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# Nitrolysis of the CN Single Bond and Related Chemistry of Nitro and Nitroso Groups

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## Key Words
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Substitution in Nitrosamines.
Electron transfer from an amino to a nitro group.
Reactions between nitroform and isocyanides.

## Abstract
Nitric acid in acetic anhydride converted N,N-dimethylbenzylamine 1 to N-methyl-N-nitrosobenzylamine 2 (76%) and benzaldehyde. Six additional acyclic and alicyclic tertiary amines similarly gave nitrosamines; 1,4-diazabicyclo[2,2,2]octane.

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tane gave an intractable mixture. An explanation for the conversions is discussed. Addition of hydrochloric acid to the reaction mixture led to recovery of the amine $1$ (36%), and to its conversion (54%) to the nitrosamine $2$ without the detectable formation of benzaldehyde; in contrast nitric acid (100%) and anhydrous hydrogen chloride in acetic anhydride converted the amine $1$ to benzaldehyde (69%) and to the nitrosamine $2$ in low yield. Nitrosamine $2$ and N-methyl-N-nitroso-$8$-phenethylamine $3$ were oxidized to nitramines $4$ and $5$.

\[
\begin{align*}
1, & n = 1 \\
2, & n = 1, x = 1 \\
3, & n = 2, x = 1 \\
4, & n = 1, x = 2 \\
5, & n = 2, x = 2
\end{align*}
\]

II. It became desirable to incorporate $\equiv$ functions into nitrosamines to provide schemes for the preparation of cage structure high energy materials. A proposed scheme is shown.

\[
\begin{align*}
\text{RNH} & \text{NHR} & \text{NHR} & \xrightarrow{\text{CH}_2\text{O or } \text{HC(OR)}_3} & \text{RN} & \text{NR} & \text{NR} \\
\text{N} & \text{ON} & \text{ON} & \text{ON} & \text{N} & \text{NO} & \text{ON} \text{NO}
\end{align*}
\]

A mono- and a dialkylated product $7$ and $8$ were obtained from the nitrosamine $6$ and benzaldehyde. Attempts to achieve trialkylation were unsuccessful.
Other alkylations of 5-membered and 6-membered alicyclic bis- and tris-nitrosamines were similarly obtained.

The preparation of α-azidodimethylnitrosamine provided the first example of introducing a nitrogen function at the α-position of a nitrosamine by the direct replacement of a hydrogen atom.

\[
(CH_3)_2NNO + (()CH_3)_2CH)_2NLi \xrightarrow{C_7H_4SO_2N_3, -78^\circ \text{C}, 3\text{h}} CH_3NCH_2N_3 \]

Attempts to extend the reaction to the tris-nitrosamine \(6\) were unsuccessful.

III. Nitroform converted p-nitrophenyl isocyanide into the mesoionic 3-p-nitrophenyl-1,2,3-oxadiazolium-5-olate \(9\) and 3-p-nitrophenyl-1,2,3,4-oxatriazolium-5-olate \(10\), together with p-nitroaniline; it converted p-tolyl isocyanide into the mesoionic 3-(2-nitro-4-methylphenyl-1,2,3-oxatriazolium-5-olate together with 2-nitro-4-methylaniline and p-methylaniline.

\[
p-O_2NC_6H_4N\xrightarrow{X} \]

\(9\) \(X = CH\)

\(10\) \(X = N\)
IV. A radical intermediate was detected by EPR during the spontaneous conversion of a tert-o-nitrobenzylamine 11 to an indazole 12. Further investigations is underway.

\[
\begin{array}{ccc}
\text{O}_2\text{N} & \text{CH}_2\text{N} & \text{O}_2\text{N} \\
\text{NO}_2 & \text{CH}_3 & \text{NO}_2 \\
11 & 25^\circ & 12 \\
\end{array}
\]
Nitrolys of CN Single and Chemistry of Nitro and Nitroso Groups.

I. Project Titles and Goals.

A. Nitramines from Tertiary Amines. Sparse information scattered throughout the literature was to be organized and a general procedure to be developed and published.

B. α-Functionalization in Nitrosamines. An exploratory investigation of functional group interchange at the α-position of nitramines was to be continued.

C. Reactions between Isocyanides and Nitroform. An investigation on the recently discovered reaction between nitroform and isocyanides was to be concluded with a publication of the results.

D. Intramolecular Electron Transfer from an Amino to a Nitro Group.

Collaboration with Dr. R. D. Pace of the Naval Research Laboratory was undertaken to elucidate radical intermediates detected by EPR in the spontaneous conversion of a tert-o-nitrobenzylamine to an indazole.

II. Project Progress Reports on I. A-D.

A. Nitramines from Tertiary Amines.

The following manuscript has been submitted for publication.
Nitrosamines from Tertiary Amines and Nitric Acid in Acetic Anhydride

By Joseph H. Boyer, T.P. Pillai, and V.T. Ramakrishnan

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Abstract. Nitric acid in acetic anhydride converted N,N-dimethylbenzylamine 13 to N-methyl-N-nitrosobenzylamine 21 (76%) and benzaldehyde. Six additional acyclic and alicyclic tertiary amines similarly gave nitrosamines; 1,4-diazabicyclo[2,2,2]octane gave an intractable mixture. An explanation for the conversions is discussed. Addition of hydrochloric acid to the reaction mixture led to recovery of the amine 13 (36%), and to its conversion (54%) to the nitrosamine 21 without the detectable formation of benzaldehyde; in contrast nitric acid (100%) and anhydrous hydrogen chloride in acetic anhydride converted the amine 13 to benzaldehyde (69%) and to the nitrosamine 21 in low yield. Nitrosamine 21 and N-methyl-N-nitroso-$\beta$-phenethylamine 22 were oxidized to nitramines 23 and 24.

