Dinitrogen Trioxide. Part VI.[1] The Reactions of Dinitrogen Trioxide with Primary and Secondary Amines

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The reactions of dinitrogen trioxide with primary and secondary amines have been studied. All secondary amines formed the *N*-nitrosamine. Primary aromatic amines gave the diazonium nitrite but the corresponding aliphatic compounds gave a variety of products including alkyl ammonium nitrites, alkyl nitrites, and alkenes. In some cases n-alkylamines gave products with a branched alkyl group.

THE reactions of amines with 'nitrous acid' have been widely studied and are commonly used to distinguish between primary, secondary, and tertiary amines. However, aqueous nitrous acid is a complex mixture containing a number of nitrosating species, *i.e.*, NO^+, $H_2NO_2^+$, NOCl, N_2O_4, N_2O_3, and HNO_2 in order of decreasing efficiency.[2]

It is generally agreed that when primary or secondary amines react with nitrous acid the products are formed in the order amine, *N*-nitrosamine, diazonium cation, and deamination products.[3] Kinetic studies of both diazotisation and deamination in dilute solutions of sulphuric or perchloric acids have given the equation, rate = k[amine][HNO_2]^2. This and other evidence suggests that the nitrosating agent under these conditions must be dinitrogen trioxide.

We therefore investigated the reactions of amines with dinitrogen trioxide under conditions such that the concentrations of all other nitrosating species were negligible. Only a few such reactions have been reported, and in all cases the reaction temperature appears to be too high for the dinitrogen trioxide to be undissociated; in some cases it is probable that water was also present.

In the present work the dinitrogen trioxide was maintained at −85° under an atmosphere of nitric oxide. Under these conditions the equilibrium concentration of other species will be negligible.[1,4] However, equilibrium is not rapidly established in this system.[5]

The active reagent could be present in very small concentration provided that it can be rapidly formed from dinitrogen trioxide. Dinitrogen trioxide may undergo self-ionisation to a very small extent, *i.e.*, $N_2O_3 \rightleftharpoons NO^+ + NO_2^-$. The nitrosonium cation is a more powerful electrophile than dinitrogen trioxide but it is unlikely to compete with the latter owing to the large difference between the concentrations of the two species. Nitric oxide and nitrogen dioxide are both free radicals and may be present in very small amounts, *i.e.*, $N_2O_3 \rightleftharpoons NO + NO_2$. Both of these species react with amines[6,7] but appear to be unimportant under the conditions of our experiments.

The reactions of dinitrogen trioxide with amines were usually highly exothermic and so an organic solvent was normally used to minimise the effect of local heating. The solvent must remain liquid at −85°, and so diethyl ether, toluene, or light petroleum was used. None of these is ideal. Both nitric oxide[8] and dinitrogen tetroxide[9] are Lewis acids, and there is reason to believe that dinitrogen trioxide may also exhibit Lewis acidity.[5] Therefore σ-donors such as diethyl ether or π-donors such as toluene may influence the chemical reactions. Diethyl ether has the added disadvantage that it reacts very slowly with dinitrogen trioxide. Light petroleum is free from these disadvantages but unfortunately dinitrogen trioxide dissociates more readily in this medium than in other solvents.[10]

RESULTS

Both aliphatic and aromatic secondary amines reacted rapidly with dinitrogen trioxide. Two products were normally obtained, one miscible and the other immiscible with the solvent. Their relative amounts are given in Table 1. The former was water-soluble and reacted with alkali to give the amine and nitrite and with acid to form nitrous acid. The ^1H n.m.r. spectrum showed the presence of the dialkylammonium cation and the i.r. spectrum indicated that nitrite anions were present. This component

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[1] Part V, A. J. Vosper, *J. Chem Soc.* (*A*), 1966, 1759.

[2] T. A. Turney and G. A. Wright, *Chem. Rev.*, 1959, **59**, 497.

[3] J. H. Ridd, *Quart. Rev.*, 1961, **15**, 418.

