Nitration of 7-Substituted 1,3,5-Triaza-adamantanes

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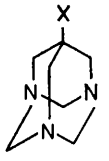
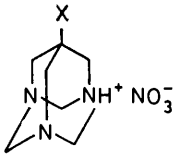
Nitrations of some 7-substituted 1,3,5-triaza-adamantanes with various nitrating mixtures are described. The products are in general *NN'*-dinitro-1,3-diazacyclohexane derivatives. The mechanism of the reactions is similar to that suggested for the nitration of hexamine with nitric acid.

As part of a programme of work related to the nitrolysis of hexamine, the synthesis of 7-nitro-1,3,5-triaza-adamantane (1) and its reactions with nitric acid and with nitric acid–ammonium nitrate have been described.[1] A further study of the nitration of this compound and of a number of other 7-substituted 1,3,5-triaza-adamantanes with various nitrating mixtures is now reported.

The following systems were used as nitrating agents:[2] concentrated nitric and glacial acetic acids (NA), concentrated nitric and sulphuric acids (NS), a mixture of fuming nitric acid, acetic acid, and acetic anhydride (NAA), concentrated nitric acid and ammonium nitrate (NAN), and fuming nitric acid.

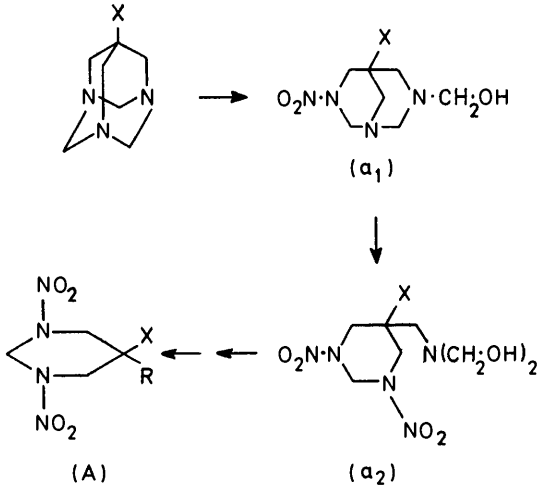


(1) X = NO_2
(2) X = NH_2
(3) X = Br
(4) X = NHAc
(5) X = N:CH·C_6H_4OMe-*p*



(6) X = NO_2
(7) X = $NH_3^+ NO_3^-$
(8) X = Br
(9) X = NHAc

The preparation of the triaza-adamantanes (1)—(5) and their nitrate salts (6)—(9) has been reported.[3] Treatment of the triaza-adamantanes (1)—(3) with NA gave only the corresponding nitrate salts (6)—(8); the imine (5) was hydrolysed under these conditions and produced the dinitrate salt of the amine (2).

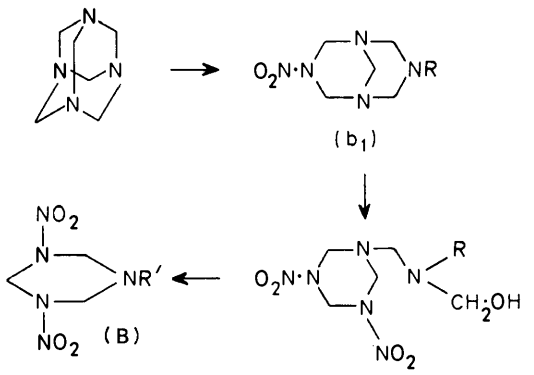


SCHEME 1

The reaction of 7-nitro-1,3,5-triaza-adamantane (1) with NAN to give a monocyclic product (10) of type (A) was considered to proceed as shown in Scheme 1.[1] Such a pathway is directly analogous to that proposed by

[1] A. F. Farminer and G. A. Webb, *J.C.S. Perkin I*, 1976, 940.
[2] T. Urbanski, 'Chemistry and Technology of Explosives,' vol. 1, Pergamon, Oxford, 1967.
[3] A. Edwards and G. A. Webb, in preparation.

several authors [4-7] to account for the formation of products of type (B) by nitration of hexamethylenetetramine (Scheme 2).