Introduction. In seeking preparations of nitramines from tertiary amines, a reinvestigation of the formation of nitrosamines from tertiary amines and nitric acid in acetic anhydride was undertaken since an oxidation would provide the final step.
Nitrosamines 1 and nitramines 2 have been produced from tertiary amines by heterolyses (eq 1, \(x = 1,2\))\(^2\) of the N-nitroso- and N-nitroammonium cations 1 and 4; but, with a few notable exceptions,\(^3\) these have failed as preparative reactions. Instead an elimination of nitroxy1 from the cation 1 (\(R = R_2CH\)) generally predominated (eq 2, \(x = 1\)). A current explanation\(^7\) for the nitrosolysis (eq 2,3; \(x = 1\)) required the intermediacy of an iminium cation 5, combination with nitrous acid, and the dissociation of a hemiaminal nitrite ester 6.\(^8,9\) Nitrosamines were also obtained from tertiary amines in reactions with tetrinitromethane (eq 4),\(^10\) with dinitrogen tetroxide either in carbon tetrachloride (eq 5)\(^11\) or in gas phase reactions,\(^12\) and with nitric acid.\(^13\)

\[
\begin{align*}
\text{NR} & \xrightarrow{\text{NO}_x} \xrightarrow{\text{N}_x\text{R}} \xrightarrow{\text{N}_x\text{NO}_x} \xrightarrow{\text{N}_x\text{NO}_x + R^+} \quad \text{eq (1)} \\
1, x = 1 & \quad 1, x = 1 \\
4, x = 2 & \quad 2, x = 2 \\
\text{NCHR}_2 & \xrightarrow{\text{NO}_x} \xrightarrow{\text{N}_x\text{CHR}_2} \xrightarrow{\text{N}_x\text{CR}_2 + \text{HNO}_x} \quad \text{eq (2)} \\
\quad x = 1,2 & \quad 5 \\
5 + \text{HNO}_2 & \xrightarrow{-H^+} \xrightarrow{\text{NCR}_2\text{ONO}} \xrightarrow{\text{NNO} + \text{R}_2\text{CO}} \quad \text{eq (3)} \\
\text{NCHR}_2 + \text{C(NO}_2)_4 & \xrightarrow{} \xrightarrow{\text{NNO} + \text{R}_2\text{CO} + \text{H}_3\text{C(NO}_2)_3} \quad \text{eq (4)} \\
\text{C}_6\text{H}_5\text{N(CH}_3)_2 & \xrightarrow{\text{N}_2\text{O}_4} \xrightarrow{\text{2,4-(O}_2\text{N}_2\text{C}_6\text{H}_3\text{N(CH}_3)_2}} \quad \text{eq (5)}
\end{align*}
\]
Investigations have been carried out on the N-methyl derivatives 7 and 8 of piperidine and pyrrolidine, N,N'-dimethylpiperazine 9, triethylamine 10, tri-n-butylamine 11, N,N-dibenzylmethylamine 12, N,N-dimethylbenzylamine 13, N,N-dimethyl-β-phenethylamine 14, and 1,4-diazabicyclo[2,2,2]octane 15.

![Chemical Structures]

\[
\begin{align*}
7, X &= \text{CH}_3 \\
8, X &= \text{CH}_3 \\
9, X &= \text{CH}_3 \\
10, R &= X = \text{C}_2\text{H}_5 \\
11, R &= X = \text{n-C}_4\text{H}_9 \\
12, R &= \text{C}_6\text{H}_5\text{CH}_2, X = \text{CH}_3 \\
13, R &= \text{C}_2\text{H}_5, X = \text{NO} \\
14, R &= \text{n-C}_4\text{H}_9, X = \text{NO} \\
15 &
\end{align*}
\]

Experimental Section.

Instruments included Perkin Elmer 237 B and 521 grating i.r., Varian A-60 and T-60 n.m.r. spectrometers. Yields were based on starting materials consumed. Elemental analyses were
provided by Micro-Tech Laboratories, Skokie, Illinois. Unless otherwise noted product identification and yield were determined by gc analysis based on comparison with authentic data. The analyses were obtained from a HP-5790 instrument with a HP-3390A integrator(column: 3% OV-17 on 80/100 Gas. Chrom Q, stainless steel 6 ft x 1/8 in; carrier gas, nitrogen, column temp. 110° to 150°C, with FID detector).

N-Methyl derivatives 7 and 8 of piperidine and pyrrolidin, N,N′-dimethylpiperazine 2, triethylamine 10, tri-n-butylamine 11, N,N-dimethylenzylamine 13, 1,4-diazabicyclo[2,2,2]octane 15, Eschenmoser's salt, nitrosonium and nitronium tetrafluoroborates, diethyl- 12 and di-n-butynitrosamine 20 were commercially available.14

N,N-Dimethyl-β-phenethylamine 14 was prepared from β-phenethylamine and formaldehyde.15 Dimethylnitramine and dimethylnitrosamine were obtained from dimethylcarbamoyl chloride and silver nitrate.16 Acetyl nitrite was prepared from nitrosyl chloride and silver acetate.17 Nitrosamines 16,18 17,19 18,20 19,21 and 2021b,22 were obtained from the appropriate secondary amine and a nitrosating agent. The α,23 m,24 and p-nitro-N,N-dimethylenzylamine25 and 2,4-dinitro-N,N-dimethylenzylamine26 were prepared from the appropriate nitro- and dinitrobenzyl halide and dimethylamine. The α-,27 and p-nitro-28 derivatives of N,N-dimethyl-β-phenethylamine were prepared by nitration. The Organic Synthesis procedure29 for preparing N-nitromorpholine from morpholine and acetone cyanohydrin nitrate was adapted for the conversion of N-methylbenzylamine14 and N-methyl-β-phenethyl-
amine to the corresponding nitramines and 24.

