[CONTRIBUTION FROM THE INSTITUTE OF SCIENTIFIC AND INDUSTRIAL RESEARCH, OSAKA UNIVERSITY, SAKAI-SHI, OSAKA, JAPAN]

A New Rearrangement of N-Alkyl-N-nitrosoamides

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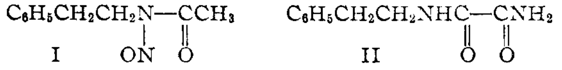
The reaction of N-2-phenylethyl-N-nitrosoacetamide with phosphorus pentachloride gives 2-phenylethyloxamide in high yield. Other nitrosoamides gave similar results. This reaction apparently involves the formation of N-nitrosoimidochloride which isomerizes by way of N-nitroso-N-2-phenylethyl-α-chlorovinylamine, in which the nitroso group was rearranged to the β-carbon atom.

N-Alkyl-N-nitrosoamides are unstable and readily decompose thermally with the evolution of nitrogen. A number of previous studies on the nitrosoamides have been concerned mainly with thermal decomposition[1a] and the preparation of diazoalkanes.[1b] In this paper, we should like to report a new rearrangement reaction of N-alkyl-N-nitrosoamides with phosphorus pentachloride, in which the N-nitroso group rearranges to the α-carbon atom of the acyl group. N-2-Phenylethyl-N-nitrosoacetamide (I) reacts exothermally with an equimolar amount of phosphorus pentachloride even at 30° with the evolution of hydrogen chloride. The product has the composition C_5H_6NO and is an isomer of the starting nitrosoamide I. Hydrolysis gave phenethylamine and oxalic acid, suggesting that the product is N-2-phenylethyloxamide (II).



$$\underset{\mathrm{I}}{C_6H_5CH_2CH_2\underset{\underset{ON}{|}}{N}-\underset{\underset{O}{\|}}{C}CH_3} \qquad \underset{\mathrm{II}}{C_6H_5CH_2CH_2NH\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}NH_2}$$

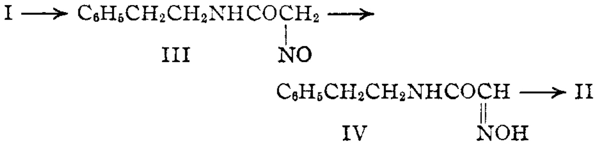
Similar reactions with N-ethyl- and N-isobutyl-N-nitrosoacetamides gave the corresponding N-alkyloxamides in excellent yield (Table I).

TABLE I

$RNHCOCONH_2$ FROM THE REACTION OF $RN(NO)COCH_3$ WITH PCl_5

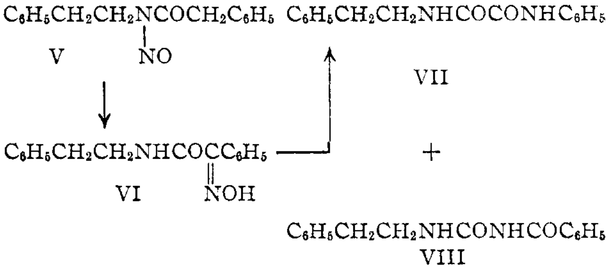
R	Yield, %	M.p., °C.
2-Phenylethyl	90	213
Ethyl	75	198.5
Isobutyl	95	205

In this reaction, the N-nitroso group of I apparently rearranges to the α-carbon atom of the acyl group and the resulting intermediate III isomerizes to the aldoxime IV, which undergoes the Beckmann rearrangement. Although nitriles are known to be obtained generally from aldoximes by Beckmann rearrangement using phosphorus pentachloride, acylamides have also been reported[2] to be obtained as in our reaction.



$$\mathrm{I} \longrightarrow \underset{\mathrm{III}}{C_6H_5CH_2CH_2NHCO\underset{\underset{NO}{|}}{C}H_2} \longrightarrow \underset{\mathrm{IV}}{C_6H_5CH_2CH_2NHCO\underset{\underset{NOH}{\|}}{C}H} \longrightarrow \mathrm{II}$$

