[CONTRIBUTION FROM DEFENCE RESEARCH CHEMICAL LABORATORIES]

REACTION OF BENZYLAMINE WITH 3-NITROSO-2-OXAZOLIDONE[1]

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Received October 27, 1952

It has been shown recently (8) that 3-nitroso-2-oxazolidone reacts with the aromatic bases *p*-anisidine and *p*-phenetidine to give carbon dioxide, nitrogen, 2-arylaminoethyl N-arylcarbamates, and N,N'-diarylethylenediamines, plus traces of acetaldehyde and acetylene.[2] On the other hand with strong alkali, the main products are acetylene, carbon dioxide, and nitrogen, the oxazolidone ring being completely broken down (3, 9). It seemed of interest to investigate the action of an amine of intermediate basic strength, and it was for this reason that the present study was undertaken. As was expected, benzylamine proved to be intermediate in its action, and products corresponding to both the above types of reaction were obtained together with two types of products not encountered previously.

The 3-nitroso-2-oxazolidone (I) was added to a solution of benzylamine in 50% aqueous ethanol. The addition was accompanied by a brisk evolution of gas, and the gradual separation of a crystalline precipitate. This crystalline solid was found to be almost pure ethylene glycol bis-N-benzylcarbamate (II). For verification, the same compound was synthesized from ethylene glycol and benzyl isocyanate. Solvent extraction of the filtrate under different conditions gave a separation of the mixture into 2-hydroxyethyl N-benzylcarbamate (III), 2-benzylaminoethyl N-benzylcarbamate (IV), and N,N'-dibenzylethylenediamine (V), along with recovered benzylamine and traces of benzyl alcohol. The last presumably arises from interaction between benzylamine and small amounts of nitrous acid present in the solution. The structure of III was confirmed by the presence of carbonyl and hydroxyl bands in its infrared spectrum, and by conversion into ethylene glycol bis-N-benzylcarbamate (II) with benzyl isocyanate. Treatment of IV with benzyl isocyanate gave N-(2-benzylcarbamylethyl)-N,N'-dibenzylurea, (VI) which was synthesized independently from N-2-hydroxyethylbenzylamine and two mole-equivalents of benzyl isocyanate. Compound V is known and was identified as its dibenzoyl and diacetyl derivatives (1). No 3-benzyl-2-oxazolidone, N-2-hydroxyethylbenzylamine, or ethylene glycol were detected.

A separate examination of the gaseous products of the reaction was carried out as described in the Experimental Section. The yields of acetylene and carbon dioxide were sufficient to account for almost all the 3-nitroso-2-oxazolidone not involved in the formation of the solid and liquid products described. It is of interest to note that the yield (56%) of acetylene obtained is substantially larger than that reported by Newman and Kutner (9) for the decomposition of

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[1] Issued as DRCL Report No. 89.

[2] Acetylene was only obtained after acidification of the reaction mixture and was apparently not a primary reaction product.

3-nitroso-2-oxazolidone by aqueous alkali, and is almost as large as their yield of phenylacetylene from 5-phenyl-3-nitroso-2-oxazolidone.

At the end of one run the solution was acidified with concentrated hydrochloric acid, about half the solvent distilled off, and the distillate tested for aldehydes with 2,4-dinitrophenylhydrazine. A mixture of products was obtained, which consisted largely of acetaldehyde 2,4-dinitrophenylhydrazone, with a small amount of benzaldehyde 2,4-dinitrophenylhydrazone. The benzaldehyde probably arises by partial oxidation of traces of benzyl alcohol by nitrous acid. About 90% of the starting materials are accounted for by the described products, which are consistent with the mechanisms suggested previously for the reaction of 3-nitroso-2-oxazolidone with aromatic amines (8) and also with aqueous alkali (9). A more detailed outline of the mechanism for the reaction of benzylamine with 3-nitroso-2-oxazolidone is given in Figure 1.

The rate of reaction of 3-nitroso-2-oxazolidone is proportional to the K_B of the amine and the amine concentration. This has been demonstrated qualitatively for the reaction of amines with various nitrosamides. Quantitative kinetic studies on this reaction will be reported at a later date elsewhere. Another consequence of the reaction scheme presented in Figure 1 is that the products of this reaction should vary quantitatively with the relative OH^- ion and amine concentrations. This fact has now been established (6–8) for both the reactions of 1-nitroso-2-nitramino-2-imidazoline and 3-nitroso-2-oxazolidine with amines. The reaction mechanism given in Figure 1 agrees with the available facts but it should not be considered final. However it does allow the prediction of the types of products to be expected from the reaction of a particular amine with 3-nitroso-2-oxazolidone.

