

Investigations on the Aprotic Deamination of Benzylamine and ($\alpha,\alpha\text{-}^2\text{H}_2$)Benzylamine

JAN M. BAKKE* and K. SVENDSEN

University of Trondheim, NLHT, Department of Chemistry, N-7034 Trondheim, Norway

The reaction of benzylamine with nitrosyl chloride in diethyl ether at -50°C gave diazotoluene (16%), benzyl alcohol (15%), benzyl chloride (31%) and α,α' -azoxytoluene (12%) together with several other products. The same reaction with ($\alpha,\alpha\text{-}^2\text{H}_2$)benzylamine gave diazotoluene (8%), benzyl alcohol (15%), benzyl chloride (30%) and α,α' -azoxytoluene (20%). These results, along with those from runs with decreasing reactant concentration showed that more than one intermediate was formed in the initial reaction. *cis*- and *trans*-Toluenediazohydroxide and toluenediazochloride were proposed as the intermediates in the parallel reaction pathways.

We have reported the direct transformation of alkylamines to the corresponding diazoalkanes. In addition, alkyl chlorides, alcohols and alkenes were formed.^{1,2} Diazohydroxides have been postulated

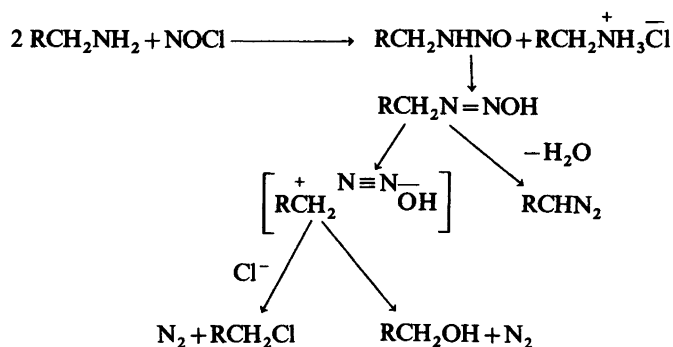
* Author to whom correspondence should be addressed at Organic Chemistry Laboratories, Norwegian Institute of Technology, University of Trondheim, N-7034 Trondheim, Norway.

as key intermediates in the deamination of aliphatic amines.^{3–6} The carbonium ion formed on nitrogen expulsion reacts with available nucleophiles, and the diazoalkanes are formed by elimination of water from the alkanediazohydroxides (Scheme 1).

To test this hypothesis we have reacted benzylamine and ($\alpha,\alpha\text{-}^2\text{H}_2$)benzylamine with nitrosyl chloride in diethyl ether at low temperature. The rate of formation of diazotoluene should show a primary deuterium kinetic isotope effect while only secondary effects are expected for the formation of benzyl chloride and benzyl alcohol.

With a common precursor (Scheme 1) this should result in a decrease in the yield of diazotoluene and an increase in that of benzyl chloride and benzyl alcohol when ($\alpha,\alpha\text{-}^2\text{H}_2$)benzylamine was the reactant as compared to benzylamine. The results in Table 1 do not support this.

The yield of diazotoluene decreased while the proportions of benzyl chloride and benzyl alcohol remained unchanged. However, the yield of α,α' -azoxytoluene increased. These results are consistent



Scheme 1.

Table 1. Reaction of benzylamine (160 mM) with NOCl (40 mM) in diethyl ether at -50°C .

Product	Yields in % of NOCl from	
	Benzyl-amine	($\alpha,\alpha\text{-}^2\text{H}_2$)-Benzylamine
Benzaldehyde	2 ± 0.5	1 ± 0.5
Benzyl chloride	31 ± 2	30 ± 2
Benzyl alcohol	15 ± 1	15 ± 1
Benzyl ethyl ether	0.1 ± 0.05	0.1 ± 0.05
Diazotoluene ^a	16 ± 1	8 ± 1
Benzyl acetate ^b		3 ± 1
Dibenzyl ether	3 ± 1	2 ± 1
Dibenzyl nitrosamine	6 ± 1	4 ± 1
α,α -Azoxytoluene	12 ± 1	20 ± 1
Dibenzylamine	3 ± 1	4 ± 1
<i>N</i> -Benzylidene-benzylamine	2 ± 1	1 ± 1

