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Aprotic Deamination of Simple Aliphatic Amines

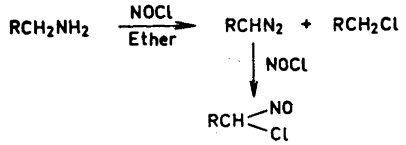
Solvent Dependence of the Formation of Diazoalkanes and Nitrosoalkanes

JAN BAKKE*

AB Bofors, Nobelkrut, Bofors, Sweden

Deamination of octylamine with nitrosyl chloride in ethyl ether, tetrahydrofuran, and ethylene glycol dimethyl ether gave diazooctane as one major product. Deamination in methylene chloride, chloroform, toluene, and heptane gave complex mixtures. In methylene chloride one of the products was nitrosooctane. The different reaction paths in the two groups of solvents was suggested to be caused by the formation of a reactive complex between nitrosyl chloride and the ethereal solvents.

The deamination of octylamine and butylamine with nitrosyl chloride in ether gives mainly diazoalkane and primary chloroalkane as products.[1] This represents a new synthesis of simple unstabilized diazoalkanes, directly from the corresponding amine. Excess amine has to be used, otherwise nitrosyl chloride reacts with the diazoalkane giving 1-chloro-1-nitrosoalkane.[1]



In an attempt to increase the yield of diazoalkane (40 % of reacted amine), the deamination of octylamine was tried in several aprotic solvents. In a few of these (tetrahydrofuran, ethylene glycol dimethyl ether), diazooctane was obtained at a somewhat higher yield (*ca.* 50 %) than in ether. In other solvents (chloroform, methylene chloride, toluene, heptane), no diazooctane could be detected (Table 2), and the reactions gave complex product mixtures.

Studies of the aprotic deamination of aliphatic amines have been performed in a variety of solvents,[2] and it is assumed that the reaction proceeds by a

* Present address: Department of Chemistry, University of Trondheim. NLHT, Trondheim,

heterolytic mechanism, usually formulated with a "hot" carbonium ion as the important intermediate. As our results from the deamination in various solvents (Table 2) indicated variation of mechanism in different solvents, it was decided to investigate this point further.

The reaction in methylene chloride was chosen for closer investigation. The reaction products are given in Table 1. The major products reported were identified by thin layer chromatography (TLC), gas chromatography (GLC), IR and/or electronic spectroscopy.

Table 1. Deamination of octylamine (51 mmol l^{-1}) with nitrosyl chloride (27 mmol l^{-1}) in methylene chloride at 50°.

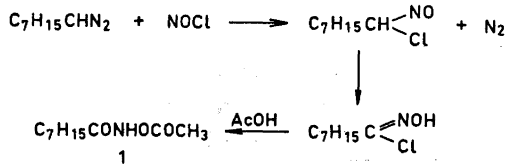
Product	Yields in per cent of added NOCl
Octyl alocohol	2
Octyl nitrite	1.5
1-Chlorooctane	20
Octanal	16
Octanal oxime	25

Octanal and octanal oxime were the most surprising products isolated, and to our knowledge this is the first report of an aldehyde or an oxime as a product of the deamination of a simple amine. Nitrosooctane would appear to be a possible precursor in the formation of octanal and octanal oxime. The reaction envisaged would proceed by isomerisation of the nitroso compound to octanal oxime, which on hydrolysis would give the free aldehyde.

Detection of nitrosooctane would be expected to be somewhat difficult, owing to its ready isomerisation to the oxime; this process in not quite as rapid as usually believed but is, however, catalysed by amines.[3] It might, however, prove to be possible to identify the nitrosoalkane by electronic spectroscopy if the unreacted amine were trapped before the reaction mixture was warmed up.

Acetic acid was used as trapping agent. After addition of acetic acid at low temperature and warming up, the reaction mixture turned blue (λ_{max} 665 nm) when approaching room temperature. The spectrum also showed a band at 290 nm; both bands are present in the spectra of aliphatic nitroso compounds.[4] 1-Chloro-1-nitrosooctane, which could have been the cause of the blue colour, has absorption maxima at 649 nm and 318 nm in methylene chloride. Calvert and Pitts [10] have reported the vapour phase electronic spectrum of 2-methyl-2-nitrosopropane. By using their ε_{max} (15 l (gmol cm)$^{-1}$), it was possible to estimate the concentration of nitrosooctane to *ca.* 6 mmol l^{-1} corresponding to 64 % of the combined isolated octanal and octanal oxime. The electronic spectrum of the deamination product together with the conclusive identification of octanal and octanal oxime identifies it as nitrosooctane. This finding of nitrosoalkane is to our knowledge the first in the deamination of aliphatic amines.