EXPERIMENTAL[3]

2-Oxazolidone. This compound was prepared by the method of Homeyer (5).

3-Nitroso-2-oxazolidone. This compound (m.p. 52–53°) was prepared in 70% yield as previously described (8).

Reaction of benzylamine with 3-nitroso-2-oxazolidone. 3-Nitroso-2-oxazolidone (30 g., 0.26 mole) was added portionwise with stirring to a solution of 60 g. (0.56 mole) of freshly distilled benzylamine in 100 ml. of 50% aqueous ethanol, the temperature being maintained below 25° with an ice-bath. The addition was accompanied by a strong evolution of gas, and the gradual separation of a colorless crystalline precipitate. After the gas evolution had ceased, the solution was allowed to stand for one hour. The precipitate was removed and washed successively with 25 ml. of water and 100 ml. of ether, leaving 5 g. of white nacreous plates, m.p. 152–155°. This melting-point was raised to 156–158° by one recrystallization from ethanol and was not depressed by admixture with authentic ethylene glycol bis-N-benzylcarbamate, yield 5.9%.

Anal. Calc'd for $C_{18}H_{20}N_2O_4$: C, 65.83; H, 6.14; N, 8.53.

Found: C, 65.61; H, 6.16; N, 8.54.

The combined filtrates were diluted with 200 ml. of water and made strongly acid by the addition of concentrated hydrochloric acid (50 ml.) in order to decompose the amine carbonates present. On standing and cooling for two hours, a crystalline hydrochloride separated and was removed (6.5 g.). This compound crystallized from aqueous ethanol in square

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[3] All melting points are corrected and were determined on a Kofler block unless otherwise stated. Microanalysis by C. W. Beazley, Skokie, Illinois.

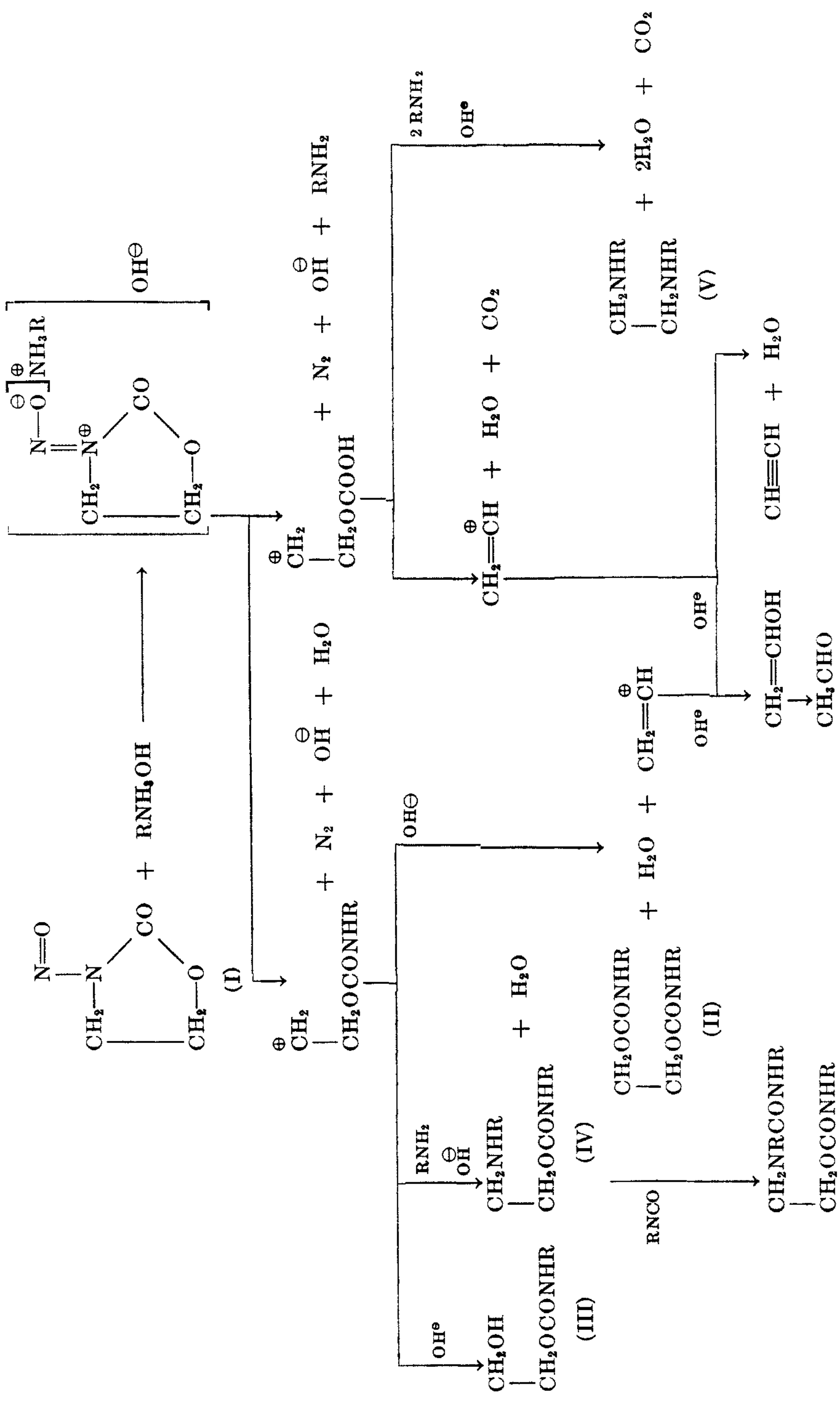
(I)
RNH₃OH
OH⊖
CH₂OCONHR
CH₂OCOOOH
N₂
RNH₂
H₂O
CO₂
2 RNH₂
OH⊖
(II)
(III)
(IV)
(V)
(VI)
RNCO
CH₂OH
CH₂NHR
CH₂NRCONHR
CH₂=CHOH
CH₃CHO
CH≡CH