Prior to use nitric acid was treated with urea to remove and/or insure the absence of nitrous acid.

**Warnings.** Mixtures of nitric acid and acetic anhydride (acetyl nitrate) can be explosive at higher temperatures. In our experience an evolution of brown fumes was moderate at 65° and excessive at 90°. Nitrosamines and nitramines can be explosive and carcinogenic.

**Amines and nitric acid in acetic anhydride. General Procedure.** Nitric acid (70%, 6.2 ml., 0.09 mol) was added dropwise with stirring to acetic anhydride (30 ml., 0.3 mol) maintained at 0°. An amine 7-15, (0.03 mol) was added dropwise (about 10 minutes), the reaction mixture was warmed and kept at 50° for 30 minutes (evolution of dark brown fumes of nitrogen dioxide) and then stirred at room temperature for 16 hours. The mixture was poured onto crushed ice, treated with an excess of solid sodium hydroxide and thoroughly extracted with ether. After drying (MgSO₄) and concentration gc analysis determined identification and yield of the nitrosamine: 16, 43%; 17, 18%; 18, 27%; 19, 32%; 20, 47%; 21, 76%; and 22, 84%. The reaction with N,N-dimethylbenzylamine also gave benzaldehyde (28%). Unidentified mixtures also obtained from amines 7-14 contained amides, detected by ir.

A mixture of dinitrogen tetroxide (excess) and N,N-dimethylbenzylamine 13 (15 mmol) in acetic anhydride (150 mmol), prepared at -50° and stirred at 25° for 14 h, gave the nitrosamine 21 (65%), a trace amount of amides (ir 1635 and 1705 cm⁻¹), and
recovered amine 13 (42%). Benzaldehyde, ir 1705 cm⁻¹, was not detected by gc (10⁻⁷ mole would have been noted).

**Amines with nitric and hydrochloric acids in acetic anhydride.**

After a stream of anhydrous hydrogen chloride bubbled through a solution of N,N-dimethylbenzylamine 13 (4.05g, 30 mmol) and nitric acid (100%, 6.2 ml, 150 mmol) in acetic anhydride (30 ml, 30 mmol) at 0°C for 15 minutes, the mixture was stirred at 25°C for 16 hours. After the usual workup benzaldehyde (69%) and the nitrosamine 21 (26%) were obtained.

In a related experiment nitric acid (70%, 6.1, 90 mmol) and acetic anhydride (30 ml, 30 mmol) were mixed at the amine 13 (4.05 g, 30 mmol) was added (10 minutes) and the mixture warmed to 50°C. Hydrochloric acid (39%, about 0.5 ml) was added dropwise as a vigorous reaction with evolution of brown fumes of nitrogen dioxide occurred. The reaction mixture was cooled to 25°C and hydrochloric acid (39%, 9.5 ml, 9.5 mmol) was added dropwise. After the reaction mixture was stirred at 25°C for 16 hours 36% of the amine 13 was recovered and 54% was converted to the nitrosamine 21. A possible conversion to benzaldehyde was limited to 10%; it was not detected. There was an unidentified product (<5%).

An experiment with methyl dibenzylamine 12 and nitric acid in acetic anhydride with hydrochloric acid at 25°C for 16 hours after mixing at 0°C gave a low conversion (14%) to N-nitroso-N-methylbenzylamine 21 (44%) and benzaldehyde (33%). Neither dibenzyl nitrosamine nor formaldehyde was detected.

A mixture of dinitrogen tetroxide (excess), N,N-dimethyl-
benzylamine \(13\) (15 mmole), concentrated hydrochloric acid (5 mmole) and acetic anhydride (150 mmole), prepared at \(-5^\circ\) and stirred at \(25^\circ\) for 14 h, gave the nitrosamine \(21\) (90%), trace amounts of amides (ir 1635, 1705, 1760 cm\(^{-1}\)), and recovered amine \(13\) (19%). Benzaldehyde was not detected by gc.

**Nitrate and nitrite esters from Eschenmoser's salt.**

Equimolar portions (5 mmol) of Eschenmoser's salt \([\text{CH}_3\text{N}=\text{CH}_2\text{I}]\), nmr (CF\(_3\)CO\(_2\)H): \(\delta\) 3.16 (s,6) and 6.46 (br s,2), and silver nitrite in acetonitrile (10 ml) was stirred at \(25^\circ\) for 16 hours. Precipitation of silver iodide was noted after 5 minutes and became quantitative. Dimethylnitrosamine was detected after 10 minutes and identified by tlc comparison with an authentic sample. In similar experiments Eschenmoser's salt failed to react with silver nitrate in acetonitrile at \(25^\circ\) for 5 days; however, in dry THF (10 ml) at \(25^\circ\) for 16 h a reaction gave a mixture of the hemiaminal nitrate ester \([\text{CH}_3\text{N}=\text{CH}_2\text{NO}_3 \leftrightarrow (\text{CH}_3\text{N})\text{CH}_2\text{ONO}_2]\), nmr (CF\(_3\)CO\(_2\)H): \(\delta\) 3.36 (s,6) and 7.50 (br s,2), and silver iodide (quantitative). Dimethylnitramine was not detected by either tlc or nmr; an authentic sample gave nmr (CF\(_3\)CO\(_2\)H): \(\delta\) 3.40 (s).

**Nitrosolysis.** To a slurry of nitrosonium tetrafluoroborate (5.2 g, 44 mmol) in dry chloroform (100 ml) a chloroform solution of \(N,N\)-dimethylbenzylamine \(11\) (2.7 g, 20 mmol) was added at \(25^\circ\) under a nitrogen atmosphere and stirred for 70 h. The reaction mixture turned light green and later became light yellow. Water was added and the organic layer was washed with sodium carbonate solution and water, and dried (MgSO\(_4\)). Removal of chloroform
left N-methyl-N-nitrosobenzylamine 21 as a yellow viscous liquid (0.45 g, 61% based on recovered amine). The aqueous solution was treated with base and extracted with ether to recover unreacted amine, (2.0 g, 75%).