From the reaction in the presence of acetic acid, *O*-acetyl-*N*-octanoylhydroxylamine (*1*) was also isolated, which may indicate the presence of diazooctane in the initial reaction mixture and its subsequent reaction with nitrosyl chloride.[1]



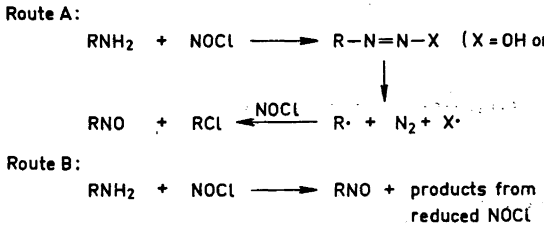
However, oximes are known to react with nitrosyl chloride to give 1-chloro-1-nitrosoalkanes,[9] and octanal oxime may be a more likely precursor than diazooctane in the present case.

As the deamination in methylene chloride had been shown to give nitrosooctane, the deamination reaction in other solvents was investigated for this product. This was done in a qualitative way by adding acetic acid to the deamination reaction before warming. An absorption maximum at 665 nm was taken as an indication of the presence of nitrosooctane. Nitrosooctane was formed in the reaction in chloroform, methylene chloride, and toluene, but not in heptane, tetrahydrofuran, or ethylene glycol diethyl ether.

These results present two questions: how was nitrosooctane formed, and why did the reaction is some solvents give mainly diazoalkanes and not nitrosoalkanes, and *vice versa*?

As to the formation of nitrosooctane, several possibilities could be considered. Firstly, it might be a secondary product. Octyl nitrite was thought to be one possible precursor, in view of the well known reactivity of nitrites;[5] it proved, however, to be stable under the reaction conditions both towards NOCl, towards diazoethane, and towards octylamine in the presence of octylammonium chloride.

A direct formation of nitrosooctane could be envisaged in at least two ways: route A by a radical mechanism in which the nitrogen in the nitroso group came from nitrosyl chloride, and route B by a direct oxidation by nitrosyl chloride, which would leave the amine nitrogen in the nitroso group.



If route A was operative, one would expect to find some octane from the reaction between the octyl radical and the solvent in the reaction mixture. GLC indicated traces of octane to be present, but only slightly more than in

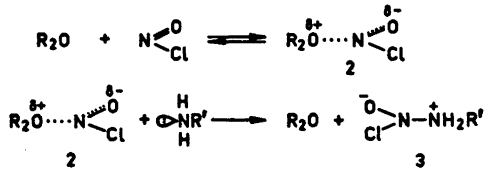
the reaction run in ethyl ether (where no nitrosooctane could be detected). Further, pentylcyclopropane, a possible product from the deamination, was not available as a reference substance. The product identified as octane by GLC may therefore have been pentylcyclopropane.

The presence of octane could thus not be used to indicate a radical mechanism for the formation of nitrosooctane, although that reaction path cannot be excluded by the present evidence.

The direct oxidation by nitrosyl chloride cannot be excluded either. The oxidation by nitrosyl chloride of *gem* chloronitrosoalkanes to the corresponding chloronitroalkanes has been reported by Ogloblin,[6] but no reports of the oxidation of an amine (primary or secondary) by NOCl have been found. This problem could probably be settled by using $^{15}NOCl$ as the deaminating agent.

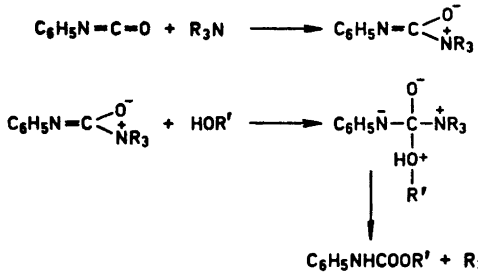
It seems, however, safe to conclude that in methylene chloride and probably also in chloroform and toluene, a major part of the reaction of octylamine with nitrosyl chloride proceeds *via* a different pathway from that in ethereal solvents (ethyl ether, tetrahydrofuran, ethylene glycol dimethyl ether).

As to the second question, why some solvents give diazooctane and others not, Table 2 shows that deamination in the solvents containing an ethereal oxygen gave diazooctane. The reason for this could be an interaction between the ethereal solvent and nitrosyl chloride.



The assumed increased reactivity of the complex *2* as compared to "free" nitrosyl chloride can be explained by the rehybridisation of the nitrogen atom in *2*, giving a transition state of lower energy than the corresponding one for "free" nitrosyl chloride. The ether may also act as base in the abstraction of a proton from the amine nitrogen in *3*, although one would expect the excess amine to be more active in this respect.

