[CONTRIBUTION FROM DEFENCE RESEARCH CHEMICAL LABORATORIES, CANADA]

# THE REACTIONS OF ETHYLAMINE AND *p*-AMINOACETANILIDE WITH 1-NITROSO-2-NITRAMINO-2-IMIDAZOLINE[1]

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The products from the reactions of *p*-aminoacetanilide and ethylamine with 1-nitroso-2-nitramino-2-imidazoline (I) are in accord with the reaction scheme previously (6) presented for the reaction of amines with this nitrosamine

*p*-Aminoacetanilide gives the cyclic compounds 1-*p*-acetamidophenyl-2-nitramino-2-imidazoline (II) and 1-nitro-2-*p*-acetamidophenyliminoimidazolidine (IV). The latter compound may exist in the tautomeric form as 1-nitro-2-*p*-acetamidophenylamino-2-imidazoline. Compound IV separates from the aqueous solution with water of crystallization. This at first was very confusing because on purification equilibrium mixtures of the hydrate and anhydrous compound IV were obtained. These mixtures always melted indefinitely at 151–162° with decomposition. When these crystals were melted during microscopic observation, it was found that two distinct crystalline forms were present. At *ca* 120–124° some of transparent yellow tablets melted and recrystallized in the same form as the majority of the crystals (opaque, yellow feather-like crystals). Finally procedures of crystallization were adopted which yielded the pure hemihydrate (III) and the anhydrous form (IV). Both the hemihydrate and the anhydrous form give a green color in the Franchimont test (2) using diethylaniline (7). The hydrate (III) could be converted readily into the anhydrous form (IV) by refluxing for a short time in *n*-propanol. The latter compound melted at 171–172° with decomposition. Either form of 1-nitro-2-*p*-acetamidophenylaminoimidazolidine is converted to N-$\beta$-nitraminoethyl-N′-*p*-acetamidophenylurea (V) by alkali or acid treatment. The other cyclic product, 1-*p*-acetamidophenyl-2-nitramino-2-imidazoline (II) was hydrolyzed with 10% sodium hydroxide to 1-*p*-acetamidophenyl-2-imidazolidone (VI). Compound VI was prepared for comparison by the method of Gabriel and Eschenbach (3) by heating 2-oxazolidone (5) with *p*-aminoacetanilide.

Although several runs of *p*-aminoacetanilide with 1-nitroso-2-nitramino-2-imidazoline were worked up, no N-[$\beta$-(*p*-acetamidophenylamino)ethyl]-N′-*p*-acetamidophenyl-N″-nitroguanidine nor the corresponding urea could be identified. If any reasonable amount of the nitroguanidine derivative were present, it would be expected to be easy to isolate. This absence of the linear derivatives was accompanied by increased yields of the cyclic products (II and IV).

Ethylamine on reaction with 1-nitroso-2-nitramino-2-imidazoline gives products similar to those obtained with benzylamine. Ethylnitroguanidine (VIII) and N,N′-diethyl-N″-nitroguanidine (IX) were obtained. There was no evidence of the cyclic compound 1-nitro-2-ethylamino-2-imidazoline. This would be expected because of the basicity of ethylamine (6). A picrate of the cyclic compound