[4] E. T. Chang and N. A. Gookeen, *J. Phys. Chem.*, 1966, **70**, 2394.

[5] A. J. Vosper, unpublished work.

[6] R. S. Drago and B. R. Karstetter, *J. Amer. Chem. Soc.*, 1961, **83**, 1819.

[7] J. L. Riebsomer, *Chem. Rev.*, 1945, **36**, 157.

[8] R. S. Drago, 'Free Radicals in Inorganic Chemistry,' Advances in Chemistry No. 36. American Chemical Society, 1962, 143.

[9] P. Gray and A. D. Yoffe, *Chem. Rev.*, 1955, **55**, 1069.

[10] J. Mason, *J. Chem. Soc.*, 1959, 1288.

TABLE 1

Reactions of dinitrogen trioxide with secondary amines

Amine	Solvent	Dialkyl or diaryl ammonium nitrite (g.)	*N*-Nitrosamine (g.)
Dimethylamine	Toluene	4·64	3·31
Diethylamine	Toluene	5·77	4·20
	Ether	8·71	6·05
	None	4·27	1·92
Di-n-propylamine	Toluene	7·62	4·28
Di-isopropylamine	Toluene	9·26	7·11
Di-n-butylamine	Ether	20·10	15·53
Di-isobutylamine	Toluene	7·96	3·77
Dibenzylamine	Toluene	10·45	8·81
Piperidine	Toluene	18·99	7·84
	None	8·63	4·23
N-Methylaniline	Toluene	Unstable	7·06
N-Ethylaniline	Toluene	Unstable	8·77
N-n-Propylaniline	Toluene	Unstable	6·20
Diphenylamine	Ether	None	12·62
Di-*p*-tolylamine	Toluene	None	3·86

was identified as the dialkylammonium nitrite and this was confirmed by analysis in some cases. Amines of low basicity such as the *N*-alkylanilines gave unstable compounds while diphenylamine and di-*p*-tolylamine gave no nitrite salt at all.

The second component was identified as the *N*-nitrosamine by its physical properties and its i.r. and ^{1}H n.m.r. spectra. This was confirmed by microanalysis in some cases. The i.r. spectra [11] all showed bands near to 1450 (N=O stretch), 1050 (N–N stretch), and 675 (N–N=O deformation) cm.$^{-1}$.

The ^{1}H n.m.r. spectra are given in Table 2. Some of these have already been reported [12,13] and our results agree well with them. The notation and assignments of configuration are based on previous work.[13] The *N*-alkylphenylnitrosamines could occur in two isomeric forms owing to restricted rotation about the N–N bond, but our spectra provide evidence for only the *syn*-isomer.[13] Thus the reaction between dinitrogen trioxide and secondary amines is as follows:

$$2R^1R^2NH + N_2O_3 \longrightarrow R^1R^2NH_2^+NO_2^- + R^1R^2N{\cdot}NO$$

TABLE 2

^{1}H N.m.r. spectra of some *N*-nitrosamines ($R^1R^2N{\cdot}NO$) at 33·1°

R^1	R^2	Solvent	Spectrum (τ values, *J* in c./sec.)	Assignment and reference (if any)
Me	Me	None	6·20 (3H, s)	*trans*-Me [12,13]
			6·93 (3H, s)	*cis*-Me
Et	Et	None	5·83 (2H, q, *J* 7·0)	*trans*-CH_2 [12]
			6·83 (2H, q, *J* 7·2)	*cis*-CH_2
			8·63 (3H, t, *J* 7·4)	*trans*-Me
			8·97 (3H, t, *J* 7·2)	*cis*-Me
Pr^n	Pr^n	None	5·94 (2H, t, *J* 7·1)	*trans*-α-CH_2
			6·50 (2H, t, *J* 7·3)	*cis*-α-CH_2
			7·9—8·8 (4H, m)	*cis*- and *trans*-β-CH_2
			8·9—9·3 (6H, m)	*cis*- and *trans*-Me
Pr^i	Pr^i	$CDCl_3$	5·00 (1H, sept, *J* 6·9)	*cis*-α-CH [13]
			5·69 (1H, sept, *J* 6·8)	*trans*-α-CH
			8·49 (6H, d, *J* 7·1)	*trans*-Me
			8·82 (6H, d, *J* 6·9)	*cis*-Me
Bu^n	Bu^n	None	5·88 (2H, t, *J* 6·7)	*trans*-α-CH_2
			6·45 (2H, t, *J* 6·5)	*cis*-α-CH_2
			8·0—9·4 (14H, m)	β-CH_2 and Me
Bu	Bu^i	None	6·07 (2H, d, *J* 7·6)	*trans*-α-CH_2
			6·61 (2H, d, *J* 7·3)	*cis*-CH_2
			7·98 (1H, m)	CH
			8·6* (1H, m)	CH
			8·8—9·2 (12H, m)	*cis*- and *trans*-Me_3
Me	Ph	None	2·4—2·8 (5H, m)	Ring protons [12,13]
			6·70 (3H, s)	*cis*-Me
Et	Ph	$CDCl_3$	2·3—3·1 (5H, m)	Ring protons [13]
			6·34 (2H, q, *J* 7·0)	*cis*-CH_2
			8·80 (3H, t, *J* 7·1)	*cis*-Me
Pr^n	Ph	Neat	2·4—3·0 (5H, m)	Ring protons
			6·07 (2H, t, *J* 7·3)	*cis*-CH_2
			8·56 (2H, q, *J* 7·0)	*cis*-CH_2
			9·27 (3H, t, 7·3)	*cis*-Me
Ph	Ph	$CDCl_3$	2·2—3·2 (10H, m)	Ring protons
p-MeC_6H_4	*p*-MeC_6H_4	CD_3CN	2·5—3·2 (8H, m)	Ring protons
			7·63 (3H, s)	Me
			7·67 (3H, s)	Me
$PhCH_2$	$PhCH_2$	$CDCl_3$	2·5—3·2 (10H, m)	Ring protons
			4·84 (2H, s)	*trans*-CH_2
			5·38 (2H, s)	*cis*-CH_2
N-Nitrosopiperidene		None	5·85 (2H, m)	*trans*-α-CH_2
			6·30 (2H, t, *J* 5·6)	*cis*-α-CH_2
			8·0—8·8 (6H, m)	β- and γ-CH_2

* This signal was partially obscured by the multiplet at τ 8·8—9·2.

A number of primary aromatic amines reacted rapidly with dinitrogen trioxide; these included aniline, the three isomeric toluidines and nitroanilines, and *p*-anisidine. Most of the product was water-soluble and in aqueous solution coupled with alkaline β-naphthol to give an azo-dye and nitrite. This azo-dye consisted of a single product (t.l.c.) with an R_F value identical with that of the synthetic azo-dye. When an aqueous solution of the product was added to hot 2N-sulphuric acid, nitrogen and nitrogen oxides were evolved, and the corresponding phenol was isolated and identified as the 2,4-dinitrobenzoate. These reactions suggest that the product was the diazonium nitrite. In the case of *p*-toluidine the i.r. spectrum of the product showed a strong band at 2270 cm.$^{-1}$ which can be attributed to the N–N stretching frequency. Attempts to isolate the products in the cases of aniline and *p*-nitroaniline resulted in violent explosions. In some cases a small amount of the diazoamino-compound was isolated. Thus the reaction between dinitrogen trioxide and primary aromatic amines is:

$$RNH_2 + N_2O \longrightarrow RN_2^+NO_2^- + H_2O$$

The experiments with aliphatic primary amines were the least satisfactory, since nitrogen was evolved and

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[11] R. N. Haszeldine and J. Jander, *J. Chem. Phys.*, 1955, **23**, 979; R. N. Haszeldine and B. J. H. Mattinson, *J. Chem. Soc.*, 1955, 4172.