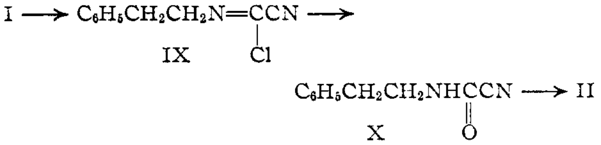
This reaction of N-2-phenylethyl-N-nitrosophenylacetamide (V) with phosphorus pentachloride gives also both N-2-phenylethyl-N′-phenyloxamide (VII) in 38% and N-benzoyl-N-2′-phenylethylurea (VIII), in 30% yield, respectively.



$$\underset{\mathrm{V}}{C_6H_5CH_2CH_2\underset{\underset{NO}{|}}{N}COCH_2C_6H_5} \longrightarrow \underset{\mathrm{VI}}{C_6H_5CH_2CH_2NHCO\underset{\underset{NOH}{\|}}{C}C_6H_5} \longrightarrow \underset{\mathrm{VII}}{C_6H_5CH_2CH_2NHCOCONHC_6H_5} + \underset{\mathrm{VIII}}{C_6H_5CH_2CH_2NHCONHCOC_6H_5}$$

These products suggest the formation of the intermediate VI as with α- and β-benzil monoxime, which are known to give dibenzamide and phenylglyoxylic acid anilide, respectively. Furthermore, the 2,4-dinitrophenylhydrazone of N-benzylpyruvamide was precipitated by 2,4-dinitrophenylhydrazine from the reaction mixture of N-benzyl-N-nitrosopropioamide with phosphorus pentachloride, although the yield was only 7.5%. These observations also suggest the formation of α-isonitrosoacetamide (IV).

Mechanism of the Rearrangement of the Nitroso Group. A. Formation of the Iminochloride as an Intermediate.—On partial hydrolysis of the reaction mixture from the nitrosoamide I and phosphorus pentachloride, there was obtained a substance, $C_{10}H_9N_2Cl$ (IX), which showed absorption at 1650 cm.$^{-1}$ indicative of the C=N (α,β-unsaturated) group. Mild hydrolysis of this product with aqueous ethanol gave a substance $C_{10}H_{10}N_2O$ (X). Further hydrolysis of X with ethanolic potassium hydroxide containing hydrogen peroxide gave N-2-phenylethyloxamide (II). Compounds IX and X were also obtained when the reaction was carried out in benzene. Earlier studies by von Braun[3] indicated that the reaction of acetanilide (XI) with phosphorus pentachloride at low temperature gave the iminochloride XII which on



$$\mathrm{I} \longrightarrow \underset{\mathrm{IX}}{C_6H_5CH_2CH_2N{=}\underset{\underset{Cl}{|}}{C}CN} \longrightarrow \underset{\mathrm{X}}{C_6H_5CH_2CH_2NH\underset{\underset{O}{\|}}{C}CN} \longrightarrow \mathrm{II}$$

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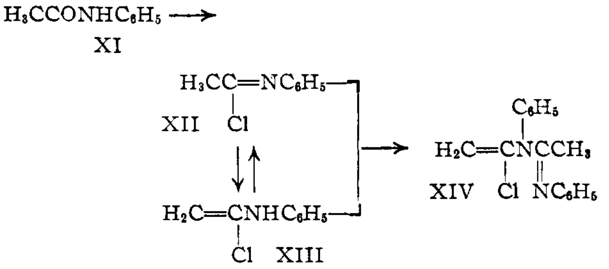
[1] (a) Previous manuscript, and references in it; (b) E. H. White, *J. Am. Chem. Soc.*, **77**, 6011 (1955), and references therein.

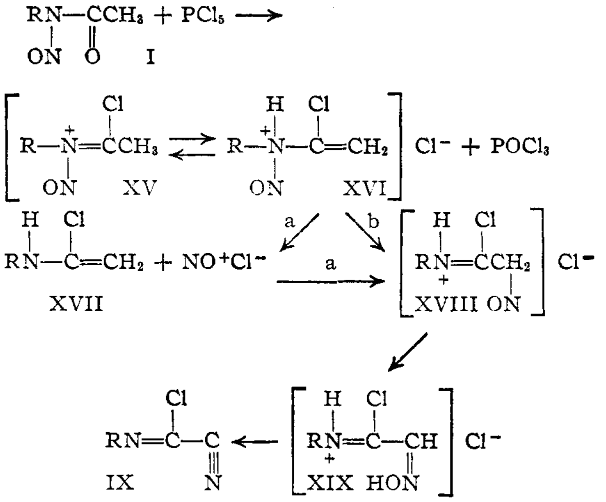
[2] E. C. Horning and V. L. Stromberg, *ibid.*, **74**, 5155 (1952).