The higher reactivity of the complex *2* has a parallel in the amine catalysed formation of urethans.[7]



No indication of a complex between ether and nitrosyl chloride could be found by electronic spectroscopy, the spectra of nitrosyl chloride in ether and methylene chloride had almost identical maxima.

Study of the N=O band [8] in IR showed it to move from 1850 cm^{-1} in methylene chloride solution to 1830 cm^{-1} in ether solution, a change in the expected direction if the N=O band had an increased single bond character in the ether solution. However, in gas phase, the NO band in nitrosyl chloride is located at 1790 cm^{-1}, and the shifts in the two solvents may be caused mainly by the polarity of the solvent. To use the shift in changing from methylene chloride to ether as an indication of the formation of a complex is therefore dubious. Nevertheless, the complex may be too weak or present in too low a concentration to be detected by the spectroscopic methods tried here.

By visual judgement, the brown colour of nitrosyl chloride disappeared more rapidly in the deaminations in ethereal solvents than in others. In these solvents, where NOCl did not react rapidly with the amine, it could react with the intermediates formed and then give the complex reaction mixtures reported here. An example of this interaction is the reported reaction between NOCl and octanal oxime or diazooctane in CH_2Cl, even in the presence of excess amine.

The results from this investigation show that an ethereal solvent is of advantage if one wishes to obtain a fair yield of diazooctane. The scope and limitations of this new synthesis of diazoalkanes will be the goal of further investigations.

EXPERIMENTAL

The IR spectra were recorded on a Perkin-Elmer infrared spectrophotometer Model 257. The electronic spectra were recorded on a Beckman DK-2 spectrophotometer, 1 cm cells being used for all measurements. Gas chromatographic separations were made on a Perkin-Elmer F 11 gas chromatograph, equipped with a hydrogen flame ionisation detector.

Run 1. Deamination of octylamine in CH_2Cl_2. Octylamine (1.0 g, 7.8 mmol) in CH_2Cl_2 (150 ml, distilled from P_2O_5) was cooled to −50°, and NOCl (100 ml gas, 4.1 mmol) was added with a syringe through a rubber serum cap. After 10 min at −50° the mixture was placed at −25° overnight. The electronic spectrum of the reaction mixture showed it to contain octylnitrite (11 mg). The solution was extracted with aqueous HCl, washed twice with water, dried (Na_2SO_4) and concentrated (yield 0.57 g). The water solution was made basic, extracted with ether, the ether phase dried (Na_2SO_4) and concentrated, giving unreacted octylamine (0.56 g, 55 % of starting material). The neutral extract was chromatographed on silica gel, eluted with $CHCl_3$: fraction 1(F1), 330 mg; fraction 2, 127 mg; fraction 3, 38 mg. GLC of fraction 1 (benzaldehyde as internal standard) showed it to contain 1-chlorooctane (30 %, 100 mg), octanal (21 %, 70 mg), and octanol (3 %, 10 mg). The presence of octanal was also indicated by thin layer chromatography and by the presence of bands at 1730 and 2710 cm^{-1} in the IR spectrum of F 1. These bands are also present in the IR spectrum of pure octanal. F2 had an IR spectrum almost identical to that of octanal oxime. F2 (liq): 3280, 2960, 2920, 2860 1670, 1550, 1470, 1380, 1350, 1050, 900, 760; octanal oxime ($CHCl_3$, 5 %): 3280, 2960, 2920, 2860, 1670, 1470, 1380, 1350, 900 cm^{-1}, F2 was crystallized from petroleum ether, giving 3 mg of a crystalline compound with IR spectrum identical to that of octaldoxime. GLC of F2 (benzaldehyde as internal standard) showed it to contain octaldoxime (35 %, 45 mg).

Run 2. Detection of nitrosooctane. This experiment was run identically with the preceding one, except that acetic acid (0.3 ml) was added at −50° and the reaction mixture then allowed to warm up. The solution turned blue: λ_{max} 665 nm ($\log (I_0/I) = 0.10$) and λ_{max} 292 nm ($\log (I_0/I) = 0.70$ after dilution 1 : 10). The electronic spectra indicated

octyl nitrite to be present in approximately the same concentration as in run 1. The electronic spectrum of 1-chloro-1-nitrosooctane in CH_2Cl_2 had maxima at: 642 nm (log $(I_0/I) = 0.09$) and 318 nm (log $(I_0/I) = 1.10$ after dilution 1 : 100), which are different from those reported above for the reaction mixture. The reaction mixture was washed with water, followed by aqueous $NaHCO_3$, dried (Na_2SO_4), concentrated and dissolved in petroleum ether. After 24 h at $-25°$, 25 mg of a crystalline compound, m.p. $82-83.5°$ was obtained. The compound had IR bands ($CHCl_3$, 5 %) at 3360, 3200, 2960, 2930, 2860, 1790, 1710, 1460, 1370, 1180, 1040, 860 cm^{-1}.