A similar reaction with N,N-dimethyl-β-phenethylamine 14 gave the nitrosamine 22 (56% based on 73% recovery of the amine 14).

A solution N,N-dimethylbenzylamine 13 (2.7 g, 0.02 mol) in acetic acid (60%, 100 ml) buffered to pH 4 - 5 with sodium acetate (13.6 g) was stirred and heated. Sodium nitrite (13.8 g, 0.2 mol) in water (50 ml) was added slowly (45 minutes) and the mixture was stirred at 90°C for two hours. It was cooled, diluted with water (50 ml) and extracted with ether (3 x 100 ml). The ether extract was washed with potassium carbonate solution (10%) until the aqueous layer was basic, and with saturated salt solution and then dried (MgSO4). Removal of the solvent left a yellow oil of benzylmethylnitrosamine 21 (1.20 g, 68%). The aqueous layer was made basic with potassium hydroxide and extracted with ether to recover dimethylbenzylamine (1.12 g, 41%).

A similar reaction with N,N-dimethyl-β-phenethylamine 14 gave the nitrosamine 22 (82% based on 50% recovery of the amine 14).

Equimolar portions of acetyl nitrite (volatile and unstable) and tri-n-butylamine (no other solvent) at 25°C for 14 hours failed to react. After the mixture was treated with water ether extraction recovered the amine.

Nitration. To a stirred slurry of nitronium tetrafluoroborate
(6.2 g, 46 mmol) in 1,2-dichloroethane (40 ml) N,N-dimethylbenzylamine 13 (3.0 g, 22 mmol) in dichloroethane solution (10 ml) was added dropwise under a nitrogen atmosphere. The reaction mixture was heated at reflux for 48 hr, cooled and treated with 200 ml of cold water. The organic layer was dried (MgSO₄) and concentrated to a semi-solid residue (200 mg) of m-nitrobenzaldehyde, a small amount of o-nitrobenzaldehyde, and a trace of p-nitrobenzaldehyde. The aqueous layer was made basic with sodium carbonate and extracted with ether to give a liquid mixture (3.7 g, 95%), of o-, m-, and p-nitro-N,N-dimethylbenzylamines (10:85:1).

A similar reaction with N,N-dimethyl-β-phenethylamine 14 gave a red-yellow oil mixture (95%) of o- and p-nitro-N,N-dimethyl-β-phenethylamines in the ratio of 1:4.

To a slurry of nitronium tetrafluoroborate (5.0 g, 37 mmol) in 10 ml of conc. sulfuric acid at 25°C in a flask with an attached tube of Drierite was added dropwise N,N-dimethylbenzylamine 13 (4.05 g, 30 mmol) in conc. sulfuric acid (5 ml). The light yellow reaction mixture was stirred at 25°C for 7 days, poured onto ice, treated with sodium carbonate, and extracted with methylene chloride (3 x 100 ml). The extract was washed with water, dried (MgSO₄), and the solvent was removed to leave a yellow liquid mixture (5.92 g, 89%) of o, m, and p-nitro-N,N-dimethylbenzylamines (7:90:1).

A similar reaction with N,N-dimethyl-β-phenethylamine 14 gave a yellow oil mixture of p-nitro-N,N-dimethyl-β-phenethylamine (65% yield) and a small amount of unidentified material.
**Nitramines.** N-nitroso-N-methyl-β-phenethylamine 22 (0.55g, 3.3 mmol) dissolved in glacial acetic acid (10 ml), was treated with hydrogen peroxide (30%, 1 ml) dropwise, heated at 90° for 7 hours, cooled, diluted with crushed ice, and extracted with ether (3 x 50 ml). The ether extracts were washed with water, aqueous sodium bicarbonate, dried (MgSO₄), and evaporated to give N-nitro-N-methyl-β-phenethylamine 24 (0.51g, 85%) as a yellow oil which crystallized from low boiling petroleum ether as a colorless solid mp 39-40°. Anal. calcd for C₉H₁₂N₂O₂: C, 59.99; H, 6.71; N, 15.55. Found: C, 59.95; H, 6.71; N, 15.55. IR(CHCl₃): 1510(s) and 1290(s) cm⁻¹ (NNO₂). Nmr (CDCl₃): δ 2.95(t, 2H), 3.18(s, 3H), 3.90(t, 2H) and 7.16(5H).

When similarly treated N-methyl-N-nitrosobenzylamine 21 gave the nitramine 22 (87%) as a yellow oil.³⁰

**Results and Discussion.** Exposure to nitric acid (70%) in acetic anhydride (acetyl nitrate) at 25° for ten hours left the amine 13 unchanged. This confirmed a dependence of amine conversion on heating the mixture at 50° until the evolution of brown fumes (nitrogen dioxide) became vigorous.¹ The amine 11 was similarly unaffected by acetyl nitrite at 25° and was recovered completely. On the other hand nitrosonium tetrafluoroborate in anhydrous chloroform at 25° converted 15 percent of the amines 13 and 14 to nitrosamines 21 and 22 — presumably by heterolysis of nitrosoammonium cations (eq 1) since nitrous acid was apparently unavailable for conversion via hemiaminal nitrites (eq 2,3). Nitronium tetrafluoroborate in dichloroethane converted no more than five percent of amine 13 to benzaldehyde, isolated as a mixture of
nitro derivatives. Insofar as it failed to convert amines 11 and 14 to nitrosamines 21 and 22 (eq 2,3) or to nitramines 23 and 24 (eq 1) the probable formation of a nitroammonium cation 4 was unproductive.