SCHEME 2

In the current study in general the 7-substituted triaza-adamantanes (1)—(5) reacted with nitrating agents to yield products of type (A). Thus, treatment of 7-amino- (2) and 7-bromo-triaza-adamantane (3) with either NAN or NS gave the salt (11) or (12), respectively. The corresponding product (10) was obtained from the reaction of 7-nitrotriaza-adamantane (1) with NAN, but treatment of the triaza-adamantane (1) with NS gave the bicyclic product (13), which presumably arises directly from an intermediate of type (a_1) (X — NO_2) as shown in Scheme 1. This reaction has a parallel in the reaction of hexamine with nitric acid, in which the bicyclic nitro-compound (14) was obtained in low yield; [4,6,8] this was given as evidence for the existence of an intermediate of type (b_1) (Scheme 2).

With NAA at room temperature 7-nitro- (1) and 7-bromo-triaza-adamantane (3) reacted similarly to give the acetates (15) and (16), respectively. However the acetate (16) is accompanied by a small amount of the nitrate salt (12), detected by ^1H n.m.r. spectroscopy. When these reactions are carried out at 0 °C a mixture of the acetate (15) and the nitrate (10) is obtained (ratio 2 : 1) from 7-nitrotriaza-adamantane (1) whereas the 7-bromotriaza-adamantane (3) under these conditions yields the nitrate salt (12) as the only detected product. Presumably the slower acetylation reaction at 0 °C fails to trap any of the hydroxymethylamine intermediates.

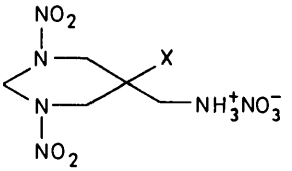
In contrast 7-aminotriaza-adamantane (2) reacts slightly differently with NAA, giving a high yield of the acetate (17) at 0 °C and at room temperature.

The isolation of the products (15)—(17) from the reactions with NAA provides clear evidence for the existence of intermediates of type (a_2).

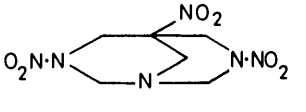
The acetamide (4) gave no isolable product on treatment with NA or NS, and the unstable, sticky solid obtained from its reaction with NAA was not identified.

However when 7-acetamidotriaza-adamantane (4) was nitrated with NAN a low yield of the spiro-compound (18) was obtained. A similar product (19) was obtained in good yield from the nitration of 7-aminotriaza-adamantane (2) with fuming nitric acid at *ca.* 2 °C. This reaction was also carried out on a small scale in an n.m.r. tube and followed by recording ^1H spectra at intervals. A spectrum recorded after *ca.* 5 min showed no trace of the amine (2), and the subsequent spectra were very complex so that the structure of any intermediate could not be determined. However as the reaction proceeded the spectrum of the product (19), emerged and the reaction was almost complete in about 45 min. These results agree with an earlier kinetic study of the nitration of hexamine with nitric acid, which indicated the immediate formation of an intermediate which in turn gave a product of type (B) (Scheme 2) by a relatively slow, rate-determining step.[7]

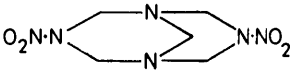
The reaction of 7-aminotriaza-adamantane (2) with fuming nitric acid when carried out at —10 °C gives a



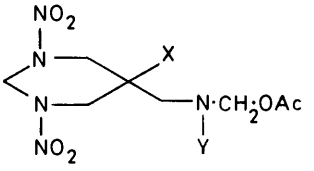
(10) X = NO_2
(11) X = $NHNO_2$
(12) X = Br



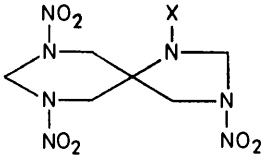
(13)



(14)



(15) X = Y = NO_2
(16) X = Br, Y = NO_2
(17) X = $N(NO_2)Ac$, Y = $CH_2O{\cdot}NO_2$



(18) X = Ac
(19) X = NO_2
(20) X = H

mixture of compound (19) (identified by comparison of ^1H n.m.r. spectra) and some other products which have not been separated and identified.