[3] J. von Braun, *et al.*, *Ber.*, **60**, 92 (1927); *Ann.*, **453**, 113 (1927); *Ber.*, **67**, 1762 (1934).

heating was converted to α-chlorovinylaniline (XIII) followed by immediate formation of vinylamidine (XIV).



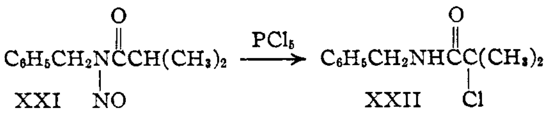
In the reaction of the nitrosoamide I with phosphorus pentachloride, the iminochloride XV may be formed first and then isomerized to α-chlorovinylamine (XVI). Then the N-nitroso group apparently migrates to the β-carbon atom of the vinyl group and the resulting C-nitroso compound XVIII isomerizes to the oxime XIX.



B. Rearrangement of the Nitroso Group.—There are two possible processes for the rearrangement of the nitroso group: one (a) involves the elimination of nitrosyl chloride and the successive electrophilic addition of the nitroso cation to the double bond; the other (b) is an intramolecular process. The former mechanism is similar to the well-known intermolecular rearrangement of N-methyl-N-nitrosoaniline to N-methyl-*p*-nitrosoaniline by hydrogen chloride.[4]

If the reaction proceeds *via* an intermolecular process, α-chlorovinylphenethylamine (XVII, R = $C_6H_5CH_2CH_2$), resulting from the reaction of N-2-phenylethylacetamide with phosphorus pentachloride, should give N-2-phenylethyloxamide (II) when treated with nitrosyl chloride. However, this reaction gave II in only 10–17% yield, while the reaction of N-2-phenylethyl-N-nitrosoacetamide (I) with phosphorus pentachloride gave II in 90% yield. This leads us to assume that the reaction is not solely intermolecular.[5]

N-Benzyl-N-nitrosoisobutyramide (XXI) was treated with phosphorus pentachloride, with the expectation of isolating a C-nitroso intermediate (XVIII) which can neither isomerize to an oxime (XIX), nor undergo Beckmann rearrangement. However, the expected compound was not formed; instead N-benzyl-α-chloroisobutyramide (XXII), m.p. 60–61°, was obtained in 46% yield.



$$C_6H_5CH_2N(NO)C(=O)CH(CH_3)_2 \xrightarrow{PCl_5} C_6H_5CH_2NHC(=O)C(Cl)(CH_3)_2$$

XXI XXII

Other Reagents for Rearrangement.—The possibility of using other reagents than phosphorus pentachloride in this rearrangement was investigated. With phosphorus oxychloride the oxamide II was obtained in 80% yield, but with phosphorus trichloride the yield of II was only 6%. Sulfuryl chloride and thionyl chloride were not effective, as the reaction did not proceed at 40–50° and thermal decomposition and the denitrosation occurred at higher temperature.

Experimental

Preparation of Nitrosoamides.—The N-nitrosoamides were prepared by the method given earlier.[1a,6]

Reaction of Nitrosoamide with Phosphorus Pentachloride.—A mixture of nitrosoamide and an equimolar amount of phosphorus pentachloride was maintained at 40–50° with occasional cooling until the phosphorus pentachloride dissolved and the evolution of hydrogen chloride ceased. Examples follow.

A. Reaction of N-2-Phenylethyl-N-nitrosoacetamide (I).—The red-brown reaction mixture of 2 g. (0.0104 mole) of I and 2.2 g. (0.0106 mole) of phosphorus pentachloride was poured into ice-water. A light yellow oil separated and solidified on standing. The crystalline solid was collected and washed with ether. Recrystallization from ethanol gave 1.8 g. of a product melting at 213°, yield 90%. Both chlorine and phosphorus were absent.

Anal. Found: C, 62.61; H, 6.40; N, 14.92. Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58.

A mixture with a sample of 2-phenylethyloxamide did not show a depressed m.p. The authentic sample was prepared by treating in 80 ml. of absolute ethanol 2 g. of oxamic acid ethyl ester[7] with equimolar amount of 2-phenylethylamine. The N-2-phenylethyloxamide which precipitated was collected and recrystallized from ethanol; m.p. 213°.