The conversion of a tertiary amine can proceed from initial attack by three different species: nitrogen tetroxide, nitrogen dioxide, and nitrous acid. Radical abstraction of an α-hydrogen atom by nitrogen dioxide, proposed earlier (eq 6), can be followed by the formation of both the pair of a nitrosamine and a carbonyl compound and the competitive oxidation to an amide (eq 9). After nitrous acid (not present initially) became available during the course of other reactions it may have converted the amine in the traditional way (eq 2,3).

\[
\begin{align*}
R_2NCH_2R & \xrightarrow{\text{NO}_2} R_2NC\text{HR} & \xrightarrow{\text{O}_2} R_2\text{NCOR} \\
\text{-HNO}_2 & \xrightarrow{[-\text{H}]^+} & \xrightarrow{\text{NO}_2} R_2\text{NCH(ONO)}R
\end{align*}
\]

\text{eq (6)}

That dinitrogen tetroxide, produced \textit{in situ} from concentrated nitric acid in acetic anhydride at 50° (eq 7-9), may have directly participated in the reaction was supported by an independent conversion 13 \rightarrow 21 by authentic dinitrogen tetroxide in acetic anhydride at 25°. IR absorption at 1705 cm\(^{-1}\) for material obtained in trace amounts was attributed to the presence of amides and not to benzaldehyde since the latter was not detected by the gc analysis which was sensitive to 10\(^{-7}\) mole of the aldehyde. Presumably the amine was initially quaternized.
Although a nitrosoammonium cation intermediate (eq 2) can account for the required productivity (eq 3) on the assumption that either dinitrogen tetroxide functioned as a nitrite reagent or there was a fortuitous generation of nitrous acid, it cannot be differentiated, at this time, from an O-nitrosohydroxylammonium cation 25. Formation of the latter after an electron transfer,33 radical pairing, and ejection of a nitrite anion (eq 10) is proposed.

\[
\text{HNO}_3 + \text{Ac}_2\text{O} \rightleftharpoons \text{AcONO}_2 + \text{AcOH} \quad \text{eq (7)}
\]

\[
2 \text{AcONO}_2 \rightleftharpoons \text{Ac}_2\text{O} + \text{N}_2\text{O}_5 \quad \text{eq (8)}
\]

\[
\text{N}_2\text{O}_5 \rightleftharpoons \text{N}_2\text{O}_4 + \text{O} \quad \text{eq (9)}
\]

\[
\begin{align*}
\text{NCHR}_2 + \text{ZNO}_2 & \rightarrow \left[ \begin{array}{c}
\text{NCHR}_2 \\
\text{ON(O)Z}
\end{array} \right] \\
& \rightarrow \text{NONZ} - \text{Z} \\
& \rightarrow \text{NNO} + \text{R}_2\text{CO}
\end{align*}
\quad \text{eq (10)}
\]

25

\[Z = \text{NO}_2\text{,C(NO}_2\text{)}_3\]

An O-nitrosohydroxylammonium cation was previously encountered in an explanation for a reaction between a tertiary amine oxide and nitrous acid (eq 11)\textsuperscript{9,34,35} and is now seen as a common intermediate for the two reactions (eq 10,11). Since the trinitromethide anion would also be an excellent leaving group, a similar explanation is available for the conversion of a tertiary amine to a nitrosamine and a carbonyl compound by treatment with
tetranitromethane (eq 4,10, \( Z = C(NO_2)_3 \)).\(^{10}\) Perhaps a lesser tendency for the similar departure of an acetate anion precluded a productive reaction between a tertiary amine and acetyl nitrate at 25°.

\[
{\text{(CH}_3\text{)}_3\text{NO}} \xrightarrow{+NO} {\text{(CH}_3\text{)}_3\text{NONO}} \rightarrow {\text{(CH}_3\text{)}_2\text{N=CH}_2} + \text{HONO}
\]

\[
- \text{H} \quad \rightarrow \quad {\text{(CH}_3\text{)}_2\text{NNO}} + \text{CH}_2\text{O}
\]

\[\text{eq (11)}\]

As expected the unsymmetrical tertiary amine 13 gave benzaldehyde (28%) with the coproduction of dimethylnitrosamine, detected chromatographically, and the nitrosamine 21 (76%) with the assumed coproduction of formaldehyde, undetected (eq 12-14).

\[
\text{13} \rightarrow \text{C}_6\text{H}_5\text{CH=N(CH}_3\text{)_2} + \text{C}_6\text{H}_5\text{CH}_2\text{N(\text{CH}_3)=CH}_2
\]

\[\text{eq (12)}\]

\[
\text{26} \rightarrow \text{27}
\]

\[
\text{26} + \text{HONO} \rightarrow \text{C}_6\text{H}_5\text{CHO} + [(\text{CH}_3\text{)}_2\text{NNO}]
\]

\[\text{eq (13)}\]

\[
\text{27} + \text{HONO} \rightarrow 21 + [\text{CH}_2\text{O}]
\]

\[\text{eq (14)}\]

Nitric acid in acetic anhydride also converted \( N \)-methyl derivatives 7 and 8 to \( N \)-nitroso derivatives 16 and 17 of piperidine and pyrrolidine, \( N,N' \)-dimethylpiperazine 9 to \( N,N' \)-dinitroso-piperezine 18, triethylamine 10 to diethylnitrosamine 19,\(^{1}\) tri-\( \text{n} \)-butylamine 11 to di-\( \text{n} \)-butylnitrosamine 20,\(^{1}\) and \( N,N \)-dimethyl-\( \beta \)-phenethylamine 14 to \( N \)-methyl-\( N \)-nitroso-\( \beta \)-phenethylamine 22.