^aDetermined by IR spectroscopy. ^bYield of benzyl acetate from runs with acetic acid added minus yield of diazotoluene determined by IR spectroscopy.

with a scheme involving two or more key intermediates, one leading to diazotoluene and α,α' -azoxytoluene and others to benzyl chloride and benzyl alcohol. The products from ($\alpha,\alpha\text{-}^2\text{H}_2$)benzylamine contained only ^2H on the benzylic carbons. They were thus not formed from diazotoluene.¹

The intermediate giving rise to diazotoluene and α,α' -azoxytoluene is proposed to be *cis*-toluenediazohydroxide (1) in equilibrium with its anion (1a). *cis*-Alkanediazohydroxides convert to diazoalkanes,^{4,5} and their anions have been alkylated to give azoxyalkanes.⁷

A possible common precursor for benzyl chloride and benzyl alcohol would be *trans*-toluenediazohydroxide (2) which on decomposition could form an ion pair analogous to that in Scheme 1. The ion pair could collapse to benzyl alcohol or react with chloride ion to give benzyl chloride. However, the results in Table 2 are not consistent with the latter assumption. When the reaction was conducted at several different concentrations, the yield of benzyl chloride increased with decreasing reactant concentrations. This is contrary to expectation for a bimolecular process as in Scheme 1. Instead, it implies that benzyl chloride is formed in a monomolecular reaction which competes with bimolecular processes. Toluenediazochloride (3) is a possible precursor of benzyl chloride. On nitrogen expulsion an ion pair would form which could

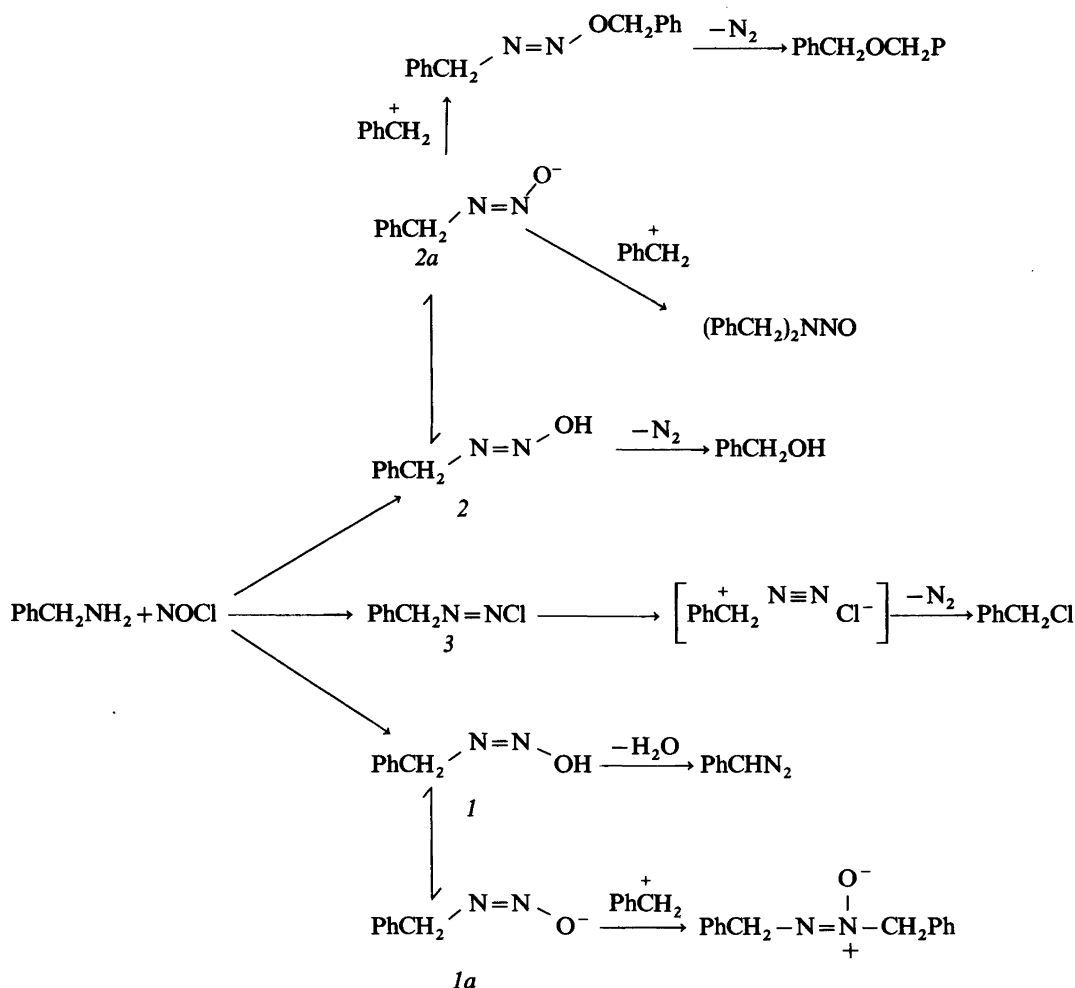
Table 2. Reactions of benzylamine with nitrosyl chloride in diethylether at -50°C . $[\text{Amine}]/[\text{NOCl}] = 4:1$.