Anal. Found: C, 62.04; H, 6.25; N, 14.90. Calcd. for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58.

Hydrolysis of II.—The reaction product, 0.3 g., was refluxed for 2 hr. in 3 ml. of 3.5 *N* methanolic potassium hydroxide solution, cooled and neutralized with hydrochloric acid. Water and methanol were evaporated, and the re-

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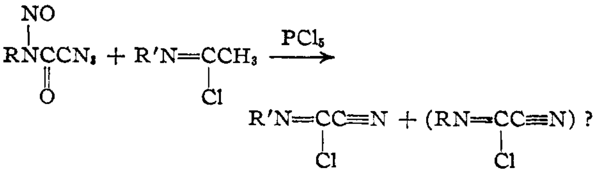
[4] P. W. Neber and H. Rauschen, *Ann.*, **550**, 182 (1942); E. H. White, *J. Am. Chem. Soc.*, **77**, 6008 (1955); Angier, *et al.*, *ibid.*, **74**, 408 (1952); V. Braun, *Ber.*, **70B**, 979 (1937).

[5] A referee suggested the use of a scavenger for NOCl to test the intramolecular character of the reaction



$$RN(NO)C(=O)CN_3 + R'N{=}C(Cl)CH_3 \xrightarrow{PCl_5} R'N{=}C(Cl)C{\equiv}N + (RN{=}C(Cl)C{\equiv}N)\ ?$$

(large excess)

We are currently testing this assumption.

[6] M. Murakami and K. Akagi, *J. Chem. Soc. Japan*, **75**, 532 (1954).

[7] A. Weadine, *J. prakt. Chem.*, **10**, 196 (1874).

sulting white residue was acidified with 0.5 ml. of concd. hydrochloric acid and extracted with ether. After drying and removing ether, colorless crystals were obtained. The product was recrystallized from carbon tetrachloride–chloroform; m.p. 99–99.5°. A mixed melting point with authentic oxalic acid (m.p. 99–99.5°) was not depressed.

Anal. Found: C, 26.58; H, 2.25. Calcd. for $C_2H_2O_4$: C, 26.68; H, 2.24.

The aqueous raffinate was treated with 5 ml. of 3 *N* aqueous solution of sodium hydroxide and extracted with ether. The extract was dried and concentrated. After acidification with concd. hydrochloric acid and evaporation, the residual yellow oil gave white crystals. Recrystallization from absolute ethanol gave a product melting at 215–217°. Its mixed melting point with 2-phenylethylamine hydrochloride (m.p. 216–217°) was not depressed.

Anal. Found: C, 60.66; H, 8.13; N, 8.57. Calcd. for $C_8H_{12}NCl$: C, 60.95; H, 7.67; N, 8.89.

B. Reaction of N-Ethyl-N-nitrosoacetamide.—The mixture of 2 g. (0.017 mole) of nitrosoamide and 3.6 g. (0.017 mole) of phosphorus pentachloride was poured into ice-water. Neutralization with sodium bicarbonate gave colorless crystals. Recrystallization from ethanol gave 1.5 g. of colorless product, m.p. 198.5°, yield 75%. Its mixed melting point with authentic ethyloxamide[8] was not depressed.

Anal. Found: C, 41.18; H, 7.11; N, 24.25. Calcd. for $C_4H_8N_2O_2$: C, 41.37; H, 6.94; N, 24.13.

C. Reaction of N-Isobutyl-N-nitrosoacetamide.—When the mixture of 2 g. (0.014 mole) of nitrosoamide and 2.9 g. (0.014 mole) of phosphorus pentachloride was poured into ice-water, a colorless crystalline solid was obtained. Recrystallization from ethanol gave 1.9 g. of the product melting at 198.5°, yield 95%.

Anal. Found: C, 49.82; H, 8.57; N, 19.08. Calcd. for $C_6H_{12}N_2O_2$: C, 49.98; H, 8.39; N, 19.43.

A mixed melting point with authentic N-isobutyloxamide (m.p. 198.5°) was not depressed. The authentic sample was prepared by a method similar to that described in section A.

D. Reaction of N-2-Phenylethyl-N-nitrosophenylacetamide (V).—When the reaction mixture of 5 g. (0.019 mole) of V and 3.9 g. (0.019 mole) of phosphorus pentachloride was treated with ice-water, a mixture of crystals and viscous light yellow oil was obtained. After washing with ether, the ether-insoluble crystals were collected. Recrystallization of the crystals from ethanol and ethyl acetate gave 1.9 g. of colorless product melting at 192°, yield 38%.

