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^{15}N Studies of the Mechanisms of Nitration of Hexamethylenetetramine and 3,7-Diacetyl-1,3,5,7-tetraazabicyclo[3.3.1]nonane

Michael R. Crampton, Michael Jones, John K. Scranage and Peter Golding[1]

Chemistry Department, Durham University, Durham DH1 3LE.

[1]Royal Armament Research and Development Establishment, Waltham Abbey, Essex EN9 1AX.

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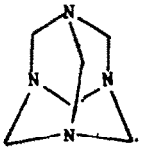
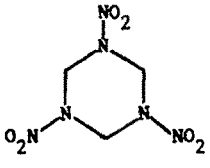
Abstract - Mechanistic studies of the nitration of hexamethylenetetramine (1) and some derivatives are reported and are compared with acetylation reactions. Nitration reactions, with nitric acid, were carried out using mixtures of [$^{15}N_4$]- and [$^{14}N_4$]-compounds and the destination of the nitrogen-isotopes in the products was determined mass spectrometrically. The results show that in nitration of (1) to give 3,7-dinitro-1,3,5,7-tetraazabicyclo[3.3.1]nonane (DPT) extensive ring cleavage occurs to give species containing single amino-nitrogen fragments. However the nitration of 3,7-diacetyl-1,3,5,7-tetraazabicyclo[3.3.1]nonane (DAPT) to 1,5-diacetyl-3,7-dinitro-1,3,5,7-tetraazacyclooctane (DADN) involves selective cleavage of the methylene bridge. A synthesis of DADN by acetolysis of DPT is reported.

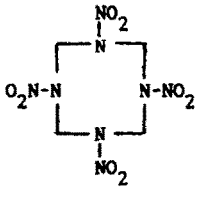
The reactions of hexamethylenetetramine, (1), with electrophiles are synthetically useful. Bachmann and co-workers[1] showed that (1) with ammonium nitrate, nitric acid and acetic anhydride produces mixtures of 1,3,5-trinitro-1,3,5-triazacyclohexane (RDX), (2), and 1,3,5,7-tetranitro-1,3,5,7-tetraazacyclooctane, (HMX), (3) in a process which forms the basis for the commercial production of these explosives. More recently[2] routes to HMX from (1) have been devised involving initial acetylation to give the diacetyl derivative DAPT, (4), or the tetraacetyl derivative TAT, (5), followed by nitration. There is current interest[3-6] in the mechanisms of these reactions and in understanding the factors which determine the ring size - six or eight membered - of the products formed. Mechanisms postulated[1,7,8] include the selective cleavage of bonds within the hexamine molecule, or the total cleavage (in the presence of electrophile) of the molecule to smaller fragments followed by recombination. Evidence for the latter pathway in the Bachmann nitration process has been adduced[9] from ^{14}C and ^{15}N tracer studies. However mass spectrometric measurements using mixtures of ^{14}N- and ^{15}N-compounds have shown[10] that acetolyses of (1) to DAPT, and of DAPT to TAT occur mainly by selective cleavage of the methylene bridges.



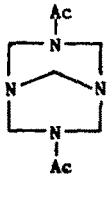
(1) Hexamethylenetetramine



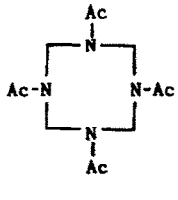
(2) RDX



(3) HMX



(4) DAPT

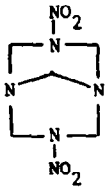


(5) TAT

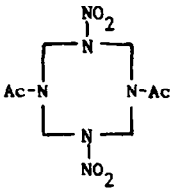
We report here studies of the mechanisms of nitration in nitric acid of (1) to 3,7-dinitro-

1,3,5,7-tetraazabicyclo[3.3.1]nonane (DPT), (6), and of (4) to 1,5-diacetyl-3,7-dinitro-1,3,5,7-tetraazacyclooctane (DADN), (7). The results are compared with those for the related acetolysis reactions. The experiments were designed to assess the extent of ring-cleavage occurring. Our general strategy was to prepare starting materials containing ca. 100% ^{15}N and to carry out synthetic reactions on mixtures of pure ^{15}N and ^{14}N compounds. The destination of the isotopes in the isolated products was determined mass-spectrometrically.

