

Acid-catalyzed Formation of Diazoalkanes. A One-pot Transformation of Alkylamines to Diazoalkanes

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We recently reported results from the deamination of benzylamine and ($\alpha,\alpha\text{-}^2\text{H}_2$)benzylamine which indicated that three products were formed in the initial reaction between the amine and nitrosyl chloride. These were the *trans*- and *cis*-toluenediazohydroxides (1 and 2) together with toluenediazochloride (3). We proposed that diazotoluene was formed by water elimination from *cis*-toluenediazohydroxide in competition with its alkylation to α,α' -azoxytoluene.¹ We now present the results of experiments which show an improvement in the direct synthesis of diazoalkanes from the corresponding amines. The method may be of special value for preparation of specifically ¹⁵N labeled diazoalkanes.

In the experiments described, nitrosyl chloride was reacted with an excess of amine.¹ The reaction mixture was therefore weakly basic during the reaction of the three intermediates. Under these conditions the formation of diazotoluene required several hours at -50°C for completion. It occurred

to us that the water loss from toluenediazohydroxide might be catalyzed by protonation of the hydroxyl group. The toluenediazonium ion (4) formed might then release a proton to form diazotoluene.

Acetic acid was therefore added to the reaction mixture prepared from benzylamine and nitrosyl chloride in diethyl ether at -75°C . The pink color of diazotoluene became visible after a few seconds and its formation appeared to be complete within a minute. Gaseous ammonia was then added to neutralize the acetic acid. The yield of diazotoluene was determined by UV/VIS and IR spectroscopy to be 31% (based on nitrosyl chloride). This should be compared to the 16% yield obtained when the reaction was carried out without acidic catalysis.¹ The other products were benzyl chloride, benzyl alcohol and benzyl acetate. The variety of other products reported earlier was either absent or present only in trace amounts (Table 1). The reaction was tried with several other alkylamines and gave fair yields from those with primary alkyl groups but low or zero yields from those with secondary alkyl groups (Table 2). There is one notable exception, 9-fluorenylamine gave a 32% yield of 9-diazo fluorene. This is understandable both from the ability of the 9-fluorenyl system to stabilize a negative charge and from its reluctance to accept positive charge.

When perchloric acid (130 mM, 70% in water) was tried as a catalyst no diazotoluene was formed. Instead an increase in the yield of benzyl alcohol was observed. If the acid was neutralized with ammonia after five min at -75°C a substantial increase in the yield of dibenzylamine was found (Table 1). This

Table 1. Reaction of benzylamine (160 mM) with NOCl (40 mM) in diethyl ether at -75°C .

Product	Yields in % of NOCl		Reaction conditions		
	a	b	c	d	e
Benzaldehyde	2±0.5	—	—	—	—
Benzyl chloride	31±2	16±1	18±1	17±1	14±1
Benzyl alcohol	15±1	10±1	64±2	41±2	10±1
Benzyl ethyl ether	0.1±0.05	—	—	—	—
Diazotoluene	16±1	31±1	—	—	23±1
Benzyl acetate	—	27±1	—	—	38±1
Dibenzyl ether	3±1	—	—	—	—
Dibenzyl nitrosamine	6±1	—	—	—	—
α,α -Azoxytoluene	12±1	—	—	—	—
Dibenzylamine	3±1	1±0.5	7±1	18±2	2±1
N-Benzylidenebenzylamine	2±1	—	—	—	—

^a Kept at -50°C .¹ ^b Acetic acid (130 mM) added after 30 min at -75°C , ammonia (80 mM) added 3 min later.
^c Perchloric acid (130 mM, 70% solution) added after 30 min at -75°C . ^d As ^c but ammonia (80 mM) added 5 min after addition of acid. ^e ($\alpha,\alpha\text{-}^2\text{H}_2$)Benzylamine reacted as under condition ^b.