FIGURE 1

plates m.p. 240–250° (uncorr.) with decomp. These crystals were shown by analysis and the following derivatives to be the hydrochloride of N,N′-dibenzylethylenediamine.

Anal. Calc'd for $C_{16}H_{22}Cl_2N_2$: C, 61.35; H, 7.08; N, 8.94.
Found: C, 61.68; H, 7.40; N, 9.44.

The *free base* was liberated with sodium hydroxide, extracted with ether, and the oil which was left after removal of the ether was treated with two mole-equivalents of benzyl isocyanate. A solid product formed almost immediately, and was crystallized twice from ethanol, giving colorless needles, m.p. 212–213°.

Anal. Calc'd for $C_{32}H_{34}N_4O_2$: C, 75.86; H, 6.76; N, 11.06.
Found: C, 75.85; H, 6.83; N, 10.80.

The *dibenzoyl derivative* was prepared in the usual manner by the Schotten-Baumann reaction, and was obtained, after one recrystallization from ethanol, as colorless needles, m.p. 184–184.5°. The reported melting-point for N,N′-dibenzoyl-N,N′-dibenzylethylenediamine is 183° (1).

Anal. Calc'd for $C_{30}H_{28}N_2O_2$: C, 80.34; H, 6.29; N, 6.25.
Found: C, 80.84; H, 6.53; N, 6.65.

The *diacetyl derivative* was also formed, by heating the free base with acetic anhydride. The crystals melted at 139–140° after one recrystallization from methanol. The reported melting-point of N,N′-diacetyl-N,N′-dibenzylethylenediamine is 139° (1).

The aqueous acid filtrate was extracted with ether (5 × 200 ml.) and then with 50% ether-chloroform (1 × 200 ml.) to remove neutral and acidic compounds. The combined extracts were dried with sodium sulfate, the solvents flashed off, and the resulting oil fractionated in a small (50 ml.) Vigreux-Claisen flask at 1 mm. pressure. The first fraction (0.2 g.; b.p.$_1$ 50–51°) was a yellow oil, smelling strongly of benzyl alcohol (b.p.$_{760}$ 205°). Treatment with α-naphthyl isocyanate in benzene gave a solid product, which after two recrystallizations from methanol melted at 131–133°. This melting-point was not depressed by admixture with authentic benzyl N-α-naphthylcarbamate, m.p. 134°.

The main part of this same ether extract (3.5 g.) distilled as a thick yellow oil b.p.$_1$ 135–145°.

Anal. Calc'd for $C_{10}H_{13}NO_3$: C, 61.54; H, 6.71; N, 7.18.
Found: C, 61.51; H, 6.52; N, 6.68.

The pot residue was transferred to a Späth bulb, and distilled at an air-bath temperature of 180° at 1 mm. This yielded a further 1.5 g. of a thick yellow oil, which gradually crystallized on standing. The crystals were filtered off, pressed free from oil with a rubber dam, and carefully washed with a few ml. of ether, leaving 0.5 g. of waxy colorless plates, m.p. 42–44°. Since it was impossible to recrystallize this substance because of its high solubility in most solvents and low melting-point, it was dried as such for analysis.

