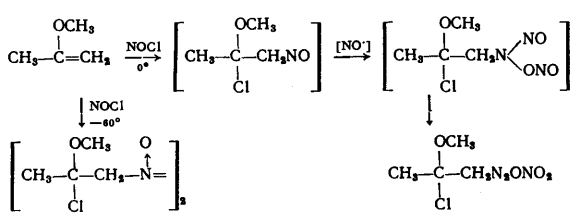
Although nitrosochlorination is widely used in synthetic practice for the preparation of chloro-nitroso- and chloro-hydroxyimino-compounds, it is nevertheless impossible in several cases to isolate the normal reaction products. The main side-processes are due to the chlorinating and oxidising action of nitrosyl chloride. The most generally occurring products of anomalous nitrosochlorination are dichlorides, dichloro-nitroso-compounds, and chloro-nitro-compounds, formed as follows:



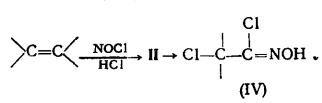
The factors determining the ratio of normal and anomalous nitrosochlorination products are extraordinarily diverse, and are often difficult to allow for exactly. Published data indicate that a substantial influence is exerted by the relative proportions of the reactants, the presence of acidic impurities in the nitrosyl chloride, the temperature of the reaction, and also the structure of the alkene. They indicate also that at elevated temperatures [33,48,81] nitration and chlorination will predominate over nitroso-chlorination.

Since in almost all cases the monomeric nitrosochlorides dimerise, Ogloblin et al. [50] explain the formation of dichloro- and nitro-chloro-derivatives in terms of the stability and the solubility of the dimeric nitrosochlorides. The formation of sparingly soluble and stable dimers would strongly diminish the yield of dichloro- and nitro-compounds; and conversely, good solubility of the dimers and ready dissociation into the monomeric forms will favour the appearance of anomalous nitrosochlorination products. These compounds are obtained by the interaction of nitrosyl chloride with the monomeric nitrosochloride of the alkene, taking place by a radical mechanism via unstable aliphatic diazo-nitrates [50].

Raising the temperature sometimes affects the formation of other reaction products in a definite manner. For example, reaction between nitrosyl chloride and 2-methoxypropene in ether at −60°C leads to formation of the nitrosochloride, whereas the same reaction at 10–15°C produces 2-chloro-2-methoxypropanediazo-nitrate, probably by a radical reaction with the monomeric nitrosochloride [30]:



As already mentioned above, in the presence of traces of hydrogen chloride the reaction of nitrosyl chloride with alkenes results in the formation of chloro-hydroxyimino-compounds [13–15,32,41]. However, cases have been observed in which chlorides of α-chlorinated hydroxamic acids can be obtained under these conditions [12–14,51,52]:



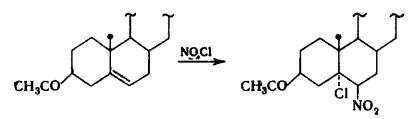
(IV)

The formation of dichloro-nitroso-compounds is obviously due to the chlorinating action of nitrosyl chloride. The interaction of oximes with this reagent results in geminal chloro-nitroso-compounds (IV) [112,113]. Therefore the formation of dichloro-nitroso-derivatives is facilitated preferentially if the reaction is conducted in the presence of excess of nitrosyl chloride. It is probable that the order in which the reactants are added plays a fundamental part in several cases.

In order that the nitrosochlorination of aliphatic alkenes should yield normal products, the double bond must have a certain nucleophilic character, and the reaction conditions must be maintained. Otherwise a complicated mixture of different addition products is formed.

In cases in which the addition of nitrosyl chloride to alkenes is difficult (i.e. in the presence of n-alk-1-enes and of alkenes containing electron-acceptor groups), the rates of chlorination and oxidation, leading to the formation of nitro-compounds, exceed the rate of addition of nitrosyl chloride, and the corresponding dichloro-compounds and chloro-nitro-compounds constitute the main products of the reaction [14,19,45,50–52,56,114–118].