N-Octanoyl-O-acetylhydroxylamine. 1-Chloro-1-nitrosooctane (0.1 g) was dissolved in CH_2Cl_2 (50 ml) at $-75°$, and octylammonium chloride (0.1 g) and octyl amine (0.05 g) was added. The blue colour disappeared immediately. Acetic acid (0.1 ml) was added to the mixture. Working up the product gave 0.06 g *N*-octanoyl-*O*-acetyl-hydroxylamine after crystallization from petroleum ether. IR spectrum and m.p. were identical to those of the crystalline product obtained in run 2.

Deamination of octylamine in other solvents. These reactions were run in the following way. Octylamine (168 mg) in solvent (25 ml) was brought to the appropriate reaction temperature and NOCl (17 ml, gas) introduced by a syringe through a rubber serum cap. After 10 min, a sample (10 ml) was filtered and investigated by IR spectroscopy. To the rest of the solution, acetic acid (0.05 ml) was added. If any blue colour could be seen, the sample was investigated by electronic spectroscopy. The amount of octyl acetate was determined by GLC (*o*-nitrotoluene used as internal standard). The results are given in Table 2.

Table 2. Deamination of octylamine (51 mmol l^{-1})with nitrosyl chloride (27 mmol l^{-1}) in aprotic solvents.

Solvent	Reaction temp. °C	Absorbance at 665 nm, log (I_0/I) ($\equiv C-NO$)	Band at 2050 cm^{-1} ($> CN_2$)	Yield of octylacetate in per cent of added NOCl
Chloroform	−55	0.06	−	< 0.5
Toluene	−45	0.03	−	< 0.5
Heptane	−23	0	−	< 0.5
Tetrahydrofuran	−55	0	+	53
Ethylene glycol dimethyl ether	−55	0	[a]	51
Ethyl ether	−70	0	+	40

−, band absent
+, band p esent
[a] Ethylene glycol dimethyl ether in 1 mm thickness was not transparent at 2050 cm^{-1}.

Octane as a possi'le reaction product. To investigate if octane was present in the deamination mixture from octylamine and NOCl in CH_2Cl_2, a reaction identical to run 1 was made. Instead of chromatographing the neutral product, this was distilled at $100-150°$. The distillate (0.3 g) was investigated by GLC. It contained less than 0.1 % octane and approximately twice the amount found in the deamination in ethyl ether: an equivalent run was made with dry ethyl ether as solvent. In this run also, less than 0.1 % of octane was detected by GLC. The GLC was able to separate octane, 1-octene, *cis*-2-octene, and *trans*-2-octene.

The reaction of octyl nitrite in the presence of octylamine and octylammonium chloride. Two solutions were made: solution A, octyl nitrite (67 mg) in CH_2Cl_2 (100 ml); solution B, octylammonium chloride (516 mg) and octylamine (107 mg) in CH_2Cl_2 (100 ml). The electronic spectrum of a mixture of solution A (5 ml) and solution B (5 ml) after 20 min at 20° was identical to that of a mixture of solution A (5 ml) and pure CH_2Cl_2 (5 ml).

The reaction of octyl nitrite with NOCl. Octyl nitrite (120 mg) in CH_2Cl_2 (200 ml) was cooled to $-70°$ and NOCl (10 ml, gas) added. After 10 min, half of the mixture was allowed to reach $+25°$. To the other half, acetic acid (0.2 ml) was added and the solution warmed up to $+25°$. In the solution without acetic acid, the electronic spectrum was the sum of the spectra of NOCl and octyl nitrile corresponding to the starting concentrations. In the sample with acetic acid added, no blue colour appeared when the mixture approached room temperature.

The reaction of octyl nitrite with diazoethane. A solution of diazoethane was made from *N*-nitroso-*N*-ethyl urea (1 g) in CH_2Cl_2 (50 ml). This solution was cooled to $-55°$, and octyl nitrite (100 mg) and octylamine (45 mg) was added. After 10 min at $-55°$, acetic acid (0.05 ml) was added and the mixture allowed to reach 25°. No blue colour could be detected; the yellow colour of diazoethane disappeared on the addition of acetic acid.

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