We also report a method for the synthesis of DADN, (7), by acetolysis of DPT, (6).



(6) DPT



(7) DADN

RESULTS AND DISCUSSION

Mass spectrometric data are given in Table 1 for 'isotopically pure' compounds obtained with nitrogen in natural abundance (^{14}N 99.63%, ^{15}N 0.37%). The peaks with masses M+1 and M+2 are due to naturally occurring ^{13}C and ^{15}N. Data are also given for ^{15}N-hexamine and ^{15}N-DAPT prepared from $^{15}NH_3$. In all cases the intensities of the M+1 and M+2 peaks, relative to M = 100, are in satisfactory agreement with those calculated theoretically, giving good evidence that our analytical technique is sound.

Table 1. Mass Spectroscopic Data for "Isotopically Pure" Compounds

Compound	Observed Intensities			Theoretical		
	M	M+1	M+2	M	M+1	M+2
^{14}N-Hexamine	100	10.1	0.5	100	8.4	0.3
^{14}N-DAPT	100	13.0	1.5	100	11.9	1.1
^{14}N-DPT	100	8.5	1.1	100	8.1	1.1
^{14}N-DADN	100	12.6	1.5	100	11.6	1.8
^{15}N-Hexamine	100	6.9	-	100	6.9	0.2
^{15}N-DAPT	100	9.7	1.6	100	10.4	0.9

Nitration of hexamethylenetetramine

Our nitration procedure was based on that of Hale.[11] This involved the reaction at 0 - 10°C of (1) with 95% HNO_3. Dilution with iced-water resulted in the precipitation of RDX, (2), which was removed by filtration. On neutralisation of the filtrate, keeping the temperature below 0°C, DPT, (6), separated from the solution and was washed with water and recrystallised from acetone (white crystals, m.p. 211°C). Two experiments were conducted, one using $^{14}NH_3$ solution as the neutralising agent and the other using $^{14}NEt_3$. This was done in order to establish whether ammonia was being incorporated in the final product, since triethylamine could not be.

Experiment (a). A mixture of ^{14}N-hexamethylenetetramine (0.25 g) and ^{15}N-hexamethylenetetramine (0.25 g) was used as starting material (atomic ratio $^{14}N:^{15}N$ = 100:96). After nitration and removal of RDX, DPT was precipitated by neutralisation with $^{14}NH_3$ solution. Data in Table 2.

Experiment (b). The procedure of expt. (a) was repeated differing only in that $^{14}NEt_3$ was used to effect precipitation of DPT. Data in Table 2.

In order to eliminate the possibility of exchange between ^{14}N-hexamethylenetetramine and ^{15}N-hexamethylenetetramine prior to nitrolysis, a third experiment, (c), was carried out.

Table 2. Relative Isotopic Composition[a] of DPT Prepared in Expts. (a) and (b)

Experiment	M $[^{14}N_4]$	M+1 $[^{14}N_3{}^{15}N_1]$	M+2 $[^{14}N_2{}^{15}N_2]$	M+3 $[^{14}N_1{}^{15}N_3]$	M+4 $[^{15}N_4]$
(a)	100	184	103	13	0
(b)	100	382	544	363	67
Random[b]	100	396	576	364	85
Selective[c]	100	0	0	4	96

[a] Mass spectrometric data obtained by chemical ionisation. The raw data were corrected for M+1 and M+2 peaks due to ^{13}C in natural abundance, and for the effects of incomplete protonation.

[b] This is the calculated relative distribution of isotopes for a random distribution with the starting composition used in expts. (a) and (b).

[c] Calculated distribution of isotopes for selective ring cleavage.

Experiment (c). A mixture of ^{14}N-(1), (0.1 g) and ^{15}N-(1), (0.1 g) was dissolved in 2M nitric acid (10 cm^3) at 20°C. The solution was allowed to stand for 5 mins. and was then cooled in an ice-bath to effect precipitation of the mononitrate salt of (1). The crystals were washed with 50% ethanol, then ethanol and then ether and dried. Monitoring, by mass spectrometry of the product indicated that < 10% of isotopically mixed species were present.