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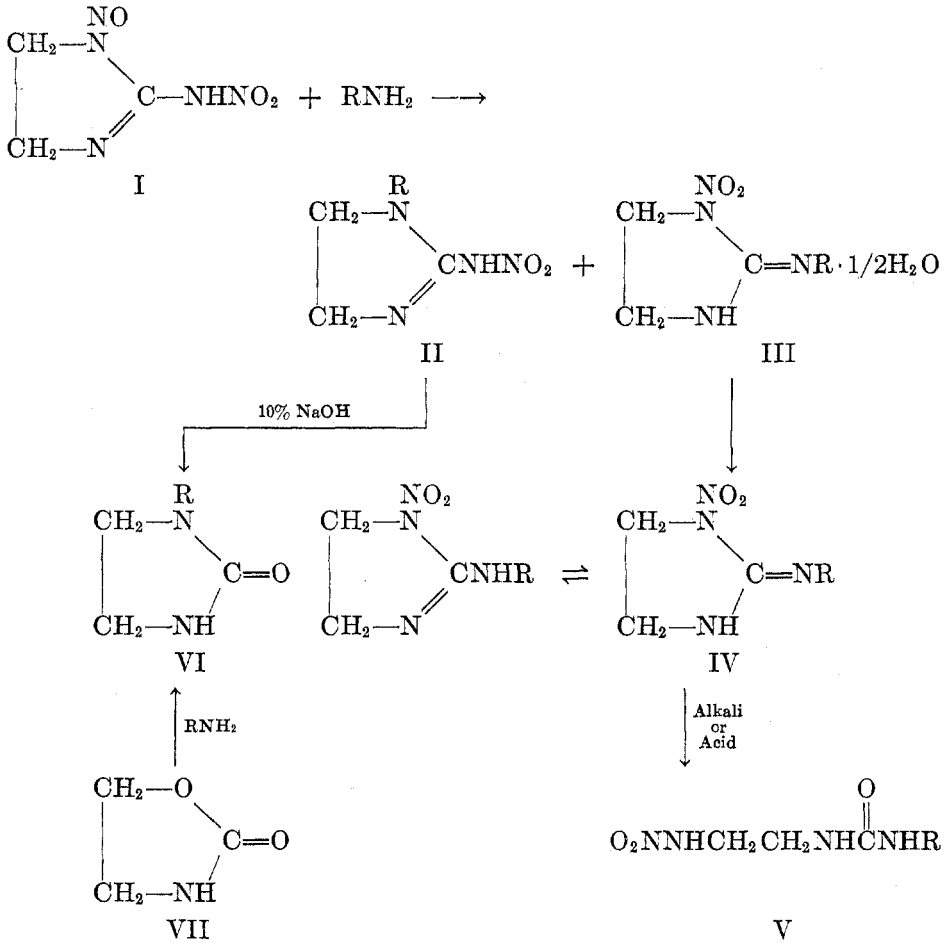
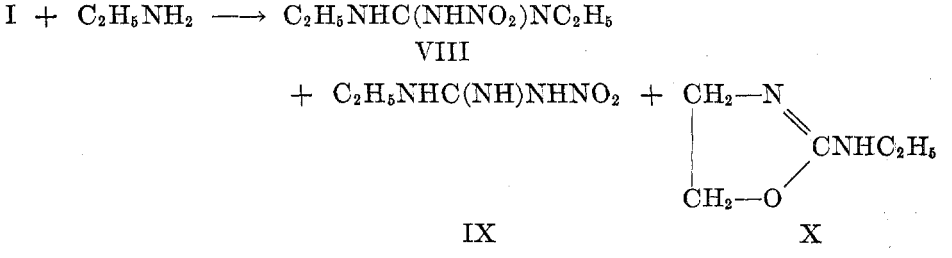



R = *p*-acetamidophenyl

2-ethylamino-2-oxazolidine (X) was obtained. It was identified by comparison with a specimen




prepared by the cyclization of N-$\beta$-chloroethyl-N'-ethylurea according to the procedure of Gabriel and Stelzner (4). Although one would expect to find 1-

ethyl-2-nitramino-2-imidazoline (7) among the products of the ethylamine run, its presence was not detected. This was explained later when other runs of ethylamine with 1-nitroso-2-nitramino-2-imidazoline were studied. It was observed that after the main reaction occurred, a secondary reaction ensued. This secondary reaction was accompanied by an evolution of gas and heat. Such a reaction could only be due to excess ethylamine reacting with one of the products. The product most susceptible to alkaline hydrolysis is 1-ethyl-2-nitramino-2-imidazolidine. It would be converted to 1-ethyl-2-imidazolidone. The later compound has been prepared (8) to examine its properties. It does not form a crystalline picrate under the usual conditions.

## EXPERIMENTAL[2]

*Reaction of p-aminoacetanilide with 1-nitroso-2-nitramino-2-imidazoline.* 1-Nitroso-2-nitramino-2-imidazoline (9) (15 g., 0.0942 mole) was added *en masse* to a suspension of 31 g. (0.206 mole) of *p*-aminoacetanilide in 100 cc. of 50% aqueous ethanol. This reaction mixture was allowed to stand at room temperature until gas evolution ceased. Several runs of this type were performed. The solid was removed by filtration and washed with 50% aqueous ethanol, yield 11.5–15.5 g. The filtrate, after dilution with water to the point of turbidity, gave a second crop of solid after standing several days, yield 2.4–6.5 g. The two crops could be divided into two fractions by crystallization from 95% ethanol or absolute ethanol. One fraction melted at 214–222° with decomposition while the other melted over a range anywhere from 146–162° with decomposition. The high-melting fractions weighed 5.86–10.13 g. (23.8–41.25%). Several recrystallizations from 95% ethanol raised the melting point of the 1-*p*-acetamidophenyl-2-nitramino-2-imidazoline to 233–234° with decomposition, yield 1.80–2.55 g. (7.31–10.38%). The greenish-yellow, felt-like crystals gave a red color in the Franchimont test (2) using diethylaniline (7).