The imine (5) when treated with the above nitrating mixtures gave only 4-methoxy-3-nitrobenzaldehyde. In fuming nitric acid a high yield of a white crystalline product was also obtained; this was shown to be a mixture of several compounds by the ^1H n.m.r. spectrum. The major product, separated by repeated recrystallization from acetone–ether, was the spiro-amine (20).

[4] T. Urbanski, 'Chemistry and Technology of Explosives,' vol. 3, Pergamon, Oxford, 1967, p. 87.
[5] G. F. Wright, 'The Chemistry of the Nitro and Nitroso Groups,' Part 1, ed. H. Feuer, Wiley, New York, 1969, ch. 9.
[6] W. L. Mosby, 'Heterocyclic Systems with Bridgehead Nitrogen Atoms,' Part 2, Interscience, New York, 1961, pp. 1393—1398.
[7] J. A. Bell and I. Dunstan, *J. Chem. Soc.* (*C*), 1969, 1559.
[8] W. J. Chute, D. C. Downing, A. F. McKay, G. S. Myers, and G. F. Wright, *Canad. J. Research*, 1949, **27B**, 218.

EXPERIMENTAL

^{1}H N.m.r. spectra were recorded for solutions in deuteriated solvents containing Me_4Si with a Varian HA-100 instrument operating at 100 MHz. ^{13}C N.m.r. spectra were recorded for solutions in deuteriated solvents containing Me_4Si with a Bruker WH-90FT instrument operating at 22.64 MHz with broad-band proton decoupling. I.r spectra (Nujol mulls) were recorded with a Unicam SP 200 instrument. M.p.s were determined with an electrothermal apparatus.

Reactions with Concentrated Nitric Acid–Glacial Acetic Acid (NA) (1 : 2).—7-Nitro-1,3,5-triaza-adamantane (1) (0.5 g) was added in portions to NA (8 ml) at 0 °C. The mixture was stirred for 2—3 h, then filtered to give 7-nitrotriaza-adamantane nitrate salt (6) (0.4 g). (This reaction at room temperature overnight gave the same product.)

Similar treatment of the amine (2) and the bromide (3) gave high yields (80—90%) of the nitrate salts (7) and (8), respectively. The imine (5) when treated with NA gave a high yield (80%) of 7-aminotriaza-adamantane dinitrate salt (7). The acetamide (4) under the same conditions gave a clear solution; addition of ethanol did not precipitate any product.

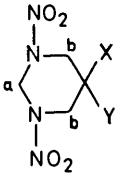
The nitrate salts were recrystallized from water or methanol and identified by comparison (m.p.s and ^{1}H n.m.r. spectra) with the authentic compounds.[3]

Reactions with Concentrated Nitric Acid–Ammonium Nitrate (NAN) (1 : 1).—(i) 7-Nitro-1,3,5-triaza-adamantane (1) (0.5 g) was dissolved in NAN (10 ml) and left at room temperature for about 2 days. The solution was then poured into ice–water to give 5-ammoniomethylene-1,3,5-trinitro-1,3-diazacyclohexane nitrate (10). The product (0.4 g) was filtered off and recrystallized from methanol; m.p. 145° (lit.,[1] 145°); $\nu_{max.}$ 1 540 and 1 570 (NO_2), 3 000, 1 620 (NH_3^+), and 1 300 cm^{-1} (NO_3^-). (This reaction was also carried out for a shorter time (3 h) and the same product was obtained in lower yield.)