Product	Yields in % of NOCl at initial concentration of NOCl		
	40 mM	20 mM	10 mM
Benzaldehyde	2 ± 0.5	0.2	—
Benzyl chloride	31 ± 2	51	58
Benzyl alcohol	15 ± 1	10	10
Benzyl ethyl ether	0.1 ± 0.05	1	2
Diazotoluene	16 ± 1	17	15
Dibenzyl ether	3 ± 1	0.1	0.1
Dibenzyl nitrosamine	6 ± 1	4	2
α,α -Azoxytoluene	12 ± 1	10	6
Dibenzylamine	3 ± 1	0.1	0.1
<i>N</i> -Benzylidene-benzylamine	2 ± 1	—	—

collapse to benzyl chloride or react with nucleophiles.

Two of the minor products, dibenzyl ether and dibenzyl nitrosamine, indicate the presence of another intermediate. A likely intermediate is toluenediazotate which on *N*-alkylation gives dibenzyl nitrosamine and on *O*-alkylation, followed by nitrogen expulsion, dibenzyl ether. It is clear that they were not formed from the same precursor as diazotoluene, *cis*-toluenediazohydroxide (2), or its anion 2a as their yields were the same from benzylamine and ($\alpha,\alpha\text{-}^2\text{H}_2$)benzylamine. Furthermore, Moss has reported that dialkyl nitrosamines are only formed in trace amounts on alkylation of *cis*-alkanediazotates.⁷ In our experiments dibenzyl nitrosamine was formed in a yield comparable to that of α,α' -azoxytoluene, indicating that the two compounds were not formed from *cis*-toluenediazotate (1a). We therefore propose *trans*-toluenediazotate (2a) as the precursor of dibenzyl ether and dibenzyl nitrosamine. As benzyl alcohol was not formed from *cis*-toluenediazohydroxide (from the results in Table 1), *trans*-toluenediazohydroxide (2) is the likely precursor of this as well. It should be noted that *cis*- and *trans*-diazotates or -diazohydroxides do not interconvert at -50°C .⁴ Dialkyl nitrosamines, with less double bond character of the N—N bond, have a barrier of ca. 25 kcal/mol⁻¹ for rotation about the bond.^{8,9}

The alkylating agent involved in the formation of the bimolecular products was not benzyl chloride since a run with benzyl chloride added did not



Scheme 2.

change the product composition. Since the yield of benzyl chloride decreased with increasing initial concentration (Table 2), toluenediazochloride (3) or the benzyl cation formed from its decomposition are the likely alkylating agent(s). On the other hand, *cis*- and *trans*-toluenediazohydroxide (1 and 2) did not act as alkylating agents. The yields of the main products from these suspected intermediates, benzyl alcohol and diazotoluene, were hardly influenced in the dilution experiments (Table 2). This difference is not surprising. Decomposition of optically active *cis*- and *trans*-diazotates gave different stereochemical results, indicating a different degree of separation of the ions in the resulting ion pairs.¹⁰

The stereochemistry of the N–N double bond and the nature of the leaving group (Cl or OH) must therefore have a strong influence on the course of the reaction.

We thus propose Scheme 2 to give a better description than Scheme 1 of the deamination reaction in solvents of low polarity. The reaction of benzylamine with nitrosyl chloride gives three products, toluenediazochloride (3), and *cis*- and *trans*-toluenediazohydroxide (1 and 2). These three then react to give the products reported in Tables 1 and 2.