*Anal.* Calc'd for $C_{11}H_{13}N_5O_3$: C, 50.20; H, 4.94; N, 26.61.
Found: C, 50.27; H, 4.90; N, 26.50.

The low-melting fraction on examination under the microscope was found to consist of two separate types of crystals. One type consisted of light yellow to transparent tablets, while the other was opaque feather-like crystals. On heating, the tablet-form crystals melted and partly resolidified to the feather-like crystals. These crystals came down together on crystallizing in the usual manner from all ordinary solvents. During one crystallization from 95% ethanol, which was conducted without prolonged heating, a crop of crystals was obtained consisting entirely of the tablet form, yield 2.08 g. These crystals give a green color in the Franchimont test using diethylaniline (7). They melted at 120–124° after which the majority of the liquid resolidified and remelted at 152–156° with decomposition. The decomposition point varied with the rate of heating. These crystals were characterized as the hemihydrate of 1-nitro-2-*p*-acetamidophenyliminoimidazolidine.

*Anal.* Calc'd for $C_{11}H_{13}N_5O_3 \cdot \frac{1}{2} H_2O$: C, 48.51; H, 5.14; N, 25.72.
Found: C, 48.64; H, 5.22; N, 25.56.

The hemihydrate of 1-nitro-2-*p*-acetamidophenyliminoimidazolidine (1.15 g., 0.0042 mole) was refluxed in 25 cc. of *n*-propanol in an open Erlenmeyer flask for four minutes. The light yellow crystals dissolved to give a deep orange solution. On cooling golden yellow crystals separated. These crystals were filtered off and washed with absolute ethanol, yield 1.10 g. (99.1%). The melting point of 153–154° with decomposition was raised to 171–172° with decomposition by one crystallization from absolute ethanol (78 cc.), yield 810 mg. The melting point of this latter compound varies with the rate of heating. It gives a green color with diethylaniline in the Franchimont test. This material proved to be 1-nitro-2-*p*-acetamidophenyliminoimidazolidine.

[2] Melting points were determined on a Kofler block and are corrected. The microanalyses were performed by Mr. C. W. Beazley, Skokie, Illinois.

*Anal.* Calc'd for $C_{11}H_{13}N_5O_3$: C, 50.20; H, 4.94; N, 26.61.
Found: C, 50.14; H, 5.13; N, 26.54.

This compound was obtained also by repeated crystallizations of the original low-melting fraction (m.p. 146–162° with decomposition) from absolute alcohol, yield 3.32 g. (9.44%).

*1-p-Acetamidophenyl-2-imidazolidone. 1. From 1-p-acetamidophenyl-2-nitramino-2-imidazoline.* 1-*p*-Acetamidophenyl-2-nitramino-2-imidazoline (1.0 g., 0.0038 mole) was dissolved in 40 cc. of 10% sodium hydroxide and refluxed for five minutes. On cooling to room temperature a white solid separated which was removed by filtration and washed with water, yield 490 mg. (58.8%). The melting point of 271° was not raised by crystallizing from 95% ethanol.

*Anal.* Calc'd for $C_{11}H_{13}N_3O_2$: C, 60.2; H, 5.94; N, 19.18.
Found: C, 59.90; H, 5.95; N, 19.31.

*2. From 2-oxazolidone.* 2-Oxazolidone (5 g., 0.057 mole) and 12.0 g. (0.08 mole) of *p*-aminoacetanilide were heated together at 190–200° for four hours. The molten material was poured into 40 cc. of water and the solid (m.p. 145–260°) was removed by filtration and washed with water, yield 5.95 g. This material after crystallization from 95% ethanol (42 cc./g.) melted at 271°, yield 1.26 g. (10%). The mother liquor on concentrating to one-half volume gave a second crop of crystals (389 mg.) melting at 263–268°. A mixture melting point between the recrystallized material and 1-*p*-acetamidophenyl-2-imidazolidone (m.p. 271°) prepared above showed no depression.