(ii) The bromide (3) (0.5 g) treated similarly gave 5-*ammoniomethylene-5-bromo-1,3-dinitro-1,3-diazacyclohexane nitrate* (12) (0.4 g) m.p. 165° (from water); $\nu_{max.}$ 1 530 and 1 560 (NO_2), 3 000, 1 630 (NH_3^+), and 1 300 cm^{-1} (NO_3^-) (Found: C, 17.25; H, 3.15; N, 24.4. $C_5H_{11}BrN_6O_7$ requires C, 17.3; H, 3.2; N, 24.2%).

TABLE 1

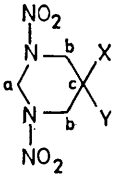
100 MHz ^{1}H N.m.r. data [solvent $(CD_3)_2SO$; δ values; J in Hz]



Compound	CH_2(a) (2 H, dd)	CH_2(b) 4 H)	X	Y
(10)	5.10, 7.15 (J 15)	4.18, 5.50 (dd, J 16)		3.65 (2 H, s), 8.6vbr (3 H, NH_3^+)
(11)	4.98, 6.83 (J 14)	3.71, 5.04 (dd, J 15)	NH not obs.	3.43 (2 H, s), 8.3vbr (3 H, NH_3^+)
(12)	5.05, 7.05 (J 15)	4.07, 5.17 (dd, J 16)		3.54 (2 H, s), 8.5vbr (3 H, NH_3^+)
(15)	5.07, 6.9 (J 14)	4.2, 5.4 (dd, J 15)		2.08 (3 H, s, CH_3), 4.7 (2 H, s, C·CH_2·N), 5.7 (2 H, s, N·CH_2·O)
(16)	4.9, 7.0 (J 15)	4.02, 4.96 (dd, J 16)		2.12 (3 H, s, CH_3), 4.25 (2 H, s, C·CH_2·N), 6.3 (2 H, s, N·CH_2·O)
(17)	5.03, 6.87 (J 14)	4.01, 5.45 (dd, J 16)	1.9 (3 H, s, CH_3)	2.08 (3 H, s, CH_3), 4.58 (2 H, s, C·CH_2·N), 5.64 (4 H, s, N·CH_2·O)
(18)	5.30, 6.48 (J 14)	4.52 (s) [dd in $(CD_3)_2CO$]	2.02 (3 H, s, CH_3), 4.02 (2 H, s, C·CH_2·N), 5.37 (2 H, s, N·CH_2·N)	
(19)	5.77, 6.24 (J 14)	4.7 (s) [dd in $(CD_3)_2CO$]	4.28 (2 H, s, C·CH_2·N), 5.68 (2 H, s, N·CH_2·N)	
(20)	5.07, 6.88 (J 15)	3.72, 4.80 (dd, J 15)	3.65 (2 H, s, C·CH_2·N), 4.62 (2 H, d, N·CH_2·N), 3.6—3.9 (NH)	

TABLE 2

22.64 MHz ^{13}C N.m.r. data [δ values w.r.t. Me_4Si; solvent $(CD_3)_2SO$]



Compound	C(a)	C(b)	C(c)	X	Y
(10)	58.6	48.7	8.16		40.6
(11)	61.1	48.6	79		57.5
(12)	59.3	54.9	60.8		44.7
(15)	59.7	49.4	85.4		20.3 (CH_3), 53 (C·CH_2·N), 74 (N·CH_2·O), 169.4 (CO)
(17)	60.8	49.7	65.8	19.5 (CH_3), 168.9 (CO)	20.3 (CH_3), 51.9 (C·CH_2·N), 70 (CH_2·O·NO_2), 74.5 (CH_2·O), 169.4 (CO)
(18)	60.4	50	60.9	23.5 (CH_3), 56 (C·CH_2·N), 64.7 (N·CH_2·N), 168.7 (CO)	
(19)	60.1	49.3	63.4	56.8 (C·CH_2·N), 66.1 (N·CH_2·N)	
(20)	59.7	50.8	62	53.1 (C·CH_2·N), 65.7 (N·CH_2·N)	