Anal. Calc'd for $C_{10}H_{13}NO_3$: C, 61.54; H, 6.71; N, 7.18.
Found: C, 61.60; H, 6.86; N, 7.05.

The infrared spectrum of a 5% solution in chloroform showed a strong carbonyl peak at 1710 cm.$^{-1}$ and a hydroxyl band at 3230 cm.$^{-1}$ The spectrum was found to be identical with that of the oil b.p.$_1$ 135–145°, and the two fractions are considered to be the same compound. The higher purity of the Späth bulb distillate is undoubtedly due to the lesser decomposition by this method of distillation. A sample of the oil was treated with exactly one mole-equivalent of benzyl isocyanate, and left for two days in a desiccator. The solid product was leached with five ml. of benzene, filtered off, and washed with a further 10 ml. of benzene. After one recrystallization from aqueous ethanol, this substance melted at 156–157°. A mixture with ethylene glycol bis-N-benzylcarbamate (m.p. 156–158°) showed no depression in melting-point. The yellow oil b.p.$_1$ 135–145° and the solid m.p. 42–44° are, therefore, considered to be 2-hydroxyethyl N-benzylcarbamate, yield 10.9%.

The acid aqueous solution from the above extraction was extracted with chloroform (5 × 200 ml.) to remove chloroform-soluble hydrochlorides. The light-brown extract was shaken with aqueous sodium hydroxide to remove hydrochloric acid, and the chloroform solution of the base concentrated to an oil *in vacuo*. The base was then reconverted to the hydrochloride, and the salt recrystallized from aqueous ethanol. There first separated

0.4 g. of N,N′-dibenzylethylenediamine dihydrochloride (confirmed as above by converting the base to its dibenzoyl derivative). Further concentration yielded 1.5 g. of a hydrochloride, m.p. 187–189°. In one run, concentration of the original chloroform extract yielded this same salt directly.

Anal. Calc'd for $C_{17}H_{21}ClN_2O_2$: C, 63.65; H, 6.60; N, 8.74.

Found: C, 63.66; H, 6.53; N, 9.20.

The free base could not be obtained crystalline, and was treated with one mole-equivalent of benzyl isocyanate in a few ml. of benzene, and left for two days in a desiccator. The product crystallized on scratching, and after two recrystallizations from methanol, was obtained as chunky colorless crystals, m.p. 92–94°. This melting point was not depressed by admixture with authentic N-(2-benzylcarbamylethyl)-N,N′-dibenzylurea, m.p. 93–94°, and the hydrochloride m.p. 189° is concluded to be that of 2-benzylaminoethyl N-benzylcarbamate. The chloroform extract left a residue (4.0 g.) which failed, however, to yield any more pure material. The above base was relatively unstable, and decomposed on attempted Späth bulb distillation, which may account for the relatively low yield (1.8%) of this compound.

The acid aqueous solution from the above extraction was combined with the mother liquors from the recrystallization of the N,N′-dibenzylethylenediamine dihydrochloride and made alkaline with sodium hydroxide. It was extracted in a liquid-liquid continuous extractor with ether. The extract, after drying with potassium carbonate and removal of the ether, was fractionated through a Vigreux column under reduced pressure. The first fraction, b.p.$_{10}$ 65–70°, consisted of recovered benzylamine (28 g.) identified by the melting point and mixture melting point of its benzoyl derivative. The second fraction, b.p.$_{1.5}$ 170–175°, yielded a further quantity of N,N′-dibenzylethylenediamine, identified as its dibenzoyl derivative. The total weight of N,N′-dibenzylethylenediamine isolated from this and previous fractions was 7.5 g. (12.1%).

Determination of gaseous products. Only acetylene and carbon dioxide were determined quantitatively. Three grams (0.028 mole) of freshly distilled benzylamine in 10 ml. of 50% aqueous ethanol were placed in a 100-ml. four-necked flask having a nitrogen lead-in, a dropping-funnel, a dephlegmator take-off, and a 10-ml. Erlenmeyer flask connected with wide 'Tygon' tubing for the addition of solid 3-nitroso-2-oxazolidone. The take-off was connected in series to a calcium chloride tube, a U-tube filled with 20 g of fresh "Ascarite", and three gas-washing bottles filled with cuprous chloride-pyridine reagent. The latter reagent was prepared as described by Siggia (10) with freshly precipitated cuprous chloride (2). A fourth cuprous chloride-pyridine bottle was added as a check on the completeness of absorption of the acetylene. When the nitroso compound had all been added, and gas evolution had ceased, 1.5 ml. of sulfuric acid in 5 ml. of water was added dropwise to decompose the amine carbonates. That absorption of the acetylene was inefficient was indicated by the fact that a copious precipitate of cuprous acetylide was obtained in all three gas-washing bottles, while some acetylene even penetrated to the fourth bottle. The yield of acetylene was 56%. The carbon dioxide yield was 77%.