Anal. Found: C, 71.68; H, 6.09; N, 10.56. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44.

A mixed melting point with authentic N-2-phenylethyl-N-phenyloxamide (m.p. 192°) was not depressed. The authentic sample was prepared by the method described in section A.

Anal. Found: C, 71.77; H, 6.21; N, 10.23: Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44.

The ether layer was dried over anhydrous sodium sulfate. When ether was removed, 3 g. of the yellow residue was obtained. Recrystallization of the residue from ethanol gave 1.5 g. of product melting at 139° yield 30%.

Anal. Found: C, 71.41; H, 5.81; N, 10.22. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44.

A mixed melting point with the authentic N-2-phenylethyl-N-benzoylurea was not depressed. The authentic sample (m.p. 139°) was prepared by benzoylation of N-2-phenylethylurea obtained by the Curtius reaction of 2-phenylpropionazide.

Anal. Found: C, 71.60; H, 6.12; N, 10.72. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44.

The Iminochloride of N-Phenylethylcarbamoyl Cyanide (IX).—The mixture of 4 g. (0.021 mole) of nitrosoamide (I) and 4.3 g. (0.021 mole) of phosphorus pentachloride was maintained at 40–50° with occasional cooling. After all phosphorus pentachloride had dissolved, it was maintained for an additional 30 minutes at the same temperature. To the reaction mixture was added 40 ml. of carbon tetrachloride and insoluble substances were filtered off. The filtrate was washed with ice-water and the carbon tetrachloride layer was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and 1 g. of oil was obtained; yield 25%. The product had b.p. 91–93° (3 mm.), $n^{23}D$ 1.5308. In the infrared, this substance absorbed as expected for C=N (α,β-unsatd.) at 1650 cm.$^{-1}$ and for C≡N at 2230 cm.$^{-1}$ but no absorption for N–H at 3200–3300 cm.$^{-1}$ was observed.

Anal. Found: C, 62.16; H, 4.88; N, 13.95. Calcd. for $C_{10}H_9N_2Cl$: C, 62.32; H, 4.71; N, 14.55.

To 5 ml. of benzene containing 1.5 g. of I, 1.6 g. of phosphorus pentachloride was added. The mixture was maintained at 45–50° for 1 hr., cooled, diluted with 20 ml. of benzene and filtered. The benzene extract was washed with ice-water, and then dried with anhydrous magnesium sulfate. When benzene was removed *in vacuo*, 0.5 g. of oil was obtained. Distillation *in vacuo* gave the iminochloride IX, b.p. 90–93° (3 mm.).

N-Phenylethylcarbamoyl Cyanide (X).—A solution of 0.5 g. of the iminochloride IX in 4 ml. of ethanol and 2 ml. of water was heated at 60–80° for 3 hr. After ethanol was removed *in vacuo*, the residual oil was extracted with ether and the extract was dried. Evaporation of solvent gave 0.45 g. of the product. Recrystallization from carbon tetrachloride gave 0.4 g. of the colorless crystals, m.p. 92°, yield 88.5%. This substance had absorption at 3250 cm.$^{-1}$ for N—H, 1680 cm.$^{-1}$ for C=O of *sec*-amide, 1550 cm.$^{-1}$ for N—H of *sec*-amide, 2230 cm.$^{-1}$ for C≡N.

Anal. Found: C, 68.91; H, 5.87; N, 15.82. Calcd. for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08.

A solution of 0.5 g. of I in 3 ml. of benzene was treated with 0.6 g. of phosphorus pentachloride. The mixture was heated at 40–45° for 1.5 hr. and then was poured into ice-water. The benzene was removed by aeration and the remained aqueous solution was kept standing for a week. The crystals formed were collected and recrystallized from carbon tetrachloride to give 0.1 g. of X, m.p. 92°, yield 22.1%.

Hydrolysis of X.—To a solution of 50 mg. of X in 3.5 ml. of ethanol was added 0.5 ml. of 10% aqueous solution of potassium hydroxide. While the mixture was heated at 45–50°, 3.5 ml. of 3% hydrogen peroxide was added dropwise. After the addition was completed, heating was continued for an additional half-hour. The reaction mixture was acidified with hydrochloric acid and the ethanol was removed under reduced pressure. The residue was recrystallized from ethanol and 30 mg. of the product was obtained, m.p. 213°. A mixed melting point with authentic 2-phenylethyloxamide was not depressed.