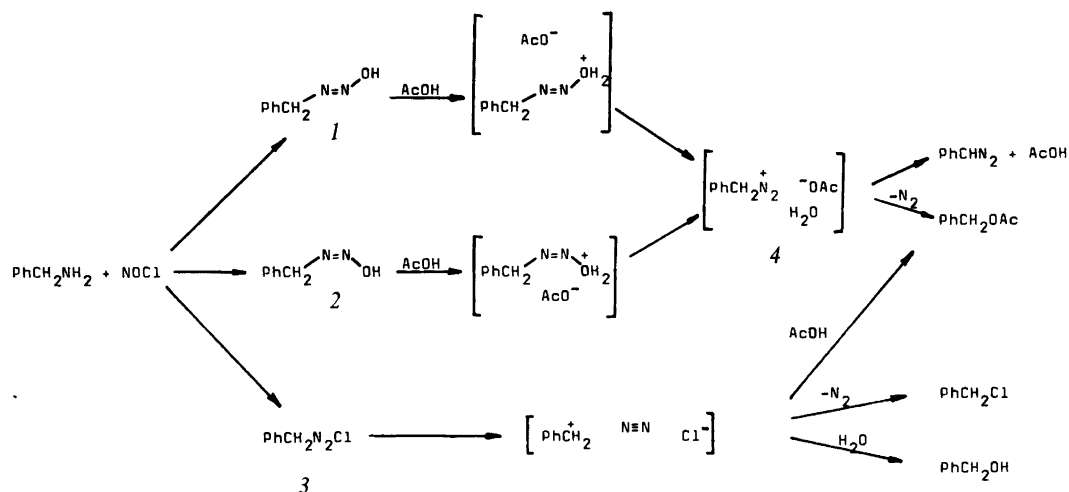
Table 2. Formation of diazoalkanes from the corresponding amines. Reaction conditions as in ^b in Table 1.

Amine reacted	Diazoalkane formed	Yields in % of NOCl
Benzylamine	Diazotoluene	31 ± 1
(α,α - ² H ₂)benzylamine	(α - ² H)Diazotoluene	23 ± 1
Octylamine	Diazoctane	40 ± 1
Methylamine	Diazomethane	22 ± 1
2-Octylamine	None	0 ± 0.3
1-Indanylamine	None	0 ± 0.3
Diphenylmethylamine	Diphenyldiazomethane	10 ± 1
9-Fluorenylamine	9-Diazofluorene	32 ± 1

suggests that the toluenediazonium ion (4) was still present in the solution and shows that benzylamine could act as a nucleophile to give dibenzylamine but not as a base which could abstract a proton to give diazotoluene even if it is a stronger base than the acetate ion. In the reaction catalyzed by acetic acid the proton abstraction must therefore have taken place simultaneously with or shortly after the departure of the protonated hydroxyl group but before the acetate ion had left the ion pair (Scheme 1). The reaction of (α,α -²H₂)benzylamine with nitrosyl chloride followed by addition of acetic acid gave results in accordance with this (Table 1). A decrease in the yield of diazotoluene was observed but no increase in the yield of benzyl alcohol, benzyl chloride or dibenzylamine. The only increase in yield was observed for benzyl acetate as would be expected from Scheme 1, where diazoalkane formation competes with decomposition of the diazonium ion to give the acetate. It is thus clear that in this case, as it was without acid catalysis,¹

diazotoluene was formed from a different intermediate than were benzyl chloride and benzyl alcohol.

Experimental. The technique for the deamination reactions has been described.¹ The acid was added after 30 min at -75 °C. The color of the diazoalkane appeared after a few seconds and no further increase in intensity of the color could be seen after ca. 1 min. Gaseous ammonia was then added with a syringe through the rubber septum. The reaction mixture was filtered and the amount of diazoalkane was determined by IR (band at ca. 2060 cm⁻¹) and UV/VIS spectroscopy. The extinction coefficients of diazotoluene were determined from the experiments with (α,α -²H₂)benzylamine. A portion (10 ml) of the reaction mixture (50 ml) was filtered and its absorbances at 2060 cm⁻¹ and 490 nm were determined. To the remainder of the mixture excess acetic acid was added. The amount of benzyl acetate was determined by GLC analysis and the ratio of (α -²H)benzyl acetate-(α,α -²H₂)benzyl acetate was



Scheme 1.

determined by MS (AEI 90). Assuming that (α - ^2H)benzyl acetate was formed quantitatively from (α - ^2H)diazotoluene and that it was formed in that way only, $\epsilon_{490}=28 \text{ M}^{-1} \text{ cm}^{-1}$ and $A_{2060}=8.5 \times 10^4 \text{ M}^{-1} \text{ cm}^{-2}$ (area of band determined by method I of Ramsey)² were found. Both these values are higher than those reported earlier ($\epsilon_{490}=22 \text{ M}^{-1} \text{ cm}^{-1}$ and $A_{2060}=5.4 \times 10^4 \text{ M}^{-1} \text{ cm}^{-2}$),^{3,4} Diazooctane,⁵ diphenyldiazomethane⁶ and diazofluorene³ were determined by known spectral extinction coefficients. The other compounds were determined by GLC analyses (Carlo Erba 4160, 15 m SE 54 WCOT column, Hewlett Packard 3390A integrator, *p*-nitrotoluene as internal standard).

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