[12] C. E. Looney, W. D. Phillips, and E. L. Reilly, *J. Amer. Chem. Soc.*, 1957, **79**, 6136.

[13] G. J. Karabatsos and R. A. Taller, *J. Amer. Chem. Soc.*, 1964, **86**, 4373.

carried away the nitric oxide, thereby causing some decomposition of the dinitrogen trioxide.. Attempts to prevent this by passing a slow stream of nitric oxide through the reaction vessel were apparently not successful, and some of the products isolated appear to result from reaction of the amine with dinitrogen tetroxide. The gases evolved during the reaction consisted mainly of nitrogen, nitric oxide, and alkenes, but smaller amounts of nitrogen dioxide and nitrous oxide were also present. Some of the product was immiscible with the organic solvent. The chemical reactions and i.r. and ^{1}H n.m.r. spectra showed that this component consisted of the alkylammonium nitrite together with a smaller amount of the nitrate. In some cases the relative quantities of the two salts were determined by analysis. Two fractions were separated from the organic solvent and identified as the alkyl nitrite and alkyl nitrate. The i.r. and ^{1}H n.m.r. spectra were identical with those reported[14] or were checked against authentic samples. In some cases the identification was confirmed by microanalysis. The relative amounts of the different products are given in Table 3. After removal of all volatile material, significant quantities remained of a high-boiling residue which was not identified.

TABLE 3

Products of reactions of dinitrogen trioxide with primary aliphatic amines

		Products			
Amine	Solvent	Alkylammonium salts (g.)	Alkyl nitrites (g.)	Alkyl nitrates (g.)	Alkenes (g.)
Methylamine	Toluene	Nitrite 5·22 Nitrate 0·63	Significant quantities	*ca.* 0·3	None
Ethylamine	Toluene	Nitrite 6·24 Nitrate 1·45	2·44	0·82	Trace
n-Propylamine	None	Nitrite + nitrate 7·17	n-Propyl + isopropyl 1·37	n-Propyl + isopropyl 0·52	*ca.* 0·3
n-Propylamine	Toluene	Nitrite + nitrate 5·10	n-Propyl 1·75 Isopropyl 0·26	n-Propyl 0·69 Isopropyl 0·1	*ca.* 0·3
n-Propylamine	Ether	Nitrite 8·64 Nitrate 2·17	n-Propyl 3·10 Isopropyl 0·63	n-Propyl 1·05 Isopropyl 0·25	*ca.* 0·4
Isopropylamine	Toluene	Nitrite + nitrate 5·35	Isopropyl 1·78	Isopropyl 0·57	*ca.* 0·25
n-Butylamine	None	Nitrite + nitrate 7·82	n-Butyl 2·77 Isobutyl 0·49	n-Butyl 2·03 Isobutyl 0·39	*ca.* 0·2
n-Butylamine	Toluene	Nitrite + nitrate 6·34	n-Butyl 3·75 Isobutyl 0·62	n-Butyl 1·84 Isobutyl 0·23	*ca.* 0·4

For the reactions with n-propylamine and n-butylamine, the ^{1}H n.m.r. spectrum of the crude nitrite and nitrate fractions showed that appreciable quantities of the isoisomer were present. For example the ^{1}H n.m.r. spectrum of the crude n-propyl nitrite contained a doublet at τ 8·64 and a septet at 4·40, which must be assigned to the methyl and methine groups respectively of the isopropyl nitrite.

Ammonia and dinitrogen trioxide react rapidly even when the latter is in large excess. The products are ammonium nitrite, water, and nitrogen, in agreement with previous work.[15]

DISCUSSION

The products of the reactions of amines with dinitrogen trioxide are extremely similar to those formed with aqueous nitrous acid. The mechanism for the latter reaction is well established[2,16] and the reactions reported here probably proceed by a similar mechanism, with the first stage involving attack by dinitrogen trioxide on the lone pair of the amine. Only in the case of primary aliphatic amines do the products differ significantly from the corresponding reactions with nitrous acid, and this is clearly due to solvolysis by dinitrogen trioxide rather than water. The molecular rearrangement of n-alkyl groups must be due to the formation of a carbonium ion. Since the products are independent of the solvent and identical with those formed in the absence of solvent, the use of donor solvents has little effect of the reaction. This work supports the idea that dinitrogen trioxide is an effective nitrosating agent for primary and secondary amines.