These reactions were generally comparable in efficiency to the similar conversions with nitrous acid; however, nitric acid in acetic anhydride offered faster reactions at lower temperature and left no unreacted tertiary amine. Aldehydes from amines 7-11 and 14 presumably underwent further changes on formation and were
not detected. No product was identified in the intractable mixture obtained from 1,4-diazabicyclo[2,2,2]octane 15.

Addition of hydrochloric acid introduced the Aqua Regia reaction, lowered the temperature required for the vigorous elimination of nitrogen dioxide,\(^1,36\) and introduced Cl(O) and Cl(\(+1\)). It did not improve the efficiency in converting an amine to a nitrosamine with the possible exception of tri-n-butylamine which gave the nitrosamine 20 in 47\% yield in the absence of hydrochloric acid and 62\% yield in the presence of hydrochloric acid (corresponding yields of 5\% and 82\% were previously reported).\(^1\)

A low conversion of dibenzylmethylamine 12 to benzaldehyde and N-nitroso-N-methylbenzylamine 21 was afforded by a similar reaction in the presence of hydrochloric acid. That nitramines were not obtained in these reactions was evidence that secondary amines were not produced as intermediates\(^9,34\) since the chloride anion was known to be a highly effective catalyst for the nitration of a secondary amine to a nitramine.\(^36\)

A dependence on the reaction medium is not completely understood. At the present time the high yield (69\%) of benzaldehyde from N,N-dimethylbenzylamine 13 in a reaction with nitric acid (100\%) and anhydrous hydrogen chloride in acetic anhydride is in sharp contrast with no detectable formation of benzaldehyde from the similar reaction with nitric acid (70\%) and hydrochloric acid (39\%) in acetic anhydride. Undetermined low yields of benzaldehyde and dimethylnitrosamine were obtained from the amine 13 and acetone cyanohydrin nitrate in exploratory experiments; neither the nitrosamine 21 nor the nitramine 21 was detected in the product mixtures. Further investigations to clarify these forma-
tions of benzaldehyde were not made.

Presumably hemiaminal nitrite ester formation (eq 3) was competitive with the formation of nitrate and acetate esters. An independent preparation of a nitrate and a nitrite ester consisted in the treatment of Eschenmoser's salt 28 with silver nitrate and with silver nitrite. Silver iodide was quantitatively obtained from each reaction (eq 15,16); the former gave a nitrate ester which did not dissociate to dimethylnitramine in agreement with other reports on the greater thermal stability of hemiaminal nitrate esters relative to nitrite esters.37 Reversibly formed hemiaminal esters would, of course, tend to be converted to nitrite esters as the latter underwent thermolysis.

\[
(CH_3)_2N=CH_2 + AgNO_3 \xrightarrow{- AgI} [(CH_3)_2NCH_2ONO_2] \xrightarrow{25^\circ} (CH_3)_2NNO_2 \text{ eq (15)}
\]

\[
(CH_3)_2N=CH_2 + AgNO_3 \xrightarrow{- AgI} [(CH_3)_2NCH_2ONO] \xrightarrow{25^\circ} (CH_3)_2NNO \text{ eq (16)}
\]

Aromatic nitro derivatives were obtained in high yields and without detectable competition from conversions to nitrosamines when the amines 11 and 14 were treated with nitronium tetrafluoroborate in either dichloroethane or concentrated sulfuric acid. The amine 11 gave predominantly (>80%) m-nitration and the amine 14 gave op-nitration (95%).38

The nitrosamines 21 and 22 were readily oxidized to N-methyl-N-nitrobenzylamine 23 and N-methyl-N-nitro-S-phenethylamine 24.39 Hydrogen peroxide in acetic acid afforded the nitramines in high yields and the nitramine 24 was quantitatively produced by m-chloroperbenzoic acid.
Acknowledgment. ONR provided financial support.

Footnotes and References

3. The heterolysis has been promoted by the formation of stable dialkylaminomethylcarbonium ions, tert-alkyl carbonium ions, and acylium cations.
13. Aconitine and other alkaloids were converted to nitrosamines by nitric acid (d 1.42) degradation of tert-amine moieties (W. A. Jacobs and L. C. Craig, J. Biol. Chem., 1940, 146, 303, 323. Earlier references are cited). It is suspected that the nitric acid contained nitrous acid.
36. Ref 4, p 633ff.
38. Nitric acid (d 1.5) at -10° to 0° converted (90%) the amine
12 to its m-nitro derivative (54% yield) and the amine 12 to its p-nitro derivative (78% yield) (F. R. Goss, W. Hanhart, and C. K. Ingold, J. Chem. Soc., 1927, 250). We found that in a mixture of concentrated nitric and sulfuric acids at 0° for one hour the amine 12 gave its m-nitro derivative (85%) with small amounts of the o-(2%) and p-isomer (12%).

B. α-Functionalization in Nitrosamines.

Introduction.

It became desirable to incorporate α-functions into nitrosamines to provide schemes for the preparation of cage structure high energy materials. A proposed scheme is shown (eq 1).

\[
\begin{align*}
\text{RNH} & \quad \text{NHR} & \quad \text{NHR} \\
\text{ON} & \quad \text{ON} & \quad \text{ON} \\
\text{CH}_2\text{O} & \text{or} & \text{HC(OR)}_3
\end{align*}
\]

eq (1)

The x-ray determination that nitration of hexahydro-2,4,6-trimethyl-s-triazine gave a trinitro derivative (eq 2) in which the methyl (axial) and nitro groups were directed to opposite sides of the mean plane of the ring implied a favorable geometry for eq (1).\(^1\)

\[
\begin{align*}
\text{CH}_3 & \quad \text{H}_3\text{C} & \quad \text{NH} \\
\text{NN} & \quad \text{NN} & \quad \text{NN} \\
\text{HN} & \quad \text{HN} & \quad \text{HN} \\
\text{R} & \quad \text{R} & \quad \text{R}
\end{align*}
\]

eq (2)

A report on the formation of a hexahydro-2,4,6-triamino-s-triazine (eq 3) tended to support the presumption of existence for the starting material in eq (1).\(^2\)

\[
\begin{align*}
\text{R-} & \quad \text{C=NH} & \quad \text{NH}_2 \\
\end{align*}
\]

\[
\begin{align*}
\text{R} = \text{HON=C(CN)} & \\
\end{align*}
\]

eq (3)
Results of Investigations.