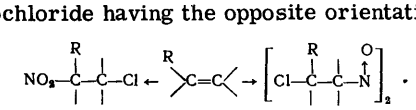
Cases are known in the literature in which chloro-nitro-compounds are formed extraordinarily readily, and are practically the sole products of the reaction [5–7]. For example, nitrosyl chloride reacts with cholesteryl acetate, the 3,17-diacetate of androst-5-ene, and 3-acetoxyandrost-5-en-17-one to form the corresponding 5-chloro-6-nitro-derivatives in high yield [5–7]:



The *trans*-diaxial positions of the chloro- and nitro-groups was established by a study of the reductive elimination of chlorine by the action of zinc dust in acetic acid [5], and also of the n.m.r. spectra [7].

Cholesteryl acetate reacts very slowly with pure nitrosyl chloride in ether at −5°C (a 53% yield of the nitrochloride was isolated after 2 months) [7]. It, however, unpurified nitrosyl chloride is used, the nitrochloride is formed quickly (in 92% yield after 5 days [5]). In the presence of nitrogen dioxide in ethereal solution the reaction is accelerated so much that the yield of the nitrochloride reaches 74% after only 2 h. This definitely indicates the possibility that this reaction is initiated by nitrogen dioxide, and in these cases the reaction probably consists in the free-radical *trans*-addition of nitryl chloride formed by the oxidation of nitrosyl chloride [12].

Such a mechanism is confirmed also by the fact that in several cases the chloro-nitro-compounds have an orientation of the nitro-group and the chlorine atom which is opposite to that to be expected for chloro-nitroso-compounds obeying Markovnikov's rule. Nevertheless, it should be noted that additions of nitryl chloride may show the opposite orientation to that observed in the reactions of nitrosyl chloride. Thus the nitrosochloride of an alkene is not the precursor of the nitrochloride of the alkene. For example, Yakubovich and Lemke [72] showed that the reaction of nitrosyl chloride with 2-methylpropene gives, together with the nitrosochloride, a small quantity of the nitrochloride having the opposite orientation:



A similar course of reaction, leading to the nitrochloride as the sole product, has been noted also by Andrianov et al.[119] in the case of 3-vinylheptamethylsiloxane:

$$2\,(CH_3)_3SiO\underset{\displaystyle CH{=}CH_2}{\underset{|}{Si}}(CH_3)OSi(CH_3)_3 + 2NOCl \rightarrow N_2 + Cl_2 + 2\,(CH_3)_3SiO\underset{\displaystyle CHClCH_2NO_2}{\underset{|}{Si}}(CH_3)OSi(CH_3)_3.$$

Thus the formation of nitro-compounds is a complicated process, and is probably unable to provide information on the stereochemistry of normal nitrosochlorination.

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It is evident from the present review that the nitrosochlorination of alkenes is a unique reaction, both in the diversity of the products obtained and in its mechanism. Even a slight change in conditions may produce substantial changes in the mechanism of this reaction and in the stereochemistry of the products. The probable reason is that at least two mechanisms—two-stage addition or via a four-centre cyclic transition state—are available for the reaction between nitrosyl chloride and an alkene. However, many aspects still remain obscure. This applies especially to the effect of catalysts on the mechanism and the stereochemistry of the process. Also only a most general study has been made of anomalous nitrosochlorination, and the mechanism of these processes is practically unknown. Very little work has been done on related nitrosohalogenation reactions. Here, too, significant anomalies can be expected in the structural and stereochemical course of the reactions, especially with nitrosyl fluoride. Coupled addition reactions, leading to the formation of nitroso-compounds, have been studied only recently. Nevertheless, the successes achieved during recent years permit us to hope for further progress in the theoretical development of the most varied aspects of this important and synthetically promising reaction.

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