Reaction of N-Benzyl-N-nitrosoisobutyramide (XXI) with Phosphorus Pentachloride.—A mixture of 2 g. (0.01 mole) of XXI and 2 g. (0.01 mole) of phosphorus pentachloride was heated at 40–45° until all the phosphorus pentachloride dissolved, then poured into ice-water. After standing overnight, it was extracted with ether. The ether extract was washed with aqueous solution of sodium bicarbonate, dried over anhydrous magnesium sulfate and concentrated. Distillation of 1.8 g. of the residue gave 1.0 g. of a fraction boiling at 120–135° under 3 mm.; yield 48.7%. This substance solidified readily and melted at 50–56°. Recrystallization from petroleum ether gave a product melting at 60–61°. A mixed melting point with N-benzyl α-chloroisobutyramide (XXII) was not depressed.

Anal. Found: C, 62.75; H, 6.77. Calcd. for $C_{11}H_{14}NOCl$: C, 62.41; H, 6.68.

Reaction of the Iminochloride of N-Benzylisobutyramide

$(C_6H_5CH_2N{=}\overset{\displaystyle Cl}{\overset{|}{C}}CH(CH_3)_2)$. **A. With PCl$_5$.**—To a solution of 2 g. (0.011 mole) of N-benzoylisobutyramide in 6 ml. of benzene was added 4.6 g. (0.023 mole) of phosphorus pentachloride which was dissolved at 60–70°. After removal of benzene under reduced pressure, distillation gave 2.2 g. of a product boiling at 137–140° under 13 mm., yield 89.4%. This substance showed absorption at 1682 cm.$^{-1}$ (C=N).

Anal. Found: Cl, 30.71. Calcd. for $C_{11}H_{13}NCl_2$: Cl, 30.80.

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(8) O. Wallach, *Ann.*, **184**, 65 (1877).

Shaking 2.2 g. of the above product with water for a minute resulted in decomposition with evolution of heat. After standing overnight the product solidified. Recrystallization of 1.9 g. of the product from petroleum ether gave crystals (XXII) melting at 60–61°.

Anal. Found: C, 62.70; H, 6.92; Cl, 17.13. Calcd. for $C_{11}H_{14}ONCl$: C, 62.41; H, 6.68; Cl, 16.77.

B. **With Nitrosyl Chloride.**—A solution of 2 g. (0.011 mole) of N-benzylisobutyroamide in 6 ml. of benzene was treated with 2.35 g. (0.011 mole) of phosphorus pentachloride at 30–40°. After solution was complete 10.6 g. (0.011 mole) of 7% solution of nitrosyl chloride in carbon tetrachloride was added dropwise. The mixture was maintained at 5–10° for 3.5 hr. with stirring and then poured into ice-water. The carbon tetrachloride layer was washed with sodium bicarbonate and dried. After removal of the carbon tetrachloride, 2.2 g. of oil was obtained. Distillation gave 1.2 g. of product boiling at 120–130° under 3 mm., yield 50.2%. This substance solidified immediately and melted at 56–58°. A mixed m.p. with an authentic sample of XXII was not depressed.

Anal. Found: C, 62.60; H, 6.93; N, 6.46. Calcd. for $C_{11}H_{14}ONCl$: C, 62.41; H, 6.68; N, 6.61.

Reaction of N-Benzyl-N-nitrosopropionamide with Phosphorus Pentachloride.—A mixture of 3.5 g. (0.018 mole) of the nitrosoamide and 3.8 g. (0.018 mole) of phosphorus pentachloride was heated 40–45° for 20 minutes, and then was poured into ice-water. After 30 min. 500 ml. of 0.2% solution of 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid was added and the mixture was heated for a few minutes. The crystalline product was collected and washed with water, ether and ethyl acetate to give 0.5 g. of yellow hydrazone, melting at 221–225°, yield 7.7%. Recrystallization from ethyl acetate gave a product melting at 229°.

Anal. Found: C, 54.09; H, 4.21; N, 19.27. Calcd. for $C_{16}H_{15}N_5O_5$: C, 53.78; H, 4.23; N, 19.60.