The preparation of \( \alpha \)-azidodimethylnitrosamine provided the first example of introducing a nitrogen function at the \( \alpha \)-position of a nitrosamine (eq 4) by the direct replacement of a hydrogen atom.

\[
\begin{align*}
(CH_3)_2N & \xrightarrow{((CH_3)_2CH)_2NLi} CH_3NCH_2N_3 \\
(C_7H_7SO_2N_3 & NO) & \text{-78° 3h oil, 30%} & \text{eq (4)}
\end{align*}
\]

This encouraged investigations of the chemistry of the methylene groups in 1,3,5-trinitrosohexahydro-1,3,5-triazine 1. Although considerable work has been reported during the last two decades on the base-catalyzed alkylation (and related reactions) at the \( \alpha \)-position of nitrosamines, similar reactions on polynitrosamines were heretofore unknown.

A mono- and a dialkylated product 2 and 3 were obtained from the triazine 1 and benzaldehyde in the presence of potassium tert-butoxide (eq 5,6). Lithium diisopropylamide, often a catalyst of choice for base catalyzed reactions of nitrosamines, underwent transnitrosation with the nitrosotriazine 1 to give diisopropylnitrosamine (eq 7). It failed to catalyze \( \alpha \)-substitutions in 1.

\[
KOC(CH_3)_3 \\
C_6H_5CHO \xrightarrow{\text{THF}} NNO \xrightarrow{-78° 2h} ONN \xrightarrow{\text{THF}} \frac{1}{2} \text{ mp 123-126°, 80%} & \text{eq (5)}
\]
Attempts to achieve base catalyzed reactions between the triazine 1 and methyl iodide, ethyl iodide, benzyl bromide, p-toluenesulfonyl azide (compare eq (1)), and 0-methylhydroxylamine were unsuccessful. It was decided to investigate 1,3-dinitrosomidazolidine 4 and 1,3-dinitrosohexahydropyrimidine 7 to gain insight and experience. Both compounds were readily alkylated (eq 8-10)
Ring size may be controlling reactivity. Deuterium exchange occurred within 15 minutes with the five membered heterocycle 4 whereas the six membered homolog 7 required 12 hours to give the comparable quantitative conversion \( \text{eq} \ (11) \). Attempted deuteriation of 1 led to decomposition.

Attempts to benzylate compound 8 to give a dibenzyl derivative of 7 have been unsuccessful.

References

2. O. Diels and E. Borgwardt, Ber. 1921, 54 [B], 1334.
C. Reactions between Nitroform and Isocyanides.

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Mesoionic Oxadiazolium-olates and Oxatriazolium-olates from Aryl Isocyanides and Nitroform

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Nitroform converted p-nitrophenyl isocyanide into the mesoionic 3-p-nitrophenyl-1,2,3-oxadiazolium-5-olate (2) and 3-p-nitrophenyl-1,2,3,4-oxatriazolium-5-olate (3), together with p-nitroaniline; it converted p-tolyl isocyanide into the mesoionic 3-(2-nitro-4-methylphenyl)-1,2,3-oxatriazolium-5-olate together with 2-nitro-4-methylaniline and p-methylaniline.

A new reaction between nitroform and p-nitrophenyl isocyanide (1) gave the mesoionic heterocycles, 3-p-nitrophenyl-1,2,3-oxadiazolium-5-olate (2) and 3-p-nitrophenyl-1,2,3,4-oxatriazolium-5-olate (3), and a trace of p-nitroaniline (4).

Equimolar portions of p-nitrophenyl isocyanide (1) and nitroform in a mixture of hexane and ether at 25°C became light yellow then brown during 20 min and evolved brown fumes (nitrogen dioxide) after about 2 h. The mixture was stirred for 14 h at 25°C. Removal of solvent left a paste which was applied to an alumina column. A mixture (1:9) of ethyl acetate and benzene eluted p-nitroaniline (4) (4%) m.p. and mixed m.p., 148-149°C and the same solvent mixtures with ratios 1:5 and 5:1 eluted the
oxatriazolium-olate (3) (42%), m.p. 167-168°C,\(^4\) i.r. (KBr): 1825 s, 1785 s (CO), 1540 s (NO\(_2\)), and 1340 s cm\(^{-1}\) (NO\(_2\)); m/z (70 eV) 178 (10%) (M - 30) and 122 (100) (O\(_2\)NC\(_6\)H\(_4\)); n.m.r. (CDCl\(_3\)): \(\delta 8.41\) (d, 2H, J 9 Hz) and \(8.65\) (d, 2H, J 9 Hz); and the oxadiazolium-olate (2) (6%), m.p. 197-198°C (decomp.),\(^5\) i.r. (KBr): 1700 m (CO), 1590 s, 1520 s (NO\(_2\)), and 1340 s (NO\(_2\)) cm\(^{-1}\); m/z (70 eV): 209 (3%) (M + 2), 191 (8), 174 (12), 164 (90), 122 (15) (O\(_5\)NC\(_6\)H\(_4\)), and 90 (100) (C\(_6\)H\(_4\)N).