The results, in Table 2, for the nitration of (1) show that extensive non-selective ring cleavage is occurring. In expt. (b) where triethylamine was used in the neutralisation process the isotopic composition in the DPT agrees closely with that predicted for a random distribution, and indicates cleavage to fragments containing single N-atoms. In expt. (a) $^{14}NH_3$ was used in the neutralisation process and the ^{14}N available from this source was in large excess of nitrogen isotopes available from the reactant. Here the ^{15}N in the product is essentially confined to two N-atoms, presumably those at the 3- and 7-positions carrying nitro-groups, and the M:M+1:M+2 ratio of 1:2:1 is that expected for a statistically random distribution in these atoms. The absence of ^{15}N at the other two positions indicates extensive incorporation of ^{14}N from the ammonia used in the neutralisation.

Nitration of DAPT (4)

The nitration of DAPT, (4), to give DADN, (7), was carried out using a literature method.[12] A mixture of ^{14}N-DAPT (0.2 g) and ^{15}N-DAPT (0.2 g) (overall atomic ratio $^{14}N:{}^{15}N$ = 100:97) was added to a stirred mixture of 95% HNO_3 (1.5 cm^3) and 98% H_2SO_4 (4.5 cm^3) over a period of 10 minutes at 25-30°C. The mixture was stirred for 1 hour, after which 75 cm^3 of ice-water was added and the solution was made alkaline by addition of solid sodium carbonate. The precipitated DADN was filtered off and washed with water (m.p. 266°C, lit.[12] 265°C). The mass spectrometric data in Table 3, clearly indicate that the nitration occurs by selective cleavage since no isotopic mixing is observed. Hence the ring structure remains intact during the reaction.

Table 3. Relative Isotopic Composition of DADN Prepared by Nitration of DAPT

	M $[^{14}N_4]$	M+1 $[^{14}N_3{}^{15}N_1]$	M+2 $[^{14}N_2{}^{15}N_2]$	M+3 $[^{14}N_1{}^{15}N_3]$	M+4 $[^{15}N_4]$
DADN	100	0	0	0	66
Random[a]	100	400	588	376	88
Selective[b]	100	0	0	4	96

[a] Calculated distribution for random isotopic distribution.

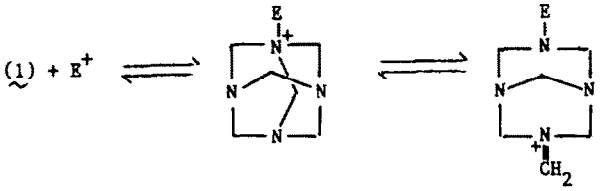
[b] Calculated distribution for selective cleavage.

Synthesis of DADN by Acetolysis of DPT

A route from DADN to the commercially important product HMX is known[2] and we sought a synthesis of DADN from DPT. Initial attempts to effect acetolysis using acetic anhydride at 120°C or various mixtures of acetyl chloride, acetic anhydride and acetic acid at 120°C failed. However a procedure was found which involved stirring 1 molar equivalent of DPT with 2 equiv. of acetyl chloride in excess acetic anhydride at 20°C for 24 hours. After addition of water and neutralisation of the acid with sodium carbonate a suspension formed which was filtered off and washed with water. Analysis by ^{1}H n.m.r. showed this to be a mixture of DADN, δ 2.3 (s) and 5.6 (s) and DPT,[13] δ 4.14 (s, CH_2 bridge), AB quartet δ 4.9, 5.65, J 13 Hz. Washing with acetone removed the DPT to leave DADN (m.p. 266°C) in 50% yield.

Comparison of Nitration and Acetolysis

Our results for the nitration of (1) with nitric acid indicate complete cleavage to species containing no more than one nitrogen atom. This is in marked contrast to the acetolysis reaction[10] where the ring structure remains basically intact, but is similar to results obtained in the Bachmann reaction.[1,9] The first step in both nitration and acetylation reactions is likely to be attack by an electrophile, E^+, at nitrogen to give a cation which can exist in a ring-opened form (equation 1). The subsequent course of the reaction may well depend on the rate



(1)