A suspension of 0.5 g. of the hydrazone in 50 ml. of ethanol was hydrogenated using Raney nickel and 61 kg. per cm.^{2} pressure of hydrogen. The reduced mixture was filtered and evaporated to dryness after acidifying with hydrochloric acid. The residue was treated with 10 ml. of 6 *N* hydrochloric acid and heated at 100° for 3 hr. After evaporating to dryness, the residue was dissolved in a small portion of water and purified with Amberlite. The eluate with 2 *N* acetic acid was decolorized with charcoal, filtered and evaporated to dryness. To the residue was added ethanol and the colorless crystals were separated. This substance was violet in ninhydrin reaction and its R_f of a paper chromatogram eluted with phenol was 0.52, as was that of alanine.

Reaction of the Imidochloride of N-2-Phenylethylacetamide with Nitrosyl Chloride.—To a solution of 1.7 g. (0.010 mole) of the amide was added at 0°, 45 ml. of a solution of 2.2 g. (0.010 mole) of phosphorus pentachloride in carbon tetrachloride. After a few minutes, 9 g. (0.010 mole) of 7.5% solution of nitrosyl chloride in carbon tetrachloride was added and the mixture was stirred at room temperature for 1 hr., then maintained at 45° for additional 1.5 hr. The colorless precipitate was collected, treated with water and 0.8 g. of the starting material was recovered. After washing and drying, carbon tetrachloride was removed from the filtrate and the residue was kept standing for a day. Recrystallization of the residue gave 0.2 g. of II, yield, 10.0%.

A solution of 1 g. (0.0061 mole) of the amide in 3 ml. of phosphorus oxychloride was treated with 1.3 g. (0.0062 mole) of phosphorus pentachloride at 40°. The mixture, when cooled in an ice–salt-bath, absorbed 0.45 g. (0.0069 mole) of nitrosyl chloride. After standing for 40 hr. at room temperature, the mixture was poured into ice-water, and the material which separated was recrystallized from ethanol to give 0.2 g. of II, yield 16.9%.

Reaction of the Nitrosoamide I with Phosphorus Oxychloride or Phosphorus Trichloride.—In 2 ml. (0.022 mole) of phosphorus oxychloride 0.5 g. (0.0026 mole) of I was dissolved. The mixture was heated at 45–50° for 3 hr., and then poured into ice-water. After standing for 2 days, white crystals had separated. The product was collected and recrystallized from ethanol to give 0.4 g. of II, yield 80%.

A mixture of 0.5 g. (0.0026 mole) of I and 0.23 ml. (0.0026 mole) of phosphorus trichloride was maintained at 45–50° for 1 hr. and then poured into ice-water. The crystalline material was collected and washed with ether. From the ether-insoluble product 0.2 g., (yield 36.4%) of I was obtained; the ether-soluble product was *ca.* 30 mg. of X (yield 6%).

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF CALIFORNIA, BERKELEY 4, CALIF.]

Cyclizations of Dialdehydes with Nitromethane. VII.[1] Preparation of *neo*-Inosadiamine-1,4[2]

BY FRIEDER W. LICHTENTHALER AND HERMANN O. L. FISCHER[3]

RECEIVED NOVEMBER 25, 1960

Cyclization of glyoxal with nitromethane at *p*H 10 yielded 1,4-dideoxy-1,4-dinitro-*neo*-inositol which upon hydrogenation gave the corresponding *neo*-inosadiamine-1,4. Structural assignment was accomplished by means of the proton nuclear magnetic resonance spectra of acetyl derivatives.

Introduction

Interest in the chemistry of the inosamines has been stimulated by their occurrence as a component of certain antibiotics.[4] Neoinosamine-2 has been isolated from hygromycin A,[5,6] while *scylloinosadiamine-1,3* (*streptamine*) occurs as part of the streptomycin molecule. The monoinosamines have been thoroughly investigated and, as a result of this, more than half of the thirty-two theoretically possible isomers have been synthesized and characterized in the last fifteen years. On the other hand, the configuration of only one of the ninety possible stereoisomeric inosadiamines, namely, streptamine, has been elucidated by unequivocal synthesis.[4,7–9] There are, however,

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[1] Paper VI in this series: A. C. Richardson and H. O. L. Fischer, *J. Am. Chem. Soc.*, **83**, 1132 (1961).

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[3] Deceased, March 9, 1960.

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