Under comparable conditions nitroform converted p-tolyl isocyanide (5)\(^1\) into the mesoionic compound (6) (48%), m.p. 140-141°C; satisfactory analyses for C, H, and N; i.r. (KBr): 1790 s (oxatriazolium-olate), 1535 s (NO\(_2\)), and 1350 s (NO\(_2\)) cm\(^{-1}\); n.m.r. (CDCl\(_3\)) and CD\(_3\)SOCD\(_3\)): \(\delta 2.65\) (s, 3H, CH\(_3\)), \(7.90\) (d, 1H, J 8 Hz), \(8.06\) (d, 1H, J 8 Hz), and \(8.16\) (s, 1H); m/z (70 eV): 192 (15%) (M - 30) and 164 (100) (C\(_7\)H\(_6\)N\(_3\)O\(_2\)); 2-nitro-4-methylaniline (8) (21%) m.p. 115-117°C,\(^6\) and a small amount of p-toluidine (7) (3%) m.p. and mixed m.p. 45-46°C.\(^7\) A trace of the isocyanide (5) was recovered; an oxadiazole was not detected.

Quilico obtained the mesoionic oxatriazolium-5-olates (11) and nitrogen dioxide in 1932 by warming arylazotrinitromethanes (10), the unstable adducts from aryladiazonium cations (9) and the anion of nitroform.\(^4\) Initial a,a-elimination of dinitrogen tetroxide from the methane (10) is proposed to enable the conversion (10) \(\rightarrow\) (11) and the dehydrobromination of the arylhydrazones (13) of bromonitroformaldehyde to produce the oxatriazolium-olates (11)\(^8\) to share a nitronitrilimine intermediate (12) and its isomerization to a nitrosaminoisocyanate (14), an open-chain
tautomer of the heterocycle (11).†

\[ \text{p-NC}_{6}H_{4}C=\text{N} \xrightarrow{\text{HCl}} \text{p-NC}_{6}H_{4}C=\text{O} + \text{NH}_{2} \]

(1)

\[ \text{p-MeC}_{6}H_{4}C=\text{N} \xrightarrow{\text{HCl}} \text{MeC}_{6}H_{4}C=\text{O} + \text{NH}_{2} \]

(5)

\[ \text{ArN}=\text{N} + \text{C(NO}_{2})_{3} \rightarrow \text{ArN}=\text{NC(NO}_{2})_{3} \]

(9)

\[ \text{Br} \]

\[ \text{ArNHNCNO} \xrightarrow{\text{NaOAc, HBr}} \text{ArNNCNO} \xrightarrow{\text{N}_{2}O_{4}} \]

(13)

(12)

(11)

(10)

(19)

(18)

\[ \text{ArNNCO} \xrightarrow{\text{NO}} \]

(11)

(14)

The anils (15) and (16) were the expected α,α-adducts from nitroform and the isocyanides (1) and (5).† Their intermediacy was supported by the isolation of the aniline derivatives (4) and (7).‡ A zwitterion (17) and the isomeric nitrosaminoketene (18) are proposed intermediates to correlate the conversion (15)+(2) with (10)+(11).†

† The complete identification of pathways for the conversions (10)+(11) and (15)+(2) awaits further investigation. A minimum of two rearrangements are required for the creation of new NN and CO bonds in each conversion.

‡ The anilines (4), (7), and (8) are formed during chromatographic separation of the product mixture. Under the conditions employed the isocyanides (1) and (5) and the heterocycles (2), (3), and (6) were not hydrolysed.
Insofar as it would have initiated a similar conversion into an oxadiazolium-5-olate which was not detected, an α,α-elimination of dinitrogen tetroxide from the anil (16) did not occur. To account for the ortho-nitro groups in the products (6) and (8) a rearrangement of the anil to the alilinoethene (19) followed by conversion into the anil (20) by a Michael addition of nitroform and an elimination of dinitromethane is proposed. Hydrolysis of the enamine (19) and/or the anil (20) could account for the formation of the aniline derivative for amine (8). The conversions (20)→(6) and (15)→(3) were apparently related.

The formation of the oxatriazolium-olates (3) and (6) from the isocyanides (1) and (5) requires a replacement of ArNC- by ArNN-. Although this conceivably could occur by interaction between dinitrogen tetroxide and anils or other intermediates, a more detailed statement awaits further investigation.

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References
2 A procedure for the conversion of tetrinitromethane into nitroform was obtained from Dr. H. Adolph, NSWC, Silver Spring, Maryland.
Ital., 1933, 63, 471 (Chem. Abstr., 1934, 28, 748).
D. Conversion of 2,4-dinitrobenzyl dimethylamine 1 to 2-methyl-6-nitroindazole 2.

Collaboration with Dr. M. D. Pace of the Naval Research Laboratory; Washington, D.C. confirmed (a) radical intermediate(s) detected by EPR for the subject conversion (eq 1). Further characterization of the intermediate(s) is underway.

\[
\text{eq (1)}
\]

\[
\begin{align*}
&\text{O}_2\text{N} & &\text{N}(	ext{CH}_3)_2 & &\text{H} \\
&\text{NO}_2 & &\text{CH}_2 & &\text{N}\text{CH}_3 \\

&\text{eq (2)}
\end{align*}
\]

It is assumed that the reaction was initiated by an electron transfer from the amino group to the nitro group (eq 2). A related electron transfer can account for the reported stabilization of the boat conformer 4 of the aminonitro compound 3 in which "interaction of the unshared electrons on N-1 with the N atom of the 4-nitro group" was claimed.¹

\[
\text{eq (2)}
\]

1. \(X = \text{CH}_3\)
2. \(Y = \text{H, NO}_2, \text{Cl, Br, I}\)
At this time a radical detected by EPR for the conversion $1 \to 2$ is thought to be related to structure 5 or 6.

Reference