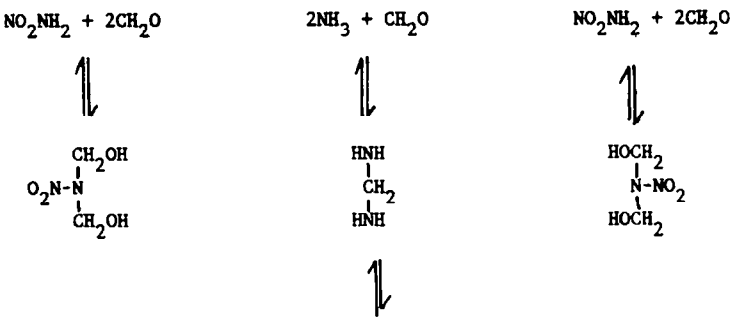
of hydrolysis of the $N{=}CH_2^+$ group compared to cleavage of other N-C bonds. In the acetolysis reaction, carried out in the presence of water and in a medium which is not highly acidic, hydrolysis will eliminate formaldehyde and yield a species which is readily acetylated to form DAPT. However in nitric acid hydrolysis of the $^+N{=}CH_2$ group, involving attack by water and proton elimination, will be more difficult so that further nitration of the molecule accompanied by C-N bond cleavage occurs preferentially. We have no direct evidence as to the precise structure of the fragments produced other than that they contain no more than one amino-nitrogen atom. However the formation of RDX, (2), is logically ascribed to the condensation of three hydroxymethyl-nitramide molecules, equation (2). It is also of interest that Wright and co-workers[14] were able

$$3(HOCH_2NHNO_2) \longrightarrow (2) + 3H_2O \qquad (2)$$

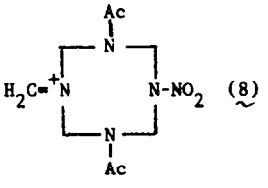
to prepare DPT, (6), by reaction in neutral solution of nitramide with formaldehyde and ammonia. They rejected the possibility that nitramide is itself produced during the nitration of (1) because of its supposed instability in acidic solutions. However recent evidence[15] shows that at the low temperature used in the nitration nitramide will decompose only over a period of hours. It is however uncertain whether cleavage all the way to nitramide occurs during nitration or whether larger fragments such as di(hydroxymethyl)nitramide are produced. The formation of DPT on neutralisation of the nitration mixture is likely to proceed as shown in the Scheme.

The selective cleavage we have observed in the conversion of DAPT, (4), to DADN, (7), shows that nitration does not necessarily result in extensive decomposition. Reaction here is likely to involve the intermediate (8). The presence of the electron withdrawing nitro- and acetyl-groups will reduce the electron density at ring-nitrogen atoms, reducing the probability of further cleavage of the molecule. Nevertheless there is evidence[9] that under the more severe conditions used in the Bachmann conversion of DPT, (6), to HMX, (3), extensive breakdown occurs.

A general conclusion of this and previous work[10] is that high yields of products containing



Scheme



(8)

eight-membered rings are only produced from hexamine derivatives by selective cleavages in which the main ring-structure remains intact. Extensive cleavage followed by recombination of fragments usually results in the preferential formation of products with six-membered rings.

EXPERIMENTAL

Preparation of ^{15}N-Hexamine

Gaseous $^{15}NH_3$ (99% isotopic abundance), obtained from Amersham International was reacted with a 37% aqueous formaldehyde solution.[16] The solution was evaporated to dryness and the ^{15}N-hexamine was extracted with chloroform. After removal of solvent the crude product was recrystallised from acetone to yield a white solid m.p. 233°C (sub). The 1% abundance of $^{14}NH_3$ leads to a product with isotopic composition of ca. 96% [$^{15}N_4$]-hexamine and 4% [$^{15}N_3$][$^{14}N_1$]-hexamine.

Preparation of isotopically pure ^{14}N- and ^{15}N-DAPT

^{15}N-DAPT was prepared from ^{15}N-hexamine by reaction with acetic anhydride in the presence of sodium hydroxide as detailed by Siele, Warman and Gilbert.[17] ^{14}N-DAPT was prepared likewise from a commercial sample of ^{14}N-hexamine.

Mass spectrometric measurements were made using a V.G. Analytical 7070E instrument. Chemical ionisation using iso-butane as reagent gas was found to be the best method of analysis for many of the compounds. This gives rise to protonated species $(M+1)^+$. Results obtained using this technique are given in terms of the parent species whose mass, M, is one unit smaller than that observed. Electron impact was used for other compounds.

Acknowledgement

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