EXPERIMENTAL

Methylamine and ethylamine were prepared by heating the corresponding hydrochloride with an excess of calcium oxide. Ammonia and the other amines were obtained commercially. Ammonia and the volatile amines were distilled from calcium oxide and fractionated; the middle fraction was used. Solid amines were recrystallised from a suitable solvent and vacuum-dried. The organic solvents were purified and dried by conventional methods. Nitric oxide was obtained from a cylinder * and purified by passing it through 90% sulphuric acid and then a cold trap at −85°.

The reactions were carried out in an all-glass high-vacuum apparatus. The organic solvent was placed in the reaction vessel, which was filled with an atmosphere of pure nitric oxide and surrounded by solid carbon dioxide and acetone. A cylinder of dinitrogen trioxide was cooled and inverted and the liquid was passed into the reaction vessel via poly(tetrafluoroethylene) tubing. Only small quantities of nitrogen oxides were lost from the apparatus. The dinitrogen trioxide was maintained at −85° under an atmosphere of nitric oxide until no further absorption took place. This normally took several days. Analysis of a

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* Obtainable from The Matheson Company Inc., 932 Paterson Plank Road, East Rutherford, New Jersey, U.S.A.

[14] P. Tarte, *Bull. Soc. chim. belges.*, 1951, **60**, 240; W. D. Phillips, C. E. Looney, and C. P. Spaeth, *J. Mol. Spectroscopy*, 1957, **1**, 35; L. H. Piette and W. A. Anderson, *J. Chem. Phys.*, 1959, **30**, 899.

[15] R. Schwarz and H. Giese, *Ber.*, 1934, **67**, 1108.

[16] A. Streitwieser, *J. Org. Chem.*, 1957, **22**, 861.

[17] G. C. Whitnack, C. J. Holford, E. St. Claire Ganz, and G. B. L. Smith, *Analyt. Chem.*, 1951, **23**, 464.

sample prepared as described above by the method of Whitnack *et al.*[17] showed that **99** mole-% of dinitrogen trioxide was present.

Ammonia and volatile amines were slowly distilled into the reaction vessel; less volatile amines were dissolved in the organic solvent and slowly added from a hypodermic syringe or dropping funnel. It was important to add the amine extremely slowly. The addition of amine was continued until the characteristic blue colour of dinitrogen trioxide disappeared. Since the amine was present in excess and the weight of dinitrogen trioxide was not known the yield of product cannot be determined and only the relative weights can be given.

For reactions involving primary aliphatic amines, considerable quantities of gases were evolved. These gases were passed through a cold trap, an i.r. cell, and then a solution of bromine in carbon tetrachloride in order to remove any alkenes as the dibromo-derivative. The quantity of alkenes evolved was calculated from the weight of the dibromo-derivative recovered and therefore represents a minimum value for this quantity. The reaction vessel and cold trap were allowed to warm up and all the gases were swept through the bromine–carbon tetrachloride solution by a stream of nitrogen. Products immiscible with the organic solvent were separated and other products were obtained from the organic solvent by distillation.

I.r. spectra were obtained with a Perkin-Elmer **457** grating instrument and ^{1}H n.m.r. spectra with a Perkin-Elmer R10 spectrophotometer.

Alkyl ammonium salts were analysed as follows. A known weight of the salt was distilled with an excess of sodium hydroxide and the amine was absorbed in standard acid and back titrated with standard alkali. The residue contained sodium nitrite and possibly sodium nitrate. The nitrite was determined volumetrically with ceric ammonium sulphate and the total nitrogen was determined by reduction with Devarda's alloy followed by an ammonia distillation.

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