*N-β-Nitraminoethyl-N'-p-acetamidophenylurea.* Conc'd hydrochloric acid (12 cc.) was added to 1.03 g. (0.0039 mole) of 1-nitro-2-acetamidophenyliminoimidazolidine. At first deep red-colored crystals formed which slowly dissolved to give a clear yellow solution. The clear solution was cooled in an ice-salt bath and neutralized with a 25% solution of potassium hydroxide. A white solid separated. It melted at 195° with decomposition, yield 1.01 g. (94.4%). One crystallization from absolute alcohol (117 cc.) gave 530 mg. of needle-like crystals which decomposed at 204°. The decomposition point varied with the rate of heating.

*Anal.* Calc'd for $C_{11}H_{15}N_5O_4$: C, 47.0; H, 5.43; N, 24.91.
Found: C, 47.17; H, 5.64; N, 24.85.

N-β-Nitraminoethyl-N'-*p*-acetamidophenylurea was also prepared in similar yields by allowing 1 g. of 1-nitro-2-*p*-acetamidophenyliminoimidazolidine or its hemihydrate to stand in presence of 10 cc. of 10% sodium hydroxide solution until solution was complete. On neutralization of the solution with 10% hydrochloric acid in the cold, the urea was precipitated.

*Reaction of ethylamine with 1-nitroso-2-nitramino-2-imidazoline.* A 70% solution of ethylamine (24 g., 0.371 mole) was diluted with 50 cc. of water and 25 g. (0.157 mole) of 1-nitroso-2-nitramino-2-imidazoline was added portionwise over a period of 20 minutes. During the reaction the temperature was held below 30°. The clear solution was allowed to stand overnight and then cooled to 4°. A crop of white crystals was obtained which melted at 80–147°, yield 7.06 g. The filtrate on evaporation to *ca.* ⅛ of its original volume at room temperature gave a second crop of crystals with considerable oil. This semi-solid weighed 2.13 g. The crystals were combined and separated by fractional crystallization from 95% ethanol into 2.0 g. (9.6%) of crystals melting at 147–148° and 1.72 g. (6.8%) of crystals melting at 111–113°. The crystals melting at 147–148° were identified as N-ethyl-N'-nitroguanidine (1) by a mixture melting point determination with an authentic sample. The material melting at 111–113° was recrystallized once more to give pure N,N'-diethyl-N''-nitroguanidine melting at 115–116°.

*Anal.* Calc'd for $C_5H_{12}N_4O_2$: C, 37.50; H, 7.50; N, 35.00.
Found: C, 37.40; H, 7.67; N, 34.80.

The original filtrate from the second crop of crystals (2.13 g.) on evaporation to dryness gave 7.60 g. of a light yellow oil. This oil in aqueous solution was treated with a saturated aqueous solution of picric acid. A crude picrate was obtained which melted at 159–162°, yield 3.0 g. (5.58%). Several crystallizations from 95% ethanol raised the melting point to 162–163°, yield 0.79 g. This picrate did not depress the melting point of an authentic sample

of 2-ethylamino-2-oxazolidinum picrate (m.p. 162–163°) prepared from N-β-chloroethyl-N′-ethylurea.

*Ethyl isocyanate* (b.p. 59.5–60°) was prepared in 87% yield by the method of Slotta and Lorenz (10).

*N-Ethyl-N′-β-chloroethylurea.* β-Chloroethylamine hydrochloride (10 g., 0.086 mole) (m.p. 147°) (11) was converted to a dry benzene solution of the free base as previously described (6). To this benzene solution was added with cooling a benzene solution of ethyl isocyanate (5 g., 0.070 mole). One-half volume of petroleum ether (b.p. 30–60°) was added and the white solid was removed and washed with petroleum ether, yield 8.80 g. (83.1%). The melting point of 98–100° (uncorr.) of the crude product could not be raised by crystallization from dilute alcohol.

*Anal.* Calc'd for $C_5H_{11}ClN_2O$: C, 40.04; H, 7.42; N, 18.61.
Found: C, 40.01; H, 7.53; N, 18.40.

*2-Ethylamino-2-oxazolidinium picrate.* A suspension of 510 mg. (0.0034 mole) of N-β-chloroethyl-N′-ethylurea in 12 cc. of water was refluxed for ten minutes. After the clear solution had cooled to room temperature, a saturated aqueous solution of picric acid was added. A yellow crystalline picrate separated immediately, yield 900 mg. (77.5%). The melting point of 162–163° was changed to 162.5–163° by one crystallization from water (58 cc.).

*Anal.* Calc'd for $C_{11}H_{13}N_5O_8$: C, 38.55; H, 3.79; N, 20.43.
Found: C, 38.80; H, 3.90; N, 20.36.

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