(iii) The reaction mixture from the amine (2) (0.5 g) with NAN when poured into ice–water gave a clear solution which was left in a fume-cupboard for a few days to evaporate. In this way *5-ammoniomethylene-1,3-dinitro-5-nitroamino-1,3-diazacyclohexane nitrate* (11) (0.25 g) was obtained; m.p. 185° (from water); $\nu_{max.}$ 1 530 and 1 550 (NO_2), 3 000 and 1 590 (NH_3^+), and 1 300 cm^{-1} (NO_3^-) (Found: C, 18.3; H, 3.75; N, 33.8. $C_5H_{12}N_8O_9$ requires C, 18.3; H, 3.65; N, 34.1%).

(iv) The acetamide (4) (0.5 g), treated as described in (iii) gave *1-acetyl-3,7,9-trinitro-1,3,7,9-tetra-azaspiro[4.5]decane* (18) (70 mg), m.p. 220—230°; $\nu_{max.}$ 1 500—1 570 (NO_2) and 1 660 cm^{-1} (C=O) (Found: C, 30.1; H, 4.1; N, 30.2. $C_8H_{13}N_7O_7$ requires C, 30.1; H, 4.1; N, 30.7%).

(v) The imine (5) when treated with NAN gave 4-methoxy-3-nitrobenzaldehyde, m.p. 81—83° (from chloroform–petroleum) (lit.,[9] 86°); $\nu_{max.}$ 1 700 (C=O), 1 610 (C=C), and 1 530 cm^{-1} (NO_2); δ ($CDCl_3$) 4.08 (3 H, s, CH_3), 7.2—8.3 (3 H, m, aromatic), and 9.9 (1 H, s, CHO).

Reactions with Concentrated Nitric Acid–Concentrated Sulphuric Acid (NS) (1 : 1). (i) 7-Nitro-1,3,5-triaza-adamantane (1) (0.5 g) was added in portions to NS (6 ml) at −5 °C. The mixture was stirred for 1 h then poured into ice–water and left for *ca.* 1 h to give *3,5,7-trinitro-1,3,7-triazabicyclo[3.3.1]nonane* (13) (0.3 g), m.p. 222° (from acetone); $\nu_{max.}$ 1 520 and 1 550 cm^{-1} (NO_2); δ_H [$(CD_3)_2SO$] 3.62 (2 H, s, CH_2), 4.22 and 5.10 (4 H, dd, 2 CH_2), and 4.65 and 5.53 (4 H, dd, 2 CH_2); δ_C [$(CD_3)_2SO$] 77.38, 67.37, and 51.91; δ_C [$(CD_3)_2CO$] 78.4, 68.4, 53.7, and 53.2 (Found: C, 27.35; H, 3.75; N, 32.05. $C_6H_{10}N_6O_6$ requires C, 27.5; H, 3.85; N, 32.05%).

(ii) The amine (2) and the bromide (3) under similar conditions gave the salts (11) and (12) in 50—60% yields.

(iii) White fumes were evolved when the acetamide (4) was added to NS and no product was isolated.

(iv) The only product obtained from the reaction of the imine (5) was 4-methoxy-3-nitrobenzaldehyde.

Reactions with Fuming Nitric Acid–Glacial Acetic Acid–Acetic Anhydride (NAA) (1 : 2 : 2).—(i) 7-Nitro-1,3,5-triaza-adamantane (1) (0.5 g) was added in portions to NAA (7.5 ml) at 0 °C.

(*a*) The mixture was then stirred at room temperature for 1.5 h and poured into ice–water, giving *5-[(acetoxymethylene(nitro)aminomethylene]-1,3,5-trinitro-1,3-diazacyclohexane* (15) (0.4 g), m.p. 114—116° (from ethanol); $\nu_{max.}$ 1 730 (C=O) and 1 550 and 1 580 cm^{-1} (NO_2) (Found: C, 26.15; H, 3.5; N, 26.85. $C_8H_{13}N_7O_{10}$ requires C, 26.15; H, 3.55; N, 26.7%).