As a result of work on alkanediazohydroxides, it has been argued that the yield of diazoalkane in the

deamination reaction depends on the stability of the diazoalkane as compared to that of the carbonium ion formed on nitrogen expulsion.^{4,11} Our results show other factors to be important as well, since the yield of diazoalkane first of all depends on the yield of *cis*-alkanediazohydroxide in the initial reaction between nitrosyl chloride and amine. In this reaction, steric and other factors not yet investigated may be of importance.

Finally, Scheme 2 offers a simple explanation of the stereochemical results from the deamination of optically active amines. These investigations showed that both the alcohol and the corresponding alkyl chloride were formed with retention of configuration.^{12,13} This is difficult to explain if the alkyl chloride was formed by reaction of an ion pair with a chloride ion. However, if the alkyl chloride and alcohol were formed on decomposition of the diazo compounds 2 and 3 and not in bimolecular reactions, the stereochemical results are analogous to those obtained on deamination of amides where the products are formed on collapse of ion pairs.³

EXPERIMENTAL

A typical deamination experiment was performed as follows. Benzylamine (1.74 g, 16.3 mmol) in diethyl ether (100 ml, distilled from lithium aluminium hydride) was cooled to -75°C and nitrosyl chloride (100 ml gas, 4 mmol) was added by a syringe through a rubber septum. The brown colour disappeared after 10 min, and the reaction temperature was then raised to -50°C . After 7 h, acetic acid (6 ml) was added, the mixture left overnight, then extracted once with 3% aqueous HCl and twice with water. The combined aqueous extracts were saturated with sodium chloride, made basic and extracted four times with diethyl ether. The basic product (1.25 g) contained (VPC) benzylamine (1.20 g, 11.2 mmol), dibenzylamine (12 mg, 0.06 mmol) and *N*-benzylidenbenzylamine (8 mg, 0.04 mmol). The neutral extract of the reaction mixture was washed with sodium bicarbonate solution and dried over sodium sulfate. The neutral product (0.43 g) contained (VPC) benzaldehyde (8 mg, 0.08 mmol), benzyl chloride (156 mg, 1.24 mmol), benzyl alcohol (65 mg, 0.60 mmol), benzyl ethyl ether (0.5 mg, 0.003 mmol), benzyl acetate (96 mg, 0.64 mmol), dibenzyl ether (12 mg, 0.06 mmol), dibenzyl nitrosamine (27 mg, 0.12 mmol) and α,α' -azoxytoluene (53 mg, 0.24 mmol). The yield of diazotoluene was also determined in separate experiments where no acetic acid was added.

Instead, the reaction mixture was filtered and the concentration of diazotoluene determined by IR spectroscopy (band at 2060 cm^{-1}).¹⁴

The reaction mixtures were analysed by VPC on a Hewlett-Packard 5985 VPC/MS system equipped with a 25 m glass capillary column (SE 54 as stationary phase) and with *p*-nitrotoluene as internal standard. All peaks in the chromatogram were identified, except for two with retention time between benzyl acetate and dibenzyl nitrosamine, both with less than 2% of total area, NMR spectra were recorded on a JEOL JNM FX 100 spectrometer. All signals in the ^1H spectrum and all but one in the ^{13}C spectrum (at δ 58.14, intensity equal to that of the down field signal of dibenzyl nitrosamine) could be assigned to the compounds in Tables 1 and 2.

($\alpha,\alpha\text{-}^2\text{H}_2$)Benzylamine was prepared by lithium aluminium deuteride reduction of benzonitrile.¹⁵ The product was worked up after addition of water. GC/MS and NMR showed the product to be 99% pure ($\alpha,\alpha\text{-}^2\text{H}_2$)benzylamine.

Role of benzyl chloride in the reaction. Benzylamine (0.87 g, 8.1 mmol) in diethyl ether (50 ml) was cooled to -75°C and benzyl chloride (0.11 g, 0.87 mmol) was added. Nitrosyl chloride (50 ml, 2 mmol) was then added, the reaction mixture was kept at -75°C for 15 min and then at -50°C for 7 h. The reaction mixture was worked up and analysed as above. The results were identical to those in Table 1 except for benzyl chloride (yield 0.17 g, 1.35 mmol).

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