Determination of aldehydic products. In a separate run, employing 2.45 g. (0.021 mole) of 3-nitroso-2-oxazolidone and 5 g. (0.047 mole) of benzylamine, the reaction mixture was filtered free from ethylene glycol bis-N-benzylcarbamate, acidified with five ml. of concentrated hydrochloric acid, and distilled into an ice-cooled receiver. After approximately 10 ml. had distilled, the distillate was treated with 0.5 g. of 2,4-dinitrophenylhydrazine and 0.5 ml. of concentrated hydrochloric acid and refluxed for two minutes. On cooling, 350 mg. of orange-red crystals separated, m.p. 100–125°. Several recrystallizations from ethanol, with hot filtration of sparingly soluble material, separated this mixture into five mg. of red crystals (m.p. 235–237°), and 135 mg. of yellow crystals (m.p. 135–142°). The red crystals (m.p. 235–237°) did not depress the melting point of a sample of benzaldehyde 2,4-dinitrophenylhydrazone (m.p. 237°). Further recrystallization of the lower-melting hydrazone raised its melting point to 159–163°. Admixture with authentic acetaldehyde 2,4-dinitrophenylhydrazone (m.p. 165–168°) further raised the melting point to 164–167°, and the two are considered to be identical.

Anal. Calc'd for $C_8H_8N_4O_4$: C, 42.86; H, 3.60.
Found: C, 42.75; H, 3.63.

Ethylene glycol bis-N-benzylcarbamate. Ethylene glycol (0.8 g., 0.013 mole) was added to 3.5 g (0.026 mole) of freshly-distilled benzyl isocyanate, and the mixture was heated on the hot-plate till homogeneous. The mixture was left overnight in a desiccator, and the solid product filtered off and washed with 10 ml. of benzene. Two recrystallizations from 95% ethanol gave 2.5 g. (58.8%) of colorless nacreous plates m.p. 156–158°.

Anal. Calc'd for $C_{18}H_{20}N_2O_4$: C, 65.83; H, 6.14; N, 8.53.
Found: C, 65.98; H, 6.19; N, 8.89.

N-2-Hydroxyethylbenzylamine. Ethylene chlorohydrin (4 g., 0.05 mole) was added dropwise to a solution of 10.7 g. (0.1 mole) of benzylamine in 25 ml. of water with stirring under reflux in a nitrogen atmosphere. After refluxing for two hours, the solution was made alkaline with sodium hydroxide, extracted with ether, and the mixture of extracted bases was fractionated under reduced pressure. After the excess benzylamine had distilled over at 65–70° at 8 mm., the desired product was obtained as a very viscous water-white oil, b.p.$_{1}$ 137–140°, yield 4.5 g. (59%). Treatment with picric acid in methanol gave a picrate which melted at 135–136°. The reported melting point for this compound is 135–136° (4).

N-(2-benzylcarbamylethyl)-N,N'-dibenzylurea. A solution of 0.52 g. (0.0034 mole) of N-2-hydroxyethylbenzylamine was treated with 0.92 g. (0.0069 mole) of benzyl isocyanate in the absence of a solvent, heated to the point of reflux on a hot-plate, and left for two weeks in a desiccator. The resulting glass was warmed with one ml. of benzene and the product induced to crystallize by scratching with a glass rod. After standing overnight in the refrigerator, the product was filtered off and recrystallized twice from 3–5 ml. of methanol. A 64% yield (0.92 g.) of chunky crystals (m.p. 93–94°) was obtained.

Anal. Calc'd for $C_{25}H_{27}N_3O_3$: C, 71.93; H, 6.52; N, 10.07.
Found: C, 72.32: H, 6.51: N, 10.10.

The authors are grateful to Dr. Hubley of Defence Research Chemical Laboratories for determining the reported infrared spectra.

SUMMARY

In a continuation of the study of the reaction between amines and nitrosoamides, the products obtained by treatment of benzylamine with 3-nitroso-2-oxazolidone have been investigated. The major products are acetylene, carbon dioxide, and nitrogen, along with smaller amounts of ethylene glycol bis-N-benzylcarbamate, N,N'-dibenzylethylenediamine, 2-hydroxyethyl N-benzylcarbamate, and 2-benzylaminoethyl N-benzylcarbamate, and traces of acetaldehyde, benzaldehyde, and benzyl alcohol. A tentative reaction scheme is presented.

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