(*b*) The mixture was stirred at 0 °C for 1 h then poured into ice–water. The acetate (15) (0.25 g) was filtered off and the filtrate was left for 1—2 days at room temperature. More solid obtained was identified (by the ^1H n.m.r. spectrum) as the nitrate (10) (120 mg).

(ii) The amine (2) when treated similarly gave an 80% yield of *5-[acetoxymethylene(nitro-oxymethylene)aminomethylene]-1,3-dinitro-5-(N-nitroacetamido]-1,3-diazacyclohexane* (17) at 0 °C or at room temperature; m.p. 155° (from acetone–ether); $\nu_{max.}$ 1 730 (C=O) and 1 530 and 1 590 cm^{-1} (NO_2) (Found: C, 29.4; H, 4.05; N, 24.65. $C_{11}H_{18}N_8O_{12}$ requires C, 29.1; H, 4.0; N, 24.65%).

(iii) The bromide (3) (0.4 g) was treated with NAA at −2 °C, giving the nitrate (12) (0.4 g). The reaction at room temperature [as described in (i) (*a*)] afford a white solid (0.25 g) mixture of the acetate (16) with a small amount of the nitrate (12), as judged by the ^1H n.m.r. spectrum. The acetate (16) was not purified; it was identified by comparison (i.r. and ^1H n.m.r. spectra) with the analogous acetates (15) and (17).

(iv) The acetamide (4) when treated with NAA at 0 °C gave a low yield of a sticky, unstable solid mixture of two or three compounds by the ^1H n.m.r. spectrum [the presence of a trace of the spiro-compound (18) was suspected].

Reactions with Fumic Nitric Acid.—(i) 7-Amino-1,3,5-triaza-adamantane (0.3 g) was added in portions to fuming nitric acid (5 ml) at *ca.* 2 °C. The mixture was stirred for 40 min then poured into ice–water. The product (0.3 g) was recrystallized from dimethyl sulphoxide–methanol–ether to give *1,3,7,9-tetranitro-1,3,7,9-tetra-azaspiro[4.5]decane* (19), m.p. 200°; $\nu_{max.}$ 1 530—1 570 cm^{-1} (NO_2) (Found: C, 22.6; H, 3.1; N, 35.25. $C_6H_{10}N_8O_8$ requires C, 22.35; H, 3.1; N, 34.7%). When carried out at −10 °C this reaction gave a white solid (0.3 g) mixture of compound (19) and some other, unidentified products (^1H n.m.r. spectrum).

(ii) The imine (5), (400 mg), treated with fuming nitric acid at −10 °C, gave a mixture of several compounds ^1H n.m.r. spectrum). 4-Methoxy-3-nitrobenzaldehyde was removed by extraction with chloroform. The remaining solid was recrystallized several times from acetone–ether until *3,7,9-trinitro-1,3,7,9-tetra-azaspiro[4,5]decane* (20) was obtained pure (120 mg); m.p. 235—240°; $\nu_{max.}$ 3 300 (NH) and 1 500—1 560 cm^{-1} (NO_2) (Found: C, 25.95; H, 4.0; N, 35.55. $C_6H_{11}N_7O_6$ requires C, 26.0; H, 4.0; N, 35.35%). The imine (5) at 0 °C gave a similar mixture, but the proportion of compound (20) appeared to be lower (n.m.r.).

N.m.r. Study of the Nitration of 7-Amino-1,3,5-triaza-adamantane.—The instrument (Varian HA-100) was locked on the proton of the nitric acid (δ *ca.* 8). The temperature was maintained at 2—4 °C. The amine (*ca.* 40 mg) was added to fuming nitric acid (0.5 ml) at 0 °C. The solution was immediately transferred to an n.m.r. tube and the spectrum recorded in the region δ 0—8 within 5 min of the addition of the amine and then at 10—15 min intervals.

Support from the European Research Office, U.S. Government, is gratefully acknowledged.

[7/377 *Received*, 3rd *March*, 1977]

[9] 'Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965.